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13. ABSTRACT *(Maximum 200 Words)*

The purpose of our study was to evaluate the effectiveness of PET-FDG in patients with metastatic breast cancer who were also being treated with high dose chemotherapy and stem cell rescue. The hypotheses of the study were as follow: 1) Active tumor sites shown by anatomical imaging methods will be associated with high levels of metabolic activity while inactive sites will be reflected by low levels of FDG uptake. 2) Reduction in tumor metabolic activity of tumors will be an early predictor of response to high dose chemotherapy. 3) Patients with no abnormal FDG uptake prior to high dose chemotherapy will live longer than patients with tumor that are metabolically active. The use of PET in this setting is potentially cost-saving considering the high costs of stem cell rescue. Non responders do not need to undergo further chemotherapy with consequent suffering and high costs, when palliation is more appropriate. On the other hand, the ability to predict the response to chemotherapy in responders might enable the physician to modulate the treatment for each patient. The study included a homogeneous group of patients entered on two University of Pennsylvania studies for the treatment of breast cancer with high dose chemotherapy. The chemotherapy protocols were protocol UPCC #3195 and Protocol PBT-1.

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INTRODUCTION

Positron emission tomography (PET) was introduced as a research modality to investigate physiological and biochemical alterations in the brain and heart[1]. Many radiopharmaceuticals have been introduced for the study of various organs, but ^{18}F-fluoro-2-deoxy-2-glucose (FDG) is generally considered the most useful radiopharmaceutical for the diagnosis of various tumors. Breast cancers have enhanced glycolytic activity and have a significant overexpression of glucose transporters[2]. Tumor hypoxia has been shown to increase FDG retention[3], and the tracer has been shown to be mainly incorporated into malignant cells[4].

There are now several reports of studies of patients with breast cancer, suggesting that the PET-FDG technique is effective in diagnosing and following patients with primary and metastatic breast tumors[5-10]. A recent retrospective study on the efficacy of PET in detecting axillary lymph node involvement has suggested potential cost savings by reducing the number of axillary dissections for breast cancer. Almost 74,000 women (75% patients) with primary breast tumors could potentially be spared axillary dissection based on the sensitivity and specificity of PET-FDG imaging to detect lymph node involvement[11].

Some groups have reported on the use of PET to evaluate tumor response to therapy. Wahl[12] described the use of PET-FDG for monitoring the treatment response of primary breast cancer. Eleven patients with large primary cancers were studied before chemohormonotherapy and at four times after initiating treatment (at days 8, 21, 42 and 63). The quantitative PET scans showed a rapid decrease in tumor glucose metabolism in all eight patients whose cancers responded clinically, but no change in the 3 non responding patients. Qualitative (visual) analysis

gave the same result. The metabolic change preceded clinical evidence of response (mammographic change), and in some patients the mammogram was difficult to interpret due to dense breast tissue. Thus, the PET-FDG appeared to be an early and accurate predictor of breast cancer response. Huovinen et al[13], using ^{11}C-Methionine, reported changes in uptake in soft tissue lesions of eight patients treated with chemotherapy, hormone therapy or radiation. The PET responses correlated with clinical responses; uptake increased in those who showed progressive disease, and decreased in patients with stable or improving lesions. Jansson et al[14] studied sixteen patients with locally advanced and metastatic breast cancers receiving chemotherapy. They noted a decrease in uptake (^{11}C-Methionine or FDG) compared to pretreatment scans in eight of twelve responders after the first course of therapy (scans were performed at 6 - 13 days after treatment). Scans done after a third chemotherapy course showed a decrease in all clinical responders. These responses were noted in lesions in breast, axillary nodes, pleura and liver.

The purpose of our study was to evaluate the effectiveness of PET-FDG in patients with metastatic breast cancer who were also being treated with high dose chemotherapy and stem cell rescue. The hypotheses of the study were as follow:

1) Active tumor sites shown by anatomical imaging methods will be associated with high levels of metabolic activity while inactive sites will be reflected by low levels of FDG uptake.
2) Reduction in tumor metabolic activity of tumors will be an early predictor of response to high dose chemotherapy.
3) Patients with no abnormal FDG uptake prior to high dose chemotherapy will live longer than patients with tumors that are metabolically active.

The use of PET in this setting is potentially cost-saving considering the high costs of stem cell rescue. Non responders should be spared from further chemotherapy which causes significant suffering and is associated with high costs. On the other hand, the ability to predict response to chemotherapy in responders might guide the physician in adopting the most effective treatment for an individual patient.

The study included a homogeneous group of patients entered on two University of Pennsylvania studies for the treatment of breast cancer with high dose chemotherapy. The chemotherapy protocols were protocol UPCC #3195 and Protocol PBT-1.

BODY

Materials and Methods

Patient Selection:

Patients selected for entry into this study were women accepted for one of two high dose chemotherapy protocols utilizing autologous stem cell support at the University of Pennsylvania. The two protocols are: Protocol UPCC #3195 ("Phase II Pilot Study of High Dose Chemotherapy With Melphalan Followed by Cyclophosphamide, Thiotepa, and Carboplatin with Cyclophosphamide and G-CSF Augmented Peripheral Stem Cell Support For Women With Responding Metastatic Breast Cancer") or Protocol PBT-1 ("Phase III Randomized Comparison of Maintenance Chemotherapy with Cyclophosphamide, Methotrexate and 5-FU vs. High Dose Chemotherapy with Cyclophosphamide, Thiotepa and Carboplatin and autologous bone marrow

support for women with metastatic breast cancer who are responding to conventional induction chemotherapy").

Chemotherapy Studies:

UPCC #3195:. This study was a University of Pennsylvania Cancer Center single institutional trial designed for patients with metastatic disease or inflammatory breast cancer. Patients with no evaluable disease or a documented complete or partial response to standard chemotherapy were treated with high dose sequential chemotherapy and peripheral stem cell rescue. Patients received high dose Cyclophosphamide followed by G-CSF to stimulate stem cell production. This was followed by apheresis to harvest stem cells. When blood count recovery occurred, high dose Melphalan was administered to the patient followed by infusion of one-third of the collected stem cells. Twenty-one days later, the patient was treated with high dose chemotherapy regimen consisting of Cyclophosphamide (1500 mg/m^2), Thiotepa (125 mg/m^2) and Carboplatin (200 mg/m^2), each drug being given daily for four days. This was followed by peripheral stem cell reinfusion.

PBT-1: The purpose of this study was to compare the time to treatment failure, overall survival and toxicity in patients with metastatic breast cancer who were treated with conventional chemotherapy alone or conventional dose chemotherapy followed by high dose chemotherapy and autologous bone marrow rescue. Patients were entered into this trial prior to receiving any chemotherapy for metastatic disease. They will then receive Cytoxan, Adriamycin and 5-FU. At the end of 4 - 6 cycles of treatment for metastatic disease, the patients were reevaluated. Those in a partial response or in a complete response were randomized either to continue the same chemotherapy (or change from Adriamycin to Methotrexate after a total dose of Adriamycin has

been given) until relapse or to receive high dose therapy and autologous bone marrow treatment with no further therapy after the transplant. The high dose regimen consisted of 4 days of Cyclophosphamide (1500 mg/m^2), Thiotepa (125 mg/m^2) and Carboplatin (200 mg/m^2). The patients who underwent bone marrow transplantation were selected for this PET study.

PET Camera:

The PENN PET 240H camera, manufactured by UGM, has been used extensively over the last 5 years for FDG and ^{15}O-water brain studies, FDG whole-body cancer studies, and FDG/^{13}N-ammonia cardiac studies. This scanner is based on NaI(Tl) position-sensitive detectors, which leads to high spatial resolution, 5.5 mm (FWHM) in the transverse and axial directions, and fine spatial sampling, 2 mm in both the transverse and axial directions[15]. The fine axial sampling, in particular, is a unique advantage of the system, leading to a maximum of 64 slices for each data acquisition, which allowed us accurate quantification and reduction of partial volume effect commonly noted with PET imaging[16]. To achieve the maximum sensitivity, the scanner operates as a full-time 3D system and takes advantage of the counts in the entire volume in the field of view.

Whole body scanning technique:

The whole-body scanning was carried out according to the protocol established in our laboratory. 114 μCi/kg of FDG was injected intravenously to the patient. Forty minutes later, the patient was positioned supine in the scanner, feet first, with her arms extended and folded behind the neck. The scanner was then moved by successive 6 cm steps to image the desired areas. This positioning scheme allowed imaging of the entire supraclavicular and axillary lymph node sites. A post-emission transmission scan was then obtained. The scanning area included the entire

chest and supraclavicular regions. During this project, new methods were implemented to reduce the transmission scanning time by the use of a single emitting Cs-137 point source. This revolutionary approach, which has since then been adopted by some commercial manufacturers, has allowed a tenfold reduction in transmission scanning time, while improving image quality and maintaining quantitative accuracy. This improvement led to acquiring a successful transmission scan in all patients enrolled in the later stages of the project, since many women found it difficult to undergo this procedure by utilizing earlier techniques.

Image Reconstruction techniques:

All the tomographic images were reconstructed with filtered back projection with a Hanning filter for a final image resolution of approximately 6 mm. We also reconstructed all studies with a new iterative reconstruction algorithm, the ordered subset expectation maximization algorithm[17, 18], to further improve image quality for qualitative and quantitative interpretation.

Qualitative interpretation:

The whole body images were read by two experienced observers, without attenuation or scatter correction. The readers were blinded to clinical and other radiological information. Anatomic sites were considered abnormal when the following criteria were met: nodal disease was considered if a clearly defined nodular abnormality could be demonstrated in lymph node groups, exceeding regional average activity; local bone involvement was considered for areas with focally increased tracer uptake higher than maximal marrow activity; diffuse bone marrow involvement was considered if the tracer activity exceeded that of liver uptake; liver and other soft tissue lesions were considered positive if clear focal areas of increased tracer uptake were identified which exceeded normal levels. Increased areas of tracer concentration corresponding

to the known normal physiologic distribution (urinary tract, bowels, muscle groups, heart, thyroid, etc.) were not considered abnormal. The rating scale utilized for recording the abnormalities is indicated in table 1.

Quantification

Quantitative analysis was carried out on attenuation and scatter corrected images by assigning regions of interest (ROI) over the area(s) of abnormal uptake which were visually determined. One quantitative measure of the degree of uptake of a given radiotracer is the standardized uptake value (SUV)[19] which was defined as follows:

SUV = (uptake activity/gram of tissue)/(injected activity/gram of patient weight).

In malignant tumors, SUV is greater than 2, and sometimes it reaches values as high as 9-10, whereas in normal tissue the SUV is approximately 1. Two types of measurements were made with this analysis. One consisted of drawing a ROI to include the entire area of abnormal uptake from which an average SUV for the abnormality was calculated. The other consisted of sampling the most active portion of the lesion to determine the maximum activity concentration in the tumor. Neither of these parameters were used so far to determine the presence or absence of active disease (qualitative assessment was adequate for this purpose), but was used in a survival study of this trial.

Results:

Thirty-nine patients were accrued into this protocol which allowed accomplishing our commitment almost entirely (98%).

We accumulated data concerning clinical evaluation, biochemical tests, and correlative imaging methods. An analysis of the results of the accuracy of PET studies are reported below.

We have also implemented an iterative reconstruction algorithm (ordered subsets expectation maximization algorithm) to improve the image quality of whole-body studies and reduce artifacts produced by non uniform distribution of activity, especially in the thorax and the pelvis[20]. In our analysis of this algorithm, we have clearly shown significant improvements in image quality, with reduction of the noise content of the reconstructed images. Combined with improvements in our techniques of attenuation correction[21], we were able to achieve optimal quantitative whole-body studies for this protocol. These improvements were applied to all studies acquired for this protocol.

Qualitative interpretation:

In total, 39 patients have had their initial PET studies before entering their high dose chemotherapy protocol. We have analyzed the results of PET examinations in patients to assess the prevalence of disease in metastatic breast cancer patients before high dose chemotherapy with stem cell rescue. The results of the PET studies were compared with the results of clinical examination and other radiological data, and are reported in tables 2 - 6. The results of the remaining 15 patients are currently being compiled for final publication.

Seventeen subjects had active disease demonstrated on the PET study (28/39, 71%), and in 11, no evidence of metabolically active disease was noted. In two subjects (8.3%), metastatic disease involvement was shown only on PET imaging (subjects 5, and 20 on table 2). In two subjects (subjects 8 and 24 on tables 2 and 4) with negative PET scans, residual lesions were shown only by bone scanning (8.3%). One of these subjects (subject 8) had a residual rib lesion that had responded well to conventional chemotherapy, and had become sclerotic on x-ray. The overall

agreement with the combined restaging procedures was 80% (31/39, 95% confidence interval 68-98%, Kappa statistic 0.60), with FDG-PET demonstrating the presence of unsuspected disease in 2/7 (29%) patients thought to be free of measurable disease at the time of entry in the high dose chemotherapy trial.

Further analysis of the regional sensitivity of FDG-PET imaging indicates that this test is sensitive for detecting lymph node disease in the chest (table 3). In this area, FDG-PET imaging agreed with the conventional assessment in 31/39 subjects (80%, 95% confidence interval 68-94%). FDG-PET demonstrated the presence of hypermetabolic lymph node involvement in the chest in 8/24 patients. Only one of these patients had a positive CT in a corresponding site (subject 19, table 3), five had negative CT, while one patient had not undergone a restaging chest CT. Six of the eight patients with FDG-PET abnormalities in the mediastinum had evidence of metastatic disease elsewhere.

For the assessment of marrow involvement (table 4), FDG-PET was in good agreement with the bone scan results for the overall assessment of the presence of metastases (21/24 subjects, 87.5%, 95% confidence interval 68-97%, Kappa = 0.75). In the evaluation of liver disease, there was moderate overall agreement between PET and CT (17/24, 71%, 95% confidence interval 49-87%, Kappa = 0.26), but there was more discrepancies between the two than in other anatomic sites (Table 5).

We have also attempted to assess the accuracy of FDG-PET utilizing short-term outcome (6 months) with clinical and imaging follow-up as a "gold standard". Using these data to calculate the performance of FDG-PET, we obtained a sensitivity of 85% (95% confidence interval 62-97%), a specificity of 100% (40-100%), a positive predictive value of 100% (80 - 100%), and a negative predictive value of 57.1% (18-90%). These results are summarized in table 6.

One of the major issues with bone marrow transplantation is the high failure rate experienced in the year following the transplant. We performed a study with the data available from this grant to assess whether a baseline PET scan could predict outcome after high dose chemotherapy in breast cancer patients (table 7). Twenty-one patients with adequate one-year follow-up were included in this study. Death or the presence of residual active disease at one year was considered an unfavorable prognosis. The absence of demonstrable disease at one year was considered a favorable outcome. A positive FDG-PET study tended to be associated with a higher incidence of unfavorable outcome at one year (relative risk = 1.47), although using the Fisher's exact test, the relationship between outcome and the FDG-PET results was not statistically significant ($p = 0.35$). Combining the PET results with those of all other imaging modalities identified patients with a higher risk of unfavorable outcome (relative risk = 1.88), but again, this did not reach statistical significance ($p=0.28$). Power calculations demonstrated that a much larger sample of patients will be needed to demonstrate such a relationship. Figure 1 describes proportion of patients surviving with and without residual disease on PET after induction chemotherapy, prior to high dose chemotherapy. There was no difference between the two groups, indicating that the residual disease after induction chemotherapy as indicated by PET cannot predict an unfavorable outcome.

Conclusion:

Our project was successfully conducted, with the expected patient accrual. The data analysis confirmed the usefulness of FDG-PET imaging in restaging breast cancer. FDG-PET imaging provides unique independent information about disease activity in patients with breast cancer prior to high dose chemotherapy. The role of FDG PET in establishing prognosis and in

assessing the outcome of treatment is being actively studied. We believe the results of this study will be of considerable importance in the management of patients with breast cancer who are being considered for bone marrow transplantation.

Publications and scientific communications supported (fully or in part) by this project:

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- Benard F, Alavi A, Alavi J, et al. The value of a baseline FDG-PET study to predict outcome after high dose chemotherapy in breast cancer patients.
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TABLE 1: PET qualitative rating scheme

PET Rating scale:
0: Normal scan
1: Probably normal scan
2: Possibly abnormal scan
3: Probably abnormal scan
4: Definitely abnormal scan

Grades 0-1 were considered negative, and 2-4 positive.

This table describes the rating scale utilized to score the degree of confidence of the reader about the overall findings on the scan.

TABLE 2

Restaging - global impression

No	PET result	PET Grade	Other Imaging	Global clinical	Status	Interval
1	+	4	+	CR	A	824,00
2	+	4	+	Tox	D	130,00
3	-	1	-	PD	D	743,00
4	-	0	-	CR	A	1254,00
5	+	4	-	Tox	D	39,00
6	+	4	+	PD	A	360,00
7	+	4	+	PD	D	301,00
8	-	1	+	PD	A	422,00
9	+	3	+	PD	D	1451,00
10	+	4	+	PD	D	937,00
11	+	3	+	PD	D	373,00
12	+	4	+	PD	D	546,00
13	-	1	-	CR	A	525,00
14	-	1	-	PD	A	888,00
15	+	4	+	PD	D	1139,00
16	+	4	+	PD	D	249,00
17	-	0	-	PD	D	637,00
18	+	3	+	PD	A	828,00
19	+	3	+	CR	A	942,00
20	+	4	-	PD	A	464,00
21	+	3	+	CR	A	462,00
22	+	4	+	CR	A	404,00
23	+	4	+	PD	D	637,00
24	-	0	+	PD	D	499,00
25	-	0	+	PD	A	395,00
26	-	1	+	PD	A	477,00
27	+	4	+	PD	D	285,00
28	+	3	+	PD	A	346,00
29	+	4	+	SD	A	221,00
30	+	4	+	PD	A	728,00
31	+	4	+	PD	A	781,00
32	-	0	+	PD	A	595,00
33	+	4	+	PD	A	420,00
34	-	0	+	PD	A	420,00
35	+	2	+	PD	D	641,00
36	+	2	+	CR	A	205,00
37	+	4	+	PD	A	463,00
38	+	4	+	PD	A	418,00
39	+	4	+	SD	A	436,00

Results of PET imaging and conventional staging in assessing residual disease after induction chemotherapy prior to high dose chemotherapy with stem cell support (CR = complete response, PD = progressive disease, SD = stable disease, Tox = death due to treatment toxicity; status A=Alive, D=Deceased; the interval to time of death or last follow-up is given in days).

Table 2 continued on Page 23

TABLE 2 (continued)

PET Grading scale:

0: Normal scan
1: Probably normal scan
2: Possibly abnormal scan
3: Probably abnormal scan
4: Definitely abnormal scan

2 x 2 Table

Convent / PET	+	-	Total
+	26	2	28
-	6	5	11
Total	32	7	39

The data above describe correlation of ratings between PET and conventional assessment in this population.

TABLE 3.

Restaging - assessment of chest disease

	PET					CT/Chest x-ray		
No	Lungs	Grade	Nodes	Grade	Chest CT?	Lungs	Nodes	Extent
1	-	0	+	4	y	-	-	PET>CT
2	-	1	-	0	n	-	-	=
3	-	0	-	0	y	-	-	=
4	-	0	-	0	y	-	-	=
5	-	0	+	4	y	-	-	PET>CT
6	-	0	+	4	y	+	-	PET>CT
7	-	0	+	4	y	-	-	PET>CT
8	-	1	-	0	y	-	-	=
9	-	0	+	3	y	+*	-	PET>CT
10	-	0	-	0	y	-	-	=
11	-	0	-	0	y	-	-	=
12	-	0	+	4	y	-	-	PET>CT
13	-	1	0	-	y	-	-	=
14	-	0	-	1	n	-	-	=
15	-	0	-	0	y	-	-	=
16	-	0	-	0	y	-	-	=
17	-	0	-	0	n	-	-	=
18	+	2	+	3	n	-	-	PET>Conv.
19	-	0	+	3	y	-	+	=
20	-	0	-	0	n	-	-	=
21	-	0	-	0	y	-	-	=
22	-	0	-	0	y	-	-	=
23	-	0	-	0	y	-	-	=
24	-	0	-	0	n	-	-	=
25	-	0	-	0	y	-	-	=
26	-	0	-	0	y	-	-	
27	+	4	-	0	y	+	-	=
28	+	2	+	3	y	+	-	PET>CT
29	+	4	-	0	y	+	+	CT>PET
30	-	0	+	4	y	-	-	PET>CT
31	-	0	+	4	y	-	+	=
32	-	0	-	0	y	-	-	=
33	-	0	-	0	y	-	-	
34	-	0	-	0	y	-	-	=
35	-	0	+	2	y	-	-	=
36	-	0	+	2	y	-	-	=
37	-	0	+	4	y	+	-	=
38	+	4	-	0	n	+	-	=
39	-	0	-	0	y	-	-	=

Results of FDG-PET study compared to those of conventional imaging in the assessment of residual disease in the chest. FDG-PET tended to demonstrate a higher number of lesions in the chest, particularly in the nodal chains.

TABLE 3 continued on page 25.

TABLE 3 (continued)

PET Grading scale:

0:	Normal scan
1:	Probably normal scan
2:	Possibly abnormal scan
3:	Probably abnormal scan
4:	Definitely abnormal scan

2 x 2 Table

Convent / PET			Total
+	9	8	17
-	0	22	22
Total	9	30	39

Grades 0-1 were considered negative, and 2-4 positive.

The data above describe correlation between FDG-PET and conventional techniques in thoracic structures.

TABLE 4 – Assessment of bone or marrow disease

No	*PET result*	*PET Grade*	*Bone scan*	*Extent*
1	-	0	-	=
2	+	4	+	BS>PET
3	-	0	-	=
4	-	0	-	=
5	-	0	-	=
6	+	4	+	BS>PET
7	-	0	+	BS>PET
8	-	0	+	BS>PET
9	-	0	-	=
10	+	4	+	=
11	+	3	+	=
12	-	0	-	=
13	-	0	=	=
14	-	0	-	=
15	+	4	+	BS>PET
16	+	4	+	PET>BS
17	-	0	-	=
18	+	3	+	BS>PET
19	-	0	-	=
20	-	0	-	=
21	+	3	+	=
22	+	4	+	PET>BS
23	+	4	+	PET>BS
24	-	0	+	BS>PET

2x2 Table

	Clinical/Imaging		
FDG-PET	**+**	**-**	**Total**
+	***10***	***0***	**10**
-	***3***	***11***	**14**
Total	**13**	**11**	**24**

The data above describe the state of the bone and bone marrow disease as determined by PET and bone scan.

TABLE 5 – Assessment of liver disease

No	*PET result*	*PET Grade*	*CT/MR result*	*Extent*
1	-	0	+	CT>PET
2	-	0	+	MR>PET
3	-	0	-	=
4	-	0	-	=
5	-	0	-	=
6	-	0	+	CT>PET
7	-	0	-	=
8	-	0	-	=
9	-	0	-	=
10	-	0	-	=
11	+	2	-	PET>CT
12	+	3	-	PET>CT
13	-	0	-	=
14	-	0	-	=
15	-	0	-	=
16	+	3	+	=
17	-	0	-	=
18	-	0	-	=
19	+	2	+	=
20	+	4	-	PET>CT
21	+	2	+	=
22	+	4	-	PET>CT
23	-	0	-	=
24	-	0	-	=

2x2 Table

	Clinical/Imaging		
FDG-PET	**+**	**-**	**Total**
+	***3***	***4***	**7**
-	***3***	***14***	**17**
Total	**6**	**18**	**24**

The data above describe the degree of liver involvement as demonstrated by FDG-PET and CT/MR imaging.

Table 6 - combined imaging data with short term follow-up

	Clinical/Imaging/Follow-up		
FDG-PET	**+**	**-**	**Total**
+	*17*	*0*	**17**
-	*3*	*4*	**7**
Total	**20**	**4**	**24**

Sensitivity =	85% (62 - 97%)
Specificity =	100% (40 - 100%)
Accuracy =	87.5% (68 - 97%)
Positive Predictive Value =	100% (80 - 100%)
Negative Predictive Value =	57% (18 - 90%)

The value reported is the percentage followed by the exact 95% confidence interval

The data above describe correlation between FDG-PET findings and determination based on clinical/imaging and follow up results.

Table 7 – predictive value of PET and conventional imaging for treatment failure

Outcome	PET		Other		Combined		Total
	+	-	+	-	+	-	
Unfavorable	11	3	10	4	12	2	14
Favorable	4	3	4	3	4	3	7
Total	15	6	14	7	16	5	21

To predict an unfavorable outcome at one year:

- Sensitivity/Specificity Conventional: 71% / 43%
- Sensitivity/Specificity PET: 79% / 43%
- Sensitivity/Specificity Combined tests: 86% / 43%
- PPV/NPV Combined: 75% / 60%

- McNemar test (PET vs Conventional): not significant (n.s.)
- Fisher's exact test (regarding a relationship between imaging and outcome): n.s. ($p = 0.16$)
- Relative risk (+ PET): 1.47 (0.21 - 10.5)
- Relative risk (+ Convent.): 1.25 (0.19 - 8.3)
- Relative risk (+ Combined): 1.88 (0.23 - 15.6)

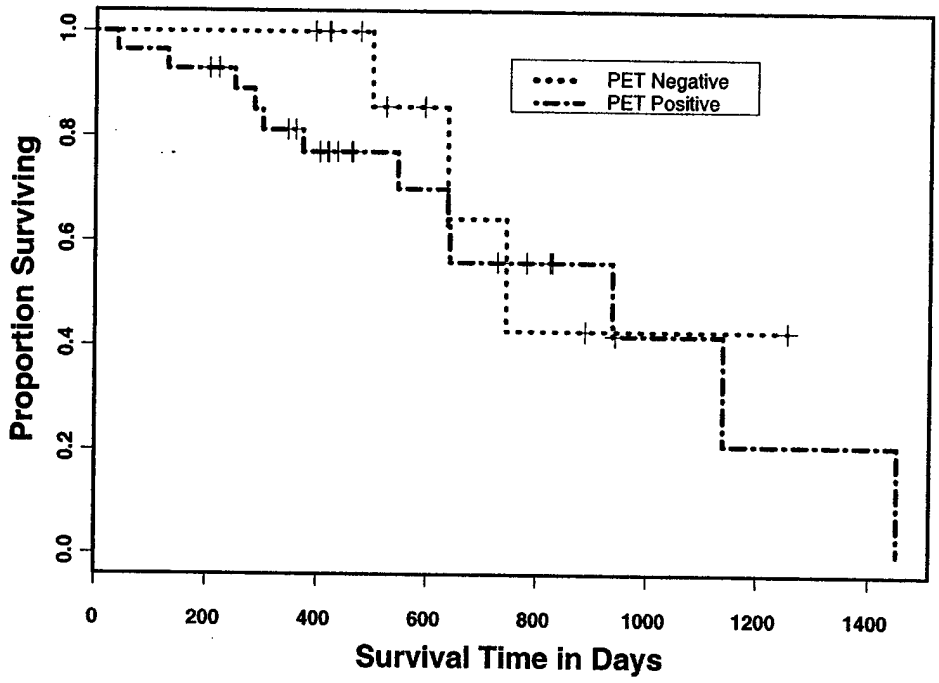
Sample size needed to confirm a statistically significant difference with the use of FDG-PET

- PPV from 71 to 75%: n = 983
- NPV from 43 to 60%: n = 67
- Sensitivity from 71 to 86%: n = 63

(assuming accurate values of sensitivity, specificity, ppv, npv)

The data above describe the predictive value of PET and conventional imaging techniques for patients with both favorable and unfavorable outcomes following treatment.

FIGURE 1.
Survival of patients entered in this protocol, after bone marrow transplantation.



This figure describes proportion of patients surviving with and without residual disease on PET imaging after induction chemotherapy, prior to high dose chemotherapy. There was no difference (logrank test; p = 0.45) between the 2 groups, indicating that the presence of residual disease after induction chemotherapy, as indicated by PET, cannot predict an unfavorable outcome.