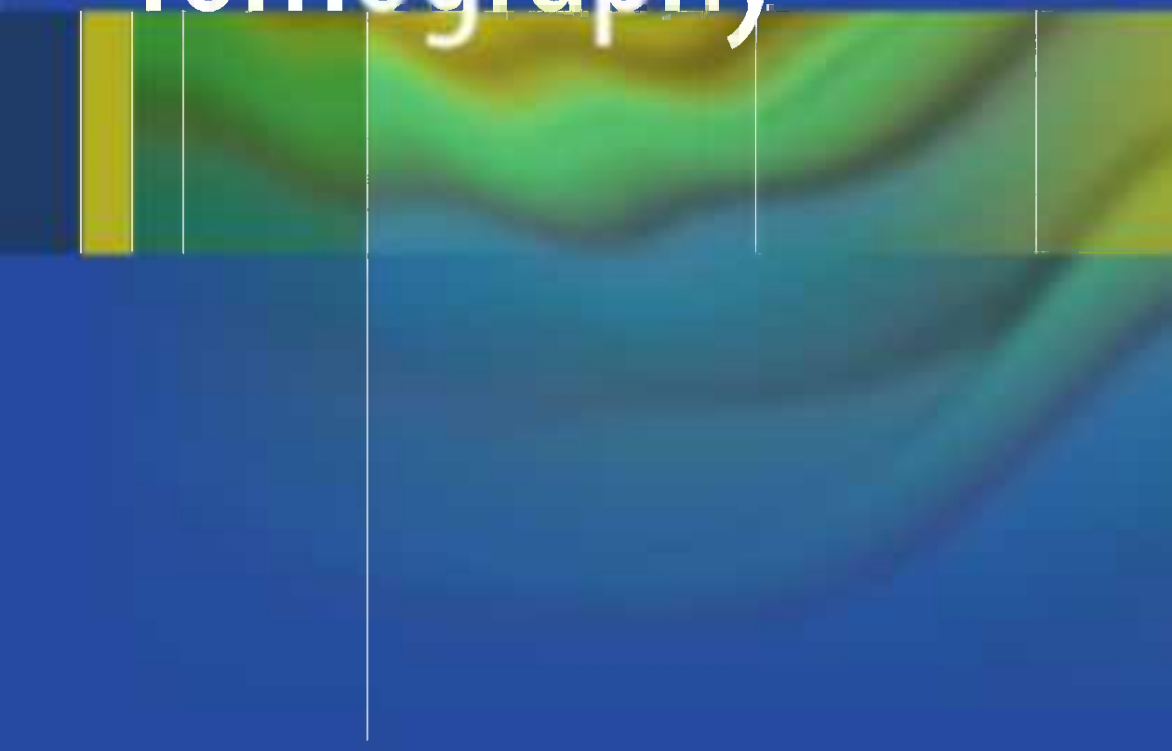
Anatoliy Granov · Leonid Tiutin
Thomas Schwarz *Editors*

Positron Emission Tomography



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Preface

Recent years have witnessed continuing increases in the incidence of malignant neoplasms, cardiovascular disease, and neurological disorders in most developed countries. At the same time, in spite of significant progress in the development of various medical technologies, there has been substantial growth in cases with an unfavorable outcome (death or disability).

It is well known that the efficient treatment of different diseases depends to a great extent on timely and precise diagnosis, and this is still especially true with regard to the most widespread, severe, and socially significant diseases. Nevertheless, many cancer patients are not diagnosed until they have advanced disease (T3 or T4). Similarly, serious difficulties are often encountered when evaluating the initial symptoms of ischemic heart disease and some neurological disorders. One solution to delayed diagnosis is offered by nuclear medicine in the form of positron emission tomography (PET), which permits precise evaluation of perfusion and metabolism in various organs and tissues and enables opportune identification of the functional disturbances underlying disease development.

PET is an imaging technique that has the distinguishing feature of employing ultra-short-lived (USL) positron-emitting radionuclides for diagnostic purposes. When positrons encounter electrons close to atoms, they both annihilate, producing a pair of gamma photons that travel from the annihilation point in strictly opposite directions and are then registered by detectors situated around the patient. PET with USL radionuclides permits the study of rapid physiological processes (like perfusion and metabolism) at the cellular and molecular level. This ability is fostered by the fact that the widely used positron-emitting radionuclides (carbon-11, nitrogen-13, oxygen-15) are components of numerous biogenic substrata that actively participate in metabolic processes. In principle it is feasible to use a variety of important biological compounds as radiotracers and to synthesize radiopharmaceutical preparations with properties necessary for clinical use.

The foundations of PET were laid in the 1970s by American scientists such as M.M. Ter-Podossian. Development of the method for use in clinical practice was slow and difficult owing primarily to technical problems. The first commercial tomographs appeared only in the late 1970s. They had a restricted number of detectors, they gathered information very slowly, and they had a low resolution.

Distinct visualization of anatomic structures was impossible with these early tomographs. However, in spite of their numerous flaws, the method immediately attracted

close attention from a broad circle of specialists in clinical medicine, including oncologists, cardiologists, neurologists, and surgeons. The very first results of research showed the unique potential of PET to study non-invasively the physiological and biochemical processes taking place in both a healthy and a diseased organism. Initially it was supposed that cardiology would become the main area of application of PET. Today, however, the method is most commonly applied in oncological practice, followed by cardiology and neurology. As the technique was improved and novel radiopharmaceuticals were developed, new and important data were obtained on the changes in cellular metabolism that accompany transformation of a healthy cell into a cancerous one, on the biological characteristics of tumoral involvement in different kinds of cancer, and on the reactions of tumor cells to treatment. Furthermore, research conducted in the USA, Japan, Western Europe, and Australia showed that the wide introduction of PET into clinical practice would have not only a revolutionary impact on the diagnostic process but also an economic benefit. In particular, it was noted that, in the mentioned countries, investment of $1 in the development of national nuclear medicine would permit $1.5–2.5 to be saved in other branches of public health. This is because PET improves diagnosis, permitting disease detection at an earlier stage and timely instigation of appropriate treatment; as a result, it allows the costs of required medicines to be significantly reduced, shortens the duration of in-patient and out-patient treatment, improves prognosis, and reduces disability and mortality in many oncological, cardiovascular, and other diseases.

The above-mentioned advantages of PET, confirmed by the wide clinical experience gathered at the world's leading PET centers, have led to the further rapid development of the technique in recent years. Accordingly, while in 2001 there were 140 PET centers worldwide, performing 255,000 examinations, by 2004 the number of PET centers had risen to 1,500, with 2.5 million examinations. Within the space of 4 years, the number of PET centers in the USA grew sixfold, to exceed 1,000, and the target for 2010 was a further increase to 6,000. Similar rates of development of PET are being observed in most Asian and European countries. In Russia there are currently only six PET centers (three in Moscow and three in Saint Petersburg), some of which function as independent diagnostic surgeries. This time lag in introducing PET in some countries obviously needs to be overcome.

The present handbook provides a systematic account of the physical and technical basis of PET, discusses the organizational principles and methods of examination, and above all examines the clinical use of PET for diagnosis, evaluation of treatment outcome, and detection of disease relapse in various organs and systems. The world's scientific literature has been analyzed and the book also summarizes the authors' 12 years of experience in examining oncological, cardiological, and neurological patients at the PET center of the Russian Research Center for Radiology and Surgical Technologies. The authors hope that their efforts will be of value for specialists starting to master this diagnostic method, for physicians working in one of the branches where PET is applied (oncology, cardiology, neurology, etc.), and for the broad circle of specialists who have recourse to PET in order to solve particular clinical tasks.

Any critical remarks will be accepted with gratitude and taken into account in further editions.

Contents

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List of Abbreviations

^{11}C-MET	^{11}C-Methionine
^{11}C-PIB	[^{11}C]2-(4′-methylaminophenyl)-6-hydroxy-benzothiazol
^{11}C-PMP	^{11}Ñ-Methylpiperidine-4-yl propionate
^{11}C-SB	^{11}C-Sodium butyrate
^{123}I-IMT	Tyrosine 1-3-^{123}I-methyltyrosine
^{18}FDDNP	2-(1-{6-[(2-[^{18}F]Fluoroethyl)(methyl)amino]-2-naphthyl} ethylidene)malonitrile
^{18}F-FDG	^{18}F-Fluoro-desoxyglucose
^{18}F-FDOPA	3,4-dihydroxy-6-18F-Fluoro-L-phenylalanine
^{18}F-FLT	^{18}F-Fluorethyletimidine
^{18}F-FLT	^{18}F-Fluorothimidine
^{18}F-FMISO	^{18}F-Fluoromisonidazole
^{18}F-FTHA	14(R,S)-[18F]-Fluor-6-thia-heptadecan acid
^{18}FMPPF	[^{18}F]Fluorobenzamido]ethyl]piperazine
3D SSP	3-Dimensional stereotactic surface projection
5HT-receptors	5-Hydroxytryptamine receptors
^{68}Ga-DOTATOC	[^{68}GA]-DOTA-D-Phe1-tyr3-octreotide
AA	Amino acids
AA	Anaplastic astrocytoma
AAD	Aromatic amino acid decarboxylase
ACD	Acute cerebrovascular disease
ACE	Acetylcholinesterase
Acetyl-CoA	Acetyl-coenzyme A
AD	Alzheimer's disease
AFP	σ-Fetoprotein
AIDS	Acquired immunodeficiency syndrome
ARVD	Arrhythmogenic right ventricular dysplasia
ATP	Adenosine triphosphoric acid
AVM	Arteriovenous malformation
BA	Benign astrocytomas
BAT	Bronchioloalveolar tumor
BBB	Blood–brain barrier
BC	Breast cancer
BCC	Bronchioloalveolar cell carcinoma

BDR	Benzodiazepine receptors
BGO	Bismuth germanate oxide
BM	Benign meningiomas
CBF	Cerebral blood flow
CBV	Cerebral blood volume
CC	Compact cyclotron
CEA	Carcinoembryonic antigen
CFA	Coenzyme fatty acid
CG	Continued growth
CG	Chorionic gonadotropin
CHD	Coronary heart disease
CHD	Coronary heart disease
CIT-FP	[^{123}I]-2α-Carbometoxy-3α-(4-iodophenyl)-*N*-(3-fluoropropyl) nortopane
CLBBB	Complete left bundle branch block
CM	Cancer metastases
CNS	Central nervous system
CPP	Cerebral perfusion pressure
CPP	Chronic pseudotumoral pancreatitis
CRC	Colorectal cancer
CT	Computed tomography
CT	Computer tomography
CVA	Cerebrovascular accident
CVD	Cerebrovascular disease
DCIS	Intraductal carcinoma in situ
DCMP	Dilatation cardiomyopathy
DCMRI	Dynamic contrast magnetic resonance imaging
DICOM	Digital imaging and communications in medicine
DLB	Dementia with Levy's bodies
DNA	Deoxyribonucleic acid
DOPA	Dihydroxyphenylalanine
DTBZ	(+)-σ-[^{11}C] Dihydrotetrabenazine
DWBS	Diagnostic radioiodine (^{131}I) whole-body scans
EC	Esophageal cancer
ECG	Electrocardiography
EEG	Electroencephalography
EF	Epileptic focus
ESR	Erythrocyte sedimentation rate
FA	Fatty acids
FABPpm	Fat acid binding protein of the plasma membrane
FADN	Flavine adenine dinucleotide
FAM	Fibroadenomatosis
FAT	Fatty acid translocase
FATP	Fatty acid transporting protein
FBP	Filtered back-projection

FDG	2-18F-deoxy-D-glucose
FFA	Free fatty acids
FLE	Fiducial localization error
FLE	Frontal lobe epilepsy
fMRI	Functional magnetic resonance imaging
FNH	Focal nodular hyperplasia
FRE	Fiducial registration error
GABA	γ-Aminobutyric acid
GB	Glioblastoma
Gd-DTPA	Gadoliniumdiethylenetriaminepentaacetic acid
GE	General Electric
GIT	Gastrointestinal tract
GLUT	Glucose transporter
GMP	Good manufacturing practice
GMP	Good medical practice
GMR	Glucose metabolism rate
Gr	Grade
GSO	Gadolinium oxyorthosilicate
HBA	Human brain atlas
HC	Huntington's chorea
HCC	Hepatocellular carcinoma
HCG	Human chorionic gonadotropin
HCM	Hypertrophic cardiomyopathy
HCMP	Hypertrophic cardiomyopathy
HD	Hodgkin disease
HD	Huntington's disease
HIV	Human immunodeficiency virus
HMPAO	d,1-Hexamethylpropyleneaminoxime
HNC	Head and neck cancer
HPLC	High performance liquid chromatography
keV	Kiloelectron-volt
LAT	Large amino acid transporter
LC	Lung cancer
LCIS	Lobular carcinoma in situ
LDH	Lactate dehydrogenase
LSO	Lutetium oxyorthosilicate
LVMH	Left-ventricular myocardial hypertrophy
LYSO	Lutetium-yttrium oxyorthosilicate
MALT	Mucosa-associated lymphatic tissue
MAO	Monoamine oxidase
MBF	Myocardial blood flow
MBq	Megabecquerel
MDCT	Multi-detector computed tomography
MFAU	Myocardial fatty acid utilization
MG	X-ray mammography

MGC 20	in Russian – Compact Cyclotron 20
ML	Malignant lymphoma
MLE	Maximum likelihood estimation
MMSE	Mini-Mental State Examination
MnDPDP	Manganese dipyridoxal diphosphate
MRCPG	Magnetic resonance cholangiopancreatography
MRI	Magnetic resonance imaging
MSA	Multisystem atrophy
MSCT	Multislice spiral computed tomography
mSV	Millisievert
MTC	Medullary thyroid cancer
NADN	Nicotinamide adenine dinucleotide
NIIEFA	Scientific Research Institute of Electrophysical Apparatus. DV Ephraim
NINCDS	The National Institute of Neurological Disorders and Stroke
OCD	Obsessive–compulsive disorder
OEF	Oxygen excretion fraction
OML	Orbitomeatal line
OMR	Oxygen metabolism rate
OSE	Optimization-space exploration
Palmitoyl-CoA	Palmitoyl-coenzyme A
PAS	Periodic Acid-Schiff
PBT	Primary bone tumors
PC	Prostate cancer
PCHN	Planocellular cancer of the head and neck
PD	Parkinson's disease
PET	Positron emission tomography
PI3K	Phosphatidyl-inositol-3-kinase
PNP	Progressive supranuclear palsy
PSA	Prostata-specific antigen
PTSM	Pyruvaldehyde-bis-4-*N*-methylthiosemicarbazone
RAMLA	Row action maximum likelihood algorithm
Rb	Rubidium
RCA	Right coronary artery
ROI	Region of interest
RP	Radiopharmaceutical(s)
RSCRST	The Russian Scientific Center of Radiology and Modern Surgery Technologies
RT	Radiotherapy
SAH	Subarachnoid hemorrhage
SC	Stomach cancer
SLM	Solitary lung masses
SLR	Short-lived radionuclides
SOP	Standard operating procedure
SPECT	Single photon emission computed tomography

SPM	Statistical parametric mapping
STT	Soft tissue tumors
SUV	Standard uptake value
SVT	Whole body scintigraphy
T/NT ratio	Tumor to nontumor ratio
T1-WI	T1-weighted image
T2-WI	T2-weighted image
TG	Thyroglobulin
TH	Thyroid cancer
THF	Tetrahydrofuran
TL	Temporal lobe
TLE	Temporal lobe epilepsy
TRE	Target registration error
TRUS	Transrectal ultrasound
TS	Tourette's syndrome
TSH	Thyroid stimulating hormone
US	Ultrasound
USLR	Ultra-short-lived radionuclides
VHL	von Hippel–Lindau tumor suppressor
WBS	Whole-body scintigraphy
WDTC	Well-differentiated thyroid cancer (carcinoma)
WHO	World Health Organization

Part I

Background

The Physical Basis of Positron Emission Tomography

1

1.1 Characteristics of Positron Emission

The method of positron emission tomography (PET) is based on the phenomenon of spontaneous *positron emission* by the nuclei of some unstable ultra-short-lived radionuclides (USLRs), in which the number of protons exceeds that of neutrons. The positron annihilates with an electron, releasing two gamma-photons having the same amount of energy (511 keV) and moving in opposite directions at almost 180° apart (close to collinearly) (Kukekov and Fadeev 1986). Annihilation does not take place in the orbit of its own atom since the positron must first lose its kinetic energy. The length of the flight of the positron from the emission point to the annihilation point depends on its own energy and on the density of the environment. It can fluctuate within a wide range. For example, in the muscle it varies from 1 to 8 mm. This is one of the reasons why PET has a smaller resolving capacity than some other radiodiagnostical methods (MRI, CT). Probably in modern positron emission scanners in which space resolution is 1–6 mm (FWNM), the physical limit of the method's resolving capacity has been reached (Phelps 2004; Gevorski and Plotkin 2006).

1.2 Principles of Detection of Positron Decay

The main components of a PET scanner are: gantry, movable support (bed) to position a patient in the ring, computer stations to collect and store raw data (the so called sinograms), as well as to reconstruct, process and store images and to obtain hard copies. An important component of the detector ring is the detector block, composed of several crystals connected with a group of photomultipliers in one case. The physical characteristics of the scanner depend to a great extent on the size, form and properties of the materials composing the crystals in the detector block as well as on the diameter of the detector ring.

The interaction between the gamma-photon and the crystal induces scintillation of the latter. As a reaction to scintillation, an electric pulse occurs in the

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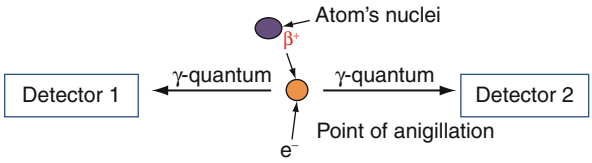

Fig. 1.1 Scheme of positron decay detection

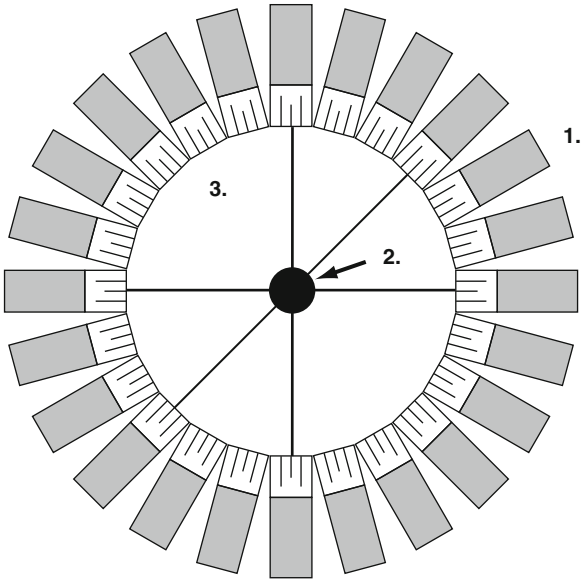

Fig. 1.2 Mechanism of positron (two-photon) emission. Note: *1* the ring of detector-blocks, *2* radiation source, *3* lines going through the radiation source and connecting pairs of detector-blocks

photomultiplier, which can be detected and processed by a computer complex (Gevorski and Plotkin 2006; Khmelev et al. 2004).

In the detector ring of the PET scanner, pairs of highly sensitive detectors, housed in rings, work for coincidence. If a pair of detectors located opposite each other detect two gamma photons within the range of coincidence, we can state that the annihilation point is on the line that unites them (coincidence line) (Fig. 1.1). Annihilation need not necessarily occur exactly in the middle between the detectors. That is why the so called "coincidence window" is used for PET, admitting a temporary deflection of the detection of radiation by pairs of detectors from 4.2 to 12 ns. The event is detected and recorded in the form of polar coordinates (the angle and the radius) in a sinogram. A sinogram is a curve representing the number of recorded events for every coincidence line. The location of every crystal has a space representation in the electronic matrix of the computer which sets the space coordinates of the radiation point. The detection of several lines going through a given annihilation point permits to precisely determine its coordinates (Fig. 1.2). The number of pulses obtained in a given crystal depends on the physical properties of the radioactive

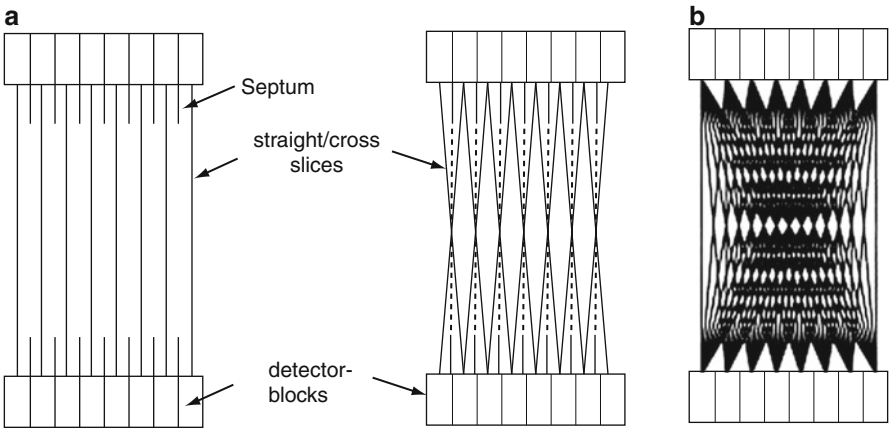

Fig. 1.3 (**a**) Two-dimensional scanning mode. (**b**) Three-dimensional scanning mode

source and reflects its qualitative characteristics. The sinogram is processed (reconstructed) by the computer in order to determine the distribution of radioactivity in the slice and to visualize the examined object (Khmelev et al. 2004; Phelps 2004).

Besides genuine coincidences, scattered and random coincidences resulting from different annihilations are detected. Scattered coincidences are related to the Compton effect, according to which they change their movement directions. To separate genuine radiation from scattered and random photons with lower energy, an energy window is used with a center of 511 keV (Khmelev et al. 2004; Phelps 2004; Gevorski and Plotkin 2006).

The above-mentioned characteristics of PET permit a genuine signal to be singled out and detected, satisfying energy and time demands. The indicated way of detecting the signal realized in positron tomographs was called "electronic collimation". Electronic collimation has replaced the use of physical collimators. Consequently, the sensitivity of PET became higher by a factor of a hundred or thousand compared with single photon emission computer tomography and correct measurements of fast biochemical processes on tomographic slices of any organ or tissue became possible (Khmelev et al. 2004; Gevorski and Plotkin 2006).

To process a signal, some (although not much) time is required during which the detector is not able to detect new events – the so-called "*dead time*". The degree of signal loss due to the dead time depends on the speed of the scanner and on the value of radioactivity in the field of view of the tomograph. Contemporary PET scanners are able to maintain a wide range of computing rates without significant losses in resolving capacity (Phelps 2004; Gevorski and Plotkin 2006).

To reduce the number of scattered and random coincidences in PET scanners, limiting screens of lead or tungsten (*septa*) are used. The radiation detection process using a septum is called a two-dimensional (2D) regime; without a septum it is called a three-dimensional (3D) regime (Fig. 1.3). Using a 2D mode permits images with a low-level noise and the highest resolving capacity to be obtained. However, in this

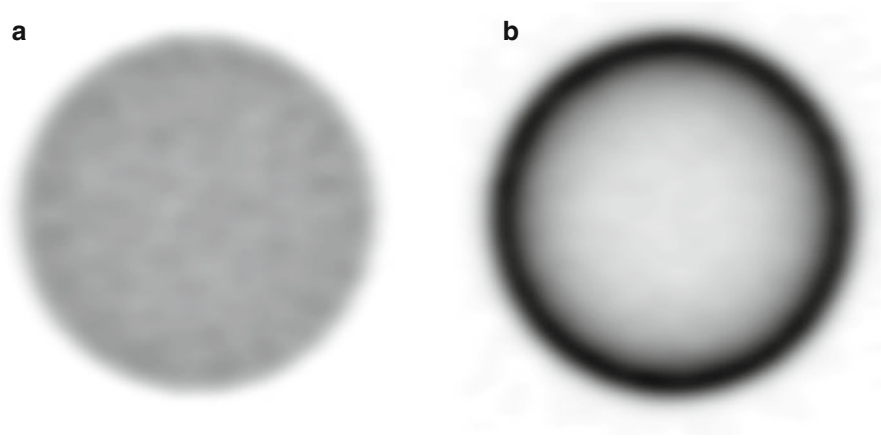

Fig. 1.4 Attenuation correction. (**a**) Image of the homogeneous ^{68}Ge phantom performed with attenuation correction. (**b**) The same image performed without attenuation correction

case the sensitivity of the tomograph (i.e., the relation of the number of annihilation acts detected in the field of view of the tomograph with regard to their genuine number in the field of vision) decreases several times; scanner sensitivity being defined by the properties of detector blocks, the diameter of the detector ring, the mode of data acquisition (2D or 3D) and the duration of scanning. The maximum positron scanner sensitivity is achieved by scanning without a septum in the 3D mode (Fig. 1.3b). However, in this case the noise level grows twice and dead time losses increase. The 2D mode, compared with 3D mode, permits a greater accuracy in quantitative analysis and treatment efficiency control to be attained. So, the choice of the scanning mode is conditioned by a particular clinical task. Presently, hybrid PET-CT scanners are produced where there is no septum and only the 3D mode is used.

In PET scanners, photon absorption correction is provided – that is correction for the irregularity of absorption of ionizing radiation by tissues (*attenuation correction*) from radioactive transmission sources of ^{68}Ge and ^{137}Cs (Ruhlmann et al. 1999; Phelps 2004; Gevorski and Plotkin 2006). This attenuation correction is necessary to compensate for radiation distortion and to attain a higher accuracy of reproducing the distribution of the radionuclide label in tissues. In contemporary tomographs, transmission sources are built into the detector ring. The control is remote, which ensures security and lessens exposure to radiation of the personnel. For example, in Fig. 1.4 we show images of a homogeneous photon of ^{68}Ge with attenuation and without it. The picture shows that the accurate reproduction of radioactive label distribution in a tomographic slice is impossible without absorption irregularity correction. The correction of the irregularity of radiation absorption by tissues is also a necessary component of the quantitative analysis of PET images. In PET-CT combined scanners, digital data are used for this purpose, which are obtained by means of CT. The efficient beam energy of X-rays in CT is 70–80 keV. Consequently, PET images corrected with help of CT attenuation correction differ from images obtained by

using radioactive sources with an energy of 511 keV. For the same reason, PET-CT data processing results in non-linear attenuation coefficients which induce a distortion of the genuine distribution and leads, to overstating radiation accumulation in dense tissues, particularly in the bones. As a result, quantitative measurements of the same formations and tissues done by means of PET and PET-CT scanners can differ by 1.5–2 times (Khmelev et al. 2004; Gevorski and Plotkin 2006). Using contrast agents in CT brings about additional distortions and results in the appearance of artifacts on PET-images, significantly overstating the real radioactivity value in the focus of accumulation of the contrast agent (Gevorski and Plotkin 2006).

In first-generation PET scanners, some part of the equipment was situated outside the tomograph due to its large size and required separate rooms. There were problems concerning speed, screening, and conditioning. The improvement of hardware and video technique and the appearance of personal computers permitted to significantly lessen the size of the main components of PET scanners and to optimize their construction. As a result, the most important parts of modern scanners are located directly in the detector ring. Owing to this circumstance, tomographs became more compact; their speed increased and so did their stability, protection and reliability.

1.3 Reconstruction of Images, Data Processing and Analysis

The initial raw PET data concerning the examined object are collected in the computer in the form of sinograms. The reconstruction procedure permits an image based on sinograms to be obtained. Reconstruction can be performed in several ways. The choice of the particular way of reconstruction depends on the task and on the examined organ. For image reconstructions of such organs as brain or heart, the method of filtered back-projection (FBP or iterative method) is usually used. The iterative method has several modifications, such as MLE, OSE, and RAMLA. In case of whole-body examination, the iterative reconstruction algorithm OSEM is most frequently used, since it ensures the optimal quality of the image owing to smoothing. When brain and heart are examined, it is preferred to use simpler filters which distort least the genuine distribution of radiopharmaceuticals (RPs) in the slices. However, it should be noted that insufficient smoothing, especially when combined with low statistics can increase image heterogeneity, which provides more difficulty in interpreting the results. Too much smoothing can reduce resolution and finally bring about a loss of informativity of the image. Most scanner manufacturers recommend using factory protocols and reconstruction installations, as most are elaborate. A number of reports contain detailed descriptions of the image reconstruction principles and other physical characteristics of the PET method (Khmelev et al. 2004; Phelps 2004; Gevorski and Plotkin 2006).

The course of further image processing (postprocessing) and the obtention of the hard copies of images depend on the particular clinical task. At the first stage, PET-image processing includes their visual analysis in three projections (axial, sagittal and coronal projections). In the case of the whole-body examination, 3D image analysis

is applied, which provides a more accurate idea of the localization and anatomical links of the examined area. The image standardization procedure is described separately for each organ in the corresponding chapters of the present book.

A necessary condition of a successful analysis is the precise knowledge of the normal distribution and pharmacokinetics of the RPs which are used. The notion of the physiologic (normal) distribution is specific for each RP and depends on its properties. Therefore the presentation of the results obtained comprises both the visualization of the state of the unaffected organs examined or of the whole body and the characteristics of the lesion area, including its localization, scintigraphic size, and regularity of RP distribution, contour accuracy and its relation to unaffected tissues. These tasks are solved as a rule by using image contrast range, colour scales and threshold level. The absence of anatomic reference points in the functional images provides certain problems concerning the interpretation of scintigraphic images. This is why in a number of cases accurate matching or fusion of images with different modalities is needed. Matching of functional PET images and the data of structural imaging (CT, MRI) is first of all required for an accurate anatomic localization of the revealed changes; it is also needed in the presence of significant physiological (individual) fluctuations of the levels of RP uptake in tissues. Besides, superimposing is necessary when the formation's size is small and close to the resolving capacity of the tomograph and also when the formation has a high structural heterogeneity.

At the second stage, quantitative or semiquantitative PET-image analysis in absolute and relative values are applied. For semiquantitative analysis of the objects examined in whole-body examination, and since recently also in brain examination, a dimensionless value is used – the so-called standardized uptake value (SUV). SUV is defined as the relation of specific radioactivity in the measured zone (kBq/cm^3) to the value of the introduced radioactivity per body mass MBq/kg. SUV is automatically calculated by the software of the scanner, taking into account the physical half-life period of the radionuclide. In image analysis using SUV, it should be noted that imprecise information on the patient's weight and stature, the value of the introduced radioactivity and the time of its introduction as well as on the detector drift can induce serious errors. This is why it is accepted to consider as significant an SUV change during treatment which is more than 25% of the initial value.

Tumor/nontumor (T/NT) ratio is used to express the relation of radioactivity accumulated in the affected area to radioactivity in unaffected tissues (referent zones). In some cases it is appropriate to apply mathematical models implying dynamic scanning of the examined organ to calculate the "input function" – a curve of activity-time in arterial blood. To measure blood radioactivity, it is most convenient to scan the left ventricular cavity. Mathematical models are widely used in heart examinations: on the one hand, the high variability of metabolic processes in this organ limits the possibility of using simple quantitative analysis methods; on the other hand, the presence of the left ventricular cavity in the field of view of the tomograph makes it simpler to obtain the inline function.

1.4 Pet Data Quality Control

PET data quality control methods are divided into acceptance trials, regular control and parameter change of the tomograph during its exploitation. Acceptance trials are done during the installation of the equipment. In the process of trials, initial data on the operation factors of the scanner are obtained, which then serve as a model in daily or recurrent technical state control. Modern scanners are provided with reliable and easy-to-use means of control and image quality correction as well as of quantitative data reproducibility: normalization, cross-calibration and other procedures. During daily control, the deviation of the readings of detectors from the mean is automatically calculated, which permits evaluation of their state, revealing deviations from the admissible parameters and identifying and localizing faults. Normalization is carried out if the admissible deviation of the sensitivity of the opposite pairs of detectors is exceeded by more than 2.5%. For this purpose, a standard calibration phantom with determined specific radioactivity is brought into the field of view of the scanner. During normalization, the so-called "blank scan" is created which is necessary to align as much as possible the field of view of the scanner during image reconstruction. During normalization, the calibration factor (ECF) is also calculated, which is an integrated factor reflecting detector drift, physical decay of calibration sources and some other parameters having impact on the precision of the measurement. The value of ECF is specific for a given model of tomograph and depends on its construction. This factor is used also as a criterion of quantitative data reproducibility. For example, an ECF value deviation of more than 5% from its previous value requires aligning the field of vision of each of the detector blocks (set up). Homogenous calibration phantoms are fabricated using positron-emitting radionuclides (^{68}Ge, ^{137}Cs) with a half-life of 1–10 years. Radionuclides should be evenly distributed in the phantom. Measurement of a radionuclide is possible only before its introduction into the phantom and is carried out by means of a curiemeter. RPs are injected to the patient in the form of aqueous solutions; their radioactivity measurement is done in a given PET center. For matching of factory ^{68}Ge phantom and a water phantom of known specific activity prepared in the PET center when changing calibration sources recalibration is performed. The accuracy of recalibrating the sources has an impact on the calibration factor (ECF) and on the outcome of the quantitative analysis in a given scanner (Khmelev et al. 2004; Phelps 2004; Townsend et al. 2004; Gevorski and Plotkin 2006).

Consequently, the available hardware arsenal ensures reliable PET data image and reproducibility quality control, which is crucial for clinical application of the method.

There can be hardware, software, control, biological and mixed *artifacts*. As a rule, hardware malfunctions are revealed during the daily checkup, which enables details of the damage to be determined. Sinogram analysis is also used for this purpose. The most frequent cause of hardware malfunctions is due to analog processors or bucket controllers getting out of order. When an analog processor gets out of

order a stripe appears on the sinogram which corresponds exactly to the damaged processor. If a controller is damaged, the stripe is wider and it embraces all the processors of the controller. Damage to the detector block is revealed during daily calibration. The damaged block is identified by scanning according to a special program or by a "set-up" procedure. Identifying program or mixed errors is a more difficult problem. For example, the procedure of pulling out radioactive calibration sources from containers is carried out by applying a special programme. An error in its working makes the radioactive sources stop. This can look like a breakdown of the mechanism making them move out.

The operator's errors (entering wrong information on the patient or on the introduced radioactivity) can be corrected by introducing the necessary amendments into the sinogram header with its subsequent repeated reconstruction. At the same time, errors in the data collection protocol or in positioning patients cannot be corrected retrospectively.

The causes of artifacts may also be due to injection errors, whereby some part or all of the RP is left in the injection spot, the radioactive substance flowing out from the vein together with blood and onto a soiled dressing; they may also be due to contamination with radioactive urine. When a radioactive substance gets to the patient's arms and clothes it can be also transferred to the scanner; for example, to the patient bed of the tomograph. In this situation, one or several superficially located uptake foci appear on the image which can induce false-positive diagnostics of some diseases, for example in melanoma. Contamination detection always provides some difficulty. This is why an important way of dealing with artifacts is observing the methodology and having an accurate idea on the possibility and place of their appearance. In case of a suspicion of a contamination artifact, one can try to wash the radioactive substance off the skin surface, take off the contaminated clothes, change linen on the tomograph and wipe its surface. Another cause of artifacts is the patient's displacement during scanning or moving organs (e.g., heart or lung excursion), which bring about a fuzzy image.

1.5 Modern Positron Emission Scanners and Hybrid PET/CT Scanners

Intensive work on developing and modifying PET scanners carried out in the 1980s resulted by the early 1990s in creating the generally accepted multiring scheme using highly sensitive detectors on the basis of crystals of bismuth germinate oxide (BGO). For example, in 1984 large-scale production of PET scanners of the ECAT series was started in the USA (CTI) and Germany (Siemens), which were widely used in the world in several modifications. At present, the main positron emission scanner manufacturers are Siemens, GE, (USA) and Philips (The Netherlands). The successive development of PET technology resulted in creating in 2000 a micro-PET system and then a micro-PET-CT system which have a high resolution (~1 mm) and are needed for laboratory research.