UDC: 616-006:615.849.1:615.07

Challenges in nuclear oncology

L. Pávics[1], K. Hideghéty[2], Zs. Lengyel[3], S. Kovács[1], Zs. Besenyi[1]

[1]University of Szeged, Department of Nuclear Medicine, Szeged, Hungary, [2]Universitiy of Szeged, Department of Clinical Oncology, Szeged, Hungary, [3]Positron Diagnostics Ltd. Budapest, Budapest, Hungary

Introduction: Modern oncologic care utilizes FDG-PET/CT imaging not only in cancer detection, diagnosis and staging, but also during radiation therapy planning. Furthermore FDG-PT/CT may also play a role in monitoring response to the therapy. The aims of the current study were to compare radiotherapy targeted tumor volume based on conventional topoCT and FDG-PET/CT imaging and to determine weather additional metabolic information leads to a modification of previously devised therapeutic regimens.
Methods: 85 oncologic patients with primary head-neck, esophagus and lung cancer were enrolled in the current study. /Age 31-75/. Within 3 weeks difference CT and FDG-PET/CT image acquisition was completed in regards to the planned irradiation position. During radiotherapy planning delineation of target volume and organs at risk were carried out both on conventional CT based topometric slices and FDG-PET/CT images. Radiotherapy target volume was calculated (PTV-cm^3) by using both modalities.
Results: In regards to the total population radiotherapy target volume as assessed by FDG-PET/CT differed in 92 % from target volumes calculated by topoCT. According to metabolic information the planned irradiation field was greater in 14 cases (16 %) (5 of which involved other regions as well) and smaller in 65 cases (76 %). The previously devised oncologic therapeutic regimen was altered in 18% of the patients based on the FDG PET/CT examination results.
Conclusion: FDG-PET/CT imaging may allow for better radiation therapy target volume planning and viable tumor mass definition, while lessening organ at risk radiation exposure. Radiotherapy planning based on the combination of structural and metabolic information with implementation of modern radiotherapy techniques (IMRT, SIB) may also improve the efficacy of cancer therapy.

Key words: Diagnostic Imaging; Radiotherapy Planning, Computer-Assisted; Positron-Emission Tomography; Tomography, X-Ray Computed; Head and Neck Neoplasms; Esophageal Neoplasms; Lung Neoplasms

UDC:616.12-071.5:616.071:537.635

Hybrid imaging in nuclear cardiology

P. Muto

Dipartimento dei ServiziDiagnosticiA.O.Ospedali dei Colli
Ospedale Monaldi Via Leonardo, Napoli, Italy

PET has significantly contributed in the past to improve the understanding of the physiology and pathophysiology of heartfailure, as a powerful tool to quantify in vivo physiological processes of the myocardium. Initially, it had however limited clinical applications due to high cost and limite davailability of machine and tracers.
In recent years, it has regained an important role in the clinical management of patients affected with coronary artery disease (CAD) and dysfunctional of the Left Ventricle (LV). PET optimal intrinsic characteristics contributed to this growing recognition, such as the better spatial/temporal resolution, diagnostic accuracy superior than SPECT, cardiac gating leading the assessment of Left Ventricular (LV) contractile function and respiratory gating for resolution of artifacts and, not least, the FDA approval dedicated radiopharmaceuticals.
At state, nuclear cardiology provides accurate data concerning both myocardial perfusion and contractile function at baseline and stress conditions, via blemyocardium and adrenergicinnervation. PET is the optimal tool for the absolute quantification and for the detection of ischemicalterations in coronary blood flow (MBF in ml / min / g tissue) and coronary flow reserve (CFR), using radio labeled PET tracerssuchas ^{13}N-ammonia, ^{82}Rb and ^{15}O-labeled water. This approach is very interesting by helping to move the diagnostic target from the obstructive coronary artery disease (CAD) at preclinical disease, with early definition of patients at risk of developing CAD. Furthermore, hybrid PET or SPECT scanner/multislice CT, by combining morphological data concerning CoronaryCalcium Score and vessel lumen with myocardial flow, perfusion and contractility, combine into a single model both anatomical extent and functional severity of coronary disease.
So,hybrid techniques provide complementary evaluation in patient diagnosis, with greater expertise pertaining the culprit vessel, in patient prognosis, by stratifying patients into different risk categories. Similarly, very important prognostic information are provided by MBF and CFR measurement, considering that a reduced CFR is a strong predictor of poor outcome in patients affected with idiopathic LV dysfunction, regardless the dysfunction degree, and with hypertrophic cardio myopathy.
Finally, PET and MRI, relying on different biological and physiological mechanisms, are truly complementary in their ability to detect stress-induced myocardial ischemia and tissue viability. This complementary ability of the two modalities opens up new perspectives in the assessment of cardio vascular disease.
In conclusion, integrated data optimizes the overall information content by providing the clinical cardiologist a wide-ranging of CAD induced abnormalities, difficult to achieve so comprehensive by the other non-invasive approaches.

Key words: Diagnostic Imaging; Multimodal Imaging; Coronary Artery Disease; Myocardial Ischemia; Tomography, Emission Computed, Single-Photon; Positron-Emission Tomography; Magnetic Resonance Imaging

UDC: 616.65-006:615.849.1

Prostate Ca scintigraphy with ^{99m}Tc PSMA antagonist

S. J. Goldsmith

Department Nuclear Medicine & Molecular Imaging/Radiology, New York-Presbyterian/Weill Cornell Medical College, New York, NY, USA

Introduction: Prostate Specific Membrane Antigen [PSMA] is expressed on Prostate tissue and to a lesser extent other secretory organs such as the parotid glands and the pancreas. The expression of PSMA increases in prostate carcinoma, apparently proportional to the degree of aggressiveness of the tumor as determined by the Gleason Score. For a number of years, efforts to image PSMA to determine extent of disease in patients with prostate ca have depended upon radiolabeled antibodies that clear slowly from the circulation, thus requiring relatively long-lived radiotracers such as Indium-111 which provide sub-optimal images. ***Aim:*** To determine if small molecules that recognize the enzymatic properties of PSMA can be used as an alternative agent to identify and image PSMA distribution and clear rapidly enough to allow use of short-lived tracers like ^{99m}Tc.
Methods: Small molecules, consisting of 2 amino acids (usually glutamine-glutamine or glutamine lysine) linked via a urea moiety, have a high affinity for PSMA and can serve as ligands and antagonists depending upon other components of the complex. Two small molecules were selected based on *in vitro* binding studies. These ligands for the enzymatic function of PSMA (MIP 1404 and 1405) were labeled with ^{99m}Tc [t1/2=6 hrs] and were administered to normal volunteers and patients with prostate cancer.
Results: Both 1404 and 1405 cleared rapidly from the blood stream resulting in high target to background ratios within 1-2 hrs after injection. Of the two, MIP 1405 clears more rapidly from the blood pool. Whole body retention of 1405 at 4 hrs is 63% and 25% at 20 hrs in normal subjects and prostate cancer patients. By contrast, 1404 has 93% retention at 4 hrs and 84% at 20 hrs, resulting in differences in the body background. Hence, target to background ratios as well as differences in the bladder activity and bowel excretion are observed but both radiotracers were useful. SPECT images of the pelvis provide maps of tumor distribution within the prostate that correlate well with histopathology mapping following resection of the prostate gland. The degree of uptake appears to correlate with the aggressive of the tumor as quantified by the Gleason Score. In patients with metastatic disease, both agents also detected prostate ca metastases. In the limited experience to date, the ^{99m}Tc labeled peptide heteromers are more sensitive for the detection of osseous lesions than bone scintigraphy and more sensitive to detect metastatic disease than ^{111}In radiolabeled antibodies.
Conclusion: Small molecules (peptide-urea-peptide heterodimers) with high affinity for the enzymatic site of PSMA have been radiolabeled with ^{99m}Tc. They clear rapidly from the blood stream providing high resolution images that identify intra-prostatic distribution of aggressive prostate ca as well as metastases to bone and soft tissue.

Key words: Prostatic Neoplasms; Prostate- Specific Antigen; Molecular Imaging; Radionuclide Imaging; Neoplasm Grading; Neoplasm Metastasis; Antigens, Surface; Technetium

UDC: 616.65-006:577.11:616-085:616.71

Fluorocholine (^{18}F) PET/CT in prostate cancer

J-N Talbot, L. Michaud, V. Huchet, K. Kerrou, S. Balogova

Hopital Tenon & Univsité Pierre et Marie Curie, Paris, France

PET/CT has been recognised as an important tool for cancer staging, restaging and monitoring. Prostate cancer (PC) is the most common malignancy in men. However, fludeoxyglucose (^{18}F) or FDG is not accurate in most cases of PC, with a low aggressiveness. For detecting prostate bone metastases, FDG PET has a high positive predictive value but its sensitivity is too low, less than that of planar bone scintigraphy (BS) with bisphosphonates (^{99m}Tc).Therefore, at least for detecting extra-osseous lesions, a PET radiopharmaceutical taken-up by PC of a low aggressiveness has been actively searched for. The only one which is currently registered in many countries of EU is fluorocholine (^{18}F) or FCH, analogue of lipids constituting the cell membrane.

FCH for detecting PC inside the prostate gland
From a few studies on this topic, it may be concluded that FCH PET can serve to localise the dominant areas of malignancy but may fail to identify sextants with smaller volumes of malignancy and may show non-specific uptake in benign hypertrophy or in prostatitis.

FCH for staging PC
Clinical nomograms based on prostate-specific-antigen (PSA) serum levels, Gleason score at biopsy, and clinical stage at presentation have been generated for pretreatment risk stratification and prediction of the probability for local recurrence or distant metastatic spread.Patients with high risk and some patients with medium risk may benefit from FCH PET/CT. At that early stage of the evolution, detection of lymph node metastases is highly specific (95%), but of a low sensitivity (49%) when the standard of truth is lymph node dissection. But FCH PET/CT can detect foci consistent with bone metastases, even in the absence of histologically malignant lymph nodes.

FCH for detecting PC in case of biochemical recurrence or for restaging PC
This setting is in our experience the most frequent cause of referring PC patients to FCH PET/CT. We have coordinated a multicentre trial in France that showed a very significant impact of FCH PET on patient management in case of occult biochemical recurrence with non-contributive MRI and bone scintigraphy.

FCH for therapy monitoring
At a late stage, when PC becomes castration resistant, FCH is still capable to image PC and to detect disease progression, although FDG may also be effective in the most aggressive forms. This is important since various therapeutic modalities are now available, and the management should be changed in case of disease progression that can be missed or delayed with follow-up based on PSA serum levels.

Key words: Prostatic Neoplasms; Prostatic Diseases; Diagnostic Imaging; Neoplasm Metastasis; Bone Neoplasms; Choline; Positron-Emission Tomography; Tomography, X-Ray Computed

616.65-006:616.24-006:616.441-006:615.849.1

FCH in Europe: Current status

M. Hodolič

Research Department, IASON GmbH, Graz, Austria

Choline is a substrate for the syntesis of phosphatidylcholine, a major phospholipid in the cell membrane. It can be labelled with ^{11}C or ^{18}F. At present ^{18}F-fluorocholine (FCH) has marketing authorization is 16 European countries in the following indications: detection of bone metastases of prostate cancer, localization of lesions of well differentiated hepatocellular cancer as well as characterization of liver nodules and/or staging of hepatocellular carcinoma, when FDG PET/CT is non conclusive and/or when surgery is scheduled.
FCH foci can also reveal secondary lesions of prostate cancer not only in the skeleton but also in soft tissue.
FCH seems to be a suitable PET tracer for brain tumor imaging as it shows a low accumulation in normal brain tissue and allows detection of the brain tumour with a high tumor to background ratio. In conjunction to MRI it is valuable diagnostic tool for identification of meningeomas and pituitary adenomas.
FCH foci may also correspond to other slow growing malignancies, or sources of false negative FDG PET results, as in bronhoalveolar carcinoma.
Thyroid nodules and hyperfunctioning parathyroid glands are FCH avid.
FCH appear to be more sensitive than FDG PET for the detection of bony myelomatous lesions.
Most of inflammatory lesions can pick-up FCH and that point is decreasing the value of FCH in sense of specificity.
All these data have to be confirmed in a larger series of patients.

Key words: Choline; Fluorine Radioisotopes; Diagnostic Imaging; Europe; Prostatic Neoplasms; Carcinoma, Hepatocellular; Brain Neoplasms; Adenocarcinoma, Bronchiolo-Alveolar; Thyroid Nodule; Multiple Myeloma; Inflammation

UDC: 616.65-006:615.849.2

A long waited novel 'magic bullet' for castration-resistant prostate cancer patients with metastatic bone disease: general aspects and practicalities of Radium-223 dichloride treatment

S. Dizdarević

Department of Nuclear Medicine, Brighton and Sussex Universtiy Hospitals NHS Trust and Brighton and Sussex Medical School, Brighton, UK

Introduction: The first original β-emitting radionuclide targeted therapy, the nearest 'magic bullet' I-131 has been used in clinical practice since 1940s. This review describes the preclinical development and clinical implementation of a novel first clinical α-emitting radiotherapeutic,Radium-223 dichloride which is the most recent 'magic (smart) bullet' for treatmentof patients with castration-resistant prostate cancer (CRPC) with symptomatic metastatic bone disease and no known visceral metastases. The review also addresses Ra-223 radiobiology and physics, efficacy and safety aspects, with an emphasis on phase III randomized trail (ALSYMPCA study), general aspects and practicalities for service establishment and delivery and current clinical data available. A comparison with β-emitting bone palliation agents, service modeling for outpatients' clinics set up within a cancer network with uro-oncology–nuclear medicine interface and further potential research will also be discussed.
Methods: A systematic review of the published relevant literature with a predefined search strategy has been conducted.
Results: Radium-223, an α-emitting alkaline earth metal ion produced from $^{227}Ac/^{227}Th$ generator system, similar to calcium ions, forms complexes with the bone mineral hydroxyapatite at areas of increased bone turnover and with the high linear energy transfer leads to a high frequency of double-strand DNA breaks in adjacent cells (range of less than 10 cells diameters), resulting in an anti-tumor effect on bone metastases with limited damage to the surrounding normal tissue. Ra-223 is the first α-emitting radiotherapeutic to demonstrate a significant overall survival (OS) advantage and delay in time to first symptomatic skeletal event (SSE) in patients with CRPC treated at four weeks interval with 6 i.v injections (50kBq/kg) with excellent safety profile. β-emitting, bone-seeking radionuclides control pain with pain response rates in the order of 60% to 70%. However, most of the published trials were underpowered to detect differences in survival, but there is evidence of the potential for disease modification when these agents are used in combination with chemotherapy or in multiple cycles.
Conclusion: Due to the success in improved survival and not just bone palliation, Ra-223 is securing an important place in standard care of patients with CRPC in the spectrum of newly approved agents in post-docetaxel setting and has huge potential in combination strategies and for earlier use in the natural course of disease. New indications such as treatment of breast cancer skeletal metastases, other predominant bone malignant disease, including primary bone tumours (e.g. osteosarcoma) are also emerging.

Key words: Prostatic Neoplasms, Castration Resistant; Antineoplastic Agents; Radium; Bone Neoplasms; Neoplasm Metastasis

UDC: 621.313.12:57.088

Registration of $^{68}Ge/^{68}Ga$ generators: Why, how, what for?

Y-M. Chevalme

ANSM, French Medicine Agency, Saint-Denis cedex, France

The aim of this presentation is to explain the necessity and address some of the difficulties in the registration of $^{68}Ge/^{68}Ga$ generators, which is frequently seen as a barrier to more widespread application of ^{68}Ga-labelled innovative PET tracers in nuclear medicine practice.

Why? $^{68}Ge/^{68}Ga$ generators can be stored and used on site in any PET centre. Since the half-life of the parent ^{68}Ge is 271 days, the generator can remain functional and storable for almost one year. ^{68}Ga, eluted from the generator, is a positron emitter with a half-life of only 67.8 minutes and allows the labeling in radiopharmacies using aseptic procedures in a sterile environtment of many peptides and other small molecules owing to rapid diffusion, localisation at the target and fast blood clearance, for non-invasive PET/CT molecular imaging.

How? Like $^{99}Mo/^{99m}Tc$ generators, $^{68}Ge/68Ga$ generators respond to the definition of radiopharmaceutical medicines according to the directive 2001/83/EEC. The criteria of quality, safety and security should be guaranteed. All types of generators include a column bearing the radionuclides and an eluent, but there are currently many different types of generators of a very different structure used in Europe under various regulatory frameworks. For example, $^{68}Ge/^{68}Ga$ generators have been developed with many different solid phases such as TiO_2, SnO_2 or organic resin-based columns and different eluents, mostly hydrochloric acid (HCl) at different concentrations. GMP-certified facilities are required to satisfy the standard of the authorities. Some points are very critical such as production and availability of the mother radionuclide ^{68}Ge, a sufficient ^{68}Ga elution yield, the removal of ^{68}Ge from the eluates (breakthrough), the purity and the concentration of the eluates. Since June 2011, a monography n° 2464 has been available in the European pharmacopeia for the gallium-68 chloride solution for radiolabelling, which should facilitate the registration of generators. It seems important to the medicines regulatory bodies that those generators, the eluted solution is an important part of an agent to be injected in Humans, will be checked, verified and finally registered with marketing authorisations granted to pharmaceutical companies, in view of dossiers fulfilling all the EMA requirements. Since no direct application of the direct injection of the eluted solution has been reported for the moment, a highly simplified clinical part of the dossier appears adequate.

What for? The success of ^{68}Ga-labelled somatostatin analogues, which are today used worldwide but in different indications and legal framework according the countries, illustrates the need for approved generators. It is likely that many other PET radiopharmaceuticals will be labelled with ^{68}Ga in the near future, in particular when a moderate daily use will not justified the production of high activities of fluorine-18 labelled radiopharmaceuticals that requires radionuclide production in a cyclotron.

Key words: Radionuclide Generators; Positron-Emission Tomography; Radiopharmaceuticals; Gallium Radioisotopes; Germanium; Device Approval; Reference Standards

UDC: 621.313.12:615.1:615.849

Ga-68 DOTA-Peptides in NET. Advantages and disadvantages versus other radiopharmaceuticals

P. Castellucci

Department of Nuclear Medicine, Policlinico S. Orosla Malpighi, Bologna, Italy

Aim: to compare advantages of Ga-DOTA-peptides in comparison with other radiopharmaceurticals in the study of NET.

Methods: many different radiopharmaceuticals can be used to image NET, since these groups of cancers can be imaged from different point of view either using $\beta+$ or γ radiopharmaceuticals. Molecular imaging can probe the synthesis, storage, and release of hormones using ^{11}C-hydroxy-ephedrine (HE) or ^{11}C-metomidate; also different amine precursors can be used such as ^{11}C-hydroxy-tryptophane (HTP) or ^{18}F-dihydroxy-phenylalanine (DOPA) and finally a metabolic compound such as ^{18}F-fluorodeoxyglucose (FDG) have it's role in the study of NET. We will compare advantages and disadvantages of the use of the above mentioned radiopharmaceuticals with the use of somatostatin receptors ligands either labeled with γ emitters (^{111}In-DTPAOC-scan) or $\beta+$ emitters ^{68}Ga -DOTA- peptides (NOC, TOC, TATE, etc).

Results: Main technical advantages of the use of Ga-DOTA-peptides are: no need of a cyclotron, since Ga is produced by a Ge-Ga Generator; the relatively low cost of the Generator and the easy labeling procedure: 20 minutes to label ^{68}Ga to DOTA-peptides.

Main clinical advantages are: better accuracy either in staging, restaging or asses therapy response in well differentiated NET, in comparison with other radiopharmaceuticals; lower costs; better dosimetry. However it is necessary to remind that there are some limitations in the use of Ga DOTA petides: 1) the use is strictly reserved to well or moderately differentiated NET (according to Ki 67 expression) in these cancers the use of FDG is strongly recommended since not only it has proved a better accuracy in comparison with Ga-DOTA-peptiedes but also it is a significant prognostic factor 2) in medullary thyroid cancer the use of F-DOPA has proved a better accuracy in comparison with Ga-DOTA- peptides or FDG.

Conclusion: Despite some few limitations, the use of Ga-DOTA-peptides to image NET has many technical and clinical advantages in comparison with other radiopharmaceuticals.

Key words: Radiopharmaceuticals; Neuroendocrine Tumors; Gallium Radioisotopes; Diagnostic Imaging

UDC: 616-006.48-616.37-006:616.33-006:615-85

Therapy of neuroendocrine tumours

J. Fettich, M, Hodolič

Bled Diagnostic Centre, Bled, Slovenia

Malignant well-differentiated neuroendocrine tumours (NETs) of the pancreas and the gastrointestinal tract are rare and clinically challenging heterogeneous neoplasms. Low- to intermediate-grade NET constitutes a group of indolent malignancies that share the capacity for secreting hormones and neuroamines. NETs can be clinically symptomatic (functioning) or silent (non-functioning).
Radical surgery is the sole effective therapeutic approach. In case of metastatic tumours surgical removal of metastatic burden, medical treatment and protein receptor radiotherapy (PRRT) in somatostatin receptor expressing tumours are also options.
The aim of this presentaton is to present the role of nuclear medicine in the therapy of NETs.
Surgery: Surgical resection of the primary and metastases remains the only curative treatment with 60-70% 5-year survival and 35% 10-year survival rates, radioguided surgery is a useful addition. Hepatic metastases develop in 85% of patients and may be treated by local ablative therapy e.g. surgical resection, radiofrequency ablation, (radio)embolisation, or liver transplantation.
Medical treatment: Expression of receptors for somatostatin is the basis of treatment of NETs with somatostatin analogues as antisecretive and antiproliferative agents. Unfortunately the anti-tumour effect of somatostatin analogues, despite efficient symptom control, is limited.
NETs are generally resistant to conventional chemotherapy, while new drugs everolimus and sunitinib significantly improve progression-free-survival.
PRRT: An exciting therapeutic strategy for cytoreduction, both for stabilisation of tumour growth and inhibition of hormone production, is the use of targeted radionuclide therapy.
The results that were obtained with ^{90}Y-octreotide and ^{177}Lu-octreotate are very encouraging in terms of tumour regression. The side effects are few and mild, if kidney protective agents are used. Severe toxicities for ^{177}Lu-octreotate are few and included myelodysplastic syndrome in 0.8%, hepatic insufficiency in 0.6%, and renal insufficiency in 0.4%. The median duration of the therapy response for these two radiopharmaceuticals was 30 and 40 months, respectively
Conclusion: Due to their complex nature and the wide range of therapeutic options, the involvement of specialists in a multidisciplinary team setting is vital to provide optimal treatment of this disease.
Nuclear medicine procedures are important for surgical treatment of NETs (localisation of the disease, radioguided surgery and radioembolisation), medical treatment (tissue characterisation – determination of expression of somatostatin receptors) and targeted radiation treatment (PRRT).

Key words: Neuroendocrine Tumors; Radiopharmaceuticals; Diagnostic Imaging; Radiotherapy; Octreotide; Somatostatin

UDC:658.56:539.1:615.07

Quality assurance and quality control of SPECT/CT systems

M. Dimcheva, S. Sergieva

Department of Nuclear Medicine, Sofia Cancer Center, Sofia, Bulgaria

The aim of this work was to present a comprehensive set of test procedures including acceptance testing and routine quality control measurements as a part of quality assurance program for equipment used in nuclear medicine.
Quality control national programs ought to be designed to follow international guidelines such as those from International Atomic Energy Agency (IAEA), European Association of Nuclear Medicine(EANM), American Association of Physicists in Medicine (AAPM), and Association of Electrical Equipment and Medical Imaging Manufacturers (NEMA). Extensive series of parameters have been developed over the years for acceptance testing and performance characterization of SPECT/CT systems. These sets of tests, including their objectives and frequencies are discussed in this work.
The results of the acceptance tests of the equipment after installation should be recorded as a comperable base for future tests. Routine quality control measurements should be made at regular intervals, and also after any major change of components, updating by the manufacturer, or repairs.
In conclusion, thorough acceptance testing at the time of initial installation, and adherence to a regular quality control program are essential for better image quality and accurate image interpretation.

Key words: Tomography, Emission-Computed, Single-Photon; Tomography, X-Ray Computed; Quality Control; Quality Assurance; Equipment Safety

UDC: 616-006:615849.1:537.1

Clinical Application of SPECT-CT in Radiotherapy Planning

S. Sergieva[1], I. Mihailova[2], M. Dimcheva[1]

[1]Department of Nuclear Medicine, Sofia Cancer Center, Sofia, Bulgaria, [2]Department of Radiotherapy, National Oncological Hospital, Sofia, Bulgaria

SPECT-CT studies enable full anatomical and functional visualization in a single acquisition. The ability to have information on the target and crucial structures gives confidence that the patient is correctly planned. The role of fusion imaging SPECT-CT method is currently being investigated in radiotherapy treatment planning. Up to date image-guided radiotherapy extensively involves CT and MRI image data. The quality of target radiotherapy directly depends on the precise determination of:

1. The Gross Tumor Volume (GTV) – macroscopic tumor tissue is based on imaging and histopathological modalities.
2. The Clinical Target Volume – this volume includes GTV with margin accounting for subclinical microscopic invasion e.g. CTV=GTV+0.5 cm. CTV is anatomical-clinical volume.
3. GTV and CTV are purely oncological concepts independent for any technology. Corresponding radiotherapy terms are Planning Risk Volume (PRV), */G.Boisseri. Cancer Radiother: 2001;5 Suppl 1:15s-35s/*.
4. Planning Target Volume (PTV): this volume includes CTV with safety margin from organ motion, daily patient setup, radiation technique, intra treatment variation. PTV is geometrical concept.
5. The Volume of the Organ at Risk (OAR) – organs at risk have a tolerance dose that depends on the dose per fraction, but the dose must be kept as low as possible.

SPECT studies provide extra information for GTV delineation. SPECT functioning imaging tool allows access to a wide variety of gamma emitted tracers representing different aspects of tumor cell proliferation and function, improving the sensitivity of radiotherapy planning including SLN mapping, bone scintigraphy, tumor imaging with ^{99}mTc-MIBI/TF, ^{131}I thyroid scintigraphy.
SPECT-CT can determine correct localization of radionuclide uptake, differential diagnosis of physiological from pathological biodistribution, benign from malignant lesions, recurrent tumor masses from the fibrous tissue.
The integration of modern multiple approaches such as SPECT-CT/ PET-CT may lead to better identification of target and non-target structures using morphological, functional and biological information better than applying each single imaging modality.

Key words: Tomography, Emission-Computed, Single-Photon; Tomography, X-Ray Computed; Neoplasms; Radiotherapy Planning, Computer-Assisted; Magnetic Resonance Imaging; Gamma Cameras

UDC: 616.24:615-085:615.849.1

Role of FDG PET/CT imaging in evaluation of chronic sarcoidosis

D. Šobić Šaranović

National PET Center, Center of Nuclear Medicine, Clinical Center of Serbia, Belgrade, Serbia

Sarcoidosis is a granulomatous multi-system disease of unknown etiology. The diagnosis is confirmed by histological verification non-caseating granuloma and presence of typical clinical and radiographic findings and after exclusion of other granulomatous diseases. Lungs and/or thoracic lymph nodes are most commonly involved, while extrathoracic manifestations are present in around 30 % typically in combination with thoracic sarcoidosis. Sarcoidosis spontaneously remits in up to one third of patients, but the chronic and progressive form occurs in up to 30%.
FDG PET/CT has an increasingly role in evaluation of patients with sarcoidosis. The objective of this review, based on our own experience and literature date, is to highlight the clinical role of FDG PET/CT in evaluation of patients with chronic sarcoidosis. The advantages of this technique are that it can visualize FDG accumulation in activated inflammatory cells and simultaneously provide PET and CT images. The performance of FDG PET/CT in specific clinical situations is of special interest: in staging and identification of occult sites and sites suitable for biopsy, in assessment of inflammatory active sarcoidosis in patients with prolonged symptoms, especially when other markers of the disease are within normal values. This method is important and better than other visualization techniques in detecting extrathoracic sites of active sarcoidosis, such as bones, liver, spleen, retroperitoneal lymph nodes. Cardiac sarcoidosis is of special clinical interest because it is potentially life threatening and quite often present in asymptomatic patients. Focal uptake of FDG in the heart indicates cardiac involvement of the disease, which is important in therapy planning and monitoring of those patients. FDG PET/CT has also role in planning therapeutic decision, monitoring treatment response, as well as in performing follow up in patients with chronic persistent sarcoidosis.

Key words: Sarcoidosis; Chronic Diseases; Diagnostic Imaging; Inflammation; Positron-Emission Tomography; Tomography, X-Ray Computed; Fluorodeoxyglucose F18

UDC: 616-006:616.071:616.71

FDG PET/CT imaging in multiple myeloma

J. Mihailović

Department of Nuclear Medicine, Oncology Institute of Vojvodina, Sremska Kamenica, Serbia

Multiple myeloma is a malignant disease of bone marrow plasma cells accounting for 1% of all malignancies and 10% of all hematological neoplasms. Each year, 5.9 new cases appear per 100,000 men and women. Early detection and staging of myeloma patients are important for prognosis and outcome of disease. A plain x-ray survey remains the gold standard in detection of lytic myeloma bone lesions and is used for radiological screening. However, in comparison to whole body plain radiography, whole body low dose CT (LDCT) has greater accuracy in the evaluation of extent of bone lesions, and correlates with MRI for staging. Recently, MRI and PET/CT have been incorporated into Durie-Salmon plus staging system to evaluate focal bone lesions and bone marrow involvement. At the time of initial diagnosis, FDG PET/CT is an excellent indicator of the extent of disease, exceeding the sensitivity and specificity of the traditional bone survey.

FDG avidity on PET/CT demonstrates the extent of active disease. Early in the course of marrow involvement, a hypermetabolic focus will be identified without CT evidence of osteolysis. FDG avidity is demonstrable in active osseous lesions as well as non-osseous, soft tissue lesions known as plasmacytomas, carrying a poor prognosis. Following successful treatment and cessation of focal disease activity, the lytic lesions will remain and will be identifiable on CT but without corresponding FDG avidity. In addition, FDG PET/CT scan may differentiate FDG avid active myeloma from MGUS or smoldering disease which usually presents with low FDG uptake without detectable diffuse or focal bone marrow lesions. FDG PET/CT is a sensitive technique for patient monitoring by identifying the new sites of involvement; to assist in the treatment strategy (radiation therapy or orthopedic manipulation).

The FDG avidity is the best indicator of extent of disease and confirmation of the active disease sites in the assessment of treatment response. Steroids are known to interfere with energy utilization and will result in decreased FDG uptake. This effect is steroid type and dose dependent. Therefore, it is suggested that at least a week without steroid exposure is necessary before treatment assessment determined by SUV can be used as a reliable indicator of the clinical response (1 week after treatment with Prednisone; 1-2 weeks after Dexamethasone).

Recent studies with Carbon 11-methionine have been promising for the imaging of active myeloma and may be more specific and independent of the steroid effect observed with FDG imaging. However, there remains a need to develop a consensus regarding the imaging protocol for PET/CT as well as a protocol for response criteria, in a similar way as for the assessment of solid tumors.

Key words: Multiple Myeloma; Diagnostic Imaging; Positron-Emission Tomography; Tomography, X-Ray Computed; Fluorodeoxyglucose F18

UDC: 616-006:615.849.1:615.07

Current status of PET/CT in radiotherapy treatment planning

A. Balenović

Health Center Zagreb, Zagreb, Croatia

Substantial technological progress in radiation oncology enabled dose delivery to the tumor with a high geometric precision. The introduction of stereotactic radiotherapy, radiosurgery, intensity modulated radiotherapy (IMRT) and three-dimensional brachytherapy require a re-evaluation of the standard methods for target volume delineation. During recent years new methods for tumor visualization have been introduced in oncology, such as positron emission tomography (PET), single-photon emission tomography (SPECT) and magnetic resonance spectroscopy (MRS). Bringing PET into current radiotherapy (RT) practice was enabled due to the significant development in PET/CT scanners, especially by decreasing resolution of the system up to 2 mm in new generations of PET cameras. Primary tumor can be identified more accurately which resulted in reshaping the gross tumor volume (GTV). More accurate tumor identification could lead to the better normal tissue sparing. The second important advantage is that other tumor characteristics besides size, which are relevant for radiation sensitivity, can be visualized. PET imaging can identify the degree of radiosensitivity of the tumor and hypoxic areas, which are resistant to the treatment. Finally, intratumoral biological heterogeneity can be identified ("biological target volume") and sub-volumes of the tumor, which are resistant to the radiation receive an extra dose delivered with a high precision on a small volume. This represents advanced dose escalation strategy, called "dose painting", which is expected to provide better therapeutic gain, namely reducing local recurrences.

The current interest focuses on three evidence based causes of radiation therapy failure in the clinic: tumor burden, cell proliferation and hypoxia, therefore radiopharmaceuticals (RF) currently used for RT planning are stratified according to that. Many studies are published on the use of ^{18}F-FDG PET/CT to improve target definition /tumor burden in RT planning. The two most widely used applications in detecting overall tumor volume are in the treatment of patients with lung cancer and head and neck tumors. Clinical outcome data shows the importance of the volume of a cancer as a driver of local outcome after RT. Limited data are available on GTV delineation and RT dose adaptation with other metabolic tracers, such as methionine (^{11}C-MET) and fluoroethyl-tyrosine (^{18}F-FET) in gliomas, ^{68}Ga-DOTATOC in meningeomas and glomus tumors, choline (labeled with ^{11}C or ^{18}F) for prostate cancer. The tumor cell proliferation is a well established cause of local failure after radiation therapy for many tumors. The intensive research resulted in developing thymidine analog, ^{18}F-fluorothymidine (FLT), which is often called a "proliferation tracer" and actually provides a map of growth fraction of tumor cells. The comparison of FLT scans at baseline and 2 weeks after the fractionated radiotherapy has been used in order to define targets for sub-volume boosting.

Tumor hypoxia is a well known strong contributor to radiation resistance and is associated with progression of the disease and a poor outcome after therapy. The strongest evidence exists for squamous cell carcinoma of the head and neck, prostate and uterine cervix.

Key words: Neoplasms; Diagnostic Imaging; Radiopharmaceuticals; Positron-Emission Tomography; Tomography, X-Ray Computed; Radiotherapy Planning, Computer-Assisted; Treatment Outcome; Radiation Tolerance

UDC: 61:519.23:001.89

Hazard ratio, odds ratio, and relative risk

J. Stare

Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia

Odds ratio (OR) is a statistic often encountered in medical literature. Most readers perceive it as relative risk (RR), although they usually don't know why that would make sense. Since this perception is usually correct, there is nothing wrong with it. Still it is probably useful to be occasionally reminded about the connection between the odds ratio and the relative risk, to avoid situations when such equating is wrong. Another statistic which is also understood as an estimator of the relative risk is the hazard ratio (HR). It is always reported when we use the Cox proportional hazards model to analyze survival data. Under proportional hazards a 'natural' argument is this: if at any time probability of dying in one group is k times the probability in the other group, then the relative risk must be k, regardless of where we are in time. Well, we shall see if this really is so.

Key words: Biostatistics; Data Interpretation, Statistical; Risk; Odd Ratio; Proportional Hazards Models

UDC: 616.132.2:616.071:616-037

Clinical value of gated SPECT MIBI early post-stress imaging in patients with intermediate Duke treadmill score

D. Šobić Šaranović

Center of Nuclear Medicine, Clinical Center of Serbia, Belgrade, Serbia

We have recently introduced early post-stress Gated SPECT MIBI imaging protocol in clinical practice as a part of IAEA Coordinate research project. We assume that shorter time to complete the study is more convenient for patients and translates into more cost-effective services. In addition, the duration of a transient post-ischemic left ventricular dysfunction after stress varies with the extent and severity of ischemia in patients with suspected or known coronary artery disease. These changes may remain partially or completely unnoticed due to a current standard delay of 45 to 60 minutes between the tracer injection and data acquisition with the technetium perfusion compounds. Therefore, early gated SPECT MIBI imaging with acquisition 15 minutes after stress, could detect more wall motion abnormalities and stunning especially in patients with mild left ventricular dysfunction or normal function and intermediate Duke treadmill score. Duke treadmill score is one of the most clinically useful scoring system for interpretation an exercise treadmill test and for prediction prognosis and planning further management for patients with suspected coronary artery disease. In the score three independent variables (exercise time, ST segment deviation, and angina index) were taken into account to interpret the result of the test. A score between 4 and –10 indicates intermediate risk. Such patients usually require further investigation with functional imaging such as gated SPECT MIBI. In spite of potential advantages, clinical utility of early gated SPECT MIBI acquisition may be limited by larger artifacts in the inferior wall due to a high liver and subdiaphragmatic uptake. The results of our investigation and experience in clinical practice indicate that the quality of early stress images is suitable for clinical interpretation. In comparison to coronary angiography as the gold standard, early stress gated SPECT MIBI parameters have high sensitivity and specificity for detecting significant coronary stenosis in patients with intermediate Duke Treadmill score. Finally, lower stress than rest ejection fraction and severe reversible perfusion abnormalities are the significant predictors of future cardiac events. Therefore, gated SPECT MIBI early post-stress imaging has noticeable diagnostic and prognostic clinical value in diagnosis of coronary artery disease in patients with intermediate Duke Treadmill Score.

Key words: Cardiac-Gated Single-Photon Emission Computer-Assisted Tomography; Exercise Test; Coronary Artery Disease; Magnetic Resonance Imaging; Perfusion Imaging; Technetium Tc 99m Sestamibi

UDC: 616.13:616-005.4

Nuclear cardiology; in the era of the interventional cardiology – Or do we have diagnostic approach to recognize culprit lesion in patients with multi vessel disease to determinate therapy

B. Baškot

Ordinacija "Dr Baškot", Belgrade, Serbia

One of the most powerful uses of myocardial perfusion imaging (MPI) is the evaluation of the risk for future events in patients with suspected or known coronary arteriography disease (CAD). It has a dual role!
Prior to coronary angiography, MPI is extremly useful in documeting ischemia and determining the functional impact of single or multiple lesions indentified subsequently.
After coronary anatomy is known, MPI remains the test of choise for indentifying the lesion responsible for the ischemic symptoms, or so colled culprit lesion.
That is extremly useful for futher management decisions with respect to percutaneous interventions. The current definition of culprit lesion that is zone of ischemia under the coronary stenoses is not quite wright, because that is not definy two pathophysiologic aspects of ischemia; severity and extent.
Coronary angiography, considered the "gold standard" for the diagnosis of CAD, does not often provide information about the physiologic significance of atherosclerotic lesions, especially in borderline lesions. More importantly, it does not provide a clear marker of risk of adverse events, especially in patients with moderate disease severity. Andreas Gruentzig said; "*When coronary angiography founded coronary artery disease, I would like to have diagnostic procedure who will give me functional significance that lesion.*"
MPI and determination of culprit lesion is more predicitble of cardiac events than coronary angiography. MPI provides information on the extent and location of myocardial ischemia. The assessment of jeopardized myocardium may be performed and provides a measure of the relative value of PTCA in terms of the amount of jeopardized myocardium.

Key words: Myocardial Perfusion Imaging; Coronary Angiography; Coronary Artery Disease; Myocardial Ischemia

UDC: 616.12-07:616-037:615-085

Value of perfusion scintigraphy in patients with left bundle-branch block

K. Nikoletić

Department of Nuclear Medicine, Oncology Institute of Vojvodina, Sremska Kamenica, Serbia

Myocardial perfusion scintigraphy (MPS) is an important imaging modality in the management of patients with cardiovascular disease, improving patients diagnosis, establishing prognosis, assessing the effectiveness of therapyand evaluating viability.
In normal conditions, conduction system of the heart originates in the sinoatrial node, the impuls further travels through the right atrium to the atrioventricular node. After exiting from atrioventricular node, the impuls is divided into right and left bundle branches, traveling furher to the right ventricle and left ventricle to initiate contraction.
Left bundle-branch block (LBBB) represents abnormality in the conduction system when the signal cannot pass through the leftbundle branch. As a result, conduction to the left ventricule is delayed because it comes from the right ventricle. As a result of presence of LBBB, septum moves toward the right on gated studies. These paradoxal movement of the septumt can result in a septal defect on myocardial perfusion imaging, which may be mistaken for myocardial infarction or ischemia. Since this phenomenon is accentuated by increasing heart rate, and thus is far less frequent if pharmacological vasodilators with dipyridamole or adenosine are used for stress-testing instead of ergobycicle.
The presence of LBBB is associated with false positive perfusion defects particularly in the septal area resulting in numerous coronary angiograms revealing normal coronary arteries. The mechanism for the apparently false positive perfusion defect has not been completely established but likely results from compromise of diastolic blood flow due to the delayed septal contraction, decreased septal perfusion due to asynchronous contraction of the septum, shortened duration of the diastole, diminished septal oxygen demand due to impaired septal wall thickening, and septal small vessel disease or fibrodegenerative changes.It does not mean that a perfusion defect in the septum is necessarily due to the LBBB rather than coronary artery disease, but this can present a diagnostic dilemma.

Key words: Myocardial Perfusion Imaging; Bundle-Branch Block; False Positive Reactions; Coronary Artery Disease; Cardiovascular Diseases

UDC: 616.441-008.61:577.175.4:615-085

Radioactive I-131 in the treatmant of hyperthyroidism - Single institution study

Š. Cerić[1], E. Kučukalić-Selimović[1], N. Bešlić[1], A. Valjevac[2], S. Begović-Hadžimuratović[1]

Department of Nuclear Medicine, University Clinical Center Sarajevo, Sarajevo, BIH, [2]Physiology Department, Medical Faculty, University of Sarajevo, Sarajevo, BIH

Introduction: The causes of hyperthyroidism are Graves's disease (GD), toxic adenoma (TA) and multinodular goiter (MNG). The treatment options for hyperthyroidism are antithyroid drugs, radioactive iodine (RAI) and surgery. We evaluated our results in the treatment of hyperthyroid diseases with RAI.
Methods and patients: In this study 115 patients were included (with GD, TA and MNG). All patients were treated with fixed doses of RAI, and we analyzed hormonal status of thyroid gland after six and twelve months.
Results: There were 60 (52.2%) patients with TA, 42 (36, 5%) with GD and 13 (11, 3%) with MNG. Mean dosage for patients with TA was 12.3±4.0 mCi. After 6 months of follow up 38 patients (63,3%) with TA were euthyroid, 8 (13,4%) were hypothyroid and 14 (23,3%) were hyperthyroid. After 12 months of follow up 44 patients (73,4%) with TA were euthyroid, 9 (15%) were hypothyroid, and 7 (11,6%) were hyperthyroid. Mean dosage for patients with GD was 10,6±3.5 mCi. After 6 months of folow up 19 patients (45,2%) with GD were hypothyroid, 10 (23,8%) were euthyroid and 13 (30,9%) were hyperthyroid. After 12 months of follow up 25 (59,5%) were hypothyroid, 10 (23,8%) were euthyroid and 7 (16,6%) were hyperthyroid. Mean dosage for patients with MNG was 13.0±2.1 mCi. After 6 months of follow up 12 (92,3%) patients were euthyroid and 1 (7,7%) was hyperthyroid. After 12 months of follow-up all 13 patients with MNG were euthyroid.
Conclusion: RAI I-131 is efective as treatment of choice for hyperthyroidsm. Our recomondations are to treat patients with higher doses of RAI I-131 for obtaining euthyroid state.

Key words: Hyperthyroidism; Iodine Radioisotopes; Treatment Outcome; Graves Disease; Goiter; Adenoma; Thyroid Neoplasms

UDC: 616.447:577.175.4:577.11:615.07

Analysis of biochemical and hormonal parameters in primary hyperparathyroidismus: The relationship with dual - wash ^{99m}Tc -MIBI parathyroid scintigraphy findings

Lj. Bojić[1], A. Filipović[2], M. Obradović[1], S. Novosel[1], D. Dragašević[1]

[1]Nuclear Medicine Department, Clinic of Oncology and Radiotherapy, Clinical Center of Montenegro, Podgorica, Montenegro, [2]Clinic of Vascular and Endocrine Surgery, Clinical Center of Montenegro, Podgorica, Montenegro

Introduction: Primary hyperparathyroidismus (pHPT) is a clinical disorder, which occurs due to the increased activity of the parathyroid glands and it is diagnosed by the presence of hypercalcemia and elevated levels of parathormon. Dual-wash ^{99m}Tc-MIBI scintigraphy is widely used technique for preoperative localization of hyperfunctional parathyroid glands. The purpose of this retrospective study was to evaluate biochemical and hormonal parameters in patients with clinically diagnosed pHPT. We compared serum levels of calcium: total (Ca) and ionisated (Ca^{++}), intact parathormon (iPTH), and phosphorus (P) between the group with positive and the group with negative dual -wash ^{99m}Tc-MIBI parathyroid scan. We also evaluated the relationship of the values of those parameters with positive scintigraphic findings in patients who were referred for minimally invasive parathyroidectomy.
Methods: Serum iPTH, Ca (total and ionisated) and phosphorus (P) levels measurements were performed in 82 patients with clinical diagnosis of pHPT. The value of PTH > 68 pg/ml, Ca total >2.55 mmol/l, Ca^{++} >1,32 mmol/l, and P<0.87 mmol/l were considered abnormal. All the patients where referred for dual -wash ^{99m} Tc-MIBI parathyroid scan at the department of Nuclear medicine between November 2011 and September 2013. Planar and SPECT scintigrams of neck and mediastinum were taken 20' and 120' after i.v. administration of 740 MBq of ^{99m} Tc-MIBI.
Results: Dual-wash ^{99m} Tc- MIBI scintigraphy was clearly positive in 51/82 patient (62%), and negative in 31/82 patient (38%) .A high statistically significant difference between the groups was found, respectively: iPTH :192 vs. 102 pg/ml (p<0.001); Ca: 2.93 vs. 2.6 mmol/l (p<0.05); Ca^{++}: 1.49 vs. 1.29 mmol/l (p<0.05) and P: 0.82 vs. 1.1 mmol/l (p<0.001). There was no significant correlation between iPTH and Ca (total and ionisated) in group with positive MIBI scan who underwent minimally invasive parathyrodictomy. A significant correlation of reverse direction was found between PTH and P levels (p<0.05) in this group of patients. Sensitivity, specificity, positive and negative predictive value of iPTH (cut-off value > 127 pg/ml) for positive parathyroid scan was: 80.6%; 87.1%; 86.2% and 81.1%. Dual-wash ^{99m}Tc-MIBI scintigraphy had a diagnostic accuracy 96% for preoperative localisation of hyperfunctional parathyroid glands at the level PTH >140.5 pg/ml.
Conclusion: Increased values of iPTH (cut-off level >127 pg/ml) showed high sensitivity, specificity, positive and negative predictive value for positive parathyroid scan. Dual- wash ^{99m}Tc-MIBI parathyroid scintigraphy showed high diagnostic accuracy in preoperative localization of hyperfunctional parathyroid glands, especially when PTH level is increased, and P level is decreased.

Key words: Hyperparathyroidism, Primary; Parathyroid Glands; Technetium Tc 99m Sestamibi; Radiopharmaceuticals; Calcium; Parathyroid Hormone; Phosphorus

UDC: 616.65-006:616.71:616.071

Correlation between bone metastases detected by bone scintigraphy and prostate specific antigen and Gleason score value in patients with prostate cancer

Lj. Bojić, M. Obradović, S. Novosel, D. Dragašević

Department of Nuclear Medicine, Clinic of Oncology and Radiotherapy, Clinical Centre of Montenegro, Podgorica, Montenegro

Introduction: Prostate cancer represents one of the most common malignant tumors in men and significant health problem in developed countries. *Aim:* To find out diagnostic correlation of prostate specific antigen levels (PSA) and Gleason's score (GS) with bone metastases in newly diagnosed prostate cancer.
Methods: This retrospective study included 112 patients with newly diagnosed prostate carcinoma who were referred for bone scintigraphy for staging at the department of Nuclear medicine - Clinical Center of Montenegro, over two years starting from January 2011 to April 2013. Levels of PSA within one month at diagnosis, GS after transrectal ultrasound - guided prostate biopsy and scintigraphic findings were recorded and analysed.
PSA >4 ng/ ml values were considered as abnormal.
Results: Bone metastases were confirmed at 47/112 (42%) patients. It has been determined that there is a high statistically significant correlation between PSA values and bone metastases presence at test subjects (Kendall's tau = 0.583; $p < .001$).
For determined cut-off value PSA > 29.6 ng/ml, sensitivity (SN), specificity (SP), positive predictive value (PPV) and negative predictive value (NPV) was: 71%, 88%, 87% and 73%.
High statistically significant correlation of positive direction and stable fortitude has been determined between bone metastases presence and GS (Kendall's tau = 0.439; $p < .001$). For determined cut-off value GS > 6, SN, SP, PPV, NPV was: 76%, 65%, 67% and 75%. In addition, high significant correlation was found between PSA and GS (Rho = 0.478; $p < 0.001$).
Conclusion: This study has shown that PSA and GS values are strongly correlated with bone metastases in patients with prostate cancer. Both, PSA and GS have proved as potential independent predictors of bone metastases in patients with prostate cancer.

Key words: Prostatic Neoplasms; Neoplasm Metastasis; Bone Neoplasms; Prostate-Specific Antigen; Neoplasm Grading; Radionuclide Imaging

UDC: 616.24-006:681.3:57.086:616.071

Synchronous B1 thymoma and lung adenocarcinoma

D. Ilinčić, M. Bjelović, M. Milošević, D. Đurić, M. Koledin, I. Kuhajda

Chest Surgery Clinic, Institute for Pulmonary Diseases of Vojvodina, Sremska Kamenica, Medical Faculty, University of Novi Sad, Novi Sad, Serbia

Introduction: Thymoma has been reported to have increased risk of extrathymic malignancy and ranges between 9% and 28%. The most frequent combination includes hematological disorders and cancers arising from the digestive tract. However, the synchronous occurrence of thymoma and lung adenocarinoma is rare.
Case: A 77-year-old male patient with long lasting productive cough, fatigue, chest pain and dyspnea was admitted to our department. Computed tomography (CT) showed mediastinal mass in the central part of the mediastinum (84x77 mm), adherent to the pericardium and lung emphysema with two irregular hypodense lesion (13 and 10 mm) the upper left lung lobe corresponding to residues of previously inflammatory process. Bronhoscopy finding was normal. A right thoracotomy was performed with complete extirpation of mediastinal tumor, histology diagnosis was thymoma (WHO classification - B1, Masaoka staging - I). Three months after patient was admitted to our Institution because of hemoptysis. CT showed no signs of rest/recurrence in the mediastimun, but progression of changes in the upper lobe of the left lung. In further evaluation FDG-PET was done, confirming no rest/recurrence in mediastinum, but high uptake (SUVmax - 32,8) in lession in lung left lobe (S3). Left thoracotomy with upper left lobectomy and mediastinal lymphadenectomy was done, with complete tumor resections, histology diagnosis of non small cell lung carcinoma – adenocarcinoma.
Conclusion: The simultaneous occurrence of thymic and extrathymic intrathoracic malignancies poses several diagnostic problems. FDG PET/CT could be useful in initial diagnosis in this patient and enable better operational planning.

Key words: Thymoma; Carcinoma, Non-Small-Cell Lung; Diagnostic Imaging; Neoplasms, Multiple Primary; Positron-Emission Tomography; Tomography, X-Ray Computed; Fluorodeoxyglucose F18

UDC: 616.447:616-089.8:577.175.4

Diagnostic value of ^{99m}Tc-MIBI SPECT in preoperative localization for minimally invasive video assisted parathyroid surgery

D. Ilinčić[1], B. Koledin[1], B. Ilinčić[2], M. Vukmirović Papuga[2], R. Žeravica[2]

Institute for Lung Disease Sremska Kamenica, Clinical Centre of Vojvodina, Medical Faculty, University of Novi Sad, Serbia

Introduction: Experienced surgeons can cure primary hyperparathyroidism with bilateral neck exploration in most patients (up to 95% of cases) without the aid of any preoperative imaging. Considering that a solitary parathyroid adenoma is the most frequent cause of primary hyperparathyroidism (in 80%– 85%), bilateral neck exploration is considered overtreatment in most cases. Accurate preoperative localization is required to enable selective minimally invasive video assisted parathyroid surgery (MIVAP) and to reduce the operative failure rate.

Aim of the study: The purpose of this study was to evaluate the diagnostic value of early parathyroid SPECT as compared with planar imaging and color Doppler sonography (CDS) in patients undergoing MIVAP. A total of 15 consecutive patients with primary hyperparathyroidism underwent planar and SPECT parathyroid scintigraphy before MIVAP (dual-phase technique using ^{99m}Tc-methoxyisobutylisonitrile (99mTc-MIBI) and a double-tracer subtraction technique using a delayed ^{99m}Tc-pertechnetate scan).

Results: The average time for surgery was 35 min (range, 25–40 min). Serum calcium, phosphorus and parathyroid hormone (PTH) levels of patents before surgery was (Ca – 2.87+/-0.32 mmol/l, iCa – 1.4 +/-0.2 mmol/l, P – 0.79+/-0.16, PTH – 185 pg/ml (Me)) and 24 h after surgery (Ca – 2.51+/-1.2 mmol/l, iCa – 1.1 +/-1.2 mmol/l, P – 0.82+/-0.76, PTH – 100 pg/ml (Me)). All patients had histopathologic examination of the removed glands (single adenoma). SPECT was superior to planar imaging in 2 patients with multinodular goiters, compared with CDS in patients with goiters and ectopic adenoma. Planar parathyroid imaging (80%, 3 false negative findings) and CDS (74%, 4 false negative findings) are less sensitive compared with SPECT (93%, 1 false negative findings).

Conclusion: Preoperative scintigraphic imaging in patients with primary hyperparathyroidism is essential for accurate localization of parathyroid adenomas and for the selection of patients who are candidates for MIVAP.

Key words: Diagnostic Imaging; Preoperative Period; Technetium Tc 99m Sestamibi; Hyperparathyroidism, Primary;Video-Assisted Surgery; Tomography, Emission-Single-Photon; Ultrasonography, Doppler, Color

UDC: 616.447:616-091.8:615.07

Does BMI contribute negative scintigraphic findings in patients with primary hyperparathyroidismus?

B. Ilinčić, M. Vukmirović Papuga, Z. Đermanov, R. Žeravica, V. Crnobrnja, A. Jakovljević

Clinical Centre of Vojvodina, Medical Faculty, University of Novi Sad, Novi Sad, Serbia

Introduction: Localizing studies seem to be the key for determining the optimal surgical strategy in patients with primary hyperparathyroidism (PHPT). Understanding the factors that affect the accuracy of parathyroid localization test ^{99m}Tc-MIBI (MIBI) scanning will allow the surgeon to develop a successful surgical strategy in a given patient. *Aim:* The aim of this study was to identify factors that affect the success of localizing study in patients with PHPT.

Material and methods: The study group included 52 patients with PHPT who underwent MIBI scan and parathyroidectomy at Clinical centre of Vojvodina. The disease is in all cases verified pathohistologicaly. We analyze variables age, body mass index (BMI), ionizing calcium (Ca), phophorus (P), serum PTH level, and gland volume (GV) versus the detection rate of individual abnormal glands on MIBI. Nonparametric tests for statistic significance and multiple regression analyses were used.

Results: Of the total of 56 abnormal glands analyzed, 92% involved single adenomas in PHPT and 8% double adenomas in PHPT. Scintigraphic sensitivity was 85%, 100 % specificity with 7 false negative findings. Patients with false negative findings were overweight, but not obese (BMI – 27+/- 1.5 kg/m^2) with lesser GV (median 12.5 cm^3 oposite 27.3 cm^3 in possitive group), signiffcantly lower ionised Ca and higher P. Serum PTH was not different between groups. In patients with negative scintigraphic findgings we found negative significant correlation between BMI and GV (r -0.5).

Conclusion: Gland size is the strongest independent predictor of successful localization. Preoperatively, higher Ca levels, lower P in patients with lesser BMI are good indicators about the accuracy of localizing tests.

Key words: Hyperparathyroidism, Primary; Radionuclide Imaging; Technetium Tc 99m Sestamibi; Sensitivity and Specificity; Diagnostic Errors; Body Mass Index

UDC: 616.441:612.017:519.23:616-037

Association of thyroid volume and biochemical markers of thyroid autoimmunity

S. Nikolić[1,3], R. Mijović[1,3], B. Ilinčić[2,3], R. Žeravica[2,3], B. Miličić[1], N. Ćurić[1,3]

[1]Center for Laboratory Medicine, Clinical Center of Vojvodina, Novi Sad, Serbia, [2]Center for Nuclear Medicine, Clinical Center of Vojvodina, Novi Sad, Serbia, [3]Faculty of Medicine, University of Novi Sad, Serbia

Background: Regarding the thyroid tissue destruction and inflammation in earlier stages of Hashimoto`s thyroiditis (HT) the aim of the study was evaluation of relations between the level of anti-thyroid auto-antibodies and thyroid volume.
Methods: The study included 38 patients suffering from HT who have been taking levothyroxine replacement therapy (median;12 months). The control group consisted of 18 sex and age matched, healthy subjects. Biochemical parameters of thyroid gland function fT3, fT4, TSH, as well as markers of thyroid autoimmunity, anti-TPOAb and anti-TgAb were estimated. All subjects underwent thyroid ultrasound. Thyroid gland volume was measured using ultrasound (Shimadzu SDU1,200 Tokyo, Japan) with a 7.5 MHz linear transducer. The volume of each lobe was calculated according to the formula: width x length x thickness x 0.479 and the lobe volumes were summed (volume of isthmus was not included). All the results were statistically processed by Data Analysis package.
Results: Statistically significant higher values of TSH (6.43±4.56 vs. 1.47±0.66), anti-TPOAb (815.71±278.33 vs. 0.61±0.35) and TgAb (56.3;1.3–1000.0 vs. 0.9;0.4-2.5) were observed in patients with HT than in controls. Thyroid volume of patients with HT was significantly higher (21.88±9.63 vs. 13.78±3.91) compared to the control group. In patients with HT, a significant positive correlation between the thyroid volume and the increased titer of TPOAb ($r=0.322$; $p<0.05$) was estimated opposed to positive, but weak correlation of anti-TgAb and thyroid volume ($r=0.18$; $p>0.05$).
Conclusion: Significant positive correlation of increased titer of anti-TPOAb regarding the weak correlation of anti-TgAb with thyroid volume in HT indicates that anti-TPOAb reflects activity of the disease and subsequent thyroid tissue destruction better than anti-TgAb.

Key words: Hashimoto Disease; Thyroid Gland; Organ Size; Ultrasonography; Autoimmunity; Biological Markers; Thyroglobulin; Autoantibodies; Thyrotropin; Iodine Peroxidase

UDC: 616-006:616-089.8(497.11Serbia)

Use of Tc-99m rhenium sulphide at Clinic for Surgical Oncology NCRC of Serbia

A. Martinović, N. Santrač, M. Oruci, M. Kocić

Clinic for Surgical Oncology, Institute for Oncology and Radiology of Serbia, Belgrade, Serbia

Background: Technetium – 99m (Tc – 99m) is metastable nuclear isomer which is used in great number of medical diagnostic procedures and represents the most used radioisotope in human medicine . We use it to mark and trace radioactivity in human body by GAMMA probe. Because of his short half-life it allows us to collect precious data whilst patient´s body irradiation is minimal. Tc-99m is user friendly only in diagnostics, not for therapeutic use.We injected Tc-99m rhenium sulphide (NanoCIS) for dynamic lymphoscintigraphy as well as handheld probe for sentinel lymph node (LN) detection. Once being detected by GAMMA probe, „hot" LN is removed and sent to frozen section analysis. NanoCIS is used as well for marking and tracing of non-palpable lesions in breast. *Aim:* To present our experience in usage of NanoCIS for localization of „hot" LNs.
Materials and methods: During year 2013, NanoCIS was applied in 46 patients - 35 female and 11 male. Localizations were: breast 25 pts. (76%), axillae 11 pts. (23.9%), groins 8 pts. (17.3%) and neck 2 pts. (4.3%). Written consent and multidisciplinary team decision is mandatory, as well as supervision by nuclear medicine specialist. Hour before operation surgeon injects 0.2 – 0.5 ml of radiocoloid into dermis or epidermis of adequate localization. Usage of protection equipment and containers is mandatory.
Results: Breast pathology – 25 pts. with average readings of GAMMA probe of 4500 units. After tissue removal and frozen section, repeated readings were zero with clear surgical margins. Twenty findings were negative and five were positive: 2 ductal carcinoma in situ, 2 carcinoma lobulare invasivum and one invasive ductal carcinoma. Axillary pathology – 11 pts. Average readings were 2900 units. "Hot" LNs were sent to frozen section - 7 detected LNs were negative and 4 were positive (melanoma). After positive reports, we performed axillary dissection. Groin pathology – 8 pts. Average readings were 300 units. Eight LNs were removed and sent to frozen section - 5 were negative, 2 positive (one for melanoma and one for genital carcinoma) and 1 sent to standard pathology. Also, after positive report we performed groin dissection. Head and neck pathology – two patients with two negative LN findings.
Conclusion: Usage of NanoCIS is medically justified because removing positive LNs and adequate amount of breast tissue helps us to achieve both oncological and aesthetical goal. Combined treatment with methylene blue dye in so called "double mapping" technique, results with extraordinary high level of sensitivity.

Key words: Diagnostic Imaging; Technetium Tc 99m Sulfur Colloid; Rhenium; Sentinel Lymph Node Biopsy; Lymph Nodes; Methylene Blue; Breast; Head and Neck; Groin; Axilla

UDC: 612.466:618.2:519.23

Impact of anteroposterior pelvic diameter on ^{99m}Tc-mercaptoacetyltriglycine diuretic renography

A. Jakovljević, R. Žeravica, B. Ilinčić, V. Crnobrnja, M. Vukmirović Papuga, F. Dujmović

University of Novi Sad, Medical Faculty, Clinical Centre Vojvodina, Novi Sad, Serbia

Introduction: Antenatal hydronephrosis is the most commonly detected abnormality during fetal development. The aim of the study was to evaluate whether the size of the prenatal and postnatal renal pelvic anteroposterior diametar (APD) has prediction of obstruction drainage finding on diuretic renography and impaired renal function.
Methods: We prospectively studied 32 renal units with prenataly diagnosed hydronephrosis, that was confirmed on postnatal ultrasonography. The renal pelvic APD was measured in pregnancy between 17th and 35th week of gestation, and between 1st and 4th week after birth to confirm hydronephrosis. The initial ^{99m}Tc-MAG3 was performed in all patients between 4th and 8th week after birth. All patients were divided into two groups: the first group included patients with obstructive diuretic renography finding and the second one included patients with non-obstructive finding.
Results: Out of 32 renal units with hydronephrosis, 14 had obstructive pattern on diuretic renography, and 18 had non-obstructive hydronephrosis. The average of prenatal renal pelvic APD in the first group was statistically higher than in the second one (p=0.009). The average of postnatal renal pelvic APD in the obstructive group was also statistically higher than in the non-obstructive group (p=0.0006). The presence of impared renal function (less than 40%) was significantly more frequent in the obstructive group.
Conclusion: Our study showed that the grade of both renal pelvic diametar, more prominent postanatal, have a significant impact on scintigraphy finding.

Key words: Hydronephrosis; Kidney Pelvis; Ultrasonography; Prenatal Diagnosis; Radioisotope Renography; Infant, Newborn; Technetium Tc 99m Mertiatide

UDC: 616.65-006:616.71:616-072

Correlation between Gleason score level, prostate specific antigen levels and bone scintigraphy in newly diagnosed prostatic cancer patients

V. Crnobrnja[1], B. Ilinčić[1], R. Žeravica[1], M. Vukmirović Papuga[1], A. Jakovljević[1], S. Živojinov[2]

[1]Clinical Centre of Vojvodina, Center for Laboratory Medicine, Departmant of Nuclear Medicine, Medical Faculty, University of Novi Sad, Novi Sad, Serbia, [2]Clinical Centre of Vojvodina, Clinic for Urology, Medical Faculty, University of Novi Sad, Novi Sad, Serbia

Introduction: The aim of this study was to identify correlation between Gleason score (GS), and prostate specific antigen levels (PSA), with bone metastasis in newly diagnosed prostate cancer patients.
Methods: This retrospective study included 298 patients with prostatic cancer in region of Vojvodina from 2012 to 2014., who had PSA, histological confirmation of prostatic cancer (GS) and bone scan. PSA was measured using hemiluminescent method, on Architect i2000SR automatic system, and histological examination was graded according to Gleason's grading system as: well differentiated (GS ≤6), moderately differentiated (GS =7), and poorly differentiated (GS ≥8). Bone scintigraphy was perform 2 to 4 hours after i.v aplication of radiotracer agent ^{99m}Tc- diphosphonat (DPD) in dose of 555 MBq. The patients were divided into 2 groups based on bone scintigraphy findings.
Results: The patients with negative bone scan(129/298) had the average level of PSA 14 ng/ml, the mean age was 69.8+/-6.4 years and GS was 6.5+/-1.24. The patients with possitive bone scan (169/298) finding had the average PSA level 50 ng/ml, mean age was 70+/-7 years and GS was 7.4+/-1.3. The patients with normal scintigraphic finding had statistically significant lower values of serum PSA (p< 0.0001) and Gleason score (p< 0.0001), comparing to patients with positive bone scan. The correlation between those parametars was better in group of patients with positive bone scan (Spearman correlation r=0.4).
Conclusion: The baseline level of PSA more than 50 ng/ml and Gleason score higher than 7 are excellent predictors of positive bone scan in patients with newly diagnosed prostatic cancer.

Key words: Prostatic Neoplasms; Radionuclide Imaging; Neoplasm Grading; Prostate-Specific Antigen; Neoplasm Metastasis; Bone Neoplasms

UDC: 616.127:616-072:537.1

The assessment of viable myocardium in patients with dilated cardiomyopathy with Tc-99m MIBI SPECT during nitrate administration

A. Jakubović Čičkušić, M. Malohodžić, B. Izić, M. Sulejmanović

Radiology and Nucler Medicine Clinic, University Clinical Centre Tuzla, Tuzla, BIH

Background: Tc-99m-MIBI myocardial SPECT has shown promise for evaluation of coronary artery disease, but its role in predicting myocardial viability is still under investigation. The aim of the study was to determine clinical use and efficacy of the Tc-99m-MIBI with sublingual nitrate (ISDN) administration for detection of viable myocardium in patients with dilated cardiomyopathy.
Methods: Thirty-seven patients (27 male and 10 female) with dilated cardioyopathy were studied. All patients were examined under baseline study at rest and after administration ISND. The data were reconstructed in transaxial slices and then reoriented into short, vertical long and horizontal long axis slices. The images were divided into seven different segments for qualitative analysis. The images were interpretated by two independent observers.
Results: The results showed that out of 68 segments with hypoperfusion at resting SPECT, 29 segments (42.67%) had an increase in Tc-99m-MIBI uptake during administration ISDN. The degree of improvement in perfusion was related to the age of patients.
Conclusion: The data suggest that the use of Tc-99m-MIBI SPECT in patients with dilated cardiomyopathy during administration ISDN may be useful for assessing myocardial viability because ISDN augmented Tc-99m-MIBI protocol in Cardiac SPECT imaging resulting in improved detection of viable but hypoperfused segments.

Key words: Cardiomyopathy, Dilated; Myocardial Perfusion Imaging; Isosorbide Dinitrate; Cardiac-Gated Single-Photon Emission Computed-Assisted Tomography; Technetium Tc 99m Sestamibi

UDC: 616.441-006:616.071:546.15

Two-week low iodine diet does not have effect on post-LID diagnostic radioiodine scans

M. Dobrenić, M. Žuvić, D. Huić

Department of Nuclear Medicine and Radiation Protection, University Hospital Center Zagreb, Zagreb, Croatia

Background: Low iodine diet (LID) is designed to decrease the total body stabile iodine concentration prior to radioiodine administration. Most centers advise a two-week low iodine diet prior to the ^{131}I application.
Iodine concentration in the morning specimens provides an adequate assessment of recent dietary iodine intake. Urinary iodine concentration < 50 μg/L indicates a moderate iodine deficiency and optimal preparation for radioiodine administration, while urinary iodine concentration between 50 and 100 μg/L reflects a mild iodine deficient state and is considered as suboptimal but adequate preparation for ^{131}I application. This study is designed to evaluate the influence of two-week LID on radioiodine tissue avidity.
Patients and methods: Fifty two patients with differentiated thyroid cancer, serum thyroglobulin (Tg) > 2 μg/L, negative Tg-antibodies, and negative radioiodine scans underwent two-week LID. Iodine concentration in the morning urine samples were measured in each patient, a day before and the 15th day after starting LID.
For impact evaluation of LID on radioiodine tissue avidity, diagnostic radioiodine scans before and after LID were compared.
Results: Following LID, the patients were able to reduce their iodine body content by 51% (range 15-72%). Thirty seven patients (71%) achieved mild iodine deficiency (50-99 μg/L) and seven patients (14%) accomplished targeted moderate iodine deficient state (<50 μg/L). Eight patients (15%) were iodine sufficient nourished even after two-week LID.
All diagnostic post-LID scans were negative.
Conclusion: This study demonstrated that two-week LID is effective way to decrease total body iodine content, although without visible effect on post-LID diagnostic ^{131}I scans.

Key words: Diet; Iodine; Thyroid Neoplasms; Radionuclide Imaging; Iodine Radioisotopes

UDC: 616.447:616.441:616-008.6

Uncommon primary presentation of multiple endocrine neoplasia – case report

M. Vukmirović Papuga, B. Ilinčić, Z. Đermanov, R. Žeravica, V. Crnobrnja, A. Jakovljević

Clinical Centre of Vojvodina, Medical Faculty, University of Novi Sad, Novi Sad, Serbia

Introduction: Multiple endocrine neoplasia type 1 (MEN 1) is a syndrome characterized by neoplasia involving the parathyroid glands, enteropancreatic tumors, anterior pituitary adenoma and other neuroendocrine tumors with variable penetrance. MEN 1 has estimated prevalence of 2 – 20 per 100 000 in the general population. Although the most commonly involved gland is the parathyroid gland, the variable penetrance of several neoplastic components can make the differential diagnosis and treatment challenging. We report herein the case of MEN 1 based on clinical, biochemical and pathological studies.
Case: The patient was a 49-year-old woman, who presented with acromegaly caused by pituitary adenoma. She underwent transsphenoidal resection of adenoma and was on bromokriptin therapy. After six years she was admitted to hospital because of reevaluation of active acromegaly. In further diagnostics there were found elevated PTH level (125.8 pg/ml) with normal ionized calcium levels and slightly elevated bone turnover markers and euthyroid nodular goiter. Dual phase parathyroid scintigraphy with 99mTc-MIBI showed adenoma of right superior parathyroid gland and hot nodule in left lobe of thyroid gland. She underwent paratiroidectomy due to enlarged right superior parathyroid gland that was shown histologically to be a parathyroid adenoma.
Conclusion: Although MEN 1 syndrome is most commonly primarily presented as hyperparathyroidism, patients with pituitary adenoma as potential presentations of MEN 1, should be monitored to prevent complications of developed syndrome.

Key words: Multiple Endocrine Neoplasia Type 1

UDC: 616-006:616-052:2-468.6

Separation of strontium and yttrium by supported liquid membrane extraction

Đ. Petrović[1], K. Kumrić[2], M. Stoiljković[3], T. Trtić-Petrović[2], D. Đokić[1]

[1]Laboratory of Radioisotopes, Vinča Institute of Nuclear Sciences, Belgrade, Serbia, [2]Laboratory of Physics, Vinča Institute of Nuclear Sciences, Belgrade, Serbia, [3]Department of Physical Chemistry, Vinča Institute of Nuclear Sciences, Belgrade, Serbia

Introduction: Radionuclide ^{90}Y is one of the most suitable radionuclide for the radiotherapy of solid and non-operable malignant tumors. ^{90}Sr is an ideal source for obtaining carrier-free ^{90}Y. The aim of the present study was to investigate the separation of Y(III) from Sr(II) by supported liquid membrane extraction (SLME) in a hollow-fibre contactor under continuous mode of operation and using di(2-ethylhexyl) phosphoric acid (DEHPA) as a carrier in the organic phase.
Methods: The SLME was performed in hollow fiber contactor containing polypropilene hollow fibers. The donor solution (25 mL of 500 ppm Sr(II) and 20 ppm Y(III) in 0.1M HCl) was fed along the shell side of contactor in a recirculated mode of operation by a peristaltic pump (4.5 ml/min). The acceptor solution (4 mL of 3 M HCl) was fed along the lumen of the hollow fiber in a recirculated mode of operation by a peristaltic pump (0.8 ml/min). The concentrations of both metal ions were determined in donor and acceptor by Inductively Coupled Plasma - Optical Emission Spectrometry (ICP-OES) solutions during the extraction which lasted 6 hrs.
Results: It was found that separation factor (α) depends on pH of aqueous solution, DEHPA concentration, and the organic solvent. The highest α (82900) was obtained from aqueous solution pH 1 (0.1 M HCl) and 15% DEHPA in n-dodecane.
The removal efficiency (R) of Y(III) increases during the SLME and reached the maximum of 85%. The extraction efficiency (E) of Y(III) also reised during the SLME, and after 6 hrs of extraction E is 60%. It means that 25% of extracted Y(III) was captured in the membrane. The changing of Sr(II) concentration in the donor solution was not observed. Also, Sr(II) was not detected in the acceptor phase.
Conclusion: The obtained results show that SLME is an effective method for separation Y(III) from Sr(II) and for obtaining carrier-free Y(III). The method described in this paper can be used for obtaining yttrium, suitable for therapeutic use in the treatment of non-operating tumors.

Key words: Pharmaceuticals Preparation; Radioisotopes; Strontium; Yttrium; Liquid-Liquid Extraction; Membranes, Artificial; Spectrophotometry, Atomic

UDC: 616-006:616.071:616.71

Is Technetium-99- 2-methoxyisobutylisonitrile uptake in newly diagnosed multiple myeloma correlated with extense of disease activity?

R. Žeravica[1], B. Ilinčić[1], V. Crnobrnja[1], A. Jakovljević[1], M. Vukmirović Papuga[1], N. Rajić[2]

[1]Clinical Center of Vojvodina, Medical Faculty, University of Novi Sad, Nuclear Medicine Department, Novi Sad, Serbia, [2]Clinical Center of Vojvodina, Medical Faculty, University of Novi Sad, Clinic of Haematology, Novi Sad, Serbia

Technetium-99m 2-methoxyisobutylisonitrile (Tc-99m-MIBI) has been proposed as a useful tracer for the detection of disease sites in patients with multiple myeloma (MM).
The purpose of this study was to evaluate the role of the Tc-99m-MIBI uptake in disease detection and to assess the correlation between the uptake of this scintigraphy agent and prognostic factors in newly diagnosed MM patients.
Thirty-two untreated patients with multiple myeloma were studied using Tc-99m-MIBI. Anterior and posterior whole-body imaging were obtained 10 min after I.V. injection of 370 MBq Tc-99m-MIBI and scored according to intensity (I) and extent (E) of the radiotracer uptake. A summed score (SS) for the Tc-99m MIBI scan was calculated for each patient. The correlation between known prognostic factors of MM and a SS of Tc-99m-MIBI uptake was assessed.
There was a positive correlation between a SS of Tc-99m-MIBI uptake and erythrocyte sedimentation rate (ESR; r=0.553, P = 0.001), C-reactive protein (CRP; r=0.434, P = 0.01), β2- microglobulin (β2M; r=0.358, P = 0.04), fibrinogen (r=0.463, P = 0.008) and bone marrow plasma cell infiltration (r=0.613, P = 0.0001). An inverse correlation was found between a SS of Tc-99m-MIBI uptake and hemoglobin (r=0.442, P = 0.012) and serum albumin (r=0.603, P = 0.0003).
In conclusion, the results of this study suggest that a higher uptake of the radiotracer correlated with more extensive disease activity, as determined by high levels of CRP, β2M, fibrinogen and bone marrow plasma cell infiltration.

Key words: Multiple Myeloma; Diagnostic Imaging; Technetium Tc 99m Sestamibi; Prognosis

UDC: 616.12-073.7:616.071

Comparison of left ventricular functional parameters evaluated by quantitative ECG-gated SPECT and echocardiography

E. Matovina, J. Mihailović, K. Nikoletić, D. Srbovan

Department of Nuclear Medicine, Oncology Institute of Vojvodina, Sremska Kamenica, Serbia

Introduction: Prognosis and therapeutic decisions are often based on functional parameters of left ventricle (LV) such as: end-diastolic volume (EDV), end-systolic volume (ESV) and LV ejection fraction (LVEF), which means that these parameters need to be accurately measured. This can be done by many imaging modalities. Each of these modalities is subject to measurement errors that can lead to the inaccurate calculation of these parameters. The aim of this study was to compare the LV functional parameters calculated using quantitative electrocardiography (ECG)-gated myocardial perfusion single photon emission computed tomography (SPECT) with those measured by ultrasound echocardiography (UCG).
Methods: We examined 40 patients (20 men and 20 women). In both groups we had the same number of patients with and without the presence of prior myocardial infarction. By the gated SPECT using technetium (Tc)-99m methoxyisobutylisonitrile (MIBI) perfusion and 4DM software, we calculated the following parameters: LV end-diastolic volume (EDV), end-systolic volume (ESV), ejection fraction (EF). The same parameters were measured by UCG. The measurements were performed within 6 month of each other. No new cardiac events were registered and no interventions were performed between measuring. The correlations between the cardiac parameters by UCG and those by SPECT/4DM were examined by linear regression analysis. A value of $p < 0.05$ was considered statistically significant.
Results: There was a significant correlation between EDV, ESV and EF measured by SPECT/MIBI and UCG (EDV, $r = 0.71$, $p < 0.001$; ESV, $r = 0.82$, $p < 0.001$; EF, $r = 0.75$, $p< 0.001$).
Conclusion: The LV systolic and diastolic parameters evaluated by SPECT/4DM correlated with those by UCG. The SPECT/4DM offers useful information regarding functional parameters of left ventricle in both men and women. Although the correlation between values obtained with gated-SPECT and blood pool ventriculography was acceptable, the differences show that the two techniques cannot be considered equivalent.

Key words: Cardiac-Gated Single-Photon Emission Computed-Assisted Tomography; Echocardiography; Myocardial Perfusion Imaging; Gated Blood-Pool Imaging; Ventricular Function, Left

UDC: 616.441-006:616.428-006:616-076

Frequency of lymphonodal metastases in thyroid microcarcinomas verified by sentinel lymph node biopsy in clinically N0 patients

R. Džodić[1,2], M. Oruci[2], N. Santrač[2], I. Marković[1,2], I. Đurišić[2], M. Buta[2], G. Pupić[3], Z. Milovanović[3], D. Gavrilović[4]

[1]University of Belgrade, School of Medicine, Belgrade, Serbia, [2] Surgical Oncology Clinic, Institute for Oncology and Radiology of Serbia, Belgrade, Serbia, [3] Department of Pathology, Institute for Oncology and Radiology of Serbia, Belgrade, Serbia, [4] Data Center, Institute for Oncology and Radiology of Serbia, Belgrade, Serbia

Aim: The aim of this study was to determinefrequency ofthyroid microcarcinomas (TMC) lymphonodal metastases in jugulo-carotid chain (JCC) and central neck compartment, as well as to examine whether sentinel lymph node (SLN) biopsy ofJCCis an accurate technique to select patients with true positive,but clinically and ultrasonically negativelymph nodes, for modified radical neck dissection (MRND).

Methods: In total 206 patients were operated in our Institution from 2002 to 2014 for multinodal goitre, Hashimoto's thyroiditis, adenomas, Graves' disease or increase of serum calcitonin concentration, with incidental finding ofpapillary TMC on frozen section and pathohistology confirmation of medullary TMC. As a standard procedure, SLN mapping was performed with 0.2ml of 1%methyleneblue injected just beneath thyroid gland capsule.All patients underwent total thyroidectomy, central neck dissection and SLN biopsy. SLNs, identified inJCC, were examined by frozen section. If positive, additional MRND was done.

Results: In our study, 93.69% of patients had papillary TMC, 5.34% medullary TMC, while 0.97% had these two combined. Multicentric carcinomas were recorded in approximately 30% of patients. In patients with lymphonodal metastases (30%), JCC metastases were found in 14.63%, central in 24.51%. Definitive pathohistology findings on SLNs showed a 97% match with frozen-section analysis results – these were no false positive findings. The patients with positive SLNs were treated with MRND of the positive JCC. The analysis showed more frequent lateral metastases in patients with tumors 5mm or less in diameter. Specificity and sensitivity of method are 100% and 67%, positive and negative predictive values are 100% and 97%. Method's accuracy is 97%.

Conclusion: The data showed that SLN biopsy is a method more precise than ultrasound or computerized tomography in detection of thyroid carcinoma lateral lymphonodal metastases, even in patients clinically and ultrasonicallystaged N0.In thyroid microcarcinomas, a prognostically most favorable group of patients, this method selected precisely 15% of patients with lateral metastases. Using SLN biopsy for intraoperative assessment of lateral compartment one can avoid unnecessary MRND, as well as to prevent under-treatment of patients with good prognosis. In addition, this method helps optimizing ablative radioiodine treatment.

Key words: Thyroid Neoplasms; Thyroid Diseases; Neoplasm Metastasis; Lymph Nodes; Sentinel Lymph Node Biopsy; Preoperative Period; Neck Dissection; Thyroidectomy

UDC: 616.441-006:616-089.8

Prophylactic central neck dissection in patients with papillary thyroid cancer… whether there is any benefit what so ever

I. Paunović

Center for Endocrine Surgery, KC Serbia, Belgrade, Serbia

In the field of thyroid surgery, nowadays, we rapidly moved from discussion of hemithyroidectomy and/or total thyroidectomy as a preferable operation for papillary thyroid cancer (PTC) to the discussion whether prophylactic central node dissection (PCND) for PTC with clinically negative neck lymph nodes is minimizing the risk of disease recurrence and metastatic spread. The role of PCND in these PTC patients still remains controversial although endocrine surgeons are overwhelmed by a huge number of publications "pro" and " contra" PCND.

The main objective of surgical technique in thyroid surgery is to identify the point of neurovascular intersection as well as to preserve the vascularisation of parathyroid glands. Consequently, there are two major complications in thyroid surgery: permanent recurrent nerve palsy (pRLN) and/or permanent hypoparathyroidism (pHPT).

Meticulous operative technique in dissection of RLN to achieve compartmental clearance of the paratracheal nodes that flank the nerve is absolutely required for PCND. The same operative technique is required for preserving vascularisation of parathyroid glands which is often impossible because inferior parathyroid gland lies in the level VI space and can be easily misunderstood as a lymph node. The above factors make PCND technically demanding, so this procedure should be performed by experienced endocrine surgeon.

Oncologic benefit of PCND compared to potential complications is still questionable. From the author's point of view very large sample size and long-term follow-up are required to demonstrate an oncologic benefit of prophylactic PCND and randomized, controlled trial regarding PCND is likely infeasible.

An endocrine surgeon must always have a clear idea about surgical approach for PTC, because, the majority of PTC patients are coming to surgical institution "healthy" and the primary goal is that they leave the institution in the same condition as at admission. pRLN and/or pHPT after PCND for PTC incapacitate patients' life more than the fact that they had PTC.

Key words: Thyroid Neoplasms; Carcinoma, Papillary; Secondary Prevention; Neck Dissection; Thyroidectomy

UDC: 616.441:611.018.1

Cyto-histological correlation of thyroid nodular disease

S. Tatić, M. Havelka

Institute of Pathology, School of Medicine, University of Belgrade, Belgrade, Serbia

Fine-needle aspiration (FNA) has an essential role in the evaluation of euthyroid patients with a thyroid nodule. It reduces the rate of unnecessary thyroid surgery for patients with benign nodules and appropriately triages patients with thyroid cancer to adequate surgery.
The Bethesda System for Reporting Thyroid Cytopathology recommends six diagnostic categories: Nondiagnostic or Unsatisfactory, Benign, Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance, Follicular Neoplasm or Suspicious for a Follicular Neoplasm, Suspicious for Malignancy, and Malignant.
For a thyroid FNA specimen to be satisfactory for evaluation, at least 6 groups of benign follicular cells are required, each group composed of at least 10 cells.
The term Benign follicular nodule applies to the most common benign pattern: an adequately cellular specimen composed of varying proportions of colloid and benign follicular cells. If resected, virtually all benign follicular nodules turn out to be nodules of a multinodular goiter or follicular adenomas.A benign result is obtained in 60% to 70% of thyroid FNAs.
Atypia of undetermined significance is very heterogenous category. An effort should be made to use this category as a last resort and limit its use to approximately 7% or fewer of all thyroid FNAs.
The purpose of category Follicular neoplasm (FN) or Suspicious for a follicular neoplasm (SFN) is to identify a nodule that might be a follicular carcinoma (FC) and triage it for surgical lobectomy. FNA is diagnostic of many thyroid conditions (eg. papillary carcinoma, Hashimoto thyroiditis), but, with regard to follicular (and oxyphilic) carcinoma, it is better considered a screening test. About 15% to 30% of cases called FN/SFN prove to be malignant. Of those that prove to be malignant, many are FCs, but a significant proportion are follicular variants of papillary carcinoma.
Many thyroid cancers, most especially papillary thyroid carcinoma (PTC), can be diagnosed with certainty by FNA (enlarged nuclei with pale chromatin, intranuclear cytoplasmic inclusions, nuclear grooves etc.).
Approximately 3% to 7% of thyroid FNAs have conclusive features of malignancy, and most are PTC. Malignant nodules are usually removed by thyroidectomy, with some exceptions (eg. undifferentiated carcinomas, lymphomas, and metastatic tumors). The positive predictive value of a malignant FNA interpretation is 97% to 99%.

Key words: Thyroid Nodule; Thyroid Diseases; Thyroid Neoplasms; Diagnosis; Biopsy, Fine-Needle; Cytodiagnosis

UDC: 616.441-006-616-089.8:615.849

Controversies in I-131 therapy of thyroid carcinoma - an individualized approach

M. Luster

Department of Nuclear Medicine, University Hospital of Marburg, Marburg, Germany

The concept of individualized therapy is rapidly gaining importance in the care of differentiated thyroid cancer (DTC) patients and represents a paradigm shift in DTC treatment with multiple implications for clinical practice. There are several areas of DTC management which have undergone or are currently undergoing a development towards personalized treatment. In the majority of DTC cases with an inherently good prognosis the extent of surgery as well as the need for and dosaging of I-131 therapy and the aim of levothyroxine therapy are subject of differentiation towards individualization based both on initial stage as well as response to therapy. In those individuals with advanced disease, newer imaging techniques, insights in I-131 therapy and targeted molecular therapies such as tyrosine kinase inhibitors, some of which are especially indicated in patients with specific mutations, have provided new options for tailored care of patients for whom until recently no effective therapies were available. Another aspect of individualized therapy concerns the reduction of adverse effects, especially the sometimes debilitating hypothyroidism which used to be necessary for effective I-131 treatment and major salivary gland damage, which is one of the most common, but most unpleasant side effects of I-131 therapy. In spite of ongoing research, many aspects concerning the individualized treatment remain to be clarified. In a perfect scenario pre-interventional testing should prompt tailored therapeutic strategies and in selected cases prevent further therapy but rather lead to a watch and wait policy. Patients should be treated by surgery that is appropriate for the extent of the tumor, should then be administered a personalized I-131 activity which optimally should be based on the absorbed dose to be delivered after which follow-up and treatment with levothyroxine should be adapted continuously to the response to treatment.

Key words: Thyroid Neoplasms; Iodine Radioisotopes; Molecular Targeted Therapy; Thyroxine; Protein-Tyrosine Kinases; Patient Care Planning

UDC: 616.441-006:616-089.8:615-085

The role of I-131 ablation and therapy in the management of thyroid carcinoma: Personal clinical experience and Serbian guidelines

J. Mihailović

Department of Nuclear Medicine, Oncology Institute of Vojvodina, Sremska Kamenica, Serbia

Differentiated thyroid carcinoma (DTC) accounts for less than 1% of all human malignancies, thus presenting a rare neoplasm. It has characteristics of normal thyroid gland expressing the sodium iodide symporter which is important for specific iodine uptake. If adequate on-time treatment is performed, in general DTC patients have a good prognosis and outcome. Ablation is defined as an elimination of residual normal thyroid tissue detected after thyroidectomy. The goals of ablation are: to eliminate thyroid remnants in order to increase sensitivity and specificity of patient monitoring by Tg determination and dx WBS; to allow post-therapeutic Rx WBS which may detect previously unknown metastases (occult), and to treat microscopic tumor deposits within the remnant or in lymph nodes or other tissue even if there is no evidence that there is residual tumor. Remnant ablation facilitates detection of recurrences during the patient monitoring. RAI represents adjuvant therapy which decreases the risk of recurrent disease and disease specific mortality by destroying suspicious metastases. Moreover, RAI treats the persistent disease. RAI is a standard procedure in all patients with DTC. However, the therapy of very low and low risk thyroid cancers is controversial since majority of data showed no statistically significant improvements in disease specific survival despite reduced recurrence rates. Our own results show significantly lower probability or recurrence in patients with differentiated thyroid microcarcinoma treated with RAI than those who did not (p=0.005). These authors suggested total or near total thyroidectomy followed by RAI ablation as an optimal treatment resulting in better patient monitoring and recurrence detection. In contrast, they recommend a simple follow-up for those who initially underwent unilateral lobectomy as low risk patients National Serbian guidelines for the management of DTC recommends no radioiodine ablation in unifocal tumors ≤1cm with favourable histology without metastases; minimally invasive follicular carcinoma without vascular invasion <20mm; in those with no evidence of invasion beyond thyroid capsule. In contrast, RAI is indicated in metastases that are present, if uncompleted tumor resection was performed, in patients with completed tumor excision with tumor extension beyond thyroid capsule and if local/locoregional metastases are present. Possible indications for ablation are: less than total thyroidectomy, tumors >10mm<40mm, tumors <10mm with unfavourable histology (papillary: tall-cell, columnar-cell, diffuse sclerosing and follicular: poorly differentiated, wide invasive), multifocal tumors <10mm. The most common method for radioiodine application is method of fixed doses or empiric method:suggested activity for ablation of thyroid remnant is 3.7 GBq; ablation of tumor remnants, regional and/or distant metastasis 5.55-7.4 GBq. Dosimetric studies are also suggested as an alternative method to fixed acitivities. Guideline is established to help in diagnosis and treatment. However, the physician's final decision must be based on the independent decision of referring physicians individually for each patient.

Key words: Thyroid Neoplasms; Ablation Techniques; Iodine Radioisotopes; Neoplasm Recurrence, Local; Practice Guideline; Serbia

UDC: 616.441-006:616-089.8:615.357

Somatostatin-receptor-based localisation diagnostics in thyroid cancer patients with negative iodine whole-body scan

M. Vlajković[1], M. Matović[2]

[1]Faculty of Medicine, University of Niš and Center of Nuclear Medicine, Clinical Center Niš, Niš, Serbia, [2]Faculty of Medicine, University of Kragujevac and Center of Nuclear Medicine, Clinical Center Kragujevac, Kragujevac, Serbia

Total thyreoidectomy followed by radioiodine ablation and thyrotropin hormone suppressive therapy with thyroxin, considered the basis for management the majority of the patients with differentiated thyroid carcinoma (DTC). During the lifelong follow up period it may be formidable to identify recurrent disease in some cases presented with elevated thyreoglobulin (Tg) and negative high-activity iodine-131 whole body scan. Findings indicating the loss of ability to trap iodine while retaining the ability to produce Tg are frequent in both poorly differentiated thyroid carcinomas and the cases of de-differentiation of previously iodine-positive DTC lesions.

The precise localization of thyroid cancer lesions is essential when deciding on the therapeutic strategy, especially in patients unable to benefit from radioiodine therapy. Since thyroid tumor cells express somatostatin receptors, the aim of this review is to present radiopharmaceuticals for somatostatin receptor scintigraphy (SRS) as a potential tool for the detection of recurrences in patients with non-iodine avid DTC, and to indicate possible criteria for the selection of these patients for peptide radio-receptor therapy. This paper describes several radiopharmaceuticals for SPECT and PET SRS used for localization diagnostics in thyroid cancer patients. These include the following: ^{111}In-DTPA-D Phe1-octreotide, ^{111}In-DOTALAN, ^{111}In-DOTA-TOC, ^{99m}Tc-EDDA/HYNIC-TOC, ^{68}Ga-DOTA-TOC PET, ^{68}Ga-DOTA-NOC PET and ^{68}Ga-DOTA-TATE.

Key words: Diagnostic Imaging; Radiopharmaceuticals; Thyroid Neoplasms; Iodine Radioisotopes; Receptors, Somatostatin

UDC: 616.441-006:615.849.2

Treatment of dedifferentiated thyroid cancer

I. Virgolini

Department of Nuclear Medicine, Medical University of Innsbruck, Innsbruck, Austria

Standard treatment of well-differentiated thyroid cancer includes total/near-total thyroidectomy, radioiodine treatment ($^{13}1$I) and long-term thyroid hormone suppressive therapy. Whereas the survival of patients with radioiodine-positive thyroid cancer, even in those patients with persistent tumor, is high, patients with radioiodine-negative cancer have limited therapeutic options. ^{18}F-FDG PET scanning provides a valuable diagnostic tool for characterization of tumor biology, and may help to select the therapeutic modality. Risk stratification in patients with radioiodine-negative thyroid cancer is also based on repeated measurement of thyroglobulin levels, which indicates occult tumor/metastases.Median survival of patients with tumor persistence after radioiodine treatment with proven radioiodine non-avid lesions is reduced to 3 years.

Re-differentiation attempts with rosiglitazone have not shown significant response rates in the long-term follow-up. Response to chemotherapy and external beam radiation is associated with high rates of comorbidity. Phase II trials of chemotherapeutic regimens neither proved effectiveness, with doxorubicin being the substance with the highest response rates along with significant toxicity. In anaplastic thyroid cancer, a case series of five patients has shown good response rates using docetaxel in combination with external beam radiation.

Imaging of somatostatin receptors (SSTR) using ^{68}Ga-DOTA-Tyr3-octreotide (DOTA-TOC) as a tracer for PET has been adapted to the diagnostic assessment of these patients. We have demonstrated that ^{68}Ga-DOTA-TOC-PET provides a sensitivity of 50% and a specificity of 88% and an overall accuracy of 57% for the detection of thyroid cancer lesions compared to ^{18}F-FDG-PET, while these values were 59%, 73%, and 66% compared to radioiodine avidity. ^{68}Ga-DOTA-TOC-PET is of high diagnostic value concerning extension and localization of disease, allowing more comprehensive diagnosis in radioiodine-positive as well as radioiodine-negative thyroid cancer and also in mixed tumor patterns and allows assessment of feasibility of peptide receptor radionuclide therapy (PRRT).

If patients are not eligible for PRRT, molecular targeted therapy using multikinase inhibitors or proteasome inhibitors can be taken into consideration (sunitinib, sorafenib, vandetanib, bortezomib, and others). We have used bortezomibi.v. at a dose of 1.3 mg/m^2 on day 1, 4, 8, and 11. All patients underwent 3 therapeutic cycles with an interval of 10 days in between. Stable disease was seen after this protease inhibitor therapy in 4/7 patients.

In conclusion, in patients with radioiodine-negative thyroid cancer treatment regimens need to be adapted to tumor entity, stage of the disease, and patient condition.

Key words: Thyroid Neoplasms; Radionuclide Imaging; Receptors, Peptide; Molecular Targeted Therapy; Protein Kinase Inhibitors; Proteasome Inhibitors

UDC: 616-052:640.522:004.378.52

Remote radiation monitoring system for patients treated with high doses of radionuclide therapy – personal experience

M. Matović[1], M. Jeremić[2], V. Urošević[3], M. Ravlić[4], M. Vlajković[5]

[1]Department of Nuclear Medicine, Clinical Center Kragujevac and Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia, [2]Department of Nuclear Medicine, Clinical Center Kragujevac, Kragujevac, Serbia, [3]Polytechnic School in Čačak, Čačak, University of Kragujevac, Serbia, [4]Prizma Company, Kragujevac, Serbia, [5]Department of Nuclear Medicine, Clinical Center Niš and Medical Faculty University of Niš, Niš, Serbia

Following the application of the radionuclide therapy, the patient must remain hospitalised for a certain amount of time in special restricted access premises until radiation in their body drops below a certain level. This period usually lasts 2-5 days, and its duration depends on several factors. The most important two are certainly: the radiation dose applied and the ammount of the tumor tissue. But the other factors are of significant importance as well, e.g. those affecting individual biokinetics and biodistribution of used radiopharmaceutical, such as kidney function, the use of various medications, etc. Having in mind the costs of medical treatment on the one hand, and the spatial limitations of the hospital premises for radionuclide therapy on the other, it is of vital importance to estimate as early as possible, when the radiation in a patient's body is expected to drop below the set limit. We have developed our own online remote radiation monitoring system, which measures the exposition dose by means of a pancake probe (LND, model 7312). This detector is connected to a PTZ (PanTiltZoom) device, which enables precise positioning of the detector on the given patient's body part. The positioning of the detector is visually controlled by a high sensitivity micro camera, placed at the centre of detector's point of view. A digital video recorder (DVR) and the appropriate software enable us to control the position of the detector and have a video control of its position at the same time. Furthermore, there are four laser pointers placed around the detector, which can also be controlled by the DVR and which at all times precisely mark the area which detector is 'seeing'. The acquisition of the measured data from the detector to PC is performed using hardware/software developed by Theremino R Italian group.

The entire system enables most precise positioning of the detector during the measurement, as well as the initiation of the measurement through either an Intranet or the Internet. It also enables the WEB based online remote monitoring of radiation levels from different body parts of the patient. The measurements are performed at chosen reference part of the patient's body, at a 1m distance. Thus we can choose the referential zone of highest radiation in accordance with which we can monitor changes in the radiation levels (0, 1, 3, 6, 9 and 12 hours after the application of the radionuclide therapy) and be able to predict, based on those results, when it would drop below the set limit. To process this data, we used our own developed software, which fits the measured data by means of the exponential function. The obtained data can help predict when the radiation levels would reach the set limit. In other words, we can predict when the patient would be released from hospital.

By using this system, we can decrease the overall expenses of health insurance for hospitalised patients in the special, restricted area. Moreover, we can optimise the use of limited hospital space allotted to radionuclide therapy.

Key words: Neoplasms; Radiotherapy; Radiation Monitoring; Radiometry; Radiotherapy Dosage; Software

UDC: 621.039.9:303.4:62-54

Quality Management System in nuclear medical practice

V. Antić[1,2]

[1]University Clinical Centre of Serbia, Belgrade, Serbia, [2]University of Belgrade, School of Electrical Engeenering, Belgrade, Serbia

QUANUM ("Quality Management of Nuclear Medicine Practices") mission have the aim to give incentive for the routine management of systematic process of verification of compliance with the standards of the objective factual perceptions, to apply good clinical practice, improve professionalism and professionalization of identifying improvements that can be implemented. In that sense, the crucial support is given by EARL („European Research Association Ltd"), with appropriate accreditation programs. The complete aspect of quality management in nuclear medicine practice is included: Strategy, Management, Administration, Human Resource Development, Radiation Protection from Ionising Radiation, Quality control of all devices in the Nuclear Medicine Center, Computer Systems, Radiopharmacy, General Clinical Services, Quality Assessment of Nuclear Medical Diagnostic Procedures and Radiotherapy. In order to provide Quality Assurance in nuclear medicine practice in the Republic of Serbia, it is necessary to improve the existing legislation and to form a national expert committee, which is supposed to carry out a general review and to train personnel to be able to satisfactorily operate regular internal auditing.

Key words: Nuclear Medicine; Quality Control; Quality Improvement; Reference Standards; Legislation, Medical; Quality Assurance, Health Care

UDC: 616-006:577.11:616-052

Tc-99m Tektrotyd SPECT/CT in assessment of patients with suspicion of NETs

M. Trogrlić, S. Težak, M. Žuvić, D. Huić

Clinical Department of Nuclear Medicine, University Hospital Centre, Zagreb, Croatia

Aim: Radiolabeled somatostatin analogs have proved very useful in localization of somatostatin receptor expressing tumours. The aim was to evaluate the potential usefulness of ^{99m}Tc EDDA/HYNIC-Tyr3-octreotide (Tektrotyd) SPECT/CT in patients with suspected NET.

Materials and methods: In this retrospective study 21 patients with biochemical (increased tumour markers: chromogranin A (n=14), 5-HIAA (n=5), NSE (n=2)) and/or clinical suspicion of NET, were examined with Tc-99m Tektrotyd between November 2010 and April 2012. Whole body and tomographic acquisition were taken 2 and 4 hours after administration of 666 MBq of Tc-99m Tektrotyd. All the patients underwent SPECT/CT 4 hours after injection of the tracer.

Results: SPECT/CT results were compared with conventional imaging (CT, MRI, EUS) and clinical follow up (range, 22-39 months). Somatostatin receptor positive lesions were found in 9 out of 21 (43%) patients and negative in 12 out of 21 (57%) patients. SPECT/CT results were true-positive in 6 cases, true-negative in 12 and false-positive in 3 cases. Tc-99m Tektrotyd had an overall sensitivity of 100%, specificity of 80%, a positive predictive value (PPV) of 67%, and a negative predictive value (NPV) of 100%. The diagnostic accuracy was 86%. The prevalence of NETs in the studied population was 29% (6 of 21).

Conclusion: Tc-99m Tektrotyd SPECT/CT showed excellent sensitivity in evaluation of patients with suspicion of NETs.

Key words: Diagnostic Imaging; Neuroendocrine Tumors; Radiopharmaceuticals; Tomography, Emission-Computed, Single-Photon; Tomography, X-Ray Computed; Magnetic Resonance Imaging; Organotechnetium Compounds; Somatostatin; Octreotide; Endosonography

UDC: 621.039:004.4:615.07

Validation of numerical outputs of International Atomic Energy Agency Software Package for the Analysis of Scintigraphic Renal Dynamic Studies in healthy individuals

S. Beatović[1,2], D. Šobić-Šaranović[1,2], E. Jakšić[1,2], M. Janković[3], M. Blagić[1], V. Obradović[1,2]

[1]Department of Nuclear Medicine, Clinical Center of Serbia, Belgrade, Serbia, [2]Faculty of Medicine, University of Belgrade, Belgrade, Serbia, [3]Faculty of Electrical Engineering, University of Belgrade, Belgrade, Serbia

Introduction: Under the auspices of International Atomic Energy Agency (IAEA) a software Package for the Analysis of Scintigraphic Renal Dynamic Studies was recently developed and distributed among nuclear medicine institutions. It is expected that implementation of the Software will reduce the heterogeneity in acquisition and processing among departments. The Software enables comprehensive analysis of renal dynamic studies with calculation of excretory parameters and kidney transit times. The aim of study was to validate numerical outputs of IAEA Software for Tc-99m MAG3 renography in healthy individuals. The normal ranges of the following parameters were determined: time to maximum counts (Tmax), time to half-peak counts (T1/2), normalized residual activity (NORA 20/2), postvoid normalized residual activity (NORA PM/2), output efficiency (OE 20), mean transit time (MTT) and mean parenchymal transit time (MPTT).
Patients and methods: 52 potential kidney donors aged 23 to 74 years (mean: 44.4 years) were included in the study. Dynamic scintigraphy was done 22 minutes after bolus injection of 110 MBq Tc-99m MAG3. For all parameters, mean values, lower and upper bound of 95% confidence interval were calculated
Results:
Values of Tmax (min) were: 3.5; 2.5; 5.2.
T1/2 (min): 6.9; 4.7; 10.4.
NORA 20/2: 0.31; 0.24; 0.45.
NORA PM/2: 0.02; 0.01; 0.04.
OE 20 (%): 92; 89; 95.
MTT (min): 2.5; 1.5; 3.5.
MPTT (min): 1.7; 1.2; 2.5.
Conclusion: Implementation of IAEA Software enables the normal limits of quantitative MAG3 parameters to be established. That would improve standardization of renography and facilitates the comparison of reports between physicians and departments.

Key words: Nuclear Medicine; Radioisotope Renography; Technetium Tc 99m Mertiatide; Software Validation

UDC: 612.446:616-053.2:004.4

Diagnostic performance of IAEA software package for the analysis of renal dynamic scintigraphy in children with antenatal hydronephrosis

S. Beatović[1,2], D. Šobić-Šaranović[1,2], E. Jakšić[1,2], M. Janković[3], M. Blagić[1], V. Obradović[1,2]

[1]Department of Nuclear Medicine, Clinical Center of Serbia, Belgrade, Serbia, [2]Faculty of Medicine, University of Belgrade, Belgrade, Serbia, [3]Faculty of Electrical Engineering, University of Belgrade, Belgrade, Serbia

Aim: The objectives of study were to use IAEA Software Package for the Analysis of Scintigraphic Renal Dynamic Studies to obtain values of curve parameters and excretory parameters in children with hydronephrosis (HN) and to validate the reliability of these numerical outputs by comparing with values established by consensus reports.
Patients and methods: 50 children with HN (median age 16 months; 30 boys, 20 girls; 99 kidneys) underwent Tc-99m-MAG3 diuresis renography. Studies were analyzed by two observers and, according to the assessment of images, renograms and differential function, kidneys were classified as normal (42, kidneys contralateral to hydronephrotic kidney), hypotonic unobstructed (49) and obstructed (8). IAEA Software was applied to each renogram. The parameters analyzed were: normalized residual activity at 20 minute (NORA 20) and on the postmicturition acquisition (NORA PM), output efficiency at 20 minute (OE 20), postvoid to maximum renal count ratio (PM/max) and mean transit time (MTT).
Results: Mean values for normal, hypotonic unobstructed and obstructed kidneys were: NORA 20: 0.25; 0.57; 2.16; OE 20 (%): 94.5; 87; 57; NORA PM: 0.02; 0.03; 0.27; PM/max: 0.01; 0.02; 0.13; MTT (min): 1.9; 3.5; 8.9. The difference between obstruction/dilatation and normal/dilatation was significant ($p<0.0001$), as well as the correlation between NORA 20/OE 20 ($R= - 0.982$). The cutoff values to predict obstruction were: NORA20: 1.6; OE 20: 73%; NORAPM: 0.11; PM/max: 0.06; MTT: 8.23 min.
Conclusion: IAEA Software Package gives reliable values of numerical parameters of renal excretion. The use of the software improves diagnostic accuracy of diuresis renography in children.

Key words: Diagnostic Imaging; Hydronephrosis; Radionuclide Renography; Technetium Tc 99m Mertiatide; Diuresis; Child; Software Validation

UDC: 616.441-006:616-053.2:616-089.8

Surgical managment of differentiated thyroid carcinoma in children and adolescents

M. Buta, I. Marković, I. Đurišić, M. Oruci, Z. Milovanović, G. Pupić, R. Džodić

Institute of Oncology and Radiology of Serbia, Belgrade, Serbia

Background: Papillary thyroid carcinoma in children and adolescents is rare but it shows extremely aggressive behavior. Gross lymph node metastases and distant metastases are common on first clinical presentation.
Patients and methods: Forty five children and adolescents were operated at the Institute of oncology and radiology of Serbia due to differentiated thyroid carcinoma (DTC). The median age was 16.6 years (range 7-21). At the time of diagnosis 13% had lung metastases. The total thyroidectomy or completion of thyroidectomy was performed in all cases followed with central neck dissection and frozen section examination of lower jugulo-carotid compartments
Results: The median tumor size was 1.9cm. PTC was found in 44 and FTC in one patient. Multifocal tumors were found in 37% and capsular invasion in 29% and vascular invasion in 24% of cases. LNM in either central or lateral neck compartments were found in 76% of patients. Capsular and vascular invasion were significantly more frequent in children less than 16 years of age. The median follow-up was 127 months. The overall survival rate was 100%.
Conclusion: DTC in children is characterized with high incidence of loco-regional aggressiveness, multifocality, lymph node metastases and distant metastases at the time of diagnosis. Extensive surgical approach should be performed in both primary and recurrent disease in young patients with DTC.

Key words: Thyroid Neoplasms; Thyroidectomy; Neck Dissection; Child; Adolescent

UDC: 616.441-006:616-089.8:615-085:616.071

TBC findings in patient with TENIS Sy referred 18F-FDG PET/CT – case report

D. Srbovan[1], K. Nikoletić[1], R. Jović[2], J. Mihailović[1], E. Matovina[1]

[1]Department of Nuclear Medicine, Oncology Institute of Vojvodina, Sremska Kamenica, Serbia, [2]Clinic of Otolaryngology, Clinical Center of Vojvodina, Novi Sad, Serbia

Introduction: Well differentiated thyroid cancer (DTC) represents about 1% of all malignant tumors. The biological behavior of DTC is known to be a very slowly growing tumor. One year after the initial treatment (surgical treatment and radioiodine therapy), the negative whole body radioiodine scintigraphy (^{131}I-WBS) and optimal serum thyroglobulin (TG) level (<1ng/mL) are the evidence and proof of stable remission of the patient. The elevation of TG and negative ^{131}I-WBS (TENIS Sy-Thyroglobulin Elevation Negativ Iodin Scyntigraphy) indicates further diagnostic procedures –^{18}F-FDG PET/CT to distinguish the spread of disease and to detect the recurrence of disease.
Case report: This case report is about 60-year old patient who underwent TT in 2009 year. Histological findings show papillary cancer-T2bN0M0 stage II. Patient referred to ^{18}F-FDG PET/CT for detection of recurrent disease. The patient was previously treated with III radioiodine (RAI) therapy. After the III RAI therapy ^{131}I-WBS was negative with elevated TG (28.18 ng/mL) under the good endogenous stimulation (TSH-75.25 mIU/mL) and normal level of antithyroglobulin antibodies (ATA). The TG was also elevated under the suppressive hormone therapy with L-thyroxin. ^{18}F FDG PET/CT scan was positive, with FDG avid foci in right para tracheal lymph node of mediastinum SUVmax 11.63, approximates 2cm large. After ^{18}F FDG PET/CT scan, the patient underwent surgery - dissection of mediastinal lymph nodes and of the neck. PH finding of 23 extirpated lymph nodes showed no presence of tumor (PH: Lymphadenitis granulomatosa necroticans mediastini most likely tuberculosis). One month after operative treatment level of TG was decreased (0.569 ng/mL) under the hormone therapy of L-thyroxin.
Conclusion: The results of our study show that FDG PET/CT, although is highly sensitive in the detection of recurrent disease in DTC patients, is not tumor specific tracer. We know that the main reason of false positive TG and true negative WBS can be interference of circulating ATA, and producing Tg from benign lesions (possibly containing thyroiditis) of persistent residual thyroid tissue or nonthyroidal tissue. Our data suggest that in some inconclusive cases we need more radical proof, PH specification is highly recommended to avoid unnecessary treatment procedures.

Key words: Thyroid Neoplasms; Radionuclide Imaging; Diagnosis; Neoplasm Recurrence, Local; Positron-Emission Tomography; Tomography, X-Ray Computed; Fluorodeoxyglucose F18

UDC: 616.33-006:616-079.4:537.1

Highly specific conventional nuclear-medicine method in differential diagnosis of abdominal tumor

M. Todorović-Tirnanić[1,2], S. Pavlović[1,2], D. Šobić-Šaranović[1,2], V. Artiko[1,2], V. Obradović V[1,2]

[1]Faculty of Medicine, University of Belgrade, Belgrade, Serbia, [2]Department of Nuclear Medicine, Clinical Centre of Serbia, Belgrade, Serbia

Introduction: Nuclear medicine diagnostic methods are very sensitive but usually suffer from lack of specificity. The aim of this work is to present a highly specific non-invasive nuclear-medicine method that helped in differential diagnosis of an infraumbilical abdominal mass suspected to be the left ovarian tumor.

Material and methods: A 20 year old female patient with severe left iliac region pain, nausea, vomiting, and an infra-umbilical mass referred to hospital. The left ovarial tumor was suspected and the patient underwent an operation that could not confirm the ovarial tumor, but a mass with 15 cm diameter looking like splenic tissue. Two months later ultrasonography could not detect the splenic tissue in the left hypochondrium, but revealed a splenic-like tissue above the symphisis, suggesting a wondering spleen. The patient has reffered to our department in order to prove or reject the presence of the splenic tissue in this formation. Selective spleen scintigraphy was performed using heat-damaged erythrocytes (20 minutes in 49,5^{0}C water-bath) labelled with ^{99m}Tc. A dynamic study lasting 30 minutes (30s/frame) and static scintigrams of the pelvic region thereafter were obtained. Splenectomy and histopathology were performed after this examination.

Results: Fast sequestration of ^{99m}Tc-labelled heat damaged erythrocytes was registered in the pelvic mass (already during the first minutes after their intravenous injection). Static pelvic scintigrams depicted not only their homogenous trapping in the enlarged pelvic mass (15 x 11 cm), but also in a small, posteriorly located 2 cm in diameter accessory spleen, positioned above the ectopic spleen. During the operation a small accessory spleen in the region of pancreatic tale was found and left in its place. The histopathology of the enlarged spleen (15 x 11 x 5 cm) revealed the normal structure of the spleen.

Conclusion: Selective spleen scintigraphy is a highly specific conventional nuclear-medicine diagnostic method for splenic tissue detection, as well as for differential diagnosis between splenic tissue and tumor masses. In our patient it resolved differential diagnostic problem and lead to splenectomy indicated for the reason of the splenomegaly.

Key words: Abdominal Neoplasms; Diagnosis, Differential; Ovarian Neoplasms; Splenic Diseases; Radionuclide Imaging; Spleen

UDC: 616.24:615-085:615.849.1

Usefulness of FDG PET/CT in evaluation of therapy response in patients with chronic sarcoidosis

I. Grozdić Milojević, D. Šobić-Šaranović, V. Artiko, J. Videnović Ivanov, V. Vučinić, N. Kozarević, N. Petrović, M. Todorović Tirnanić, S. Odalović, M. Stoiljković, V. Obradović

Clinical Center of Serbia Belgrade, Belgrade, Serbia

Aim: To assess usefulness of ^{18}F-FDG PET/CT in evaluation of therapy response in patients with chronic sarcoidosis.

Methods: Study included 66 patients with chronic sarcoidosis and evidence of active inflammation on baseline ^{18}F-FDG PET/CT for which they received therapy. After 12±5 months, 30 patients returned for the follow-up ^{18}F-FDG PET/CT due to evaluation of therapy response. On the follow-up, patients were also asked to indicate changes in clinical status. Baseline characteristics of patients who did and did not return for the follow-up were compared to assess selection bias.

Results: ^{18}F-FDG PET/CT scans on the follow-up revealed absent inflammatory activity in 9 patients, less inflammatory activity in 12 patients and more inflammatory activity in 9 patients. SUVmax was significantly lower at the follow-up examination in all patients (8.46 ± 3.52 vs. 4.90 ± 0.96; $P < 0.05$) especially in mediastinal lymph nodes. Changes in the location of disease were also found on follow-up. ACE et the follow-up was not significantly different from baseline (49.80±19.25 vs. 46.35 ± 25.58, $P = 0.522$). Changes in 18F-FDG PET/CT were consistent with changes in clinical symptoms ($P = 0,019$). There was no difference in baseline characteristics of patients who did and did not return for the follow-up.

Conclusion: ^{18}F-FDG PET/CT is able to detect changes in the magnitude and extent of inflammatory activity after treatment for chronic sarcoidosis. It is a valuable adjunct to clinical evaluation for monitoring of therapy response in patients with active chronic sarcoidosis, especially when the ACE level is normal.

Key words: Sarcoidosis; Chronic Diseases; Treatment Outcome; Positron-Emission Tomography; Tomography, X-Ray Computed; Fluorodeoxyglucose F18

UDC: 616.12-073.7:616.071

Thyroid metastases from a renal cancer diagnosed by fine-needle aspiration biopsy: Case report

E. Matovina[1], K. Nikoletić[1], J. Mihailović[1], D. Srbovan[1], S. Knežević-Ušaj[2], S. Božanić[2]

[1]Department of Nuclear Medicine, Oncology Institute of Vojvodina, Sremska Kamenica, Serbia, [2]Department of Pathology, Oncology Institute of Vojvodina, Sremska Kamenica, Serbia

Introduction: Renal cell carcinoma is a potentially lethal cancer with aggressive behavior and a propensity for metastasis, following occasionally unpredictable patterns of spread. The thyroid gland is an uncommon site for metastasis in cytology practice. Although secondary involvement of the thyroid gland by renal cell carcinoma (RCC) is rare, it is still one of the more common neoplasms to metastase to the thyroid gland.

We report a case of metastatic lesion in the thyroid from renal carcinoma which was recognized in a fine-needle aspiration (FNA) biopsy.

Study design: The patient was a 67-year old woman with a diffuse enlarged, inhomogeneous right thyroid lobe, seen on chest CT, associated with propagation to upper/front mediastinum and bilateral bronchopulmonary lymphadenopathy. Thirteen years ago she had undergone radical right nephrectomy due to renal carcinoma. Ten years later atypical resection of left upper pulmonary lobe was perfomed, followed by chemio- and radiotherapy due to metastatic disease.

Results: Ultrasonography of thyroid bed showed hypervascularized, heteroechogenic soft mass in right thyreoid bed with slitely extended isthmus. The left lobe had normal ultrasonographic features. Laboratory showed slightly increased free threeiodothyronine (FT3), with normal free thyroxine (FT4) and tireoglobulin values. Anti-thyroid peroxidase antibodies as well as anti thyroglobulin antibodies were negative. Ultrasonography guided FNA biopsy of the right thyroid lobe was performed in three directions. Cytology showed light cell adenocarcinoma, most likely metastasis of renal origin.

Conclusion: Every new aggregate in the thyroid in patients with even a long-term history of cancer should be considered as potentially metastatic until proved otherwise. FNA could be helpful in the diagnosis of thyroid metastatic lesion.

Key words: Carcinoma, Renal Cell; Neoplasm Metastasis; Thyroid Neoplasms; Diagnosis; Biopsy, Fine-Needle; Ultrasonography