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# Role of 18F-FDG-PET/CT in the staging of metastatic rhabdomyosarcoma: A report from the European paediatric Soft tissue sarcoma Study Group

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| Abstract: | Background : Initial staging of rhabdomyosarcoma is crucial for prognosis and to tailor the treatment. The standard radiology workup (SRW) includes MRI, chest CT and bone scintigraphy, but 18 F-FDG-PET/CT (PET-CT) use is increasing.<br>The aim of our study is to evaluate the impact of PET-CT in the initial staging of patients with metastatic rhabdomyosarcoma enrolled in the European protocol MTS2008.<br>Methods : Two authors retrospectively reviewed the SRW and PET-CT reports comparing the number and sites of metastases detected. For bone marrow involvement, PET-CT and bone marrow aspirates/biopsies were compared.<br>Results : Among 263 metastatic patients enrolled from October 2008 to December 2016, 121 had PET-CT performed at diagnosis, and for 118/121, both PET-CT and radiological reports were available for review.<br>PET-CT showed higher sensitivity than SRW in the ability to detect locoregional (96.2% vs. 78.5%, p-value=0.0013) and distant lymph node involvement (94.8% vs. 79.3%, p-value= 0.0242), but sensitivity was lower for intrathoracic sites (lung 79.6% vs. 100%, p-value=0.0025). For bone metastasis, PET-CT was more sensitive than bone scintigraphy (96.4% vs. 67.9%, p-value=0.0116). The PET-CT sensitivity and specificity to detect marrow involvement were 91.8% and 93.8%, respectively.<br>The mean number of metastatic sites was 1.94 (range 0-5) with PET-CT and 1.72 (range 0-5) with SRW. In 4 (3.4%) patients, PET-CT changed the staging from localized to metastatic disease.<br>Conclusion : PET can identify metastatic disease not evident on SRW in a small |

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| | number of patients. This is due to its higher ability to recognize lymph node and bone involvement. Chest-CT remains essential to detect lesions in intrathoracic sites, which can be performed in a one stop-shot routine examination or on a dedicated chest-CT scan. PET-CT could replace bone scintigraphy to study bone involvement. |

# Role of $^{18}$F-FDG-PET/CT in the staging of metastatic rhabdomyosarcoma: A report from the European paediatric Soft tissue sarcoma Study Group

## Highlights

- PET/CT in the staging of rhabdomyosarcoma is increasingly used
- PET/CT is more sensitive than conventional radiology in detecting nodal metastases
- Chest-CT is essential for the evaluation of intrathoracic lesions
- PET/CT could replace bone scintigraphy to study bone involvement
- Systematic use of PET/CT will modestly increase the number of metastatic patients

 

# Role of $^{18}$F-FDG-PET/CT in the staging of metastatic rhabdomyosarcoma: A report from the European paediatric Soft tissue sarcoma Study Group

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## ABSTRACT

Background: Initial staging of rhabdomyosarcoma is crucial for prognosis and to tailor the treatment. The standard radiology workup (SRW) includes MRI, chest CT and bone scintigraphy, but $^{18}$F-FDG-PET/CT (PET-CT) use is increasing.

The aim of our study is to evaluate the impact of PET-CT in the initial staging of patients with metastatic rhabdomyosarcoma enrolled in the European protocol MTS2008.

Methods: Two authors retrospectively reviewed the SRW and PET-CT reports comparing the number and sites of metastases detected. For bone marrow involvement, PET-CT and bone marrow aspirates/biopsies were compared.

Results: Among 263 metastatic patients enrolled from October 2008 to December 2016, 121 had PET-CT performed at diagnosis, and for 118/121, both PET-CT and radiological reports were available for review.

PET-CT showed higher sensitivity than SRW in the ability to detect locoregional (96.2% vs. 78.5%, p-value=0.0013) and distant lymph node involvement (94.8% vs. 79.3%, p-value= 0.0242), but sensitivity was lower for intrathoracic sites (lung 79.6% vs. 100%, p-value=0.0025). For bone metastasis, PET-CT was more sensitive than bone scintigraphy (96.4% vs. 67.9%, p-value=0.0116). The PET-CT sensitivity and specificity to detect marrow involvement were 91.8% and 93.8%, respectively.

The mean number of metastatic sites was 1.94 (range 0-5) with PET-CT and 1.72 (range 0-5) with SRW. In 4 (3.4%) patients, PET-CT changed the staging from localized to metastatic disease.

Conclusion: PET can identify metastatic disease not evident on SRW in a small number of patients. This is due to its higher ability to recognize lymph node and bone involvement. Chest-CT remains essential to detect lesions in intrathoracic sites, which can be performed in a one stop-shot routine examination or on a dedicated chest-CT scan. PET-CT could replace bone scintigraphy to study bone involvement.

## INTRODUCTION

Rhabdomyosarcoma (RMS) is a highly aggressive tumour thought to derive from primitive cells demonstrating myogenic differentiation. It is the most typical form of soft tissue sarcoma in children and young adults. It accounts for 4-5% of all childhood malignancies, with an annual incidence of 5.3 per million children under the age of 15[1]. Histologically childhood RMS is classified as embryonal (80% of all RMS) or alveolar subtype (15 - 20%), with the majority of alveolar tumours characterized by the reciprocal chromosomal translocations t(2;13) or t(1;13).

Effective multidisciplinary treatments have been progressively developed in the last decades, but results are not homogenous, and a patient's chance of survival depends on a series of prognostic factors[2]. The most important factor is the presence of metastases at diagnosis which occur in approximately 20% of patients, most frequently involving lungs, bone and bone marrow, and distant nodes. The long term survival in localized RMS is higher than 70%[1], whereas the expected 5-year overall survival in metastatic RMS is less than 35%, but with substantial variation according to age, primary tumour location, bone or bone marrow involvement, and the number of metastatic sites as demonstrated in the prognostic scoring system devised by Oberlin et al.[2] Therefore accurate staging is of paramount importance to determine prognosis and tailor treatment.

The European paediatric Soft tissue sarcoma Study Group (EpSSG) performed an international protocol dedicated to children and young adults with metastatic RMS. When the protocol was launched, $^{18}$F-FDG-PET/CT was considered optional but was performed in a substantial number of patients.

This study retrospectively investigated the impact of $^{18}$F-FDG-PET/CT in defining tumor extent and stage in pediatric and young adult patients with rhabdomyosarcoma.

## MATERIAL AND METHODS

A prospective international, multi-institutional, clinical trial entitled MTS2008 was conducted in 74 centers in 11 countries from October 2008 to December 2016 as an amendment to the existing RMS 2005 study in localised RMS[3] .

All participating centers were required to obtain written approval from their local authorities and ethics committees and written informed consent from the patient and/or his/her parents or legal guardians. Inclusion criteria were patients aged $\leq$ 21 years with metastatic rhabdomyosarcoma histologically proven and not previously treated.

The standard radiology workup included CT and/or MRI of the primary tumour, chest CT scan, and radionuclide bone scintigraphy. $^{18}$F-FDG-PET/CT was optional but if performed results had to be considered to determine tumour extent and define tumour stage. Staging investigations included bone marrow aspirate and biopsy

The imaging reports were systematically reviewed by two authors (FM and GB) supported by a nuclear medicine doctor (PZ); the number and sites of metastatic lesions detected by standard radiology workup and $^{18}$F-FDG-PET/CT were noted separately. In case of discrepancy among the reviewers the reports were discussed and agreement obtained. A total of 118 $^{18}$F-FDG-PET/CT, 116 CT scan, 101 MRI and 46 bone scan reports were reviewed. As we were more interested to understand how the use of $^{18}$F-FDG-PET/CT influenced patients management we did not perform a review of images but, in case of doubt, we contacted the patients' treating physicians to clarify the interpretation of the reports.

The sensitivity of the different investigation methods was calculated using as reference the final clinical interpretation by the treating physician, i.e. if the lesion demonstrated by the radiological investigations were considered, and treated, as a metastasis or not.

The result of bone marrow aspirate/biopsy were used as the reference for calculating the sensitivity and specificity of $^{18}$F-FDG-PET/CT in detecting bone marrow metastases.

The population was divided into two group (patients who underwent PET vs patients who did not) and the difference in the distribution was verified using the Chi-square test. Fisher's exact test was used to compare the sensitivity of F-FDG-PET/CT and SRW.

The level of statistical significance was established for p values<0.05. All statistical analyses were performed with SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

## RESULTS

### *Patients Characteristics*

Overall, 263 patients with a metastatic RMS were registered from September 2008 to

December 2016. $^{18}$F-FDG-PET/CT was performed at diagnosis in 121 patients and for 118 of 121 patients MRI and/or CT scan of the primary tumor, chest-CT and $^{18}$F-FDG-PET/CT PET reports were available. These 118 patients were the subjects of our analysis. The characteristics of patients and the comparison between those who did or did not undergo $^{18}$F-FDG-PET/CT are summarized in **Table 1**.

There was great variability in the use of $^{18}$F-FDG-PET/CT in different countries. $^{18}$F-FDG-PET/CT was more frequently performed in France and The Netherlands (in 77.8 and 84.2% of patients, respectively) than in the UK (15.9%). In addition, the use of $^{18}$F-FDG-PET/CT increased over the years (32.7% in 2008-2012 vs 53.6% in 2013-2016). In the UK 71.4% of patients had a PET in 2016, the last year of the study.

The use of $^{18}$F-FDG-PET/CT was also significantly more frequent in older patients, particularly in those older than 7 years, in tumours with alveolar histology and with locoregional nodal involvement (N1).

In the study group 13/118 patients had both MRI and CT scan of the primary tumor, 89 had MRI alone and 16 CT scan alone. Chest CT scan was performed in in all patients.

The total number of metastatic sites found with standard radiology workup and $^{18}$F-FDG-PET/CT was 203 and 229 (p=0.0005), respectively, with a mean number per patient of 1.72 (range 0-5) for standard radiology workup and 1.94 (range 0-5) for $^{18}$F-FDG-PET/CT.

In 40 patients $^{18}$F-FDG-PET/CT detected a higher number of involved organs (6 patients: 2 sites more than standard radiology workup; 34 cases: 1 site more than standard radiology workup). In 65 patients the two methods showed the same number of sites involved. Conversely in 13 cases standard radiology workup showed a higher number of involved sites. In 4/118 (3.4%) patients in which the standard radiology workup was negative for metastatic disease, the$^{18}$F-FDG-PET/CT identified metastases: bone metastases (with bone scan negative) and distal nodal involvement (with small nodule not considered pathologic by MRI) were detected in 2 cases each.

The capacity of $^{18}$F-FDG-PET/CT to detect distant metastasis varies between different organs (**table 2).** Considering regional and distant nodal involvement $^{18}$F-FDG-PET/CT identified a higher number of lymph nodes involved than standard radiology. In particular, $^{18}$F-FDG-PET/CT detected in-transit involved nodes in 5 patients (4 popliteal, 1 of the elbow), not found by standard radiology workup. With the limitation of small numbers $^{18}$F-FDG-PET/CT was also able to identify a higher number of subcutaneous metastases.

Conversely chest CT scan showed better sensitivity than $^{18}$F-FDG-PET/CT in detection of lung lesions.

In 7 patients with lung lesions detected on CT scan alone, 6 had multiple nodules $\leq$ 6 mm in size. In 4 patients, the lesions detected on CT scan were greater in number and smaller ($\leq$5 mm) than those detected by $^{18}$F-FDG-PET/CT scan.

Comparing the role of $^{18}$F-FDG-PET/CT and bone scintigraphy in the detection of bone metastases, 46 patients had both investigations at diagnosis and $^{18}$F-FDG-PET/CT demonstrated bone lesions (**table 3**), with a higher sensitivity but lower specificity.

Of 114 patients who underwent Bone Marrow Aspirates/Biopsies and $^{18}$F-FDG-PET/CT, bone marrow involvement was detected using $^{18}$F-FDG-PET/CT with a sensitivity and specificity above 90% (**table 4**).

## DISCUSSION

The diagnostic value of $^{18}$F-FDG-PET/CT has been demonstrated in various adult malignancies[4], but there are limited data in paediatric oncology[5,6,7,8,9]; the exception being lymphoma where $^{18}$F-FDG-PET/CT is standard of care for staging and treatment response evaluation[10,11].

Recent data indicates that $^{18}$F-FDG-PET/CT combined with standard imaging provides additional information for staging of sarcomas[12]. $^{18}$F-FDG-PET/CT was not mandatory for staging in MTS2008 protocol but was increasingly used given positive reports of its use in adult sarcomas patients[4,13], and a few small case series in paediatric patients demonstrating better detection of nodal and bone involvement[14,15,16,17].

We found that the use of $^{18}$F-FDG-PET/CT varied among European countries although this difference became less evident as it's use increase in the UK towards the end of the MTS2008 trial period. $^{18}$F-FDG-PET/CT was performed more frequently in older patients probably due to the higher expected rate of lymph node and distant metastases[2] and less frequently performed in younger patients who would need general anaesthesia.

The more frequent use in patients with alveolar RMS may have been related to the known higher propensity of this histotype to metastasise.

One limitation of our study is that imaging review was not performed. Instead we relied on imaging reports and clinician reports of metastases and when the reports were unclear or inconsistencies appeared between separate imaging modalities we contacted the treating centre for clarification . However this limitation provides a more realistic application of the utility of $^{18}$F-FDG-PET/CT in normal clinical practice. Another limitation is that without a tissue (nodes or distant metastases) diagnosis for staging confirmation, it is difficult to compare the results of different image-staging investigations with the exception of bone marrow assessment, where biopsy is routine. Detection of false positive and false negative results in $^{18}$F-FDG-PET/CT may be difficult without histological confirmation. Another possible limitation is that $^{18}$F-FDG-PET/CT was performed more frequently in older children, however there is no reason to suspect that the detection of metastatic lesions by $^{18}$F-FDG-PET/CT should be different according to age.

In this retrospective study we tried to analyse the impact of PET in clinical practice

The strenght of this study is that it provides the largest series to date in the use of $^{18}$F-FDG-PET/CT in the staging of metastatic RMS in a paediatric population. In addition, the multicentre, multicountry nature of the study enables the potential benefit of $^{18}$F-FDG-PET/CT to reflect real world application outside individual centres of PET imaging expertise.

The higher number of patients with nodal involvement in the $^{18}$F-FDG-PET/CT group seems to reflect the increased capacity of this investigation to detect tumour involvement in regional and distant nodes[18]. This finding is in agreement with Norman et al.[16] who reviewed 4 studies on paediatric rhabdomyosarcoma including a total of 82 patients[5,14,17,19]. They found that the diagnostic accuracy of $^{18}$F-FDG-PET/CT had a sensitivity and a specificity in the range of 80-100% in comparison with a 67%-86% sensitivity and 90-100% specificity for conventional imaging (CT scan, MRI and bone scan). A high capability of $^{18}$F-FDG-PET/CT to detect nodal involvement has been reported also by Eugene et al.[15]. It is of interest that in 5 patients with primary limb tumours, $^{18}$F-FDG-PET/CT showed in transit lymph nodes, not detected by standard radiology workup. Some studies report a  high avidity of RMS for FDG, and therefore $^{18}$F-FDG-PET/CT seems particularly useful in recognizing small involved lymph nodes[18].  In cases where standard radiology workup shows small or doubtful nodes, there is a benefit derived from the metabolic parameter extracted from the PET/CT examination, yet, being aware of the possible false positive results [16].

In line with other published studies [14,17] chest CT is more reliable than $^{18}$F-FDG-PET/CT for pulmonary lesions, that are often of limited size and therefore under the limit of detection of $^{18}$F-FDG-PET/CT, PET/CT protocols often use free breathing which can induce motion artefacts. A single-breath chest CT can be performed with a standard multi-slice CT scan–PET, to improve lung nodules dectection. High-resolution Lung Reformat of the CT scan with smaller field of view and sharp reconstruction filter and 2-mm slice thickness does provide higher lung nodules detection [20,21]

Considering bone involvement, $^{18}$F-FDG-PET/CT detected a higher number of lesions compared with bone scintigraphy. The lower sensitivity of bone scintigraphy is probably related to the limited value of this investigation in the detection of osteolytic lesions, while it is useful for detection of osteoblastic metastatic lesion. In addition $^{18}$F-FDG-PET/CT may be able to recognize bone lesions at an earlier stage, due to an increased glycolytic activity, even in osteolytic lesions[22].–These data, and the review by Norman[16], support replacing bone scintigraphy with $^{18}$F-FDG-PET/CT in RMS.

$^{18}$F-FDG-PET/CT showed a high ability to detect bone marrow involvement. However, in our series 2 false positives occurred when using BMA or trephines as gold standard: $^{18}$F-FDG-PET/CT  may show a pathological uptake in bone marrow also during a systemic inflammation and the typical highly cellularity of hematopoietic bone marrow in children; this may be difficult to differentiate from neoplastic infiltration[23]. Our data, in which 4 patients presented bone marrow involvement in BMA/BMB not shown on $^{18}$F-FDG-PET/CT, suggest that marrow aspirate/biopsy cannot be omitted from the initial staging of RMS, as is the case for other tumors such as Hodgkin's lymphoma[10,24] and more recently proposed for Ewing sarcomas.[25] The possible omission of BMA/BMB should be investigated in future prospective studies or based on histological and nuclear medicine imaging review.

Only a few studies[5,15,17,9] reported the influence of $^{18}$F-FDG-PET/CT in patients staging. We found that 4 patients were upstaged from localized to metastatic disease and therefore have been treated more intensively: chemotherapy included antracyclin and was longer and metastatic site were irradiated. How this may influence prognosis is difficult to establish but it is expected that the increased use of $^{18}$F-FDG-PET/CT will modestly increase the number of metastatic patients in the RMS population. In addition the detection of the higher number of metastatic lesions may have changed the local treatment as the protocol reccomended irradiate all metastatic site if feasible. We have not been able to measure how this treatment change because we did not collect data on the irradiation of each single lesion.

As seen, $^{18}$F-FDG-PET/CT allows us to highlight a greater number of lesions and therefore have a better sensitivity in staging. Intuitively it might appear that improved staging would provide advantage (in terms of systemic therapy and local control), but to date there are no studies that prove this hypothesis; additional therapies may simply deliver greater toxicity without benefit. Furthermore, each additional investigation, which is associated with radiation exposure in children should be carefully assessed for its added value in achieving a cure of the patient and balanced against toxicities and late effects. On this topic, the next EpSSG protocol (FaR-RMS study) will provide further information as $^{18}$F-FDG-PET/CT become more widespread.

On the other hand, as we know PET-CT is associated with a radiation exposure, partially reduced in case of using MRI instead of CT in association with PET, as in the case of PET-MR. This will have to be taken into consideration when using this method more widely, weighing any real clinical advantage in terms of survival with the radiation load.

At the same time quality control and standardization of imaging procedures are necessary not only for radiation safety but also for comparing image results between different institutions in multicenter clinical trials.

## CONCLUSION

The use of $^{18}$F-FDG-PET/CT in the diagnostic workup of rhabdomyosarcoma is continuously increasing in clinical practice. Our study demonstrates that $^{18}$F-FDG-PET/CT has a higher capacity to detect lymph node and bone involvement and can replace the use of bone scintigraphy. However, MRI of the primary tumor is essential to evaluate primary tumor size and extent, and chest-CT exploration is essential to search for intrathoracic lesions. Further studies are needed to compare $^{18}$F-FDG-PET/CT with new methods such as total body MRI and to monitor response to treatment to guide treatment decisions.

In the next EpSSG protocol $^{18}$F-FDG-PET/CT has been included in the standard staging investigations and a randomized trial will try to evaluate the prognostic value of $^{18}$F-FDG-PET/CT response and its potential use as imaging biomarker.

## TABLES

| | PET imaging n=118 | No PET n=145 | Total n=263 | % with PET imaging | p-value |
|---|---|---|---|---|---|
| **Country** | | | | | **<0.0001** |
| Argentina | - | 8 | 8 | 0 | |
| Belgium | 4 | 3 | 7 | 57.1 | |
| Brazil | - | 8 | 8 | 0 | |
| France | 42 | 12 | 54 | 77.8 | |
| Israel | 6 | 3 | 9 | 66.7 | |
| Italy | 26 | 28 | 54 | 48.1 | |
| Norway | 3 | - | 3 | 100 | |
| Slovakia | - | 1 | 1 | 0 | |
| Spain | 7 | 5 | 12 | 58.3 | |
| The Netherlands | 16 | 3 | 19 | 84.2 | |
| UK & EIRE | 14 | 74 | 88 | 15.9 | |
| | | | | | |
| **Year of diagnosis** | | | | | **0.0008** |
| 2008-2012 | 36 | 74 | 110 | 32.7 | |
| 2013-2016 | 82 | 71 | 153 | 53.6 | |
| | | | | | |
| **Age (years) at diagnosis** | | | | | **0.0009** |
| ≤ 3 years | 9 | 31 | 40 | 29.0 | |
| >3 and ≤ 7 years | 25 | 41 | 66 | 37.9 | |
| >7 years | 84 | 73 | 157 | 53.5 | |
| | | | | | |
| **Gender** | | | | | 0.8142 |
| Female | 52 | 66 | 118 | 44.1 | |
| Male | 66 | 79 | 145 | 45.5 | |
| | | | | | |
| **Histology** | | | | | **0.0013** |
| Alveolar/Solid Alveolar/Mixed E-A RMS | 76 | 63 | 139 | 54.7 | |
| Embryonal/Botryoid/Spindle cell-Leiomyomatous RMS | 38 | 73 | 111 | 34.2 | |
| Pleomorphic RMS | 1 | - | 1 | 100 | |
| Not Otherwise Specify RMS | 3 | 9 | 12 | 25.0 | |
| | | | | | |
| **Tumour primary site** | | | | | **0.0421** |
| No primary | 8 | 2 | 10 | 80.0 | |
| HN no PM | 5 | 7 | 12 | 41.7 | |
| HN PM | 23 | 38 | 61 | 37.7 | |
| GU BP | 15 | 12 | 27 | 55.6 | |
| GU no BP | 4 | 13 | 17 | 23.5 | |
| Extremities | 34 | 30 | 64 | 53.1 | |
| Other sites | 29 | 43 | 72 | 40.3 | |
| | | | | | |
| **Primary tumour invasiveness** | | | | | 0.8222* |

| | PET imaging n=118 | No PET n=145 | Total n=263 | % with PET imaging | p-value |
|---|---|---|---|---|---|
| T1 | 29 | 36 | 65 | 44.6 | |
| T2 | 80 | 106 | 186 | 43.0 | |
| Tx | | | 12 | | |
| | | | | | |
| **Primary tumour size** | | | | | 0.5011° |
| $\leq$ 5 cm | 27 | 30 | 57 | 47.4 | |
| >5 cm | 80 | 109 | 189 | 42.3 | |
| Size not reported | | | 17 | | |
| | | | | | |
| **Regional nodal involvement** | | | | | 0.0303^ |
| N0 | 33 | 57 | 90 | 36.7 | |
| N1 | 79 | 76 | 155 | 51.0 | |
| Nx | | | 18 | | |

Excluded patients: *12 Tx, ° 17 Size not reported, ^18 Nx

Table 1: Clinical characteristics '$^{18}$F-FDG-PET/CT (PET) done' versus "$^{18}$F-FDG-PET/CT (PET) not done' patients

| SITE OF METASTASIS | SRW+ | SRW- | | *SRW sensitivity* | *PET sensitivity* |
|---|---|---|---|---|---|
| ***Locoregional Nodes*** | | | | 78.5% | 96.2% |
| **PET+** | 59 | 17 | | | |
| **PET-** | 3 | 39 | | | |
| ***Distant Nodes*** | | | | 79.3% | 94.8% |
| **PET+** | 43 | 12 | | | |
| **PET-** | 3 | 60 | | | |
| ***Lung*** | | | | 100% | 79.6% |
| **PET+** | 35 | | | | |
| **PET-** | 9 | 74 | | | |
| **Pleura** | | | | 100% | 78.9% |
| **PET+** | 15 | | | | |
| **PET-** | 4 | 99 | | | |
| **Central Nervous System** | | | | 100% | 50% |
| **PET+** | 2 | | | | |
| **PET-** | 2 | 114 | | | |
| **Peritoneum** | | | | 86.7% | 86.7% |
| **PET+** | 11 | 2 | | | |
| **PET-** | 2 | 103 | | | |
| **Liver** | | | | 100% | 75% |
| **PET+** | 3 | | | | |
| **PET-** | 1 | 114 | | | |
| **Subcutis** | | | | 66.7% | 100% |
| **PET+** | 4 | 2 | | | |
| **PET-** | | 112 | | | |
| **Other Sites** | | | | 78.9% | 89.5% |
| **PET+** | 13 | 4 | | | |
| **PET-** | 2 | 99 | | | |

Table 2: comparison between $^{18}$F-FDG-PET/CT (PET) and standard radiology work up (SRW) in detection of nodal and metastatic involvement

| | **BS+** | **BS-** | |
|---|---|---|---|
| **PET+** | 18 | 9 | *Bone Scintigraphy sensitivity 82.6%* |
| | | | *Bone Scintigraphy specificity 100%* |
| **PET-** | 1 | 18 | *PET sensitivity 95.6%* |
| | | | *PET specificity 78.2%* |

Table 3: Bone involvement. Comparison between $^{18}$F-FDG-PET/CT (PET) and Bone Scintigraphy (BS)

| | **BMA + and/or BMB+** | **BMA – and BMB -** | |
|---|---|---|---|
| **PET+** | 43 | 2 | *BMA + BMB sensitivity* 95.9 % |
| | | | *BMA + BMB specificity* 100% |
| **PET-** | 4 | 65 | *PET sensitivity* 91.8% |
| | | | *PET specificity* 93.8% |

Table 4: Bone marrow involvement. Comparison between $^{18}$F-FDG-PET/CT (PET) and Bone Marrow Aspirates (BMA)-Bone Marrow Biopsy (BMB)

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