Chr. Reiners, M. Lassmann, P. Schneider
Clinic and Policlinic for Nuclear Medicine of the University of Wьrzburg

NUCLEAR MEDICAL DIAGNOSTICS WITH MODERN GAMMA CAMERAS

Ч. Рейнерс, М. Ласман, П. Шнейдер

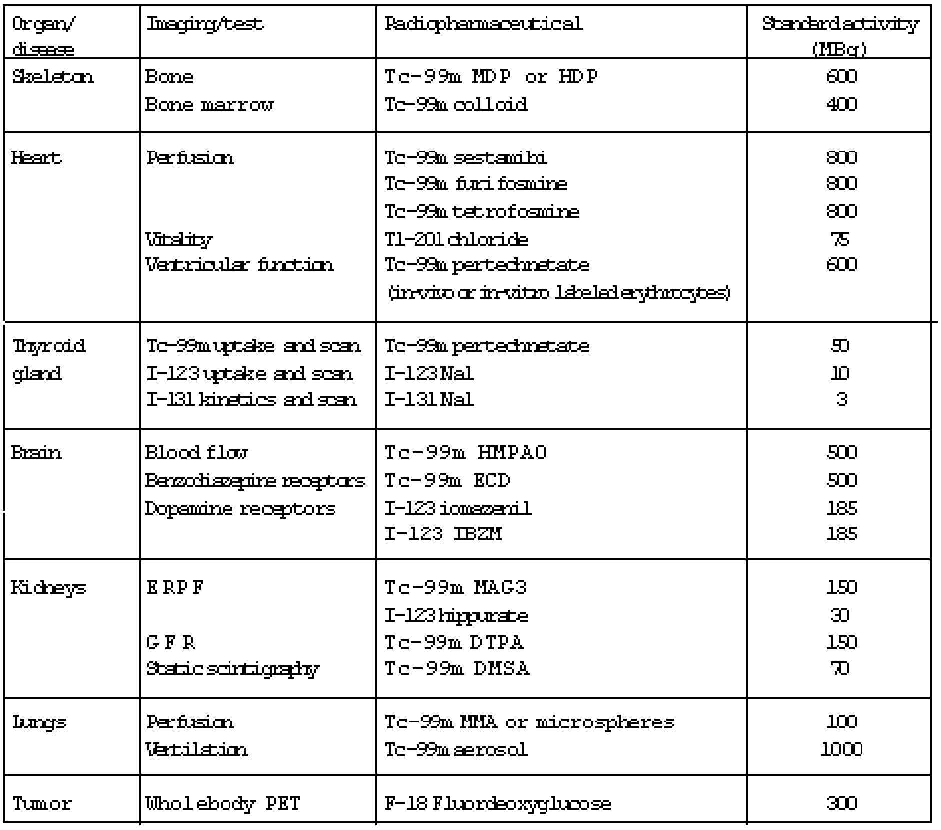
ЯДЕРНАЯ МЕДИЦИНСКАЯ ДИАГНОСТИКА С ПОМОЩЬЮ СОВРЕМЕННЫХ ГАММА-КАМЕР

Клиника ядерной медицины университета Вюрцбурга (Германия)

1. Principles of nuclear medical diagnostics In nuclear medical diagnostics, unsealed radioactive substances are used to image organ functions non-invasively. In contrast to other imaging diagnostic modalities (ultrasound, X- ray, to some extent also magnetic resonance tomography), the nuclear medical examination approach is primarily function-oriented. In this case vital processes such as blood circulation, metabolism and viability of organs or tumors can be displayed as “functional images” [1, 2]. Different radiopharmaceuticals are used for displaying blood circulation, blood volume, lung ventilation, gastrointestinal passage, absorption and secretion, phagocytosis, cell kinetics, antigen or receptor binding as well as metabolism and thus viability (Table 1).

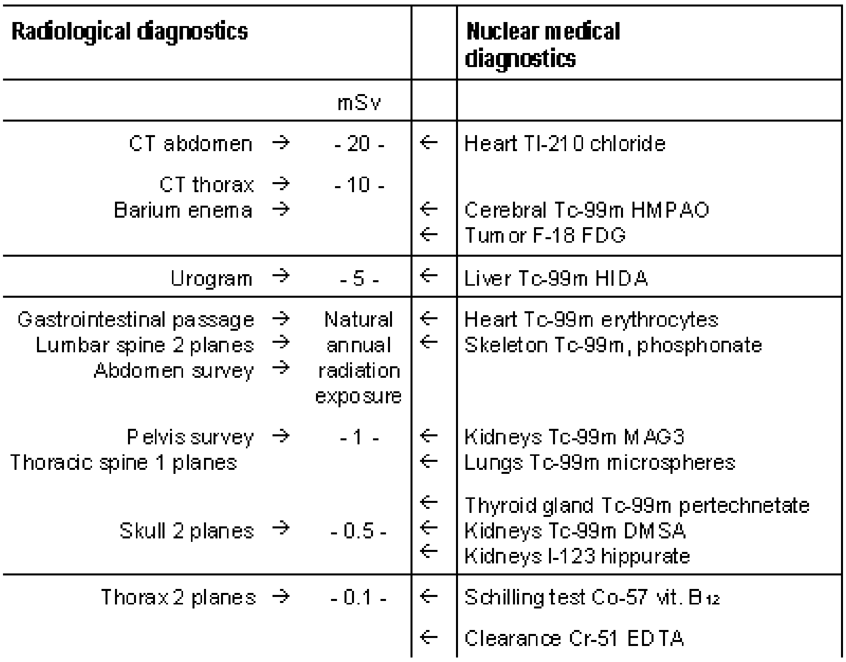
Table 1

Most frequently used radiopharmaceuticals in nuclear medicine.



Organ/ disease	Imaging/test	Radiopharmaceutical	Standard activity (MBq)
Skeleton	Bone	Tc-99m MDP or HDP	600
	Bone marrow	Tc-99m colloid	400
Heart	Perfusion	Tc-99m sestamibi	800
		Tc-99m furifosmine	800
		Tc-99m tetrofosmine	800
	Vitality	Tl-201 chloride	75
	Ventricular function	Tc-99m pertechnetate (in-vivo or in-vitro labeled erythrocytes)	600
Thyroid gland	Tc-99m uptake and scan	Tc-99m pertechnetate	50
	I-123 uptake and scan	I-123 NaI	10
	I-131 kinetics and scan	I-131 NaI	3
Brain	Blood flow	Tc-99m HMPAO	500
	Benzodiazepine receptors	Tc-99m ECD	500
	Dopamine receptors	I-123 iomazenil	185
		I-123 IBZM	185
Kidneys	ERPF	Tc-99m MAG3	150
		I-123 hippurate	30
	GFR	Tc-99m DTPA	150
	Static scintigraphy	Tc-99m DMSA	70
Lungs	Perfusion	Tc-99m MMA or microspheres	100
	Ventilation	Tc-99m aerosol	1000
Tumor	Wholebody PET	F-18 Fluordeoxyglucose	300

By far the most frequently used tracer is the artificial radioactive isotope technetium-99m which combines the advantages of optimum radiation properties (emission of exclusively gamma radiation with suitable energy, short half-life of 6 hours) and general availability as a generator nuclide. According to the pathophysiological principle of uptake in the organism, technetium-labeled radiopharmaceuticals provide answers to numerous diagnostic questions from widely differing indications. Methods of nuclear medical routine diagnostics are today used most frequently for examinations of the thyroid gland, skeleton, heart, kidneys, lungs and brain as well as of oncological and inflammatory diseases [3]. The diagnostic value of nuclear medical examinations of organ functions can be increased by interventional tests (e.g. defined ergometric stress in myocardial perfusion scintigraphy or thyroid gland hormone suppression in the diagnostics of functional thyroid gland autonomy). Here the lack of invasiveness and the comparatively low radiation exposure of nuclear medical methods are of advantage (Fig. 1).



Radiological diagnostics				**Nuclear medical diagnostics**
		mSv		
CT abdomen	→	- 20 -	←	Heart Tl-210 chloride
CT thorax	→	- 10 -		
Barium enema	→		←	Cerebral Tc-99m HMPAO
			←	Tumor F-18 FDG
Urogram	→	- 5 -	←	Liver Tc-99m HIDA
Gastrointestinal passage	→	Natural annual radiation exposure	←	Heart Tc-99m erythrocytes
Lumbar spine 2 planes	→		←	Skeleton Tc-99m, phosphonate
Abdomen survey	→			
Pelvis survey	→	- 1 -	←	Kidneys Tc-99m MAG3
Thoracic spine 1 planes			←	Lungs Tc-99m microspheres
			←	Thyroid gland Tc-99m pertechnetate
Skull 2 planes	→	- 0.5 -	←	Kidneys Tc-99m DMSA
			←	Kidneys I-123 hippurate
Thorax 2 planes	→	- 0.1 -	←	Schilling test Co-57 vit. B_{12}
			←	Clearance Cr-51 EDTA

Figure 1 Radiation exposure (effective dose) in the most frequent examination methods in nuclear medicine and radiological diagnostics in comparison to the annual fluctuation amplitude of natural radiation exposure (from [4]).

Nuclear medicine diagnostic procedures using small amounts of tracers are a prerequisite for performing dosimetry prior to therapy with radiopharmaceuticals. For this purpose uptake and kinetics of the tracers are quantitatively evaluated from scintigrams or from measurements with external probes. These data are used for the determination of the therapeutic activity. The success of therapy can be predicted by a dose assessment during or after therapy when the remaining activity in the patient is greatly reduced. Later, it can be documented using a repeated nuclear medicine diagnostic scan. The limits of nuclear medical routine diagnostics are, on the one hand, due to radiopharmacological aspects and, on the other hand, set by the equipment [1]. The easily available Tc-99m, which is ideal with regard to its physical and chemical features, cannot be coupled to all required biologically active substances, so that with this radionuclide the spectrum of radiopharmaceuticals for examinations of the organ metabolism is limited. I-123 labeled substances, which are used for many clinical questions, therefore represent an important supplement to technetium studies. Short lived positron emitters (e.g. F-18) may be used for high-resolution positron emission tomography (PET). The expenses for PET with dedicated ring tomographs are high as compared to single photon emission computed tomography (SPECT) with rotating gamma cameras.

2. Requirements for modern gamma cameras

2.1 Detectors/collimators

The gamma camera was considered for many years to be technically fully developed and no longer capable to be significantly improved [1]. The spatial resolution in planar technique was 10 mm maximum, while in SPECT technique it was around 0,5 cm3. Absolute quantification of the uptake of radiopharmaceuticals appeared to be impossible because the simultaneous attenuation measurements of the gamma radiation was not possible until recently in the SPECT technique.

Modern, multipurpose gamma cameras are nowadays equipped with rectangular detector heads (Fig. 2). A NaI(Tl)- crystal with a thickness of 0.9 cm is still used as detector material for conventional cameras. The light generated in the crystal by gamma radiation is registered according to location by a large number of coupled photomultipliers. The energy range in which the cameras can be used is determined essentially by the weight of the outer lead shield and by the response of the crystal. The practical use of gamma cameras ends at the energy level of positron-emitting nuclides.

To achieve a high inherent spatial resolution with a half-value width of 3.5-4 mm in the central field of view (CFOV) and to obtain a quantum efficiency that is as uniform as possible over the entire field of view of the detector, each photomultiplier should be connected to its own analog digital converter (ADC). In this way homogeneity values as defined by NEMA, e. g. for integral homogeneity, of less than 3% in the CFOV can be achieved. Digital processing of the data of the individual photomultipliers enables a clear improvement of the spatial resolution, of the dead time losses and of the long-term stability to be achieved with modern cameras compared with older models. In the meantime the inter action of the technical innovations and improvements has made resolutions of less than 0,5 cm3 possible in SPECT images. Direct digital signal processing is a prerequisite for using a gamma camera as a coincidence system for positron-emitting radionuclides. Today low-energy/high-resolution collimators continue to be used as the standard type of collimator. So-called fan-beam collimators are recommended for high spatial resolution in SPECT with simultaneously increased transmission

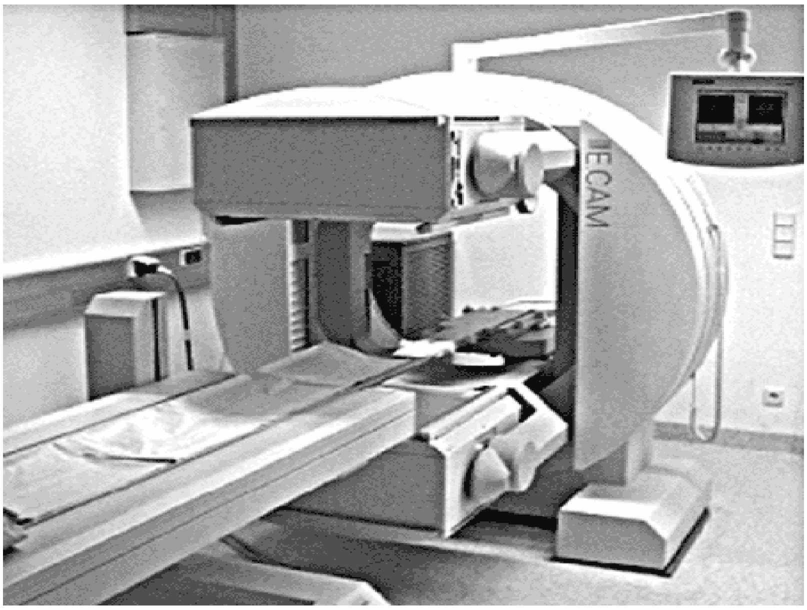


Figure 2 The E.CAM of the Clinic and Policlinic for Nuclear Medicine of the University of Wьrzburg. through the collimator. However these collimators have the disadvantage that the object to be imaged must be located close to the center of rotation of the camera in order to reduce geometrical distortions.

2.2 Gantry/table

The gantry and the table are operated today by microprocessor-controlled motors. The quality of the scintigrams is influenced by the attenuation of the gamma rays by the patient table. Due to automatic contour scanning of the patient in whole-body as well as SPECT imaging, in which the camera moves as close as possible to the patient, the quality of the scintigrams can be further improved. Thus maximum spatial resolution with a simultaneously high quantum yield is achieved. With modern cameras it must be possible to adjust the table and detector heads in as versatile a way as possible to enable the physician the necessary access to the patient even under unfavorable conditions (Fig. 3). It should be emphasized that a large rectangular field of view with these cameras clearly simplifies the examination of infants, since they can be brought up very close to the detector and thus are acquired completely by the field of view of the detector. Modern camera systems facilitate the optional positioning of the camera heads at an angle of 180° (e.g. bone SPECT) or 90° (e. g. heart SPECT). Semiautomatic or fully automatic collimator changing is a way to save time in clinics or practices in which different radionuclides are frequently used.

2.3 Computer systems

The requirements for the computer system are speed, stability in acquisition and a user interface, which is as simple as possible to operate when evaluating studies. A comprehensive package of clinical software, in which the user’s own programs can be generated and incorporated by a programming interface, is required according to the present state of the art. Currently, at Siemens the introduction of the practically platformindependent programming language IDL (Interactive Data Language), with corresponding interfaces to the ICON, is realized both in conventional nuclear medicine and in positron emission tomography (PET).

Interfaces to radiology information systems (RIS), to digital archives as well as standardized interfaces to other modalities (DICOM) today are prerequisites for the purely digital systems used in nuclear medicine.

Typical features of the hardware equipment of modern cam era computers are:

- At least 64 MByte RAM,
- 20 inch monitor with a resolution of at least 1024 x 786 for 256 colors,
- At least 2 GByte hard disk,
- Network connection.

Figure 3 Detail view of the table for the E.CAM.

Apart from acquisition and evaluation programs, the software configuration simplifies the use of additional packages for quality control, interfaces to other data processing methods as well as easy and simple archiving. The possibility of remote maintenance by modem assists in pinpointing and solving more complex software and hardware problems.

For image output, today either black and white laser printers with a resolution of at least 1200 dpi, color printers (thermal transfer, solid ink or sublimation) or X-ray film printers can be used. With the low film throughput compared with radiological diagnostics and the resulting problems with film processors, the use of digitally connected dry laser imagers is suggested in nuclear medicine.

To be open for future networking and to simplify the integration of digital nuclear medical evaluation consoles in a hospital communication system (HIS), an efficient network must be provided at least within a department/clinic. The state of the art today is a network with a star topology and with twisted-pair cabling, which currently allows data transmission speeds of up to 100 Mbit/s depending on the active network components. The networking of the computer systems within the Clinic and Policlinic for Nuclear Medicine of the University of Wьrzburg is shown as an example in Fig. 4.

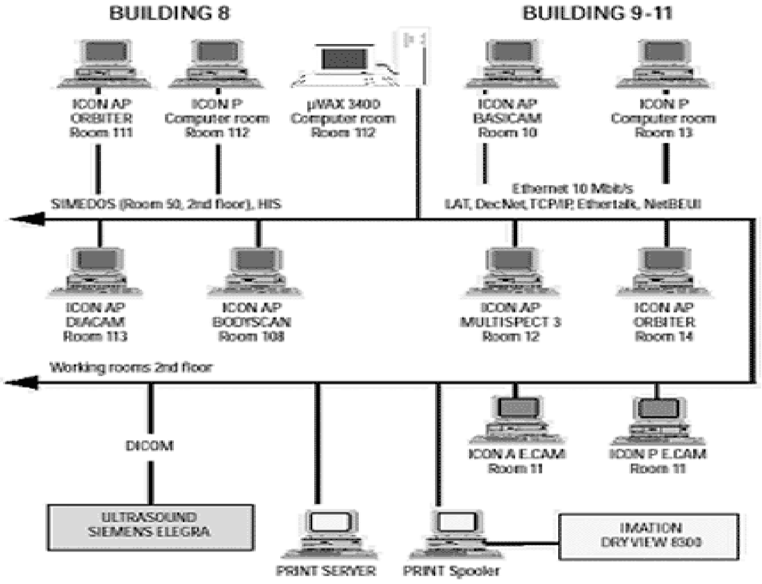


Figure 4 Networking the modalities within the Clinic and Policlinic for Nuclear Medicine of the University of Wьrzburg.

3. Clinical use of the modern gamma camera

In Germany the thyroid gland continues to be the organ most frequently examined by nuclear medicine. Even though this organ can also be examined with a modern double-head gamma camera the detectors of which can be positioned variably, both on the recumbent and on the sitting patient, in the normal case thyroid gland scintigraphy can be performed adequately with less complex gamma cameras (Fig. 5). The main areas of application for a modern SPECT-capable double-head camera are in the fields of oncology, cardiology, neurology and psychiatry.

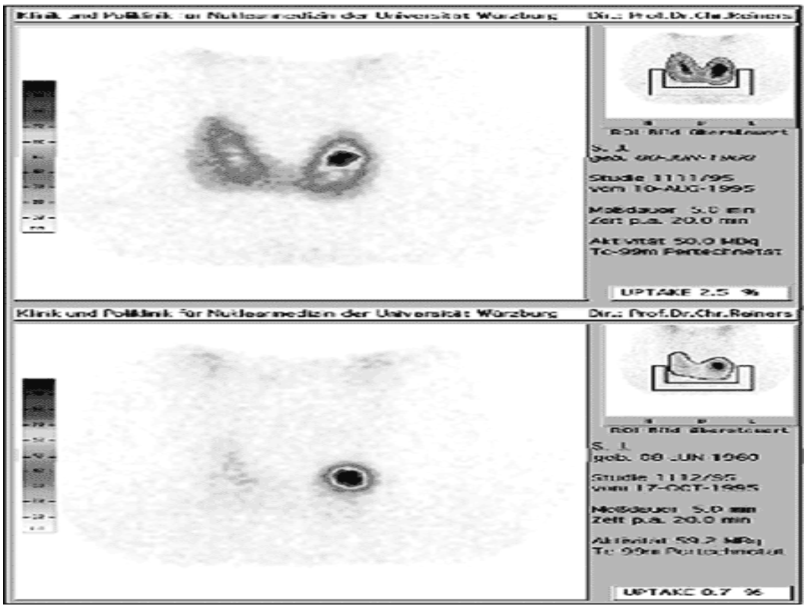


Figure 5 Thyroid gland scintigram with Tc-99m pertechnetate before (above) and after (below) suppression with triiodothyronine. There is an autonomous adenoma in the left lobe (Basicam).

Skeletal and bone marrow scintigraphy is of great importance among oncological questions. Skeletal metastatic spread can frequently be detected significantly earlier by scintigraphy than by radiography. A high image quality is expected in whole-body scintigrams (Fig. 6).

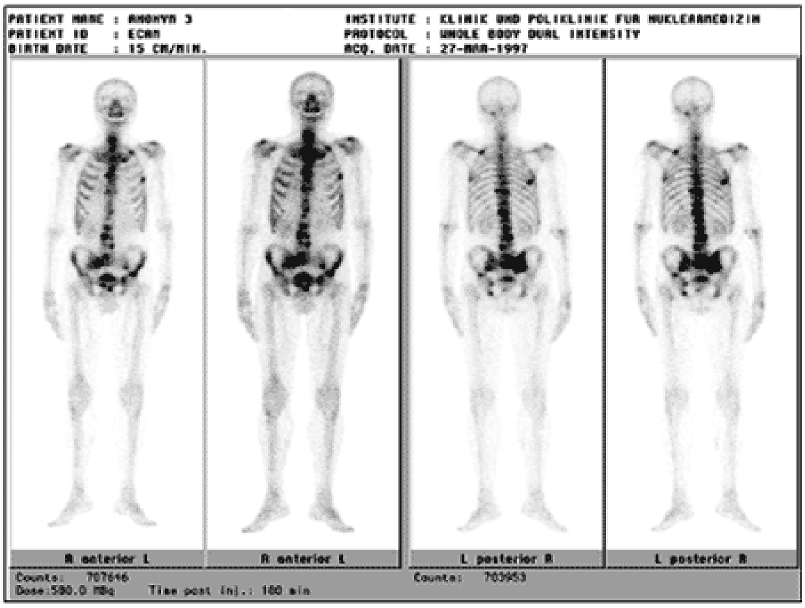


Figure 6 Tc-99m MDP whole-body skeletal scintigram of a patient with prostate carcinoma and multiple bone metastases, ventral and dorsal view (E.CAM).

Moreover, the examination should be as comfortable as possible and be performed quickly for patients suffering pain. The possibility of being able to perform single acquisitions in all planes or SPECT examinations without repositioning the patient is of advantage.

Non-specific or more specific radiopharmaceuticals are used for tumor scintigraphy. Thallium-201 or Tc-99m MIBI as well as the today largely outdated gallium-67 chloride, for instance, come in the first group. It has been shown that Tc-99m MIBI can be used for a number of problems in the field of oncology. This concerns the localization of metastatic spread of a thyroid gland carcinoma as well as of bronchial carcinomas. Fig. 7 shows an example of an intrathoracic parathyroid gland adenoma displayed with Tc-99m MIBI in planar and in SPECT technique.

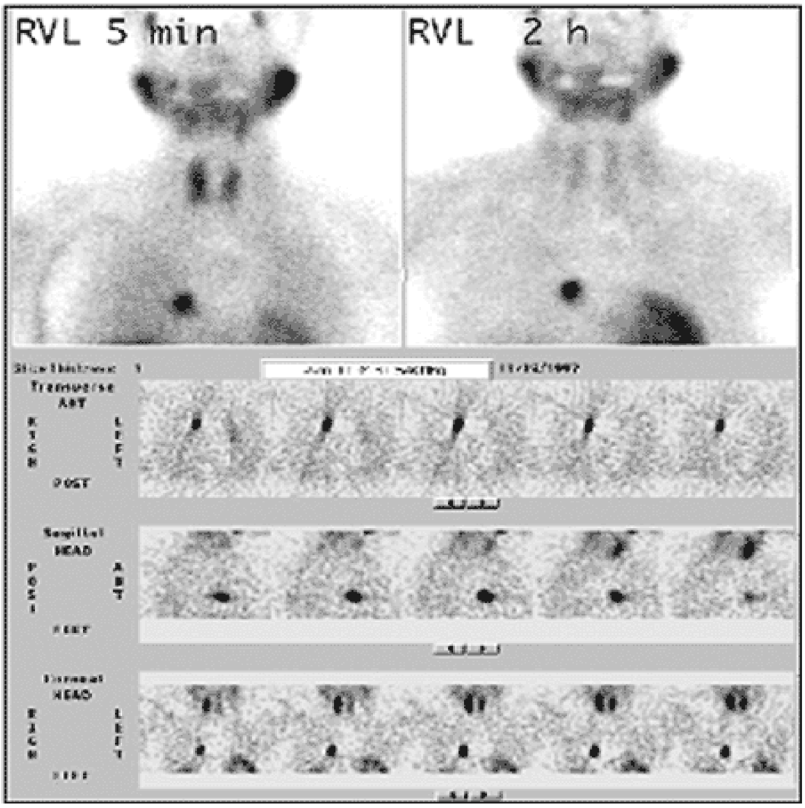


Figure 7 Tc-99m MIBI examination in a patient with an intrathoracic parathyroid gland adenoma in planar technique (above) and in SPECT technique (below) with the E.CAM.

Nuclear medical methods based on the antigen/antibody binding or the binding to specific receptors are more specific.

Recently In-111-octreotide has especially established itself as a radiopharmaceutical for the diagnosis of neuroendocrine active tumors. Fig. 8 shows a cerebral metastatic spread of such a tumor in a child.

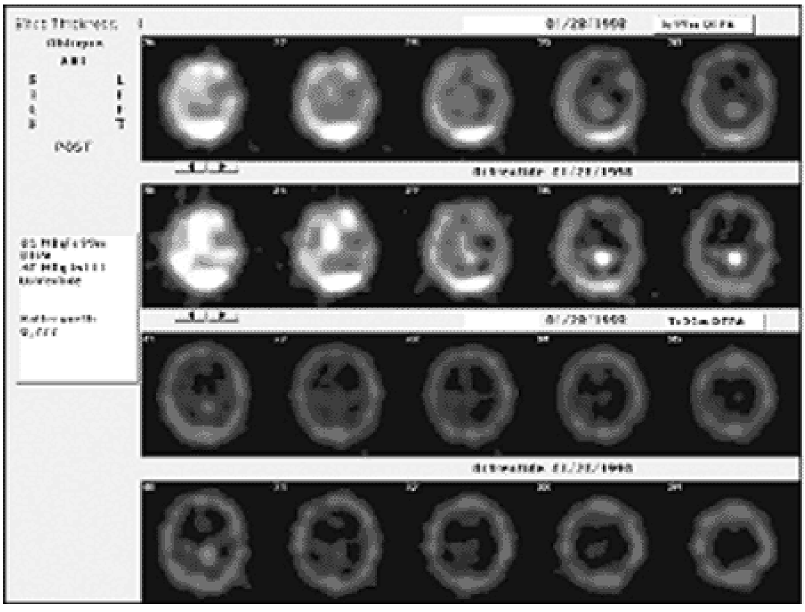


Figure 8 In-111-octreotide SPECT examination in a child with a neuroendocrine active brain tumor (PNET), transversal tomograms (E.CAM). Row 1 and 3: disturbance of blood

brain barrier shown by Tc-99m DTPA, row 2 and 4: specific uptake of In-111 octreotide in the tumor.

In nuclear medical cardiological diagnostics, MIBI labeled with Tc-99m is widely used as a perfusion marker, along with thallium-201 chloride which is a marker of myocardial viability. Myocardial perfusion scintigraphy usually is performed at rest and after defined ergometric or pharmaceutical stress (Fig. 9).

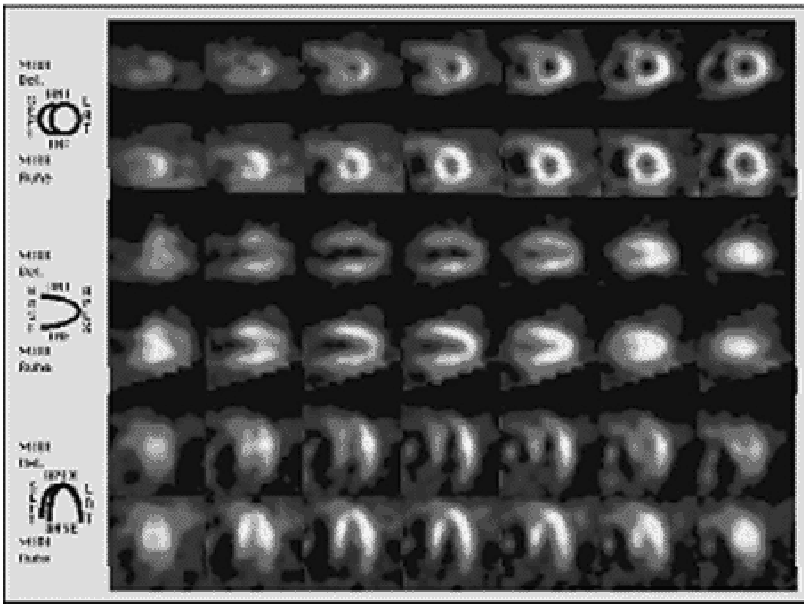


Figure 9 Myocardial SPECT examination in a patient with a reversible ischemia in the septum and the anterior wall (E.CAM). Row 1, 3 and 5: stress images, row 2, 4 and 6: study at rest.

Here, reversible ischemias can be differentiated from permanent circulatory disturbances or myocardial scars. A prerequisite is an optimized tomographic examination technique. In this case detectors that can be tilted by 90° and the possibility of an attenuation correction are of advantage. A whole series of radiopharmaceuticals is available today for the examination of the cerebral blood flow and of cerebral receptor systems. Cerebral scintigraphy is performed tomographically exclusively in SPECT technique. Networking or superpositioning with X-ray computed tomography or magnetic resonance tomography is of great importance for the evaluation of cerebral scintigraphic examinations. It is mandatory that modern gamma cameras fulfill the current standards (e. g. DICOM). Fig. 10 shows an example of the parallel viewing of SPECT tomograms and MR tomograms on an imaging console.

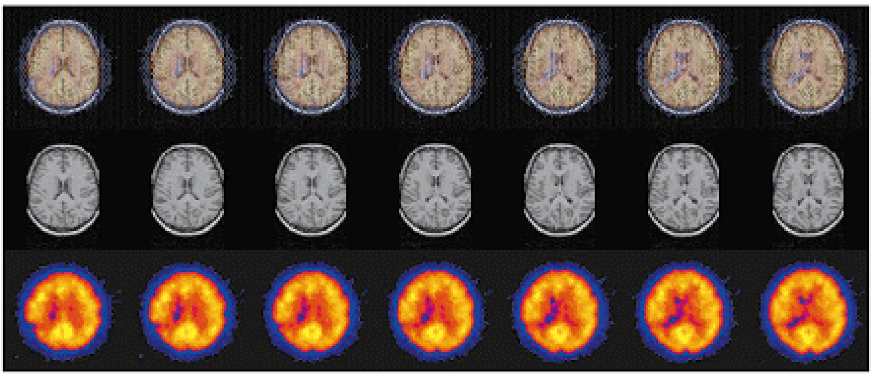


Figure 10 Use of image superpositioning in morphological and functional imaging. Upper row: fused image, middle row: MRT, bottom row: Tc-99m IMPAO perfusion SPECT. (Siemens ICON software).

4. Options/further technical development

4.1 Attenuation correction (SPECT) Simultaneous transmission/emission measurement is no longer a problem today with the improved detector electronics. Many SPECT examinations (especially of the myocardium, for instance) show artifacts because the absorption of the gamma radiation in the body is not taken into account. With a half-value layer of Tc-99m in water of 4.5 cm, approximately 50% less photons are received on acquisition from the back of an object 4.5 cm in diameter. The correction is performed in the case of multi-head cameras by the additional measurement of the attenuation of a transmission line source (Am-241 or Gd-153) in the patient. The emission data are then reconstructed with attenuation correction by the inclusion of the data of the transmission measurements. Nevertheless several problems complicate the interpretation of the reconstructed tomographic slices:

- The SPECT volume must be covered completely by the transmission measurement, since otherwise artifacts are introduced into the reconstruction due to incomplete data blocks.
- There is no correction for photon scatter in the tissue.
- The photon energies of the sources used for the transmission measurement are not identical with the nuclide used, so that there must be an energydependent adaptation to the attenuation coefficients of the emission measurement.
- The reconstruction algorithms can introduce new artifacts.
- The time required for the evaluation of the studies is increased due to the time necessary for the reconstruction of the images.

Taking account of these points, the attenuation correction allows both an improvement of the absolute quantification of the radionuclide uptake, comparable with PET, as well as avoiding incorrect findings due to attenuation artifacts. An example of the use of the attenuation correction in myocardial scintigraphy is shown in Fig. 11.

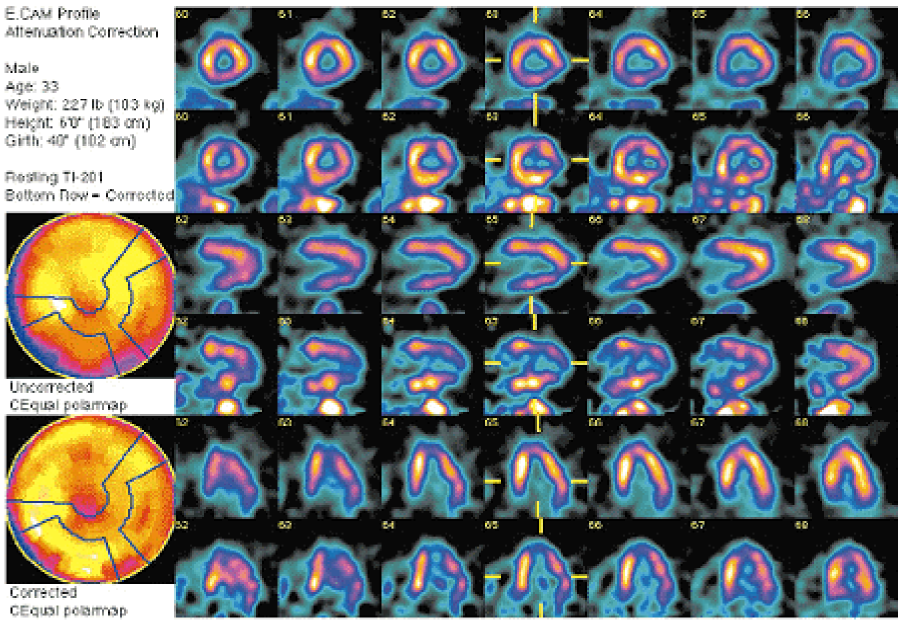
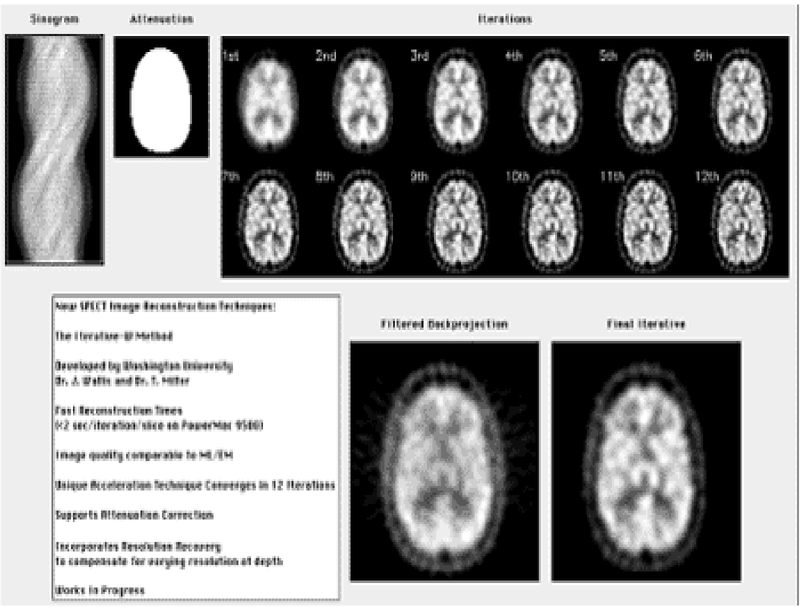


Figure 11 Use of the attenuation correction in myocardial SPECT with Tl-201. Row 1, 3 and 5: uncorrected, row 2, 4 and 6: attenuation corrected. Lower left: comparison of polar maps. (Siemens ICON software).

4.2 Iterative reconstruction (SPECT) The reconstruction of tomograms by means of filtered back projection, a common and fast evaluation method for SPECT studies today, leads on the one hand to artifacts due to its inherent properties and, on the other hand, pathological findings can be lost because of excessive smoothing or filtering.

Iterative reconstruction avoids these problems and leads to an improved evaluation of SPECT studies. For instance, the Mallinckrodt Institute of Radiology, Washington University School of Medicine, St. Louis, USA, is developing a program for Siemens for the iterative reconstruction on the ICON system using IDL. The technique of iterative reconstruction can contribute to significantly improved image quality with a clear reduction of the artifacts caused by the analytical reconstruction. This can be seen clearly in Fig. 12 (bottom left: filtered back projection, bottom right: iterative reconstruction).



New SPECT Image Reconstruction Techniques:

The Iterative-W Method

Developed by Washington University
Dr. J. Wallis and Dr. T. Miller

Fast Reconstruction Times
(<2 sec/iteration/slice on PowerMac 9500)

Image quality comparable to ML/EM

Unique Acceleration Technique Converges in 12 Iterations

Supports Attenuation Correction

Incorporates Resolution Recovery
to compensate for varying resolution at depth

Works in Progress

Figure 12 Reconstruction algorithms for SPECT. Bottom left: filtered back projection, bottom right: iterative reconstruction. (Siemens ICON software).

The problems of iterative reconstruction result from the fact that the optimum number of iterations must be found at which simultaneously no diagnostic information is lost and the computing time for the iteration must be kept as low as possible so that results can be obtained in a time acceptable for clinical routine.

4.3 Coincidence measurement with new types of detector

For about two years, the coincidence measurement of positron emitters like F-18 FDG with gamma cameras has been gaining clinical relevance for certain questions such as those arising in oncology. This measurement procedure is made possible by the uniform digitization of the camera data after the photomultipliers, improved computer capacities and thicker NaI(Tl)- crystals (1.3 cm), whose efficiency for 511 keV photons is clearly better with concurrently only slight loss of quality for conventional nuclides. Technical problems arise from the processing of high count rates due to photons with energies of less than 511 keV with simultaneously low yield for 511 keV photons. Suitable fast reconstruction algorithms for the evaluation of coincidence measurements are still required.

Such coincidence systems for PET tracers are currently being evaluated clinically. The major disadvantage of this method is, nevertheless, that an absolute quantification of activity concentrations, such as in examinations with PET ring tomographs until now is not possible (Fig. 13).

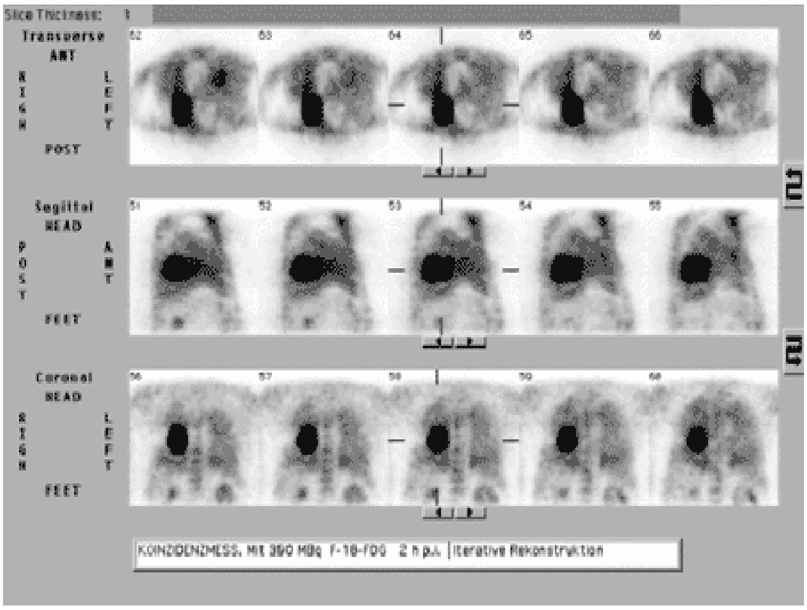


Figure 13 Coincidence PET imaging (E.CAM duet) with F-18 FDG in a patient with a non-small cell lung cancer. Intense uptake in the tumor in the right lung.

The future must show to what extent current detector developments, such as crystals of lutetium orthosilicate and yttrium orthosilicate (LSO/YSO)* for detectors with a higher quantum efficiency, as well as further optimization of the detector electronics, can replace the dedicated PET tomograph.

Literature

[1] Reiners, Chr.: Nuklearmedizinische Funktionsdiagnostik gestern – heute – morgen: Mцglichkeiten und Grenzen. Editor: Bцrner W., Holeczke F., Messerschmidt O. Gustav Fischer Verlag, Stuttgart, 1990, 30; 35-50

[2] Schicha, H.: Nuklearmedizinische Diagnostik – Prinzipien und Indikationen. Z. Дrztl. Fortbild. 91; 335-340, 1997

[3] Reiners , Chr., Sonnenschein W.: Die Strahlenexposition durch nuklearmedizinische Untersuchungen in Deutschland 1992 (alte Bundeslдnder). Nucl.-Med. 33; 254-262, 1994

[4] Hдnscheid , H. et al.: Kursus der Nuklearmedizin. http://www.uniwuerzburg. de/nuklearmedizin/kursus/kursus.htm