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review

Recent developments in nuclear medicine instrumentation

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State-of-the art gamma cameras offer two new options for nuclear medicine. Attenuation correction should enable artefact free myocardial perfusion scintigraphy. 511 keV coincidence detection may be a low-cost alternative to PET. Different solutions for both methods are implemented by the industry. However, clinical validation is at the beginning now. The present paper is dealing with the discussion of solutions, clinical relevance and future trends of nuclear medicine instrumentation.

Key words: nuclear medicine-instrumentation-trends; – PET– SPECT – coincidence – attenuation correction

Introduction

Since the early nineties basic technical requirements of both gamma cameras and nuclear medicine computers have become well-defined. Their technical performance enables high quality investigations and meets the demands for most clinical questions. Using single photon emitting radionuclides and traditional equipment, about 90% of routine "clinical requirements can be covered perfectly. However, some important technical issues remain unsolved. First, attenuation artefacts, located predominantely at the inferior wall in men and in the anterior region in women, decrease the specificity of myocardial perfusion imaging. Second, the quantification of absolute radionuclide uptake may be necessary in special cases. Both problems remain unresolved using conventional gamma cameras. Furthermore, the perspective of a broad availability of F-18-FDG and its increasing clinical importance motivates leading producers of gamma cameras to make 511 keV imaging at low cost possible.[1,2] The present paper addresses these challenges as well as possible answers and specific points, which have to be considered to make newly developed technologies useful in various clinical settings.

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Classification of imaging equipment

Definition of groups of imaging devices may be helpful both to analyse and to understand the processes of gamma camera develop-

Table 1. Nuclear medicine imaging devices

Planar gramma camera
Singl head SPECT
Dual headed SPECT
Triple headed SPECT
SPECT with 511 keV facility
Dedicated planar gamma camera

ment. Table 1 contains a list of equipment presently manufactured. The first group considers traditional planar gamma cameras. They are characterised by high image quality as a consequence of detector parameters summarised in Table 2.

State-of-the-art gamma camera detectors are partly or fully digitalized. Sophisticated possibilities for correction of homogenity as well as for linearity are standard. However, the relative number of these devices is decreasing rapidly. They are replaced step by step by single head SPECT cameras with the same detector characteristics as described above. Furthermore, recent developments resulted in high mechanical stability and user friendly handling.

Recently, dual headed SPECT cameras are increasingly penetrating the market. These universal devices are the working horses of modern nuclear medicine. The relative position of the two detectors can easily be changed between 180 degrees for whole body acquisitions and 90 degrees for cardiac studies. In most cases further individual positions are available. The open gantry enables easy patient handling and reduces claustrophobia. Even severely ill, intensive care patients can be investigated comfortably. The patient bed is extended by convenience equipment as grips, stabilising devices for head, arms etc. Reproducible patient positioning is supported by laser light. Detector movement control enables contour finding both in whole body and SPECT mode. These accessories ensure comfort feeling of the patient which eases the technician's work, and, therefore, helps to increase image quality. Today, the above listed principles are met by nearly all producers. Thus, decisions about purchasing are determined more and more by price, additional service, and by the clinical experiences of reference sites.

A further development is characterised by triple headed SPECT cameras. On one side they can not be used as universally as dual headed systems. On the other hand this limitation is somewhat compensated by an excellent tomographic image quality. Purchasing can be recommended to sites in which whole body gamma cameras as well as planar gamma cameras are already in operation and SPECT capabilities are required all day long.

Table 2. Performance parameter of gamma camera

Parameter	CFOW	UFOW
Intrinsic Spatial Resolution		
FWHM	< 4.5 mm	< 4.5 mm
FWTM	< 8 mm	< 8 mm
Intrinsic Energy Resolution		< 11 %
Intrinsic Flood Field Uniformity (W/O corr)		
Integral	< 5 %	< 5 %
Differential	< 4 %	< 4 %
Intrinsic Spatial Linearity		
Absolute	< 1 mm	< 1 mm
Differential	< 0.5 mm	< 0.5 mm
Intrinsic Count Rate Performance at 20% loss		> 160 kcps
Maximum Count Rate		> 200 kcps

A new class of SPECT cameras is suitable for 511 keV coincidence imaging. These devices have two detectors and can also be used effectively for state-of-the-art single photon imaging.

Finally, groups of dedicated equipment should be mentioned. Whole body scintigraphy, thyroid imaging or bedside imaging in intensive care units can be performed most effectively using specially developped planar gamma cameras. Dedicated SPECT systems have been introduced for heart, brain or recently, for breast imaging.

Attenuation correction

Myocardial perfusion imaging is often hampered by attenuation artefacts. Image reading reveals perfusion defects which are located typically in the anterior region in women and in the inferior wall in men. Therefore, whether an intensity deficit is caused by real perfusion defects or merely by an attenuation artefact may be uncertain in an estimated 20 % of cases in men and even in as much as 40-45 % in women. Thus, there is a real need for compensation.

From a theoretical point of view, there are four groups of methods for attenuation correction.

- Initially, a uniform attenuation coefficient was assumed in the wholebody region reconstructed. However, in practical patient management this simplified assumption is only applicable in brain studies, but it is not feasible in the thoracic region since attenuation is rather non-uniform there.

- Methods using CT images for correction are hampered by their complexity and by an additional necessity for registration of images from different equipment. To overcome these limitations, combined PET/CT devices for simultaneous data acquisition and registering for exact localisation of tumour/metastasis are under development. The principles of that equipment can be theoretically extended to attenuation correction.

- Segmentation is a new method for the identification of major structures with different attenuation features in the thoracic region.[3] For this purpose a low dose mixture of Tc-99m-MAA and Tc-99m-colloid is given for simultaneous localisation of the liver and the lungs. Additionally, a body wrap with Tc-99m highlights the patient's outline. The identified areas are then considered with their assigned attenuation coefficients. This attempt for attenuation correction seems to be very promising especially in myocardial scintigraphy, however, it is not widely used.

- Recently, transmission based attenuation correction was introduced in SPECT. The idea of measuring real attenuation in order to correct emission data is originating from positron emission tomography (PET). In PET, the measured distribution of linear attenuation coefficients is already routinely used in order to quantitatively calculate tracer distribution. To this, an external radioactive source is needed in order to generate a clearly defined radiation field. Presently, most cameras use Gd-153 for transmission imaging. Some additional experience exists with Am-241, Tc-99m, and Co-57. Technically, the source(s) may be arranged either as single fixed line sources e.g. at the focus of a fan beam collimator, as scanning line sources or as an array of fixed line sources.[2,4,5] The patient's body is positioned between the radiation source and the gamma camera detector. Consequently, distribution of attenuation coefficient within the body can be determined from the acquired transmission projection images. In the individual patient under investigation the measured attenuation can then be taken into account during reconstruction. However, an iterative reconstruction algorithm is mandatory. On the other hand, this is no more a real problem, since computing time

may be kept in the range of only a few minutes when a powerful computer is available.

Requirements of transmission based attenuation correction

There are some fundamental requirements, which should be fulfilled to ensure that transmission based attenuation correction can be usefully utilised in clinical patient management. In short, first, the method should work in a wide range of body mass independent of the patient's body size. Second, it should not increase the investigation time significantly. Third, measurement of transmission and emission should be strictly performed in the same geometric position of the patient. Fourth, attenuation correction should not generate image artefacts by itself, and therefore, it should be especially free of overcompensation. Fifth, transmission measurement should not significantly increase the radiation exposure both of the patient and of the staff. Finally, the additional costs should be acceptable. In the following, some critical points of attenuation correction are discussed in detail.

Truncation free data acquisition

An important issue to obtain correct transmission images is the careful positioning of the patient. It is well-known from SPECT technique that the target organ should be completely within the field-of-view of the gamma camera in all projections acquired. Otherwise, so called truncation artefacts may occur, and image interpretation will be hampered. Since in case of transmission imaging the total body of the patient reflects the "target organ", large field-of-view detectors with their long axis positioned perpendicular to the long axis of the patient are needed in general.

Early attempts using triple headed gamma cameras and focusing collimators exhibited truncation artefacts even in slightly overweight patients. To compensate for this, asymmetric fan beam collimators were introduced (Figure 1) in which the radiation

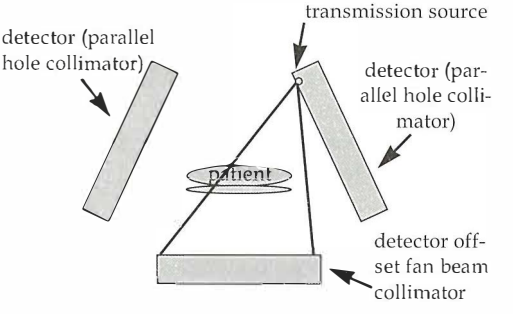

Figure 1. Measurment of attenuation using asymmetric fan beam collimator.

source is placed in the collimator focus. The radiation field then covers one half of the patient's body in each projection. Therefore, a full 360 degree-rotation is necessary to acquire a complete set of data for this rather highly sophisticated approach.

Up to now, most clinical experience has been gained using scanning line sources and large field-of-view, double headed gamma cameras (Figure 2). Using two sources and (nearly) simultaneous data acquisition, complete emission/transmission data can be obtained theoretically in the same duration which is required for a 90 degree SPECT acquisition, i.e. in about 15 minutes. This duration of acquisition meets best the clinical requirement of high patient throughput.

Cross-talk

For practical reasons, transmission images will be usually acquired following the injection of radioactivity into the patient. Therefore, transmission data may be contaminated by emitted radiation being acquired in the

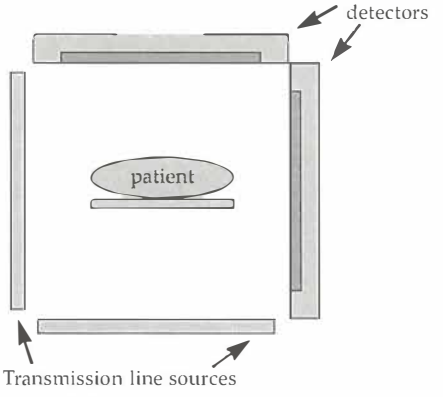

Figure 2. Scanning line sources for attenuation measurment. The sources scan along the lenght of the patient at each angle.

transmission energy window. On the other hand, radiation of the transmission source may scatter as well into the emission energy window, especially when transmission and emission data are acquired simultaneously. However, attenuation correction algorithms presume both contamination free emission and transmission data. Therefore, cross-talk described above, should be minimised sufficiently.

Gd-153, the most widely used transmission source has a gamma energy of 100 keV. Performing simultaneous emission/transmission acquisition, and using Tc-99m as an emission source, there is no cross-talk of Gd-153 into the higher energy emission photopeak window of Tc-99m. However, Tc-99m may scatter down into the Gd-153 window and contaminate the transmission data. Using Gd-153 in connection with Tl-201 myocardial scintigraphy, the relations are practically vice versa.

The most effective way to keep both transmission and emission data fairly free of cross contamination is the use of a transmission source as a scanning line source. Mechanical collimation of a moving Gd-153 line source ensures an appropriate focus of transmission radiation only to a small area of the gamma camera detector, lying opposite to the current position of the line source. On the detector surface a narrow electronic mask is established. This mask is scanning over the face of the detector in synchrony with the collimated line source. This enables only the corresponding detector area to collect transmission photons, minimising the contamination with scattered emission photons. On the other hand, the remainder area of the detector is electronically kept open for the collection of emission photons and, due to the mechanical collimation of the line source, closed for transmission data. This method reduces cross-talk to less than 1 % Gd-153 scatter into the Tl-201 window, and to less than 7 % Tc-99m scatter into the Gd-153 window.[6]

In general, cross-talk should be preferably minimised during acquisition. Subtraction routines that are employed after completed acquisition may substantially increase the amount of noise in the images.[7] On the other hand, transmission data contaminated by emission may result in overcompensation of attenuation and, therefore, may rather introduce than avoid artefacts.[4]

Additional points of view

To have a complete impression about the performance of a method introduced for attenuation correction, some additional points should be considered. First, the handling of the transmission source should be as simple as possible in order to minimise necessary interventions of the technician. This involves source placement, checking of the field-of-view, as well as the exclusion of truncation.

Second, transmission measurement is a highly sophisticated tool, thus, appropriate quality assurance should be elaborated in order to establish valid results.

Third, transmission measurements should not increase acquisition time and decrease patient throughput significantly, as in the

case when acquisition of transmission and emission data is performed successively. To avoid this, there are several attempts currently under clinical investigation.

Fourth, considering the relatively high activity and long physical half-life of radiation sources for transmission measurement problems of radiation protection including handling with old sources should be carefully analysed.

Finally, one should take into account that none of the methods developped for attenuation correction has yet been sufficiently validated and the interpretation of attenuation corrected images differs significantly from that of non-corrected images.

Way towards quantitative SPECT

Until recently, quantitative SPECT seemed to be an unrealistic dream for nuclear medicine specialists. Nowadays, intensive research is ongoing on this topic. Several camera producers are working on tools, making quantification feasible. Attenuation correction helps to come closer to images with a correct relative distribution of radioactivity. However, to make quantification possible, images should be corrected for Compton scattering and for collimator response function as well.

511 keV imaging with gamma camera

Positron emission tomography has been considered for a long time both an interesting and a highly expensive research tool. In the last few years, the glucose analogue F-18-fluorodeoxyglucose (FDG) initiated a breakthrough in answering numerous diagnostic questions.[8,9,10] Based on the results of clinical trials, well-defined indications for FDG imaging have been established and accepted both by the nuclear medicine community and by referring clinicians.

The increase of number of sites performing FDG imaging is facilitated by the fact, that the supply with the radionuclide F-18 is not limited to the place of its production. Its physical half-life of 110 minutes permits transportation within a radius of about 200 kilometers. Professional suppliers are building up distribution networks in different european countries and offer price and availability independent of the geographic location of potential users.

In conclusion, there is an increasing demand for positron imaging devices at low cost. Traditional gamma cameras are optimised for the detection of photons with an energy of 100-150 keV. To answer the question, how the performance of these devices may be extended to F-18 imaging, the spectrum of routine FDG-PET investigations should be considered. Accepted indications for FDG-PET cover about 70 % oncological, 20 % neurological and about 10 % cardiological patients with an even increasing tendency of oncological patients. In addition, within oncology one should differentiate between several questions arising in clinical patient's management, i.e. tumour detection, differentiation between malignant and benign tumour masses, staging, detection of metastases, documentation of effectivity of treatment, and last but not least diagnosis of relapse after therapy. Moreover, each of the above mentioned questions may arise in different regions of the body or in combination with each other.

Given a special clinical question technical requirements may vary. For example the detection of metastases needs technical equipment providing high geometric resolution. Follow-up of tumours may need quantification, which is not essential in staging. This demonstrates, that a particular instrument may be a good compromise for one selected clinical question, but may not meet the requirements for other clinical problems.[11]

History of 511 keV imaging using conventional gamma cameras

First attempts to obtain 511 keV images using conventional gamma cameras were undertaken using seven-pinhole collimators. Results were presented in patients with chronic ischemic heart disease, i.e. in the detection of myocardial viability. The next step was the introduction of high energy collimators for planar F-18 imaging. With increasing mechanical stability of SPECT gantries these 511 keV collimators were attached to rotating cameras as well. These initial efforts resulted in quite acceptable image quality for F-18-FDG cardiac viability studies at low additional costs. In fact, up to now these high-energy collimators can be effectively used in cardiac scintigraphy only. For other clinical questions neither the requested minimum of resolution (brain imaging) nor the necessary count rate capability (oncology) could be achieved. Due to the fixed geometry of collimators and due to the limitations regarding imaging parameters, possibilities of further developments of collimated 511 keV imaging seem to be exhausted.

Coincidence imaging

Recent developments of computer technology opened the way to introduce coincidence detection in traditional gamma cameras. This development has been facilitated by the introduction of fully digitalized gamma camera detectors, with an analogue-to-digital converter connected to each photomultiplier tube.

Data sampling in coincidence cameras is practically a 3D acquisition at any time. That means, that the whole, collimator-free detector-surface is available for coincidence events. However, this type of coincidence measurement has several technical problems. Some of them result from detector geometry others result from physical parameters of the detector itself.

The geometric position of the two detectors makes evident, that the detection of two gamma photons originating from a given positron annihilation has a higher probability, when this annihilation occurs at a position close to the middle of the detectors as compared to the detector edges. In other words, the sensitivity of the detector field-of-view is non-uniform. It is maximal at the centre and decreases toward to the edges (Figure 3).

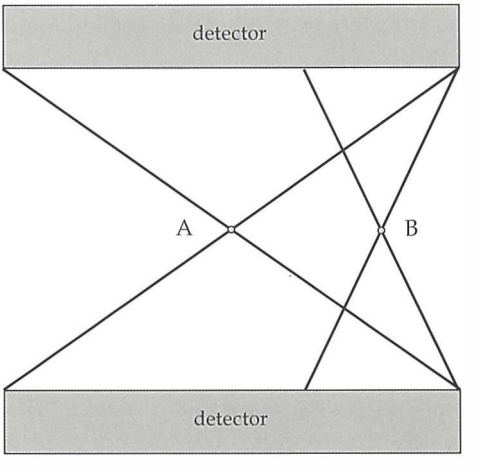

Figure 3. Relation between the position of radiation source and the coincidence count rate. Photons emitted from the source A have a higher probability to meet the detector as campaned to photons emitied from source B.

A positron emitting point source positioned under the middle of the detectors results in a higher coincidence count rate, than the same source at the periphery. This difference has to be corrected subsequently. An important consequence is an increasing statistical noise towards the edges of the images.

A further problem of coincidence imaging is in principle, that not all coincidences registered are true ones, since data are contaminated both by random as well as by scatter coincidences. Random coincidence occurs when two different events can not be separated by the time window of the processing

electronics. Consequently, an increase in the total count rate increases the probability of random coincidences as well as organs with high activity being placed close to the detectors field-of-view. The latter shows up when searching tumors or metastases in the thoracic or in the neck region. Radiation emitted from the brain, which accumulates F-18-FDG intensively, may considerably increase the number of random coincidences resulting in a decreased signal-to-noise-ratio over the area of interest. Similar problems may result in body areas close to the urinary bladder. To overcome this problem, axial collimation may be helpful.

Scattered coincidence means, that either one or both photons detected are scattered ones, but the energy window of the equipment considers them still to be true ones. These events may contain a false position information.

With these limitations in mind, an important task of coincidence imaging is to maximise both the total and the relative number of true coincidences. To meet this requirement a high total count rate is needed. Thus, the detector sensitivity has to be maximised, the processing electronics should be fast, and the pile-up in the crystal should be negligible up to high count rates. In this case, technical solutions for subsequent separation of random and scatter events still result in an acceptable high rate of remaining true coincidences.

Coincidence detection with NaI crystal

NaI based scintillation crystals have been originally developped for detecting of low energy gamma radiation. However, the traditional crystal thickness of 3/8 inch (9.5 mm), optimised for 140 keV imaging in modern gamma cameras results in a poor efficiency for 511 keV. Therefore, most producers of gamma cameras designed for 511 keV imaging use an increased crystal thickness of 5/8 inch (15.9 mm). This offers an almost twofold increase in the efficacy of absorption for 511 keV photons without significant loss of geometric resolution for Tc-99m. A further disadvantage of NaI is its relatively long duration of light pulses of about 230 ns which is a limitation in case of high count rates due to pile-up effects induced. Thus, today's maximum detector count rate is rather limited by the time resolution of the crystal than by the processing electronic. Despite some feasible electronic corrections for pile-up, the maximum count rate, the maximum patient dose, and the maximum rate of true coincidences still remain limited using NaI crystal based detectors.

The upper performance limit of modern dual headed gamma cameras is in the range of a total count rate of about 2 million cps. However, about 1% of the total count rate are detected as true coincidences only, and therefore contribute for imaging. Consequently, the sensitivity of the system is better characterised by the maximum coincidence rate, than by the maximum total count rate. Despite some sophisticated possibilities to increase sensitivity using appropriate electronic solutions, image acquisition time with coincidence cameras will always be significantly longer, than that with ring detector PET systems in 3D mode. Today's experience clearly shows, that even the fastest coincidence cameras need about 40 minutes for imaging of one single body region. The same image quality could be achieved in 3D PET in less than 3 minutes.

To increase the detector's suitability for 511 keV imaging, promising experimental results have been presented recently using lutetium oxyorthosilicate (LSO). This material has an about twofold density as compared to NaI, and consequently, an increased probability of interaction with high energy photons. Moreover, the duration of light pulses is in the range of about 40 ns, thus being

extremely short as compared to NaI. This enables a corresponding increase of the total count rate. However, the applicability of LSO for low energy radiation is limited due to its poor energy resolution. Thus, for imaging in low energy range as well as in high energy range a combination of LSO and YSO (yttrium oxyorthosilicate) as a sandwich detector is considered. First cameras are expected to be presented in the near future. Up to now, the clinical usefulness of gamma camera coincidence imaging has to be proven.

Attenuation

Unfortunately, the well-known attenuation artefacts of single photon imaging may also be present on coincidence images. This is especially problematic in cardiac imaging. The explanation for this is that the two annihilation photons after positron emission have to pass the whole body before being detected. In contrast, a gamma photon used for single photon imaging has only to pass the body layer between its origin and the detector surface. Due to the longer way, the probability of absorption or scattering is higher for the two high energy photons, than for the one photon of single photon emitters. This is only partly compensated by the 54 % higher linear attenuation coefficient of 140 keV photons.

Attenuation correction algorithms for gamma camera coincidence imaging are currently under clinical evaluation.

Reconstruction

Reconstruction of coincidence data is time consuming. Since the images are relatively noisy best results are achicved with maximum likelihood iterative methods. With state-of-the-art computers, results can be obtained within 5 minutes after completion of data acquisition. However, reconstruction time can reach about 30-60 minutes when less powerful computers have to be utilised.

Conclusions

Based on the recent successful development of the industry it can be expected, that within the next 2-3 years validated attenuation correction will be part of clinical practice in nuclear medicine. As a next step, 1-2 years thereafter, leading edge cameras will allow to perform scatter and collimator response correction and, thus, open the way to quantitative SPECT.

Considering 511 keV imaging, clinical questions still have to be defined in which PET imaging can be replaced by low cost coincidence gamma cameras without significant loss of information. The results of ongoing investigations are, however, still uncertain.

The most important task today is a careful validation of these new methods. In particular, validation should be performed for each type of devices as well as for each type of software algorithm. Carefully designed multicenter studies should be started in order to facilitate the acceptance of these new technologies.

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