Journal of
APPLIED
BIOMEDICINE

J. Appl. Biomed.
3: 147–153, 2005
ISSN 1214-0287

BRIEF COMMUNICATION

Positron emission tomography (PET) in residual post-treatment Hodgkin's disease masses

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Received 7th April 2005.
Revised 25th May 2005.
Published online 1st July 2005.

Summary
Hodgkin's Disease (HD) is one of the malignant diseases with good chances for a cure. The prognosis for cure depends on the initial stages and the outcome after initial treatment. Stages I or II at diagnosis, or a complete remission after initial treatment are good indicators for the best prognosis to patients.

A frequent problem faced by clinicians is met at the post-therapy stage because of the difficulty of distinguishing between dead tissue and disease activity in residual masses. Considering that these two situations include therapy options that run from treatment abstention to autologous stem cell transplantation, it is extremely important to distinguish them accurately.

Classical Tomography Scan (CT Scan), Gallium scintigraphy, Magnetic Resonance Imaging (MRI) or Positron Emission Tomography (PET) are used to investigate residual masses. In order to clarify the best way to confirm the post-treatment status of patients affected by HD, we describe in this paper our experience of using PET to solve those problem situations where a CT Scan or MRI were not conclusive and Gallium was negative.

Keywords: PET – Hodgkin – Residual

INTRODUCTION

Hodgkin Disease (HD) accounts for about 1% of all cancers in the western world. The incidence has increased slightly over the past 30 years, but this is more than matched by a significant decrease in mortality, reflecting the undoubted improvements in disease therapy.

It may be that this potential curability makes HD unique among neoplastic diseases. The prognosis for cure in HD is related to the stage of the disease at diagnosis and the outcome reached after initial treatment.

The essential aim of staging systems for HD is to provide information to identify groups of patients with different prognoses and to plan therapy strategies based on the individual risk of each patient (Glimelius et al. 2003).

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Two main situations are primordial for decision making in HD. One is the initial staging. Stages I or II have a significantly better outcome compared with stages III – IV. Survival curves show differences of more than 90% for long term survival for the early stage, instead of less than 50% for the advanced stages. For this reason, precision is required.

The other problematic situation faced by clinicians is observed after the end of treatment (Canellos et al. 1988). Either in the immediate post-therapy stage or in further evaluations of corresponding follow-up controls, it is extremely important to confirm the disease status, since at these points, therapy options run from treatment abstention to autologous stem cell transplantation.

To do a proper staging in HD, clinicians count on a number of different tools which include laboratory data (LDH, β2 microglobuline) and image data such as X rays, classical Tomography Scans (CT Scan), Gallium scintigraphy, Magnetic Resonance Imaging (MRI) or, more recently, Positron Emission Tomography (PET) (Hoh et al. 1997).

In order to clarify the best way to confirm the post-treatment status of patients affected by HD, we describe in this paper our experience with the role of PET solving problematic situations frequently observed by the majority of clinicians, hematologists and oncologists who treat Hodgkin's Disease.

MATERIALS AND METHODS

To demonstrate the utility of PET in complex differential diagnosis of residual masses after treatment, we will describe 2 cases of HD in young patients: A 32-year-old pregnant woman and a 39-year-old man. Both patients were healthy before the HD diagnosis was made and in both, residual masses were observed which caused a severe dilemma after the end of therapy, since the choice had to be made between further treatment or therapeutic abstention.

Methods employed to study the residual masses in these cases were CT Scan, MRI, Gallium scintigraphy and PET in both situations.

RESULTS

A description of these two cases of Hodgkin's Disease will sustain the main objective of this paper.

Case 1: A 32-year-old woman who was admitted to our Institution because of leg weakness, fatigue and anemia. This young woman was 8 months pregnant. The patient had been well until a month earlier, when she described the symptoms mentioned. On general physical examination at that time, the patient appeared severely ill. Skin inspection showed intense pallor, and prominent cervical lymph nodes. Pulmonary auscultation referred obstruction of air flow on the right side. In the small needle aspiration of one cervical node Reed Stemberg's cells were identified. Since her gestation was advanced, on the same day we did a frontal radiograph of the chest, observing an enormous mediastinal lymphadenopathy mass invading all the right pulmonary area.

We then recommended a cesarean and took a cervical node biopsy. The results were a healthy baby and a diagnosis of Sclero-Nodular Hodgkin Disease for his mother.

After staging procedures (bone marrow biopsy, laboratory tests, and whole body CT Scan and gallium scintigraphy), our patient was catalogued as Stage II B Bulky HD and received treatment with ABVD protocol (Doxorubicine, Bleomicine, Vinblastine and Dacarbazine) for 6 cycles (6 months) and mantle radiotherapy (40 Gy). The outcome control after treatment showed a complete remission at all initial sites attempted but the mediastinal mass which was reduced to more than 75% of initial size, still remained observable at CT Scan images (Figure 1).

The problem was clear: was the residual mass due to a post- radiotherapy administration fibrosis or was it an active diseased mass?

At this point, we instigated a gallium scintigraphy which is normally accepted as a good marker to detect disease activity in such cases (Kostakoglu et al. 1992, Israel et al. 1988).

The Gallium was negative and patient and doctors were satisfied. However, based on the huge size of the mediastinal on the initial attempt, we decided to administer a PET that could assure remission. The PET results showed clear activity of the radioisotope in the interior of that mass (Figure 2).

The patient underwent autologous transplantation and punctual radiation to the remaining mass. Unfortunately, a PET was again positive showing new areas of involvement (pulmonary) (Figure 3, 4). Patient is now in partial remission waiting for a new treatment schedule.

Case 2: A 39-year-old man consulted his clinician because of a 4 cm diameter inguinal left node. No B symptoms or other manifestations were referred. He underwent a surgical biopsy and an initial staging screening by the serum analysis

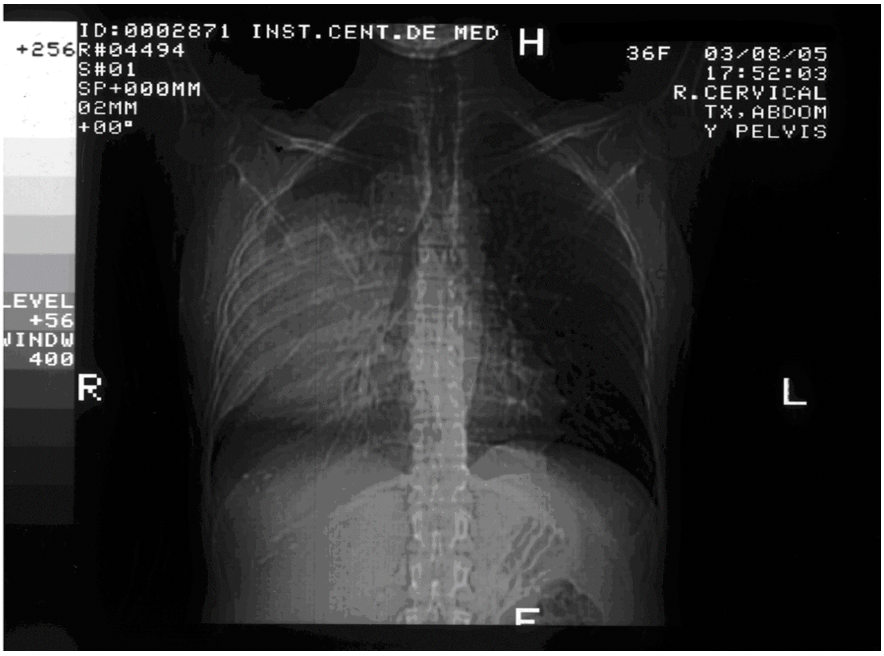

Fig. 1. **Patient 1: Initial chest CT scan**

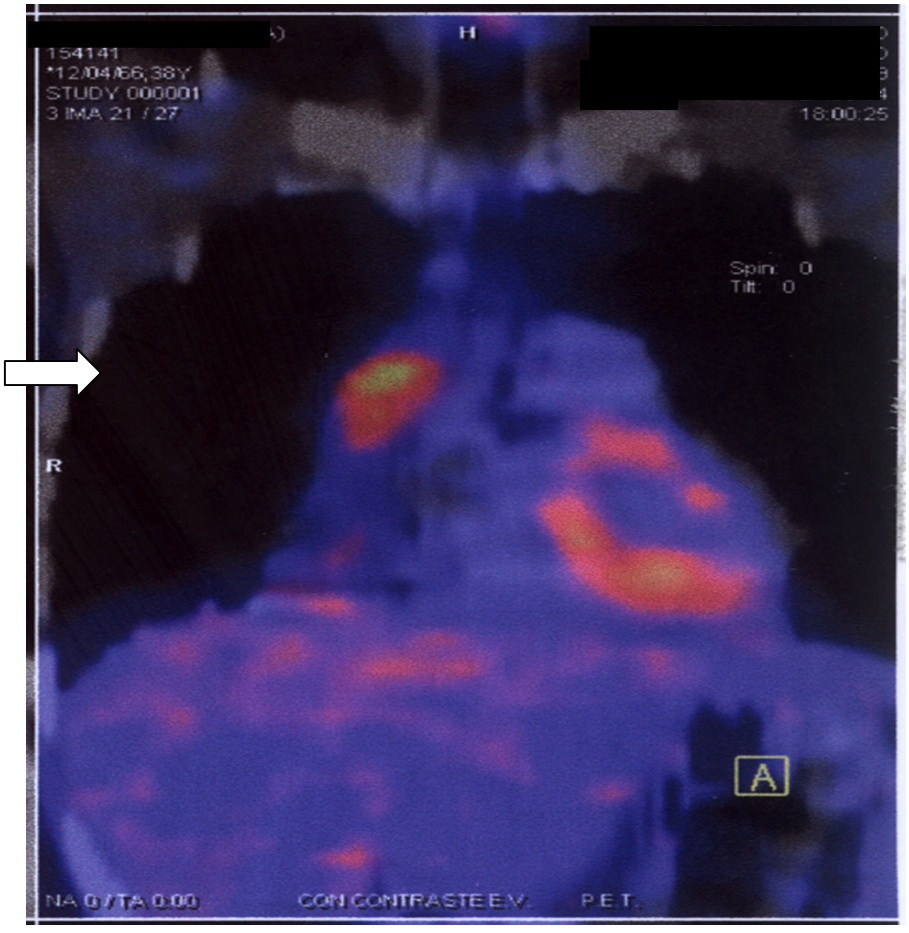

Fig. 2. **Patient 1: PET done after the initial treatment**

laboratory (proteinogram, LDH, β2 microglobuline), Cervical-Thoraco-Abdominal and Pelvic CT Scan and bone marrow biopsy. The node biopsy was confirmed as Hodgkin's disease. All other studies were normal and the patient was then catalogued as Stage I A.

Three cycles of ABVD protocol were given as well as local radiotherapy treatment.

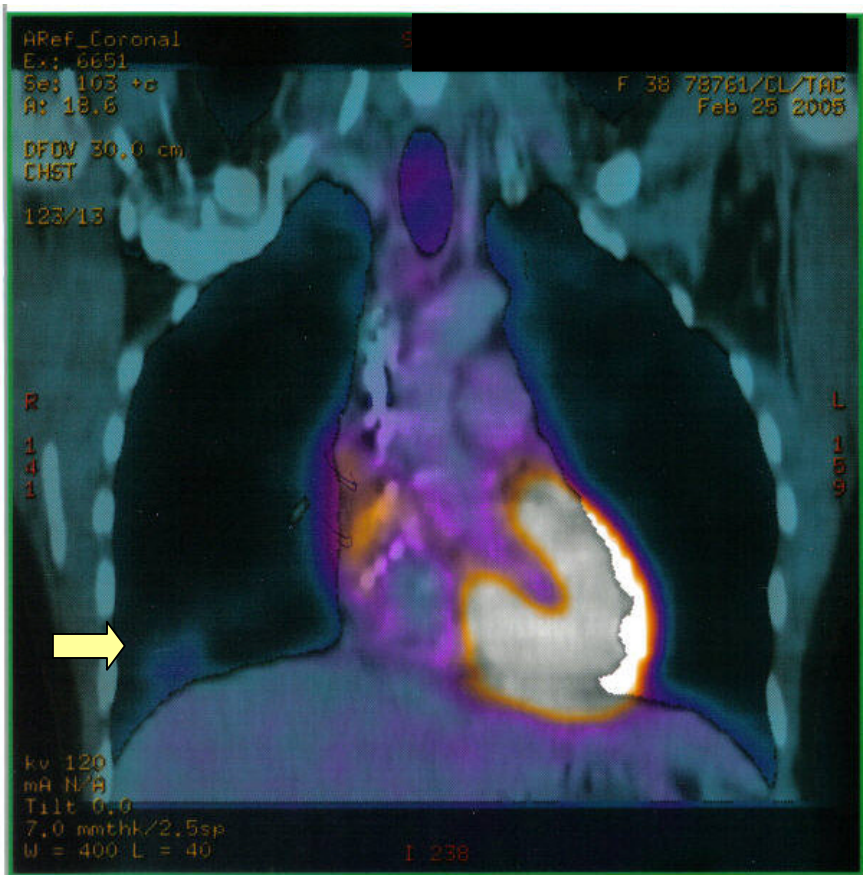

Fig. 3. **Patient 1: PET after autologous stem cell transplantation**

Post-therapy staging using exactly the sample tools used at diagnosis, showed a completed remission. The patient submitted to periodical clinical controls and scan studies at 6 months interval. At the first year's control, a very small suspicious mass image at the iliac region was observed by the CT Scan study (Figure 5).

Four possibilities were initially considered: laparotomy in order to take a biopsy of the suspicious location, MRI, gallium or empiric treatment. MRI was carried out with the same doubts that were shown in the previous Scan, laparotomy was considered extremely cruel and risky for the situation, gallium scintigraphy is useful in discriminating thorax images but is useless in abdominal masses (however it was done anyway with negative results), and empiric radiotherapy was refused by both our team and the patient.

We considered then a PET, which besides the high costs of the practice, could be useful in this particular case. The PET study confirmed activity on the iliac mass (Figure 6).

The patient underwent 3 cycles of ESHAP protocol (Etoposide, Metilprednisolone, high doses of Cytarabine and Cisplatinum). The treatment was well accepted and afterwards all studies, including a new CT Scan, which showed the mass had disappeared, and a new PET which was negative. The patient now remains in remission.

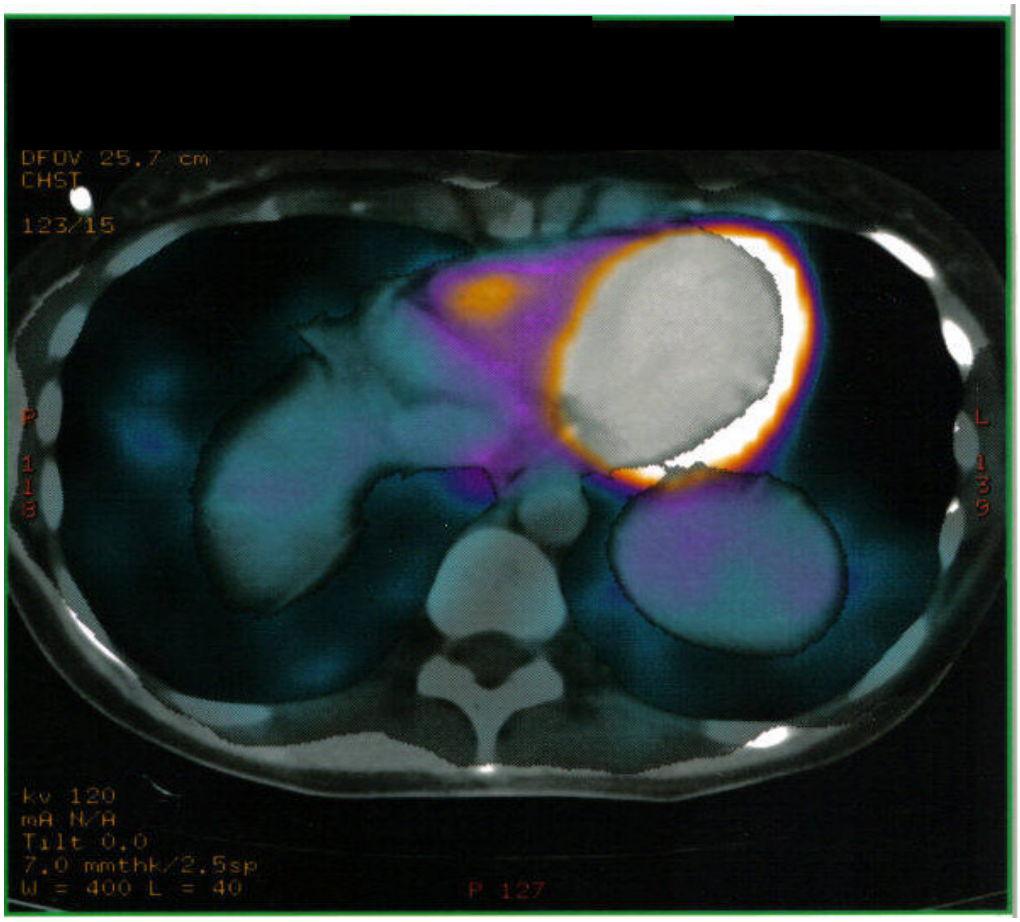

Fig. 4 **Patient 2: PET at the year's control post-treatment**

DISCUSSION

The appearance of a residual mass after initial treatment of HD can create problems for therapy management because the mass may represent an active cancer or merely be scar or dead tissue from chemotherapy damage (Canellos et al. 1988). The usual method of evaluating a residual mass is with repeated X Rays (Radford et al. 1988), CT scans, MRI (Nyman et 1989, Hill et al. 1993) or surgical biopsy. CT scans have not been very good at recognizing cancer versus scar or dead tissue since they only recognize an abnormal mass size. Often a surgical biopsy is necessary to determine whether cancer remains. However, when the mass appears to be in a difficult site for access by surgery (thoracic or abdominal cavities), the decision to submit the patient to a confirmatory biopsy is hard to take.

Guided needle biopsy can frequently avoid surgery for abdominal or thoracic lymph nodes, however, either because in several locations the use of this technique is experimental, or because the material extracted from fine needles is often insufficient for pathologists, this type of technique is not always indicated.

New methods can also help to make the right decisions in these cases.

PET (positron emission tomography) is one of these alternatives.

Positron emission tomography, also called PET imaging or a PET scan, is a diagnostic examination that involves the acquisition of physiologic images based on the detection of positrons.

Living tissue needs to undergo a metabolism of sugars. PET uses this property by injecting a sugar attached to a particularly low energy radiation (positron) into a patient Emissions of radiation can be detected after the sugar is trapped in living cancer cells. These positron emissions from living tissue that have taken up the sugar are then detected by the PET scanner. If no positron emissions are detected in the scanned area, it is unlikely that the mass in question contains living cells.

PET scans are used most often to detect cancer and to examine the effects of cancer therapy by characterizing biochemical changes in the cancer (Zinzani et al. 1999). These scans are performed on the whole body and because PET allows the study of body functions, it can help physicians to detect alterations in biochemical processes that suggest

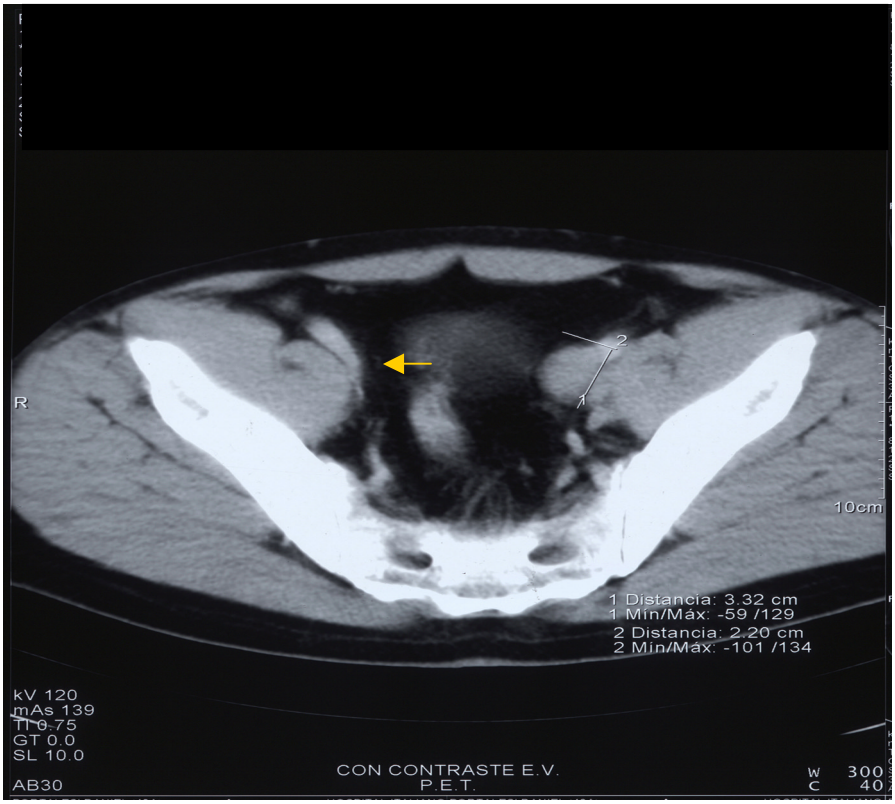

Fig. 5. **Patient 2: CT scan at the year's control post-treatment**

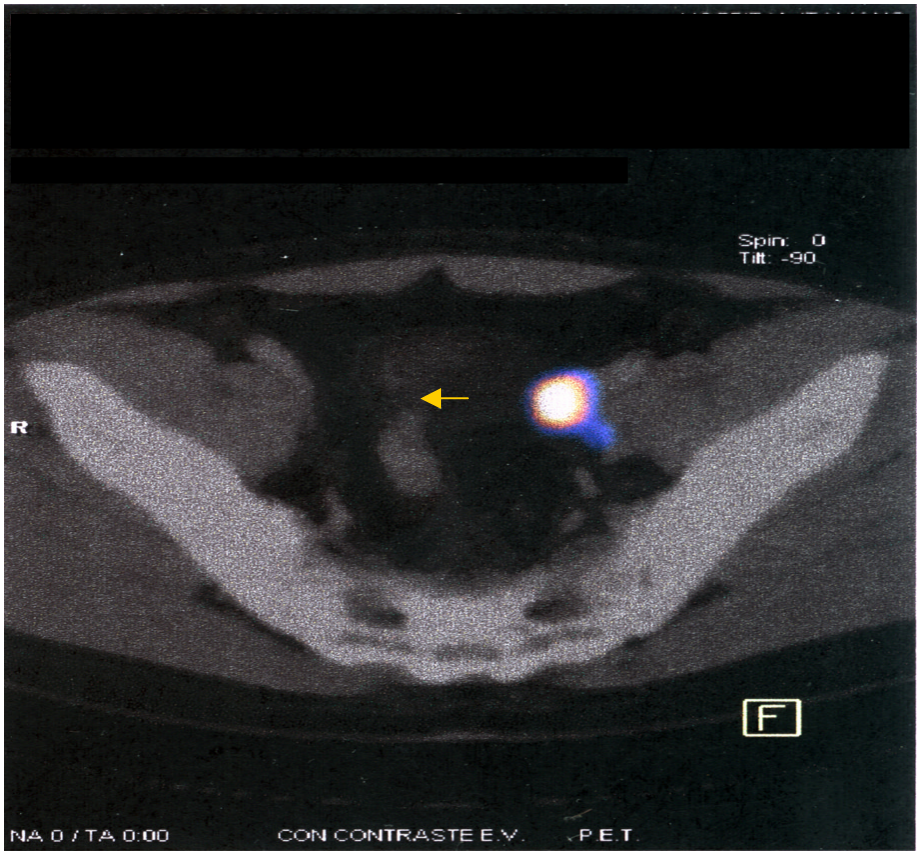

Fig. 6. **Patient 2: PET at the year's control post-treatment**

disease before changes in anatomy are apparent on other imaging tests such as CT or MRI scans (Weihrauch et al. 2001)

Since the radioactivity is very short-lived, patient's radiation exposure is extremely low and the substance amount is so small that it does not affect the normal processes of the body.

It is noteworthy, since PET's costs are several times higher compared to other methods, that indiscriminate use might put at risk Social Security or Health Insurance budgets, so, until this situation changes, doctors must be sure when this method should be ask or recommended.

It is well demonstrated by other authors (Schaefer et al. 2004, de Wit et al. 2001, Jerusalem et al. 1999), that PET is superior to the CT Scan in identifying residual mass in HD, but not to the Gallium test, which is still considered a good option to establish the activity of a non voluminous mass in the thoracic region (Setoain et al. 1997).

However, our paper shows examples where Gallium scintigraphy could gives false negative results and PET may be useful in these same cases.

In conclusion, we propose to still use the CT Scan for standard post-treatment controls. If a residual thoracic mass remains in those controls, Gallium scintigraphy must be used. In cases of a negative result of that Gallium test in a bulky thoracic mass or if that mass is located in abdominal or pelvic cavities, PET should be used to establish the difference between scar or dead tissue and remaining mass with disease activity.

In all other cases where surgical accessibility is possible (cervical or inguinal masses), a biopsy should be obtain for therapeutic decision making.

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