1. Wykład 1: Nuclear Medicine Diagnosis – Standard Approach
2. Wykład 2. Imaging of Neuroendocrine Tumours/Neoplams
3. Wykład 3. PET in Oncology
4. Wykład 4: Therapy using Radioisotopes
5. Wykład 5: Clinical use of nuclear medicine in diagnosis and therapy of CNS (central nervous system) diseases

**Seminaria:**

1. Introduction of clinical use of bone scan
2. Clinical cases of GEP-NET using diagnostic imaging

Tematyka zajęć

**Nuclear Medicine Diagnosis – Standard Approach**

**Definition**

* The method of diagnosis and treatment with radioactive substances introduced into the human body;
* The results provide a diagnosis, appropriate treatment and monitoring of therapy;
* Radioisotope studies allow an assessment of both construction and maintenance of the test organ.
* These methods often allow the identification of disease earlier than other imaging techniques.

**Principles of nuclear medicine (NM)**

* Nuclear medicine is the medical specialty that uses the radioisotopes (radiotracer) principle;
* Most often with radiopharmaceuticals, to evaluate molecular, metabolic, physiologic and pathologic conditions of the body for the purposes of diagnosis, therapy and research as well.
* The combination of anatomic information from other modalities may complement the information from radiotracers providing more information than the sum of the two separately, which allows from single image received both functional and structural information as image fusion.

**Structure of the nuclear medicine (NM)**

* + A very small amount of a suitable pharmaceutical or other agent radiolabelled with radioisotopes.
  + Almost all, does not cause side reactions, such as allergies;
  + The radiopharmaceutical is given i.v., p.o. or a body cavity such as the articular cavity;
  + Uptake of the radioactivity (increased or decreased) is a marker of disease, compar to physiological uptake of the radiotracer.
  + Distribution of the radioactivity is examined using a special device - gamma camera.

**NM Study characterization**

* + During the examination, the device (gamma camera) does not produce any additional radiation, except hybrid imaging like SPECT/CT, PET/CT which used CT.
  + The radiation dose associated with a specified radiotracer and particular diagnostic imaging proceedings is in most cases much lower than the dose in the normal course of radiological examination.
  + Labeled radiotracer is usually eliminate very rapidly from the body and practical is not harmful to the environment.

**Specificity of MN studies**

* Suitable radiotracer to study individual organs;
* Reading of the examination at various times after a radiotracer administration dependent on type of examination;
* In some studies acquisition done immediately after administration, others after few hours and another after few days later;
* MN illustrates the potential function of the organ and its pathology, but not directly the structure of the organs or tissue.

**Types of NM imaging**

* Planar;
* Dynamic;
* First pass,
* Gated;
* WB - whole body;
* Tomographic acquisition - SPECT (Single Photon Emission Computed Tomography) or PET (Position EmissionTommography).

**Imaging of NEN**

**Introduction**

* Neuroendocrine neoplasms (NEN) old name tumours (NET) are derived from the diffuse endocrine system and can be found anywhere in the body;
* The WHO classification of endocrine tumours includes neoplasms originating from endocrine glands like:
  + adrenal pheochromocytomas (Pheo), pituitary adenomas, paragangliomas, ganglioneurinomas (PGL), neuroblastomas;
  + *MTC;*
  + Most common tumours of diffuse endocrine system of gastro-entero-pancreatic area (70 % cases, 2% digestive tract tu).

**Diagnostic Imaging of NEN**

* Endoscopy, EUS – methods of choice in initial diagnosis of foregut and hindgut NET,
* MDCT after i.v. contrast enhancement;
* MRI before and after i.v. contrast enhancement (Gd)-DTPA
* Somatostatin Receptor Imaging using:
  + SPECT Scintigraphy (SRS) (99mTc HYNICTOC – Tektrotyd)
  + PET Ga68 DOTATATE, DOTATOC; 18FDG PET, 18F DOPA;
* 123I mIBG;
* Bone scane or MRI of the spine.

**Diagnostic Imaging goals using functional and structural imaging methods**

* Primary tu detection – EUS, endoscopy, US, SRS, PET, CT;
* Local tu extent - CT, MRI, EUS, SRS;
* Adjacent organs invasion - CT, MRI, SRS, EUS;
* Disease staging - CT, SRS, MRI, mIBG, US;
* Somatostatin receptor expression *in vivio -* SRS;
* Response on local/systemic therapy-CT, MRI, SRS
* Imaging „follow-up” - SRS, CT, MRI, EUS, etc.

**PET in Oncology (Positron Emission Tomography)**

**Principles of PET technology of NM imaging**

* PET allows non-invasive quantitative assessment of biochemical and functional pathological processes;
* The most commonly used tracer at present is the glucose analogue FDG.
* FDG accumulation in tissue is proportional to the amount of glucose utilization;
* The use of the phenomenon of annihilation of matter with antimatter particles;
* Radioisotopes like 18F, 11C, 13N, 15O or 82Rb emit a +b, which are annihilated after a collision with an electron – b;
* The reaction gives 2 photons 511KeV the opposite direction of propagation

**PET - General**

* PET is a tomographic technique that computes the 3D distribution of radioactivity based on the annihilation photons that are emitted by positron emitter labeled radiotracers;
* Conjunction **PET** with **CT** enables precise anatomical localization of the lesion with accumulating radiotracers (18F-FDG or others) and also differentiation of pathological tissue from normal;
* CT allows for better image quality by correcting the absorption and scattering of radiation by the patient's body tissue (called Attenuation correction & Scatter Correction);

**Limitation of FDG-PET in oncology**

* Not all cancers are FDG avid;
* Variable uptake is likely related to biological features of individual cancers, low uptake seen as follows:
  + Bronchoalveolar carcinomas,
  + Renal RCC,
  + DTC - thyroid cancers,
  + several subtypes of malignant lymphoma,
  + Well differentiated neuroendocrine neoplasm (NET/NEN);
  + Most prostate carcinomas.

**Therapy using radioisotopes**

**Clinical used of I-131**

Non-oncological (benign);

* Hyperthyroidism : Graves’ disease , hyperactive goiter, single hyperactive thyroid nodule ;
* Nontoxic goiter/ diffuse parenchymal goiter
* Postoperative ablation of residual thyroid parenchyma after surgical removal of benign multinodular goiter ;

Oncology

* Treatment remaining thyroid tissue after surgical removal of the thyroid cancer;
* Treatment of metastatic thyroid cancer ;
* Treatment of thyroid cancer recurrence at local, regional and distant metastases.

**Radiosynovectomy (RS)**

* Radiosynovectomy (RS) is a safe and repeatable treatment method of chronic synovitis with synovial overgrowth and refractory chronic or acute inflammatory joint effusion.
* It consist in the intraarticular administration of a radioactive isotope in the form of a colloid, causing the extinguishing of active synovitis;
* The radiocolloid causes permanent irradiation of the synovium with beta ray electron beams, which ultimately leads to its fibrosis and extinguishes the inflammatory process destroying the joint.

**Main indication of RS**

* Chronic/acute arthritis in the course of systemic diseases (reumatoid arthritis, psoriasis,
* Haemolytic arthritis and haemophilic arthropathy.
* Spondyloarthropathies;
* selected cases of osteoarthritis;
* recurrent effusions following surgery, e.g. arthroplasty, or other iatrogenic post-surgery AEs causing arthritis;
* pigmented villonodular synovitis and crystal synovitis;
* Crystalopathies, including gout and pseudogout, calcium pyrophosphate dihydrate arthritis - CPPD.
* Undifferentiated arthritis.

**Palliative treatment of refractory metastatic bone pain**

* Palliative therapy of refractory, metastatic bone pain using radioisotopes;
* 223Ra – radium - Xofigo® (approved in Europe and USA for prostate cancer);
* 89Sr (approved in Europe and USA for prostate cancer),
* 153Sm-lexidronam (153Sm-EDTMP);
* 186Re-etidronate (186Re-HEDP);
* Substantial advantages of bone palliation radionuclide therapy include the ability to simultaneously treat multiple sites of disease with a more probable therapeutic effect in earlier phases of metastatic disease.

**Therapy using 131ImIBG**

* **mIBG** is an iodinated guanethidine derivative, structurally **similar to natural NA**;
* **is taken into chromaffin cells** by an active transport mechanismutilising the vesicular monoamine transporters **(VMATs)**and concentrated in storage granules;
* VMAT occurs in 2 sub-groups, VMAT1and 2;
* Significant number of **NETs concentrates mIBG** like: neuroblastomas, pheochromocytoma and paragangliomas (PGL) and enterochromaffin carcinoids;

**PRRT with SSTR analogues**

* Current therapeutic options for patients with inoperable progressive metastatic GEP-NEN/NET are still limited;
* When a metastatic GEP-NET is responsible for carcinoid syndrome, treatment with SST analogues is method of choice, due to good symptoms control;
* Reduction of tumour size using „cold” SST analogues is seen rare;
* Chemotherapy, particularly in patients with midgut GEP-NEN/NET not only ineffective but also toxic;

**The goal of PRRT**

* The main goal of radionuclide peptide target therapy (PRRT) consists of the elimination of cancer cells using high energetic b-electrons;
* Lower toxicity to other normal tissues, due to direct binding of radioisotopes into tumour cells

**Radioembolisation – SIRT**

* High radiation dose to all tumors within the liver;
* Low radiation dose to the normal liver tissue;
* Infusion via hepatic artery;
* Uses 90Ymicrospheres (SIR-Spheres; TheraSphere);
  + Diameter approx. 30 µm;
  + Half life: 64 hours;
  + Beta energy max 2.27 MeV mean 0.93 MeV;
  + Penetrates mean 2.5 mm tissue; max 11 mm;
  + Achieves doses of 100–1.000 Gy to the tumour.

**Central Nervous System NM imaging and therapy**

Clinical use of functional imaging methods SPECT and PET

* Regional cerebral blood flow - rCBF;
* Metabolic exchange, base on glucose utilization using FDG-PET;
* Neurodegenerative diseases, dopamiergic transport system, D2 receptor system;
* Neuro-oncology diagnosis using FDG-PET/CT, 201Tl SPECT/CT and AA labeled with radioizotopes in PET/CT and SPECT/CT diagnosis
* Intratumoral and i.a. therapy of primary brain tumours (gliomas), short review on clinical used and direction on further progress.

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**Clinical indication SPECT/CT rCBF or PET/CT**

* Vascular disease CNS – (CVD)
* Stroke - acute;
  + - Potential complication after stroke, prognosis anf choice of correct approach in further therapy opption and clinical follow-up;
* Stroke – chronic;
  + Evaluation of rCBF with functional test (Diamox), before surgery of carotid arteries;
  + consider before open or intravascular surgery of CCAs;
* MDI – multi infarct dementia, second after AD.

**rCBF in localization of seizure foci**

* + Before surgery, lateralization and localization of epileptic foci;
  + „Ictal” and „interictal” examination in case of temporal lobe seizure.

**Dementia –rCBF (SPECT) and FDG-PET**

* + Suspicion of dementia, early differential diagnosis of dementia;
  + mild cognitive impairment (MCI), especially the amnestic form, frequent conversion to AD;
  + AD - Alzheimer's Disease;
  + DLB - Dementia "Lewy body" (the 2-nd most common);
  + MID - Vascular (multi-infarct dementia - MID), leukoencephalopatia, optimal MRI;
  + FTD - fronto-temporal dementia (including Pick's disease) (5%);
  + Movement disorders with dementia such as Parkinson and Huntington disease.

**MRI, SPECT and PET in dementia**

* structural MR imaging allows the measurement of neuronal loss (atrophy);
* SPECT role of rCBF disturbance;
* 18F-FDG PET allows the assessment of neuronal dysfunction;
* newer radiotracers (18F-florbetapir, 18F-florbetaben, 18F-flutemetamol) allow imaging of cerebral amyloid deposits.

**Summary SPECT and FDG-PET in dementia**

* The basic role in the early diagnosis of AD, MCI, and differentiating AD from other forms of dementia;
* Predicting the conversion of MCI to AD;
* Evaluation of the effectiveness of therapy;
* Analysis based on modern image analysis algorithms, measurements of volume (voxel-based) and a comparison to a standard age group;

**Neurodegeneration such as neuronal dysfunction and neuronal loss**

* Confirm or exclude interruptions in the dopaminergic neurons (Parkinson’s);
* Early diagnosis of Parkinson's disease;
* Assessment of the severity of Parkinson's disease;
* Use of presynaptic dopamine binding medium FP 123I - CIT (DaTSCAN);
* Dopaminergic system - receptors - currently 5 types of dopamine receptor (D1-D5)
* D2 ligands (differentiation of atypical Parkinson's disease);
* 123I SPECT iodobenzamide (IBZM), 123I epidepride,
* PET18F fallypride and 18F and 11C raclopiride desmethosyfallypride.