

The Value of Fusion Imaging (PET – CT) in the Diagnosis of Vertebral and Spinal Tumors

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Abstract

Fusion imaging (PET/CT), widely used in the developed countries, allows the identification of different lesions at the molecular level, enabling the emergence of a new field of advanced medicine - "molecular imaging". For example, marking with a radiotracer of a nucleic acid chain component allows the identification of the cancer at the molecular level and its treatment by radioimmuno - scintigraphic techniques. Having a great sensitivity in the early detection of some lesions in a wide spectrum of pathology, Nuclear Medicine procedures are much sought by the clinicians.

Keywords: cancer, cyclotron, radionuclides, spinal tumors

Introduction

Cancer begins at subcellular molecular level by altering a gene that controls cell growth and behavior; in particular there is a marked increase in DNA synthesis and an exaggerated local consumption of glucose as an energetic support for anarchic cell multiplication. These amendments are being "propagated" little by little, so that after a certain period of time (years) during which the disease usually progresses

asymptotically, tissues or organs come to be involved. When the number of cancer cells is large enough to be detected visually by conventional techniques (X-ray, ultrasound, CT, MRI), the disease has already passed the stage where it can be treated successfully. The challenge of medical activity is to detect cancer before the onset of clinical symptoms and dissemination in other organs and to establish an early effective treatment. Cancer is one of the main causes of mortality in the world. Recent statistical studies conducted under the auspices of the World Health Organization (WHO) show that 1 in 9 women will develop some form of breast cancer, 1 in 7 men will develop a form of prostate cancer, and 1 of 10 male will develop lung cancer. Effective treatment depends mainly on early detection of tumor process (8).

Materials and Methods

When diagnosed by the methods existing today in our country, including the high performance imaging explorations, cancer can not be cured. The established treatment - surgery, chemotherapy or radiation may provide, in relation to the evolutive stage of the disease a survival not exceeding 4-5 years (2). Medical imaging is a top field of

medicine that includes a group of modern medical techniques with different principles, which have in common the fact that provide diagnostic data through the image of the anatomical systems, internal organs or injuries. These imaging techniques can be grouped into:

- Anatomical (structural) techniques: ultrasound, computed tomography (CT), magnetic resonance imaging (MRI), angiography, digital radiography;

- Functional (metabolic) techniques: planar scintigraphy, tomoscintigraphy (SPECT), monoclonal antibody immunoscintigraphy, positron emission tomography (PET).

Anatomic and metabolic imaging fusion: integrated PET-CT, SPECT-CT, PET-RM systems are high performance techniques that enable in a single view both the pathological metabolic process examination and its precise location by co-registering the two categories of information (13, 14). Due to its increasingly large expansion and wide introduction into diagnostic and settlement protocols around the world, we will refer next to PET-CT technique. The PET-CT is an imaging technique that realizes the early detection of cancer by visualizing the excessive glucose consumption in the cancer cells (PET) and the anatomical location of the precise process by simultaneous PET and CT scanning. Since 1991 over 2000-3000 equipments have been installed over the world. WHO estimates a need of approximately one PET equipment at 1 million inhabitants.

PET technique is based on marking a normal constituent of the body (e.g. - deoxyglucose, an analogue of glucose) with a positron emission radiotracer (^{18}F , ^{14}C , ^{16}O , ^{13}N but usually ^{18}F) that after iv injection is distributed throughout the

body, depending on the distribution properties of the radiolabeled constituent. Once injected into the body, the positrons emitted by radionuclide decay migrate to short distance into the tissues, lose some of the energy, slow their motion, and annihilate after the collision with present electrons. The annihilation process will give two gamma photons emitted in opposite directions (180°), with an energy of 511 keV each. Both radiations can then be detected by forming a ring of detectors around the patient so that it becomes possible mapping the distribution of positron-emitting isotope into the body. In this way can be studied the distribution of an extremely large number of substances whose metabolism is affected in various pathological conditions (2, 12, 13). By far the most widely used positron-emitting radionuclide is ^{18}F coupled with deoxyglucose - analogue of glucose. Metabolically active cancer cells will capture the labeled glucose about 30-40 times higher than the adjacent healthy cells. The computerized system of the facility that detects the photons emitted from the positron annihilation with an electron, allows the space identification of the positronic radiotracer fixation place and also viewing the pathological process (9). The positron emitting radiotracers used for PET examination are included in the table below:

Positron emitting radiotracer	Physical T1/2
^{18}F	110 min.
^{11}C	20 min.
^{13}N	10 min.
^{15}O	2 min.

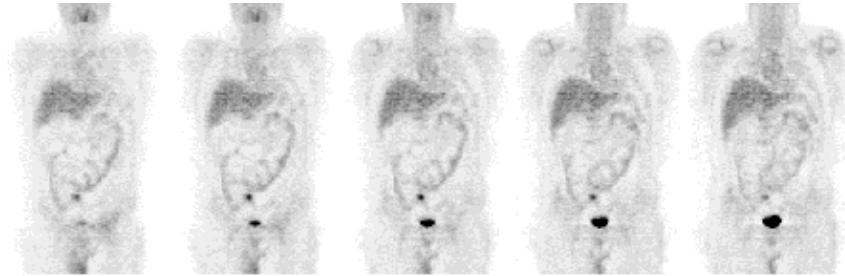


Figure 1 FDG – PET normal appearance

Because of the short physical half-life, positron emitting radionuclides need to be produced on site in a medical cyclotron (baby cyclotron). There are positron emitting radionuclides produced in a generator, e.g. - ^{68}Ga , which by coupling with different peptides allow to assess and conduct therapeutic setting for neuroendocrine tumors, but other clinical applications are currently in the research stage (10).

The method was developed in the '70s (Phelps and Hoffman) and it has been used for two decades predominantly in the clinical research of various cellular processes at molecular level by incorporating the positronic isotope into different messenger molecules (enzymes, hormones, antibodies, peptides and oligonucleotide). Imaging of apoptosis, neurotransmitters and neoangiogenesis have been translated from experimental evidence into clinical practice (Figure 1). The remarkable progress in molecular imaging determined W. Wagner jr. (from J. Hopkins Clinic - Baltimore) to assert that "the molecular medicine has revolutionized modern medicine, the nuclear medicine comes to revolutionize molecular medicine". In 1998, Townsend had the idea to combine (overlay) the metabolic PET images with the anatomic CT images, making accurate anatomical localization of

the lesions through what is called "fusion image". The first integrated PET-CT equipments produced by major companies have been introduced into clinical practice around 2000, being widely accepted by the medical community.

The PET-CT equipment through a single examination allows to obtain a fusion image that contains both metabolic information (PET) and precise anatomical details (CT).

The PET-CT main indications are: - detection and indication of the malignant or benign substrate of various tumors; - determining the actual extension of malignant tumors, the preoperative and posttherapeutic staging; -differentiating the postoperative fibrosis, the residual post irradiation tumor necrosis or the relapse; - establishing the tumor prognosis compared with the level of glucose uptake and the histological grade; -directing the therapeutic surgical approaches: minimal surgery, CT-guided percutaneous ablation, chemoembolization; -directing the selective biopsy by identifying viable component of the partially necrotic tumors (8).

The necessary equipment includes: cyclotron for obtaining the positron emitting radioisotopes; radiopharmacy laboratory for radiolabelling the active molecules (fluorine deoxyglucose, ^{11}C - methionine, ^{11}C - thymidine, ^{18}F - deoxythymidine, ^{18}F -

choline, etc.). It is possible to purchase the radiotracer from a radiopharmacy, but the latter must be at a reasonable distance from PET-CT unit because of the very short half-life of radionuclides and it is only possible for radiotracers tagged with ^{18}F ($T_{1/2} = 110$ min., compared to ^{11}C with $T_{1/2} = 20$ min. or ^{15}O with $T_{1/2} = 2$ min.!) (Figure 2).

The PET/CT scan combines the metabolic details of a PET scan (tumor cell activity, tumor viability etc.) with the anatomical details offered by a CT scan (size and location of tumor, mass, anatomical relationships etc.), giving a more accurate image than PET or CT used separately. The PET examination begins with intravenous injection of FDG (18-fluorine deoxyglucose), a glucose-like substance which is attached to the F18 isotope. The metabolically active tissues or these with abnormally high rate of multiplication (tumors) consume much higher amounts of the radioactive sugar. The radiotracer accumulation leads to gamma rays emissions that are converted by computer into images. These images indicate "hot" areas signaling tissues with high metabolic activity (abnormal increased multiplication rate) because cancer cells consume more sugar / energy than other tissues or organs. The CT scan is based on the absorption in varying degrees of the X-rays by the examined structures and on the computerized data processing to obtain the thin sections that can be reconstructed three-dimensional reproducing detailed images of body structures. The entire examination usually takes 30 minutes, providing detailed and accurate information that enables physicians to provide a quick, correct and complete diagnosis.

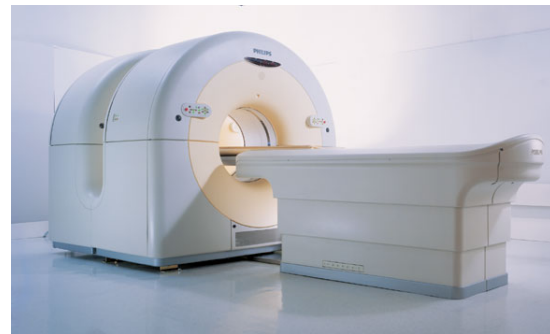


Figure 2 The integrated PET-CT equipment

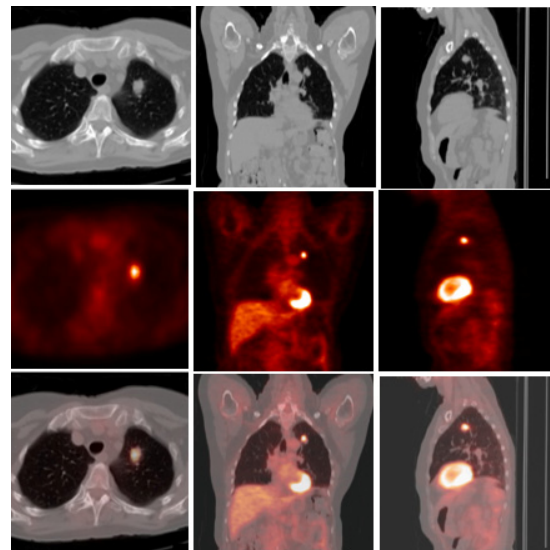


Figure 3 67 years old male patient. Rx and CT examinations: solitary pulmonary nodule. The indication of PET-CT: assessing the malignant/benign substrate of the lesion. Anatomopathological examination: small cell carcinoma

In oncology, the PET/CT investigation offers the ability to early diagnose, locate, monitor and control the development of cancer. With PET-CT, surgeons, oncologists and other specialists will be able to detect cancer more accurately, to assess recurrences, to make a complete and accurate staging, to assess the patient's likely response to therapy and to monitor more effectively the results of chemotherapy and radiotherapy. In oncology, PET-CT provides vital diagnostic information that allows monitoring of treatment outcomes and often helps avoid surgery (4).

In neurology and neurosurgery, PET - CT is used to identify areas of the brain that cause seizures and to determine whether surgery is a viable option. Also, this technology allows diagnosis of Alzheimer's disease at a stage when the disease can still be controlled with medication.

Before examination, patients are asked: - not to eat nor drink anything (or to drink only plain water) at least 6 hours before the examination, because it could affect the results (the ban also refers to sugarfree chewing gum, mints, candies and drinks of any kind); - if they take drugs, they should drink only as much water as it is necessary to swallow them; - to minimize their physical activity on the day they are examined (gymnastics, jogging, etc.) as it might affect the capture of the radionuclide; - to bring with them on the day they are examined previous CT scan, X-ray, scintigraphic or MRI examinations, tumoral markers results, anatomo-pathological test results and hospital discharge papers they have (as written reports, images or CDs); - to announce in advance whether they are diabetic, to allow physician consultation on the preparation and conduct of examination; before the actual examination begins their blood glucose level is measured

anyway. When recording high blood glucose levels which persist even after being taken measures to low them, the investigation can not be done; - to announce whether they are febrile; - to announce the existence or suspicion of pregnancy or nursing status; - to call the physician if they have questions about the scheduled procedure (15).

The examination will begin with a test to determine blood glucose level. Patients will then receive an injection containing a small amount of radioactive glucose (radioactive sugar), which will be distributed throughout the body. The radiotracers used for PET/CT scan lose their radioactivity very quickly (within two to three hours) and only very small doses are injected. Six to eight hours after injection, the remaining radioactivity is negligible. In most cases, patients will have to wait about an hour for radioactive drug to be distributed in the body.

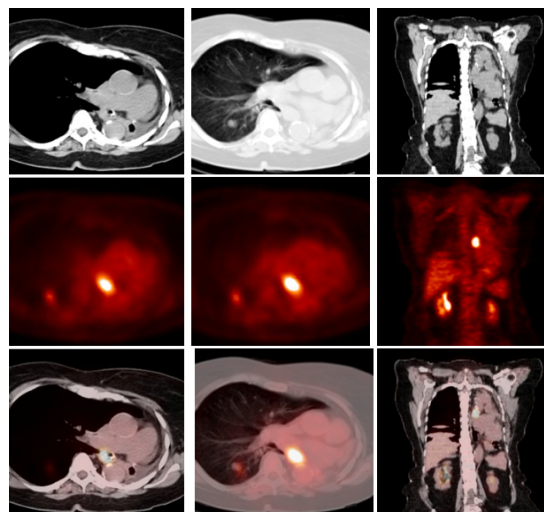


Figure 4 78 years old woman with operated squamous cell lung adenocarcinoma (post-pneumonectomy status). The indication of PET-CT: staging. PET-CT examination: tumoral relapse; right lung metastasis, on the front and left side of the T5 vertebral body

About 60 minutes after the injection, patients will go to the toilet to urinate. Patients will be asked to stand still during the scan because movement can affect the outcome of the investigation. During the scan patients breathe normally. During the acquisition of the images they will not feel anything unusual, except table movements, as some areas of the body are scanned. Throughout the examination the patients will be monitored by an operator and they may communicate with him through the microphone and through the cameras. The PET-CT scan takes between 20 and 30 minutes. The examination procedure may differ depending on the examined area (20).

The risks and precautions during the examination are not negligible and should be known. Except the restraint during the examination, there is recorded no special sensation like pain, annoying noises, temperature differences, etc. There were never reported unwanted side reactions after intravenous administration of FDG, required for carrying out the PET / CT examination. There are no contraindications for the FDG administration and only in cases of severe renal failure or high blood sugar level that not falls within lower values of 180-200 mgr/dl, the examination is not made, because these conditions make it impossible to correctly use the radiotracer. Sometimes, intravenous injection of the substance can be difficult. In this case there is a catheter inserted in advance. Any state of pregnancy, suspected or found, is a contraindication to the examination. In this case, the necessity of investigation should be determined by mutual agreement with the treating physicians. Breast-feeding should be discontinued for at least 6 hours after completion of investigation. Renal failure causes a reduction in quality of PET / CT

scan images, although it is not a contraindication to perform the examination. Patients wearing orthopaedic prostheses, pacemakers, implanted arterial or venous prostheses, etc., are not exposed to any risk, but it is appropriate to inform of their existence the physician that records the medical history (22).

After the administration of FDG follows an average wait of 60 minutes to ensure optimal distribution of the substance into the body. The image acquisition time with PET – CT equipment is about 30 minutes, but in some cases may be extended, depending on the disease (e.g.- melanomas) or on the pursuit of certain issues. The last part of procedure lasts about 15 minutes (16).

The presence of the integrated PET-CT equipment in Romania allows detection of cancer (and other diseases) to debut before the effective dissemination into the entire body, with maximum therapeutic efficiency (9).

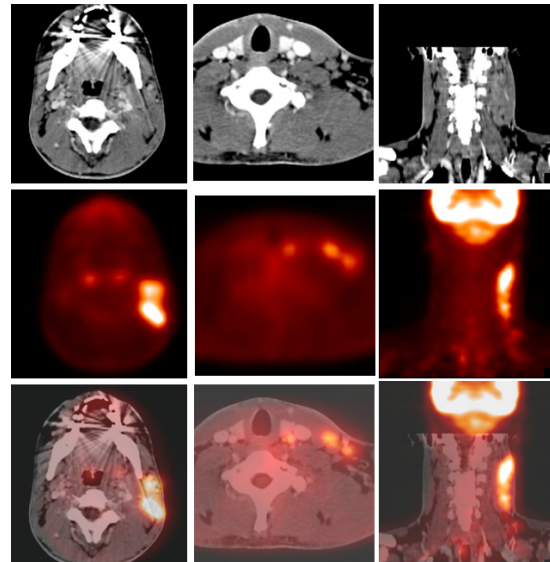


Figure 5 37 years old female patient, presenting physical fatigue, low grade fever, left laterocervical swelling / The indication of PET / CT: diagnostic-staging. Anatomico-pathological examination: Hodgkin's lymphoma

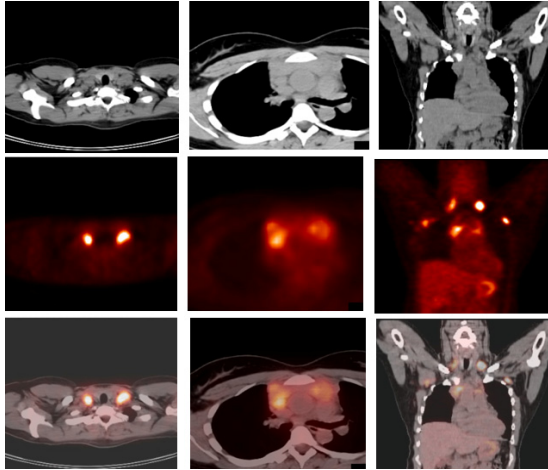


Figure 6 39 years old female, presenting fever, physical fatigue, pruritus, palpable supraclavicular lymph nodes, thoracic pains. The indication of PET-CT: staging. PET-CT examination: FDG uptake is observed in several coastal, vertebral and axillary lymph nodes outbreaks. Supraclavicular lymph nodes biopsy: Hodgkin's lymphoma

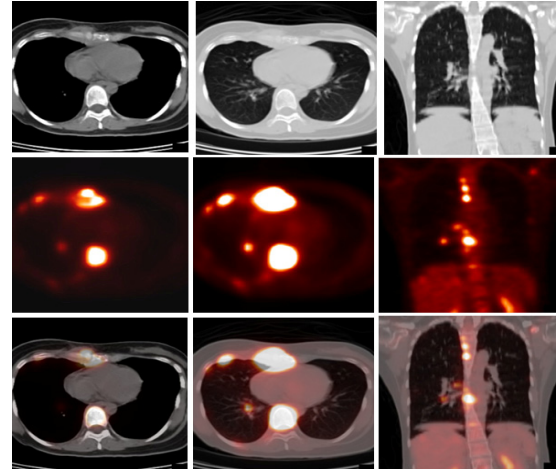


Figure 8 43 years old female patient with right mastectomy 2 years ago for breast cancer, with vertebral, lung and liver metastatic disseminations. Clinical issues: diffuse bone pains, pronounced at sternal and vertebral level. The indication of PET-CT : new staging

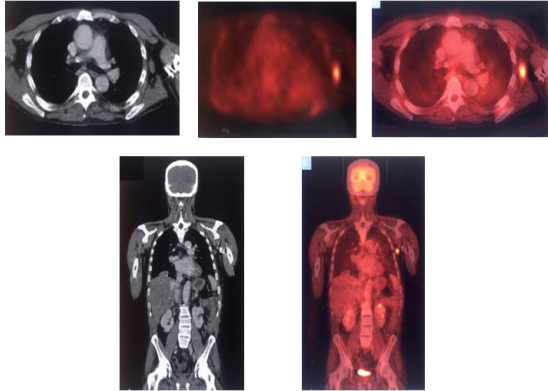


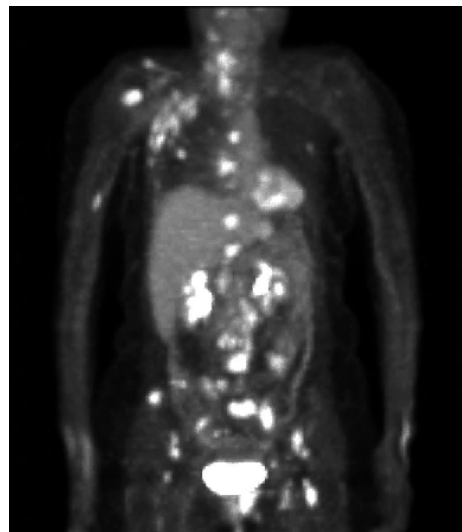
Figure 7 51 years old male with non-Hodgkin's lymphoma with mediastinal, lung, spinal and cerebral dissemination, that followed multiple courses of chemotherapy. The indication of PET-CT: evaluation 6 months after the last course of chemotherapy. PET-CT examination : axillary lymphatic dissemination after chemotherapy for non-Hodgkin's lymphoma

The World Health Organization and the International Agency for Fight against Cancer recommends a PET-CT facility at approx. 1-2000000 inhabitants (19).

Cases presentation

We present some clinical cases of patients treated in the Neurosurgery Clinic of "Dr. Carol Davila" Central University Military Emergency Hospital and investigated PET-CT at Euromedic - Fundeni Clinic (Figure 8, 9, 10, 11, 12, 13, 14).

Before chemotherapy



After chemotherapy

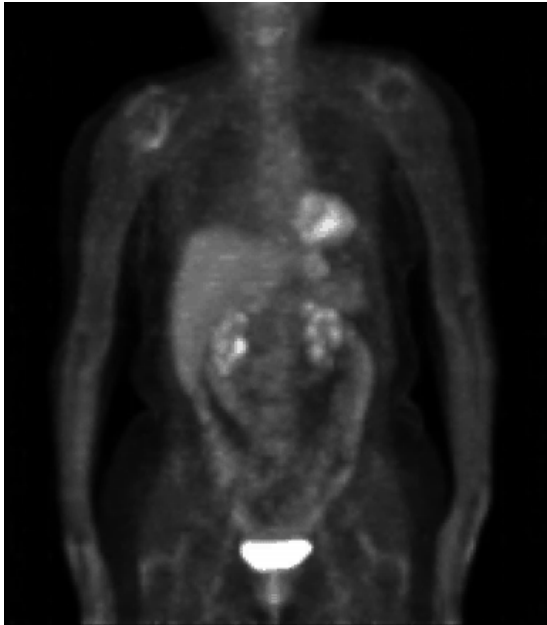


Figure 9 67 years old female with metastatic breast cancer. The indication of PET-CT: assessing the response chemotherapy

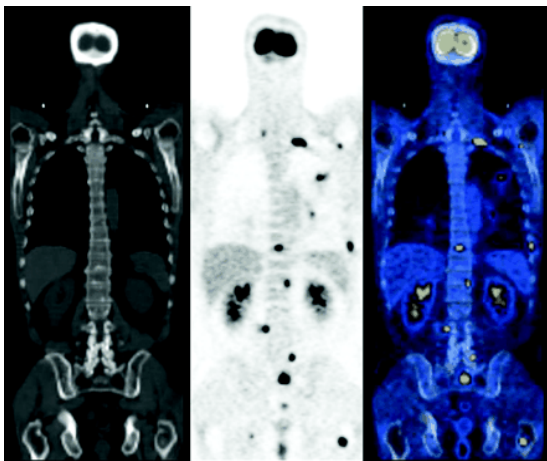


Figure 10 52 years old male patient with lung cancer: multiple bone metastases in PET and PET / CT (thoraco-abdominal contrast CT scan in normal range)

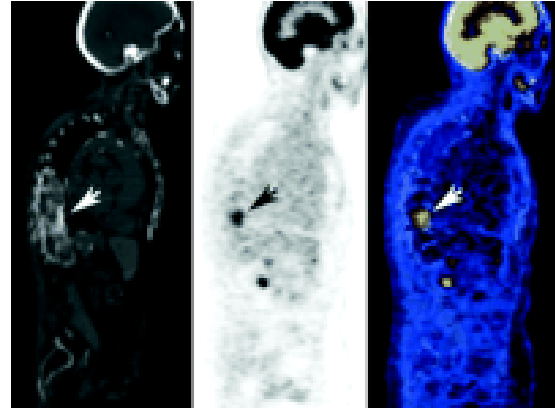


Figure 11 T11 compression in 63 years old female with multiple osteoblastic lesions

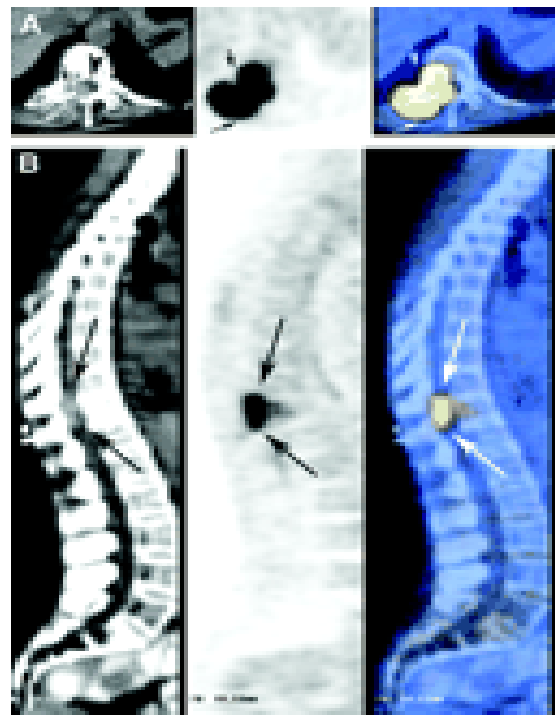


Figure 12 63 years old female with breast cancer and secondary disseminations at T10 epidural and vertebral body and pedicle level

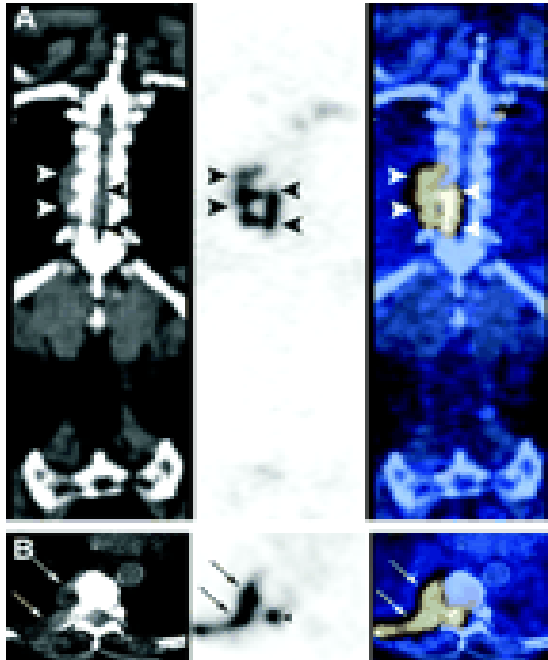


Figure 13 52 years old female with colon cancer and metastatic process involving the T11 posterior body and posterior elements, with epidural extension

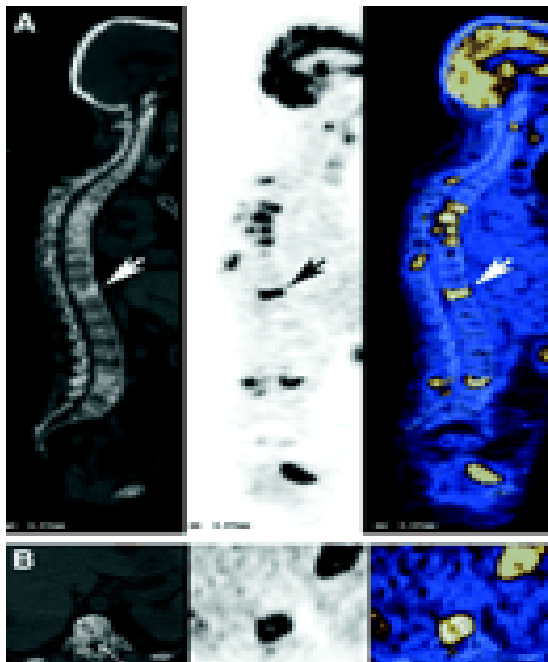


Figure 14 Tumoral mass with epidural extension through the left T11 intervertebral foramen in a 51 years old female patient with lymphoma

Discussion

The goal of surgery is to improve the quality of life as it is not always possible to cure the illness itself. It aims to:

- decompress the nerves trying to improve the patients neurological status;
- stabilize and relief pain, so the patient to be able to keep upright and walk;
- obtain a histo-pathological diagnosis followed by a specific oncological treatment (23).

Currently the vertebral and spinal pathology benefits from the contribution of new diagnostic techniques that have been developed and applied in the last two decades. Generally these techniques are known as imaging techniques that have in common the fact that provide diagnostic information on the lesion substrate using computerized processed images. In the order of their clinical applicability have been imposed: magnetic resonance imaging (MRI), computerized tomography (CT), tomoscintigraphy (SPECT) and positron emission tomography (PET-CT). These computerized techniques have revolutionized the neuroradiology replacing or restricting the applicability of conventional radiological diagnostic methods: plain or contrast radiography (myelography), conventional tomography and arteriography (22).

PET-CT scan shows a lot of benefits compared with other commonly used imaging means:

- determines how widespread the disease is;
- indicates the location of the tumor to execute biopsy, surgical treatment or planning of treatment;
- analyzes the response to and efficiency of the therapy;

- detects traces of residual disease or relapse;
- helps to avoid invasive diagnostic procedures.

Being fully compatible with the oncological radiotherapy systems (Micromultileaf, CyberKnife, Tomotherapy), PET / CT allows the urgent development of optimized treatment plans for selective irradiation of metabolically active tumoral tissue, fully preserving healthy tissues (8).

Conclusions

The investigation and treatment of vertebral and spinal tumoral injuries is necessary to comply with the best neurosurgical conduct requirements. These requirements are imposed by current knowledge of acquisitions in the field of spinal surgery, as reflected in literature. Their main purpose is to avoid the numerous errors and complications that may occur during treatment. Meeting these requirements will bring more clarity to the doctor-patient relationship, particularly in cases where after the neurosurgical treatment occurred litigations related to the quality of the medical care (17).

In spinal tumoral pathology the investigations are required to clarify the location and, if possible, the etiology of the lesion. The precise location dictates the approach path and the suspected etiology allows selection of an appropriate surgical technique. Also, for the surgery decision is necessary that the location of the lesion to be consistent with the neurological symptoms, ie the location to explain the neurological syndrome (21).

The patient should be exhaustively investigated, meaning not a lot of abusive and aimless investigations, but a full

appropriate investigation protocol, to establish an accurate diagnosis. In line with current international standards, the methods of diagnosis in spinal pathology should focus on minimally invasive investigations that provide maximum information (12).

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