

ABSTRACT BOOK

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FROM IMAGE TO DIAGNOSIS & TREATMENT
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TOTAL BODY PET IMAGING - A PARADIGM SHIFT FOR NUCLEAR MEDICINE

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Total-body PET (TB-PET) allows for the first time to extend quantitative, physiological and molecular imaging to extended axial imaging ranges of 106 cm to 194 cm, so as to assess multiple organs at the same time as well as their interplay. The introduction of TB-PET has encouraged the clinical community to optimize imaging protocols. The research community has started to investigate multi-organ interactions - the organ connectome for understanding human physiology and pathology. This talk highlights the clinical use cases, but focuses on the potential of using total-body (and whole-body) PET image information to conduct multi-organ connectome analysis for disease phenotyping. Novel data analytics schemes help realise such studies. Novel study protocols and paradigms, as well as translational research pipelines, will be required to support causal interpretations of inter-organ relationships. Ultimately, the widened adoption of total-body PET anticipates new, cross-speciality interactions among scientists, clinicians, and patients. It is our choice to engage in it now.

Keywords: PET/CT, Quantification, Data Analysis

TARGETED RADIONUCLIDE THERAPY (TRT): THE HISTORY OF RADIOPHARMACEUTICAL DEVELOPMENT

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The continuing progress in the development of radiopharmaceuticals opened avenues to a new management of many diseases, switching from a “population treatment” approach to the concept of personalized medicine or precision medicine. The goal of molecular imaging (MI) in nuclear medicine is the noninvasive localization and quantification of certain molecular events in vivo based on positron emission tomography (PET) or single photon emission computed tomography (SPECT) radiopharmaceuticals. The main objective of targeted radionuclide therapy (TRT) is the ability to selectively deliver cytotoxic radiation to cancer cells that causes minimal toxicity to surrounding healthy tissues, using optimized targeting vehicles (such as small organic molecules, peptides, and antibodies) that deliver beta (β^-) or alpha (α) emitting radionuclides into the tumor cells. Theranostics has the potential to develop patient-specific radiation dosimetry strategies based on MI studies, and cell-killing radiation strategies to deliver the optimal therapeutic dose to the right patient at the right time. More than twenty radiopharmaceuticals for MI and eleven radiopharmaceuticals for therapy are in clinical use. In addition, hundreds of radiopharmaceuticals are in preclinical, and clinical investigational studies. This presentation will review the historical development of radiopharmaceuticals for TRT in the last 80 years and covers the importance of radiochemistry strategies, drug product specifications, and clinical applications of FDA approved radiopharmaceuticals such as I-131 MIBG, Lu-177 DOTATATE, and finally Lu-177 PSMA-617. Recent developments and challenges of TRT based on small molecules and mAbs with alpha emitting radionuclides such as 225-Ac will be discussed to highlight the importance of radiation dosimetry.

Keywords: Targeted Radionuclide Therapy (TRT); Radiopharmaceuticals; Theranostics

CHALLENGES IN DEVELOPING THERANOSTIC LABORATORY

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The theranostic concept in nuclear medicine refers to the use of different isotopes for labeling the same ligand specific to the same target. Labeling of the ligand with radionuclide pairs for both diagnosis and treatment should be performed in specialized facilities called theranostic laboratories. The incidence of non-communicable diseases (NCDs) in Balkan countries is escalating, so the development of these laboratories has become increasingly popular. The first challenge in the implementation of this concept is to ensure adequate reimbursement from the national health insurance funds for medical procedures. The shortage of trained personnel in radiopharmacies is a widespread problem in the developing countries. It necessitates the introduction of postgraduate educational programs/specialization in the home country or sending the professionals to foreign countries, which have sufficient infrastructure for training, education, and fellowship programs in theranostic practice. The cooperation with European or international organizations and cooperative work with experts in the field can be very helpful in organizing education. A logistic challenge also represents import of radionuclides, precursors, cassettes, generators, and equipment from distant countries. Moreover, the lack of official technical service representatives makes more expensive the installation, qualification, and maintenance of the equipment. A non-negligible expense is the adaptation of the rooms where the isolators/laminar-flow chambers will be installed and synthesis and quality control of radiopharmaceuticals will be done. In order to improve patient management and to have better outcomes in the treatment of NCDs, some Balkan countries have already found a way to overcome all previously mentioned obstacles.

Keywords: Theranostic, Radionuclide Pairs, Radiopharmacy

THYROID NODULES AND GENETIC TESTING

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In recent years, the need for personalized diagnostics and therapy has increased requirements for improving diagnosis, disease and patient characteristics, developing more efficient and personalized therapeutic regimens, with successful outcomes and avoiding unnecessary therapeutic choices. Additionally to classical diagnostic studies in patients with thyroid nodules, progress in the understanding of molecular - structural interactions, combined with technological progress and available molecular markers, creates relevant multidisciplinary convergences and integrated classical and molecular diagnostics. Molecular profiling (MP) is useful in diagnostic and therapeutic challenge of indeterminate thyroid nodules (ITN) as well as for clinical profiles in differentiated thyroid carcinoma (DTC) and therapy of advanced disease. The choice of molecular testing of ITN should provide analytical, clinical validity and clinical utility, the information if a test can “rule out” cancer (likelihood that a nodule is benign) and reduce diagnostic surgery for benign nodules or “rule in” cancer (likelihood that the nodule is malignant) to optimize extent of surgical treatment. MP includes genomic alterations (such as point mutations, insertions, and deletions), gene fusions resulting in rearrangements or translocations, copy number variations, RNA-based gene expression, and/or micro-RNA expression. Diagnostic tests novelties, risk assessment algorithms and response in individuals and families, counseling dynamics, educational and time-related challenges for nuclear medicine specialties means that redefining the role of clinical geneticists in nuclear medicine may well be required.

Keywords: Thyroid Nodules, Differentiated Thyroid Carcinoma, Clinical Genetic

COMBINATION THERAPIES IN NET IN THE HORIZONE

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A growing body of literature reports on the combined use of peptide receptor radionuclide therapy (PRRT) with other anti-tumour therapies in order to anticipate synergistic effects with perhaps increased safety issues. The combination treatments to enhance PRRT outcome are based on improved tumour perfusion, upregulation of somatostatin receptors (SSTR), radiosensitization with DNA damaging agents or targeted therapies. Several Phase 1 or 2 trials are currently recruiting patients in combined regimens. The combination of PRRT with cytotoxic chemotherapy, capecitabine and temozolamide (CAPTEM), seems to become clinically useful especially in pancreatic neuroendocrine tumours (pNETs) with acceptable safety profile. Neoadjuvant PRRT prior to surgery, PRRT combinations of intravenous and intra arterial routes of application, combinations of PRRT with differently radiolabelled (alpha, beta, Auger) SSTR-targeting agonists and antagonists, inhibitors of immune checkpoints (ICIs), poly (ADP-ribose) polymerase-1 (PARP1i), tyrosine kinase (TKI), DNA-dependent protein kinase, ribonucleotide reductase or DNA methyltransferase (DMNT) are tested in currently ongoing clinical trials. The combination with I-131 MIBG in rare NETs (such as paraganglioma, pheochromocytoma) and new non-SSTR-targeting radioligands are used in the personalization process of treatment. The talk will provide an overview of the current status of ongoing PRRT combination treatments.

Keywords: PRRT, Combination Treatments, Neuroendocrine Tumors

TREATMENT OUTCOME AFTER PEPTIDE RECEPTOR RADIONUCLIDE THERAPY IN PATIENTS WITH NEUROENDOCRINE TUMORS-SINGLE INSTITUTION EXPERIENCE

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Neuroendocrine neoplasms (NENs) are a heterogeneous group of tumors that can arise as primary tumors in almost every organ system of the body. According to the World Health Organization classification, the Ki-67 mitotic index is used to classify them into three degrees. The treatment of these tumors poses a great challenge, with limited and often palliative options for patients with certain types of metastatic NEN. If possible, operative treatment is a primary option, followed by somatostatin analogues, chemotherapy, immunotherapy, mTOR inhibitors, and radiation therapy. Peptide receptor radionuclide therapy (PRRT) represents only one link in a chain of treatment options, especially for well-differentiated neuroendocrine tumors. The aim of this work is to show the current possibilities in the treatment of advanced NEN, as well as to demonstrate the response to treatment and survival of patients with NEN G2 treated with peptide receptor radionuclide therapy. Forty-nine consecutive patients with differently localized tumors displaying neuroendocrine expression were referred to the Center for Nuclear Medicine, 37 of whom had NEN, 8 dedifferentiated thyroid carcinoma, 2 medullary thyroid carcinoma, 1 paraganglioma, and 1 pheochromocytoma. Out of the total number, 3 patients with NEN were excluded from the treatment due to comorbidities, 1 due to the inability to regulate hyperinsulinemia, 1 (pheochromocytoma) due to a severe general condition (Karnofsky score 20%), and 1 patient with NEN G3 due to a significantly low level of radiopharmaceutical binding on the pre-therapy scan with Tektrotyd accompanied by a high degree of metabolic binding of FDG in lesions that did not show up on the somatostatin receptor scan. Thyroid cancer patients will be excluded from this work. The overall response in 34 patients was estimated using RECIST 1.1 criteria at the endpoint of 2 years after the PRRT. Thirty-three patients were treated in accordance with a standard procedure involving the administration of labeled Y-90 and/or Lu-177 peptides with a three-day amino acid renal protection protocol. One patient was treated with In-111 octreotide in Italy. The control laboratory examinations were performed one

month after each cycle, to evaluate possible hematologic toxicity or renal impairment. Before the treatment, all patients except for one underwent somatostatin receptor scintigraphy with Tc-99m Tektrotyd. The remaining patient underwent Ga-68 DOTA-NOC scanning, as it was mandatory to ensure the visualization of pathological changes with a high level of somatostatin receptor binding (Krenning score 3/4) before the treatment. The patients underwent another Tc-99m Tektrotyd scan 6-12 months after PRRT. The overall response to PRRT according to RECIST 1.1 criteria was stable disease in 24, partial remission in 4, and disease progression in 6 patients. After the first cycle of PRRT, four patients were referred for another cycle of PRRT due to progression, 26 continued biological therapy with somatostatin analogues, 2 underwent radiofrequency ablation, and two continued to receive mTOR inhibitors. During PRRT, one patient was excluded after the first cycle due to hematotoxicity, while one patient experienced deterioration of renal function. Peptide receptor radionuclide therapy is a powerful therapeutic tool that represents only one link in the chain of comprehensive treatment of NEN. It has demonstrated high level of success and safety in the control of neuroendocrine tumors, and should therefore be used during the treatment of this disease.

Keywords: Peptide Receptor Radionuclide Therapy, NET, Somatostatin Analogues

PROSTATE-SPECIFIC MEMBRANE ANTIGEN THERANOSTICS FOR CASTRATION-RESISTANT PROSTATE CANCER

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Therapeutical gorithm for prostate cancer initially include Androgen Deprivation Therapy, but eventually resistance occurs and prostate cancer transform into castration-resistant prostate cancer (CRPC). PSMA theranostics is a field of personalized medicine that involves the use of the same or similar radiopharmaceuticals for the diagnosis and treatment of patients. While PSMA is expressed at low levels in normal prostate epithelium, it is overexpressed in 90-95% of prostate cancers increasing with grade of aggressiveness, Gleason score, and resistance to therapy. The highest levels of PSMA expression were found in metastatic disease and CRPC with a poor prognosis. The differential expression of PSMA between normal tissue and tumor cells, as well as the ability of PSMA to be internalized upon binding of antibodies or targeted small molecules, makes PSMA an attractive target for therapeutic treatment with radiolabelled beta emmitters. At the same time, PSMA is a clinically validated target for prostate cancer diagnosis based on positive diagnostic scan. We summarize the first experience with Lu-177 PSMA treatment in CRPC in Serbia in several consecutive patients. Biochemical response was evaluated with clinical, biochemical and hematological toxicity as well.

Keywords: Prostate Cancer, Theranostics, Lu-177 PSMA

SEQUENCING RADIUM-223 DISCHLORIDE [Ra-223] RaCl₂ AND LUTETIUM-177 PROSTATIC SPECIFIC MEMBRANE ANTIGEN [Lu-177] PSMA IN TREATMENT OF mCRPC

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The prostate treatment landscape has continued to evolve. In some countries both Radium-223 dichloride, ([Ra-223] RaCl₂) and Lutetium-177-prostatic specific membrane antigen ([Lu-177] PSMA), received regulatory approval for patients with metastatic castration resistant prostate cancer (mCRPC). Multi-tracer imaging for patients' selection can personalized treatment directing towards the appropriate targeted treatment, sequencing or combination treatment. A large body of real-world evidence (RWE) for [Ra-223] has been published in the decade since the pivotal phase 3, ALSYMPCA study. More than 86.000 patients have been treated with [Ra-223], first targeted alpha treatment (TαT) in clinical practice. International, Prospective, Open-Label, Randomized, Multicenter, Phase 3 Trial of [Lu-177] PSMA-617 in the treatment of patients with progressive PSMA-positive mCRPC (VISION trial) has demonstrated prolonged imaging-based progression-free and overall survival. In VISION, 2.5% of patients received [Ra-223] following [Lu-177] PSMA therapy and 17.4 % received prior treatment with [Ra-223]. The radium lutetium (RALU) study showed that introduction of [Ra-223] early in the treatment sequence in patients with bone-predominant mCRPC and subsequent treatment with [177-Lu] PSMA is feasible, well tolerated and effective. Clinical data from >300 patients in retrospective studies showed that sequential use of [Ra-223] followed by [Lu-177] PSMA-617 is efficacious, without any observed safety signals. World Association of Radiopharmaceutical and Molecular Therapy (WARMTH) retrospective multi centre study indicated that prior [Ra-223] showed a positive impact on overall survival in patients with 6-20 bone metastases or diffuse bone involvement, who also received subsequent [Lu-177] PSMA-617 treatment. Conclusion: The life-prolonging radionuclide molecular therapies may be sequenced with favourable safety profile and a potential to improve patients' outcomes in patients with mCRPC.

Keywords: 223 Radium-Dichloride, 177 Lutetium-PSMA, Prostate Cancer

Ac-225 PSMA VERSUS Lu-177 PSMA TREATMENT: RUSSIAN EXPERIENCE

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Introduction: Russia has created its own radiopharmaceuticals for radioligand PSMA-therapy for mCRPC. Lu-177 PSMA has been used since 2021. At stages 1–2, pharmacokinetics, safety, dosimetry, test activity (5, 7.5 and 10 GBq) and clinical effectiveness were studied. SPECT/CT showed high accumulation of Lu-177 PSMA in metastases (similar to PET/CT). Good safety has been demonstrated. The optimal activity for repeated courses was 7.5 GBq with intervals between administrations of 6–8 weeks. However, with an individual approach, intervals and doses can be individualized. Efficiency of Lu-177 PSMA. After a single injection of 7.5 GBq after 5 weeks, a decrease in PSA by more than 30% was noted in 54% of patients, of which by more than 50% in 29%. Stabilization was observed in 36% of patients. Progression with increase of PSA level more than 30% - in 11%. Ac-225 PSMA has been in MRRC used since 2023. At stages 1–2, pharmacokinetics, safety, dosimetry, test activity (6, 9 and 12 GBq) and clinical effectiveness were studied. Efficiency of 225-Ac PSMA. After a single injection of 9 MBq after 5 weeks, a decrease in PSA by more than 30% was observed in 60% of patients, of which by more than 50% in 40%. Stabilization was noted in 30% of patients. Progression with increase of PSA level more than 30% - in 10%. Conclusions: Lu-177 PSMA and Ac-225 PSMA are effective drugs for the treatment of mCRPC. Ac-225 PSMA is more effective in reducing PSA levels even with more advanced disease. The best efficiency is achieved with high expression of PSMA. Side effects vary. The use of Lu-177 PSMA causes predominantly thrombocytopenia, and Ac-225 PSMA - leukopenia/neutropenia and damage to the salivary/lacrimal glands.

Keywords: Metastatic Castrate-resistant Prostate Cancer (mCRPC), Lu-177 PSMA, Ac-225 PSMA

THORIUM-227-ZOLEDRONATE: 3-IN-1 THERANOSTICS

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Introduction. Bisphosphonates were developed in the 19th century. Initially they were studied in the 1960s for the treatment of bone metabolism disorders. In the 1990s, the real mechanism of their action was demonstrated for alendronate (Fosamax). Bisphosphonates inhibit the activity of osteoclasts and promote their apoptosis. Zoledronic acid, or zoledronate, is a 3rd generation bisphosphonate with a selective effect on bone tissue based on a high affinity for mineralized bone tissue. It highly effectively inhibits the activity of osteoclasts, does not have undesirable effects on formation, mineralization and mechanical properties of bone tissue. It also has direct antitumor properties, providing additional effectiveness in bone metastases. Alpha-emitting isotopethorium-227 (radioactinium) is relatively easy to produce. It can be prepared indirectly by neutron-irradiation of Radium-226. Product will contain also thorium-227 parent nuclide, i.e. actinium-227 ($T_{1/2} = 22$ years). Actinium-227 can be quite easily separated from the Radium-226 target and used as a thorium-227 generator. If necessary, this process can be scaled up to an industrial level, and therefore the supply problem experienced with most other alpha-emitters being considered as candidates for molecularly targeted radiotherapy can be avoided (eg. actinium-225). Thorium-227 decays to radium-223 (Actinium X), which has a half-life of 11.4 days. Method for producing thorium-227 bioconjugate using the DOTAGA-anhydride chelator with modified zoledronic acid ensures its stability in a biological environment (blood serum and/or whole blood) and to radiolysis in solutions. Treatment of metastatic bone disease include targeted delivery of a therapeutically effective amount of thorium-227 complex therapeutic agent to bone metastases, and, subsequently, as a result of the decay of the applied thorium-227, an acceptable non-myelotoxic amount of next alpha-emitter – radium-223 is formed in vivo. Conclusion: (1) Radionuclide therapy for bone metastases is an uncontested method that allows pain relief in most patients without the use of narcotic analgesics and significantly improves their quality of life. (2) Use of therapeutic doses of zoledronate as a carrier allows parallel therapy with bisphosphonates. (3) Daughter radionuclide (radium-223) continues its therapeutic effect in pathological foci.

Ke words: Thorium-227, Zoledronate, Radium-223

VENTILATION/PERFUSION TOMOGRAPHY V/P SPECT VS. MULTISLICE COMPUTED TOMOGRAPHY MSCT IN DETECTION OF PULMONARY EMBOLISM - PROSPECTIVE STUDY

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Pulmonary embolism (PE) is a life-threatening emergency that, given the serious complications, requires the urgent application of anticoagulant therapy. The two basic imaging methods used in diagnosing PE are the radiological method-Multislice computed tomography (MSCT) and nuclear medicine method-Ventilation/perfusion single-photon emission computed tomography (V/P SPECT). Each of the two mentioned diagnostic methods (MSCT and V/P SPECT) has certain advantages and disadvantages compared to the other. The primary aim of the study is to determine the sensitivity and specificity of MSCT and V/P SPECT in the diagnosis of PE. Also, the study includes the identification of the frequency of other lung disease in patients with suspected PE using MSCT and V/P SPECT. Out of the total of 100 patients included in the study, 45 were males, and 55 were females. 37 of the total number of subjects included in the study were not diagnosed with PE, while 63 of the patients were diagnosed with PE and underwent anticoagulant treatment. The study was conducted as a prospective clinical study.

Keywords: Pulmonary Embolism, V/P SPECT, MSCT

IMAGING TUBERCULOSIS: BEYOND DIAGNOSIS AND EVALUATION OF TREATMENT

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Antiretroviral therapy (ART) improves survival in HIV-infected adults with pulmonary tuberculosis (TB) but ART mediated functional immune restoration may trigger the TB immune reconstitution inflammatory syndrome (TB-IRIS). We used FDG PET-CT to test the hypothesis that robust ART-mediated immune recovery induces pulmonary inflammation and impairs lung function in HIV/TB co-infected adults. Increases in lung TGA during the initial 4 weeks of ART tended to occur in subjects who developed an FEV1 decrease or worsening symptoms. The participants with increasing lung TGA on ART had significantly greater increases in the frequency of PPD-specific CD4+ T cells expressing TNF α and IFN γ from baseline to week 4post-ART. The most robust associations were between increase in lung TGA and increase in the frequency of PPD-specific CD4+Tcells expressing both cytokines following ART initiation ($p<0.001$). Lung inflammation on FDGPET-CT is associated with worse lung function and symptoms prior to ART initiation and that greater recovery of pathogen-specific CD4 cell function on ART is associated with increased pulmonary inflammation and decreased lung function in HIV-infected individuals with pulmonary TB. The greater baseline to week-4 increases in PPD-specific CD4+ T cell responses in those who developed worsening pulmonary inflammation and lung function on ART supports a causal role for these cells in lung damage. In the same vein, the use of molecular imaging to select potential host directed therapy is possible. Furthermore, novel molecular imaging agents like a *Ga-68 CBP8* may assist to identify patients at risk of developing post-TB lung disease (PTLD) before they start TB treatment.

Keywords: TB-IRIS, FDG-PET/CT, Ga-68 CBP8

F-18 FDG-PET/CT IN LUNG CANCER

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At present, PET-CT with 18-Fluoro-2-deoxy-d-glucose (18F-FDG) is the standard of care in the management of non-small-cell lung carcinoma (NSCLC), with an irreplaceable role in the initial evaluation (staging), follow-up, therapy monitoring, restaging and – more recent for the radiotherapy planning (an evolving indication). Moreover, FDG PET-CT is a remarkable tool for the characterization of solitary lung nodules (SLN), with a very important role in risk stratification for malignancy and subsequent management. The increased uptake of F-18 FDG-PET/CT in lung cancer cells is the result of the changes in glucose metabolism: increased levels of glycolytic enzymes and over expression of glucose transporters (GLUT1 and 3). Besides, adaptation to hypoxia results in increased dependency on glycolysis as an energy source; this phenomenon is characteristic for rapidly growing tumors. In this paper, we'll present the latest advances in the use of FDG-PET/CT in the NSCLC, particularly in the therapy planning and monitoring.

Keywords: Lung Cancer, PET/CT, 18-Fluoro-2-Deoxy-d-Glucose

LUNG NEUROENDOCRINE TUMORS – THERAPEUTIC APPROACH

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However, most often, it appears in the thorax at tracheobronchial tree and the thymus. NETs are a group of tumors with heterogenous malignancy that evolve from neuroendocrine cells, with the lung being the second target organ after the gastrointestinal tract. These rare tumors are usually asymptomatic and non-functional with little information regarding incidence in the specialty literature. The modern treatment focuses on molecular diagnosis data and by using this molecular landscape we establish a differentiation of lung neuroendocrine tumors (LNETs). The new data were revealed regarding histological evaluation, genetic aberrations. The prognosis depends on the type of LNET that were found to determine the systemic treatment . The efficient management depends on multidisciplinary approach which in turn leads to overall life expectancy, especially in patients with functional tumors.

Keywords: Lung Neuroendocrine Tumors, Molecular Diagnostic, Systemic Treatment

NUCLEAR MEDICINE IN DIAGNOSIS OF HEART AMYLOIDOSIS

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Introduction: First study indicates that heart DPD-uptake can be seen in patients with ATTR-cardiac amyloidosis that was conducted by Perugini et al in 2005, though DPD-scan became widespread used in diagnosis of cardiac amyloidosis after Gillmore et al in 2016 confirmed its high diagnostic accuracy in detection of ATTR-cardiac amyloidosis. The latter study also implicated that patients with negative DPD-scan and no light-chains in serum, have very low probability of having cardiac amyloidosis. Amyloid scan is indicated in patients with left ventricle hypertrophy >1.2 cm, measured either with ultrasonography or MR, that cannot be explained by other heart disease. Methods: SPECT-based radiopharmaceuticals: Tc-99m Biphosphonates are not expensive and easily available radiopharmaceuticals, used both for bone- and amyloid scan. Amyloid scan whole body images taken 3 hours after injection of 500-700 MBq Tc-99m (DPD/HMDP/PYP) are analyzed either with ranging the myocardium uptake after Perugini criteria (DPD/HMDP) or calculating H/CL ratio (heart/contralateral lung) between heart uptake and uptake in the corresponding area on the contralateral side (PYP). If the uptake in myocardium is grade 1-3 or has a H/CL ratio $> 1,5$, examination should proceed with SPECT/CT of the heart to both localize and determine uptake intensity in left and right ventricle. PET-based radiopharmaceuticals: PET-based amyloid-binding radiopharmaceuticals (such as F-18 florbetapir, F-18 florbetaben, F-18 flutemetamol and C-11 labeled Pittsburgh Compound-B (PiB), used regularly for diagnosis of beta-amyloid in patients with Alzheimer disease, can additionally be used in diagnosis of cardiac amyloidosis. The use of PET amyloid radiotracers show promise, however, further data are needed to define their overall accuracy and additive value in diagnosis of cardiac amyloidosis. Conclusion: SPECT-based radiopharmaceuticals are most used in diagnosis of cardiac amyloidosis, considering easy availability and low cost. Intense heart uptake, followed with blood examination excluding AL-amyloidosis, has a high specificity and sensitivity for heart ATTR.

Keywords: Cardiac Amyloidosis, PET/CT Heart Imaging, SPECT/CT Heart Imaging

THE EPIDEMIOLOGICAL AND CLINICAL CHARACTERISTICS OF AUTOIMMUNE THYROIDITIS IN THE TUZLA CANTON IN THE PERIOD FROM 2015 TO 2020

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Introduction: Bosnia and Herzegovina (B&H) is one of the countries of Southeast Europe with a need for more data about chronic autoimmune thyroid diseases (CAITD) epidemiology. **Objective:** This research aimed to assess the incidence of CAITD in the Tuzla Canton of B&H during 6 years (2015–2020). **Methods:** We retrospectively evaluated 82000 hospital records of inpatients and outpatients with possible thyroid symptoms residing in Tuzla Canton of B&H (total of 445,028 inhabitants). The study included patients with laboratory and clinical proof of autoimmune thyroid diseases (AITD). The incidence rates were calculated with age standardization using the European standard population. The trends in incidence were evaluated as moving three-year averages. **Results:** During the observed period, 1875 patients satisfied the diagnostic criteria for CAITD with a male-to-female ratio of 1: 8.01. The median age of all cases was 46 years (interquartile range: 31 to 61) and women and men were on average the same age at the time of diagnosis. The overall standardized incidence was found to be 71.25 per 105 (%95 CI=63.36–79.15). The overall standardized incidence in men was 16.25 per 105 and 123.74 per 105 in women. In the end of the observed period, AITD prevalence was 427.52 per 105 (% 95 CI=408.17-446.87). **Conclusion:** There was a slight incidence decline in our region during the observed period. This decrease might result from a combination of various factors, mainly the Corona epidemics outbreak, and emigration. Based on the lower incidence rate in Tuzla Canton, one can assume that iodine prophylaxis carried out to eradicate goiter had satisfied expectations because there had not been any enormous increase in patients with AITD.

Keywords: Chronic Autoimmune Thyroid Diseases, Epidemiology, Statistics

PREDICTING EARLY RESPONSE TO RADIOIODINE THERAPY IN PAPILLARY THYROID CARCINOMA USING SUPERVISED MACHINE LEARNING APPROACH: A PILOT STUDY

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Introduction: The three-tiered American Thyroid Association risk system primarily relies on data obtained from pathological analyses, overlooking other potential risk factors. This limitation hinders accurate prediction of occult, regional, or distant metastases after surgery. Since decisions on radioactive iodine (RAI) therapy often rely on this system, determining whether to administer therapy and deciding on the appropriate dosage becomes a challenging task. **Aim:** This pilot study assessed four machine learning (ML) classifiers to predict early responses to RAI treatment in PTC patients, aiming to identify those at higher risk of therapy failure. **Methods:** The classifiers were developed utilizing clinico-pathological, molecular, and laboratory data collected from 95 patients who underwent both surgical and RAI treatment. The therapy response assessment categorized patients into two groups: excellent response and RAI therapy failure, encompassing indeterminate, biochemical incomplete, and structural incomplete responses. The ultimate ML classifier was chosen based on the highest specificity and minimal overfitting, while maintaining high sensitivity. **Results:** Among the evaluated models, the k-Nearest Neighbor (k-NN) classifier emerged as the best fit, boasting an area under the receiver operating characteristic curve of 0.82 and sensitivity, specificity, positive and negative predictive values, and F2 score of 0.90, 0.45,

0.44, 0.91, 0.75. Notably, the most significant risk factors predicting RAI failure were the lymph-node ratio (LNR), and a postoperative stimulating thyroglobulin (sTg) level. A LNR exceeding 0.36 and a sTg level above 7.38 ng/ml predict a higher likelihood of RAI therapy failure. Conclusion: Our findings suggest that the k-NN model demonstrates potential in predicting early responses to RAI therapy, offering valuable insights into the significance of identified risk factors, such as lymph-node ratio and postoperative stimulating thyroglobulin levels.

Keywords: Papillary Thyroid Carcinoma, Radioactive Iodine Treatment, Machine Learning

SURGICAL MANAGEMENT IN ADVANCED DIFFERENTIATED THYROID CARCINOMA

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Introduction: Locally advanced thyroid cancer affects the surrounding structures, primarily larynx, trachea, pharynx and esophagus. The possibilities of surgical treatment range from radical operations to palliative interventions with the aim of deobstructing the airway. The aim of the paper is to point out the importance of good diagnostics, good planning and application of various surgical techniques for resection and reconstruction of locally advanced thyroid cancer. **Materials and methods:** Data and results of treatment of patients with locally advanced thyroid cancer were processed through a retrospective analysis. The results of treatment and types of operative techniques applied in patients treated over a period of twenty years are presented. In all of them, it is an extracapsular invasion of the cancer with involvement of the surrounding tissue, predominantly the respiratory tract. **Results:** Except for anaplastic carcinoma and lymphoma, where the treatment ended with tracheostomy, in all others it was an operable carcinoma, and one of the surgical techniques of airway resection and reconstruction was applied. The larynx resection (total or conservation laryngectomy) and tracheal resection with reconstruction were performed. None of the patients had invasion of the entire thickness of the esophagus wall, so apart from partial resection of the invaded part, no major and extensive interventions were performed on the esophagus. Palsy of the recurrent nerve, either by cancer invasion before surgical intervention or as a result of resection of the tumor-affected nerve, was solved by laterofixation with preserved nerve integrity, or by temporary tracheostomy, and later by arytenoidectomy with closure of the tracheostomy for resected nerves. Neck metastasis surgery was performed during the primary surgery. In addition to the VI group dissection, a selective neck dissection was performed unilaterally and bilaterally. In a small number, a modified radical neck dissection was applied. **Conclusion:** Although the number of patients with locally advanced thyroid cancer is not large, the achieved functional and oncological results, in differentiated cancer, indicate that surgery extended to the surrounding, affected structures of the neck is the basis of treatment for advanced thyroid cancer. A good reconstruction of the resulting defects gives good functional results.

Keywords: Advanced Differentiated Thyroid Cancer, Resection, Reconstruction

RADIOIODINE THERAGNOSTICS FOR ADVANCED DIFFERENTIATED THYROID CANCER

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This course will present the role of diagnostic radioiodine imaging and for completion of staging of thyroid cancer patients after total thyroidectomy and will address the selection of prescribed I-131 activity for adjuvant treatment and for treatment of regional and/or distant metastases. The lecture will focus on the practical knowledge in the clinical practice of thyroid cancer theragnostics. The target audience will include physicians and trainees (residents and fellows) in nuclear medicine. The course will review core clinical knowledge regarding the interpretation of classic planar radioiodine scintigraphy and therapeutic I-131 administration and will update the participants with new information regarding I-131 SPECT/CT and PET/CT in thyroid cancer. The expected outcome of the new information provided to the audience in this course is that the participants will be able to select the patients who will benefit from radioiodine therapy and be able to offer an individualized treatment plan, by integrating disease stage and risk stratification, as well as addressing the option of dosimetry calculations, when deciding the prescribed therapeutic I-131 activity. The attendees of this course will be offered a logical, comprehensive approach to the diagnostic evaluation and selection of patient-specific activities for scenarios commonly encountered in clinical practice. The state-of-the-art techniques will be reviewed for diagnostic scanning and dosimetry. Attendees will learn how to establish a thyroid cancer theragnostics practice at their respective institutions that starts with initial post-thyroidectomy evaluation and follows through to the advanced and recurrent disease.

Keywords: Radioiodine Theragnostics, Thyroid Cancer, Pre-ablation Scan

NEW RECOMMENDATIONS FROM ATA & ETA GUIDELINES IN THE MANAGEMENT OF JUVENILE DIFFERENTIATED THYROID CARCINOMA

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Juvenile differentiated thyroid carcinoma (JDTC) is a rare neoplasm, accounting for 0.5%–3% of all childhood malignancies. In 2015, The American Thyroid Association Guidelines Task Force on Pediatric Thyroid Cancer published the Management Guidelines for Children with Thyroid Nodules and Differentiated Thyroid Cancer with new recommendations. Soon after, the European Thyroid Association Guidelines for the management of pediatric thyroid nodules and DTC recommended similar management algorithm for JDTC. The goal of radioiodine treatment is to decrease the risks of recurrence and to improve mortality by eliminating iodine-avid disease. In addition, it is important to reduce/eliminate unnecessary I-131 exposure for children without increasing disease specific morbidity and mortality. Radioiodine therapy is indicated in iodine-avid persistent locoregional or nodal disease that cannot be resected and in patients with known/presumed iodine avid distant metastases. JDTC patients with persistent disease who need additional courses of I-131 treatment, should get individualized treatment approach based on clinical data and previous response. In our institution, we analyzed the probability of recurrence which was 16.7% at 5 years, 22.3% at 10 years, and 33.3% at 15 and 23 years after the initial treatment. The strong predictive factors for recurrence were age ($p < 0.001$), initial treatment ($p < 0.0001$), and tumor multifocality ($p < 0.011$). Conclusions: Recommendations for treatment of JDTC are published by the ATA and the ETA recently. Treatment with radioiodine is safe, with no adverse effects on fertility or secondary malignancy.

Keywords: Differentiated Thyroid Carcinoma, Juvenile, Radioiodine Therapy

RADIOIODINE THERAPY FOR DIFFERENTIATED THYROID CANCER IN CHILDREN: OUR OWN EXPERIENCE

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Children are not "miniature" adults! Most experts around the world recognize the differences between adult and pediatric thyroid cancer (TC) and emphasize the need for specific guidelines for the pediatric population. In comparing the two guidelines (ATA 2015 and ETA 2022) with each other and with Russian clinical guidelines for the treatment of childhood TC, we found significant differences in determining the tactics of treatment and examination during radioiodine therapy (RIT). The aim of report is to analyze our experience with RIT in children with DTC and to identify the most unresolved issues in the context of current international and Russian recommendations. From December 2021 to February 2023, 55 pediatric patients (median age 14 years (6-18), 41 girls and 14 boys) underwent 58 RIT courses at the N.N. Blokhin National Medical Research Center of Oncology (Russia). All patients underwent surgical treatment of a primary or recurrent tumor. According to postoperative histological examination, 40 (72.7%) patients were diagnosed with classic papillary cancer (PC), 8 (14.6%) patients had aggressive subtypes of PC and 7 (12.7%) patients had follicular variant of PC. The evaluation of the primary tumor process extent revealed: multifocality in 22 (40%) patients, involvement of neck lymph nodes in 47 (85.1%), lung metastases in 8 (14.5%). Adjuvant RIT to ablate residual thyroid tissue and reduce the risk of recurrence were performed at an average ^{131}I activity of 2 GBq (1.1-4 GBq), therapy of lung metastases with ^{131}I 4 GBq (1.83-4GBq). Out of 8 patients with lung metastases, 3 patients had radioiodine refractory process. Lung metastases were associated with an advanced primary process (T3-4, N1b) and high TTG-stimulated thyroglobulin levels (from 118 ng/ml to >5,000 ng/ml). Conclusion: On the way to a personalized treatment strategy for children with DTC prospective multicenter studies and the creation of international registries are needed.

Keywords: Thyroid Carcinoma, Radioactive Iodine I-131, Treatment

THE ROLE OF EXTERNAL BEAM RADIOTHERAPY IN THYROID CANCER TREATMENT

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External beam radiotherapy (EBRT) can be used in the treatment of thyroid cancer in definitive (radical), adjuvant and palliative settings in both differentiated and undifferentiated cancer type. The evidence supports the doses of at least 60Gy as definitive treatment for unresectable disease. The complete clinical response can be achieved in approximately 20% of patients. Patients with differentiated thyroid cancer (DTC) commonly have a good prognosis. However, 15–33% of DTC patients have a primary or develop during the treatment iodine refractory-differentiated thyroid cancer. Postoperative EBRT in patients with residual iodine refractory-differentiated thyroid cancer is still inconclusive, but there are results that patients could have improved local control if EBRT is used. High-risk differentiated thyroid cancer with lymph node metastases, distant metastases, extrathyroidal/extracapsular extension, tumor size > 4 cm, ages between 15 and 45, radiotherapy in patient history or FS + could benefit from EBRT. Undifferentiated types such as medullary, anaplastic or metastatic thyroid cancer benefit from adjuvant or palliative radiotherapy. There are no randomized studies to clarify the role of EBRT in medullary thyroid cancer. In the available literature, radiotherapy reduces the risk of loco regional relapse, especially in those with nodal involvement, extrathyroidal extension or residual disease without an impact on overall survival. As 70% of primary medullary cancers present with nodal involvement, 30 % demonstrate extracapsular extension and 10% have metastatic disease, it is clear that most of the patients with medullary cancer could benefit from EBRT at some point of the treatment. Modern radiotherapy techniques such as Intensity Modulated Radiotherapy (IMRT), Volumetric-arc Therapy (VMAT), Cyber knife therapy or proton therapy provide safe radiation delivery, excellent sparing of the surrounding tissues and dose escalation to the tumor or lymph nodes. Therefore, it is to be expected that EBRT can be even more used in the future. External Beam Radiotherapy in Thyroid Cancer treatment is effective treatment option, however its role still remains unclear. There is a lack of adequately powered, high-quality studies, so current practice is based mainly on the individual approach,

Keywords: External Beam Radiotherapy, Thyroid Cancer, Radiotherapy Techniques

PARATHYROID GLAND: UPDATE OF MOLECULAR IMAGING

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The primary objective of parathyroid imaging is to identify all sources of excessive parathyroid hormone secretion before surgical intervention. Scintigraphy with Tc-99m Sestamibi, or dual tracer Tc-99m pertechnetate and Tc-99m sestamibi, with or without SPECT or SPECT/CT, is considered standard practice. This molecular imaging approach detects cellular physiology, including mitochondria content found in parathyroid adenomas. The integration of structural imaging with molecular imaging in a hybrid approach allows for obtaining comprehensive structural and functional information in a single examination. Radiolabeled choline (C-11 choline or F-18 choline) has recently been explored and used as a promising PET tracer for detecting hyperfunctioning parathyroid tissue. Choline uptake is increased by choline kinase upregulation, and phospholipid-dependent choline kinase is upregulated where PTH is oversecreted. The recent advances in preoperative localization of abnormal parathyroid glands in PHPT have allowed more accurate and potentially curative minimally invasive surgical treatments for patients.

Keywords: Parathyroid Imaging, Cellular Physiology, Functional Information

SENTINEL LYMPH NODE DETECTION IN BREAST CANCER: SPECT/CT WITH RADIOCOLLOIDS AND BEYOND

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Introduction: Sentinel node lymphoscintigraphy (SLN) and biopsy have become standard practice for lymphatic staging in early-stage breast cancer. SPECT-CT can detect a precise localization of SLNs and the second echelon LNs in axillary and extra-axillary regions. The aim of our study: to evaluate SPECT-CT imaging of SLNs with different Tc-99m radiocolloids in patients with early breast cancer (BC). Materials and methods: 132 patients (pts) with early BC T1-2 N0 clinically underwent SPECT/CT visualization of SLNs and the second echelon LNs with a different size of Tc-99m radiocolloids. The tracers included: Tc-99m Phytate (Technephyte; DIAMED, Russia) - 50 pts, Tc-99m Rhenium sulfide (Nanotech; DIAMED, Russia) - 41 pts, and a relatively new radiotracer Tc-99m-Al₂O₃ (Alotech; UralPharma, Russia) - 41pts. The radiopharmaceuticals have different size of particles: Technephyte–1,000nm (large), Nanotech- 100nm (small), and Alotech <50nm (very small). The imaging of SLNs in all pts was performed 120 minutes after intra-peritumoral injection of 0.2-0.3ml (100-150MBq) of Tc-99m radiocolloids. All regional lymph nodes that accumulated radiocolloids (SLNs+ second echelon LNs) were detected on SPECT-CT images and localized according to anatomy. The number and topography of LNs detected after the injection of Tc-99m radiocolloids were evaluated. Results: In our study LNs were visualized in 95-98% cases for each type of radiocolloids. The mean number of detected on SPECT-CT imaging LN was different: 1.6 ± 0.16 for Technephyte; 2.76 ± 0.26 for Nanotech and 4.95 ± 0.48 LNs for Alotech ($p < 0.05$). We determined high differences in distribution (topography) of LNs after injecting different ^{99m}Tc-radiocolloids. The incidence of detection internal mammary SLNs was 4 in 48 pts (8%) for Technephyt, 3 in 40pts (7%) for Nanotech and 10 in 39 pts (24%) for Alotech. The extra axillary LNs detection rate was also different and found in 5 (10%), 16 (39%) and 31 (75%) cases, respectively. Conclusion: SPECT-CT examination with radiocolloids demonstrated a different localization of sentinel and the second echelon LNs in patients with breast cancer. The topography of these LNs significantly depends on the type (size) of Tc-99m radiocolloids.

Keywords: SPECT/CT, Sentinel Lymph Nodes, Breast Cancer

MOLECULAR IMAGING OF LYMPH NODE METASTASIS: FROM IMAGE TO DIAGNOSIS

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Lymph node imaging is a useful technique, aiding the clinician in determining whether nodes are benign or malignant. The most important imaging techniques nowadays are: sonography, CT, MRI (contrast MRI, DWI, MR spectroscopy, interstitial administration of lymphangiographic contrast) and nuclear medicine methods (PET, PETCT, PETMRI). Multiple diagnostic modalities are used for the assessment and characterization of lymph nodes, each with its advantages and drawbacks. The most used standard parameters in lymph node differentiation are based on nodes morphology: shape, diameter, internal structure, margins, position of the hilus, thickness of the cortex, vascularization assessment and their relationship to the surrounding structures. Modern molecular methods estimate the nature of lymph nodes according to their vascularity – MRI (enhancement kinetics, flow kinetics, blood volume microvascular permeability), elevated metabolite - MRS (elevated choline levels have been associated with metastatic lymph nodes), MRI with USPIO is an adjunct technique using ultra small superparamagnetic iron oxide particles (lymph nodes show several patterns of uptake which is helpful in the characterization of lymph nodes, interstitial administration of lymphangiographic contrast with MRI helps in identification of sentinel nodes and the course of draining lymphatics, PET has gained importance in recent years in identifying small nodal metastases F-18 FDG is the main radiotracer used, and it is avidly taken up by malignant cells with high rates of glycolysis. Despite all mentioned imaging modalities histopathology remains the gold standard for the final diagnosis.

Keywords: Lymph Nodes, Metastases, Molecular Imaging

PET/CT & BREAST CANCER

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Breast cancer is the most common malignancy in woman and its incidence is still growing. The 5-year survival rates are approximately 75% with ranges of 92% for stage I to 15% for stage IV disease. F-18 FDG PET/CT is not routine for early diagnosis of breast cancer, although it has potential for detection of malignant lymph nodes lymphoscintigraphy with sentinel node biopsy is preferred method. PET/CT scanning should be performed for patients with stage III disease or when conventional staging studies yield non-diagnostic or suspicious results. Used in this clinical setting F-18 FDG PET/CT can upstage the patients, thus influencing the further management. Having in mind the molecular subtypes of breast cancer, and the need for personalized approach in the management of breast cancer the patients novel radiopharmaceuticals have been developed that provide more information on the tumor biology hence it can provide guidance toward targeted therapy. With the use of F16a-[F-18] fluoro-17b-estradiol (F-18 FES), estrogen receptor (ER) status of the lesions can be assessed in vivo. This possibility is very useful because discrepancies in ER expression between the primary tumor and the metastasis is observed in 16%–40% of patients. PET/CT with trastuzumab labeled with Zr-89 or Ga-68 or Cu-64 can provide information on theHER2 receptor status of the lesions. The studies have been conducted to image the progesteron receptor status with [F-18]-fluorofuranyl norprogesteroneand androgen receptor status of the tumor with 16β-[F-18]fluoro-5α-dihydrotestosterone. Recently Ga-68 DOTA FAPI has proven very high sensitivity in detection of metastases from breast cancer, and also opened the way for research for the 88 Lu labeled theranostics in these patients. The functional imaging with PET tracers can provide valuable information in patients with breast cancer that have profound impact in the clinical management.

Keywords: Breast Cancer, PET/CT, Imaging

REDEFINING PROSTATE CANCER STAGING AND MANAGEMENT IN THE ERA OF PSMA PET/CT

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Prostate cancer is a systemic disease and understanding the concept of treatment is important to understand the type of imaging required at each point. The estimated burden of prostate cancer accounts for almost 29% of cancer in males and accounts for estimated 11% of cancer related deaths. The available modalities for imaging in prostate cancer includes USG/TRUS, CECT, mpMRI/WB MRI and PET-CT with F-18 Choline, F-18/Ga-68 PSMA and F-18 FDG in certain situations. The indication for PSMA PET-CT can be divided into routine clinical and potential indications. It is routinely used in the initial staging of Ca Prostate, localization of recurrence or persistent disease, localization of metastasis in patients with negative conventional imaging and in evaluation before PSMA directed RLT. Potential indications include guidance for biopsy, detection of metastatic disease and monitoring of systemic treatment. The 2022 different guidelines for imaging prostate cancer states that there is a strong evidence in not using additional imaging for staging purposes in low risk PCa and use of at least one abdominopelvic cross sectional imaging and a bone scan in intermediate or high risk disease. PSMA imaging is recommended in this setting to increase sensitivity keeping in mind the lack of outcome data of subsequent treatment changes. PSMA PET-CT imaging in initial staging is thus indicated in PCa with high risk features where it has higher accuracy in comparison to conventional imaging to the tune of 27% (Pro PSMA trial) along with high specificity for pelvic lymph nodal metastasis. In head to head comparison of Ga-68 PSMA-11 PET-CT and mpMRI with histopathology in the detection, intra-prostatic localization and determination of local extension of primary prostate cancer, it was found that both imaging modalities performed equally in detection, intra-prostatic localization and delineation of tumor extent, with mpMRI superior in delineating the T stage. PSMA PET-CT is more appropriate in N staging as compared to MRI as compared to other cross sectional imaging. PSMA PET-CT is more accurate in metastatic staging than CT or bone scan. The impact of using PSMA PET CT in staging has been highlighted in the pro PSMA trial which showed superior accuracy (92% vs 65%), greater treatment impact (28% vs 15%) and fewer uncertain results (23% vs 7%). It has also shown to have lesser exposure to radiation, high reporter agreement and fewer uncertain results. It also helps in

upstaging and down-staging along with minor or major change in RT planning in a large number of patients. PSMA PET CT has also been found to be useful in recurrence of disease, persistent disease and nmCRPC as compared to conventional imaging. The other potential applications include improved localization of lesions in PSMA PET CT guided biopsies and has been shown to be a safe procedure with a high diagnostic yield and also useful in providing incremental information in patients with high PSA and negative TRUS biopsy. PSMA PET CT has also been useful in monitoring systemic treatment. PPP & RECIP 1.0 has been proposed and validated in patients undergoing PSMA RLT. In summary PSMA PET CT has a high detection rate and superior diagnostic accuracy compared with diagnostic imaging with management plans changed more often as compared to conventional imaging. This has been useful at multiple time points throughout the course of disease from initial staging to CRPC.

Keywords: Prostate Cancer, Staging, PSMA PET-CT

THE PERFORMANCE OF BONE SPECT/CT AND FDG-PET IN THE PROSTATE CANCER DIAGNOSTICS: ARE THESE METHODS STILL USEFUL?

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For more than half a century, nuclear medicine has played significant role in diagnosis of prostate cancer (PC). Traditionally, whole body bone scan (BS) has been used as a method of high-sensitivity (91%) to assess spread of disease into the skeletal system, but with drawback of low specificity in differentiation between benign and malignant lesions (69%). The addition of SPECT-CT to BS enabled precise anatomical localization and attenuation correction of radiotracer uptake, which helped to detect fractures, degenerative changes or joint infection on CT. That leads to increased specificity of the technique (92%). F-18 FDG PET/CT, which is inevitable in diagnostics of many tumors that express high affinity to glucose, did not have significant historical role in monitoring PC patients, due to low uptake of labeled glucose in the cells of PC. Because of that, FDG PET/CT should not be used routinely for staging of primary PC. However, 18F -FDG can be used as an auxiliary method to analyze glucose metabolism in PC cells and find new targets and methods for diagnosis and treatment of the tumor. Intraprostatic uptake of FDG imaged by PET/CT suggests aggressive behavior and castration resistance of the tumor. The other possible indications for FDG PET/CT in PC are based on the increasing of the expression of hexokinase2 when progressing to CRPC, which enables detection of metastatic disease in patients with biochemical PSA relapse, in whom scan sensitivity increases with increasing serum PSA level. Accordingly, FDG PET/CT can be used in the assessment of extent of metabolically active castrate resistant metastatic disease, as well as in monitoring of the response to androgen deprivation therapy and other treatments, and also in prognostication. The new era in nuclear medicine diagnostics of PC began after discovering a new, highly specific molecular target on the tumor cells, prostate specific membrane antigen (PSMA). Anti-PSMA antibodies and small ligands were labeled with either positron (Ga-68, F-18) or gamma emitters for PET/CT and SPECT/CT. The most extensive use of PSMA imaging was performed in biochemical recurrence after radical prostatectomy (RRP) or radiotherapy (RT), since PSMA expression is upregulated when castrate resistant phenotype evolves. PSMA enabled the detection of disease relapse at very low PSA levels (> 0.2 ng/mL). The excellent performance of PSMA was also shown in detection of primary tumor, as well as

in the selection of appropriate candidates for radioligand therapy (RLT) with Lu-177 PSMA. In those cases, FDG PET/CT can also help to exclude patients who exhibited high uptake of labeled glucose. However, the recent EAU ESTRO Guidelines on PC do not propose PSMA PET/CT and SPECT/CT as standard methods for staging of PC, although PSMA PET/CT was more accurate than CT and bone scan for high-risk disease. It was also stressed that the PSMA PET/CT finding could not influence the decision about change of the treatment in patients with PC, in view of current available data. Bone scan is still recommended for metastatic screening in the intermediate-risk disease and high-risk localized disease/locally-advanced disease.

Keywords: Prostate Cancer, Bone Scan, Molecular Imaging

SPECT/CT IMAGING OF THORACIC NETs

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Neuroendocrine tumors (NETs) of the thorax, including bronchial and thymic tumors, belong to foregut NETs. Carcinoid bronchial tumors are only 2% of all lung neoplasms and 20-30% of all NETs, developing from enterochromaffin or Kulchitsky cells, located in the bronchial mucosa. Primary NETs of the thymus account for less than 5% of all anterior mediastinal neoplasms and 2 % of thymic lesions. Bronchial NETs are classified according to the grade of biological aggressiveness and extent of tumor cell differentiation. The well-differentiated neoplasms comprise typical and atypical carcinoids. Large-cell neuroendocrine carcinomas (LCNEC) as well as small cell carcinomas (SCNEC) are poorly differentiated. Somatostatin-receptor imaging using In-111 pentetreotide/Tc-99m Tektrotyd with SPECT or Ga-68 labelled somatostatin analogues with PET is used to obtain essential information for staging, assessing SSTR status and decision making for personalized therapy in patients with NETs. Tc-99m Tektrotyd with SPECT/CT can be used as an alternative when PET/CT SSTR scanning is not available. Tc-99m Tektrotyd is a radiopharmaceutical indicated for imaging of primary and metastatic NETs which overexpress somatostatin receptor SSTR2, SSTR3 and SSTR5. The main indications for SPECT-CT SSTR imaging are as follows: 1. To image the primary tumor in cases of metastatic NET with unknown primary and to point the most appropriate lesion for biopsy, 2. To assess SSTR expression in order to predict the therapy response and thus effectively influence the management of patients with NETs, 3. To stage pre-treatment patients, 4. To indicate patients with negative SSTR status, where FDG-18 PET/CT should be performed, and 5. To follow-up the treatment response.

Keywords: SPECT/CT Imaging, Thoracic NETs, Indications

MODERN PRODUCTION OF TECHNETIUM-99m GENERATORS

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The production of technetium-99m generators is typically a resource-intensive endeavor, due to its categorization as a sterile radiopharmaceutical with a complex production process. To address this, we have designed a cost-effective, automated system tailored for the needs of smaller-scale producers in developing countries. This system operates within a single hot cell, segmented into three distinct areas. Initially, the molybdenum-99 (Mo-99) solution's vial is unpacked in the first compartment. The next area is designated for the preparation of the Mo-99 solution, which is then loaded into the generators. The final compartment houses a charger that not only dispenses the molybdenum-99 solution into generators but also performs quality control checks on the eluates and secures protective caps on the generators, thereby making them ready for shipment in their transport containers. This charger is capable of handling 13 generators at a time, with the option to repeat the charging process for larger batches. The preparation and loading of the Mo-99 solution into the generators occur in a sterile Class "A" environment, adhering to EU-GMP standards. Automation of the entire procedure is achieved through a PC, which manages the operations via specialized software. Impact of blood markers on success of peptide receptor radionuclide therapy in patients with neuroendocrine tumors.

Keywords: Technetium-99m Generators, Production, Automation

FDG-PET/CT IN THE EVALUATION OF FOCAL ADRENAL LESIONS

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Introduction: Focal adrenal lesions (incidentalomas) can be found in approximately 5% of CT imaging in the general population. Around 80% of focal lesions are non-functional, benign adenomas. In patients with known malignancies approximately 40- 57% of focal adrenal lesions are benign, and it is very important to have an accurate differential diagnosis, especially when staging of the disease is done. F-18 FDG-PET/CT is a diagnostic tool that is very effective in the differential diagnosis of focal adrenal lesions, but there is always a possibility for false-positive findings and therefore it is very important to correlate with clinical, laboratory findings and other diagnostic modalities.

Material and methods: In our study we analysed 90 focal lesions of the adrenal gland in oncology patients that underwent PET/CT examination in the period from 2019 to 2024. Most of the patients had colorectal carcinoma, lung carcinoma, lymphoma and cervical carcinoma. The FDG PET/CT was done using standard protocols, with normal glycaemia and after 4 - 6 hours of fasting.

Results: In the analysed material we found that 90% of focal adrenal lesions were consistent with adenomas which correlated with the clinical settings and other imaging modalities. In 60% of patients even a control FDG PET/CT was done, where no metabolic or morphologic progression of the focal adrenal lesion was verified.

Conclusion: Benign and malignant focal lesions of the adrenal gland can show increased FDG uptake, therefore it is very important to know the intensity of the uptake in correlation with the clinical data and other diagnostic modality findings to give an accurate differential diagnosis. FDG PET/CT is a very important diagnostic tool in the evaluation of focal adrenal lesions with a very high sensitivity and specificity in the differential diagnosis of benign and malignant lesions.

Keywords: Focal Adrenal Lesions, F-18 FDG-PET/CT, Adenoma

PROBABILITY OF SURVIVAL IN DIFFERENTIATED THYROID CARCINOMA PATIENTS WITH RECURRENT DISEASE: ITS PROGNOSTIC FACTORS AND OUTCOME

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Background: If treated on time, differentiated thyroid carcinoma (DTC) usually has a good prognosis. However, during the follow-up some patients can develop recurrence. Aim: The purpose of the study was to evaluate the disease-specific survival (DSS) of DTC pts with recurrent disease. Patients and methods: From 2007 to 2022, 765 DTC patients were initially treated with surgery and I-131. There were pT1=488 (63.8%) patients, pT2=125 (16.3%) patients, pT3=133 (17.4%) patients, pT4=19 (2.5%) patients. During the follow-up 765, 61 (7.97%) patients developed recurrence. After the relapse, patients were treated surgically, while some of them underwent RAI and/or external beam radiation. The probability of DSS and the influence of prognostic factors were analyzed with the Kaplan-Meier method. The significance of differences was tested by log-rank test. A *p* value of less than 0.05 was considered significant. Results: We analyzed 33 (54.1%) males and 28 (45.9%) females, 39 (63.9%) patients <55 years old and 22 (36.1%) patients ≥55 years old; 57 (93.44%) patients had papillary carcinoma, 2 (3.28%) patients had follicular carcinoma, and 2 (3.28%) patients had Hurthle cell carcinoma. Total thyroidectomy (TT) was performed on 42 (68.85%) patients, while 19 (31.15%) patients underwent TT with neck dissection. There were 17 (27.87%) N0M0 stage, 37 (60.66%) N1M0 stage, and 7 (11.47%) N1M1 stage. The median follow-up was 7.4 years, range: 1.1-27.4 years. The probabilities of DSS at 5, 10, and 15 years after initial therapy were 96%, 86%, and 86%, respectively. The histological type of the tumor (*p*=0.007) was the predictive factor that significantly influenced the probability of recurrence. Other factors including age, gender, tumor stage, and type of initial treatment did not influence recurrent disease (*p*=0.269, *p*=0.672, *p*=0.248, and *p*=1.00, respectively). At the last check-up, 24 (39.34%) patients had complete remission, 30 (49.19%) patients had partial remission while 7 (11.47%) patients have died due to disease-related deaths. Conclusion: Recurrent disease reduces DSS in DTC patients. It is important to detect recurrence on time and to perform adequate treatment.

Keywords: Differentiated Thyroid Carcinoma, Recurrence, Survival

DEMOGRAPHIC AND PATHOLOGICAL DIFFERENCES BETWEEN UNIFOVAL AND MULTIFOVAL PAPILLARY THYROID CARCINOMA

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Introduction: Papillary thyroid carcinoma (PTC) is the most common type of thyroid malignancy. Tumor multifocality is often observed in PTC but its prognostic value is controversial. **Aim:** The aim of our study was to compare demographic and pathological features between unifocal and multifocal PTC. **Material and methods:** Medical records and pathologic results of patients who underwent total or near-total thyroidectomy at our Institute between January 2016 and January 2023 were reviewed retrospectively. Having these results, 330 patients were included in the study because of PTC and they were divided into 2 groups - 129 patients (39.09%) with multifocal PTC were included in Group 1, and 201 patients (60.91%) with unifocal PTC were included in Group 2. Demographic parameters including age and gender and pathological parameters including lymphnode metastasis (LNM), capsular invasion, lymphovascular invasion (LVI) and extrathyroidal extension (ETE) were analyzed and compared in both groups. **Results:** There were no significant differences between Group 1 and Group 2 in age and gender. However, the significant differences ($P < 0.05$) were observed in LNM, capsular invasion, LVI and ETE. LNM was detected at 24.03% and 12.44% in Group 1 and Group 2, respectively; the difference was significant between the two groups ($p=0.006$). Multifocal tumors were also more likely to have capsular invasion (25.58% vs. 10.95%, $p<0.001$), LVI (34.88% vs. 14.43%, $p<0.001$) and ETE (23.26% vs. 9.45%, $p<0.001$). **Conclusion:** Multifocal PTC accounts for the 39.09 % of all PTC in our study population and comprises a more aggressive form of PTC in terms of LNM, capsular invasion, LVI and ETE in comparison to the unifocal PTC.

Keywords: Papillary Thyroid Carcinoma, Multifocal, Unifocal

IMPACT OF BLOOD MARKERS ON SUCCESS OF PEPTIDE RECEPTOR RADIONUCLIDE THERAPY IN PATIENTS WITH NEUROENDOCRINE TUMORS

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Introduction: Peptide receptor radionuclide therapy (PRRT) is effective treatment option for well-differentiated, somatostatin receptor-positive, unresectable or metastatic neuroendocrine tumors (NETs). There is a lack of reliable biomarkers to predict effect of therapy in patients. The aim is to determine the prognostic significance of blood biomarkers on therapy success in patients with NETs undergoing PRRT treatment. **Methodology:** We retrospectively analyzed 46 patients with NETs treated with PRRT at the Department for nuclear medicine, University Clinical Center Kragujevac, Serbia. We assessed hematological, blood-based inflammatory markers and biochemical markers on disease progression. In accordance with the disease progression, the patients were divided into a progression group (n=16) and a non-progression group (n=30). The data were compared between the two groups. **Results:** The study included 46 patients (47.8% female, 52.2% male). The average age was 57.41±12.11 years (range 35–75 years). Tumors were localized in the GEP in 52.2% of the patients, 21.7 % in lung and 26.7% in other localizations. The pathological findings were NET-G1 in 25% patients, NET-G2 in 45.8% and NET-G3 in 29.2%. The neutrophil to lymphocyte ratio (NLR) and CRP/Alb ratio were significantly higher in patients with progression than in those without progression (median NLR: 2.40 vs 1.90, p = 0.001, median CRP/Alb 0.34 vs 0.0196, p=0.022). **Conclusion:** The study's results suggest that certain biomarkers may serve as indicators for therapy success in patients with NETs undergoing PRRT. The findings can potentially help to identify patients who are at higher risk of disease progression and tailor treatment strategies accordingly.

Keywords: Neuroendocrine Tumors, Peptide Receptor Radionuclide Therapy, Biochemical Markers

FDG-PET/CT IN THE DETECTION OF METASTASES IN NON-SMALL CELL LUNG CANCER: COMPARISON WITH MULTI-DETECTOR COMPUTED TOMOGRAPHY

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Background: Integration of positron emission tomography (PET) and computed tomography (CT) increases diagnostic performance in the evaluation of disease staging in oncology patients. **Purpose:** The purpose of this study was to compare the findings of FDG PET/CT and multi-detector CT (MDCT) in the detection of metastases and the staging in NSCLC. **Patients and Methods:** A total of 103 consecutive patients (67 ± 10 years, 65 (63%) were men) with histological confirmation of NSCLC were included in the study in order to compare findings of MDCT and PET/CT performed in median 17 days. The whole body PET/CT was performed 60 minutes after i.v. application of 5.5 MBq/kg body weight of ^{18}F -FDG. MDCT was performed using standard protocol for neck, chest, abdomen and pelvis when necessary and findings were found in the patients' history. **Results:** FDG PET/CT and MDCT differ in the staging of patients with NSCLC ($\kappa=0.084$, $p=0.439$). There was a moderate agreement between these two methods in determining the class T ($\rho=0.531$, $p<0.001$), and a poor agreement in determining the class N ($\rho=-0.009$, $p=0.933$) and class M ($\rho=0.252$, $p=0.021$). It was also found a poor agreement in the detection of metastases in the lymph nodes on ipsilateral side of the mediastinum ($\rho=0.351$, $p=0.001$), and for the detection of metastases in the lymph nodes on the contralateral side of the mediastinum and supraclavicular lymph nodes ($\rho=0.012$, $p=0.913$). It was similarly shown in the detection of metastases in distant lymph nodes ($\rho=-0.090$, $p=0.416$), lung ($\rho=0.260$, $p=0.018$), bones ($\rho=0.116$, $p=0.295$), and adrenal gland ($\rho=0.302$; $p=0.006$). **Conclusion:** Our results indicate that F-18 FDG PET/CT integrates the advantages of PET in the evaluation of the metabolic status of the lesion and CT, which enables anatomical localization and change measurements. In comparison to MDCT findings, PET/CT is better in evaluating metastases in contralateral, supraclavicular and distant lymph nodes, with more precise N3 staging. PET/CT is also better in evaluating distant metastases in bones and suprarenal glands, implicating better staging of patients with NSCLC, as well as treatment planning.

Keywords: FDG-PET/CT, Non-Small Cell Lung Cancer, Computed Tomography

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GATED SPECT MIBI STRESS IMAGING IN DETECTION OF ISCHAEMIA IN PATIENTS WITH INTERMEDIATE DUKE SCORE: COMPARISON WITH STRESS ECHO STUDY

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Background: Both, stress gated SPECT MIBI imaging and stress echo have IA class indications for detection of ischemia in patients with intermediate probability of coronary artery disease (CAD). However, both functional tests have advantages and drawbacks. **Purpose:** To compare Gated SPECT MIBI early post stress findings with stress echo in patients with suspected or known coronary artery disease, normal left ventricular function and intermediate Duke score. To evaluate sensitivity and specificity of Gated SPECT MIBI early post stress protocol in comparison to coronary angiography served as gold standard. To assess possible added value of Gated SPECT MIBI over stress echo in specific localization of myocardial ischemia. **Patients and Methods:** The sample included 113 patients, mean age 60 ± 9 years, 87 men and 26 women with normal left ventricular function and intermediate exercise Duke Score. They underwent 2-day stress-rest gated SPECT MIBI protocol with early post stress data acquired 15 minutes after i.v. injection of 555 MBq of Tc-99m MIBI. Perfusion and functional parameters were assessed by 4D-MSPECT programme. Stress echo was performed within two days and CA within one month of gated SPECT MIBI investigation. **Results:** There was no significant difference between early gated SPECT and stress echo findings in detection CAD (Mc Nemar, $p=1.000$) with good agreement between methods ($\kappa=0.697$, $p<0.001$). Spearman correlation between early gated SPECT and stress echo was also significant ($s=0.558$, $p<0.01$) Early gated SPECT has added value over stress echo findings (NRI index = 0.2466, $p<0.001$) in detection of ischemia especially in inferior-lateral wall. Overall sensitivity of ES was 95% and specificity 84%. **Conclusion:** Our data demonstrate comparative utility of early gated SPECT MIBI imaging and stress echo for non-invasive evaluation of CAD in patients with normal left ventricular function. The advantage of gated SPECT MIBI over stress echo is ability to concurrently detect and quantify ischemia in inferior-lateral wall and in patients with poor acoustic window.

Keywords: Gated SPECT MIBI Stress Imaging, Stress Echo, Ischemia Detection

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FDG-PET/CT IN THE FOLLOW-UP OF THE PATIENTS WITH LARYNGEAL CARCINOMA AFTER THERAPY

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Objective: The aim of this investigation is to estimate the diagnostic performance of positron emission tomography/computed tomography using fluorine-18 fluoro-deoxyglucose (FDG PET/CT) in the follow up of the post-treatment laryngeal squamocellular squamous cell cancer carcinoma (SCC), as well as survival rate. **Material and Methods:** Total of 68 patients (57 males and 11 females), mean age (69.1±6.8), with post-treatment laryngeal SCC were investigated. FDG PET/CT findings were compared to clinical follow-up of up to 12 years after imaging. The degree of metabolic activity was analyzed visually and semi-quantitatively using maximal standardized uptake value (SUVmax). **Results:** High accumulation of radiopharmaceutical was found in 48 (70.6%) patients (42 males and 6 females) who were considered true positive, physiological in 17 patients (25%) (13 males and 4 females) and only 3 (3.5%) (2 males and one female) were false positive. The overall sensitivity of FDG PET/CT was 100%, specificity 85.0%, positive predictive value 94.0%, negative predictive value 100% and accuracy 95.6%. In 25 cases (36.8%) PET/CT findings significantly influenced further management of the patients. **Conclusion:** FDG PET/CT is a valuable tool for follow-up of laryngeal SCC due to its high sensitivity, specificity, PPV, NPV and accuracy. It can influence the patients' management in significant number of cases. SUVmax was not proven to be a strong predictor of patients' disease-free survival.

Keywords: PET/CT, Laryngeal Carcinoma, Therapy

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THE ROLE OF SPECT AND SPECT/CT SRS IN THE DETECTION OF RESIDUAL AND RECURRENT MEDULLARY THYROID CARCINOMA

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Introduction: The aim of our research was to evaluate the usefulness of somatostatin receptor scintigraphy (SRS) with SPECT and SPECT/CT in detecting of residual/recurrent disease of surgically treated MTC patients with elevated serum calcitonin levels. **Material and methods:** In the period from May 2021 to March 2023, 28 patients, mean age 59.7 ± 7.8 years, were referred to our center for SRS with calcitonin serum levels still being elevated 3 months after surgery. The study was performed 2 hours after application of radiopharmaceutical, using SPECT/CT. Foci of increased Tc-99m-HYNIC TOCuptake on both SPECT and SPECT/CT images were interpreted visually by two nuclear medicine specialists and interpreted according to Krenning score system. **Results:** From 28 MTC patients with elevated serum calcitonin, 12 (42.9%) were interpreted with positive SPECT/CT findings, later confirmed to be MTC metastases. Of those 12 patients, 6 patients had very low Krenning score (grade 1 or 2) while remaining 6 patients had high Krenning score (grade 3 or 4). Based on SPECT images alone, only those patients with high Krenning scores were interpreted as positive, accounting for only 6/28 (21.4%) patients. **Conclusion:** Based on the limited number of patients with elevated serum calcitonin levels, Tc-99m HYNIC TOC scintigraphy can reveal residual/recurrent MTC in above 40% of the cases. When comparing SPECT and SPECT/CT, the latter was found to be superior in correctly identifying MTC metastases, especially in patients with low Krenning score.

Keywords: SPECT/CT, Medullary carcinoma, Thyroid

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SOMATOSTATIN RECEPTOR SCINTIGRAPHY WITH SPECT/CT IN THE MANAGEMENT OF NEUROENDOCRINE NEOPLASMS OF APPENDIX

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Aim/Introduction: To establish the role of somatostatin receptor scintigraphy (SRS) with SPECT and SPECT/CT in the follow up of patients with Neuroendocrine Neoplasms of Appendix (ANETs). **Materials and Methods:** The total of 58 patients were investigated, 36 females and 22 males, average age (48.3 ± 17.8 years). All patients had histological diagnosis of ANET (55 carcinoids of appendix and 3 tubular carcinoid). SRS was performed for restaging in all the patients after surgery. In 45 patients only planar view and SPECT were performed, while SPECT/CT was performed in 13. **Results:** There were 23 true positive (TP), 29 true negative, 4 false positive and 2 false negative SRS result. The sensitivity of the method (including both SPECT and SPECT/CT) was 92%, specificity was 87.9%, positive predictive value was 85.2%, negative predictive value was 93.6% and accuracy 89.7%. Single photon emission computed tomography contributed diagnosis in 12 TP findings in comparison to planar images. SPECT/CT contributed in 7/15 patients, in 5 confirming the positive finding (Krenning score 2) and in 2 excluding it in comparison to SPECT. In 12 patients Krenning score was 4, in 6 patients it was 3 and in 5 it was 2. In 21 patients SRS significantly changed the management of the patients. **Conclusion:** In conclusion, our results confirmed the value of SRS in the follow-up of the patients with ANET after surgery, if recurrences or metastases are suspected, with added value with SPECT and particularly with SPECT/CT.

Keywords: Neuroendocrine Tumors, Scintigraphy, SPECT/CT

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ENDOCRINE DISRUPTING AIR POLLUTANTS ASSOCIATED WITH THE INCIDENCE OF AUTOIMMUNE THYROID DISEASE

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Background: Endocrine disrupting air pollutants such as sulphur dioxide (SO₂), carbon monoxide (CO), nitrogen dioxide (NO₂), fine particle matter (PM_{2.5}), and ozone (O₃) can affect thyroid gland function on the level of synthesis, metabolism, and the action of its hormones. **Objective:** The aim of this study was to establish whether increased air pollution could contribute to an increased incidence of autoimmune thyroid diseases (AITD). **Methods:** A retrospective analysis was conducted of the medical records of 82000 patients at the University Clinical Centre in Tuzla, Bosnia and Herzegovina. The target group of this study comprised a total of 174 patients from the Lukavac area. Daily data on concentrations of air pollutants were collected from the air quality monitoring station located in Lukavac. The study covered the period from 2015 to 2020. **Results:** The results of the monitoring confirmed the presence of air pollutants in concentrations above the permitted limits throughout the entire observed period. Concentrations of PM_{2.5}, SO₂, NO₂, CO, and O₃ were in the range of 1.90–431.40 µg/m³, 3.60-620.50 µg/m³, 3.40-66.20 µg/m³, 48.00-7002.00 µg/m³, and 0.70-89.40 µg/m³, with means of 64.08 µg/m³, 77.48 µg/m³, 22.57 µg/m³, 1657.15 µg/m³, and 31.49 µg/m³, respectively. Hashimoto's thyroiditis was found in 33 patients (18.97%), whilst 141 patients (81.03%) were diagnosed with atrophic thyroiditis. The highest total incidence of autoimmune thyroiditis was recorded in 2017, when it reached 99.49, 95% CI. **Conclusion:** The effects of chronic exposure to a mixture of air pollutants on the function of the thyroid gland are still not sufficiently well-known, but the numerical tendency towards a higher incidence of AITD in this study, albeit without statistical significance ($p > 0.05$), still underlines the need for additional research.

Keywords: Autoimmune Thyroiditis, Air Pollutants, Endocrine Disruptors

THE GENDER BASED DIFFERENCES – URBAN AIR POLLUTION ASSOCIATED WITH THE INCIDENCE OF AUTOIMMUNE THYROID DISEASES

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Background: Environmental pollutants disrupt the function of the thyroid gland through several mechanisms, including the synthesis, metabolism, secretion and action of thyroid hormones. **Objective:** The aim of this study was to determine whether increased air pollution could contribute to an increased frequency of autoimmune thyroid diseases (AITD) more in women or men. **Methods:** A retrospective analysis was conducted of the medical records of 82000 patients at the University Clinical Centre in Tuzla, Bosnia and Herzegovina. The target group of this study comprised a total of 174 patients from the Lukavac area. People included in the study were patients older than 14 years, of both gender, with all forms of clearly defined AITD, living in the area of Lukavac period from January 2015 to December 2020. **Results:** The results of the monitoring confirmed the presence of air pollutants in concentrations above the permitted limits throughout the entire observed period. During the six-year period, 174 cases of AITD were registered, of which 150 (86.21%) were women and 24 (13.79%) men. Hashimoto's thyroiditis was found in 33 patients (18.97%), whilst 141 patients (81.03%) were diagnosed with atrophic thyroiditis. **Conclusion:** In our study, the disease was significantly more frequent in women than in men (25:4). It has been reported that women are more sensitive to polluted air and that they have a greater chance of dying from pollution than men. One of the explanations may be that women more often suffer from AITD. Another reason is that oestrogen and progesterone may contribute to the gender disparity.

Keywords: Autoimmune Thyroiditis, Women, Men

BONE SCAN WITH INCIDENTAL EXTRAOSSEOUS Tc-99m-DPD ACCUMULATION FOLLOWING URINOTHERAPY – CASE REPORT

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A bone scintigraphy is an essential imaging modality to evaluate skeletal diseases. Uptake of bone seeking tracers normally is seen in the osseous structures and to some degree in the kidneys and bladder. However, there are some reports about extraskelatal uptake on bone scans. The pathogenesis of this finding is not always apparent. A 66-year-old male with a newly diagnosed prostate cancer (Gleason score 7, PSA level 45), was referred for a bone scintigraphy as a part of cancer workup. A wholebody bone scan and SPECT study showed no definite evidence of bone metastasis. Surprisingly, significant radiotracer accumulation was noted in abdomen, most likely of intestinal origin. The possible causes of bone seeking radiotracer uptake in the intestines are neuroblastoma, protein-losing enteropathy, enterovesical fistula, gastrointestinal bleeding, intestinal infraction, etc. But in our case, the cause was of different origin. After considering all possible causes of intestinal radiotracer uptake that did not match the patient's medical history, we interviewed the patient again. He admitted that he drinks his own urine as a form of alternative treatment for prostate cancer. Therefore, after the intravenous injection of radiotracer, the patient drank his own radioactive urine before the start of imaging which led to the intestinal visualization. It is important to recognize the specific conditions causing extraskelatal accumulation of bone seeking tracers, because it greatly enhances the diagnostic value of the study. In some cases it is of great importance to think unconventionally, or from a new perspective.

Keywords: Bone Scan, Intestinal DPD Uptake, Urinotherapy

PET/CT AND NECROTIZING
MEDIASTINAL LYMPHADENOMEGLY
IN PATIENTS WITH LUNG SARCOIDOSIS - CASE REPORT

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Introduction: Sarcoidosis is a chronic granulomatous inflammatory disorder which can affect any organ and/or organ system. Thoracic sarcoidosis starts with enlarged hilar and mediastinal lymph nodes with formation of multiple changes in the lung parenchyma, leading possibly to fibrosis. Its typical pathological presentation is mediastinal lymphadenomegaly, symmetric hilar, in most cases non-necrotic granulomas. The presence of necrotic granulomas can represent a diagnostic problem. Positron emission tomography-computed tomography (PET-CT) gives important information about morphofunctional cell state and helps recognize the advanced disease/ establish the stage of the disease. Case report: A 37-year old man presented with palpitation and shortness of breath. The chest X-ray and computed tomography confirmed hilar and mediastinal lymphadenopathy without any visible pathologic lung parenchyma changes. The lung biopsy finding was presented with epithelioid cell granulomas with Langhans cell reaction and noncaseous necrosis inside a few granulomas like unusual sarcoidosis presentation. All cultures were negative on mycobacteria. PET-CT confirmed avid foci of bilateral hilar end mediastinal enlarged lymph nodes and indicated the disease involved the hepatoduodenal lymph node. According to the decision of the Commission for granulomatous lung diseases, corticosteroid therapy is not indicated for the patient. Further clinical and radiological follow-up is suggested. Conclusion: PET-CT cannot indicate the difference between different granulomatous diseases, but it plays an important role in assessing the extent of the disease. Excellent knowledge of atypical clinical-pathologic and diagnostic criteria plays

a crucial role in the timely diagnosis and application of appropriate treatment of the disease.

Keywords: PET/CT, Sarcoidosis, Lymphadenopathy

TC-99m LABELLED RED BLOOD CELLS IN DIAGNOSTIC DECISION MATRIX: CASE REPORT

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Mapping out different treatment of liver metastatic tumors may be challenging as they can resemble other space-occupying liver lesions. Technetium-99m pertechnetate-labeled RBC scintigraphy offers a non-invasive approach to distinguishing hemangiomas from other space-occupying lesions in cases where there are inconsistencies between clinical and radiological findings. In this paper, we present the case of a 65-year-old patient with suspected liver metastasis of choroidal melanoma referred to nuclear medicine department by an interventional radiologist. On the performed standard MR examination of the liver, twenty lesions were observed, and three of them had the characteristics of hemangioma. On the repeated MR exam with liver specific contrast due to biopsy planning, described lesions had the characteristics of secondary deposits without clear differentiation in relation to liver hemangiomas. To minimize the risk of inadvertently sampling lesions resembling hemangiomas, liver scintigraphy with Tc-99m labeled erythrocytes was suggested. In the early dynamic study, homogeneous perfusion of the liver was seen with no areas of focally increased or decreased radiotracer activity. On the delayed static studies and on the SPECT study, a clear focus of decreased uptake occurred, while the other lesions seen on MR did not have the scintigraphic characteristics of a hemangioma. A liver biopsy was successfully performed without any complications. Liver scintigraphy with Tc-99m labeled red blood cells, being non-invasive, readily accessible, and relatively cost-effective, can contribute to the clinical puzzle solving when navigating towards the correct diagnosis and treatment.

Keywords: Tc-99m labelled Erythrocytes, Scintigraphy, Liver Hemangioma

THE ROLE OF BONE METABOLIC AND TUMOR BIOCHEMICAL MARKERS IN THE PREDICTION OF BONE METASTASES IN PROSTATE CANCER PATIENTS

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Introduction: Bone scintigraphy is recommended as the first step imaging method for bone metastasis screening in medium-to high risk patient group as a non-invasive and reliable diagnostic tool. **Aim:** To compare biochemical markers (total PSA, free PSA, free PSA/total PSA ratio, Gleason score and alkaline phosphatase (ALP) with Tc-99m-DPD bone scintigraphy results in prediction of bone metastases. **Material and methods:** Retrospectively, 53 prostate cancer patients underwent standard protocol Tc-99m-DPD whole-body bone scintigraphy with medical records of PSA, free PSA, free PSA/total PSA ratio, alkaline phosphatase values and Gleason score. Biochemical serum markers were determined no later than 2 weeks before scintigraphy was performed. **Results:** The mean age of the patients was 70.60±9.15 (minimum-maximum: 52.00–87.00). The number of bone metastases moderately correlates with levels of alkaline phosphatase ($r=0.507$), very weakly correlates with total PSA ($r=0.185$) and weakly correlates with Gleason score ($r=0.372$), free PSA ($r=0.295$) and free PSA/total PSA ratio ($r=0.323$). The ROC curve of sensitivity versus the specificity of free PSA, total PSA, free PSA/PSA ratio, ALP and Gleason score for detection of bone metastases determined that the ALP variable was statistically significant and have a valuable diagnostic value (respectively AUC=0.870; $p=0.016$). The ALP cutoff value was 105.30 U/L, with sensitivity rate of 82% and a specificity rate of 86.4%. **Conclusion:** The results of this study show that ALP with cutoff value of 105.30 U/L had a good prognostic value with sensitivity of 82% and specificity of 86.4%.

Keywords: Bone Scintigraphy, Prostate Cancer, Biochemical Markers

IMPORTANCE OF LYMPHOSCINTIGRAPHY FOR SENTINEL NODE MAPPING IN HEAD AND NECK MELANOMAS

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Introduction: Head and neck melanomas present a challenge for diagnosis and treatment, because they often do not follow standard lymphatic drainage. Therefore, the adequate sentinel lymph node mapping is of great importance. The Aim of this study was to determine if there is a difference in the number of drainage basins in relation to the two most common histological types of melanoma. **Materials and methods:** We retrospectively analyzed 46 patients (29 male, 17 female mean age 65 years) who underwent lymphoscintigraphy from January 2019 to December 2023. Tc-99m antimony sulphide colloid was injected intra-dermally in all patients. **Results:** 28 patients (61%) out of 46 patients had superficial spreading type, while 18 patients had nodular type of melanoma. The average tumor thickness was 3.7 mm (0.7-13 mm). In the nodular melanoma group, 67% of patients (12/18) had sentinel lymph nodes in two or more drainage basins, while in the group of patients with superficial spreading type, sentinel lymph nodes in two or more drainage basins were detected in 47% of cases (9/19) **Conclusion:** We observed that nodular type of melanoma in the head and neck region is expected to have more drainage basins and it is necessary to map all isolated sentinel lymph nodes. For these reasons, multidisciplinary management is essential for patients with head and neck cutaneous melanomas

Keywords: Melanoma, Sentinel Lymph Node, Lymphoscintigraphy

PAROTID VERSUS SUBMANDIBULARY GLAND PHENOTYPE OF FUNCTION IMPAIRMENT IN ANA NEGATIVE AND ANA POSITIVE PATIENTS

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Introduction: Dynamic scintigraphy of the salivary glands is used in patients with primary and secondary Sjogren's syndrome to objectify the feeling of dryness in the mouth and to evaluate the severity of salivary glands damage. **Aim:** To examine the degree of severity of function damage of the salivary glands in patients with dry mouth syndrome (parotid phenotype, submandibular phenotype, mixed phenotype). **Material and methods:** Retrospectively, 41 female patients who underwent standard protocol 99m-Tc salivary scintigraphy (GE HealthCare Discovery NM830). The patients underwent laboratory ANA screen testing (indirect immunofluorescence test) and were divided in two groups, ANA+ and ANA-. Based on the visual assessment of two nuclear medicine specialists, categorization of salivary gland function was established-finding 1 (F1)-preserved function, F2-parotid damage, F3-submandibular damage and F4 damage to both pairs of glands. **Results:** No statistically significant difference was observed in the mean life years of patients in relation to the presence of ANA [ANA (+) 52.8+/-16.3 vs (ANA-) 57.6+/-11.5 years, P=0, 24)]. It was observed in ANA (-) (F1-9/20; F2-6/20; F3-2/20; F4-3/20) and ANA (+) (F1-1/21; F2-2 /21; F3-6/21; F4-12/21). In relation to the degree of damage to the salivary glands, a statically significant difference was observed in the frequency of disorders in relation to the presence of ANA antibodies (p=0.001). Cramer's V between presence of ANA and damage category is ($X^2=15.79$; $\phi_c =0.62$, p=0.001). **Conclusion:** The submandibular phenotype of salivary gland damage is more frequent with ANA positivity in patients with dry mouth syndrome.

Keywords: Salivary Gland Scintigraphy; Antinuclear Antibodies; Sjogren's Syndrome

A PILOT STUDY: THE FUNCTIONALITY OF THE THYROID NODES IN RELATION TO TSH LEVELS

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Introduction: The functionality of the thyroid nodes (TN) have a significant role in making clinical decisions for the process of selecting an adequate therapeutic treatment. **Aim:** The aim of the study was to examine the functionality of thyroid nodes in relation to thyroid stimulating hormone (TSH) levels. **Materials and methods:** The clinical records of patients who underwent thyroid scintigraphy with Technetium-99m (Tc-99m) in Department of Nuclear Medicine Clinical center of Vojvodina from 2022 to 2024 year was used for this retrospective study. Out of total 322 thyroidscintigraphy we processed consecutive sample of patients with single TN. We observed age, gender, serum concentration of TSH, presence of thyroid autoantibodies and TN functionality according to scintigraphy findings. **Results:** Patients (n=40, 19 female, 11 male) were observed according to the TSH concentration [low TSH 0.02 (0.006-0.25 mIU/L vs. normal 0.88 (0.36 - 5.74) mIU/L]. No significant difference was observed between the age (low TSH 63 (23.5) vs. normal TSH - 54 (18) years of age, p=0.32). Presence of Hypo/afunctional nodes were 23/40 (TSH - 1.14 +/-1.2 mIU/L, 12 /40 had positive thyroid autoantibodies) vs functional 7/40 (TSH - 0.67 +/-0.66 mIU/L) and hyperfunctional 10/40 (TSH - 0.15 +/- 0.23 mIU/L). **Conclusion:**In patients with single TN, we found hypo/functional nodule as the most common scintigraphy finding with low normal TSH values.

Keywords: Thyroid Node, Scintigraphy, TSH Level

COMPARATIVE ANALYSIS OF THYROID NODULE GUIDELINES: INSIGHTS FROM INTERNATIONAL PERSPECTIVES

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Thyroid nodules are a common clinical entity, and their management poses a significant challenge to clinicians worldwide. This abstract presents a comparative analysis of thyroid nodule guidelines from three esteemed medical associations: the European Thyroid Association (ETA), the American Thyroid Association (ATA), and the Korean Thyroid Association (KTA). The 2023 ETA guidelines advocate for ultrasound as the primary imaging modality and recommend fine-needle aspiration cytology (FNAC) for nodules ≥ 1 cm in size or suspicious nodules < 1 cm. The risk stratification is based on the Thyroid Imaging Reporting and Data System (EU-TIRADS), with active surveillance recommended for low-risk nodules. The 2015 ATA guidelines also emphasize ultrasound as the initial imaging modality and suggest FNAC for nodules ≥ 1 cm, with consideration of surgery based on risk stratification. The ATA risk stratification system categorizes nodules into low, intermediate, and high-risk groups. ATA introduced the concept of the "Bethesda System for Reporting Thyroid Cytopathology," which standardizes reporting of fine-needle aspiration results. Additionally, the guidelines emphasize the role of molecular testing for indeterminate nodules, offering a more personalized approach. The 2023 KTA guidelines align with the ETA and ATA recommendations, emphasizing ultrasound and FNAC for nodules ≥ 1 cm and incorporating the KTA TIRADS for risk stratification. They place significant emphasis on the role of elastography and shear wave velocity in assessing nodules, complementing traditional ultrasound features. The active surveillance is recommended for low-risk nodules, with surgery reserved for intermediate and high-risk nodules or those with rapid growth. This comparative analysis highlights variations in diagnostic approaches, risk stratification systems, and management strategies across different regions, while underscoring the importance of individualized patient care guided by international best practices.

Keywords: Thyroid Gland, Nodules, Guidelines (ETA, ATA, KTA)

IS THERE ANY EXCUSE FOR DTC BONE METASTASES
DEVELOPED DUE TO IMPROPER INITIAL TREATMENT?
– CASE REPORT

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Background: Differentiated thyroid cancer (DTC) usually has a favorable prognosis if adequate treatment is performed. This case aims to highlight the importance of proper initial treatment algorithms in DTC patients. Case presentation: We present the case of a 55-year-old man admitted to our institution for a PET/CT exam which detected non-hypermetabolic lytic lesions in VL1 and the right ischiadic bone, as well as a new hypermetabolic focus in the left iliac bone. He was diagnosed at another institution on December 6, 2011, with papillary thyroid carcinoma, follicular type, pT3NxMx, after the right thyroid lobectomy followed by LT4 replacement. Eleven years later, because of the pain in the right leg he underwent a CT scan which detected bone metastases in the VL1 and right iliac bone (ischiadic and pubic bone). Soon after, on October 21, 2022, the biopsy of the right ischiadic bone was performed, and metastatic papillary carcinoma was confirmed histologically. One month later, the bone scintigraphy detected bone metastases in the VL1 and right iliac bone (pubic bone and ishiadic bone). Thyroidectomy was completed with left thyroid lobectomy on January 27, 2023. Radioiodine therapy with 5.55 GBq I-131 was applied on March 3, 2023, in another institution. Between March 28 and April 13, 2023, the patient received external beam radiation to the lumbar spine and right hemipelvic region (total dose of TD30 Gy/10 fractions). Later this year, from July 31 to August 21, the patient underwent additional radiation (stereotaxic beam radiation treatment, SBRT-X knife) to the VL1 and right ischiadic bone (16 Gy). A couple of months later, on October 10, an additional course of radioiodine therapy with 5.55 GBq I-131 was administered. Post-treatment WBS revealed bone metastases in the VL1 and right ischiadic bone. Lab analyses showed: TSH=83.5 uIU/ml; Tgb=>500 ng/ml; TgbAb=14.7

U/ml. At the moment, the patient awaits an additional course of radioiodine therapy in the amount of 7.4 GBq that is scheduled for next month. Conclusion: Initial management of DTC routinely includes total thyroidectomy followed by I-131 treatment and long-life hormonal therapy. However, if initial treatment is improper, DTC patients develop metastatic disease.

Keywords: Differentiated Thyroid Cancer, Radioactive Iodine, Therapy

LINGUAL THYROID IN A YOUNG ASYMPTOMATIC FEMALE PATIENT WITH HYPOTHYROIDISM – A CASE REPORT

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Introduction: Lingual thyroid (LT) is a rare ectopic localization of thyroid tissue that is presented as a nodule on the base of the tongue due to an abnormality in embryogenesis. The exact prevalence of lingual thyroid is unknown since many asymptomatic individuals never come to a clinical examination. **Case report:** We report a case of a 29-year-old female who was presented to our department with a clinical history of hypothyroidism. The patient did not report any symptom that could indicate the presence of a lingual thyroid. The neck ultrasound showed hypoplastic thyroid tissue and a solitary nodule in the submandibular region. An oropharyngeal examination revealed a solid mass on the base of the tongue. In our department, a Tc-99m thyroid scintigraphy study was performed on a single photon emission computed tomography (SPECT/CT) gamma camera. SPECT/CT images have shown functional thyroid tissue on the basis of the tongue with the larger diameter of 16 mm and no functional glandular tissue in the central cervical position. **Conclusion:** The presence of lingual thyroid in asymptomatic patients can be diagnosed using oropharyngeal examination, neck ultrasound and Tc-99m scintigraphy with a hybrid camera that provides functional and anatomical images and looks for other locations of ectopic thyroid tissue.

Keywords: Lingual Thyroid, Ectopic Thyroid, Hypothyroidism

A CASE OF A LETHAL OUTCOME IN A PATIENT WITH PAPILLARY THYROID CARCINOMA IN AN ECTOPIC THYROID TISSUE

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Introduction: The presence of ectopic thyroid tissue is caused by abnormal embryogenesis of the thyroid gland. Thoracic cavity is the most common non-cervical location for ectopic thyroid tissue. Any disease affecting the thyroid gland may also involve the ectopic thyroid, including malignancy. **Case report:** A 66-year-old patient with history of colorectal carcinoma was operated for the mediastinal mass found on a computed tomography (CT) scan. Histopathologic examination revealed an ectopic thyroid tissue with foci of papillary thyroid carcinoma (PTC). Thyroid ultrasound and ^{99m}Tc thyroid scan were performed and did not show any abnormality. After the subsequent total thyroidectomy, no PTC was found in thyroid gland which confirmed that it was a case of primary PTC in the ectopic tissue. Patient received radioiodine therapy and I¹³¹ post-therapy whole body scan (WBS) had shown only focal uptake in thyroid bed region and upper mediastinum. Two months later, bone scan and PET/CT with FDG were performed due to progressive pain in both legs and right palm and revealed bone metastasis. Consequently, patient was treated with an external beam radiotherapy and 4 cycles of peptide receptor radionuclide therapy (PRRT) that showed relatively high uptake in majority of the lesions. Control PET/CT showed partial therapy response and patient reported lower level of pain. One year after last PRRT, patient developed a solitary brain metastasis that was completely surgically removed, and the PTC metastasis was confirmed. Due to progression of the disease, tyrosine kinase inhibitors (TKI) therapy was prescribed but three months later, a progressive worsening of the patient general condition occurs. Control PET/CT showed a progression of the disease in terms of multiple confluent metastases in all parts of the skeleton and liver. Metastases of PTC were confirmed by a biopsy. The patient died 5 years after the initial diagnosis of PTC. **Conclusion:** Ectopic thyroid tissue is rare primary location of PTC and it is reasonable to expect a worse prognosis due to a challenging and often delayed detection.

Keywords: Ectopic Thyroid, Papillary Thyroid Carcinoma, Thyroid Gland

THYROID PAPILLARY CARCINOMA ARISING IN ECTOPIC THYROID TISSUE: A CASE REPORT

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Introduction: Ectopic thyroid tissue results from abnormal embryologic development and migration of the thyroid gland. True malignant transformation in ectopic thyroid tissue is extremely rare and is always diagnosed after surgical excision of the lesion by pathology examinations. **A case report:** A 40-year-old female patient was referred to our institution due to swallowing difficulty, worsening in last two weeks. Her medical and family histories were non-specific. The neck ultrasonography revealed heterogeneous thyroid nodules on both sides, the largest on the left side up to 22 mm. Thyroid functional tests, calcitonin and thyroid antibodies were within normal limits. The USG-guided fine needle aspiration cytology (FNAB) was performed on the left side thyroid nodule and PC findings indicated a benign colloid nodule. Tc-99m scintigraphy indicated the existence of a hypo/afunctional nodule on the left with a larger focal uptake in the upper mediastinum that might correspond to the image of retrosternal ectopic thyroid tissue. On I-131 scintigraphy, this focus was not noticed. Due to the worsening swallowing symptoms and weight loss, thyroid operative treatment was performed. The histopathological examination showed retrosternal ectopic multicentric papillary carcinoma. Afterwards, the patient underwent a successful radioiodine ablation therapy and was put on Levothyroxine suppression therapy. **Conclusion:** Ectopic thyroid cancer is an extremely rare type of thyroid cancer, which is easy to be misdiagnosed. Preoperative use of US, radionuclide scanning, computed tomography /Magnetic resonance imaging and FNAB can significantly reduce the misdiagnosis rate of this disease.

Keywords: Ectopic Thyroid, Retrosternal Propagation, Thyroid Cancer

A CASE REPORT OF ADENOMA OF THE PARATHYROID GLAND

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Introduction: Preoperative planar Tc-99m-sestamibi scintigraphy, complemented by SPECT/CT (Single-Photon Emission Computed Tomography with Computed Tomography) imaging of the neck and chest, offers higher sensitivity in detecting hyperfunctioning parathyroid glands, facilitating successful parathyroidectomy. **Case report:** We present a case of a 33-year-old female patient who had been diagnosed with tumor measuring 9x22x55 mm (APxLLxKK), located between the right lobe of the thyroid gland and the common carotid artery on neck CT, initially suspected to be an aberrant blood vessel. Subsequent neck MRI (*Magnetic Resonance Imaging*) confirmed the tumor. The laboratory analyses showed an increase in following parameters: PTH 310 (up to 68) and Ca 2.92 (up to 2.55) with a normal vitamin D. Due to that the patient was referred for scintigraphy of the parathyroid glands, which was performed in another institution, and scintigraphy yielded negative results. For further evaluation of the disease, the patient was referred to the Institute of Oncology and Radiology of Serbia, where the repeat scintigraphy was done but with SPECT/CT. SPECT/CT examination revealed a hypodense soft tissue mass measuring 9x22x50mm (APxLLxKK), which was located between the right thyroid lobe, common carotid artery and jugular veins. The described mass intensively accumulates the radiopharmaceutical and corresponds to the hyperfunctionally altered right parathyroid gland. The suspected hyperfunctional parathyroid gland was surgically removed, confirmed to be an adenoma. After the operation a decrease in value of the PTH was registered. **Conclusion:** This case emphasizes the significance of Tc-99m-sestamibi planar scintigraphy coupled with additional SPECT/CT imaging of the neck for accurate identification of parathyroid glands and subsequent treatment planning.

Keywords: Parathyroid Gland, Adenoma, Tc-99m-Sestamibi SPECT/CT

FDG-PET AND SPECT IN PRESURGICAL EVALUATION OF FOCAL PHARMACORESISTANT EPILEPSY

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Introduction: Multimodal imaging techniques provide information on the relationship between the epileptogenic lesion (morphological MR), the irritative zone (interictal EEG), the ictal onset zone (ictal EEG, SPECT, FDG-PET), the functional deficit zone (interictal FDG-PET), the eloquent cortex (functional MR) and represent the standard for the non-invasive phase of pre-surgical evaluation of patients with pharmacoresistant focal epilepsy. **Objective:** To indicate the importance of FDG-PET and SPECT imaging in presurgical lateralization and localization of the epileptic focus. **Materials and methods:** FDG-PET was performed in 83 patients (5-65 years) with focal temporal and extratemporal pharmacoresistant epilepsy, and in 8 patients ictal and interictal HMPAO-SPECT. The findings were visually analyzed and compared with the epileptogenic zone detected by video EEG monitoring and MRI findings. **Results:** Interictal FDG-PET showed a hypometabolic zone: temporal unilateral (44 patients), bilateral (5), frontal (14), parietal (4), frontoparietal medial (1), multifocal (7 patients). Ictal PET was obtained in 4 patients (2 nonconvulsive status epilepticus, 1 epilepsy partialis continua, 1 complex partial seizures), the epileptogenic zone was shown as a hypermetabolic region. Epileptogenic focus was detected in 69 patients (84%) using FDG-PET. SPECT showed ictal hyperperfusion and interictal hypoperfusion in the temporal region with an epileptic focus. **Conclusion:** SPECT and FDG-PET can visualize the epileptogenic focus as a zone of hyperperfusion and hypermetabolism ictally, hypoperfusion and hypometabolism interictally and are significant methods in the presurgical evaluation of patients with focal pharmacoresistant epilepsy, especially if the MR findings are normal or the MR and video EEG findings are discordant.

Keywords: FDG-PET, SPECT, Pharmacoresistant Epilepsy

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PET/CT - DIAGNOSTIC POTENTIAL, APPLICATION AND SIGNIFICANCE

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Introduction: PET/CT is a hybrid machine that has a double perspective, because in the same examination we get the morphology and the relationship between different structures and organs, but also the evaluation of the function of the organs and their various physio-pathological processes. PET/CT is based on the coincidence detection of two 511 KeV annihilation photons. In the resulting image, we can see the tracer concentration as a three-dimensional image of the metabolic process in the body. FDG-fluorodeoxyglucose (FDG) is a glucose compound labeled with fluorine-18, a positron emitter, with a half-life of 110 min, and a high energy of 511KeV. FDG is the most commonly used radiopharmaceutical. **Conclusion:** Thanks to the great diagnostic potential of PET/CT, the establishment of an accurate diagnosis is significantly accelerated, more precise results of the course of treatment are obtained, and radiotherapy planning is improved. Patients are deprived of unnecessary, less useful, invasive diagnostic procedures. The goal is to improve one's health and prolong human life.

Keywords: PET/CT, Diagnosis, Application

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THERAPY OF HYPERTHYROIDISM USING I-131

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Introduction: Radioiodine therapy is most often used for the treatment of diffuse toxic goiter - Graves' disease (GB), toxic adenoma, Plummer's disease, thyrotoxic crisis, for reducing the volume of non-toxic polynodous goiter (less often), therapy of subclinical hyperthyroidism. Radioiodine with its β -particles leads to irreversible DNA damage, which starts the destruction of the thyroid gland tissue and ultimately leads to a decrease in the function and/or size of the gland. **Objective:** Assessment of the effectiveness and safety of radioiodine therapy. **Materials and methods:** In the Center for Nuclear Medicine-CCS, in the period 2006-2013, 1113 patients were evaluated. After consultation with an endocrinologist and an endocrine surgeon, it was decided to apply a therapeutic dose in order to treat hyperthyroidism. Oral application is done on our own, with a little water. The patient is invited to the first control examination 3 months after the application of radioiodide. **Results:** The results of patients treated in 2006-2013, who received an individual dose, were analyzed. Out of 1113, the largest number were women with GB disease (504), and 97 men. 271 people (223 women, 48 men) were treated for toxic adenoma; polynodosis struma 231 (199 women, 32 men), 10 patients due to subclinical hyperthyroidism. One year after the application of a therapeutic dose of ^{131}I , 468 patients were euthyroid (406 women, 62 men). 341 of them had hypothyroidism (278 women, 63 men). 809 patients (610 women, 199 men) received only one dose during treatment, 304 patients who were treated with two/more doses remained hyperthyroid (241 women, 63 men). **Conclusion:** ^{131}I therapy once again confirms the effectiveness, safety and simplicity of application in the treatment of benign thyroid diseases.

Keywords: Radioiodine, Hyperthyroidism, Therapy

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PERSONNEL EXPOSURE TO IONIZING RADIATION DURING THE SEPARATION AND APPLICATION OF FDG RADIOPHARMACIES WITH SEMI-AUTOMATIC AND AUTOMATIC SINGLE DOSE SEPARATORS

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Introduction: The introduction of the latest equipment in working with open sources of ionizing radiation is of great importance in reducing the exposure of medical personnel. The greatest exposure of personnel occurs during the separation and application of individual patient doses. **Objective:** The comparison of personnel exposure doses when working with semi-automatic and automatic dose separators. **Materials and methods:** A semi-automatic separator has been used in the national PET center since 2010, and an automatic separator has been used since 2015. The exposure doses of personnel were measured with an electronic dosimeter and calculated over a period of one year using both dose separators. **Results:** The results are given as the mean value of the results obtained by reading the electronic dosimeters of the personnel who worked with the semi-automatic and automatic separator, over a period of one year. The exposure dose of technicians when working with a semi-automatic separator, per patient, is 0.1-0.2 μSv during separation, 0.7-0.9 μSv during application, and 0.8-1.0 μSv in total. The values when working with an automatic separator, per patient, are: 0.07-0.1 μSv during separation, 0.08-0.13 μSv during application, and 0.15-0.23 μSv in total. **Conclusion:** The automatic activity separator shows greater accuracy and precision in the separation and application of individual doses and reduces the exposure time of the personnel, which results in a lower exposure dose of the personnel when working with the automatic separator compared to the semi-automatic dose separator.

Keywords: Ionizing Radiation, Personnel Exposure, Automatic Dose Separator

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NUCLEAR MEDICINE DIAGNOSTIC BONE SCINTIGRAPHY

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Diagnostic scintigraphy is a highly sensitive method for detecting bone diseases, which often allows early diagnosis and primarily overview of the entire skeleton. The goal of scanning in patients with breast cancer, prostate cancer, bronchial and other carcinoma is the detection of bone metastases. Methods and materials: Two and a half hours after the i.v. injection of 555 MBq of Tc-99m-labeled MDP whole body imaging in anterior and posterior projections is done. If necessary, additional spot images or SPECT images are performed. A small number of patients sent by the physician or orthopedist come to the bone scan to determine benign lesions of the bones-infection or inflammation. In these cases we perform the three-phase bone imaging. Before injection of the radiotracer, the patient is positioned on the gamma camera so the area of interest can be imaged. The technologist starts imaging and injects the patient. Images are obtained at 1-3 seconds per frame (when using digital images) for a video clip lasting 60 seconds which is referred to as "dynamic imaging." Each frame is a summation of the radioactivity counts for the obtained image. This dynamic imaging demonstrates and characterizes relative perfusion to a particular area and is called the "flow phase" or "angiographic phase." Following this step, a second image is obtained in the same field of view and is termed the "blood pool" phase. This characterizes blood pool accumulation in the soft tissues and bone (or lack thereof) as a result of flow and capillary dilatation. Two 3 hours after initial injection, the third "delayed" phase, includes images of the same location as the earlier phases and will also include the whole body. Results: In the past year 1761 patients were scanned: - patients (8.5%) underwent tomography skeleton- 94 patients (5%) underwent targeted bone scintigraphy-29 patients (2.5%) underwent three-phase bone scintigraphy. Conclusion: We have concluded that the diagnostic method of imaging the skeleton may reveal changes in the bones much earlier than X-ray imaging. Tomographic and target capture as an additional method significantly contribute to the precise interpretation of the findings. In case of suspicious changes in the spinal column tomographic scanning is a better additional method, whereas imaging target is better with long and flat bones.

Keywords: Bone Diseases, Scintigraphy, Tc-99m-MDP

THE USAGE OF AUTOMATIC F-18 FDG INTEGO DOSE APPLICATOR: FROM THE TECHNOLOGIST POINT OF VIEW

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Automatic applicator and dose divider is used during work on PET/CT diagnostics. The use of this device represents a measure of protection of both staff and patients against radioactive radiation. Using the Intego device The Co-57 source is used to calibrate the device and the calibration is performed by an authorized service technician, once, after installing the software. Checking the linearity of the dose calibrator is a procedure that needs to be performed during the maintenance program. The test is performed according to the written instructions provided by the manufacturer. A source with a minimum dose of 3.7 MBq is used. Daily testing of Intego is performed before each start of work on the apparatus with a Cs-137 source. The device is turned on by pressing the Power button. Work modes appear on the touch screen, where we select the Clinical button to work with the patients (when we select Training mode, the device can only be used for exercise). After switching on, it takes 15 minutes to warm up the ionization chamber and it's not possible to use function of the device. We start daily testing by clicking on the offered activity OK (Daily QC should be performed)-Daily QC-Start. Upon receiving the instructions, the source of Cs-137 is placed in the ionization chamber using the support provided for it. After testing has been completed, we remove the Cs-137 and return it to the lead safe provided for storing the source. The test results appear on the screen with the possibility of printing the results or running a new test if the test is not successful. We test Pinch Valves by selecting the Valve Calibration function. To place the work sets, move the cover towards the front of the cart to open the insulated chamber. Open the package of SAS and place it according to the manufacturer's instructions in the provided guide and connect the physiological solution to it. Place the PAS according to the manufacturer's instructions. On the screen select the Summary-New function and then enter the data about the FDG number (Lot Number), date (Date), time (Time), source type (RP), activity (Activity), volume and confirm everything with the OK function. After that, pressing the Prime application starts filling the SAS with physiological solution as well as the software calculation of the activity of the dose that is currently in the device. The device is then ready to work with

patients. We then enter the patient's data (name and surname) as well as the recommended isotope dose by the doctor's instructions (which are determined based on the body weight). We connect PAS set to the cannula that we previously placed on the patient. The technician presses on the control button Prepare and Infuse, applies the isotope. After the application has been finished, by selecting the Print function, we print a label (with the name and surname of the patient, the time of application and the dose of applied F-18 FDG) from which precise data about the dose and the time of application of the dose are further used in the PET/CT imaging procedure. We remove the used PAS set together with the cannula and dispose it in a special place for disposal of radioactive waste. By placing a new PAS set, the device is ready for dose application to the next patient. After finishing work with the Intego device, the SAS set and the shielding with the FDG bottle remain in the device until at least 10 isotope half-life times have passed ($T_{1/2}$ FDG-18 is 110 min), and all in order to protect the staff.

Keywords: Automatic Dose Applicator, Dose Divider, F-18 FDG-PET/CT Imaging

ARTIFACTS OF CONVENTIONAL RADIONUCLIDE PLANAR BONE SCINTIGRAPHY

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Bone scintigraphy is one of the most frequent nuclear medicine diagnostic procedure. It is routinely performed in the evaluation of oncologic patients for suspected bone metastases as well as in various benign musculoskeletal conditions. Materials and methods: The Tc-99m methylene diphosphonate (Tc-99m-MDP) is the most common used radiotracer for bone scintigraphy, and shows excellent contrast between normal and diseased bone. The excretion of Tc-99m MDP is primarily renal and 70% of the administered dose is eliminated by 6 hours. For routine planar bone scans, the patient is normally injected intravenously with 370-740 MBq of Tc-99m-MDP and imaged 2-4 hours later. Bone scans show high sensitivity, but variable or limited specificity. To increase the specificity of bone scan interpretation it is necessary to reduce the false interpretation. Since purely lytic metastases may not generate a visible osteoblastic response, the bone scan is not recommended technique for bone evaluation in myeloma. Bone scintigraphy artifacts can be technical or patient related. The technical artifacts include equipment, radiopharmaceutical, and image processing-related issues. The equipment-related artifacts may be due to inadequate quality-control procedures and calibration. The extravasation of the radiopharmaceutical at the site of injection is a common artifact that may mimic bone abnormality. In such cases, the radiotracer will be slowly resorbed. In addition, lymphatic drainage may also occur, resulting in the visualization of one or more lymph nodes, not infrequently seen in the axilla or supraclavicular region on the side of an upper extremity injection. To avoid this artifact, it is important to document the site of injection in all patients. Another artifact, so called "glove phenomenon", may be due to inadvertent arterial injection of the radionuclide. It presents as localized areas of increased activity in an extremity distal to the site of injection. Urinary contamination is another frequent problem, which may simulate focal bone lesions. In this case, it is necessary to remove the patient's clothes or to wash the patient's skin and repeat the scanning (spot images). For valid bone interpretation of the pelvic region, it is important that patient should empty the bladder prior the acquisition. Conclusions: To minimize the misinterpretation of the bone scan, it is important to have a comprehensive knowledge of normal variants, common patterns and artifacts of bone scintigraphy.

Keywords: Bone Scintigraphy, Tc-99m-MDP, Artifacts

F-18 FDG-PET/CT IMAGING: ARTIFACTS AND PITFALLS

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The proper patient's preparation is important to avoid pitfalls of PET/CT scan interpretation. Patients are advised to fast approximately 4-6 hours before image acquisition and to abstain from beverages with sugar. Following application of the F-18 FDG radiotracer, patients are placed in a quiet room with instructions to rest, stay calm without excessive movement to minimize skeletal muscle uptake. To avoid possible brown fat activation, the injection room should be kept at warm temperature. Increased metabolic activity in brown adipose tissue is visualized as symmetric, bilateral increased FDG uptake within the supraclavicular fossae, within the neck, the thorax, axillae and the paraspinal and retroperitoneal fat. Due to brown fat activation, nodal involvement may be difficult to appreciate on PET imaging in patients with primary tumors of the head and neck or lymphoma. Patients are also advised to minimize muscle activity 24 hours before image acquisition to avoid increased muscular FDG uptake. Talking during the FDG uptake phase results in increased uptake within the muscles of phonation and vocal cords, in the lingual region and masseter muscles. Patient motion during image acquisition can lead to misregistration artifact and should be registered. Dental prosthetics, metallic implants or chemotherapy ports represent common artifacts in PET/CT imaging. In the presence of these high density materials, standardized uptake value (SUV) measurement is compromised. The patient's medical history data have to be collected prior to the PET/CT exam. These data should include exact timing of patient's prior diagnostic and therapeutic procedures, as well as surgical interventions. Conclusions: The artifacts, pearls and pitfalls may impede the accurate PET/CT interpretation and can potentially lead to misdiagnosis. The normal biodistribution of PET radiotracers as well as the technical aspects of image acquisition and inadequate patient preparation affect the quality of PET/CT imaging. In order to allow correct image interpretation, it is necessary to have a comprehensive knowledge of the normal anatomy and to be familiar of potential imaging pitfalls.

Keywords: F-18 FDG-PET/CT Imaging, Artifacts, Pitfalls

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