Evaluation of Neoadjuvant Therapy Response of Osteogenic Sarcoma Using FDG PET

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According to the current treatment protocol of the Cooperative Osteosarcoma Study (COSS), monitoring preoperative chemotherapy response and estimating grade of tumor regression in patients with osteosarcoma is mandatory before surgical removal of the tumor, particularly if a limb salvage procedure is intended. In addition, response to neoadjuvant chemotherapy is considered as an important prognostic indicator. The aim of this prospective study was to assess the usefulness of 2-(^{18}F) fluoro-2-deoxy-D-glucose (FDG) PET in the noninvasive evaluation of neoadjuvant chemotherapy response in osteosarcoma. **Methods:** In 27 patients with osteosarcoma, we determined tumor-to-background ratios (TBRs) of FDG uptake with PET, before and after neoadjuvant chemotherapy according to COSS 86c or COSS 96 protocols, respectively. We compared changes in glucose metabolism of osteosarcomas with the histologic grade of regression in the resected specimen, according to Salzer-Kuntschik, discriminating responders (grades I–III; n = 17) and nonresponders (grades IV–VI; n = 10). **Results:** The decrease of FDG uptake in osteosarcomas expressed as a ratio of posttherapeutic and pretherapeutic TBRs showed a close correlation to the amount of tumor necrosis induced by polychemotherapy ($P < 0.001$; Spearman). With a TBR ratio cutoff level of 0.6, all responders and 8 of 10 nonresponders could be identified by PET. In addition, lung metastases of osteosarcoma were detected with FDG PET in 4 patients. **Conclusion:** FDG PET provides a promising tool for noninvasive evaluation of neoadjuvant chemotherapy response in osteosarcoma. This could imply consequences for the choice of surgical strategy, because a limb salvage procedure cannot be recommended in patients nonresponsive to preoperative chemotherapy unless wide surgical margins can safely be achieved.

Key Words: osteosarcoma metabolism; osteosarcoma drug therapy; evaluation studies; osteosarcoma surgery; osteosarcoma radionuclide imaging

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The histologic response to neoadjuvant chemotherapy not only represents an important prognostic indicator for disease-free survival after multimodal treatment of osteogenic sarcoma (*1,2*), but should also influence the surgical procedure. Data evaluated by the Cooperative Osteosarcoma Study (COSS) indicate that the risk of a local recurrence is linked to both the response to preoperative therapy and the type of surgery. Although the overall local failure rate was 4.8%, it rose to 14.3% in patients with poor response (defined as less than 90% tumor destruction) when treated by a limb salvage procedure (*3*). In a study by Picci et al. (*4*), patients with inadequate surgical margins but excellent response to neoadjuvant treatment had a lower incidence of local relapse than patients with adequate surgical margins but poor response to preoperative chemotherapy.

Because local recurrence of osteosarcoma is associated, as a rule, with synchronous or metachronous metastatic spread, even amputation does not offer a curative perspective. Therefore, the response to neoadjuvant chemotherapy should be determined and considered as precisely as possible before definitive operative tumor removal, particularly if a limb salvage procedure is planned. In patients with large tumor volume and a low response, ablative surgery or rotation plasty should be preferred.

Standard techniques for noninvasive evaluation of tumor regression are three-phase bone scintigraphy using ^{99m}Tc methylene diphosphonate (*5*) and static or dynamic gadolinium diethylenetriamine pentaacetic acid (DTPA)-enhanced MRI (*6–8*). A new approach for this problem could be diffusion-weighted MRI, which revealed a high sensitivity in discerning viable osteosarcoma tissue and tumor necrosis in an animal model (*9*).

Elevated uptake of 2-(^{18}F)-fluoro-2-deoxy-D-glucose (FDG) determined by PET has been reported in malignant mesenchymal tumors in a small number of studies. FDG PET was proposed as a diagnostic tool for discriminating benign and malignant soft tissue and osseous lesions (*10–13*), for the grading of sarcomas (*12,14,15*) and for the detection of local recurrences (*16*). Garcia et al. (*17*) found the sensitivity of FDG PET in diagnosis of recurrent or residual musculoskeletal sarcoma to be significantly higher compared with ^{99m}Tc-methoxyisobutyl isonitrile (MIBI) SPECT. In addition, FDG PET was proposed for detection of pulmonary metastases in osteogenic sarcoma (*18*).

Several studies have analyzed the role of FDG PET scanning in the assessment of therapeutic response in patients with various carcinomas (*19–26*) and in malignant

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lymphoma (*27–29*). In a recent study, Jones et al. (*30*) presented FDG data of nine patients with soft-tissue sarcomas and malignant primary bone tumors, including three osteosarcomas, who received neoadjuvant therapy. Changes of glucose metabolism could be correlated to the amount of tumor necrosis induced by the preoperative treatment. Using repeated examination with FDG PET, van Ginkel et al. (*31*) found a significantly different glucose consumption in patients with partial and complete response after isolated limb perfusion for soft-tissue sarcoma. However, in their study, specificity of the method was compromised by an FDG accumulation due to surrounding inflammatory reaction.

The aim of this study was to analyze whether FDG PET represents a more accurate tool for evaluating neoadjuvant chemotherapy response in osteosarcoma compared with established imaging techniques, such as contrast-enhanced MRI and three-phase bone scintigraphy.

MATERIALS AND METHODS

Patient Selection

In a current prospective study initiated in January 1993, 27 patients (17 male, 10 female; age 5–36 y, median 17 y) with osteogenic sarcoma were examined by FDG PET before biopsy and again after neoadjuvant polychemotherapy. Selection criteria included first manifestation of a histologically ascertained classic high-grade osteosarcoma and completion of neoadjuvant polychemotherapy according to COSS-86c or COSS-96 protocol. There was no restriction regarding the age of the patients. PET was performed in all patients referred to the surgical department of our institution with evidence of a malignant primary bone tumor, on the basis of radiologic findings, including plain x-rays and contrast-enhanced MRI.

All patients underwent an open biopsy, and the diagnosis of osteosarcoma could be confirmed histologically in 32 patients. Tumor staging comprised a CT scan of the chest to exclude pulmonary metastases; CT data were compared with the thoracic PET findings. Excluded from the study were 2 patients with parosteal osteosarcoma, 1 patient with periosteal osteosarcoma and 1 patient with central low-grade osteosarcoma, because they did not require neoadjuvant therapy. Of 28 patients who were selected for the investigation, 1 patient with stage IIIB osteosarcoma underwent rotation plasty without PET examination before definitive surgery; therefore data of 27 patients could be evaluated.

Table 1 summarizes patient data, including histologic subtype, tumor location and stage of disease. Biopsy was performed within 5 d after the initial PET scanning, and chemotherapy was initiated within 14 d thereafter. According to COSS 86c or COSS 96 protocol, doxorubicin, high-dose methotrexate, ifosfamide and cisplatinum were administered consecutively.

All patients in the study were examined with a second PET scan immediately before surgical treatment of the tumor. The minimum interval to the last combined administration of ifosfamide/cisplatinum was 12 d; the maximum interval was 18 d.

All patients or their parents gave written informed consent to receive chemotherapy per COSS 86c or COSS 96 protocols and to be scanned with FDG PET twice preoperatively.

TABLE 1
Individual Data, Histologic Subtype, Tumor Stage, Site and Surgical Procedure of 27 Patients with Osteosarcoma Eligible for the Study

Patient no.	Age (y)	Sex	Subtype	Stage	Location	Surgery
1	14	M	Chondroblastic	IIB	Left femur	LS
2	17	M	Chondroblastic	IIB	Right femur	LS
3	17	F	Osteoblastic	IIB	Left fibula	LS
4	18	M	Osteoblastic	IIB	Left tibia	AM
5	14	F	Osteoblastic	IIIB	Right femur	—*
6	12	F	Osteoblastic	IIB	Right femur	AM
7	8	M	Chondroblastic	IIB	Right femur	RP
8	15	F	Osteoblastic	IIB	Left femur	LS
9	23	M	Chondroblastic	IIB	Left pelvis	LS
10	29	M	Osteoblastic	IIB	Right femur	LS
11	17	M	Mixed†	IIB	Left femur	RP
12	11	M	Osteoblastic	IIB	Right femur	LS
13	19	M	Osteoblastic	IIB	Right humerus	LS
14	14	M	Chondroblastic	IIB	Rib	LS
15	18	M	Osteoblastic	IIB	Left femur	LS
16	15	M	Chondroblastic	IIB	Left femur	LS
17	8	M	Osteoblastic	IIB	Left femur	RP
18	14	F	Osteoblastic	IIB	Right femur	RP
19	13	F	Osteoblastic	IIB	Left femur	RP
20	22	F	Chondroblastic	IIIB	Right pelvis	—*
21	20	F	Osteoblastic	IIB	Left humerus	LS
22	5	F	Teleangiectatic	IIB	Cervical spine	LS
23	22	M	Mixed†	IIB	Left femur	LS
24	36	M	Osteoblastic	IIIB	Left femur	LS
25	17	M	Osteoblastic	IIB	Right femur	LS
26	34	M	Osteoblastic	IIB	Left femur	LS
27	19	F	Chondroblastic	IIB	Left femur	LS

*No surgical therapy because of advanced tumor stage.
†Osteoblastic and chondroblastic differentiation.
LS = limb salvage; AM = amputation; RP = rotation plasty.
Tumor stage graded according to Enneking (*45*).

FDG PET

FDG PET studies were performed as described by Stollfuss et al. (*32*) with a commercially available scanner (ECAT 931–08–12; Siemens/CTI, Knoxville, TN) that allows simultaneous acquisition of 15 contiguous 6.75-mm thick sections with an axial field of view of 10.1 cm. The resolution was 7 mm (full width at half maximum) at the center of the field of view. Attenuation correction was performed with a rotating $^{68}Ge/^{68}Ga$ source. Depending on tumor size, transmission scans with a duration of 8 min per bed position were obtained in at least three bed positions without overlap before emission scans on the same day. Thus, repositioning of the patient was necessary using multiple laser-guided landmarks. Patients fasted for at least 8 h before the study, and normal plasma glucose levels were documented before FDG administration. According to a previous study by Ichiya et al. (*23*), static emission scans of the tumor site and the corresponding contralateral area, with two or three contiguous bed positions starting no earlier than 45 min (range 45–60 min) after intravenous administration of a body mass dependent dose of 120–300 MBq FDG, were used for semiquantitative assessment of tumoral FDG uptake. Acquisition time was 10 min per bed position. In addition, emission scans of the chest were obtained. Image reconstruction was performed with a multiplicative iterative reconstruction algorithm (*33*).

Data Analysis

Qualitative and quantitative evaluation of the PET scans was performed by analyzing the hypermetabolic zones on transaxial, coronal and sagittal sections. Regions of interest (ROIs) were individually defined for each osteosarcoma, excluding areas of lower uptake within the tumor, if present. ROIs were defined in the scan expressing maximum uptake and were larger than 2.6 cm^2 in each case. The neoplasm was demarcated readily from surrounding tissue, and the boundaries of the ROI were just within the apparent hypermetabolic zone of the tumor. Quantitative assessment of FDG uptake was obtained from transaxial sections exclusively. Tumor-to-background ratios (TBRs) were calculated with an ROI of identical configuration at the analogous site of the contralateral extremity, pelvic bone or chest, respectively. In a case with a vertebral lesion (patient 22), an adjoining unaffected vertebral body was used as reference region. The average activity within each ROI was corrected for radioactive decay. Ratios of TBR before and after neoadjuvant treatment were calculated for each patient and compared with the histologic extension of tumor destruction. To assess the interobserver error, TBR values were obtained by two independent physicians without knowledge of the clinical data and were averaged for statistical evaluation.

In 25 patients, tumor regression defined as a percentage of devitalized tumor was determined histologically within the resected specimen and graded according to Salzer-Kuntschik et al. (*34*), discriminating responders (grades I–III) and nonresponders (grades IV–VI). In patient 20, who had a locally inoperable iliosacral tumor with multiple pulmonary metastases, the effect of chemotherapy was assessed by repeated biopsy. One patient with stage IIIB disease (patient 5) developed a local and pulmonary progress under chemotherapy and died without further surgery. In this case, grade of regression was estimated with the use of follow-up investigations with contrast-enhanced MRI and three-phase bone scan.

Statistical Analysis

The Mann-Whitney U test was used to compare TBRs of responders and nonresponders. The Spearman rank correlation test was used to compare ratios of pretherapeutic and posttherapeutic TBRs with the grade of histologic response (*34*). The 95% confidence intervals (CIs) were calculated according to Clopper and Pearson (*35*).

RESULTS

Interobserver deviation of TBR values ranged from 2%–11% (median 4%). TBRs before neoadjuvant chemotherapy ranged from 3.3 to 33.2 (median 10.3). No correlation of quantitative PET data to age, sex, tumor site, volume or histologic subtype was apparent. Pretherapeutic median TBR in the responder group (n = 17) was 10.34 (range 3.89–33.2) and in the nonresponder group (n = 10) 9.64 (range 3.26–22.2). Post-therapeutic values differed significantly ($P \leq 0.01$) for responders (median 2.27, range 0.32–17.5) versus nonresponders (median 6.37, range 2.24–20.33). Patients with thus far disease-free survival (n = 15) had a pretherapeutic median TBR of 7.79 (range 3.26–33.2), whereas patients with metastatic disease, development of a relapse or lethal course (n = 10) presented a median TBR of 11.19 (range 5.13–32.4). Two patients were not eligible for this evaluation: 1 patient died during a traffic accident 13 mo after surgery, and the other patient succumbed to a septic complication related to postoperative chemotherapy 9 mo after tumor resection.

Individual data on pretherapeutic and posttherapeutic TBRs, the histologic grade of regression, follow-up period and current status are listed in Table 2. Patient 5 with stage IIIB osteosarcoma of the femur showed pulmonary metastases simultaneously; under chemotherapy both local and pulmonary progress were observed. MRI follow-up 3 mo after biopsy revealed an extended tumor mass in the thigh without reduction of gadolinium uptake compared with the initial examination. Three-phase bone scintigraphy displayed an increased tracer uptake in all phases. Thus, on the basis of the clinical findings, this patient had to be classified as a "nonresponder," and the grade of regression was estimated ≥5. The patient died 3 mo after confirmation of the diagnosis; her deteriorated state precluded any further surgery.

Ratios of post-therapeutic and pretherapeutic TBRs showed

TABLE 2
Histologic Grade of Regression, Oncologic Outcome and Data Evaluated by FDG PET

Patient no.	Grade of regression	Follow-up period (mo)	Current status	TBR_1	TBR_2	TBR_2/TBR_1
1	1	70	NED	17.97	2.27	0.13
2	4	66	NED	3.26	2.92	0.90
3	3	62	NED	6.79	2.27	0.33
4	4	60	NED	7.79	5.74	0.74
5	≥5*	3	DD	22.00	20.33	0.92
6	3	50	DD	8.44	1.93	0.23
7	3	30	DD	13.42	2.11	0.16
8	3	47	NED	6.83	2.74	0.40
9	4	8	DD	5.13	2.24	0.44
10	4	16	DD	11.48	7.00	0.61
11	3	6	DD	32.40	17.50	0.54
12	1	28	NED	5.27	1.89	0.36
13	4	9	D	6.15	4.79	0.78
14	3	25	NED	10.34	1.99	0.19
15	3	23	NED	23.20	4.80	0.21
16	2	23	NED	3.89	0.32	0.08
17	2	13	D	4.20	0.47	0.11
18	2	19	NED	6.56	1.61	0.25
19	2	13	DD	10.60	2.50	0.24
20	3	10	ADM	6.70	2.80	0.42
21	4	9	DD	13.10	8.30	0.63
22	6	8	NED	3.40	3.10	0.91
23	4	8	NED	22.20	11.10	0.50
24	3	7	ADM	10.89	3.10	0.28
25	3	6	NED	33.20	7.10	0.21
26	5	5	NED	18.9	18.6	0.98
27	3	5	NED	17.6	3.10	0.18

*Estimated grade of regression.

TBR_1 = tumor-to-background ratio before biopsy; TBR_2 = tumor-to-background ratio after neoadjuvant chemotherapy; NED = no evidence of disease; DD = died of disease; D = died of unrelated cause; ADM = alive with metastases.

a close correlation to the histologic extent of tumor destruction (Spearman correlation coefficient 0.82, $P < 0.001$; Fig. 1). However, the dispersion of TBRs within the individual regression groups did not permit a precise prediction of the quantitative amount of tumor necrosis. A major reduction of glucose metabolism developed in 2 patients (9 and 23), indicating a good response to preoperative therapy, although their morphologic grade of regression was IV (nonresponder). By using a TBR cutoff level of 0.6 for detecting responders (prevalence 63.0%), there were two false-positive but no false-negative results. The sensitivity was 100% (CI 80.5%–100%), the specificity 80.0% (CI 44.4%–97.5%), the accuracy 92.6% (CI 75.7%–99.1%), positive predictive value 89.5% (CI 66.7%–98.7%) and negative predictive value 100% (CI 63.1%–100%). Figure 2 demonstrates the findings of patient 8 (responder); Figure 3 shows patient 4 (nonresponder).

PET examination of the chest revealed lung metastases in patients 5, 20, 24 and in an 8-y-old boy with osteoblastic osteosarcoma stage IIIB of the distal femur, who had to be excluded from the study because no PET scan was obtained after neoadjuvant chemotherapy. This patient underwent rotation plasty because of impending tumor exulceration and subsequent bilateral removal of pulmonary metastases. Pulmonary dissemination suspected by PET could be confirmed by CT scanning in all 4 patients, and also by histologic examination in the drop-out case previously mentioned. According to CT data, no false-negative or false-positive results concerning lung metastases were observed in this series.

DISCUSSION

Established imaging methods to assess neoadjuvant therapy response in osteosarcoma comprise three-phase bone scintig-

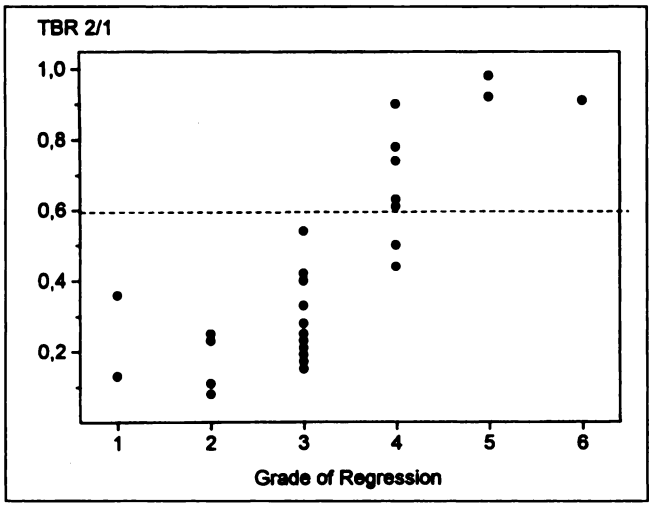

FIGURE 1. TBR quotients of 27 patients with osteosarcoma after (TBR_2) and before (TBR_1) neoadjuvant chemotherapy, correlated to histologic grade of regression (Spearman rank correlation coefficient 0.82, $P < 0.001$). Using cutoff level of 0.6, responders could be discriminated from nonresponders in all but 2 patients.

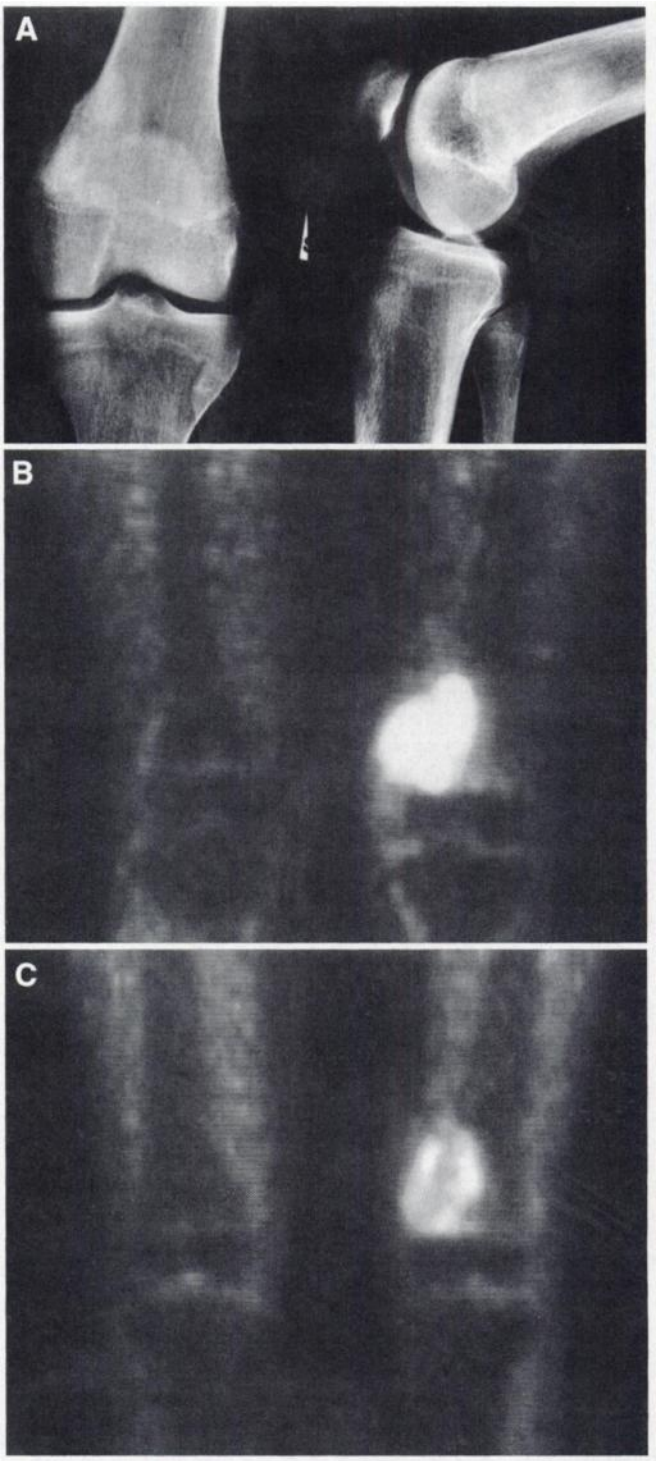

FIGURE 2. Fifteen-y-old girl with osteoblastic osteosarcoma stage II B of left femur (patient 8). (A) Anteroposterior and lateral plain radiographs show sclerotic lesion of medial part of distal femoral metaphysis. (B) Initial coronal FDG PET scan shows strongly hypermetabolic area in projection to distal femoral metaphysis before chemotherapy. (C) Coronal FDG PET scan after neoadjuvant chemotherapy. Marked reduction of glucose metabolic activity is expressed within lesion. Histologic examination of resected specimen revealed viable tumor fraction of 9%, so patient was classified as responder grade III.

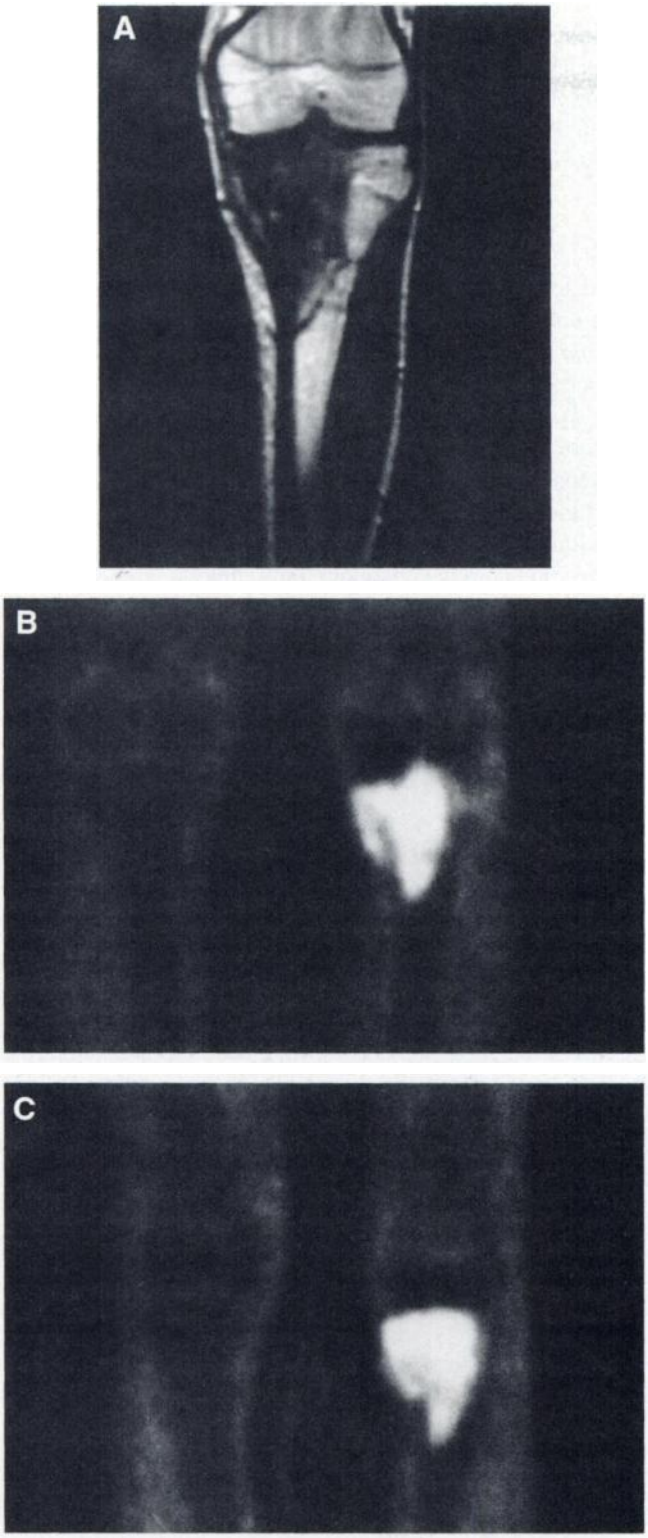

FIGURE 3. Eighteen-y-old man with osteoblastic osteosarcoma stage IIB of left proximal tibia (patient 4). (A) T1-weighted unenhanced coronal spinecho MR image shows extension of lesion. (B) Coronal FDG PET scan before incision biopsy shows highly elevated glucose metabolism of tibial head. (C) Coronal FDG PET scan after neoadjuvant chemotherapy. Hypermetabolic area appears unchanged. With viable tumor fraction of 22%, patient had to be classified as nonresponder grade IV.

raphy and contrast-enhanced dynamic MRI. The accuracy of bone scanning for quantitative estimation of tumor necrosis in osteogenic sarcoma was calculated at 93% by Bielack et al. (*5*) and 80% by Erlemann et al. (*6*). In a study comparing three different radioactive substances (*36*), ^{201}T1-chloride and ^{67}Ga-citrate were superior to ^{99m}Tc-methylene-diphosphonate (MDP) in predicting bone tumor response to chemotherapy; MDP bone scanning might be affected by factors other than tumor activity (e.g., osseous blood flow), giving an accurate correlation with clinical and pathologic response in only one of seven cases (*36*). A close correlation of ^{201}T1 uptake changes to the grade of chemotherapy-induced tumor regression in osteosarcomas was confirmed by Ohtomo et al. (*37*) and by Imbriaco et al. (*38*). An 86% accuracy of dynamic MRI in predicting tumor response was reported by Erlemann et al. (*6*). In our series, FDG PET attained a similar level of accuracy. It might be considered an advantage that PET directly assesses glucose metabolism, which is maintained in viable tumor cells only, whereas MRI and bone scanning are restricted to an indirect estimation of tumor necrosis by monitoring blood perfusion.

Our study attempts to evaluate preoperative monitoring of osteosarcoma using FDG PET with emphasis on prediction of tumor response to neoadjuvant chemotherapy, because surgical strategy must consider response behavior. Parameters for quantification of FDG uptake are represented by standardized uptake values (SUVs) and TBRs. For reasons of practicality and independence of transmission scanning, we have used TBR instead of SUV. Because SUV is the more conventional method of quantification, it will have to be shown that the validity of TBR matches that of SUV for such purposes. Because TBR is dependent on metabolic background activity, it does not reflect absolute glucose uptake, but only changes relative to some ill-defined "normal" tissue. If that tissue is muscle, it is known that muscle FDG uptake varies with activity and rest.

For evaluation of tumor response to fluorouracil in colorectal cancer liver metastases, it has been shown that semiquantitative analysis by FDG SUV is not as reliable as the tumor-to-liver ratio (*21*). This is indicative of the problems of introducing extra measurement variables when trying to establish a semiquantitative method. Inadequate injection with extravasation of some of the FDG at the time of intravenous administration most likely led to an underestimate of the tumor SUV. This problem did not affect the TBR, because it is purely a ratio of the observed radioactivity in the two ROIs, therefore injected activity is irrelevant. As a further potential confounding factor for SUV calculation, a competing organ such as the myocardium could take up a greater proportion of the injected FDG dose, leaving less for the tumor. If this is present only on the pretreatment or post-treatment scan, it may result in a misinterpretation of tumor response.

From studies concerning potential confounding factors for SUV calculation, it appeared that the time to scanning did not have any impact on the SUV. When planning the

timing of the scans, it was initially considered that 45–60 min from the time of FDG injection was an appropriate period for tumor FDG levels to plateau. This was based on data from normal brain studies and colorectal liver metastasis studies. A subsequent study of 68 scans in 47 patients suggested a good correlation between the fractional rate of tracer uptake from Patlak plots and SUVs at 60 min for a range of tumor types (*39*). Furthermore, in most of the studies concerning therapy monitoring of malignant tumors, semiquantitative analysis of tumor FDG uptake for evaluation of therapy response was performed on static emission scans from 45–60 min (*19–30*). Hamberg et al. (*40*) reported the results of a study examining this issue. In eight patients with non-small cell lung cancer, they found that FDG SUV (or dose-uptake ratio) plateau in these tumors was not reached by 90 min in the majority of scans, both before and after treatment. The average time to reach 95% of the plateau SUV in pretreatment scans was about 300 min (range 130–500 min) and in post-treatment scans was about 150 min (range 65–400 min). They calculated that because the time-activity curve is increased more steeply in the pretreatment scans, probably because of a treatment-induced reduction in glycolytic rates, there will be an underestimation of the change with treatment when based on 60 min data. In this study, however, FDG PET correctly identified all responders, whereas 2 patients with tumor necrosis rates below 90% after preoperative chemotherapy showed a decrease of glucose metabolism similar to the responders and, therefore, were falsely classified as responders with FDG PET. The timing of scans in relation to the FDG injection needs further investigation to determine the impact or the utility of the clinical method, although it did not appear to be a major factor in this study.

In this study, the exclusive use of TBR values resulted in a high accuracy concerning the evaluation of chemotherapy response in osteogenic sarcomas. However, assessment of relative decrease of TBR values before and after chemotherapy did not permit a precise quantification of tumor necrosis, but enabled a discrimination of responders and nonresponders, except for 2 patients (9 and 23) with a pelvic and a femoral lesion, respectively. Each had a tumor necrosis rate after preoperative chemotherapy below 90%, but showed a decrease of glucose metabolism similar to the responders. The reason for this result is not yet clear. Methodologic difficulties in PET examination of pelvic tumors may arise from nonspecific FDG uptake by the bowels closely adjacent to the innominate bone and from the complex anatomy of the osseous structures. To overcome this problem, Wahl et al. (*41*) suggested fusion of PET data with CT or MR images ("anatometabolic tumor imaging"). As a general problem with FDG PET in monitoring chemotherapy response in malignant tumors, the glucose analog FDG is known to accumulate not only in tumor cells but also in macrophages and granulation tissues (*42*), as well as in inflammations (*43*) such as osteomyelitis (*11,44*). This might result in increased post-therapeutic FDG accumulation not exclusively caused by viable tumor cells. In this series we did not observe a false-positive result caused by inflammatory processes or nonspecific postoperative hypermetabolism. None of our patients had inflammatory complications, and because the second PET scan was obtained at least 10 wk after the biopsy, relevant reparative activity could not be expected.

CONCLUSION

Because FDG PET depicts metabolic activity rather than topographic information, it has been shown to be especially valuable for monitoring therapy response in patients with advanced tumor disease. Likewise, data from our ongoing study suggest that FDG PET provides a promising noninvasive tool to identify responders after neoadjuvant treatment in osteogenic sarcoma. This could imply consequences for the choice of surgical strategy, because a limb salvage procedure cannot be recommended in patients nonresponsive to preoperative chemotherapy unless wide surgical margins can be achieved safely. Another advantage of FDG PET scanning compared with current imaging modalities, such as bone scintigraphy and dynamic MRI, is the possibility of simultaneous whole-body tumor staging, which enables the detection of occult skeletal, lung and visceral metastases.

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