Practical Nuclear Medicine 2nd ed

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Practical Nuclear Medicine

Second Edition

Preface to the second edition

Since the first edition of this book was published, the face of medical diagnostic imaging has continued to develop. MRI continues to find new applications, most notably, so far as nuclear medicine is concerned, in the development of functional imaging. The application of X-rays has also moved forward, with the continued development of digital systems, once the prerogative of nuclear medicine, and spiral CT.

Nuclear medicine itself has also moved forward. No self-respecting nuclear medicine department will now wish to be seen without a dual-headed camera and even triple-headed cameras are to be found in some departments. The dual headed camera offers real advantages for bone imaging and SPECT. Analogue position circuitry in gamma cameras, which has changed little since Anger's day, is now being supplanted by fully digital approaches, offering the advantage of greater reliability and the ability to handle higher count-rates. The holy grail of accurate quantitation from SPECT has been brought closer with the introduction of transmission imaging. In the field of radiopharmaceuticals ^{99m}Tc labelled myocardial perfusion agents are well established; one of them, MIBI, has been used in other areas such as parathyroid imaging. ^{99m}Tc HMPAO is now widely used, not only for brain blood flow imaging but also for white cell labelling in order to image infection. Nuclear medicine's role in oncology is increasing, for example in the application of ^{123}I MIBG and ^{111}In Octreotide.

The success of the first edition has shown that there was a need for the practical manual format of the book and this has been maintained in the second edition. Nothing is perfect, however, and changes have been introduced. The techniques of nuclear medicine are wider than imaging. A chapter has now been included specifically dealing with non-imaging. Recently one of the areas being strongly promoted by manufacturers has been the potential use of dual-headed cameras for positron emission tomography (PET). In conjunction with central radionuclide production facilities this offers the opportunity for a wider clinical use of the longer-lived PET radiopharmaceuticals, in particular ^{18}F fluorodeoxyglucose. A chapter on PET imaging has therefore been introduced.

A surprisingly large number of the original authors have been prepared to revise their contributions; to them we are, once again, very grateful. We would also like to warmly thank the new contributors. Link Medical and Amersham International kindly provided financial help towards the cost of the colour plates. Once again we would like to acknowledge the support of our colleagues and of our long-suffering families.

Aberdeen
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Abbreviations

ACD	acid citrate dextrose
ACTH	adrenocorticotrophic hormone
ADC	analogue-to-digital converter
AFTN	autonomously functioning nodules
ALRA	as low as reasonably achievable
ALI	annual limits on intake
ARDS	adult respiratory distress syndrome
AVM	arterio-venous malformation
BBB	blood brain barrier
BGO	bisthmus germanate
CAD	coronary artery disease
CCK	cholecystokinin
CEA	Carcinoembryonic antigen
CFOV	central field of view
CGP	circulating granulocyte pool
CoR	centre of rotation
CoV	coefficient of variation
CPU	central processing unit
CRH	corticotropin releasing hormone
CSF	cerebrospinal fluid
CT	computed tomography
DMSA	2,3-dimercaptosuccinic acid
DSA	digital subtraction angiography
DTPA	diethylene triamine pentaacetic acid
DVT	deep vein thrombosis
EDE	effective dose equivalent
EPA	Environmental Protection Agency
ERPF	effective renal plasma flow
FDG	^{18}F-fluorodeoxyglucose
FoV	field of view
FWHM	full width at half maximum
FWTM	full width at tenth maximum
GFOV	geometrical field of view
GFR	glomerular filtration rate
GI	gastrointestinal
GMP	The Guide to Good Pharmaceutical Manufacturing Practice
HIDA	hepatic iminodiacetic acid
HIG	Human polyclonal immunoglobin
HIPDM	N-trimethyl-N-(2-hydroxyl-3-methyl-5-iodobenzyl)-1,3-propanediamine
HM-PAO	hexamethylpropyleneamine oxime
HPLC	high performance liquid chromatography
HSA	human serum albumin
IBD	inflammatory bowel disease
IMP	N-isopropyl-[^{123}I]-p-iodoamphetamine

ITLC	instant thin layer chromatography
IVC	inferior vena cava
IVU	intravenous urography
LAL	Limulus Amoebocyte Lysate
LDL	low density lipoprotein
LET	linear energy transfer
LLD	lower level energy discriminator
LOR	line of response
LSF	line spread function
LSO	lutetium oxyorthosilicate
MAA	human albumin macroaggregates
MAB	monoclonal antibodies
MAG3	benzoylmercaptoacetyltriglycerine
MCA	multichannel analyser
MDP	methylene diphosphonate
MGP	marginating granulocyte pool
MIBG	^{123}I labelled meta-iodo-benzyl guanidine
MIBI	2-methoxy-isobutyl-isonitrile
MIRD	Medical Internal Radiation Dose Committee
MRI	magnetic resonance imaging
MTF	modulation transfer function
MTT	mean transit time
MUGA	multiple gated acquisition
NEC	noise equivalent counts
NP-59	^{131}I-6β-iodomethyl-19-norcholesterol
OIH	orthoiodohippurate
PCP	pneumocystis carinii pneumonia
PE	pulmonary embolism
PET	positron emission tomography
PHA	pulse height analyser
PMT	photomultiplier tube
PPP	platelet-poor-plasma
PRP	platelet-rich-plasma
PTH	parathyroid hormone
PUO	pyrexia of unknown origin
PV	plasma volume
QA	quality assurance
RAIU	radioiodine thyroid uptake
RAM	random access memory
RBC	red blood cells
RBE	relative biological effectiveness
rCBF	regional cerebral bloodflow
RCP	radiochemical purity
RCV	red cell volume
ROI	region of interest
ROM	read only memory
RPA	radiation protection adviser
SD	standard deviation
SDAT	senile dementia of the Alzheimer type
SeHCAT	^{75}Se-labelled tauroselcholic acid
SestaMIBI	2-methoxy-isobutyl-isonitrile
SPECT	single photon emission computed tomography
SUV	standardized uptake value
TAC	tiame activity curve
TBV	total blood volume

TLC	thin layer chromatography
TLD	thermoluminescent dosimetry
TRH	thyrotropin-releasing hormone
TSH	thyroid stimulating hormone
UTI	urinary tract infection

Contents

Chapter 1
Nuclear medicine imaging

Peter F Sharp

1.1 Introduction

In nuclear medicine clinical information is derived from observing the distribution of a pharmaceutical administered to the patient. By incorporating a radionuclide into the pharmaceutical, measurements can be made of the distribution of this radiopharmaceutical by noting the amount of radioactivity present. These measurements may be carried out either *in vivo* or *in vitro*. *In vivo* imaging is the most common type of procedure in nuclear medicine, nearly all imaging being carried out with a gamma camera (see Section 1.3). It offers the potential, unique among imaging techniques, of demonstrating function rather than simply anatomy.

Where a knowledge of the precise amount of activity present in an organ is required and an image of the distribution is not essential, collimated scintillation probe detectors aligned with the organ of interest are used [1] or, in specialized centers, the technique of positron emission tomography may be available (see Chapter 19). If the amount of radioactivity present is very low then high-sensitivity whole-body counters, consisting of heavily shielded probe detectors, are necessary [2].

In vitro measurements are made on samples of material taken from the patient, such as breath, urine, and faeces, to determine the amount of radiopharmaceutical present. Such measurements are made using gamma- or beta-sample counting techniques (see Chapter 3).

The diagnostic information is provided by the action of the pharmaceutical, and the role of the radioactivity is purely a passive one enabling the radiopharmaceutical to be localized. For this reason it is possible to use low levels of radioactivity and so the potential hazard to the patient can be kept small (see Chapter 7).

Table 1.1 Ideal characteristics of a radiopharmaceutical

Half-life should be similar to the length of the test
The radionuclide should emit gamma-rays and there should be no charged particle emissions
The energy of the gamma-rays should be between 50 and 300 keV
The radionuclide should be chemically suitable for incorporating into a pharmaceutical without altering its biological behavior
The radionuclide should be readily available at the hospital site
The pharmaceutical should localize only in the area of interest
The pharmaceutical should be eliminated from the body with a half-life similar to the duration of the examination
The radiopharmaceutical should be simple to prepare

1.2 The ideal radiopharmaceutical

The specific features looked for in the ideal radiopharmaceutical are summarized in Table 1.1. It must be emphasized, however, that no single radiopharmaceutical actually has all these properties. As the radionuclide label and the pharmaceutical perform different functions, the particular features regarded as desirable for them can largely be considered separately.

1.2.1 Radionuclides

Half-life

The half-life of the radionuclide determines how quickly the radioactivity will decay. Obviously, if the half-life is very short then the activity will have decayed to a very low level before imaging has started. On the other hand, if it is too long then the patient will remain radioactive for a considerable time, and in order to reduce the possibility of radiation damage the amount of activity

administered will have to be kept low. Roughly, the half-life should be of a similar length to that of the examination, usually a few hours.

Type and energy of emission

For imaging it is first necessary that the radiation given off should be sufficiently penetrating to allow it to be detected externally even though it may need to pass through several centimetres of tissue. This limits the choice to gamma- or X-rays. The energy of the radiation will also affect its ability to penetrate tissue: the higher the energy the better it will be. However, the higher the energy the more difficult it will be to stop the gamma-ray in the detector of the imaging device. In practice gamma-rays with energies between 50 keV and 300 keV are preferred, about 150 keV being ideal.

The radiation dose received by the patient must also be considered. It is necessary to avoid those radionuclides which have significant particulate (i.e. alpha and beta) emissions, which owing to their short range will simply increase radiation dose without contributing to the image quality. As the purpose of radioactive decay is to redress an imbalance in the ratio of protons to neutrons in the nucleus, it is clear that simple gamma-decay will be accompanied by the emission of a charged particle, usually a beta-ray. There are, however, two decay processes which avoid this problem: isomeric transition and electron capture. Particles will still be emitted, namely Auger and conversion electrons, but at a considerably lower rate than the one per gamma experienced with other modes of decay.

Pharmaceutical labelling

While the prime consideration in choosing a radionuclide is that its manner of decay should be suitable for *in vivo* imaging, it must not be forgotten that this material must be incorporated into a pharmaceutical. Unfortunately all the elements of biological interest, such as carbon, nitrogen, and oxygen, do not have radioisotopes meeting the criteria of Table 1.1. These particular elements do, however, have radioisotopes which emit positrons. These positively charged electrons annihilate with an electron to produce a pair of 511-keV gamma-rays. While the energy of these gamma-rays is such that the sensitivity of detection in the crystal of a standard gamma camera will be low, nevertheless several cameras have been adapted for positron imaging either by fitting them with a high-energy collimator or by using coincidence electronics. The most effective way of imaging positron-emitting radiopharmaceuticals is still with specialized equipment (see Chapter 19).

Despite the potential problems, pharmacists and radiochemists have been very successful in incorporating some of the most unlikely material, such as the widely used radioisotope of technetium, into a large range of pharmaceuticals. This problem will be considered in Chapter 6.

Production of radionuclides

Radionuclides can be produced from three sources: the nuclear reactor, the cyclotron, or a generator. It is not intended to go into detail about the process of production of radioactive material and the interested reader is recommended to read references [3] and [4].

The reactor radionuclides are produced either by introducing a target of stable material into the neutron flux found inside the reactor, or by separating out fission products from the fuel rods or a uranium target. As neutron irradiation increases the number of neutrons relative to the number of protons in the nucleus it will produce radionuclides which decay predominantly by beta-decay.

The cyclotron produces a beam of charged particles, such as alphas and deuterons, which can be aimed at the target. The resulting radionuclide will have an excess of charge and so will decay either by emission of a positively charged particle (a positron) or by the capture of a negative charge (electron capture). The latter, as has been mentioned earlier, is a particularly useful decay process as it has a gamma-to-beta ratio greater than unity.

Obviously in most instances radionuclides produced by these two routes will be shipped to the hospital from a central manufacturing site. This creates a problem, since short-lived radionuclides will decay significantly during transportation. Fortunately the third mode of production, the generator, provides an answer, at least for certain radionuclides. The generator will be discussed in Chapter 6 but basically it depends upon the existence of a long-lived radionuclide which decays into the required short-lived radionuclide. All that is then needed is for this long-lived parent to be supplied in the form of a generator from which the short-lived daughter can be chemically extracted when required. This generator is the source of the radionuclide most commonly used in nuclear medicine, technetium-99m, the parent material in this case being molybdenum-99.

A list of commonly used radionuclides is given in Table 1.2 together with their mode of production and characteristics of decay.

Selection of pharmaceutical

The most important feature required of the pharmaceutical is that it should be taken up rapidly and completely in the biological system of interest. In practice most radiopharmaceuticals also localize in other parts of the body, and if these are radiosensitive the amount of activity which can be administered will be limited (see Chapter