

# Chosen abstracts of XL Days of Nuclear Medicine of Czech Society of Nuclear Medicine

## LUNG

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### IMAGING OF PULMONARY EMBOLISM

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The aim of this review is to discuss the current opinion on the value of imaging methods for the diagnosis of pulmonary embolism (PE). The rapidly developing field of the CT pulmonary angiography (CTPA) will be pointed out. During the eight decade of the last century, large Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) study, focused on the diagnostic value of the ventilation/perfusion scanning (V/Q, comparison with conventional pulmonary angiography — AG). Positive predictive value (PPV) of high probability V/Q results is 88%, negative predictive value of normal finding reaches 91%. However, there are roughly two thirds (!) of indeterminate results where the PPV ranges from 10 to 70%. Typically, this occurs in patients with preexisting cardiopulmonary disease. Pulmonary AG is still considered to be the gold standard, but it is reluctantly indicated method (0.5% mortality) with limited availability. The implementation of CTPA into the clinical practice offers noninvasive alternative for the direct diagnosis of PE. Literary data show high sensitivity and specificity (90–95%) for the depiction of emboli up to the level of segmental arteries. Newest multidetector devices allow even the confident diagnosis of isolated peripheral PE. The important advantage of chest CT is also the capability to show the alternative pathology as a cause for clinical symptomatology. Moreover, concurrent CT venography of the legs and abdomen can be accomplished with the same amount of iodinated contrast agent. In our institution, the V/Q scan is performed mainly in patients with no history of cardiopulmonary disease and normal or near-normal chest X-ray, because in this situation it provides convincing results. The other patients undergo CTPA. Pulmonary AG is only indicated when subsequent endovascular treatment of massive peracute PE is planned.

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### PULMONARY PERFUSION SCINTIGRAPHY AT HIGHT ALTITUDE (4559M)

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**Aim:** To assist in understanding of the pathophysiology of high-altitude pulmonary oedema (HAPE).

**Material and methods:** Pulmonary perfusion scintigraphy was performed in the group of 21 mountaineers (9 of them with a previous history of HAPE documented by X-ray) in basal conditions at 550m and 6 hours after the rapid climb to 4559m. In 6 subjects HAPE developed 18 to 36 hours after the scintigraphy at high altitude. They were treated with NO-inhalation, the scintigraphy was repeated again before and after therapy. The area of perfusion (number of pixels) and the inhomogeneity of perfusion were calculated (determined by standard deviation — as the percentage difference from the average value).

**Results and conclusions:** Pulmonary perfusion area is significantly greater (35% difference in control group, 29% difference in HAPE group) at high altitudes in comparison with the results in basal conditions at low altitude. The pulmonary perfusion, especially in the apical parts, is inhomogeneous at high altitudes (standard deviation increased from 31 to 35% without significant difference between control and HAPE group). The distribution of pulmonary perfusion improves and the O<sub>2</sub> saturation increases after NO-inhalation. To our knowledge, until today we have performed scintigraphy at the highest altitude all over the world during this study.

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### NUCLEAR MEDICINE METHODS IN THE DIAGNOSIS OF PULMONARY EMBOLISM

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The aim of the presentation is to give the overview of the role of lung scintigraphy in the period of changing approaches to diagnostic procedures in diagnosis of pulmonary embolism. The major contribution of nuclear medicine to the pulmonary imaging was the report from the PIOPED study in the beginning of nineties. The results showed very good output for high probability, very low probability and normal scans (92–95%), but scans with intermediate probability are mostly non-diagnostic. This group represents major problem in competition to other imaging methods. At present many papers document enhancing of the sensitivity using tomographic techniques in lung scintigraphy. The most valuable is the negative predictive value of normal VQ scans, which still plays very important role in differential diagnosis mainly in patient with subacute or chronic dyspnoea. The other question to discuss is the detection of silent embolia when deep venous thrombosis is present and the other problem is follow up of reperfusion of defects in known embolia. Most of errors by evaluation of VQ scans are related to delay in performing VQ scan after the onset of symptoms, when the reperfusion already occurs and the second main problem is presence of the unresorbed previous embolism (35% of cases). The radiation burden is in lung scintigraphy several times lower comparing to CT angiography and also use of the iodine contrast falls off.

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### LUNG PERFUSION SCINTIGRAPHY — INDICATIONS, AVAILABILITY AND LOGISTIC PROBLEMS OF STANDARD DIAGNOSTICS OF PULMONARY EMBOLISM

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The retrospective evaluation of standard scintigraphic examination — lung perfusion scan (PSP) provided in regional nuclear medicine department — Banská Bystrica for one year — 2001 were done. Due to economic problems of our hospital we could not use ventilation pulmonary scan (VSP).

**Material and methods:** 365 (11,3%) examinations of PSP in year 2001 were performed. The mean age was 56.6 ± 17.5 (2–88 years), 49% patients over 60 years. 301 patients (102 M, 199 F) were evaluated. Second examinations were done to 61 patients. Waiting period for the first examination was 3,6 days.

**Results:** About 45 PSP 100 000 inhabitants were provided in Slovakia during the year 2001. In district of Banská Bystrica it was similar — 45 and in the Czech Republic (CR) it was 15-times more — 360 per 100 000 inhabitants. Very good correlation (R = 0.79) was found between distance (km) of ordering specialists from ONM and the number of examinations per 100 000 inhabitants. This value was decreasing from 60 (for 20 km) to 15 (for 120 km). The pulmonary embolism is a major indication of PSP in 93.4%. The results of PSP were: 30% negative (gr. 0 a 1) and more than 30% certainly positive (gr. 3) findings. During controls after the therapy in one third of cases the normalization was found. We investigated correlation of % of negative results on extent of information in order form. (1 entry — 51%, vs. 4 and more entries — 21%). We confirmed relation between the percentage of positive PE results on interval between time of acute events and PSP (to 4 days — 50% over 14 days — 29%).

**Conclusions:** PSP is useful examination in diagnostics and stratification of patients with pulmonary embolism. About a third of results (grades 2 and 2+) is necessary to reevaluate by VSP or by other examination. Probably the best one is a spiral CT. PSP is relatively rarely provided in Slovakia, about 6.4% of the level in the Czech Republic. Calculated incidence of PE in our region is about 100/100 000 inhabitants therefore real number of examinations could be about 270 PSP/100 000 and with controls to 360–400/100 000, which is near to value in the CR. The result of 50% and more positive (pathological) results PSP (during the first examination) indicate very good diagnostic level of ordering clinical department. The use of diagnostic algorithm of PE with PSP is in the region of Central Slovakia is insufficient due to important logistic problems with transport of patients.

## ONCOLOGY

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**THE VALUE OF FLUORODEOXYGLUCOSE IN THE DIAGNOSTICS TODAY**

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Ten years after the first synthesis of 2-fluoro-2-deoxy-D-glucose (FDG) by Josef Pacak, the atom of fluorine was replaced by its radioactive form  $^{18}\text{F}$  by T. Ido. It happened in USA 25 years ago. Due to imperfection of PET scanners at that time,  $^{18}\text{F}$ FDG was used for brain research only. Later, a clinical application was recognised in seizures and in the assessment of biological behaviour of brain tumours. But the expansion of MRI considerably limited  $^{18}\text{F}$ FDG-PET in the brain imaging. Concerning PET investigation of brain tumours, it could be expected replacement of  $^{18}\text{F}$ FDG by labelled amino-acids like  $^{11}\text{C}$ -MET or  $^{18}\text{F}$ FET in the future.

Since 1986  $^{18}\text{F}$ FDG has been applying for studies of myocardial metabolism. Later,  $^{18}\text{F}$ FDG-PET became the gold standard in the assessment of its viability. In spite of development of other imaging modalities,  $^{18}\text{F}$ FDG-PET partially plays this role till now. The uptake of  $^{18}\text{F}$ FDG in the vast majority of neoplasm is high enough, that modern PET scanners enable to discover tumour foci of 5 mm in diameter, e.g. non-enlarged lymph nodes invaded by tumour, that cannot be recognised by anatomical imaging modalities (CT, MRI). An improvement of PET scanners in the last decade enabled whole body investigations.  $^{18}\text{F}$ FDG-PET encountered great success in the localisation of unknown primary tumours, in the biological evaluation of known tumours, in the staging of tumour diseases, in the assessment of the effect of therapy and in the early diagnostics of tumour recurrence.

That's why (thanks to  $^{18}\text{F}$ FDG) PET represents the most dynamically developing imaging modality up to date. In the Czech Republic (CZ) one of the milestones of worldwide development of PET was settled 35 years ago. It is gratifying, that two  $^{18}\text{F}$ FDG producers operate in CZ now, and that CZ belongs to the most developed countries in the clinical usage of  $^{18}\text{F}$ FDG-PET after 4 years of operation of PET Centre Prague. Recent installations of two state of the art PET scanners including hybrid PET/CT are promising for the future of PET in CZ.

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**PALLIATIVE THERAPY OF PAINFUL BONE METASTASES WITH BONE-SEEKING THERAPEUTIC RADIOPHARMACEUTICALS**

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Bone is a common site of metastatic disease and is the most common site of metastatic spread in breast cancer and prostate cancer. The pain is the most important consequence of bone metastases and is present in majority of the patients. Radiotherapy represents one of effective therapeutic options in the palliation of bone pain. Currently, radiation may be delivered either by external irradiation (loco-regional, half-body) or intravenous administration of bone-seeking therapeutic radiopharmaceuticals as is  $^{153}\text{Sm}$ Samarium-EDTMP,  $^{186}\text{Re}$ Rhenium-HEDP,  $^{90}\text{Sr}$ Strontium-chloride,  $^{32}\text{P}$ Phosphorus-orthophosphate. These radiopharmaceuticals produce beta radiation, and are concentrated in areas of enhanced osteoblastic activity.

Palliative therapy with bone-seeking radiopharmaceuticals is indicated in patients with refractory bone pain and disseminated bone metastases. Contraindications for this therapy are anaemia, leucopenia, trombocytopenia, renal insufficiency and simultaneous administration of chemotherapy a radiotherapy.

Results of studies from home and abroad with bone-seeking therapeutic radiopharmaceuticals will be presented during the lecture.

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**FIRST EXPERIENCE WITH POSITRON EMISSION TOMOGRAPHY WITH  $^{18}\text{F}$ -FLUORODEOXYGLUCOSE (FDG-PET) IN PEDIATRIC ONCOLOGY**E. Kabickova<sup>1</sup>, O. Belohlavek<sup>2</sup>, D. Sumerauer<sup>1</sup>, M. Chanova<sup>1</sup>, E. Cumilivska<sup>3</sup>, R. Kabsan<sup>3</sup>, R. Kodet<sup>4</sup>, J. Koutecky<sup>1</sup>

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**Aim:** The purpose of our study was to evaluate the role of FDG PET imaging in the management of children with cancer.

**Material and methods:** Twenty four children with malignant solid tumors underwent thirty-two FDG-PET studies between January 2001 and December 2002. There were 8 children with soft tissue sarcoma, 12 with bone sarcoma, two with neuroblastoma, one with testicular germ cell tumor and one with nephroblastoma. The median age was 15.7 years (range 5.3 to 18.5). In 9 children PET was the part of primary staging, 16 PET studies were undertaken for therapy monitoring after completion of treatment and in 7 children PET was performed for suspected relapse. PET scans were compared with follow-up clinical data, results of conventional imaging methods (CIMs) and histology.

**Results:** In three of nine children referred for initial staging PET revealed more extensive disease than expected. These positive findings resulted in a change of the stage (from III to IV). After completion of therapy CIMs suggested residual abnormalities in 10 of 16 children, 19 of them accumulated FDG. True-positive were 7 PET studies, in two children was PET false-positive. Six of seven patients assessed for suspected relapse accumulated FDG, developed relapse was proven by biopsy or with clinical follow-up. One patient with negative PET remains in complete remission (follow-up 10 months).

**Conclusions:** In this preliminary study, FDG-PET was useful in the evaluation of a variety of pediatric malignancies: for primary staging, post-therapy assessment and early detection of relapse. Approximately one third (9/24, 38%) of investigations resulted in modification of scheduled treatment. Further experience is necessary to define the precise role of FDG-PET in pediatric oncology.

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**POSITRON EMISSION TOMOGRAPHY WITH  $^{18}\text{F}$ -FLUORODEOXYGLUCOSE (FDG-PET) IN CHILDHOOD MALIGNANT LYMPHOMAS**E. Kabickova<sup>1</sup>, O. Belohlavek<sup>2</sup>, D. Sumerauer<sup>1</sup>, E. Cumilivska<sup>3</sup>, M. Kynci<sup>3</sup>, R. Kodet<sup>4</sup>, J. Koutecky<sup>1</sup>

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**Aim:** Children with malignant lymphomas (ML) generally are treated according to stage and risk profile. Metabolic imaging by FDG PET offers the advantage of functional tissue characterization that is independent of morphologic criteria and contributes to more accurate primary staging and better assessment of response to therapy. The aim of our study was to assess the clinical value of FDG PET for initial staging and restaging of childhood lymphomas.

**Material and methods:** Fifty four children and adolescents with Hodgkin's disease or non-Hodgkin's lymphoma (NHL) underwent 78 FDG-PET studies between March 2001 and May 2003. The median age was 15.8 years (range 4.1 to 18.3). The indication for FDG PET examination was initial staging in 40 children and restaging after completion of first-line chemotherapy in 38 children. PET scans were compared with clinical follow-up, results of conventional imaging methods (CIMs) and histology.

**Results:** Thirty three of 40 children referred for initial staging had concordant FDG-PET and CIMs imaging (82%). PET correctly upstaged seven patients (18%). PET showed no abnormal uptake in retroperitoneal lymph nodes in 3 children with positive lymphangiogram.

At the end of treatment CIMs suggested residual abnormalities in 19/38 children, only six of them accumulated FDG. Three children had true-positive PET studies and received additional therapy. In 3 children PET was false-positive.

Thirty two children showed a normal post-treatment PET scan, all but one are in complete remission, with a median follow-up of 16.5 months (11-24). One patient with NHL relapsed two months after a normal PET scan.

**Conclusions:** FDG-PET contributed to more accurate initial staging. Post-treatment PET studies were useful for detection of viable tumor, false positive results were observed due to inflammatory lesions (outside of known residual masses) or tumor "healing". Information from FDG-PET imaging resulted in a change in clinical management in 20% of children with ML (11/54).

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**SENTINEL LYMPH NODES DETECTION IN PATIENTS WITH ENDOMETRIAL CARCINOMA**P. Koranda<sup>1</sup>, M. Kudela<sup>2</sup>, V. Hušák<sup>1</sup>, P. Dzviničuk<sup>2</sup>, D. Lubušky<sup>2</sup>, M. Mysliveček<sup>1</sup>, M. Kamínek<sup>1</sup><sup>1</sup>Department of Nuclear Medicine, <sup>2</sup>Department of Gynaecology and Obstetrics, Palacky University, Olomouc, Czech Republic

**Aim:** The sentinel lymph node (SLN) biopsy is already established procedure reducing unnecessary extent of surgical management in various malignancies. This pilot study was performed to determine the feasibility of preoperative lymphoscintigraphy and intraoperative gamma probe guided biopsy in women with endometrial carcinoma (EC). Outcome and measured count rate from SLN were compared with those in patients with vulvar carcinoma (VC).

**Material and methods:** A consecutive series of 21 women was studied using standard protocol. There were 16 pts with EC (FIGO stages — 2 pts IA, 6 IB, 3 IC, 2 IIA, 2 IIB, 1 IIIA) and 5 pts. with VC (T category — 1 T1, 2 T2, 2 T3). All patients received 50 MBq of <sup>99m</sup>Tc-nanocolloid divided into 4–6 portions. In women with EC radiopharmaceutical was injected peritumorally in a total volume of 2.5 ml, injection sites were oriented according to ultrasonographic and in some cases also hysteroscopic findings. A series of static lymphoscintigrams was performed 20–90 min p.i. In women with VC radiopharmaceutical was administered intrademally and submucosally around the tumour in a total volume of 0.5 ml and a 5 min dynamic scintigraphy was performed. Subsequently, a series of static lymphoscintigrams was acquired 5–90 min p.i. Surgery started 2–3 hours p.i., mean operation time being 3 hours. 9 patients with EC were studied using blue dye.

**Results:** In EC patients SLNs were detected using gamma probe intraoperatively in 10/16 cases and in surgical specimens in 13/16 cases (internal iliac SLN 12/16, external iliac 5/16, common iliac 4/16, obturator 2/16, periaortic 2/16). In all 5 VC patients SLNs were detected both intraoperatively and in surgical specimens. Median count rate from excised SLN in EC was 45 cps and in VC 250 cps (gamma probe sensitivity 10 cps/kBq), respectively. The mean dose to surgeon's chest measured by personal electronic dosimeters was  $2.3 \pm 1.9 \mu\text{Sv}$  per procedure. SLN were detected using blue dye technique in 4/9 women with EC, 1 patient being negative using radionuclide method.

**Conclusions:** The preoperative lymphoscintigraphy and intraoperative gamma probe guided biopsy are able to detect SLNs in significant number of patients with EC, despite some difficulties accompanied by the procedure. The SLN count rates in women with EC were lower compared with those in women with VC; therefore we recommend to practice one-day protocol.

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**VALUE OF GALLIUM SCINTIGRAPHY IN THE AGE OF PET**

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Gallium 67 — citrate is used to functional imaging some types of tumors and inflammations more than 30 years. Nowadays gallium scintigraphy is a classical method of nuclear medicine. It provides important diagnostic and prognostic data especially in patients with malignant lymphomas and malignant melanomas. In inflammatory diseases gallium scintigraphy, besides imaging, can assess the activity of inflammation. Dual heads gamma cameras equipped with 300 keV collimators, standard protocols with whole body scintigraphy and SPET increased the sensitivity and specificity of examination.

During the last years PET with <sup>18</sup>F-DG has expanded in many indications where gallium scintigraphy was superior. Both methods in comparison show higher sensitivity and specificity for PET, thanks to better resolution and different mechanism of the radiopharmaceutical uptake. The great advantages of PET are possibility to image tumors without gallium avidity, lower radiation dose and better comfort for patients (1-day procedure). Disadvantages of PET are the higher price and not so simple approach in our country. Gallium scan is generally accessible in the most nuclear medicine departments.

In the right indications (the staging and follow-up of malignant lymphomas and melanomas, monitoring tumor response to treatment and early detection of recurrence, detection of activity some inflammations) gallium scintigraphy has slightly worse results, but is still profitable.

During the last five years we have performed 450–490 gallium scans per year in our department and the demands for examination have not changes. In the course of time we observed changes in their spectrum. Number of patients to reveal malignity and staging is decreasing, but demands for follow-up patients after therapy and detection of recurrence are increasing.

Gallium scintigraphy is a good functional modality for some tumors and inflammations. In future it will be replaced with PET and <sup>18</sup>F-DG in many indications. But we suppose that gallium scintigraphy will be still for a long time important diagnostic method thanks to the good results, lower price and good availability.

**NEUROLOGY**

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**INVESTIGATION OF DAT SYSTEM USING DATSCAN. COMPARISON OF VISUAL AND SEMIQUANTITATIVE ASSESSMENT**J. Bakala<sup>1</sup>, A. Gatková<sup>2</sup>, Z. Kalita<sup>2</sup>, P. Minář<sup>1</sup>, J. Bernátek<sup>2</sup>, A. Keder<sup>1</sup><sup>1</sup>Department of Nuclear Medicine, Bata's Hospital, Zlín, <sup>2</sup>Department of Neurology, Bata's Hospital, Zlín, Czech Republic

**Aim:** To compare the visual and semiquantitative assessment of the investigation of DAT system in Parkinson disease using DATSCAN.

**Material and methods:** Since year 2000 there were altogether 52 patients investigated. All procedures were done with the radiopharmaceutical DATSCAN — 123I ioflupane (Amersham). For the study 35 patients were selected (selection criteria was the same gammacamera). All have been investigated on double head gammacamera AXIS (Philips) connected with the ODYSSEY computer system.

The same system was used for determination of basic parameters with the Alderson phantom. The patients were 19 men (average age 64 ± 8 years) and 16 women (average age 58 ± 7.6 years). Three hours after application of 185 MBq 123I ioflupane the acquisition was done. Altogether 128 images were used in the matrix 128 × 128; time per frame was 45 sec. iterative transversal reconstruction (16 iterations) was used. Postfiltration with Butterworth filter, order 10, cut-off 0.35.

The final assessment was done primary visual on the coloured display individual by the transversal oblique, sagittal and coronal sliced, finally using 3D.

Visual assessment:

0 — normal tracer uptake;

I — asymmetric tracer uptake in putamen only;

II — asymmetric tracer uptake both in putamen and nucleus caudatus;

III — dramatic decrease of tracer uptake both in putamen and nucleus caudatus;

Semiquantitative assessment:

Integration of 15 slices (each 2.7 mm) from transversal reconstruction was done.

Binding potential was calculated using different methods:

1 — RR ROI basal ganglia (BG) × occipital region (OR);

2 — IR ROI BG × IR OR;

3 — IR nucleus caudatus (NC) × IR OR;

4 — IR putamen (P) × IR OR.

**Results:**

	BG INT	DX NC INT	PU INT	BG INT	SIN NC INT	PU INT
group 0	84.0 ± 27.3	112.8 ± 40.3	87.1 ± 37.6	85.5 ± 29.1	111.3 ± 41.1	96.6 ± 38.9
group I. DX +	40.5 ± 14.5	61.3 ± 20.8	24.0 ± 7.4	54.1 ± 15.7	78.5 ± 21.8	38.7 ± 13.0
group I. SIN +	66.2 ± 23.4	92.3 ± 27.7	43.3 ± 24.2	51.6 ± 27.7	72.4 ± 31.2	36.4 ± 35.1
group II. DX +	64.3 ± 14.1	82.3 ± 26.7	57.6 ± 11.6	80.1 ± 15.7	107.0 ± 26.8	65.6 ± 16.8
group II. SIN +	74.7	104.8	44.6	57.8	80.7	31.3
group III. DX +	26.4 ± 5.9	42.2 ± 11.0	18.2 ± 0.7	33.7 ± 14.7	51.2 ± 20.6	23.9 ± 7.3

**Conclusions:** Both visual and semiquantitative assessment correlates with the clinical results. Semiquantitative assessment will allow us in the future to interpret the results of neuroprotection during the therapy of PD.

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**ICTAL BRAIN SPECT BEFORE REPEATED EPILEPSY SURGERY**M. Buncová<sup>1</sup>, J. Hadač<sup>2</sup>, K. Sixtová<sup>2</sup>, K. Stegurová<sup>2</sup><sup>1</sup>Department of Nuclear Medicine, Institute for Clinical and Experimental Medicine, <sup>2</sup>Department of Pediatric Neurology FTN, Prague, Czech Republic

The aim of epilepsy surgery is seizures elimination and improvement quality of life. The localisation of the epileptogenic region is an assumption of expected result. The brain SPECT of regional cerebral perfusion can be a useful tool for it. Reoperation should be necessary, if the first epilepsy surgery has failed. We are presenting our experience we obtained at repeated ictal brain SPECT in 3 children (2 girls age 8m, 11y and 1 boy age 4y). Ictal brain SPECT was accomplished before first surgery and repeated examination before reoperation. We image epileptogenic region that need not be identical to more evident morphological lesion which is attractive for surgeon. The importance of ictal brain SPECT before epilepsy surgery and before reoperation especially results from the comparison of the anatomical imaging and functional imaging brain SPECT.

## CARDIOLOGY AND ANGIOLOGY

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## POSSIBILITIES OF DETECTING PERFUSION DEFECTS OF LOWER LIMBS IN DIABETIC PATIENTS WITH THE AID OF 99mTc TETROPHOSMIN PERFUSION SCINTIGRAPHY AND LASER DOPPLER

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**Aim:** The diagnostics of microangiopathy and mediocalcinos of LL (lower limbs) are still difficult procedures despite the introduction of new methods of examination. For the detection of muscular perfusion in the lower limbs of diabetic patients without claudications we used 99mTc Tetraphosmin in the performance of myocardial scintigraphy, assuming that according to Cosson et al. perfusion defects in the proximal parts of the lower limbs are attributed to microangiopathy and distal defects to macrovascular disease. We compared the findings with a Laser Doppler (examination) of the periphery of the lower limbs with thermal provocation.

**Material and methods:** We involved in the observation 11 diabetic patients, whom we divided into two groups: the first one without confirmed microvascular complications and the second one with confirmed microvascular complications. There were 6 patients in the first group (3 women, 3 men, Type 1 DM 3, Type 2 DM 3), group age  $42.2 \pm 10.3$  years, length of duration of DM  $11.5 \pm 4.6$ , all treated with insulin, 2 smokers, 4 non-smokers, HbA<sub>1c</sub>  $7.9 \pm 0.7\%$ , 2 dyslipidemia. In the second group 5 patients (2 men, 3 women, Type 1 DM 4, Type 2 DM 1), group age  $46 \pm 6.6$  years, length of duration of DM  $23.5 \pm 8.1$ , all treated with insulin, non-smokers, HbA<sub>1c</sub>  $9.1 \pm 1.2\%$ , 3 dyslipidemia, 3 patients had confirmed nonproliferative retinopathy and nephropathy, 1 autonomic neuropathy in the region of the cardiovascular system and 1 diabetic thick skin and tissue (carpal tunnel syndrome, Dupuytren's contractures). All patients underwent examination by biothesiometer, color duplex sonography and Doppler with ABI (ankle brachial index) measurements. Perfusion periphery LL was evaluated by Laser Doppler with thermal provocation in the big toe area. Further exercise myocardial SPECT (single-photon emission computed tomography) imaging was performed, followed by planar scintigraphy of both lower limbs on gamma camera AP (anteroposterior) and PA (posteroanterior) view. Rest scintigraphy followed by planar imaging at the same locality was executed in the following stage.

**Results:** The images were evaluated visually and semi-quantitatively using ROI (region of interest). In the first group without microvascular complications vibratory thresholds for right LL were found to be  $17.8 \pm 9.9$  V, for left LL  $17 \pm 9.7$  V, ABI for right LL  $1.2 \pm 0.2$ , for left LL  $1.2 \pm 0.3$ , sonographically  $2 \times$  mediocalcinos of the crural arteries, rest Laser Doppler  $13 \pm 7.8$  PU (perfusion units), after thermal provocation  $72.4 \pm 49.6$  PU, time for achieving maximum value of perfusion  $2.3 \pm 1.7$  min, and rate  $19.4 \pm 12.6$  PU/min. Scintigraphically after exercise 1 patient with sonographically confirmed mediocalcinos was found to have defective perfusion of the calf. In the second group with confirmed microangiopathic complications vibratory thresholds for right LL were  $24.4 \pm 15.9$  V, for left LL  $24.8 \pm 5.3$  V, ABI for right LL  $1.2 \pm 0.2$ , for left LL  $1.1 \pm 0.3$ ,  $4 \times$  mediocalcinos, rest Laser Doppler  $8.7 \pm 5.9$  PU, after provocation  $90.3 \pm 41.3$  PU, time for achieving maximum value  $2.4 \pm 0.7$  min, ( $p = 0.9$ ), rate  $46.2 \pm 29.9$  PU/min ( $p = 0.1$ ). Scintigraphy revealed: 1 defect in the region of the calves, 3 patients with perfusion defects of the thighs and one patient with borderline rates for a perfusion defect of the thighs.

**Conclusions:** Patients with confirmed microvascular complications manifested a lower rest perfusion of the periphery, a longer period for attaining the maximum value when examined by Laser Doppler, and these findings were correlated with proximal defects of thigh perfusion in scintigrams. The defective perfusion of calves after exercise may be a manifestation of silent macrovascular disease. Both methods appear to be adequate for more detailed noninvasive diagnostic procedures concerning vascular disease of the LL in patients with diabetes.

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<sup>201</sup>Tl AND <sup>99m</sup>Tc-MIBI GATED SPECT IN PATIENTS WITH LARGE PERFUSION DEFECTS: COMPARISON OF 4D-MSPECT SOFTWARE WITH CONTRAST LEFT VENTRICULOGRAPHYM. Kamínek<sup>1</sup>, M. Škvařilová<sup>1</sup>, J. Ostřanský<sup>1</sup>, M. Mysliveček, O. Lang<sup>2</sup><sup>1</sup>Department of Nuclear Medicine, <sup>2</sup>Department of Internal Medicine, University Hospital, Olomouc, <sup>3</sup>Department of Nuclear Medicine, University Hospital, Prague-Královské Vinohrady, Czech Republic

**Aim:** Left ventricular ejection fraction (LVEF) is a major prognostic factor in coronary artery disease and may be computed by gated SPECT (GSPECT). Previous validation studies in patients with large perfusion defects have been performed using Cedars QGS software. We evaluated the feasibility and accuracy of new quantitative software 4D-MSPECT in assessing LVEF in patients with large perfusion defects. A difference in <sup>201</sup>Tl and <sup>99m</sup>Tc-MIBI studies was also studied.

**Methods:** A total of 111 consecutive patients (86 men, 25 women, 49 with a history of myocardial infarction, mean age  $63 \pm 8$  y) who underwent both rest GSPECT and contrast left ventriculography (LVG) were studied. A cardiac cycle was divided into 8 frames either for <sup>201</sup>Tl ( $n = 42$ ) or <sup>99m</sup>Tc-MIBI studies ( $n = 69$ ). Sixty-four projection views were obtained over  $180^\circ$  using a  $90^\circ$  dual-head camera Siemens e.cam equipped with low-energy high-resolution collimators. Images were reconstructed using filtered backprojection, the summed rest perfusion score (SRS) and the LVEF were assessed using 4D-MSPECT software. Correlation coefficients between LVG LVEF and GSPECT LVEF were calculated using Pearson's method.

**Results:** Average SRS was 7.2 (range 0–47), mean LVG LVEF was  $52.5 \pm 10.6\%$  (range, 20–70%) and mean GSPECT LVEF  $52.1 \pm 10.9$  (range 18–74%). Correlation coefficients were high for all patients ( $r = 0.92$ ), for subgroup of patients with mild to moderate perfusion abnormality (SRS 4–13,  $r = 0.92$ ), for subgroup of patients with large perfusion defects (SRS > 13,  $r = 0.93$ ), for <sup>99m</sup>Tc-MIBI and <sup>201</sup>Tl studies  $r = 0.90$  and  $0.92$ , respectively.

**Conclusion:** Correlation coefficient between LVG LVEF and GSPECT LVEF was high ( $r = 0.92$ ). In agreement with previous studies performed using GSPECT with Cedars QGS, the LVEF measurement is feasible using 4D-MSPECT in patients with large perfusion defects. The superiority of <sup>99m</sup>Tc-MIBI over <sup>201</sup>Tl was not observed in the LVEF measurement.

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## CONJUNCTION OF BICYCLE STRESS WITH ATROPINE FOR MYOCARDIAL PERFUSION SCINTIGRAPHY — PRELIMINARY STUDY

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**Introduction:** Many patients are not able to achieve appropriate (85% of maximal) heart rate during stress myocardial perfusion scintigraphy (SMPS). It implies lower sensitivity. These patients are usually shifted to pharmacological stress with dipyridamole or dobutamine. However, change of the type of stress during the test infers more time required.

**Aim:** To determine the efficacy of atropine injection added to bicycle stress in patients unable to achieve appropriate heart rate during SMPS.

**Material and methods:** Atropine was used in 21/194 patients sent to our departments for SMPS. There were 15 men and 6 women with mean age of 57 years (41–75). 13 patients took beta-blockers. All except one withdrawn beta-blockers for 48 hours, 3 did not. Atropine was injected intravenously in the dose of 1 mg if the patient demonstrated inability to continue stress and his/her heart rate was not appropriate. <sup>99m</sup>Tc MIBI was injected within one minute and patients continue stress for another minute at the same level or one step lower.

**Results:** Heart rate was lower on average by 14 (from 4 to 29) beats per minute (bpm) than appropriate in the time of atropine injection. Atropine was injected on average in the 7<sup>th</sup> (from 4 to 10) minute of stress, stress was finished on average in the 9<sup>th</sup> (from 6 to 12) minute. Heart rate increased on average by 25 bpm (from 15 to 40) after atropine administration. All patients except one achieved or exceeded appropriate heart rate. Only one patient complained xerostomia, others had no side effects. 15 patients had negative, 1 patient borderline and 5 positive SMPS results.

**Conclusion:** Use of atropine in conjunction with physical stress to increase heart rate is effective, safe and it saves operating time. Its diagnostic efficacy should be assessed on a larger group of patients.

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## ASSESSMENT OF BLOOD FLOW VELOCITY THROUGH LARGE ARTERIES OF LOWER EXTREMITIES

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Supposing the passage of radionuclide through lower limbs arteries corresponds their blood flow velocity.

Evaluation of blood flow velocity precedes standard bone scintigraphy. Patients are in supine position on the scintibed using AP projection over pelvis. The mark is drawn on the skin 1–2 cm bilateral up the iliac crests to assist the localisation of the aorta bifurcation. On this mark is positioned <sup>57</sup>Co marker. Dynamic study (120 frames — 1s, matrix  $128 \times 128$ ) starts immediately after the injection.

We follow the aorta bifurcation passage activity on the screen. Just after the bolus phase is over the scintibed is shifted without any interruption of dynamic study to catch start activity in the insteps and toes. Time-activity curves from the bifurcation ROI and feet ROIs are generated. The assessment of time interval corresponds to the duration of the radiopharmaceutical passage from aorta bifurcation to feet. Distance from mark on the skin to toe is measured. Blood flow velocity is calculated — extremity length/time interval.

Blood flow velocity in normal (22 person — i.e. 44 extremities) was assessed  $2.24$ – $8.54$  cm/s, on the right limb  $4.45 \pm 1.56$  cm/s, the left  $4.57 \pm 1.73$  cm/s. There was no significant side difference.

10 patients were examined for Charcot osteoarthropathy. On the extremity with more patol.alteration, the flow velocity was from  $5.29$  cm/s to  $12.33$  cm/s, on the contralateral lower extremity from  $2.28$  cm/s to  $7.4$  cm/s. On the affected side was blood flow velocity significant increased. Asymmetric velocity was detected by osteomyelitis on lower extremity and iliofemoral bypass, too.

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### STRESS MYOCARDIAL PERFUSION SCINTIGRAPHY IN PATIENTS WITH IMPLANTED PACEMAKER

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**Introduction:** Artificial heart pacing is a common therapeutic method stimulating myocardial contraction by electric pulses. Stimulating electrode is most frequently placed into the apex of the right ventricle, in dual-chamber stimulation also into the right atrium. Appropriate type of stress should be applied if such a patient is referred for stress myocardial perfusion scintigraphy (SMPS) for good accuracy.

**Aim:** To evaluate the influence of pacemaker on myocardial perfusion by retrospective assessment of patients referred to SMPS.

**Material and methods:** 77 patients (pts) with pacemaker were enrolled into analysis. There were 44 men and 33 women with mean age of 72 years (54–83). Finally we analyzed only 56 pts without previous myocardial infarction. Single-head gamma camera with LEAP collimator was used; we employed one-day stress-rest protocol; data were processed by CEQUAL™. 11/14 patients stressed only by bicycle had pacemaker set on DDD mode. 5 pts were stressed only with dipyridamole, 3 with VVI and 2 with DDD mode of pacemaker. Remaining 37 pts underwent combine stress with dipyridamole and exercise, 33 pts had pacemaker set on DDD mode. 21/56 pts underwent coronary angiography.

**Results:** Fixed perfusion defects were detected in 42/56 (74%) pts, remaining 14 pts had homogeneous perfusion. Defects were consistently localized in the apical part of the inferoseptal wall and their extent was from 2% to 10% of the myocardium of the left ventricle. 10/42 pts with fixed perfusion defect underwent coronary angiography and their findings were normal. 11/14 pts without perfusion defect revealed also normal coronary arteries (5/11) or < 50% stenoses (6/11).

**Conclusion:** 74% of patients with pacemaker and without previous myocardial infarction can reveal small fixed perfusion defect consistently localized in the apical part of the inferoseptal wall despite normal coronary arteries. Histological changes, mainly fibrosis, around the tip of electrode can cause these perfusion defects. We should be aware of interpreting these defects as a positive result to avoid false positive findings.

## KIDNEY

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### DMSA SCINTIGRAPHY AND THE INFLUENCE OF APPLIED METHODOLOGY OF INVESTIGATION ON THE DIAGNOSTIC VALUE OF METHOD

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**Aim:** According to the world standard the investigation of renal parenchyma from planar images includes the evaluation of scans at least in four projections in order of correct assessment number, shape, size and character of cortical lesions. But there are still some departments where only two projections of DMSA scan are used for the evaluation. The objective of this study was to evaluate the sensitivity, specificity and diagnostic accuracy of the method using for DMSA results interpretation only 2 projection and to compare variability between two above mentioned DMSA methods. The method using 4 projections in the investigation of renal parenchymal abnormality was considered as a reference one. Studies obtained from January 2000 were retrospectively interpreted. The second aim of our study was to determine an occurrence of mobile kidney (ren migrans), because this kind of renal abnormality stay often unknown and it might caused some difficulties in patients.

**Material and methods:** Planar anterior, posterior, right and left posterior oblique images of both kidneys were obtain in supine position for 3 min each, 2–4 hours post injection of <sup>99m</sup>Tc-DMSA. There have been used five projections for qualitative assessment of renal parenchymal abnormalities in our department since January 2002. The fifth projection presents planar posterior in standing patients and it allows the evaluation of mobile kidney. 735 studies were obtained from January 2000 to December 2002, whereby six types of findings were considered: without any lesion, presence of one, two or three renal cortical abnormalities, shrank kidney and missing kidney.

**Results:** Shrank and missing kidneys were excluded from statistic interpretation of findings, there were evaluated 707 of right kidneys and 701 of left kidneys. The method using 2 projections in the investigation of renal parenchymal abnormality showed 74% sensitivity, 88% diagnostic value in left kidneys and 75% sensitivity, 87% diagnostic value in right kidneys. The finding of mobile kidney was presented in 5.5% in 2002.

**Conclusions:** Applying five planar projections in the assessment of renal parenchymal abnormalities definitely increases the diagnostic value of the planar scintigraphy. Applying only 2 projections as a method of DMSA results interpretation decreases number of positive findings specially in case of small or single lesions. We have also proved that mobile kidney appears proportionally often and it can be detected only by changing the position of patient during the investigation.

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### NEW METHODS FOR EVALUATION OF DYNAMIC RENAL SCINTIGRAPHY

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Dynamic renal scintigraphy contains more diagnostic information than it is usually extracted by traditional methods for descriptive analysis of time-activity curves.

**Aim:** The aim of this contribution is to provide definition and description of newer parameters and procedures based on physiological models, to demonstrate principles of calculations and clinical applications.

**Material and methods:** Algorithms for calculation of diagnostic parameters of renal function were compiled using recent papers by K.E Britton, A.M.Peters, and M.D.Rutland. They were implemented in MATLAB (MathWorks Inc) on a personal computer (PC), and used to evaluate data of dynamic renal scintigraphy transferred to PC from different types of scintillation cameras in the Interfile format.

**Results:** An interesting alternative to classic representation of plasmatic and renal clearance [ml/min] that is independent of both the distribution volume of a radiopharmaceutical and body size, is the value of clearance normalised by the volume of plasma or extracellular fluid (ECT). The result is given as rate in [s<sup>-1</sup>]. However, its reciprocal value, a residence time of the tracer in plasma or ECT [s], seems to be a more practical number. It represents an average time for which a molecule of the tracer persists in respective volume (i.e. plasma or ECT) before it is excreted by one or both kidneys. Preliminary clinical results show that (in comparison with classic formula) the clearance given as the residence time is more sensitive to changes of renal function, it is not affected by changes of body fluid volumes, and it is also less dependent on patient's gender and age. It reduces differences between men and women, and in children it sooner approaches adult values. Accepted criterion of renal outflow becomes renal output efficiency (ROE). It is a portion of activity excreted by the kidney up to a specified time related to the total activity theoretically accumulated by that kidney up to the same time (either before or after administration of a diuretic). Clinical results show that with ROE it is possible to reduce the proportion of uncertain reactions to a diuretic (F +20) from usual 15% down to 2% — the value that is otherwise achievable only by repeated examination using F –15.

**Conclusion:** Residence time of the tracer in plasma or ECT and ROE are simple but potentially useful diagnostic parameters based on physiological models which promise to improve accuracy of quantitative description and evaluation of dynamic renal scintigraphy. Clinical significance of both parameters remains to be validated in more extensive clinical trials.

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**VALUE OF DYNAMIC RENAL SCINTIGRAPHY AND INDIRECT RADIONUCLIDE CYSTOGRAPHY IN EXAMINATION OF MICTURITION DISORDER IN CHILDREN**

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**Aim:** The aim of the study was to evaluate benefit of <sup>99m</sup>Tc MAG3 dynamic renal scintigraphy (DRS) and following indirect radionuclide cystoradiography (IRC) in children who were examined for micturition disorder. Furthermore, to compare our results with results of urodynamic study(UD) and ultrasound examination which were obtained at urological department of Children surgery.

**Matreial and methods:** In period — September 2000–April 2003, at Department of Nuclear medicine of IKEM were examined 12 boys of the age 10.3 ± 3.4 years, and 5 girls of the age 10.6 ± 4.9 years, mainly with diagnosis: nocturnal enuresis and neurogenic bladder.

Evaluation was performed by program MAG3 on computer system Vision 101 — General Electric

Urodynamic study — MENUET system — Dantec.

**Results:** In 7/17 patients with normal findings on UD and IRC, was found disorder in dynamic renal scintigraphy as alteration of excretory fase. In the majority of cases it was relative urine retention for hypotony of renal pelvis or ureter.

Despite psychological influence during the micturition, in 11/17 patients were results of IRC and UD identical.

**Conclusion:** Advantages of indirect radionuclide cystoradiography:

1. Technically is possible to obtain investigation in any child who is toilet trained — almost from the age of 2;
2. Physiological conditions of micturition (in older children there is certain influence of surrounding);
3. Radiation exposure is not increased from the preceding dynamic renal scintigraphy;
4. During the same examination we obtain complete information about condition of intra- and extrarenal urinary tract, VUR and micturition.

**INFECTION AND INFLAMATION**

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**RADIOLOGY IN DIAGNOSIS OF INFLAMMATORY DISEASES**

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This announcement is a thought on how a modern radiology can take place in the diagnosis of inflammatory diseases in the climate of a large hospital, where the opportunities of CT, MR and ultrasound imaging are available. It is aimed to demonstrate how radiology takes place in detection of severe inflammatory diseases, where imaging plays the main role. It also discuss the threats and opportunities of each method and the risk of an exaggerated diagnosis and reliance of each method and also bad clinical interpretation of a well done examination.

We point out the need of a good technical performance in examining, which plays an important role in order to determine a further imaging strategy. We also emphasise the requirement of a complex interpretation of all radiology an non-radiology examinations and the confrontation with the clinical data of a patient and his laboratory results as well. We refer to a change of findings in time and on several case we document the variation of image in a period of short time.

We discuss the benefit of relevant clinical and history data and the necessity of a cooperation between all departments. We point out the benefit of a functional data and information system, that also includes the results of all radiology examinations, now days useful for two health service institutions. (By the way we also point out on the opportunity to send the image data to a requesting physician).

The underestimation of technical and organisational requirements can lead to a severe failure of the reliability of the radiology method a examination and can thereby discredit each method in the diagnosis of inflammatory diseases in general as well. This misunderstanding can then lead to a failure tendency to replace the concrete radiology method by other non-radiology examination method, in the situation where the radiology method would be a useful and optimal way to reach the goal.

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**POSITION OF RADIONUCLIDE IMAGING METHODS IN THE DIAGNOSIS OF OSTEOMYELITIS IN PATIENTS WITH DIABETIC FOOT SYNDROME**

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**Introduction:** Ulcerations of foot in diabetics are frequent but virtually serious complication. Ulcers commonly cause poly-microbial infection of soft tissue but it can involve a bone. Osteomyelitis especially together with ischemia frequently lead to lower extremity amputation.

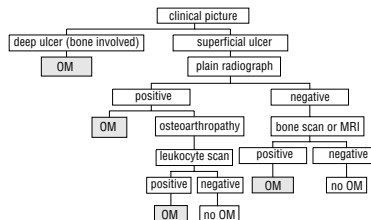
**Aim:** To introduce a review of available radionuclide methods and their position in the diagnostic process.

**Material and methods:** Many different imaging methods can be used for osteomyelitis imaging. This review is focused on radionuclide methods mainly on bone and leucocyte scans. Polyclonal human immunoglobulin G scan, gallium scan and new methods are also briefly reported.

**Results:** Diagnostic efficacy of particular method depends on patient population examined, localization of inflammation, clinical course of the disease and other factors. Moreover there is no gold standard which could be used as a reference method currently. Bone scan sensitivity between 83% and 100% and specificity 50% to 75% is referred in the literature. Labeled white blood cells sensitivity is referred between 86 and 94%, specificity 90% to 100%. Combined sensitivity is referred 77% to 93% and specificity 83% to 100%. No method can be used alone for diagnosis of osteomyelitis.

**Conclusion:** Plain radiograph is a first choice method in the diagnostic process of osteomyelitis in patients with diabetic foot syndrome, bone scan or magnetic resonance imaging follows. In the case of neuropathic osteoarthropathy white blood cells scan is usually essential — see diagram.

Diagnostic diagram (OM — osteomyelitis; MRI — magnetic resonance imaging)



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**IMAGING INFECTION INTO THE 21<sup>ST</sup> CENTURY**

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The scintigraphic imaging of infection has become a well established part of routine clinical practice, though for 40 years the dynamic bone scan has been used for osteomyelitis and the HIDA scan for nearly 50 years in cholecystitis. It was the advent of Ga-67 which in 1969 ushered in the era of more specific infection imaging. Ga-67 is still useful in disease such as TB, spinal osteomyelitis but its use is hampered by the non-specific uptake into a variety of normal tissues and non-infected pathology. Therefore the search for more specific tracers has continued with In-111 labelled leukocytes in 1977 and Tc-99m HMPAO labelled cells 10 years later. These are often considered the gold standards of infection imaging but the cell labelling requires skill and time. Therefore the search for an easy to use Tc-99m labelled radiopharmaceutical continues. The early 1990's saw the production of Tc-99m antigranulocyte antibodies and Tc-99m HIG. These agents still have their enthusiasts but have not been widely accepted. The last 5 years has seen the launch of Tc-99m selusamab, a radiolabelled Fab', with the ability to image soft tissue and bone infections. More specific infection imaging was also promised by Tc-99m Ciprofloxacin but recent reports suggest this may also be a non-specific marker. Latest developments have also concentrated on PET, however the most commonly used agent F-18 FDG is very non-specific and may not be ideal for use in infection, though new infection specific tracers for PET await development.

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**VALUE OF BONE SCINTIGRAPHY AFTER THE TREATMENT OF THE BONE CYST**E.Urbanova<sup>1</sup>, P.Sponer<sup>2</sup>, K.Urban<sup>2</sup>, J.Vizda<sup>1</sup><sup>1</sup>Department of Nuclear Medicine, <sup>2</sup>Department of Orthopaedic Surgery, University Hospital Hradec Kralove, Czech Republic

**Aim:** To assess the role of the bone scintigraphy after the treatment of unicameral and aneurysmal bone cysts. The cause of the lesions is unknown. Pathologic fractures are common. As a bone substitute bioactive glass ceramics, bone allograft and autograft can be used. Fresh autogenous bone is the best grafting material, but its supply is limited especially in children. Bioactive glass ceramics were reported to have the character of osteoconduction and capability for binding directly with the living bone tissue. In orthopedic surgery material BAS-O Lasak Praha in granules is used.

**Material and methods:** In our study 13 patients (pts) were treated by curettage and filling of the bone defect with bioactive glass ceramic. Patients were in age range 8–23 years. Aneurysmal bone cyst was present in 3 pts, in 10 pts unicameral bone cyst was proofed. Involvement of femur was in 8 pts., humerus in 3 pts and tibia in 2 pts. Clinical examination, plain radiography and 3-phase bone scintigraphy and SPET were performed to follow up the patients 3–11 years after the operation. Scintigraphic data were acquired with dual head gamma camera after intravenous injection of <sup>99m</sup>Tc-methylenediphosphonate. Regions of interest (ROI) were selected bilaterally within 4 consecutive coronal tomograms and each ROI was compared to equivalent reference ROI.

**Results:** In all patients were no significant changes in perfusion and blood pool. Normal osteoblastic activity in implanted area was in six cases, slightly increased in 4 and high in 3 cases (these pts suffered pain). No signs of glass ceramic loosening and no periosteal reaction were observed on plain radiographs. Clinical examination proofed no inflammatory changes of the soft tissues in all cases.

**Conclusions:** This small study suggests that 3-phase bone scintigraphy and quantitative SPET analysis are sensitive methods to follow up patients for monitoring bony repair after aneurysmal or unicameral bone cyst operation. The next step will be comparison between similar groups of patients where bioactive glass ceramic, allogeneous and autogenous bone grafts were used for filling.

This study was supported by the Czech Ministry of Health Grant Agency, No. 6853-3/2001.

**INSTRUMENTATION**

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**PET/CT — THE NEW MODALITY (NUCLEAR MEDICINE POINT OF VIEW)**

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**Aim** of this presentation is to discuss the first experience with hybrid PET/CT investigation from the nuclear medicine point of view.

**Material and methods:** The scanner used Siemens Biograph duo LSO is equipped by LSO detectors. It operates in 3D mode exclusively. So it is possible to shorten the data acquisition by factor of 2 and administer lower amount of activity at the same time in comparison to the standard 2D mode at BGO scanners. CT data serve as well for attenuation correction.

**Results:** 400 PET/CT investigations were carried out during the first 3 months of operation. The image quality in 3D mode is fully comparable to up to now used BGO PET scanner ECAT EXACT in 2D mode. Moreover exact anatomical localisation of hypermetabolic lesions is enabled. Some typical findings and image patterns will be presented to illustrate capability of the new PET/CT modality.

**Conclusion:** PET/CT imaging should be considered as the substantial milestone in the development of PET. It brings complex and rapid (one stop shop) investigation of the patients, but on the other hand it requires to solve plenty of new questions arising by fusion of nuclear medicine and radiodiagnostics.

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**VARIA**

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**UNDERGRADUATE TEACHING OF NUCLEAR MEDICINE IN EUROPEAN COUNTRIES**

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**Introduction:** Education schemes of undergraduate teaching of nuclear medicine of students is an important problem for international nuclear medicine community. The students of today will be tomorrow our clinical partners. Therefore the amount of knowledge in nuclear medicine graduate have when leaving the university should be an object of care of nuclear medicine lecturers.

This paper overviews the curricula of nuclear medicine undergraduate training in 68 European medical faculties and for comparison 8 extra-European ones. The data show high variation in number of hours devoted to nuclear medicine, varying between 0 to 62 hours. In most cases this teaching is integrated with the one of radiology or clinical modules, in some cases also with training in clinical physiology. The average curriculum of nuclear medicine in our sample was 15.7 hours, in extra-European universities 8.8 hours. If the nuclear medicine was taught as an independent course the average was 25.2 hours, when integrated with radiology and/or radiotherapy 14.7 hours, when integrated with clinical modules 5.2 hours.

**Conclusions:** in pregraduate education of nuclear medicine there are tremendous differences country-to-country. This may exert the problems with intra-European diploma acceptance. Moreover, it should be considered, whether the integration of teaching with other clinical modules is a good thing for nuclear medicine community.

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**UNDERGRADUATE TEACHING OF NUCLEAR MEDICINE TECHNOLOGISTS IN EUROPEAN COUNTRIES**

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This article overviews the training of nuclear medicine technologists in chosen European countries, Australia, the USA and Canada. There are basically two types of this training: either at medical schools following secondary school, without any university degree, usually on a two- or three-year basis, or else as a university course, leading to a BSc degree after three years, in some countries an MSc degree after an additional two years. In the USA/AU/CAN both systems coexist, in Europe it varies from country to country. Also the number of hours devoted to nuclear medicine varies in particular curricula — from 2.500–4.400 hrs BSc, 4.500–6.200 MSc. Some efforts are being made to unify this system by transition to the university model of education in many European countries (BG, CH, CZ, I, PL and others)

There are following questions facing the future of nuclear medicine technologists training:

- professional schools or university-based training?
- radiology, radiotherapy and nuclear medicine technology — together or separated?
- role of MSc of NM technology.

Those questions are the challenge for the community of technologists and educationalists.

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**INTO THE FUTURE OF NUCLEAR MEDICINE**

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Any attempt to predict the future of any medical specialty is fraught with problems. Personal preference will play a part as will wishful thinking and possibly the ravings of a mad or alcohol soaked mind. Therefore this vision of the future will be very personal.

There are three main areas where Nuclear Medicine will develop in the next 10 years and all have in common the fact that it is important to exploit the differences between functional imaging and radiology and not try to compete head on. The first of these is PET, clearly this technology will be the area of greatest investment in machines, however if PET is to truly succeed then new tracers must be found, if we allow PET to be a CT contrast agent we will have failed to deliver the range of knowledge possible in nuclear medicine.

The second area is the development of single photon agents which will allow *in-vivo* monitoring of highly specific and important physiological processes. These will be linked to our growing knowledge of the genomics and proteomics of diseases such as cancer. Therefore Tc-99m MIBI is a known substrate for MDR1 expression and Tc-99m Annexin-V can be used to identify apoptosis. Soon it may be possible to use nuclear medicine to identify manipulations of the patient's genome.

The third area is therapy, the advance of Y-90 Zevalin for non-Hodgkins lymphoma is showing the way and underdevelopment is a whole raft of new antibodies and peptides. These treatments will not be cheap but will provide highly efficacious treatment with reduced toxicity and will need to be thought of as a cancer therapy and not a nuclear medicine imaging agent.

Therefore the next 10 years in nuclear medicine may be the most exciting since the 1960s and the first use of Tc-99m we are in for a revolution — I hope we enjoy it.

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**FIVE YEARS OF DEPARTMENT OF NUCLEAR MEDICINE IN THE NEW ONCOLOGY PAVILION IN UNIVERSITY HOSPITAL IN HRADEC KRALOVE**

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Department of Nuclear Medicine was moved to new oncology pavilion in University Hospital in autumn 1997. Therefore modern history of nuclear medicine in Hradec Kralove has been started to write before five years.

New oncology pavilion was built in years 1994-1997. Digital double-head SPECT gamma camera, two computers X-Pert Pro with processing software and equipment for radiation monitoring (indicators of radioactive contamination of surface, indicators of radioactive contamination of hands and feet and digital personal dosimeters) were bought to new department. Next double-head SPECT gamma camera and planar gamma camera was moved to new department too. All acquisition and processing computers were connected by network. We are doing central archiving of image data and print of hard copy by laser printer. Two laminar boxes were bought for division of nuclear pharmacy.

Department of nuclear medicine is doing administration of therapeutic radiopharmaceuticals ( $^{131}\text{I}$ ,  $^{32}\text{P}$ -orthophosphate,  $^{89}\text{SrCl}$ ,  $^{153}\text{Sm-EDTMP}$ ,  $^{90}\text{Y}$ -colloid) and disposes of six single bedrooms. These bedrooms are being shielded by heavy spar and toilets are connected by separate plumbing with sump of radioactive waters.

Our balance in years 1998-2002: 38 630 scintigraphy (for example: whole body bone scan 12 414, lung perfusion scintigraphy 5 398, dynamic renal scintigraphy 3 241, DMSA scan 1 465, whole body gallium scan 2 331, SPECT 7 380). We administered therapeutic radiopharmaceutical in 930 patients (for example:  $^{131}\text{I}$  — 666 patients,  $^{153}\text{Sm}$  — EDTMP — 86 patients,  $^{90}\text{Y}$  — 60 patients).

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**THE NUCLEAR MEDICINE TECHNOLOGIST IN EUROPE — CURRENT STATUS AND FUTURE PROSPECTIVE**

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The practice of nuclear medicine technology requires skills of various disciplines. For this reason it needs a specialist training and Education. The nuclear medicine technologist (NMT) should be able to apply the knowledge of at least eight areas when imaging or treating patients with radiopharmaceuticals. These 8 areas are patient care, radiochemistry, dosimetry, use of technology, radiation safety, organisation and management, quality assurance and education. In order to carry out his/her task, the NMT must successfully complete didactic and clinical training. It is recognised that the practice of nuclear medicine varies from department to department within a country and from country to country. The Education should be certified to be sure that the NMT meets the criteria for these basic competencies. In 1998 the EANM Technologist Committee delivered the competencies for the European Nuclear Medicine Technologist. This document represents what is thought to be good practice. For five years the Technologists Committee of the EANM established an Education subcommittee with members from different countries in Europe to get Educators in Europe on the same line. The language and the laws in the different countries in Europe make it difficult to provide a uniform system of education. We feel that this problem will be solved in the next decade. Communication between Educators in all European Countries should be encouraged. A register of certified NMT should be made. Initially in the separate countries, later one European register of certified NMT should be established.

With all the technical innovations and new developments in Nuclear Medicine there is a Huge need of Continuing Education (CE). In the Netherlands there is an experience of 14 years of CE courses, while in other countries no CE courses are available. Therefore at each EANM Congress Continuing Education sessions for NMT are running during the whole Congress in English, with a programme of assessment via Multiple Choice Examination. In 2003 The EANM Technologist Committee established a PET learning course for NMT in Vienna (Austria) in order to provide the highest standard of education on PET and its relation to other imaging modalities in Europe. The language barrier is still a problem, but will be solved in the next decade, as more and more young people in Europe will be educated in English language during their school period. An Exam of the CE courses needs to be expanded into a credit system. This credit system should lead to a review of the registration of a certified Nuclear Medicine Technologist.

To promote good practice for Nuclear Medicine Technologists a new publication on "The advanced Performance a Responsibility guidelines for the Senior NMT" is produced in 2001 by the EANM Technologist committee.

All these efforts must lead to a high standard of work of Nuclear Medicine Technologists in all the different countries in Europe.

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# Chosen abstracts of Serbia and Montenegro SNM Congress

## ONCOLOGY

1

### SCINTIMAMMOGRAPHY AS A METHOD OF DIAGNOSIS AND FOLLOW-UP OF PATIENTS WITH BREAST CANCER

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**Aim:** To evaluate the scintimammographic findings used in the diagnosis and follow up of patients with breast cancer on our material.

**Material:** In 31 women scintimammography was made, age of 19–70, average age 51.06 years. By the breast changes women were divided into 3 groups. Group I (n = 13) were patients with clinical and scintimammography findings suggesting breast malignancy, with PH verification. Group II (n = 13) patients with earlier PH certified breast malignancy and later developed recurrence. Group III (n = 5) was made of women who had clinical and ultrasonography signs for fibroadenoma and dysplasia.

**Methods:** Scintimammography was made with <sup>99m</sup>Tc-MIBI with an activity of 555 MBq, 10 minutes after intravenous application in the cubital vein on the contralateral side where the breast changes were detected. Gamma camera Orbiter 45 Siemens was used, with mattress 128 x 128 in prone and anterior position of both breasts. Only the sensitivity and accuracy of the method could be determined.

**Results:** Group I: in 69.2% (9/13) a breast amputation was made and in 30.8% (4/13) breast quadrantectomy. All the scintimammography findings were true positive (TP) regarding the PH results, so this method had SE = 100% and A = 100%. Group II were patients with proven malignancy and later developed recurrence: in 53.8% (7/13) the scintimammographic findings were negative and in 46.2% (6/13) they were positive for recurrence. Only one patient from this group was reoperated (TP). Group III: two scintimammography findings were negative and three were positive. None of the women from this group had PH verification of the scintimammographic findings. In 19.2% (5/26), in whom the malignancy was PH verified, accumulation in the axilla was detected and in 11.5% (3/26) multifocality of the changes in both breasts were detected.

**Conclusion:** Scintimammographic findings can help a surgeon make a decision if a breast amputation or quadrantectomy is to be made, in cases of recurrence it can help make a decision about further therapy, a positive scintimammographic finding in cases of benign lesions should be verified.

2

### TREATMENT AND OUTCOME OF SMALL (PT0 AND PT1) DIFFERENTIATED THYROID CARCINOMA

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**Aim:** The analysis of treatment and outcome of differentiated thyroid carcinoma (DTC) patients (pts) whose primary tumor was in diameter to one centimeter (pT0 and pT1).

**Material and methods:** 391 DTC pts were treated from 1977 to the end of 2000, followed to the end of 2002. In 55 (14.1%) of them the primary tumor was pT0 (4 pts) or pT1 (51 pts). They were divided into groups: A — 25 (45.5%) pts with regional metastases (N1) — 3 of them had distant metastases (M1) too; B — 30 (54.5%) pts without regional and distant metastases (NOM0).

**Results:** The frequency of N1 in pT0-pT1 pts was not significantly different comparing to other DTC pts (p > 0.1), but M1 were significantly less frequent (p < 0.05). Papillary carcinomas (94.5%) were significantly more frequent than follicular (5.5%) comparing to other DTC pts (p < 0.05). The probability of 20-years survival was 0.94 ± 0.04. In the group A — nearly total or total thyroidectomy was done in all 25 pts, nodal dissection in 24 pts, radioiodine therapy was applied in 24 pts, hormonal therapy in all 25 pts, external beam therapy in 2 pts and chemotherapy in one patient; complete remissions were achieved in 15 (60%) pts, 7 (28%) pts had relapses, and 2 (8%) pts died from disease related deaths. In the group B — nearly total or total thyroidectomy was done in 15 pts, in 7 pts subtotal thyroidectomy, in 8 pts lobectomy, partial lobectomy or nodulectomy, hormonal therapy in all pts and one patient was treated by external beam therapy; complete remissions were achieved in 24 (80%) pts, 2 (6.7%) pts had relapses, while disease related deaths were not registered.

**Conclusion:** The small (pT0 or pT1) DTC were papillary in most pts. Nearly half of them had N1, but rarely M1. The probability of 20-years survival was very high. In pts with N1 complete remissions were less frequent, relapses more frequent, and there were a few disease related deaths comparing to N0 pts; in our opinion in N1 pts radical surgery and radioiodine therapy are mandatory, followed by life-long hormonal treatment. In T1N0M0 pts acceptable is less capacious surgery and life-long hormonal therapy, while RAI treatment in most of them is not necessary.

3

### FREQUENCY OF METASTASES AND LETHAL OUTCOME IN PATIENTS WITH LOCALLY INVASIVE DIFFERENTIATED THYROID CANCER (DTC)

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**Aim:** To analyze the frequency of metastases and lethal outcome in DTC pts staged pT4, related to the DTC pts staged pT1-pT3.

**Material and methods:** We treated 267 pts whose primary tumor status was exactly staged (pT1-pT4) in a period of 1977–2000. They were followed up until the end of 2001. Among them were 117 (43.8%) pts staged pT4, 49 (18.4%) pts staged pT3, 78 (29.2%) pts staged pT2 and 23 (8.6%) pts staged pT1. All pts were treated surgically, by radioiodine and by hormonal therapy, while some of them underwent external radio therapy and/or chemotherapy.

**Results:** In pT4 stage we found regional metastases in 68 pts, distant metastases in 21 pts and lethal outcome in 10 pts (58.1%; 17.9% and 8.5%, respectively). In pT1 stage we found regional metastases in 21 pts, distant metastases in 2 pts and lethal outcome in 2 pts (91.93%, 91.3% and 8.7%, respectively). In pT2 stage we found regional metastases in 37 pts, distant metastases in 8 pts and lethal outcome in 5 pts (47.4%, 10.3% and 6.4%, respectively). In pT3 stage we found regional metastases in 14 pts, distant metastases in 11 pts and lethal outcome in 5 pts (28.6%, 22.4% and 10.2%, respectively). Regional metastases were significantly more frequent in pT4 stage than in DTC pts staged pT2 and pT3 (p < 0.05, p < 0.001, respectively), but they were significantly the most frequent in pT1 stage (p < 0.001). Distant metastases were significantly more frequent in DTC pts staged pT4, related to the pts in pT1 and pT2 stage (p < 0.005, p < 0.005, respectively), but there were no significant statistical difference related to the pts staged pT3 (p > 0.2). We didn't find any statistical difference between pts staged pT4 and pts staged pT1, pT2 or pT3 stage (p > 0.9, p > 0.4, p > 0.5, respectively).

**Conclusions:** Patients with DTC staged pT4 have significantly more frequent regional and distant metastases than DTC pts staged pT2-pT3, with exception of pts staged pT1 stage who were detected because of the presence of regional metastases. DTC pts staged pT4 had no influence to the lethal outcome, related to pts staged pT1, pT2 and pT3 stage.

4

### FLUORINE-18-FDG COINCIDENCE IMAGING IN PATIENTS WITH LYMPHOMA

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The continued improvement in chemotherapy and radiation therapy strategies has resulted in high overall survival rates in patients with Hodgkin's disease (HD) and non-Hodgkin's lymphoma (NHD). Computed tomography is still the principal imaging modality for monitoring of lymphoma, but it is unable to differentiate residual disease from fibrosis. The aim of this study was to compare FDG coincidence imaging with CT and other conventional diagnostic method.

35 studies were performed in 31 patients (14 female, 17 male; median age 35 years, range 16–66 years; 21 with HD, 10 with NHD; 15 patients — stage III–IV, 16 patients — stage I–II) following chemotherapy, radiotherapy and in a few cases after or before bone marrow transplantation. In almost all patients FDG study was done for clarification of residual post-therapy abnormalities that fall under the category of unconfirmed/uncertain complete remission. All patients were injected with 296–370 MBq of FDG after one night fasting. Acquisition, consisting of whole-body scan and tomographic studies of the thorax and abdomen, was started one-hour p.i. The system used was triple-head Philips IRIX, Inc, Cleveland, OH. Reconstruction was performed by an iterative method. In 19 studies FDG scan was negative, in 16 positive. In 11 studies FDG scans found out more lesions than CT and other methods. In many patients unsuspected lesions were detected. The modality of treatment was changed in 10 patients (29%). All FDG-negative patients remained in remission one year after the study. Our preliminary data indicate that this non-invasive metabolic imaging performed with "hybrid" coincidence technology is superior to CT and other conventional diagnostic method in the post-therapy staging of lymphoma. More patient studies and longer period of time are needed to assess the prognostic value of this method in follow-up.

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**RADIOGUIDED INTRAOPERATIVE LOCALIZATION OF SMALL COLORECTAL LESIONS**B. Vidregar-Kralj<sup>1</sup>, I. Edhemović<sup>2</sup>, A. Schwarzbartl-Pevac<sup>1</sup>, I. Žagar<sup>1</sup><sup>1</sup>Institute of Oncology, Department of Nuclear Medicine, <sup>2</sup>Department of Surgery, Ljubljana, Slovenia

**Aim:** Accurate intraoperative localisation of small non-palpable colorectal lesions is often difficult. Based on our previous experience with radioguided occult lesion localisation (ROLL) in the breast, we have recently introduced similar ROLL method for the detection of small colorectal lesions with <sup>99m</sup>Tc-labelled macroagregates (<sup>99m</sup>Tc-MAA).

**Material and methods:** Five patients (4 males and 1 female, age 55–73 years) were candidates for surgery of small colorectal lesions (3/5 located in the rectum, 2/5 in the colon sigmoideum) that were expected to be identified with difficulties during open surgery. During colonoscopy performed 18–20 hours before operation, <sup>99m</sup>Tc-MAA (74–111 MBq in 0.5 ml volume) was injected into the base of the lesion using sclerotherapy needle. All the patients underwent planar scintigraphy of abdomen with simultaneous emission-transmission scanning using a <sup>57</sup>Co flood source, 1–2 hours before surgery. The location of injected radiopharmaceutical was intraoperatively detected with gamma probe.

**Results:** In 4/5 patients scintigraphy revealed intensive focal uptake, in 1/5 patients the focal uptake was only faintly seen, probably because of intraluminal leakage of radiopharmaceutical. Intraoperatively, all the marked lesions were easily detected with gamma probe and later confirmed by histopathological examination.

**Conclusions:** Our work suggests that intraoperative radioguided detection of small non-palpable colorectal lesions after preoperative endoscopic injection of <sup>99m</sup>Tc-MAA is simple and accurate method.

**INFECTION AND INFLAMMATION**

6

**THE VALUE OF SCINTIGRAPHY BY RADIOLABELED CIPROFLOXACIN IN THE DETECTION OF ORTHOPEDIC INFECTIONS**V. Obradović<sup>1</sup>, V. Artiko<sup>1</sup>, B. Davidović<sup>1</sup>, Ć. Vučetić<sup>2</sup>, N. Petrović<sup>1</sup>, N. Nikolić<sup>3</sup>, D. Janković<sup>3</sup>, D. Djokić<sup>3</sup><sup>1</sup>Institute for Nuclear Medicine; <sup>2</sup>Clinical Center of Serbia, <sup>3</sup>Institute for Orthopedics, Clinical Center of Serbia, <sup>4</sup>Vinča Institute for Nuclear Sciences, Laboratory for Isotopes, Belgrade, Serbia and Montenegro

The aim is detection of the infective foci in orthopedic patients using <sup>99m</sup>Tc-ciprofloxacin (Laboratory for radioactive isotopes, Vinča).

Total of 35 patients with clinical suspicion on orthopedic infection was investigated. In all the patients, whole body skeletal scintigraphy was performed. Ciprofloxacin chloride (3.5 mg) was mixed with 555 MBq of <sup>99m</sup>Tc in 3 ml of physiological solution and incubated for 20 min. After slow i.v. injection in a cubital vein, dynamic acquisition (1 f/min) was performed during first 60 min in the position of interest, followed by static acquisition (500.000 imp) of the whole body, anterior and posterior view after 1h and 4 h in all patients. When necessary, additional scintigrams were acquired after 24 h. In all the patients with negative or equivocal findings of planar scintigraphy, emission computerized tomography (SPECT) was performed (60 positions, 6 degrees). Interpretation was made by three independent observers. Additional data were provided using clinical finding, ultrasonography, radiography, computed tomography and magnetic resonance imaging, laboratory analyses, and surgical or microbiological confirmation of infection.

In our study, the highest uptake of radiopharmaceutical was present in liver and urinary bladder, while there was no free pertechnetate in a thyroid gland.

There were 18 TP findings (4 with septic arthritis, 5 with osteomyelitis of femur, after fracture and osteosynthesis, 4 with flegmona of crural region and the foot caused by diabetes, and 5 with infection of the hip prosthesis), 12 TN (5 with osteoporosis, 5 with hip luxation and 2 with femoral fracture and osteomyelitis without infection), three FP (femoral osteomyelitis without infection and loosening of hip prosthesis without infection), while two FN (one due to TBC vertebral osteomyelitis, and the other with resistance to antibiotic therapy). The smallest lesion found was 15 × 20 mm. Scintigraphy after 4h reduced the number of FP findings from 7 to three, and increased the number of TP from 14 to 18, while scintigrams taken after 24 h did not influence the results of the study. Sensitivity was 90%, specificity 80%, positive predictive value 86%, negative predictive value 86% and accuracy 86%. In all 18 patients infection was caused by *Staphylococcus aureus*, in three associated with *Staphylococcus alpha haemoliticus*, *Pseudomonas* and *Acino bacter*. In one patient with FN finding, infection was caused by *Micobacterium tuberculosis*, and in the other resistant to antibiotic.

According to our results, scintigraphy with radiolabeled ciprofloxacin is a useful method for detection and assessment of exact localisation of orthopaedic infections.

## CARDIOLOGY

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**LOW DOSE DOBUTAMINE AND LOW DOSE DIPYRIDAMOLE RADIONUCLIDE VENTRICULOGRAPHY IN DETECTION OF MYOCARDIAL CONTRACTILE RESERVE IN PATIENTS AFTER MYOCARDIAL INFARCTION**

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**Aim:** To evaluate the ability of low dose dobutamine and low dose dipyridamole radionuclide ventriculography to detect contractile reserve in patients after myocardial infarction and functional recovery after coronary angioplasty.**Material and methods:** The study group consisted of 20 consecutive patients (52 ± 10 years, 17 male) with previous myocardial infarction and resting regional dyssynergy, in whom diagnostic cardiac catheterization revealed significant one-vessel coronary artery stenosis suitable for angioplasty. Each patient underwent equilibrium 99mTc radionuclide ventriculography which was performed at rest and during low dose dipyridamole (0.28 mg/kg over 2 minutes) and low dose dobutamine infusion (up to 10 mcg/kg/min). Left ventricular global and regional ejection fractions were determined. Increase of regional ejection fraction for > 5% (inferoapical and posterolateral regions) or > 10% (anteroseptal regions) during low dose dobutamine and dipyridamole in infarcted regions, as well as in the follow up period, was considered as index of contractile reserve. After 8 weeks of successful angioplasty, resting radionuclide ventriculography was repeated in all patients in order to identify functional recovery of the infarct zone.**Results:** Out of the 180 analyzed segments (20 × 9), 90 regional ejection fractions have shown depressed contractility. The mean of the regional ejection fractions showing depressed contractility increased from the resting value of 34 ± 12% to 42 ± 14% in the follow-up period (p = 0.06). Of the 90 with baseline dyssynergy, 46 were responders during low-dose dobutamine (51%), whereas 32 segments were responders (36%, p = 0.05 vs. dobutamine) during low dose dipyridamole. Positive predictive value of dobutamine and dipyridamole for predicting functional recovery was 72% and 75% (p = ns), respectively. Negative predictive value of dobutamine and dipyridamole was 48% and 69% (p = 0.05), respectively. In the group of patients with most severe dyskinesia (regional ejection fraction < 35%, 42 segments) positive predictive value was 73% and 82%, while negative predictive value was 42% and 64% for low dose dobutamine and low dose dipyridamole respectively (p = NS).**Conclusions:** Although low dose dobutamine induced higher rate of positive responses during radionuclide ventriculography imaging, dipyridamole radionuclide ventriculography has shown superior, particularly negative, prognostic value for predicting functional recovery of infarcted regions.

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**FREQUENCY AND PROGNOSTIC VALUE OF REPORTED SIDE EFFECTS DURING DIPYRIDAMOL STRESS TEST IN MYOCARDIAL PERFUSION SCINTIGRAPHY**

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**Aim:** To evaluate occurrence and prognostic value of side effects of pharmacological vasodilatation induced by dipyridamol on the outcome of myocardial perfusion scintigraphy.**Material and methods:** Study group comprised 95 patients (M 58, F 35, mean age 58 years, range 33–76 years). Gated or non-gated SPECT 180° myocardial perfusion scintigraphy (99mTc-MIBI or 99mTc-Tetrofosmin) was performed according to stress-rest two days protocol. Average dose of intravenous dipyridamol was 0.56 mg/kg, infused over 4 minutes (maximal vasodilatory effect achieved in average 5.5 minutes). Subjective symptoms and clinical cardiac (chest pain, ST-T segment change in ECG, hypotension, Ventricular ectopia, AV block) and non-cardiac side effects (headache, nausea, dyspnea, fatigue, bronchospasm, nonspecific pain, flushing, sweating) were registered during test.**Results:** 66 patients (69.5%) had subjective symptoms or clinical signs during pharmacological stress test. The most frequent cardiac sign was chest pain reported in 23 patients (24.2%) (associated with ST-T segment changes in 4 patients and hypotension in 1 patient). One patient had transitory AV block grade I. Headache (35.8%), fatigue (26.3%), nausea (22.1%) and flushing (15.4%) were the most frequent non-cardiac symptoms. 14 patients received Aminophyllin treatment for substantial side effects. Neither fatal nor nonfatal myocardial infarction, or endangering arrhythmias were registered. Myocardial perfusion test findings were positive in 43% of the patients with severe side effects (3 or more symptoms or signs), 44% of the patients with moderate side effects (1–2 symptoms or signs) and 48% of the patients with no side effects (statistically insignificant).**Conclusion:** Dipyridamol stress test performed during myocardial perfusion scintigraphy presents safe diagnostic procedure. Subjective symptoms and clinical signs registered during pharmacological vasodilatation had no prognostic value for the outcome of myocardial perfusion scintigraphy.

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**ACCURACY OF 99mTc-MIBI MYOCARDIAL SCINTIGRAPHY IN THE EVALUATION OF CORONARY ARTERY DISEASE**S. Popadic<sup>1</sup>, J. Vojcic<sup>1</sup>, M. Malesevic<sup>1</sup>, S. Dodic<sup>2</sup>, K. Kermeci<sup>1</sup>, J. Mihailovic<sup>1</sup>, A. Peter<sup>1</sup><sup>1</sup>Department of nuclear medicine, Institute of oncology in Sremska Kamenica, Novi Sad, <sup>2</sup>Institute of Cardiovascular Diseases, Sremska Kamenica, Serbia and Montenegro**Aim:** To assess the accuracy of myocardial 99mTc-MIBI scintigraphy with tomographic imaging (SPECT) comparing to coronary angiography in the evaluation of coronary artery disease.**Material and methods:** Sixty-six patients (40 males — 60.6%, 26 females — 39.4%; mean age 53 ± 8.68), with suspected or known coronary artery disease who underwent both investigation within six months, were included in the study. Significant disease was defined by ≥ 75% luminal coronary artery stenosis in one or more coronary artery or major branch or in a saphenous vein graft or arterial mammary graft.**Results:** Overall results are shown in the Table:

	(N = 66) scintigraphy (pts)	Myocardial 99mTc-MIBI Coronary angiography (pts)
Normal finding	24 (36.4%)	42 (63.6%)
One-vessel disease	26 (39.4%)	15 (22.7%)
Multi-vessel disease	16 (24.2%)	9 (13.6%)

According to our results, we found the myocardial 99mTc-MIBI scintigraphy overall sensitivity of 92%, specificity of 55% and accuracy of 53% with positive predictive value of 39% and negative predictive accuracy of 96%.

**Conclusion:** On the basis of its high sensitivity and high negative predictive value myocardial 99mTc-MIBI scintigraphy appear to be an useful diagnostic tool for coronary artery disease, with especially high value in predicting the low-likelihood of future cardiology events.

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**ANALYSIS OF TC-99M-MIBI MYOCARDIAL PERFUSION SCANS IN PATIENTS WITH NORMAL OR NON-SIGNIFICANT FINDINGS ON CORONARY ANGIOGRAPHY**J. Vojcic<sup>1</sup>, S. Popadic<sup>1</sup>, M. Malesevic<sup>1</sup>, S. Dodic<sup>2</sup>, J. Mihailovic<sup>1</sup>, D. Srbovan<sup>1</sup>, K. Kermeci<sup>1</sup>, A. Peter<sup>1</sup><sup>1</sup>Institute of Oncology, Department of Nuclear Medicine, Sremska Kamenica, Serbia and Montenegro, <sup>2</sup>Institute of Cardiovascular Diseases, Sremska Kamenica, Serbia and Montenegro**Aim:** To analyze Tc-99m-MIBI myocardial perfusion scans (MPS) in patients (pts) with normal, or findings of non-significant stenoses on coronary angiography (CA).**Materials and methods:** We retrospectively analyzed 41 patients (22 males, 19 females; mean age 51.13 ± 5.3 years) who presented with findings of normal or non-significant stenosis on CA in the past two years. Findings of MPS and CA were analyzed comparatively in each patient. Positive MPS findings were divided according to the vessels involved compared to CA findings, into 3 categories: A — same vessels involved as in CA, B — same vessels plus additional vessels, C — different vessels. **Results:** In 41 pts with normal/nonsignificant findings on CA, we found 16 (39%) with negative MPS (true negatives) and 25 (61%) with positive MPS findings (false positives). Out of those 25, there were 6 in category A, 6 in category B, and 13 in category C (5 of those could be characterized as unrecognized attenuation). Since the same vessels were involved in both CA and MPS, category A and B pts could also be accounted for true positives, rendering only the patients in category C as false positives. Having in mind the 5 unrecognized attenuation pts, there would be only 8 pts (20% of all) as false positives.**Conclusions:** Coronary angiography is often considered golden standard for myocardial perfusion imaging. However, these results show that in some pts the significance of stenosis on CA could be underestimated. Also, it is essential to recognize artifacts in order to achieve more accurate results of myocardial perfusion imaging.

## KIDNEY

11

**THE ROLE OF DYNAMIC SCINTIGRAPHY WITH TC-99M DMSA IN THE QUANTIFICATION OF RENAL BLOOD FLOW**

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**Aim:** To evaluate whether blood flow to kidney (RBF) could be estimated by the analysis of the vascular transit of DMSA and to determine the sensitivity of this parameter in assessing perfusion of native and transplanted kidney.

**Material and methods:** Investigation was carried out in 58 subjects, who were divided into four groups. The first two groups consisted of healthy individuals: group A of 23 potential kidney donors and group B of 18 children in remission after first urinary tract infection. Group C consisted of 10 pts. with well-functioning transplant and group D of 7 pts. with suspected acute rejection. Dynamic scintigraphy was done 14 min after bolus of 370 MBq DMSA. For the first 40 seconds two frames per second were recorded. The blood flow to kidney is estimated from a derived first pass activity plateau in renal region of interest as the difference between the maximal slopes of renal and arterial TA curves.

**Results:** Mean values of RBF in group A were 18.28%CO and of one kidney BF 9.14. In group B values were 20.83 for both kidneys and 10.96 for one kidney. Transplant blood flow (TBF) in group C was 13.99 and in group D 6.73. Values of RBF in group C were 53% higher than one kidney RBF in group A and 23% lower than global RBF in group A. In group D, RBF was 66% lower than global RBF in group A and 56% lower than RBF in group C. Statistical difference was significant. There was no overlapping between group D and C, as well as between group D and A. Correlation between RBF and biochemical parameters of renal function was significant: RBF/C<sub>cr</sub> r = .90, RBF/Cr r = .73 and RBF/BUN r = .70.

**Conclusions:** Fractional renal blood flow, derived from the first-pass activity plateau as the upslope ratio of kidney curve and arterial curve is sensitive method for quantifying renal perfusion. Flow is generated in physiological units of percentage cardiac output. Method is independent of time interval between the arterial and organ time-activity curves; many other techniques require this to be simultaneous. Method gives physiological values of blood flow in healthy adults and infants. Well functioning transplants could receive a fraction of CO similar to that delivered to two normal kidneys. Flow to the rejecting allograft is markedly reduced.

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**GASTRIC EMPTYING AND HORMONE LEVEL CHANGES AFTER GASTRIC ULCER SURGERY**

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The aim was to examine influence of peptic ulcer surgery on the gastric emptying (GE) and serum levels of the gut hormones.

Seven healthy volunteers (C), 7 patients after Billroth I (BI), 11 after Billroth II (BII), 7 after BI with selective vagotomy — Harkins 1 (H1) and 10 after BII with selective vagotomy Harkins 2 (H2) were examined. After ingestion of the high density test meal dynamic scintigraphy of the gastric region was performed during 120 min. From the gastric emptying curve the lag phase duration (min) and emptying rates (%) after 30, 60, 90 and 120 min were analysed. The serum levels of gastrin, motilin, somatostatin and neurotensin were determined by RIA techniques just before the test meal, at the beginning and every 10 min of GE study.

The lag phase duration was reversely related to GE rates, and the GE pattern was linear in both controls and operated patients, except in BII group in which the GE pattern was exponential. In relation to C group, GE was slower in BI (p < 0.05), H1 and H2 groups (p < 0.01), and faster in BII group (p < 0.01). Slower GE in operated patients except BII group, could be explained by massive gastric motility disorders (H1, H2) and by decreased anastomotic patency (BI, H1). Faster GE in BII group could be a consequence of increased anastomotic patency (large stoma) and lack of the duodenal inhibitory activity. Lower serum gastrin values obtained in all patients, in relation to C group (p < 0.01), were explained by an absence of the secretory active antral mucosa. The serum motilin values showed peaks during the first 60 min in all groups. Higher values of this gastric motility accelerator obtained in patients after the selective vagotomy (p < 0.01) could be explained by its attempt to normalize marked GE retardation (H1, H2). Since somatostatin also stimulates the gastric motility, its higher serum values recorded in BI and H1 groups (p < 0.01) might be explained as a compensation of decreased anastomotic patency, while such an effect was not necessary in other operated patients. The highest serum values of neurotensin obtained in BII group (p < 0.01) might be a result of an attempt of this GE inhibitor to retard the most rapid GE in those patients, while increased values obtained in H1 and H2 groups could not be explained by this effect.

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**EVALUATION OF LIVER TRANSPLANT FUNCTION BY NUCLEAR MEDICINE METHODS**V. Artiko<sup>1</sup>, V. Obradović<sup>1</sup>, N. Petrović<sup>1</sup>, B. Radević<sup>2</sup><sup>1</sup>Clinical Center of Serbia, Institute for Nuclear Medicine, Belgrade, <sup>2</sup>Clinic for Cardiovascular Diseases "Dedinje", Belgrade, Serbia and Montenegro

The aim was to evaluate the perfusion, morphology and the biliary tree patency of the liver transplants by the two scintigraphy methods successively performed.

The study was performed in 10 controls and 18 patients after orthotopic transplantation (up to two years). "First pass" acquisition was performed with scintillation camera, after bolus injection of 360 MBq <sup>99m</sup>Tc-diethyl-IDA, (60 frames/60s), continued by 59 minutes (1 frame/min) slower dynamic study. From the liver and kidney activity during "first pass" study, hepatic perfusion index (HPI) was calculated using slope-analysis. Hepatobiliary scans obtained during second phase of the study were analysed for morphology, and parenchymal and hepatobiliary TA curves were generated and analysed according to the time to maximal activity (T<sub>max</sub>) and the time to half of maximum activity (T/2).

In comparison to the controls (HPI = 0.64.5 ± 0.05%) portal perfusion was slightly (0.68 ± 0.04%), but not significantly (p > 0.05) increased. In 3 patients, biliary phase of hepatobiliary scintigraphy showed increased accumulation of radiopharmaceutical in the left (n = 1) or right (n = 2) hepatic duct. Uptake of the radiopharmaceutical (T<sub>max</sub> = 18.5 ± 2.9 min) was slightly, but not significantly (p > 0.05) delayed in comparison to the controls (14.2 ± 3.4 min), while excretion was significantly (p 0.05) prolonged (31.3 ± 3.7 min) in comparison to the controls (25.7 ± 3.5 min) while extrahepatic one is high significantly (p < 0.01) prolonged (89.0 ± 14.3 min) than physiological (45.0 ± 7.2 min).

The single injection hepatic radionuclide angiography and hepatobiliary scintigraphy are noninvasive, sensitive and valuable for the follow up of the liver transplants.

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**SALIVARY SCINTIGRAPHY IN THE EVALUATION OF DRUG INDUCED XEROSTOMIA**

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Drug induced xerostomia is a common clinical problem that is frequently underestimated. This condition is often associated with the use of calcium channel blockers and sedatives.

**Aim:** To evaluate xerostomia induced by calcium channel blockers and sedatives by dynamic quantitative salivary scintigraphy.

**Material and methods:** 15 healthy subjects and 12 patients with clinically verified xerostomia who were on medication with calcium channel blockers and sedatives. Following an intravenous application of 190MBq <sup>99m</sup>Tc pertechnetate a dynamic images were recorded for 35 minutes at 20 sec per frame. At 25 min post-injection salivary excretion was stimulated by vitamin C pill. The parameters used for evaluation of salivary gland function were uptake ratio (UR), excretion time (ET), percent of excretion (PE) and velocity of excretion in the first minute after stimulation (VE). They were determined by drawing regions of interest and generating time-activity curves.

**Results:** showed that 33 % of the patients had normal salivary gland function while other 67 % showed abnormal findings. The parameters that were deteriorated were ET, PE and VE. The parameter that was deteriorated in all patients with disordered salivary scintigraphy was VE. UR was low only in one patient.

**Conclusion:** is that patients with drug-induced xerostomia showed deterioration of parameters that reflect the process of salivary excretion. Salivary scintigraphy is useful tool in the evaluation of patients with drug induced xerostomia.

## RADIOPHARMACEUTICALS

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MEMBRANE BASED EXTRACTION OF  $^{177}\text{Lu(III)}$  WITH DI (2-ETHYLHEXYL) PHOSPHORIC ACIDK. Kumrić<sup>1</sup>, T. Trtić-Petrović<sup>2</sup>, E. Koumarianou<sup>3</sup>, S.C. Archimandritis<sup>3</sup>, J. Čomor<sup>1</sup>

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Metallo-radiopharmaceuticals are pharmaceuticals composed of a metallic radionuclide, e.g.  $^{67}\text{Cu}$ ,  $^{90}\text{Y}$ ,  $^{99\text{m}}\text{Tc}$ ,  $^{177}\text{Lu}$ ,  $^{188}\text{Re}$ ,  $^{213}\text{Bi}$ ,  $^{149}\text{Tb}$ , etc., and a bioactive-targeting molecule, e.g. antibodies, peptides or receptor ligands [1]. Metallo-radiopharmaceuticals can be used for diagnosis or endoradiotherapy depending on the radiophysical characteristics of the incorporated radionuclide. Lanthanide radioisotopes are of particular interest for radiotherapy as they are readily forming stable complexes with linking chelators.  $^{177}\text{Lu}$  is a lanthanide radionuclide with good characteristics ( $t_{1/2} = 6.7$  days and  $E_{\beta} = 0.497$  MeV) for application in endoradiotherapy. The labeling of a bioactive molecule with metallo-radionuclides consists of several phases. The most important phase is the separation of the labeled compound from the free radionuclide [1, 2].

The aim of this study was to investigate the feasibility of membrane extraction of  $^{177}\text{Lu(III)}$  from the separation of free  $^{177}\text{Lu(III)}$  from the bioactive compound labeled with  $^{177}\text{Lu(III)}$ .

$^{177}\text{Lu}$  was produced by the research nuclear reactor at NCSR Demokritos by direct neutron activation of  $^{176}\text{Lu}_2\text{O}_3$ . After the irradiation the samples were dissolved in 0.1 mol-dm<sup>-3</sup> HCl, the solution was evaporated to dryness and than re-dissolved in deionised water. The specific activity of  $^{177}\text{Lu}$  was 114 MBq·mg<sup>-1</sup>. The final  $^{177}\text{Lu}$  activity in the solution for extraction of 26.6 MBq·cm<sup>-3</sup> was obtained by dilution with 0.05 mol-dm<sup>-3</sup> ammonium citric buffer of pH = 5.3. Supported liquid membrane based extraction of  $^{177}\text{Lu(III)}$  has been performed in a small membrane module with a microporous flat polypropylene membrane. The membrane was impregnated by soaking in a solution of 40% di(2-ethylhexyl) phosphate (DEHPA) in kerosene for 30 min. The extraction of  $^{177}\text{Lu(III)}$  was performed from a donor phase consisting of 36.9 mg·dm<sup>-3</sup> Lu in 0.05 mol-dm<sup>-3</sup> ammonium citric buffer, pH = 5.3, into the acceptor phase, which was 1 mol-dm<sup>-3</sup> HNO<sub>3</sub>, pH = 0.5. The donor phase was pumped continuously through the donor channel at a flow rate in the range from 0.06–0.3 cm<sup>3</sup>·min<sup>-1</sup>, while the acceptor phase was stagnant. Samples of donor phase leaving the module were taken every 2 min and a sample of acceptor phase was taken at the end of the procedure.

The influence of donor flow rate on the efficacy of removing of Lu(III) from the donor phase was determined. It was found that the extraction efficiency decreased by increasing the flow rate of the donor phase. The most efficient stripping of Lu(III) from the donor phase, 93%, was obtained at the donor phase flow rate of 0.06 cm<sup>3</sup>·min<sup>-1</sup>.

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COMPARISON OF DIFFERENT FORMULATIONS OF THE  $^{99\text{m}}\text{Tc}$  — CIPROFLOXACINN.S. Nikolić<sup>1</sup>, D. Janković<sup>1</sup>, D. Đokić<sup>1</sup>, I. Pirmettis<sup>2</sup>

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**Aim:** Technetium-99m ciprofloxacin (Infecton) has recently become established as a new radiopharmaceutical for the imaging of infection. The antibiotic chelated with  $^{99\text{m}}\text{Tc}$  make possible the area of bacterial infection should be identifiable during imaging. Different formulations of this radiopharmaceutical were prepared. The radiochemical purity and stability, determination of octanol/saline partition coefficients and total human serum protein binding, as well as in vitro binding  $^{99\text{m}}\text{Tc}$ -CIP to bacteria *S. aureus* ATCC 25923 were studied.

**Material and methods:** Ciprofloxacin hydrochloride used in this work was Bayer product.  $^{99\text{m}}\text{Tc}$  eluate from Universal  $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$  generator (Vinča Institute of Nuclear Science, Laboratory for Radioisotopes) was used for labeling. All other chemicals were Merck products. The *in vitro* binding to bacteria was studied on bacteria *S. aureus* ATCC 25923.

Four formulations are investigated:

**Formulation No. 1** The vial of inactive preparation contained: ciprofloxacin (3.8 mg),  $\text{SnCl}_4 \times 2 \text{H}_2\text{O}$  (0.39 mg) and NaCl (4.4 mg), pH value was adjusted to 3.4 using acetic acid/sodium acetate buffer solution; all ingredients were dissolved and mixed under nitrogen. Each single vial with freeze-dried product was formulated for one application. After reconstitution with  $^{99\text{m}}\text{Tc}$  pertechnetate (0.2–0.5 mCi, 3ml) vial is incubated for 30 min.

**Formulation No. 2:** ciprofloxacin (1.9 mg),  $\text{SnCl}_4 \times 2 \text{H}_2\text{O}$  (0.19mg) and NaCl (2.2 mg);

**Formulation No. 3:** ciprofloxacin (3.8 mg),  $\text{SnCl}_4 \times 2 \text{H}_2\text{O}$  (0.39 mg), mannitol (7.6 mg) and NaCl (4.4 mg);

**Formulation No. 4:** ciprofloxacin (1 mg),  $\text{SnCl}_4 \times 2 \text{H}_2\text{O}$  (0.2 mg), mannitol (10 mg) and ascorbic acid (1.5 mg).

**Results:** Ciprofloxacin was labeled with  $^{99\text{m}}\text{Tc}$ -pertechnetate using  $\text{SnCl}_4 \times 2 \text{H}_2\text{O}$  as reducing agent. The reaction volume of 3 ml has shown minimum contain of impurities.

For determination  $\text{TcO}_3^-$  species (free  $^{99\text{m}}\text{Tc}$ -pertechnetate,  $\text{Rf} = 1$ ) SG strips (MEK or saline) and silica gel 60 layers on aluminum sheets (methanol/acetone 1:1) were used. The concentration of  $\text{TcO}_3^-$  species (reduced-hydrolysed  $^{99\text{m}}\text{Tc}$ ) with  $\text{Rf} = 0$  were determined with SG strips (butanol/acetic acid/water 2:2:1). The results obtained with these chromatographic methods were in a good agreement. In the bacterial binding assay,  $^{99\text{m}}\text{Tc}$ -CIP prepared by formulation No. 1 gave highest binding to bacteria, formulation No. 2 and 3 showed lower values, while No. 4 showed significantly lower binding.

**Conclusion:** Radiopharmaceutical  $^{99\text{m}}\text{Tc}$ -ciprofloxacin has been developed for detection infectious foci, which localize in high concentrations in living bacteria. The procedure was simple and the product was easy for handling. After reconstitution of the inactive kit with sodium pertechnetate, no additional manipulations are necessary before *i.v.* application.

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PREPARATION OF  $^{188}\text{RE}$ -HEDP FOR TARGET RADIOTHERAPY — LABELLING AND PRELIMINARY ANIMAL STUDIESI. Pirmettis<sup>1</sup>, M. Papadopoulos<sup>1</sup>, S. Archimandritis<sup>1</sup>, A.D. Varvarigou<sup>1</sup>, D. Djokić<sup>2</sup>, D. Janković<sup>2</sup>

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Rhenium radioisotopes  $^{186}\text{Re}$  and  $^{188}\text{Re}$  have favorable properties for therapy. They emit high energy beta particles and emission of the 155 keV and 137 keV gamma photons respectively, which permits the biodistribution evaluation of Re-radiopharmaceuticals *in vivo* with gamma camera. While  $^{188}\text{Re}$  could be obtained from  $^{188}\text{W}/^{188}\text{Re}$  radionuclide generator system,  $^{186}\text{Re}$  is reactor produced radioisotope.

$^{99\text{m}}\text{Tc}$ -HEDP is well known radiopharmaceutical for diagnostic of bone metastases. In these investigations HEDP was used as a model for labelling with  $^{186/188}\text{Re}$ .

Rhenium was prepared by irradiation of the target in the nuclear reactor of Demokritos. The weighed amount of natural Rhenium ( $^{185}\text{Re} + ^{187}\text{Re}$ ) was placed in quartz ampoule sealed by flame and aluminum can. After irradiation, the  $\text{H}^{186/188}\text{ReO}_4^-$  was prepared in reaction with  $\text{H}_2\text{O}_2$ , which takes 2 hours at least. After that the prepared  $\text{H}^{186/188}\text{ReO}_4^-$  was added to a vial with HEDP. For this purpose standard kit prepared in Demokritos was modified, which means pH of HEDP solutions was adjusted to 2.0–2.5. Then the vial was heated for 30 min in boiling water. As labelling was in acid medium, after cooling sodium acetate buffer (pH 8.7) was added.

The radiochemical quality control of  $^{186/188}\text{Re}$ -HEDP was determined using ITLC-SG and Whatman 3 MM strips as stationary phase and two solvent systems: methyl-ethylketone as well as etidronate solution as mobile phase. In this way both free perhenate and reduced-hydrolysed rhenium could be obtained. Prepared  $^{186/188}\text{Re}$ -HEDP was of high radiochemical purity (RCP ? 95% 30 minutes and RCP ? 98% 24 h after labelling).

For biodistribution study Wistar rats were used. After dilution, 0.3 ml of  $^{186/188}\text{Re}$ -HEDP was injected. The one group of animals was sacrificed 1 hour and another 24 hours post injection. The organs of interest were measured in gamma counter. The biodistribution study showed that the complex is localized in the skeleton (28% and 21% ID/organ at 1 and 24 hours), while the remaining activity was excreted via the urinary system. No significant activity was to be found elsewhere.

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## CHEMICAL AND BIOLOGICAL EVALUATION OF TECHNETIUM (I) — TRICARBONYL COMPLEXES WITH EHIDA AND DPD

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The first results on synthesis of  $[\text{}^{99\text{m}}\text{Tc}(\text{CO})_3(\text{H}_2\text{O})_3]^+$ , the air and water stable organometallic aqua complex obtained directly from  $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$  generator, were presented 1998 (Albeto and co workers). This precursor allows complexation of  $^{99\text{m}}\text{Tc(I)}$  aqua ion with different mono-, bi- and tridentate ligands based on the tricarbonyl technetium (I) core, by changing of three labile coordinated  $\text{H}_2\text{O}$  molecules with other ligands.

A number of  $^{99\text{m}}\text{Tc}$ -phosphate compounds and  $^{99\text{m}}\text{Tc}$ -IDA complexes, made by adding  $^{99\text{m}}\text{TcO}_3^-$  to the kits, have been applied for bone and gallbladder imaging respectively. They form mixed-metal complexes containing Tc (+3, +4 or +5) and Sn (II) in undetermined proportions. The results of the labelling of DPD as well as the EHIDA with  $[\text{}^{99\text{m}}\text{Tc}(\text{CO})_3(\text{H}_2\text{O})_3]^+$  and investigation of their chemical and biological behaviour, in comparison with the same one for  $^{99\text{m}}\text{Tc}$ -DPD and  $^{99\text{m}}\text{Tc}$ -EHIDA complexes, were presented.

DPD and EHIDA were synthesised and prepared in kit form in INS Vinča. Carbonyl labelling agent Isolink<sup>TM</sup> (Mallinckrodt Medical B.V.) and carbonyl precursor NCRS Demokritos prepared according a direction for use, were applied. The samples (0.1 ml) of each ligand dissolved in water and with pH adjusted to desired value were added to a vial containing 0.9 ml of  $^{99\text{m}}\text{Tc}$ -carbonyl neutralised to pH  $\approx$  7.5 and pH  $\approx$  5.5 respectively. After heating (30 min) and cooling down to room temperature, reaction products were analysed by HPLC equipped with UV and  $\gamma$ -detector, with TEAP 0.05 M, methanol and water as solvent.

Biological evaluation of  $^{99\text{m}}\text{Tc(I)}$ -DPD and  $^{99\text{m}}\text{Tc(I)}$ -EHIDA complexes involve the bio distribution examination on Wistar rats. The animals were sacrificed sixty and 3.5 min after application of 0.1 ml of  $^{99\text{m}}\text{Tc}$ -carbonyl tagged DPD and EHIDA ( $\approx$  74 kBq) respectively. The radioactivity in the organ of interest was measured and the percentage of radioactivity related to the administrated dose was determined. In the same way, the biodistribution of  $^{99\text{m}}\text{Tc}$ -DPD and  $^{99\text{m}}\text{Tc}$ -EHIDA were done.

The results confirmed that hydrophilic organometallic  $[\text{}^{99\text{m}}\text{Tc}(\text{CO})_3(\text{H}_2\text{O})_3]^+$  precursor allows forming of Tc (I) complexes with diphosphate and IDA derivatives, based on the tricarbonyltechnetium (I) core. The changes in structure of DPD and EHIDA labelled molecules influence the biological behaviour. Thus Tc (I) complexes of DPD did not accumulate in bone (< 1% of complex was found out in femur),  $^{99\text{m}}\text{Tc}(\text{CO})_3$ -EHIDA has shown faster filtration throw the kidneys and slower biliary excretion, so the radioactivity in liver was higher, but in the intestine lower.

## RIA

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**EXTERNAL QUALITY ASSURANCE — THE RESULT OF THYROXIN DETERMINATION BY RIA T<sub>4</sub>-INEP IN THE INTERNATIONAL MEASUREMENT EVALUATION PROGRAMME IMEP 17**

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External quality assurance (EQA), previously named as external quality control, is the set of procedures operated by an external agency for objective comparison of the laboratory results with an agreed target. The Isotope Measurement unit of the Institute for Reference Materials and Measurements (IRMM) develops and performs reference measurements using primary methods, produces certified isotopic reference materials, and organises international measurement evaluation programmes (IMEP) in the nuclear and non-nuclear fields. IMEP aims at establishing SI-traceable reference values through application of primary methods of measurements. The Consultative Committee for Amount of Substance (CCQM) of the International Committee for Weights and Measures (CIPM) defines these as methods having the highest metrological qualities. In July 1999, IRMM launched IMEP 17, the evaluation programme for trace and minor constituents in human serum. The programme is organized in collaboration with C-AQ IFCC (Committee for Analytical quality of the International Federation for Clinical Chemistry and Laboratory Medicine) and members of EQALM (European committee for the External Quality Assurance programmes in Laboratory Medicine). The preparation of two test materials from pools of fresh human serum started in 2000 by DEKS Herlev University Hospital and Statens Seruminstitut, Copenhagen, Denmark. The pool of Material 1 was left unmodified to resemble a normal patient serum. This material was used for thyroxin determination. Isotope dilution mass spectrometry (IDMS) was used as the primary method for thyroxin quantitation. Immunoassays were used for routine laboratory measurements, and thyroxin was the only constituent measured by immunoassay in IMEP 17. The reason is probably that EQA of immunoassay present some additional problems arising from the use of biological reagents.

Participating laboratories has received certified test samples, which were analysed using routine measurement procedure. INEP participated through the Society of Medical Biochemists of Serbia and Montenegro. Ten replicates were measured following the protocol, by immunoassay RIA T<sub>4</sub>-INEP. The measurement was done in June 2002 and the result was sent to regional coordinator. The outcome of the programme was available at the beginning of 2003. IMEP-17 reference value for thyroxine is 97.6 nmol/L and the value measured in INEP was 94.1 nmol/L i.e. deviation from the certified value is below 5%.

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**MEASUREMENT OF SERUM THYROGLOBULIN LEVELS — DO WE NEED STANDARDS AND NATIONAL GUIDELINES?**

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Thyroglobulin (Tg) is synthesized and secreted by both normal and malignant thyroid cells. Hence, serum Tg levels are convincing indicator of thyrocytic activity. Detectable and increasing Tg levels in patients with thyroid carcinoma after "total" thyroidectomy or radioiodine therapy indicate considerable amount of active thyroid tissue or cancer recurrence. An understanding of the malignant disease, its natural history and biochemistry of Tg allows laboratories to determine the characteristics of suitable Tg assays. In current laboratory practice there are several immunoassay methods such as radioimmunoassay, immunoradiometric assay, enzyme-immunometric assay and immunoluminometric assay. Results are often subject to significant variations regardless of the method used. Interferences of Tg autoantibodies are already known (giving as a rule false negative results) as well as the use of heterophile anti-Tg antibodies in analytical procedure (giving as a rule false positive results). In Serbia, unlike in the EU countries there are no national or international standards for serum Tg measurements. The use of various analytical procedures, lack of standards and national guidelines may lead to clinical malpractice. The most important recommendations can be summarized: a) there should be precise national guidelines scheme of specimen requirements and sample stability; b) the use of international Tg reference standards such as CRM-457 is highly recommended; c) manufacturers of the assay kits should verify and quote the lowest detectable dose (LDD) calculated on precision profiles derived from "binned" patients samples; d) manufacturers and laboratories should detect the analytical range of the assay based on the 10% CV on LDD and upper limit of the normal values; e) it is recommended that laboratories should notify clinicians of interference due to endogenous Tg antibodies and indicate the most likely nature of the interference; f) Tg autoantibodies should always be detected simultaneously using a sensitive immunoassay rather than a haemagglutination method; g) for a particular Tg method the results of a clinical assessment of the assay performance should be available. The clinical sensitivity and specificity (positive and negative predictive values) of the assay should be clearly quoted; h) laboratories should run internal QC samples which encompass the range of results reported by the laboratory. A sample with a Tg concentration close to the LDD should be run with each assay to ensure that the quoted LDD is being achieved; i) an external quality assessment should be established to facilitate method comparison and monitoring assay performance.

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**STANDARDIZATION OF HETEROGENOUS ANTIGENS IMMUNOASSAYS**

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Biological standardization is organized and promoted by the World Health Organization (WHO). According to standards of International Organization for Standardization (ISO), the standardization of diagnostic assays should be achieved within the context of a reference system comprising: reference material, reference measurement procedure and reference measurement laboratories. The role of reference system is to ensure that a numerical value assigned to the reference material is traceable through the defined reference method, associated with a specified uncertainty and that is commutable with clinical values. Standardization of glycoprotein immunoassay is complicated by several problems including microheterogeneity, crossreaction, matrix effects as well as the need to measure concentrations close to the detection limit. Different immunoassays, based on antibodies with different specificities, could measure a mixture of protein isoforms differing with respects to glycosylation, degradation or complex formation. During WHO Consultation on International Biological Standards for *in vitro* Diagnostic Procedures held in Geneva in September 2000, it had been proposed that the reference system for heterogenous analytes should be achieved through a process of consensus. The proposal is that the term international conventional reference material (ICRM) would be used for such analytes, instead of a primary international biological reference material. The assignment of a numerical value to an ICRM would be achieved using an international reference measurement procedure within an international conventional reference measurement system. Reference measurement laboratories would be embedded in a network that can prove their competence. The aspects of competence include the low uncertainty in the measurement results, the Quality System and consistently excellent performance in proficiency/external quality assessments. The developing technology poses a number of problems for the WHO biological standardization programme: in meeting the increased demand, in using recombinant materials on place of natural materials, in moving towards the use of more transparent units, and in standardization of complex heterogenous preparations. Heterogenous antigen immunoassay standardization include all of these problems. The results of heterogenous analytes determination by immunoassay from different manufacturers will be discussed.

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**CLINICAL ACCURACY OF TOTAL THYROXINE, T<sub>4</sub>/TBG RATIO AND FREE THYROXINE MEASUREMENTS IN HYPOTHYROIDISM AND HYPERTHYROIDISM**I. Petrović<sup>1</sup>, S. Savin<sup>1</sup>, D. Cvejić<sup>1</sup>, S. Spasić<sup>2</sup>, N. Paunković<sup>3</sup>, D. Paunković<sup>3</sup>, Z. Jelić-Ivanović<sup>2</sup><sup>1</sup>Institute for the Application of Nuclear Energy-INEP, Zemun-Belgrade, <sup>2</sup>Institute for Medical Biochemistry, Faculty of Pharmacy, University of Belgrade,<sup>3</sup>Nuclear Medicine, Medical Center Zajecar, Serbia and Montenegro

Clinical laboratory diagnostics of thyroid function disorders comprises a number of analyses. Most of all thyroid function panels include measurements of total and/or free thyroid hormones. The aim of this study was to evaluate the clinical accuracy of total T<sub>4</sub>, free T<sub>4</sub> and T<sub>4</sub>/TBG ratio and to establish their usefulness in evaluation of hypothyroidism and hyperthyroidism.

Total T<sub>4</sub>, T<sub>4</sub>/TBG ratio and FT<sub>4</sub> were first determined in healthy, euthyroid subjects (n = 102) and then in patients with hypothyroidism (n = 33) and hyperthyroidism (n = 66). The reference range for each parameter was determined in each group. The values of the areas under the ROC curves were significantly higher ( $t > t_{tab}$ ,  $p = 0.05$ ) for T<sub>4</sub>/TBG ratio and FT<sub>4</sub> (0.9924 i.e. 0.9976) than for total T<sub>4</sub> (0.9260) in hypothyroid patients while there were no significant difference between these parameters in patients with hyperthyroidism.

In conclusion, for the diagnosis of hypothyroidism, determination of the proportion of free thyroxine is of the greatest importance. No significant difference between T<sub>4</sub>/TBG ratio and FT<sub>4</sub> was found. Determination of total T<sub>4</sub> is not a preferable parameter because of its significant lower clinical accuracy. Each of these three parameters could be used with equal certainty in the diagnosis of hyperthyroidism.

## ENDOCRINOLOGY

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**SENSITIVITY OF DUAL TRACER TC-99M-TETROFOSMIN/TECHNETIUM-99M PARATHYROID SCINTIGRAPHY**

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**Aim:** To estimate sensitivity of dual tracer subtraction scintigraphy with Tc99m-tetrofosmin and Tc99m in detection of abnormal parathyroid glands in patients with primary and secondary hyperparathyroidism.

**Material and methods:** Sixteen patients, ten with primary and six with secondary hyperparathyroidism underwent parathyroid scintigraphy preoperatively. All patients had pathohistological confirmation of diagnosis. Abnormal parathyroid glands weighed from 0.1 to 7 g. After *i.v.* injection dynamic scintigraphy for 25 minutes (one minute, one picture) using 555MBq of Tc-99m-tetrofosmin and three hours later, using 111MBq of Tc-99m was performed. Tc-99m-tetrofosmin dynamic study was followed by static scintigraphy of neck and chest. After normalisation, motion correction and subtraction Tc-99m from Tc-99m-tetrofosmin picture.

**Results:** Abnormal scintigraphic finding was in 15 patients with sensitivity of 93.7%. Overall sensitivity for detecting 25 from 31 abnormal parathyroid glands was 78.5%, (for primary hyperparathyroidism sensitivity was 90%, and for secondary 67%).

**Conclusions:** Positive scintigraphy in 15 from 16 patients (sensitivity 93.7%) and detecting 25 from 31 gland (sensitivity 78.5%), shown high sensitivity of dual tracer subtraction scintigraphy with Tc-99m-tetrofosmin and Tc-99m in detection of abnormal parathyroid glands.

## INSTRUMENTATION

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**CURRENT STATE AND PERSPECTIVES OF APPARATUS BASE FOR MODERN SPECT**A.V. Gektin<sup>1</sup>, B.V. Griniev<sup>1</sup>, A.V. Demin<sup>1</sup>, A.N. Kalashnikov<sup>2</sup>, V.R. Luybysky<sup>3</sup>, O.V. Shishkin<sup>1</sup>.<sup>1</sup>Institute of Scintillation Materials NAS of Ukraine, Kharkov, <sup>2</sup>SDTB "ORIZON", Smela, <sup>3</sup>Joint Venture "Amcrys-H, Ltd", Kharkov, Ukraine

Methods of diagnostics with use of radiopharmaceuticals are widely adopted in clinical practice. With the help of these methods different diseases at early stages are diagnosed. Sale of emission tomographs in the international market of medical devices steadily grows. At present such firms-creators as Philips (38% of market share), General Electric (30%), Siemens (28%) dominate in the market. The other firms possess about 4% of the market. In particular such firms as Toshiba, Mediso, IS<sup>2</sup> Research and others.

In order to understand the tendencies of development and usage of gamma cameras we give data from the report of the enterprise Frost and Sullivan, in this report the situation on gamma-camera market from 1997–2007 is analyzed.

In the CIS countries implementation of methods of radionuclide diagnostics is held back due to absence of modern equipment.

Within the period of 1996–1998 STC "Institute for Single crystals", Kharkov and SDTB "ORIZON", Smela on basis of tomographic gamma-camera GKS-301 (which was developed in 1990 in Moscow) created a noticeably modernized gamma-camera "Tamara" and by the year 2002 more than 30 sets of this kind of equipment were produced mainly for the health care service of Ukraine. In 2001 STC "Institute for Single crystals" and SDTB "ORIZON" developed new tomographic camera "OFECT-1" with rectangular view field of large scale. This tomograph passed all tests and works successfully in the Romodanov Institute of "Neurosurgery" of AMS of Ukraine, Kiev.

The construction of tomograph allows placing inlet window of detection block practically in any possible way and to carry out investigations in any comfortable for patient position — "lying", "sitting", "standing".

Two or more personal computers may be connected to the tomograph for the convenience of simultaneous survey, data collection, processing, archivation and transmission of the data. Tomograph set includes portable cardiograph that allows examining cardiovascular system, to determine series of parameters of central and organ hemodynamic, to evaluate volume of blood circulation, to reveal and evaluate concealed hemorrhages and to carry out synchronized equilibrium ventriculography.

It is possible to carry out EKG synchronized tomographic studies with the purpose to determine size and severity of defects of myocardium walls and contractility of left ventricle of heart.

Device of digital scaling is implemented in the tomograph; this device allows to improve resolution of scintigraphic images by means of enlarging of image of the object under study within the limits of the selected region of interest up to matrix size of the image at proportional reduction of matrix pixel. Scale of region of interest of the object under consideration may vary from 100% to 400% at step 20% and to change position of region of interest.

Control over the removal of region of interest as well as determination of region of interest is carried out by software with usage of graphic interface of user.

Tomograph software support meets all modern requirements.

Technical parameters of tomograph fully comply with modern requirements and do not yield to foreign samples.

## VARIA

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**COMPARISON OF TWO METHODS FOR OPTIMAL RED CELL MASS AND PLASMA VOLUME ESTIMATION**

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It is well known that using ml/kg method leads to inappropriate red cell mass and plasma volume (RCM&PV) interpretation (particularly in obese individuals).

**Aim:** To present and compare the results of two proposed methods for optimal RCM&PV estimation, and their impact to the interpretation of obtained results.

**Material and methods:** 120 patients (81 male and 39 female) with the diagnosis of polycythaemia rubra vera were subjected to the RCM&PV determination using autologous erythrocytes *in vitro* labelled with <sup>51</sup>Cr-sodium chromate. Two methods were performed for optimal volume determination:

1. Retzlaff's tables, based on patients sex, body weight and height;
2. The method recommended by the ICSH based on body surface area, sex and age of patients [1].

**Results:** There was no significant difference in the age of the investigated persons. Males were 22–76 years old (mean value = 55 years, SD ± 15 years), females 32–81 years (mean value = 58.5 years, SD ± 13 years). Body mass in males ranged from 52 to 139 kg (mean value = 83.3 kg), and in females 43.5–104 kg (mean value: 66.6 kg). The difference in real and ideal body mass was highly significant for males (mean difference = 7.1 kg, SD ± 13.2 kg), while it was not the case for female patients (mean difference = 1 kg, SD ± 12.5 kg). ICSH method yielded lower optimal values in comparison to Retzlaff's method. ICSH and Retzlaff's methods differed highly significantly ( $p < 0.01$ ) in male subjects for RCM&PV and blood volume. Plasma and blood volume optimal values were significantly lower with ICSH than Retzlaff's method in female patients ( $p < 0.05$ ), while the differences were not significant for RCM.

Concordant interpretation of RCM&PV using the two methods for optimal RCM&PV calculation was obtained in 110/120 patients (91.7%): absolute erythrocytosis in 69/110 (62.72%), normal results in 37/110 (33.64%) persons and PV depletion in 4/110 (3.64%) subjects.

Incongruent interpretation was registered in 10/120 patients (8.3%): RCM was augmented in four patients using ICSH method (Retzlaff's method yielded normal findings), RCM was normal in two patients (Retzlaff's method yielded lowered plasma volume), RCM was depleted in one patient (Retzlaff's method indicated normal findings). In three patients ICSH method indicated lowered plasma volume (while Retzlaff's method yielded lower limit plasma volume value twice and lower limit RCM value once).

**Conclusion:** Two methods for optimal RCM&PV estimation differ significantly and lead to different interpretation of obtained results in 8.3% of patients. ICSH method yields somewhat lower values for optimal RCM&PV compared to the Retzlaff's method.

**References:**

1. ICSH, International Council for Standardization in Haematology. Br. J. of Haem., 1995; 89: 749–756.