

Publications · Brochures

Principles and Practice of PET/CT

Part 1 A Technologist's Guide



Editors

Peter Hogg Head of Diagnostic Imaging Research University of Salford Salford, UK

Contributors

Suzanne Dennan Department of Diagnostic Imaging St. James Hospital, Dublin, Ireland

Thomas Kane Consultant in Radiology & Nuclear Medicine Victoria Hospital, Blackpool and Lancashire PETCT Centre, Preston, UK

Jean-Marc Vrigneaud Medical Physicist Nuclear Medicine Department Centre Georges-François Leclerc Dijon, France

Sylvianne Prevot Radiation Safety Officer Centre Georges-Francois Leclerc Dijon, France

Angela Meadows Unit Manager Preston PET/CT Centre Alliance Medical Royal Preston Hospital Lancashire Teaching Hospitals NHS Trust, UK

Ronald Boellaard

Associate Professor and Head of Physics Department of Nuclear Medicine and PET Research VU University Medical Centre Amsterdam, The Netherlands **Giorgio Testanera**

Istituto Clinico Humanitas Department of Nuclear Medicine Rozzano, Italy

Ann Heathcote Regional Manger Alliance Medical Limited Warwick, UK

Amy Wareing Senior PET CT Technologist Preston PET CT Centre Royal Preston Hospital Lancashire Teaching Hospitals, UK

Peter Julyan Clinical Scientist North Western Medical Physics The Christie NHS Foundation Trust, UK

Katy Szczepura Medical Physics Lecturer Department of Diagnostic Radiography University of Salford Greater Manchester, UK

Simona Cola Technologist of the Department of Nuclear Medicine S. Maria Nuova Hospital Reggio Emilia, Italy

Contents

-	
Foreword Suzanne Dennan	
Preface and Glossary of Terms and Abbreviations	
Peter Hogg and Giorgio Testanera	
Chapter 1: The value and limitations of PET-CT in routine clinical practice: a UK radiologist's perspective	
Thomas Kane and Peter Hogg	
Chapter 2: Practical radiation protection in PET-CT Jean-Marc Vrigneaud, Sylvianne Prévot, Angela Meadows and Peter Hogg	
Chapter 3: PET imaging instrumentation and principles of PET protocol optimisation Ronald Boellaard	
Chapter 4: CT instrumentation and principles of CT protocol optimisation Ann Heathcote, Amy Wareing and Angela Meadows	
Chapter 5: Quality assurance and quality control for PET-CT Peter Julyan	
Chapter 6: PET isotope production Katy Szczepura	
Chapter 7: Patient care in PET-CT Simona Cola and Peter Hogg	
Chapter 8: Radiographer and technologist competencies – education and training in PET-CT Peter Hogg and Angela Meadows	
Imprint 99	

Foreword Suzanne Dennan

The EANM Technologist Committee was established in 1996 to represent European nuclear medicine technologists and radiographers within the EANM. Key aims of the Technologist Committee include the promotion of high professional standards and participation in EANM education and continuing education initiatives. During the lifetime of the committee, the field of nuclear medicine has undergone considerable change, particularly with the advent of hybrid PET-CT imaging.

Since 2004, an annual "Technologists' Guide" has been produced by the EANM Technologist Committee. This successful series aims to develop expertise in key areas of nuclear medicine and to assist with the development of high standards of professional practice. The current book is dedicated to PET-CT and will be the first of a comprehensive three-part series devoted to this important topic. I am grateful for the efforts and hard work of the authors, who have ensured the educational value and quality of this guide. Special thanks are extended to the editors, Professor Peter Hogg and Mr. Giorgio Testanera, for their dedication to the success of this publication. In particular, many thanks are due to Siemens Medical for their support and generous sponsorship.

It is hoped that this PET-CT book will serve as an invaluable educational tool for all professionals working in PET-CT departments and that it will contribute to the quality of their daily work. I also hope that this book will benefit those with no or limited PET-CT experience, helping them to start to develop their understanding of the field. I look forward to the next two books in 2011 and 2012.

Suzanne Dennan Chair, EANM Technologist Committee

Preface and Glossary of Terms and Abbreviations

Peter Hogg and Giorgio Testanera

PET-CT is expanding rapidly in many countries and has quickly established its place in the diagnosis and management of several prominent diseases. This has come about through a growing and convincing evidence base in regard to its efficacy, combined with sound financial reasons. Taken together, these provide a firm argument for routine use of PET-CT in certain disease processes. With this in mind, this book, the first in a series of three about PET-CT, comes at a timely moment. The next two books in this series will be published in 2011 and 2012. Each chapter has a reference list, though we have tried to keep these lists to essential references only. Finally, most chapters also have a short reading list, which seeks either to develop fundamental background knowledge that should be present prior to reading the chapter or to give direction on how to extend your knowledge after reading the chapter.

This book covers some fundamental aspects of PET-CT in preparation for the two subsequent books. It commences with a chapter on a radionuclide radiologist's perspective about the use of PET-CT in his medical practice. This is an important starting point because it makes a clear statement about how PET-CT is evolving in a particular country with a view to providing a routine service. Having introduced this perspective, the book progresses to a number of equipment-related chapters. These outline how PET-CT imaging and radionuclide production equipment work and also they explain what quality checks might be conducted to ensure optimal performance. Given that PET-CT radiation protection requirements are complex, we have included a substantial chapter on this. This comprises three elements – 'staff', 'patient' and 'department design'. There is also a chapter on patient care, and, as with radiation protection, we have anticipated an existing level of general knowledge about these particular issues. The final chapter presents arguments on how competence to practice could be achieved and what considerations should be borne in mind when designing educational curricula.

Building on this book, the second in the series will explore some more fundamental issues (such as radiochemistry QC) before progressing to the detail of how PET-CT procedures are conducted. We hope that you enjoy reading this book and the two related ones. More importantly, we hope that this book will serve as a valuable resource when conducting PET-CT procedures and also designing educational processes that seek to ensure staff are competent in their roles.

Finally, as part of this preface, we have included below a concise glossary of terms and abbreviations that aim to give a simple insight before you begin reading this book.

Peter Hogg and Giorgio Testanera

PET

Positron emission tomography (PET) is a tomographic imaging technique which allows non-invasive quantitative assessment of biochemical and functional processes. A range of positron emitters are available for use but ¹⁸F (combined with FDG – fluorodeoxyglucose) is the most commonly used. PET-CT has particular value in cancer diagnosis and management but it does have value in many other pathologies, too.

CT

Computed tomography (CT) is a technique that uses an x-ray beam to generate images that have a very good resolution to demonstrate anatomy.

PET-CT

Integrated PET with CT in a single unit (PET-CT) has become an established and valued imaging modality in clinical routine. Integrated PET-CT has been shown to be more accurate for lesion localisation and characterisation than either PET or CT alone. PET-CT is an example of hybrid imaging.

Image fusion and hybrid imaging

Image fusion involves the bringing together of two image datasets with the intention of registering them as closely as possible. Generally the two image datasets would have been produced on different types of medical imaging device. Various problems have been incurred when using two geographically remote imaging devices and consequently in recent times there has been a move towards the fusion of the two medical imaging devices into one physical unit. The use of one imaging unit to produce two different image datasets has become known as hybrid imaging. Examples of hybrid imaging devices include SPECT/CT, PET-CT and PET/MR.

Molecular imaging

Molecular imaging can be broadly defined as the in vivo characterisation and measurement of biological processes at the cellular and molecular level. Molecular imaging differs from traditional imaging in that probes (known as biomarkers) are used to help image particular targets or pathways. Biomarkers interact chemically with their surroundings and in turn alter the image according to molecular changes occurring within the area of interest. PET is an excellent molecular imaging modality.

Cyclotron

A cyclotron is required to generate the positron-emitting radionuclides that are used in PET imaging. Ideally cyclotrons are located as close as possible to the PET scanner because the positron-emitting radionuclides tend to have short half-lives.

Chapter 1: The value and limitations of PET-CT in routine clinical practice: a UK radiologist's perspective

Thomas Kane and Peter Hogg

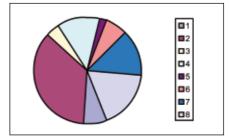
Introduction

When considering the value and limitations of PET-CT in routine clinical practice it is important to set the context as there can be marked variations both between and within countries. The first part of this chapter sets out some national UK PET-CT service issues and then gives background information about a PET-CT service in the north of England. The second part of the chapter explores what that PET-CT service is used for; particular emphasis is placed on cancer detection and staging.

Tom Kane is a dual gualified radionuclide radiologist. He practices radiology and gamma camera nuclear medicine in a large district general hospital located in the North West of England. His private radiology practice is within a nearby private hospital. His clinical PET-CT practice is conducted at a large teaching hospital, the Preston PET Centre, that is approximately 15 miles from the district general hospital. This teaching hospital provides a range of acute services to local residents, serving a population of approximately 390,000 people. It also provides specialist services, such as plastic and brain surgery, to a catchment of 1.5 million people over a broad geographical area. The teaching hospital also has a radiotherapy unit which serves approximately 180 to 200 patients each day. In addition to the clinical PET-CT practice. Tom has been involved in a national audit programme for PET-CT provision using mobile scanners across the south of England. This involved him in 'quality assuring' clinical reports of PET-CT cases that had been produced by radiologists and nuclear medicine physicians.

The Preston PET Centre, established in 2007, houses a General Electric 64-slice CVT system with cardiac and respiratory gating capabilities. The majority of its workload is focussed on oncology (97%), with a small group of patients referred in the neurology category (for brain imaging and investigation of paraneoplastic syndrome). The Centre has three injection rooms which allow for efficient use of scanner time, with a maximum throughput of 15 patients per day. Generally the Centre operates an 8-hour day. A cyclotron facility is located on hospital premises and it produces two radiopharmaceutical runs per day. The number of injections per vial produced varies, but generally no more than 5 patient doses are put into a multidose vial. The Centre has its own multi-professional team of staff and its workload is shown in Fig. 1.

Figure 1: Profile of referrals to the Preston PET Centre, categorised by tumour type. 1, single pulmonary nodule; 2, non-squamous cell lung cancer; 3, lymphoma; 4, colorectal (pre surgery); 5, colorectal (post surgery); 6, head and neck cancer; 7, oesophageal cancer; 8, 'other' (where the evidence base alters patient management)



Courtesy of Alliance Medical Ltd, Alliance Medical Lancashire PETCT Centre, Royal Preston Hospital. Within the UK the development of PET services has been slower than in many other countries. In 2005, a national Framework [1] suggested that research evidence was sufficiently robust to support the country-wide implementation of PET facilities. To help inform resource issues and finance, this Framework also provided an outline of what would be required to establish and operate a PET scanning service; an element of future proofing was included through inferences of where growth areas might lie. On the basis of this Framework, proposals were put forward to establish PET imaging services and cyclotrons. Fundamentally this Framework initiated a planned and coordinated national roll-out of UK PET imaging. An interesting feature of the Framework was that PET-CT, and not PET in isolation, was to be the preferred imaging system.

The UK intention was that there would eventually be a large number of fixed PET-CT sites with some mobile provision. It was considered that mobile provision would be important in the early stages; this conclusion was not reached without good reason. Crowe [2] gives a clear indication as to why mobile services would be a good starting point for establishing a PET service. He indicates that mobile PET-CT would distribute the financial risk when entering the market; that mobile PET-CT would get around the local problem of not having readily available trained personnel; and that one mobile unit could offer PET-CT to several geographical sites on a regular basis. Another catalyst in advancing the availability of PET-CT scanners within the UK was the production of national guidelines (2005) for lung cancer management [3]. These guidelines stipulated that specific geographical areas must have rapid access to PET-CT scanning and that the provision should be a uniformly high-quality service irrespective of where a patient lives. An interesting departure from the norm within the UK was that a sizeable proportion of the PET-CT scanners would be commissioned from private companies; reimbursement to the private company would come from taxation, which is in line with the principles of the National Health Service. The present position of PET-CT within the UK is that a geographically limited routine service is provided, but the number of PET-CT centres is increasing annually in line with the 2005 Framework ambitions.

Having set the context in which the practice sits, let us now explore what that practice consists of.

Radiopharmaceutical

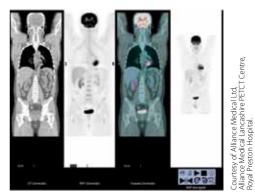
The most extensively used radiopharmaceutical in UK clinical practice is ¹⁸F-FDG (fluorine-18 fluorodeoxyglucose), and two factors account for this. First, the majority of PET-CT scanning is conducted to assess malignant disease and there is robust published evidence to support the use of ¹⁸F-FDG in this context [4, 5, 6, 7, 8, 9]; second, because of the general lack of geographical proximity of cyclotrons to PET-CT scanners, short-lived radioisotopes cannot be used easily. ¹⁸F and FDG have good characteristics, e.g. high spatial resolution, a relatively long half-life that permits longer synthetic procedures to be engaged with (labelling) and sufficient activity in a sample for the distance between the cyclotron and the PET scanner to be quite large. FDG is a modified glucose molecule that is taken up into cells by the same pathway as glucose, usually via the GLUT-3 transporter, but it cannot be metabolised beyond initial phosphorylation to FDG-6-phosphate. FDG uptake therefore depicts normal and abnormal metabolic activity.

Figure 2 illustrates normal biodistribution of ¹⁸F-FDG in an adult. Normal metabolic activity is minimised in clinical imaging by asking patients to starve for a period of hours prior to injection, with the intention of achieving a hypoglycaemic state (low blood sugar). There is normally a high uptake within the brain, which has obligatory glucose metabolism. There is also high activity in the urinary system as FDG is not trapped by the renal tubular cells, unlike normal glucose. There is usually low-grade FDG activity in the liver due to glycolysis and there can be variable uptake in myocardial cells. Muscle that has recently been exercised will also show FDG uptake and for this reason patients are encouraged to limit physical activity prior to injection and scanning.

Figure 2 demonstrates intense uptake in the grey matter and basal ganglia of the brain, moderately intense myocardial uptake, and

intense activity in excreted urine in the renal collecting systems and bladder. Lower grade activity due to glycolysis is shown in the liver, and there is similar activity in bone marrow. The lungs, although having low-level metabolic activity, are apparently totally free of activity due to over-correction from the very low CT value of air-containing lung in the attenuation correction process.

Figure 2: Normal biodistribution of ¹⁸F-FDG in an adult. From left to right, images are: coronal CT, coronal PET, fused PET-CT and MIP PET



PET-CT in routine practice

Within the Preston PET Centre, FDG is used almost exclusively for cancer detection, staging and recurrence. This is consistent with PET-CT practice elsewhere; world-wide, around 90% of PET-CT clinical workloads generally are for cancer detection. In the context of cancer staging, PET-CT is most often used to target potentially curative therapy, often by reducing the frequency of unnecessary surgery. This is particularly true for lung cancer, where metastatic spread may occur remotely without more local tumour spread. The wholebody ability of PET-CT, combined with its high sensitivity, is therefore of considerable clinical value in comparison with other contemporary imaging modalities.

Until the Preston PET Centre opened as a mobile service in 2005, and subsequently as a fixed site in 2007, cancer imaging depended upon other radiological techniques, such as magnetic resonance (MR), ultrasound (US), computed tomography (CT) and gamma camera nuclear medicine (NM). For many common cancers the accuracy of CT staging can be limited: MR, US and gamma camera NM also have limitations. Between 2005 and 2006 Tom's perspective on the use of medical imaging for the evaluation of cancer changed because the increased specificity and sensitivity of PET-CT, compared with conventional imaging alternatives, became increasingly apparent. The role of PET-CT was also becoming apparent to physicians and surgeons through the peer-reviewed journals within their own specialities. This led to pressure for the provision and use of PET-CT in clinical pathways for common cancers within the newly opened Preston PET Centre

For the purpose of the rest of this chapter we shall consider only two cancers that are diagnosed and managed within the Preston PET Centre – non-small cell lung cancer (NSCLC) and colorectal cancer.

Non-small cell lung cancer

Of all the cancers, lung cancer is the most frequent and the most lethal. Predisposing factors for this cancer include smoking and passive smoking, asbestos, air pollution and exposure to radon. On occasion lung cancer has no symptoms; on other occasions the symptoms can be varied and include: persistent cough, dyspnoea, chest discomfort, haemoptysis, hoarseness, anorexia and weight loss for no known reason.

NSCLC comprises several cancers (e.g. adenocarcinoma, squamous cell carcinoma and large cell carcinoma) and each has its own characteristics. For most patients with NSCLC, current treatments do not cure the cancer. NSCLC can be diagnosed or excluded by using a broad range of diagnostic tools and techniques, including physical examination, chest x-ray, CT, sputum cytology, fine-needle aspiration, bronchoscopy and PET-CT. Nearly all types of NSCLC are FDG avid. Figure 3 illustrates an FDG scan on a patient with NSCLC. Using the TNM staging classification [10], this patient has T2, N0, M0. As can be seen from the scan, there is intense FDG update in a small hilar tumour with no abnormal FDG uptake elsewhere

Courtesy of Alliance Medical Ltd, Alliance Medical Lancashire PETCT Centre, Royal Preston Hospital.

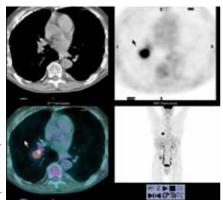
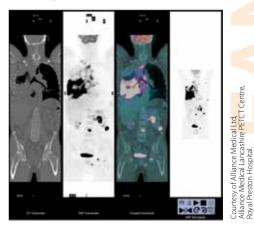


Figure 3: ¹⁸F-FDG scan on a patient with NSCLC; note the intense uptake in the tumour

By contrast, Fig. 4 shows a patient with an extensive lung tumour, with FDG uptake in infected lung around this. Conventional imaging had suggested this might be amenable to radical lung resection, but PET-CT revealed multiple tumour deposits in bone, seen on these images in the spine and bony pelvis as well as the left humerus, and a tumour nodule in the abdomen adjacent to the left kidney.

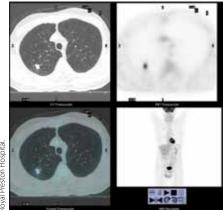
Figure 4: ¹⁸F-FDG scan on another patient with NSCLC, showing multiple tumour deposits in bone and a tumour nodule adjacent to the left kidney



For the solitary lung nodule, PET-CT has been shown to be highly accurate at differentiating benign from malignant disease [11]; this approach has a particular value when CT and chest radiography alone are indeterminate. PET-CT also has value where biopsy is risky.

FDG PET-CT has a very low false negative rate for both NSCLC and small cell lung cancer, although this rate increases significantly in small lesions. Most centres regard 7 mm as the lower limit for reliable exclusion of FDG uptake, and for this reason most published guidelines use 10 mm as the lower size limit for FDG assessment. However, for FDG-negative lesions above 10 mm, most authors would support a policy of observation using serial CT. Management of FDG-positive lesions is complicated by potential false positive findings; FDG uptake is not inevitably due to malignancy, and in particular granulomatous infection (e.g. tuberculosis or, in North American populations, histoplasmosis) can give very high FDG uptake. Again, most authors would recommend either excision or percutaneous biopsy, depending on the patient's general state of health and the likelihood of curative treatment. Figure 5 illustrates an example of a patient presenting with a chest mass which all imaging modalities (including PET-CT) suggested to be a small lung cancer, but which was found following surgery to be a focal tuberculous infection.

Fig. 5. Imaging results in a patient with a focal tuberculous infection mimicking lung cancer



In proven NSCLC the prognosis is strongly related to tumour staging; in patients in whom curative surgical resection or radical radiotherapy is not possible, the 5-year survival is effectively zero. In the British population fewer than 20% of cases of NSCLC will present at stage 1 or 2a, where curative surgery may be considered. Conventional imaging assesses nodal stage by size criteria; however, in the mediastinum, size can be a poor predictor of tumour spread due to the presence of reactive nodal enlargement. FDG has been shown to have a greater predictive value in assessing mediastinal nodes, though there are a number of publications showing that FDG uptake can vary, again due to reactive change. A local study in the Preston PET Centre confirmed an approximately 8% error rate, both for FDG uptake in benign nodes and for FDG-negative involved nodes. This has led to current advice being to surgically sample FDG-negative enlarged nodes, and FDG-positive nodes that are not unequivocally malignant, prior to a treatment decision. FDG has shown a clear ability to detect occult metastatic disease, particularly in the skeleton, over conventional CT staging. Currently the staging of NSCLC forms the single largest referral group in the Preston PET Centre, at 45% of referrals.

Courtesy of Alliance Medical Ltd, Alliance Medical Lancashire PETCT Centre, Royal Preston Hospital.

Colorectal cancer

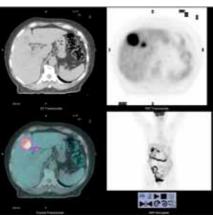
Colorectal cancer is the second most prevalent cause of death by cancer in developed countries. Symptoms include rectal bleeding, change in bowel habit, an abdominal lump, weight loss and anaemia. Colon cancer can be diagnosed or excluded by using a broad range of diagnostic tools and techniques, including barium enema, colonoscopy, CT colonoscopy, blood tests, US, MR and PET-CT [12]. Anatomical methods of imaging colorectal cancer have been found to be suboptimal, not least because microscopic spread reduces cure rates and late diagnosis by anatomical methods confounds this. PET-CT can be valuable for assessing the extent of metastatic disease and as such it is useful in differentiating patients in whom surgery is particularly valuable, i.e. those with locally resectable disease.

PET-CT is not generally used for primary detection or screening but it does have particular value in identifying loco-regional and disseminated disease. It can also be used to detect tumour recurrence when blood tests [e.g. carcino-embryonic antigen (CEA)] raise suspicion and when other radiological tests are normal. Additionally, PET-CT has value in assessing CT-detected abnormalities, particularly soft tissue thickening at the site of previous surgical resection. The presence or absence of FDG uptake has a high predictive value in distinguishing surgical scarring from tumour recurrence, though evaluation can be hampered in the presence of infection.

In the Preston PET Centre the commonest referral indication in colorectal cancer is to stage patients whose primary tumour has been resected and who are subsequently being assessed for suitability for either liver or lung resection for presumed localised metastatic disease. As in other cancers, the exclusion of other sites of disease is considered highly predictive of curative success for localised resection. Whilst PET-CT has been shown to have a lower sensitivity for liver lesions compared with MR, and a lower specificity as compared with CT portography, the ability of PET-CT to detect metastatic disease at other sites outside the liver or lung has given this technique an overall greater predictive power for surgical planning. Figure 6 illustrates a patient who presented with colon cancer. Conventional imaging had indicated a solitary metastatic deposit in the liver (the large FDG-avid lesion), and liver surgery was being considered. FDG PET-CT, however, showed additional metabolically active nodes in the liver hilum and adjacent to the porta hepatis, indicating inoperable tumour.

Fig. 6a A liver deposit (large lesion) and a small liver hilum node are visible in a patient with colon cancer. Fig. 6b Further FDG-avid nodes





6b



How will the PET-CT service develop?

For the Preston PET Centre there is a relatively low referral rate of lymphoma cases, which for the UK PET-CT practice generally form the single largest patient group. This low referral pattern is highly likely to change in time and there should be an increasing trend to image this patient group. As elsewhere in the UK, there is an increasing number of referrals to assess the potential for secondary deposits from oesophageal cancer that are being considered for surgery or radical therapy. There is also an increasing trend for imaging pathologies which fall outside the currently agreed referral pathways; these include malignant melanoma, gynaecological cancers and nodal staging of cervical carcinoma. This also reflects UK practice, where recent assessment by the UK PET-CT Advisory Board shows clinical practice evolving as PET-CT becomes a more mature and established medical imaging technology.

 a + 6b: Courtesy of Alliance Medical Ltd, Uliance Medical Lancashire PETCT Centre toyal Preston Hospital.

References

1. A Framework for the Development of Positron Emission Tomography (PET) Services in England. Department of Health 2005, Crown. <u>http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAnd-</u> Guidance/DH_4121029

2. Crowe P. Making PET and PET-CT a clinical reality through mobile PET services. In: Von Schulthess G, editor. Clinical molecular anatomic imaging. Philadelphia: Lippin-cott Williams and Wilkins; 2003.

3. National Institute for Clinical Excellence. The diagnosis and treatment of lung cancer. 2005. www.nice.org.uk/nice-media/pdf/CG024niceguideline.pdf

4. Wechalekar K, Sharma B, Cook G. PET-CT in oncology – a major advance. Clin Radiol 2005;60:1143–55.

5. Israel O, Keidar Z, Bar-Shalom R. <u>Positron emission to-</u> mography in the evaluation of lymphoma. Semin Nucl Med 2004;34:166-79.

 Schöder H, Yeung H. Positron emission imaging of head and neck cancer, including thyroid carcinoma. Semin Nucl Med 2004;34:180-97.

7. Dehdashti F, Siegel B. <u>Neoplasms of the esophagus and</u> stomach. Semin Nucl Med 2004;34:198-208.

8. Delbeke D, Martin W. <u>PET and PET-CT for evaluation of</u> <u>colorectal carcinoma</u>. Semin Nucl Med. 2004;34:209-23.

9. Eubank W, Mankoff D. <u>Current and future uses of positron</u> <u>emission tomography in breast cancer imaging</u>. Semin Nucl Med 2004;34:224-40.

10. National Cancer Institute. National Cancer Institute Fact Sheet. Staging: questions and answers. Available at: <u>http://</u> <u>www.cancer.gov/cancertopics/factsheet/Detection/staging</u>, 2009

11. Jeong S, Lee K, Shin K, Bae Y, Kim B, Choe B, et al. Efficacy of PET-CT in the characterization of solid or partly solid solitary pulmonary nodules. Lung Cancer 2008;61:186-94.

12. Lonneux M. <u>FDG-PET and PET-CT in colorectal cancer</u>. PET Clinics 2008;3:147-153.

Suggested reading

Barrington SF, Maisey MN, Wahl RL. Atlas of clinical positron emission tomography. 2nd ed. London: Hodder Arnold; 2006.

Christian P, Waterstram-Rich K. Nuclear medicine and PET-CT – techniques and technology. 6th ed. St. Louis: Mosby/ Elsevier; 2007.

Czernin J, Dahlbom M, Rabit O, Schiepers C. Atlas of PET-CT imaging in oncology. Berlin Heidelberg New York: Springer; 2004.

Von Schulthess G, editor. Clinical molecular anatomic imaging. Philadelphia: Lippincott Williams and Wilkins; 2003.

Chapter 2: Practical radiation protection in PET-CT

Jean-Marc Vrigneaud, Sylviane Prévot, Angela Meadows and Peter Hogg

a) THE PATIENT Jean-Marc Vrigneaud

Introduction

Radiation exposure to the patient from a PET-CT scan is both external, from the CT scan, and internal, from the injected PET radiotracer. Accordingly, the radiation burden to the patient can be relatively large, with a total effective dose of 25 mSv commonly cited in the case of PET-CT studies [1]. Dose reduction can be achieved by careful attention to the CT imaging parameters and the administered activity of the PET tracer; this is particularly important in children. This review will outline the factors that affect radiation dose in both modalities and will try to give some insights into dose reduction in PET-CT imaging.

PET dosimetry

Considering the intention of optimisation in radiation protection, the aim is to achieve the minimum patient radiation dose consistent with diagnostically acceptable image quality. In nuclear medicine, this can be done primarily by:

- Appropriate selection of the best available radiopharmaceutical and its activity, with special requirements for children
- Appropriate image acquisition and processing

Optimisation of administered activity

Radioactive doses should be as low as reasonably achievable but high enough to obtain the desired diagnostic information. The radiation dose to the patient may depend on factors associated with the PET scanner, in that these factors influence the amount of administered activity required to provide an image quality good enough to produce a reliable diagnosis (see next section).

¹⁸F-FDG is by far the most commonly used radiopharmaceutical in PET. The radiation dose from ¹⁸F-FDG can be calculated using tables from International Commission of Radiation Protection (ICRP) Publication 80 [2]. These tables provide dose data, using ICRP publication 60 dosimetry, in the case of standardised individuals (children aged 1, 5, 10 and 15 years and adults). Accordingly, these data do not account for differences among individuals in terms of their pharmacokinetics and should not be used to evaluate the risk to a given individual. However, they do provide generic assessments of organ and effective doses that are sufficient to permit comparison of different techniques or different medical examinations. For instance, in the case of ¹⁸F-FDG, the adult dose per unit activity administered is 19 µSv/MBg. This leads to an effective dose of almost 7 mSv for a typical administered activity of 370 MBg. The organ receiving the highest absorbed radiation dose is the bladder

Whenever possible, diagnostic reference levels should be used to identify situations where the levels of administered activity are unusually high or low. Special attention should be drawn to paediatric patients as they are known to be more radiosensitive with respect to carcinogenesis. At our institution, the standard protocol for clinical studies is to inject 5 MBg/kg of ¹⁸F-FDG but an even lower dose level may be adopted depending on the equipment (see next section). Other approaches exist to balance the paediatric dose according to appropriate criteria (e.g. body surface area). For example, Table 1 summarises administered activity as a function of patient weight, according to the new European Association of Nuclear Medicine (EANM) paediatric dosage card [3].

Optimisation of image acquisition and processing

Determination of optimal performance is a very difficult task in PET imaging as no simple metrics exist to define image guality. Recently, attempts have been made to adjust administered activity as a function of the noise equivalent count rate (NECR), which is essentially a metric related to the signal to noise ratio in PET [4]. Basically, PET image guality is also influenced by spatial resolution, quantitative accuracy of the tracer concentration and noise. If there is significant noise, then resolution and accuracy are lost. PET acquisitions require a low noise level within the image and no patient motion. The heavier the patient, the higher the noise because of increased attenuation and increased scatter and random fractions

(3D acquisitions) [3]					
Weight (kg)	10	19	32	55	70
Age (yr) ¹	1	5	10	15	Adult
¹⁸ F-FDG administered activity (MBq)	38	65	102	163	196
Effective dose (mSv) ²	3.6	3.3	3.8	4.0	3.7

Table 1: Radiation dose from ¹⁸F-FDG according to the new EANM paediatric dosage card (3D acquisitions) [3]

¹Estimated from anatomical data

² Estimated from ICRP publication 80 [2]

Careful attention should be paid to administration of the lowest possible activity in children that is consistent with maintenance of diagnostic value. It must be borne in mind that if repetition of the examination is necessary, this will cause unnecessary radiation exposure. In contrast, smaller patients may benefit from reduced scan time or reduced injected dose if image quality is good enough. Ultimately, a compromise may be required between imaging time and the possibility for the patient to keep still during the examination.

Considering PET scanners, acquisition and reconstruction parameters should be chosen such that the image quality is optimum. For example, in paediatric studies where the radiation burden can be an issue, 3D acquisition mode should be used because of the enhanced sensitivity of the PET scanner in 3D mode compared with 2D mode. Reconstruction parameters should also be optimised as a function of the region being scanned. In general, iterative algorithms are the standard in PET because of the relatively high statistical noise originating from the emission data. In the most recent implementation of these algorithms, better image guality is achieved by including all the corrections needed (geometry, normalisation, dead time, scatter, attenuation, random events) in the iteration loop.

New technologies will continue to improve image quality, providing the physician with the opportunity to reduce scan time per bed position or to lower the injected dose. For instance, time-of-flight (TOF) imaging seems to be particularly promising in terms of achieving a lower level of noise and better resolution compared with non-TOF imaging. This benefit has already been shown in large patients, with the TOF gain being more significant when limited acquisition time and high attenuation reduce the total counts in the image [5]. In the same way, dynamic studies with low statistics should also benefit from the enhanced image quality achieved with TOF imaging.

CT dosimetry

CT delivers a relatively high radiation dose to the patient. Its use has increased rapidly as a result of the tremendous advances in CT technology that make it extremely user-friendly for both the patient and healthcare workers. In Western countries, though it represents only a small fraction of all medical procedures involving ionising radiation, its contribution to the collective effective dose is quite large (up to one-third).

Overview of factors affecting radiation dose in CT

The factors affecting radiation dose can be classified as intrinsic and extrinsic. Intrinsic factors are related to the geometry and design of the scanner (tube, focus, collimator, filtration, detector design, etc.) and cannot be modified by the user. Extrinsic factors are those parameters that can be adjusted by the user, and it is these parameters that mainly determine the patient dose. Optimisation of CT radiation dose is rather challenging and requires a good knowledge of how the various factors affect the absorbed radiation dose; these concerns are summarised in Table 2.

Table 2: User-adjustable factors affecting radiation dose in CT

	5
mA	The tube current is linearly related to radiation dose.
Time per rotation	The exposure time per rotation is linearly related to radiation dose.
mAs	The product of the tube current and time. Linearly related to radiation dose. Reducing the mAs reduces the radiation dose but increases the noise by $(1/\sqrt{mAs})$.
kVp	The tube voltage measured in kilovolt peak. X-ray output is approximately proportional to (kVp) ² . With respect to other exposure parameters, changing the voltage from 140 to 120 kV reduces patient dose by 40%.
Pitch	With respect to other exposure parameters, dose is inversely proportional to pitch. However, on multiple detector-row CT, tube current is automatically increased as pitch is increased to maintain image noise. As a consequence, when the effective mAs or mAs/slice is used, radiation dose is unaffected by pitch. Effective mAs or mAs/slice = true mAs/pitch.
Scan length	The average radiation dose within the volume may vary slightly when using a larger scan region but the effective dose increases linearly as the length of the patient irradiated increases because of the exposure of additional tissues and organs.
Collimation	Multiple detector-row CT systems have been observed to have a radiation dose inefficiency at the narrow beam collimation required for narrow slice widths.
Slice thickness	This parameter affects the patient dose indirectly by governing the noise in the image. The noise is proportional to $1/\sqrt{\text{slice thickness}}$.
Patient size	With the same acquisition parameters, the smaller patient receives a higher radiation dose than the larger patient.
Slice thickness	inefficiency at the narrow beam collimation required for narrow slice widths. This parameter affects the patient dose indirectly by governing the noise in the image. The noise is proportional to 1/√(slice thickness). With the same acquisition parameters, the smaller patient receives a higher radia-

Displayed CT dosimetric quantities

The CTDI_{vol} (Computed Tomography Dose Index in mGy) is displayed on the user console prior to scan initiation. It represents the average dose within the scan volume for a standardised CTDI phantom. It can be used to study the influence of technical parameters on patient dose or to compare the radiation dose with diagnostic reference levels.

The CTDI_{vol} does not represent the average dose for objects of substantially different size, shape or attenuation than the CTDI phantom. For example, in the case of paediatric patients,

the CTDI_{vol} can be underestimated by a factor of 2. Accurate determination of CTDI_{vol} in paediatric applications requires the use of appropriate phantoms adapted to child size.

The dose-length product (DLP in mGy·cm) is another displayed quantity. The DLP reflects the total energy absorbed that is attributable to the complete scan acquisition. It takes into account the length of the scan acquisition. Effective dose can be estimated from the DLP [6] using appropriate conversion coefficients as a function of the region being scanned (head, neck, thorax, abdomen or pelvis).

Dose reduction in CT

As in PET, patient dose in CT is interconnected with image quality (spatial resolution, noise, slice thickness). For example, to reduce the level of noise by a factor of 2 with respect to spatial resolution and slice thickness, it is necessary to increase the dose fourfold. When optimising patient dose, this trade-off should always be kept in mind and the CT parameters should always be adapted according to the contrast needed in a given region. Protocols should also take the individual patient into account by selecting parameters according to patient size, age and gender and the clinical question.

Amongst all parameters listed in Table 2, the tube current (mA) is often the least standardised. Tube voltage and gantry rotation time are generally fixed for a given clinical application. Lower tube voltages can be used for small adult patients or children or in specific protocols that require a low radiation dose (e.g. in pregnant woman). Reducing the tube voltage improves image contrast but also reduces the penetration of x-rays and increases the noise in the image. The fastest rotation time should be used to minimise motion blurring and artefacts. Ultimately, the CT operator should take patient size into account when selecting the mA (or mAs). Several technique charts exist to adjust mA according to various criteria (e.g. patient weight or patient thickness) [7]. For example, for body CT imaging, a reduction in mA by a factor of 4-5 from adult techniques is acceptable in infants [8]. On the other hand, a large patient will need a higher than average mAs to counteract the effect of increased attenuation. Reducing the scanning length and minimising the number of scans in an imaging study are also helpful in optimising patient dose.

On modern CT scans, automatic exposure control (AEC) systems adjust the x-ray tube current (mA) in real time during gantry rotation in response to variations in x-ray intensity at the detector. AEC systems enable the CT user to prescribe a measure related to image quality so as to modulate the tube current as a function of size, shape and geometry of the region being scanned. The main advantage of this technique is the consistent image quality obtained within a patient as the patient's attenuation varies but also from one patient to another, irrespective of the patient size. These systems should be used with caution to ensure that the required image quality is always specified appropriately. To this end, the displayed dosimetric quantities can be checked to identify any misuse of these systems.

PET-CT dosimetry

PET-CT dosimetry will depend strongly on imaging protocols. In most cases, patients referred for a PET-CT procedure do not require stand-alone diagnostic CT or contrast-enhanced CT. Highquality anatomical details are not essential and a higher level of noise can be tolerated in the images. Also, there is no need to discriminate between various kinds of soft tissue. Indeed, the CT component is used mostly for anatomical correlation of the PFT data and attenuation correction This means that there is a great potential for dose reduction compared with diagnostic guality images required in radiology departments. If the CT component is used only for co-registration and localisation, a reduction in CT parameters is possible while maintaining acceptable image guality for anatomical correlation. For example, the mAs can be as low as 10-40 mAs depending on the patient weight [9]. This trend is even more relevant if only attenuation correction is needed. Here, the only requirements are to obtain an accurate representation of the attenuating tissue, with linearity maintained and without any CT artefacts. In this case, it is possible to further reduce the radiation exposure without compromising

the quality of the attenuation-corrected emission data [10]. The tube current can be as low as 10 mA and the tube voltage can be reduced to 80-90 kVp in small adult patients or children.

Another specificity of PET-CT imaging is the axial extent of the CT scan. The current method for whole-body imaging is to scan each patient from the mid thighs to the eyes. The resultant effective dose can be relatively high if the CT parameters are not optimised. Table 3 shows examples of effective dose obtained from a whole-body CT scan operating at different mAs per slice. In some cases, it may be more appropriate to tailor this approach and adapt scan length and scan quality according to the clinical indication.

Table 3: Radiation exposure from a whole-body CT scan for PET-CT studies as a function of mAs. Simulations were carried out for a GEMINI GXL PET-CT scanner (10-slice CT) operating at 120 kV, 10x1.5 mm, pitch 0.7, scan length 1 m (CT-Expo 1.7, © G. Stamm, Hannover and H.D. Nagel, Hamburg)

			mAs/slice		
	20	40	80	120	150
CTDI _{vol} (mGy)	1.4	2.9	5.7	8.6	10.7
DLP (mGy·cm)	147	293	587	880	1100
Effective dose (mSv)	2	4	8	12	15

As a consequence, the patient exposure from PET-CT studies will depend on the imaging protocols, the number of CT scans performed and, to a lesser extent, the amount of PET tracer injected. According to Table 3, for an adult patient, the effective dose from the CT scan may be in the range of 2-15 mSv. From the first part, we learnt that the internal adult dose due to the ¹⁸F-FDG tracer is approximate-

ly 7 mSv. The total radiation burden for the adult patient will thus be 9-22 mSv depending on the imaging protocol chosen. Children are known to be more radiosensitive than adults and they also have a potential for a longer life relative to adults. Whenever possible, paediatric adjustments should be used in both PET and CT to maintain doses as low as reasonably achievable.

b) THE STAFF Sylviane Prévot

Introduction

Compared with the radiation exposure of staff traditionally used to handling ^{99m}Tc and other low-energy radiopharmaceuticals, the radiation doses reported from PET are much higher [11, 12, 13]. In the last few years the rapid expansion of PET-CT facilities and the introduction of positron emitters in conventional nuclear medicine departments have given rise to new radiation safety concerns for radiographers and nuclear medicine technologists. As a consequence, working practices have had to be reviewed and sometimes modified in order to minimise individual and collective radiation exposures.

General principles of radiation protection

The principle of optimisation [ALARA (as low as reasonably achievable) philosophy] has been part of the European basic safety standards since the 1980s. It was re-emphasised in the Euratom Council Directive 96/29 [14], which had its roots in ICRP 60 [15]. In the context of the optimisation of occupational exposure, radiation safety issues need to be addressed before PET tracers are handled. Source-related restrictions on the prospective doses to individuals in planned situations – dose constraints – must be used when designing new premises. The layout of the department must be considered as well. This careful approach aims to ensure the safe practice of PET-CT imaging.

Staff doses must be maintained as low as possible. National regulation limits are applied as part of the control of practice (Table 4). Operational protection will be based on the following:

- Prior risk assessment and optimisation of protection in all workplaces
- Delineation of areas (controlled/supervised); avoidance of any accidental entrance
- Classification of workers into two categories (A/B) according to the doses likely to be incurred in normal working conditions
- Information and training of exposed workers
- Appropriate measures to protect pregnant staff from the hazards of ionising radiation
- Monitoring of exposures and adequate medical surveillance
- Monitoring of the working environment

	Effective dose (E)		Equivalent dose (H)	
	Whole body	Lens of eye	Skin	Extremities
Exposed workers, apprentices & students aged 18 years or over	20 mSv per year (average over a 5-year period) Max. 50 mSv in 1 year	150 mSv	500 mSv·cm ⁻²	500 mSv
General public	1 mSv	15 mSv	50 mSv⋅cm ⁻²	
Fetus	1 mSv over pregnancy			

Table 4: Dose limits according to Euratom Council Directive 96-29 [14]

Radiation safety issues in FDG PET-CT Computed tomography (CT) studies

CT uses an x-ray beam. During the CT scan, scattered radiation from the patient results in a high risk of external exposure for staff in the room. Adequate shielding in walls and doors avoids scattered radiation out of the scanner

attered radiation out of the scanner datory (Table 5).

Table 5: Attenuation of x-rays in radiology

Voltage	HVL	Attenuation (%)	Attenuation (%)	Transmission (%)
(kV)	(mm Pb)	0.35 mm Pb	0.5 mm Pb	2 mm Pb
50	0.1	91	97	$<1 \times 10^{-6}$
100	0.2	70	82	$<1 \times 10^{-3}$
150	0.26	61	74	<5 × 10 ⁻³

HVL, half-value layer

¹⁸F-fluorodeoxyglucose (FDG) PET imaging

Physical characteristics of ¹⁸F

Positrons (e⁺) are emitted from a proton-rich nucleus undergoing β^+ decay. A positron travels a few millimetres, losing kinetic energy through collision with matter before it combines with a free electron (e⁻). The mass of the e⁺ and e⁻ is converted into two annihilation photons of 511 keV, emitted in opposite directions, 180° apart. ¹⁸F emissions are shown in Table 6.

Table 6: ¹⁸F emissions (Delacroix et al. [16])

room. In normal working conditions, operators

are isolated from the source/patient within the

control room. Occasionally the presence of

someone beside the patient may be justified.

In that case a 0.5-mm lead apron providing

more than 74% attenuation of x-rays is man-

	Gamma		Beta (E _{max})		Elec	tron
	E (keV)	%	E (keV)	%	E (keV)	%
E1	511	194	634	97	1	3

Risk of internal exposure

External contamination of skin or internal contamination by inhalation or ingestion may result in internal exposure. ¹⁸F has a short half-life ($T_{1/2} = 110$ min) and radiotoxicity is moderate; consequently the risk of internal exposure is relatively low despite β emission.

Risk of external exposure

With a gamma ray constant in air being approximately 10 times higher than the 140-keV emissions from ^{99m}Tc, 511-keV annihilation photons result in a high and sometimes underestimated risk of external exposure for staff.

¹⁸F-FDG in a vial or syringe is a source emitting high-energy gamma photons and beta particles. Despite a high dose rate, 0.63-MeV positrons have ranges of 0.9 mm in glass and 1.7 mm in PMMA. Most of them are stopped in the walls of a vial. Exposure rates at short distances without a shield can be extremely high: more than 1 Sv-h⁻¹ in contact with a syringe (Table 7). The dose limit for extremities can be reached in only 21 min when holding 500 MBq of ¹⁸F in an unshielded syringe, whereas it takes 3 h with ⁹⁹mTc (Table 8).

Table 7: Exposure rates from ¹⁸F without a shield (Delacroix et al. [16])

	Exposure rate (mSv·h-1) On contact At 10 cm At 40 cm		
Multidose, 10-mL vial, 6 GBq	4200	96	6
Single dose, 10-mL vial, 500 MBq	350	8	0.5
Syringe, 5 mL, 500 MBq	1450	-	-

Table 8: Exposure rates when holding various radionuclides in an unshielded syringe

Radionuclide	Dose rate on contact (µSv·h ⁻¹ ·Bq ⁻¹ ª)	Exposure rate for 500 MBq (mSv·h ⁻¹)	Time required to reach dose limit (500 mSv)
^{99m} Tc	3.5×10 ⁻⁴	174	2.9 h
131	1.1×10 ⁻³	550	54 min
¹⁸ F	2.9×10 ⁻³	1450	21 min

^aDelacroix et al. [16]

Following administration, beta particles are stopped in soft tissues. The patient is a moving source emitting scattered 511-keV photons. The mean dose rate measured with a Babyline 81 (Nardeux) at 0.5 m from the patient's abdomen is 0.26±0.04 µSv·h⁻¹·MBq⁻¹ immediately after injection and 0.15±0.04 µSv·h⁻¹·MBq⁻¹ 1 h later, just before installation after emptying the bladder (Table 9).

Padianharmacoutical	Exposure rate (µSv·h⁻¹)		
Radiopharmaceutical	On contact	At 0.5 m	
^{99m} Tc-HDP (470 MBq) following injection	180	24	
^{99m} Tc-HDP (922 MBq) installation (+3 h)	40	9	
¹⁸ F-FDG (350 MBq) following injection	590	91	
¹⁸ F-FDG (350 MBq) installation (+1 h)	364	52	
HDP bydrowymathylana diphasphanata			

Table 9: Exposure rates measured on contact and at 0.5 m from a patient

HDP, hydroxymethylene diphosphonate

These figures clearly demonstrate that the doses likely to be incurred when holding ¹⁸F-FDG sources or when at a short distance from a patient without a shield can be much higher than those involved in standard nuclear medicine procedures. Three situations must be considered critical in terms of external exposure:

- Dose dispensing
- Injecting the patient
- Positioning the patient on the scanning bed

Therefore, specific shielding devices and handling procedures have to be developed so that exposures can be reduced and maintained at a minimum level.

Practical steps to control external exposure

A protection strategy must be implemented in every PET-CT facility according to the layout of the department and local working practices, including:

- Appropriate delineation of areas with restricted access to properly trained staff
- Adherence to well-established standard policies and procedures to maintain best practice in radiation safety
- Use of the three basic radiation protection principles: time, distance, shielding
- Close attention to staff training
- · Close monitoring of exposures
- Radiological surveillance of the working
 environment

Dose dispensing is performed in the hot laboratory, which is designated as a controlled area. Injecting/resting rooms and the scanner room are controlled areas as long as a radioactive patient is present and/or during the CT study. The rest of the time they are designated as supervised areas, as is the scanner control room.

Optimisation of staff exposures

Absorbed dose – average dose over a tissue or an organ – is a function of the dose rate and of the time spent near the source of radiation. In well-managed operations, protection benefit involves a balance between several factors so that dose rates can be significantly reduced without a corresponding substantial increase in time.

Minimising time

- Prepare every process very carefully and perform all radioactivity tasks as swiftly as possible
- Check volume required before drawing up then dispense dose as rapidly as reasonable
- Conduct all patient examinations, give clear explanations and allow time for questions **before** FDG is injected
- Optimise the injection procedure gaining a good IV access (e.g. cannula with a threeway tap) before handling the activity
- Spend only as long as necessary when positioning patients

Experienced and well-trained radiographers and nuclear medicine technologists generally perform manipulations more rapidly. Staff rotation also contributes to reducing the time of individual exposure.

Maximising the source-operator distance

- Make use of the inverse square law
- Use long tongs (25-40 cm) to place and remove unshielded vials in the dose calibrator
- Draw up with a spinal needle (20G×90 mm)
- Use a trolley to carry doses from the hot laboratory to the injecting room
- Avoid staying beside the patient unnecessarily after injection
- Use the intercom to communicate with patients
- Use remote viewing to oversee patients in the resting area/scanning room
- Direct patients rather than escort them unless they need support

The mean dose rate measured at the patient's abdomen just before installation is 2.5 times lower at 1 m than at 50 cm.

<u>Placing adequate shields between the source</u> <u>and the operator to be protected</u> Attenuation is a stochastic process depending on:

- The nature and energy of the source
- The thickness and density of the attenuator

Before choosing the most appropriate attenuator, it is first necessary to determine the thickness required for attenuation or complete absorption of the emissions from the source. The half-value layer (HVL) of 511-keV photons from ¹⁸F, i.e. the thickness resulting in 50% attenuation, is 4 mm in lead (Pb) and 2.7 mm in tungsten (W). Compared with ^{99m}Tc, whose HVL in lead is 0.2 mm, ¹⁸F shielding requirements are about 16 times greater. Therefore, thicker shields are required when handling ¹⁸F-FDG, as follows:

Shielded hot cell and dose calibrator (50 mm
 Pb) to avoid whole-body exposure (Fig. 1)

Figure 1: Hot cell (Lemer-Pax)



 Adequate dispensing pots (Pb≥30 mm or W, 20-25 mm) and caps (W≥20 mm) with an aperture through which the needle is inserted, providing more effective protection when dispensing manually [17] (Fig. 2)

Figure 2: Manual dispensing



 Syringe shields (W≥5 mm) in sizes to fit all the syringes used for administration of doses (Fig. 3)

Figure 3: Syringe shields



Courtesy of Medisystem.

 Shielded trolley (Pb, 30 mm) to move shielded syringes from the hot laboratory to the administration room Lead mobile screen (≥30 mm) highly recommended to reduce whole-body exposure when standing next to the patient (injection process, removal of cannula) or when operating the scanner from the gantry (Figs. 4–6)

Figure 4: Manual injection

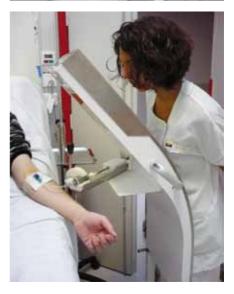


Figure 6: Operating camera from gantry



Figure 5a,b: Remote injection (Medisystem)





• Lead containers (≥10 mm) for waste and sharps

Courtesy of Centre Leclerc.

The relative importance of different aspects of working techniques is set out in Table 10 [18]. Shielding is the most important factor affecting finger doses [19]. Syringe shields providing good visibilities are now available; they should also be used for injections. In addition, shielding contributes to the optimisation of wholebody doses [12], protecting the environment against ionising radiations emitted from their content. Unshielded syringes should never be handled directly.

Table 10: Likely impact of protection factors [18]

Methodology	Protection	Impact
Whether or not a syringe shield is used	S + T	High
Shielding used for the vial	S	High
Position of the fingers of the hand holding the syringe	D+T	Medium / High
Speed with which unshielded manipulations are performed	Т	Medium / High

T, time; D, distance; S, shielding; High, >40% attenuation; Medium, 20-40% attenuation

Since thick vials and syringe shields are very heavy to manipulate, automation of the dispensing process is of particular relevance (e.g. Comecer Althea and Trasis UniDose). The administration process is then performed using specific protective techniques. Automatic systems combining safe dispensing and infusion of ¹⁸F-FDG are also available (e.g. MEDRAD Intego[™] and Lemer-Pax Posijet). Both of the aforementioned systems are designed to replace the manual process of dose preparation and injection. The number of studies reported for the preparation/injection of ¹⁸F-FDG is limited. Nevertheless, automated techniques seem a very promising means of lowering finger doses (Fig. 7).

Figure 7: Automatic injection using the MEDRAD Intego[™] system



Monitoring of occupational exposure

The rapid increase in ¹⁸F-FDG PET-CT studies raises the question of whether whole-body and extremity exposures are being maintained below the regulation limits. Close monitoring of staff doses is required to confirm that the highest level of protection is achieved.

All staff working in a PET-CT facility must wear a personal dosimeter (OSL, TLD, film badge, electronic dosimeter) (Fig. 8). In addition, staff preparing and injecting FDG doses should wear finger dosimeters to demonstrate that equivalent doses do not exceed the annual limit of 500 mSv (Fig. 9). Regular exposure close to the limit is not in accordance with the fundamental ALARA principle. Occasionally, if an individual is found to be exposed at a consistently high level, close to the individual dose limit, so that the accumulated effective dose may be approaching an unacceptable level, then special attention should be given to the optimisation of protection [15].

Dosimeters should be worn routinely and at appropriate positions [20]. An evaluation of working practices requires all users to wear their dosimeters every day and always in the same place. Ring dosimeters should be worn on the same fingers and in the same orientation with respect to the radiation source. The most exposed parts of the hands are likely to be the tips of the index and middle fingers. An empirical multiplying factor may be applied to doses recorded by ring dosimeters dependFigure 8: Personal whole-body dosimeters



Figure 9: Ring dosimeters



Courtesy of Centre Leclerc

ing on which side of the hand the dosimeter element is worn (palm or back) [19].

Several studies investigating the doses received by PET staff are available [11, 12, 13, 17]. Whole-body doses vary considerably between centres and depending on local working practices. Roberts et al. [12] reported an estimated dose of 4.1 μ Sv per PET procedure, injection of FDG contributing the most to radiation exposure.

In our institute, the average equivalent dose, H_p(10), measured with electronic dosimeters (DMC 2000 XB, MGP) over the last 3-year period is 3 μ Sv per examination, leading to 6 mSv for 2000 patients a year. Installation of patients on the scanning bed results in 96% of whole-body exposure. In 2009, the mean effective dose received by ten radiographers rotating weekly through PET-CT and three nuclear medicine cameras was 2.15±0.52 mSv, including radiopharmacy and ¹³¹I-therapy procedures.

Dealing with staff exposure remains an everyday challenge in any nuclear medicine department. PET tracers must be manipulated with care. Appropriate shielding devices and a robust radiation safety programme are required to minimise staff exposure. Optimisation is an iterative process requiring a collective ongoing effort to achieve the best possible level of protection in all situations involving exposure. The radiation doses received by properly trained radiographers and nuclear medicine technologists can be maintained as low as reasonably achievable and well below the regulation limits without compromising best patient care and welfare.

c) DEPARTMENT DESIGN Angela Meadows and Peter Hogg

Introduction

This short section considers radiation protection measures fundamental to the design of a PET-CT department so as to minimise radiation dose to staff, patients and members of the public. Our intention is not to review the design of conventional gamma camera nuclear medicine departments or to outline detailed building requirements for a PET-CT department. Should you wish to engage in this important background reading, we have included suggested reading at the end of the section. This section will highlight important constructional and layout considerations when using 511-keV radionuclides, particularly when the use of x-radiation is a requirement, as with most modern PET-CT systems.

Regulation and guidance

Each country will have its own law and guidance relating to radiation protection, and the guidance will advise on the construction of PET-CT centres and the layout of a PET-CT facility. However, what is of central significance, regardless of geography, is that a responsible employer will understand the importance of minimising the amount of radiation dose to which staff, patients and the public are exposed. In order to achieve this, a number of practical measures need consideration.

As with gamma camera nuclear medicine, there will be a requirement to include design features that seek to minimise the spread of radioactive spills and these will be notable in dispensing and administration area surfaces and flooring etc. (Fig. 10). Dispensing and administration areas will also require designation as either 'controlled' or 'supervised' in accordance with dose limits and guidance. Radiation warning signs are also required as appropriate.

Figure 10: Smooth, easy to clean surfaces are appropriate in view of the risk of a radioactive spill. Radiation warning signs denote potential hazards



Department design must also extend to the 'designation' of sinks, toilets and drains for the disposal of limited quantities of radionuclides. It is essential that there are sufficient designated'hot toilets' as a significant proportion of the administered patient injection (approximately 30%) will be excreted by the patient as they empty their bladder prior to their PET-CT scan.

Generally speaking, the traditional gamma camera nuclear medicine department will not afford any radiation shielding within its walls, and personnel will not have been required to stand behind secondary radiation shields during patient imaging procedures. It is essential that such practical considerations are taken into account for PET-CT, particularly if modernising an existing nuclear medicine imaging facility for this purpose.

Problems and solutions for 511-keV photons

The fact that 511-keV photons are more penetrating than the low- or medium-energy photons commonly associated with ^{99m}Tc and ¹¹¹In has led to the imposition of additional department design requirements on PET-CT centres. Both distance and shielding must be used to good effect for the purpose of radiation dose reduction for staff and the public.

In order to address this issue, as a first step the administration/uptake rooms can be made larger, particularly in length, so that people passing by the doorway are less likely to be subject to exposure from a radioactive patient. Figure 11 demonstrates a good example of this. Here the uptake couch is several metres from the entrance to the room, thereby making maximum use of distance to minimise dose to staff and members of the public in nearby corridors. Single occupancy uptake rooms are recommended as opposed to shared bay facilities since they will help to minimise the additional radiation dose to staff and other patients and will also allow for 'quiet time' during the uptake period. Furthermore, optimising the number of rooms will assist in optimising scanner usage and ensuring efficient throughput. A busy city hospital could warrant up to four uptake rooms, although this judgment is wholly dependent on potential workload.



Figure 11: Typical administration/uptake room

area based on the dimensions and layout of the rooms. Department design and recommended shielding will depend on the facility, and a team of experienced professionals will be required in the work-up and implementation of department design.

Figure 12 demonstrates an example of a 15mm lead brick that can be used in wall construction. Typically lead bricks are used as additional shielding in wall construction when high-energy photons are to be used. They are contained within the wall between the control and the scan room, demonstrated in Fig. 13. In addition, lead salts are contained within the glass window of the patient viewing area demonstrated in this image.

Figure 12: A 15-mm lead brick; such bricks help to provide additional shielding



Equally the external aspects of the uptake rooms require consideration and unless additional shielding is used in wall construction then distance again can be used where possible. For instance, beyond the rear wall in Fig. 11 is an enclosed area of land where public access is restricted. Furthermore, when considering location of a facility on a hospital site, it is prudent to ensure that it is not located next to a maternity or paediatric unit.

Knowing that the PET scan can take a significant amount of time to complete (up to 1 hour), shielding materials within the scan room walls to protect staff are essential. Depending on the chosen layout of the department, assessment must be made to measure typical dose rates from a patient in a particular

33

Figure 13: Control room where shielding with lead salt glass and lead bricks is used in the adjoining wall to the scan room



An additional consideration is the imaging and uptake room doors: again, increased lead shielding is recommended, as illustrated in Fig. 14.

Figure 14: Side view of the scan room door. Lead lining approximately 4 mm wide can be seen and provides additional shielding



4 mm lead

X-ray considerations

Fortunately, in terms of cost limitation, the inclusion of lead within scan room walls and doors has a dual benefit in shielding from x-rays produced by the CT scanner. The path of the x-rays must be considered and dose rates measured around the scan room and adjacent rooms during acceptance testing phases. A typical CT scatter plot image seen in Fig. 15 provides a visual representation of x-ray distribution during the CT element of the scan. This helps to demonstrate the importance of considering the distribution of shielding in room design and illustrates that, for example, shielding must be of significant thickness between the control and the scan room.

Figure 15: Typical CT'scatter plot' depicting the path of x-rays during exposure

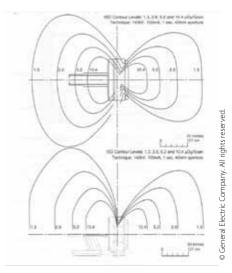


Figure 16: External flashing radiation warning sign during CT x-ray exposure

CONTROLLED

The additional design requirements imposed by the CT scanner also include a 'flashing' warning sign (Fig. 16) to indicate that an x-ray exposure is underway. In some departments a 'pull across' tape over the scan room door also makes it clear that an x-ray exposure is occurring (Fig. 17) and provides an additional warning measure to restrict access. Figure 17: Additional measures to ensure restricted access



In summary, fundamentally the principles of radiation protection are similar to those in conventional nuclear medicine imaging, in that we ensure we use time, distance and shielding as measures to adhere to radiation protection guidance. However, in PET we are dealing with much higher energies and as a result careful consideration must be given to additional shielding and layout of the facility at the outset. Furthermore, it is strongly advised that a team of professionals experienced in radiation protection support the work-up at the design phase, ensuring that shielding is appropriately distributed in relation to the space and layout available and that the design conforms to all relevant legislation and law.

References Chapter 2

References

1. Townsend DW. Positron emission tomography/computed tomography. Semin Nucl Med 2008;38:152-66.

2. International Commission of Radiation Protection. Radiation dose to patients from radiopharmaceuticals. ICRP Publication 80. London: Pergamon Press; 1997.

3. Lassmann M, Biassoni L, Monsieurs M, Franzius C. The new EANM pediatric dosage card: additional notes with respect to F-18. Eur J Nucl Med Mol Imaging 2008;35:1666–8.

 Watson CC, Casey ME, Bendriem B, Carney JP, Townsend DW, Eberl S, et al. Optimizing injected dose in clinical PET by accurately modeling the counting-rate response functions specific to individual patient scans. J Nucl Med 2005;46:1825-34.

5. Karp JS, Surti S, Daube-Witherspoon ME, Muehllehner G. Benefit of time-of-flight in PET: experimental and clinical results. J Nucl Med 2008;49:462-70.

6. European guidelines on quality criteria for computed tomography (EUR 16262 EN, May 1999).

7. Arch ME, Frush DP. Pediatric body MDCT: a 5-year followup survey of scanning parameters used by pediatric radiologists. Am J Roentgenol 2008;191:611-7.

8. McCollough CH, Zink FE, Kofler JM, Matsumoto JS, Thomas KB. Dose optimization in CT: creation, implementation and clinical acceptance of size-based technique charts. RSNA 2002 Scientific Program, Supplement to Radiology 2002;225:591.

9. Alessio AM, Kinahan PE, Manchanda V, Ghioni V, Aldape L, Parisi MT. Weight-based, low-dose pediatric whole-body PET/CT protocols. J Nucl Med 2009;50:1570–8.

10. Fahey FH, Palmer MR, Strauss K, Zimmerman RE, Badawi R, Treves ST. Dosimetry and adequacy of CT-based attenuation correction for pediatric PET. Radiology 2007;243:96-104.

11. Benatar NA, Cronin BF, O'Doherty MJ. Radiation doses rates from patients undergoing PET – implications for technologists and waiting areas. Eur J Nucl Med 2000;27:583-9.

12. Roberts FO, Gunawardana DH, Pathmaraj K, Wallace A, U PL, Mi T, et al. Radiation dose to PET technologists and strategies to lower occupational exposure. J Nucl Med Technol 2005;33;44-7.

13. Guillet B, Quentin P, Waultier S, Bourrelly M, Pisano P, Mundler O. Technologist radiation exposure in routine clinical practice with 18F-FDG. J Nucl Med Technol 2005;33:175-9.

14. Council Directive 96-29 Euratom of 13 May 1996 laying down the basic safety standards for the protection of the health of workers and the general public against the dangers arising from ionizing radiation

15. ICRP (International Commission on Radiological Protection). 1990 Recommendations of the International Commission on Radiological Protection. ICRP Publication 60. Oxford: Pergamon Press; 1991.

16. Delacroix D, Guerre JP, Leblanc P. Radionucléides et radioprotection. Les Ulis: EDP Sciences; 2006.

17. Prévot S, Touzery C, Houot L, et al. Optimization of technologists' hands exposure: impact of vial shielding when preparing ¹⁸F-FDG doses. Eur J Nucl Med Mol Imaging 2008;35:Suppl 2:T13.

18. Martin CJ, Whitby M. Applications of ALARP to extremity doses for hospital workers. J Radiol Prot 2003;23:405-21.

19. ICRP (International Commission on Radiological Protection). Radiation dose to patients from radiopharmaceuticals. ICRP Publication 106. New York: Elsevier; 2009.

20. Donadille L, Carinou E, Ginjaume M, Jankowski J, Rimpler A, Sans Merce M, et al. An overview of the use of extremity dosimeters in some European countries for medical applications. Radiat Prot Dosimetry 2008;131:62-6.

Suggested reading

Christian P, Waterstram-Rich K. Nuclear medicine and PET/ CT – techniques and technology. 6th ed. St. Louis: Mosby Elsevier; 2007.

European Guidelines on Quality Criteria for Computed Tomography. EUR 16262, EU 1998.

Martin C, Sutton D. Practical radiation protection in healthcare, Oxford: Oxford University Press; 2002.

Saunders SE. <u>Computed tomography: physical principles</u>, <u>clinical applications, and quality control</u>. 3rd ed. Philadelphia: W.B. Saunders; 2008.

Seerum E. Rad Tech's guide to radiation protection. Malden, Mass.: Blackwell Science; 2001.

Statkiewicz Sherer MA, Visconti PJ, Ritenour ER. Radiation protection in medial radiography. 5th ed. St. Louis: Mosby; 2006

Chapter 3: PET imaging instrumentation and principles of PET protocol optimisation

Ronald Boellaard

Introduction

Positron emission tomography (PET) is a medical imaging technique which allows guantitative in vivo measurements of 3D distributions of positron-emitting tracers. ¹⁸F-fluorodeoxyglucose (FDG) is the most commonly and widely used PET tracer in oncological applications. FDG basically provides a measure of glucose consumption and it is mainly used to detect malignancies [1, 2]. By using different tracers, various physiological or pharmacokinetic parameters may be derived, such as blood flow, glucose and oxygen consumption, neuroreceptor density and affinity, drug delivery and uptake and gene expression. Furthermore, PET can be used for assessment of therapeutic responses as a clinical application or for the evaluation of the efficacy of new drugs [3, 4]. PET imaging combines high sensitivity with high spatial resolution [nowadays up to ~2.5 mm full-width at half-maximum (FWHM) for clinical PET scanners].

For some of these applications, the visual inspection of PET images provides sufficient information. Typically, in oncology, visual inspection of whole-body FDG images is used for tumour staging and patient management [5, 6]. Nevertheless, as PET is a quantitative imaging modality it is likely that it will be used in a quantitative manner more extensively. Applications in which quantification of PET is important are the assessment of tumour response on therapy and the use of PET as a prognostic indicator based on 'standardised uptake values' (SUVs) [7], as will be explained in more detail later. Quantification of PET studies, however, depends on parameters/settings and the methods used during PET acquisition, image reconstruction and data analysis. It is therefore of the utmost importance to realise to what extent these parameters may affect quantification. Limitations of PET regarding quantification should be considered carefully and taken into account during evaluation of PET studies. In this paper some background on the principles of PET and PET instrumentation will first be presented. The second section will focus on the factors affecting SUV and optimisation of PET imaging for multi-centre studies.

PET imaging and instrumentation PET-CT and PET/MRI

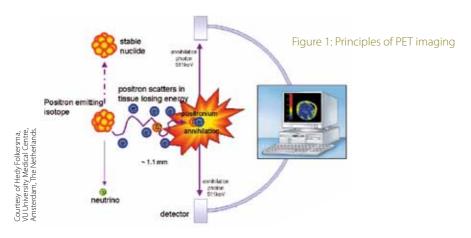
Nowadays most PET systems are combined multimodality PET-CT systems. An excellent overview on PET-CT technology was recently published in the European Journal of Nuclear Medicine and Molecular Imaging by Mawlawi and Townsend [8]. At present there are five vendors offering PET-CT systems: Philips Healthcare, Siemens Medical Solutions, Hitachi Medical, Toshiba Medical Corporation and GE Healthcare. All PET-CT systems have a sequential, but integrated, system design in which the CT scanner is placed in front of the PET part either within one large cover or in two separate covers, allowing the two systems to be moved apart. The latter option may allow for easier patient access and/or improve patient comfort (e.g. claustrophobia).

At present, clinical (prototype) PET-MRI systems are being built with different designs, as follows: (a) a PET insert placed within the MRI scanner, thereby allowing for truly simultaneous PET and MRI acquisitions, but restricting the system's application to brain imaging; (b) a design in which MRI and PET are placed side by side, i.e. a similar arrangement to that used for PET-CT systems. In the latter case, acquisitions will be nearly but not exactly simultaneous, but these systems allow for whole-body acquisitions. Major challenges with PET-MRI acquisitions are the development of PET detectors that are insensitive to the magnetic field of the MRI scanner and use of MRI data for attenuation (and scatter) correction of the PET data. Much progress has been reported in addressing these issues [9].

The remainder of this paper will, however, focus on PET(-CT) imaging as PET-CT is widely available and used in a routine clinical setting [10, 11].

Principles of PET

PET is a molecular imaging technique which measures the distribution of a radioactive tracer in vivo [12]. Upon administration of very small amounts (pico- or nanomoles) of a radiotracer to the patient it distributes among and within the organs. The radioactive atom of the radiotracer emits positrons. The emitted positron combines with an electron after travelling a distance up to several millimetres in tissue. The positron and electron are then converted into two photons, each having an energy of 511 keV, which are emitted in nearly opposite directions. PET image acquisition is based on the simultaneous (coincidence) detection of these two photons. A PET scanner consists of many photon detectors surrounding the patient. During a PET scan millions of coincidence detections are collected, providing information about the distribution of the radiotracer in tissue. Figure 1 demonstrates the principles of PET imaging.



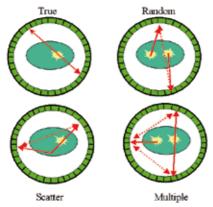


Figure 2: Illustrations of true (top, left), random (top, right), scatter (bottom, left) and multiple (bottom, right) coincidences

Unfortunately, not all coincidences contribute to the signal, i.e. the 'true' 3D distribution of the tracer. Background noise is added to the signal due to photons that are scattered before detection or by coincidence detection of two uncorrelated photons, i.e. so-called random coincidences. Figure 2 illustrates the differences between true, random, scatter and multiple coincidences. True coincidences arise from the simultaneous (coincident) detection of two annihilation photons generated by one positron emission. Ideally, only true counts are detected. A large fraction of the emitted photons (up to 50%) is scattered before leaving the patient. When one of the photons has been scattered, it will result in a dislocation of the 'true' coincidence detection. Moreover, when two photons from two different positron emissions are accidentally (randomly) detected simultaneously (while the others are undetected), the

PET camera will notice a random coincidence detection. It may be clear that these random coincidences result in image distortions (appearing as the addition of a smooth background). Finally, multiple detections can occur when three or more photons are detected at the same time. These multiples are usually discarded.

Quantification of PET studies requires that the contributions of scattered and random coincidences are accounted for Moreover, due to attenuation (=scatter and absorption) of photons in the patient, a large fraction of the emitted photons is not detected. Fortunately, in PET, attenuation does not depend on the location of the positron emission along the line of response, i.e. the line connecting the detectors where a coincidence is measured. Consequently, by acquiring transmission and/or CT scans, the effects of attenuation can be corrected for exactly. In practice, however, attenuation correction is somewhat hampered by patient motion. Random, scatter and attenuation correction methods will be discussed later in more detail

Acquisition and image reconstruction: 2D versus 3D

Although PET is a 3D imaging method, in the past a lot of PET and PET-CT scanners were equipped with septa, i.e. lead or tungsten annular shields positioned within the field of view (FOV). These septa served to shield the detectors from photons emitted or scattered outside the transverse or transaxial plane (Fig. 3). The main purpose of using these septa (2D mode) was

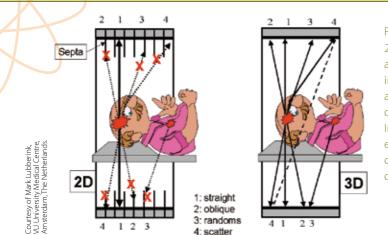


Figure 3: Illustration of 2D (left) and 3D (right) acquisitions. Red crosses indicate photons that are shielded from the detectors by the septa. Indices above and below each 'detector' indicate corresponding types of coincidences

to reduce the contribution of random coincidences, scattered photons and photons coming from activity outside the FOV at the cost of reduced sensitivity compared with 3D (no septa) acquisitions. It was generally considered that the reduced contribution of random and scattered photons in the case of 2D acquisitions improved the quantitative accuracy of PET studies, although this is nowadays a matter of debate [13]. Most modern PET and PET-CT scanners are no longer equipped with septa, and acquisition in 3D mode (without septa) is the only option. 3D acquisition includes lines of response (LORs) that are located in obligue planes (Fig. 3). 3D acquisitions have a higher detection probability, resulting in increased sensitivity but also in increased random and scatter contributions. Fortunately, most of these scanners are also equipped with new and fast detectors using new scintillation crystals (Table 1). These new crystal materials result in better count rate performance as they show a faster scintillation rise and decay time. Consequently, a shorter coincidence time window can be applied, resulting in a reduction of random (and scatter) coincidences. Use of these new crystals therefore partly compensates for the increase in random and scattered photons with 3D acquisitions.

Property	Nal	BGO	LSO	GSO
Density (g/ml)	3.67	7.13	7.4	6.7
Effective Z	51	74	66	61
Decay time (ns)	230	300	35-45	30-60
Photons/MeV	38000	8200	28000	10000

Table 1: Characteristics of common scintillation crystals

BGO, bismuth germinate; GSO, gadolinium oxyorthosilicate; LSO, lutetium oxyorthosilicate; Nal, sodium iodide

Random correction

As indicated above, random coincidences arise from the 'simultaneous' detection of two uncorrelated photons, i.e. photons coming from two different positron emissions. As these randoms are uncorrelated, their mutual directions are also uncorrelated and an almost uniform background is added to the measured 3D activity distribution.

Nowadays most PET-CT systems use sophisticated random correction methods based on using either block singles or a delayed coincidence time window method [12]. A detailed explanation of these methods is beyond the scope of this chapter. In short, the delayed coincidence time window method is based on counting coincidences using a time-shifted coincidence window. As the time window is shifted, measured coincidences come from photons of uncorrelated positron emissions by definition. The 'measured' randoms using this technique provide an accurate estimate of the randoms distribution and contribution. A randoms-corrected sinogram can then be obtained by subtracting this randoms sinogram from the measured total coincidence sonogram, resulting in a 'trues' sinogram. In most cases this correction is performed online during acquisition, although randoms correction can be applied in a more sophisticated and accurate way during image reconstruction.

Attenuation correction

Attenuation of photons in the patient causes loss of coincidences. The number of measured coincidences depends on the patient's 'radiological' thickness. The effects of attenuation can be easily compensated for by acquiring transmission or CT scans. In short, during transmission scans the radiological thickness of the patient is measured for each possible LOR. The transmission through the patient is obtained by taking the ratio of the measured transmission scan counts to those obtained during a blank scan, i.e. a transmission scan acquired without the patient in the FOV. This ratio (transmission) is a direct measure of the attenuation loss per LOR. Correction can be performed by multiplying a 'trues' sinogram by this (inverse) ratio, although more sophisticated implementations within the reconstruction algorithm are usually applied [14]. Occasionally it may be necessary to compensate for emission spillover, i.e. emission counts measured during transmission scanning, and/ or to enhance the quality of the attenuation correction using dedicated segmentation algorithms – an approach usually referred to as transmission image segmentation or seqmented attenuation correction [15].

In PET-CT systems the CT data are used to derive the attenuation correction (CT-AC). CT scans do not suffer from a poor signal-to-noise ratio (SNR) compared with ordinary transmission scans and emission spillover. A CT scan is made by rotating an x-ray tube around the

patient. The energy of the photons generated by the x-ray tube is much lower than 511 keV. A CT image therefore represents the distribution of attenuation coefficients for lower photon energies (~70 to 90 keV). The coefficients are not directly applicable for 511 keV and the CT image needs to be converted into a "511-keV attenuation coefficient image". Moreover, CT scans may suffer from beam hardening artefacts as the x-ray beam consists of a spectrum of photon energies and the attenuation depends on the photon energy. A single scaling factor may not be used to 'convert' the CT scan into a "511-keV attenuation coefficient image". Normally this conversion is performed by applying conversion functions per tissue class (e.g. bilinear scaling functions) to rescale Hounsfield units (HU) to "511-keV attenuation coefficients". Next, this rescaled image is used to derive the attenuation correction factors per LOR.

The accuracy of both transmission scan- and CT scan-based attenuation correction may be affected by patient motion. Clearly, any displacement of the patient between the transmission or CT scan and the emission scan causes a spatial mismatch between the two data sets and results in an incorrect attenuation correction. Patient motion should therefore be restricted as much as possible. Clearly, respiratory motion can be quite pronounced in the case of CT-based AC. A CT scan provides almost a 'snapshot' of the patient as a (spiral) CT scan is acquired very rapidly. Emission data are col-

lected over various respiratory cycles, while the CT-AC provides a series of images each acquired during only a short phase of the respiratory cycle. CT-AC images therefore do not match the emission data and some interface artefacts may appear. A common strategy to reduce (but not to avoid) these artefacts is to instruct the patient to breathe shallowly.

Finally, CT-AC may provide incorrect attenuation correction in a number of special cases. For example, special attention is needed in the case of metal implants. While these implants seem relatively opaque on 511-keV transmission scans, they give rise to severe artefacts on CT-AC images. When an implant is overlooked, there will be a false impression of an increased signal on the PET scan at the location of the implant. Similarly, use of contrast agents produces a high-intensity signal on the CT scan and results in an incorrect attenuation correction, although it seems that with current CT-AC processing algorithms the impact of contrast agents on the accuracy of CT-AC is moderate. Finally, in some PET-CT scanners the FOV of the CT is smaller than that of the PFT scanner. When the patient is only partially visible on the CT scan, e.g. sometimes the arms of the patient are truncated, it is not possible to calculate the attenuation for those LORs. passing through the arms fully correctly and attenuation correction could be wrong. A review on the use of PET-CT and the limitations of CT-AC has been provided by Von Schulthess et al. [16].

Scatter correction

The above information on random and attenuation corrections might seem complicated, and it is true that many factors can influence their accuracy. Yet, development of accurate scatter correction algorithms is still one of the most challenging topics in PET physics, especially in the case of 3D scans (no septa). As most modern systems are 3D only, this section will summarise scatter correction issues for 3D scans only.

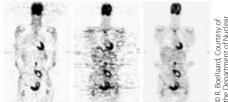
Scattered coincidences occur when one or both photons are scattered and thereby deflected from their original direction (Fig. 2). The main cause of scattering events for 511-keV photons is Compton scattering, where the photon interacts with ('hits') an electron. After scattering, the photon has a lower energy (depending on the angle of deflection from its original direction) and it obtains a different direction. Scattering results in an almost random direction of the scattered photon (although forwardly peaked) and adds a low-frequency background onto the image (thereby reducing contrast).

The most frequently applied scatter correction method in PET is based on estimating the scatter distribution/contribution using a single scatter simulation method described by Watson et al. [17]. This method initially reconstructs a first estimate of the distribution of the activity in the patient without scatter correction. Next, this initial estimate is used in combination with the transmission scan data to calculate a scatter sinogram. The method assumes that scatter is mainly caused by single scatter events of one of the photons and it tries to simulate scatter using the fact that almost all scattered events are caused by Compton scattering. Compton scattering has been characterised well and is used within the simulation. A detailed description of this method can be found in [17]. As the method is based on the physical principles of photon scattering and takes distribution of activity and attenuation into account, it seems to be an accurate scatter correction method, and is nowadays routinely available.

Image reconstruction methods

PET measures coincidences, which are usually stored in sinograms. A sinogram contains the projections over all angles of the activity distribution in the patient. The process of calculating the 3D activity distribution in the patient from the measured sinograms including correction for randoms, scatter, attenuation, normalisation and dead time is called image reconstruction. Image reconstruction algorithms can be classified into analytical and iterative methods and into 2D and 3D methods.

The most commonly used analytical image reconstruction method is filtered back-projection (FBP). This method is linear and quantitatively robust. However, the method is sensitive to noise and reconstructed images may contain severe streak artefacts. For these reasons, iterative reconstruction algorithms have been developed such as ordered subset expectation maximisation (OSEM). Other iterative methods have been developed as well, such as least square [18] and RAMLA [19]. In general, during iterative reconstruction an image is generated by repeatedly (iteratively) estimating an image and its corresponding sinogram. Iterations are continued until there is an optimal match between the estimated and the measured sinogram. The drawback of these methods is that both quantitative accuracy and SNR depend on the number of iterations [20]. Too few iterations result in quantitative inaccuracy (no convergence), while too many iterations amplify noise to unacceptable levels. A trade-off has to be found for each specific application. Moreover, in the case of iterative reconstruction, convergence (i.e. the image reaching the 'true' activity distribution) depends on the underlying source distribution, and optimal reconstruction settings may therefore be different for different types of PET study (body part under investigation or different scan statistics). For oncological whole-body studies, in comparison with FBP, OSEM reconstruction clearly provides images with better (visual) image guality (Fig. 4) and with almost equal quantitative accuracy [14, 21, 22]. However, in the case of dynamic PET studies consisting of many frames with short scan durations and thus poor statistics, iterative reconstruction may show biases (i.e. quantitative inaccuracies). Consequently, FBP is often still the preferred reconstruction method for dynamic PET studies [20].



© R. Boellaard, Courtesy of the Department of Nuclear Medicine & PET Research, VU University Medical Centre, Amsterdam, The Netherlands.

Figure 4: Examples of whole-body FDG PET images. Left, images reconstructed using FBP without attenuation correction; middle, FBP with attenuation correction; right, OSEM iterative reconstruction with attenuation correction

A second classification of image reconstruction methods is based on 2D or 3D reconstructions. In both cases 3D volumetric information about the activity distribution in the patient is obtained. 2D reconstruction methods reconstruct images plane-wise. When acquisitions are performed in 3D, the 3D sinogram containing obligue planes is first converted into a 2D sinogram containing axial planes only. The latter process is called rebinning. Fourier rebinning (FORE) [23] is generally used for this purpose and is presently the most accurate rebinning method implemented for most systems. After (Fourier) rebinning, a 2D sinogram is obtained and reconstructions can be performed plane by plane (2D). Reconstruction speed was the main rationale of using rebinning in combination with a 2D reconstruction. The drawback of rebinning is that it reduces the resolution at increasing radial distance from the centre of the axial FOV This

resolution-degrading effect of FORE depends on and increases with the axial aperture of the scanner and sinogram rebinning is therefore not feasible for all scanners.

To avoid resolution loss due to rebinning, 3D reconstruction methods are nowadays applied which use the full 3D sonogram or all LORs. As a 3D sinogram contains many more LORs, it can be easily understood that fully 3D reconstructions are computationally more demanding. Modern PET-CT systems are therefore equipped with dedicated computer clusters to reconstruct the image within a reasonable time and fully 3D reconstruction has become the standard.

Recent technologies: time of flight and resolution recovery

In the past few years, PET-CT systems with time of flight (ToF) capabilities have become commercially available [24]. ToF is based on the difference in arrival or detection time of both 511-keV annihilation photons when the annihilation took place at off-axis locations. The difference in detection time contains information about the position of the positron emission along the LOR. ToF requires a high timing accuracy and fast detectors with high sensitivity and fast electronics, which have only recently become available. At present, assessment of the exact location (within a couple of millimetres) with ToF is not feasible. The current ToF technology provides a positional accuracy within about 10 cm FWHM. However, by using the estimated position of the positron emission and taking its uncertainty into account within the reconstruction method, ToF reduces image noise and seems to enhance contrast recovery. In other words, ToF is presently used to improve image quality.

A second new development, which has recently also become available on clinical scanners, is the use of recovery correction during image reconstruction [25]. This image reconstruction method uses the (measured) spatially variant point spread function, either image or sinogram based, during the reconstruction process to reduce partial volume effects and thereby enhance the spatial resolution of the reconstructed images. First clinical evaluations using these methods have been published [26]. Further evaluation of the impacts on quantification and on image quality is warranted, but first results are promising.

Optimisation of PET imaging for multicentre study quantification

As pointed out above, accurate corrections to account for many factors at a technical or data collection level, such as random coincidences, scattered photons, attenuation effects and dead time, have been developed and are being applied in most modern PET-CT systems. PET is therefore essentially a quantitative medical imaging technique that can measure the distribution and uptake of a radiotracer quantitatively in vivo. Moreover, PET provides a quantitative measure of the underlying biology, such as metabolism, receptor density or occupancy, transporter activity or information on signaling pathways, depending on the radiotracer being used. FDG is presently widely used in the clinic and provides a quantitative index of glucose metabolism.

High rates of glucose metabolism are associated with malignancy and FDG PET-CT studies are therefore used for staging, prognosis and response monitoring purposes (using changes in glucose metabolism as a measure of tumour response). There is more and more evidence that quantitative measures of FDG uptake or its change can be used as a prognostic factor, for response assessment or as a surrogate endpoint for therapy outcome evaluations [27, 28, 29]. Widespread use of quantification of FDG uptake has been hampered, however, by the vast variability in methodology applied to derive quantitative measures of FDG uptake, such as the standardised uptake value (SUV). The outcome of SUV depends on many factors, as recently pointed out in the supplement issue of the Journal of Nuclear Medicine [30]. As a consequence, conclusions drawn based on SUV data obtained in one centre are not valid for studies performed elsewhere. In this section, the factors that affect SUV quantification will be briefly discussed, followed by an explanation on how to optimise FDG PET-CT scanning procedures for use in multi-centre studies, i.e. to make SUV data exchangeable among institutes [31].

Factors affecting SUV quantification

Although PET is a quantitative imaging technique, there are still many factors that affect quantification of FDG PET-CT studies using SUVs. These factors have been described in [30] and are summarised below. The average or estimated magnitude of the impact of these factors on SUV variability is indicated in parentheses:

Biological factors

- Uptake period (15%)
- Patient motion and breathing (30%)
- Blood glucose levels (15%)

Technical factors

- Relative calibration between PET scanner and dose calibrator (10%)
- Residual activity in syringe (5%)
- Incorrect synchronisation of clocks (10%)
- Injection vs calibration time (10%)
- Quality of administration (50%)

Physics/data analysis-related factors:

- Scan acquisition parameters (15%)
- Image reconstruction parameters (30%)
- Use of contrast agents (15%)
- Region of interest (ROI) or volume of interest (VOI) method (50%)

Different types of PET-CT system from different vendors are being used today. These scanners have different hardware configurations (detectors, scintillator material, electronics etc.) and use different software and algorithms for image reconstruction, corrections and data analysis. These differences will not be overcome and different scanners show different quantitative performances. Yet, variability of SUVs in multi-centre studies can be substantially minimised by taking a number of precautions and by employing procedures that minimise the variability of SUV caused by the above-mentioned factors. Optimisation of image quality for exchangeability and comparability of SUV measures is thus based on principles that aim at reducing SUV variability across sites [6, 32, 33, 34]. Standardisation of PET procedures addresses:

- Patient preparation procedures
- FDG administration procedures
- PET study statistics, image quality and SNR
- Clinical image' resolution/contrast recovery
- Data analysis procedures and SUV normalisation
- Specific multi-centre quality control measures

These specific topics will be discussed briefly below, with a focus on the practical consequences. It is recommended that interested readers consult several other papers in which these items are outlined in more detail [2, 21, 35, 36, 37, 38, 39, 40].

Patient preparation procedures

Patient preparation procedures describe all measures to be taken into account prior to FDG administration and the PET-CT study. Adequate patient preparation is needed to maximise uptake in tumours and minimise uptake in healthy tissues, thereby optimising PET study image quality for both diagnosis and quantification. Below the two most important issues that affect the clinical procedure from a practical point of view are discussed.

FDG uptake varies over time. Therefore the time interval applied between FDG administration and the start of the PET study must be matched as closely as possible between scans performed at various sites. Generally an interval of 60 min with a tolerance of +/- 5 min is considered acceptable. When PET studies are performed for response monitoring purposes, an appropriate interval between the end of the therapy cycle and the PET study needs to be considered as FDG uptake may vary strongly shortly after (chemo-)therapy [6]. The optimal interval is study specific and requires further investigations [3].

As both glucose and FDG are actively transported into cells, glucose levels in blood affect the uptake of FDG and thereby the SUV. High blood glucose levels will result in lower uptake of FDG and thereby lower SUVs. When not properly taken into account, a high blood glucose level may erroneously result in (incorrect) lower SUV data and will also hamper visual interpretation of the PET images. It is therefore important that blood glucose levels are within a normal range before FDG administration. Usually normal blood glucose levels (<7 mmol/L) can be reached by 4–6 hours' fasting prior to the PET examination. Blood glucose levels should be checked before administration of FDG. If blood glucose values are elevated (>7mmol/L), the PET-CT study should preferably be rescheduled [31], if clinically feasible.

FDG administration

The net administered FDG dose needs to be known exactly. Paravenous injection should be avoided and residual activity in the syringe or administration system should be minimal (<3%) or must be measured so that it can be accounted for. It is recommended to implement proper administration procedures that ensure that the net administered dose is known Discrepancies in assumed versus true net administered dose will result in incorrect SUV data Calculation of net administered dose should also include appropriate corrections for decay and requires accurate synchronisation of clocks throughout the department. Decay correction should be applied between the FDG dose calibration time and the start time of the PET study.

It should be noted that three time points are essential for correct SUV assessments: (a) FDG dose calibration time or dose assay time, i.e. the time at which the amount of FDG (MBq) that is to be administered to a patient is specified; (b) injection or administration time and (c) start of the PET-CT acquisition. The difference between injection time and start of the PET-CT acquisition provides the uptake period, which should be as close as possible to 60 min. The time difference between dose calibration time and PET-CT acquisition time is needed to derive the decay-corrected FDG dose at the start of the PET-CT study. Alternatively, the FDG dose at injection time may be entered in the PET-CT system during setup of the patient acquisition. In the latter case, decay correction must be applied for the interval between FDG dose calibration (or assay) time and injection time, assuming that the scanner software then accounts for decay between injection and scan start time (which should be checked)

Image quality

The quality of a PET study depends on many technical factors, which have been addressed in the first section of this chapter. In clinical practice, differences in image quality may occur due to differences in scanner sensitivities, relative bed overlap between subsequent bed positions and patient weight. These factors could therefore also increase variability in SUV between scanner, institutes and patients. Moreover, poor scan statistics result in an upward bias of SUV [35]. Differences in scan statistics amongst centres and subjects may be minimised by prescribing FDG dosage as a function of patient weight, relative bed overlap of subsequent bed positions and emission scan acquisition mode (2D vs 3D) and acquisition duration (per bed position). The EANM guidelines for oncological FDG PET-CT studies provide recommendations for FDG dose [31]. Although these recommendations are an improvement over a flat dosing procedure, i.e. all subjects receive the same FDG dose regardless of type of scanner and patient weight, further optimisation of FDG dose as a function of the above-mentioned parameters is needed and may be scanner dependent.

'Clinical' image resolution or contrast recovery The resolution and/or contrast recovery seen in clinical practice is determined to a large extent by the reconstruction settings applied. Iterative reconstruction algorithms are being used mostly for reconstruction of FDG whole-body PET studies. Various parameters of these algorithms, such as number of iterations and subsets, relaxation factors, voxel size and post-reconstruction image filter settings, determine the 'clinical' contrast recovery seen in practice [41, 42]. Moreover, a sufficient number of iterations (or its product with the number of subsets) is needed to ensure sufficient convergence of image reconstruction. Insufficient convergence results in a lower contrast recovery (and thus lower SUV) and makes lesion SUV more dependent on that of its surrounding. Differences in contrast recovery are probably one of the main factors contributing to variability of SUV amongst centres [21]. Matching of contrast recovery across centres and scanners is therefore essential in multi-centre studies as long as methods to correct for partial volume

effects are not widely available or validated/ approved. Contrast recovery can be achieved by strict prescription of reconstruction settings per type of scanner and should be determined using dedicated QC phantom experiments.

Data analysis procedures and SUV normalisation The first step in deriving SUV is the assessment of tracer uptake by placing an ROI over or in the tumour as seen in the PET-CT images. Various ROI strategies can be applied, such as manually defining 2D and 3D ROIs or semi-automatic ROI generation, fixed size ROIs and use of the maximum intensity voxel. All ROI strategies have specific disadvantages and benefits regarding ease of use, accuracy and precision. Use of the maximum voxel value might be attractive as it is less dependent on the performance of manual or semi-automatic ROI procedures, but it may suffer from upward bias in the case of increased noise levels [35]. Clearly, the uptake (SUV) derived from the PET study depends on the ROI methodology and a method should be used consistently across all scans and institutes in a multi-centre study.

In most cases SUV is normalised by body weight (SUV-BW), as indicated in Eq. 1. Other normalisations are also used, such as lean body mass and body surface area [37]. The most appropriate normalisation factor is, however, still a matter of debate. Therefore, it is recommended that patient height should be measured in addition to patient weight in order to allow for application of all the various SUV normalisations. Moreover, the SUV calculation may include a correction for plasma glucose level (Eq. 2). However, although in theory more accurate results may be obtained by correcting SUV for plasma glucose, the introduction of an additional correction factor into the SUV calculation may worsen reproducibility, especially when not properly measured [43]. Equation 1

$$SUV = \frac{ACvoi(kBq/ml)}{FDGdose(MBq)/BW(kg)}$$

$$SUVglu = \frac{ACvoi(kBq/ml)}{FDGdose(MBq)/SUVglu} \times \frac{Pglu(mmol/l)}{5.0}$$

In Eqs. 1 and 2 ACvoi represents the average activity concentration within a VOI over the tumour, FDGdose is the net administered dose corrected for decay between dose calibration time and start time of the PET study and BW represents the measured body weight. In Eq. 2 the plasma glucose level (Pglu) is normalised by a population average value of 5.0 (round-ed-off value).

Specific multi-centre quality control measures The quality control measures specific for multicentre PET studies should focus on three items: (a) correct functioning of the PET or PET-CT camera according to specifications; (b) accurate (within 10%) relative calibration of the PET or PET-CT scanner against the dose calibrator used for measuring patient FDG doses and (c) verification of activity concentration or contrast recovery as a function of sphere size to assure resolution or contrast recovery matching amongst centres in a multi-centre study. All scanners are equipped with (semi-)automated procedures for daily quality control of the PET-CT system. The test usually reports hardware failures or drifts resulting in unacceptable image quality loss. The procedures are scanner specific and provided by the manufacturer. In the case of PET-CT scanners, all daily tests should be performed for both the PET and the CT components of the scanner. Clearly, all tests should be passed without errors before (any) clinical use.

The relative calibration of the PET-CT scanner against the dose calibrator used for measuring patient FDG dose provides information about potential discrepancies in the calibration of PET-CT and that of the dose calibrator. Cross-calibration (and its verification) is equally important as the calibrations of the individual devices themselves. This can be easily understood from Eq. 1. In the SUV calculation the FDG uptake measured with PET enters the equation in the nominator, while the injected dose measured using a dose calibrator is used in the denominator. Consequently, any discrepancy in absolute calibration results in incorrect SUVs. For correct SUV data, an accurate relative (cross-)calibration is therefore even more important than the accuracy of the (separate) calibrations of the individual devices (dose calibrator and PET scanner).

Differences in spatial image resolution or contrast recovery between various PET-CT systems in a multi-centre study make a large contribution to inter-institute SUV variability [21]. Prescriptions for acquisition and reconstruction parameters may be defined for each type of scanner to fulfil resolution and convergence criteria. However, these prescriptions will become obsolete with ongoing development of new PET-CT scanners and (reconstruction) software. Moreover, resolution is generally measured using point sources, which may provide an optimistic estimation of 'clinical' resolution in the case of iterative reconstruction methods Therefore contrast recovery coefficients provide a more clinically relevant measure of resolution and convergence. The activity concentration recovery coefficient is the ratio between FDG uptake in a sphere measured by the PET-CT system compared with the real FDG uptake. Recovery coefficients can be measured using phantoms containing variously sized spheres.

The absolute values of the contrast recovery coefficients and their relative change with sphere size provide a good measure of the overall partial volume effects seen under conditions which are clinically more relevant [21]. When different systems provide similar (absolute) recovery coefficients measured in a standardised way, resolution (and partial volume effects) is sufficiently matched to allow interchangeability of clinical SUV data across institutions/centres.

Summary

PET is essentially a quantitative imaging modality. This chapter has first described some background on the principles of PET and PET instrumentation, thereby providing the reader with a fair understanding of the quantitative nature of PET. As quantification of PET studies also depends on the methods and procedures used during PET acquisition, image reconstruction and data analysis, it is of importance to understand the effect of such factors on the main clinical quantitative parameter, the socalled standardised uptake value. The second part of this chapter has therefore focussed on explaining a few of the main factors affecting SUV and (corresponding) procedures for optimisation of quantitative PET imaging.

Acknowledgements

Hedy Folkersma and Mark Lubberink are thanked for providing illustrations.

References Chapter 3

References

 Smith TAD. FDG uptake, tumour characteristics and response to therapy: a review. Nucl Med Commun 1998;19:97-105.

2. Fletcher JW, Djulbegovic B, Soares HP et al. Recommendations on the use of F-18-FDG PET in oncology. J Nucl Med 2008;49:480-508.

3. Weber WA. PET for response assessment in oncology: radiotherapy and chemotherapy. Br J Radiol 2005;78:42-9.

4. Weber WA. Chaperoning drug development with PET. J Nucl Med 2006;47:735-7.

5. Cheson BD, Pfistner B, Juweid ME, Gascoyne RD, Specht L, Horning SJ, et al. Revised response criteria for malignant lymphoma. J Clin Oncol 2007;25:579-86.

6. Juweid ME, Stroobants S, Hoekstra OS, Mottaghy FM, Dietlein M, Guermazi A, et al. Use of positron emission tomography for response assessment of lymphoma: Consensus of the Imaging Subcommittee of International Harmonization Project in lymphoma. J Clin Oncol 2007;25:571-8.

7. Geus-Oei LF, van der Heijden HF, Corstens FH, Oyen WJ. Predictive and prognostic value of FDG-PET in nonsmall-cell lung cancer: a systematic review. Cancer 2007;110:1654-64.

8. Mawlawi O, Townsend DW. Multimodality imaging: an update on PET-CT technology. Eur J Nucl Med Mol Imaging 2009;36 Suppl 1:S15-S29.

9. Pichler BJ, Judenhofer MS, Wehrl HF. PET/MRI hybrid imaging: devices and initial results. Eur Radiol 2008;18:1077-86.

10. Beyer T, Antoch G, Muller S, Egelhof T, Freudenberg LS, Debatin J, et al. Acquisition protocol considerations for combined PET-CT imaging. J Nucl Med 2004;45 Suppl 1:25S-35S.

11. Beyer T, Antoch G, Bockisch A, Stattaus J. Optimized intravenous contrast administration for diagnostic wholebody 18F-FDG PET-CT. J Nucl Med 2005;46:429-35.

12. Townsend DW. Physical principles and technology of clinical PET imaging. Ann Acad Med Singapore 2004;33:133-45.

13. Lubberink M, Boellaard R, van der Weerdt AP, Visser FC, Lammertsma AA. Quantitative comparison of analytic and iterative reconstruction methods in 2- and 3-dimensional dynamic cardiac 18F-FDG PET. J Nucl Med 2004;45:2008-15. 14. Lartizien C, Kinahan PE, Swensson R, Comtat C, Lin M, Villemagne V, et al. Evaluating image reconstruction methods for tumor detection in 3-dimensional whole-body PET oncology imaging. J Nucl Med 2003;44:276-90.

15. van der Weerdt AP, Boellaard R, Knaapen P, Visser CA, Lammertsma AA, Visser FC. Postinjection transmission scanning in myocardial 18F-FDG PET studies using both filtered backprojection and iterative reconstruction. J Nucl Med 2004;45:169-75.

16. von Schulthess GK, Steinert HC, Hany TF. Integrated PET-CT: current applications and future directions. Radiology 2006;238:405-22.

17. Watson CC. New, faster, image-based scatter correction for 3D PET. IEEE Trans Nucl Sci 2000;47:1587-94.

18. Anderson JM, Mair BA, Rao M, Wu CH. Weighted leastsquares reconstruction methods for positron emission tomography. IEEE Trans Med Imaging 1997;16:159-65.

19. Browne J, de Pierro AB. A row-action alternative to the EM algorithm for maximizing likelihood in emission tomography. IEEE Trans Med Imaging 1996;15:687-99.

20. Boellaard R, van Lingen A, Lammertsma AA. Experimental and clinical evaluation of iterative reconstruction (OSEM) in dynamic PET: quantitative characteristics and effects on kinetic modeling. J Nucl Med 2001;42:808-17.

21. Westerterp M, Pruim J, Oyen W, Hoekstra O, Paans A, Visser E, et al. Quantification of FDG PET studies using standardised uptake values in multi-centre trials: effects of image reconstruction, resolution and ROI definition parameters. Eur J Nucl Med MoI Imaging 2007;34:392-404.

22. Visvikis D, Cheze-LeRest C, Costa DC, Bomanji J, Gacinovic S, Ell PJ. Influence of OSEM and segmented attenuation correction in the calculation of standardised uptake values for [18F]FDG PET. Eur J Nucl Med 2001;28:1326-35.

23. Defrise M, Kinahan PE, Townsend DW, Michel C, Sibomana M, Newport DF. Exact and approximate rebinning algorithms for 3-D PET data. IEEE Trans Med Imaging 1997;16:145-58.

24. Karp JS, Surti S, Daube-Witherspoon ME, Muehllehner G. Benefit of time-of-flight in PET: experimental and clinical results. J Nucl Med 2008;49:462-70.

25. Brix G, Doll J, Bellemann ME, Trojan H, Haberkorn U, Schmidlin P, et al. Use of scanner characteristics in iterative image reconstruction for high-resolution positron emission tomography studies of small animals. Eur J Nucl Med 1997;24:779-86.

26. Mourik JE, Lubberink M, van Velden FH, Kloet RW, van Berckel BN, Lammertsma AA, et al. In vivo validation of reconstruction-based resolution recovery for human brain studies. J Cereb Blood Flow Metab 2010;30:381-9.

27. Weber WA. Positron emission tomography as an imaging biomarker. J Clin Oncol 2006;24:3282-92.

28. Avril N, Sassen S, Schmalfeldt B, Naehrig J, Rutke S, Weber WA, et al. Prediction of response to neoadjuvant chemotherapy by sequential F-18-fluorodeoxyglucose positron emission tomography in patients with advancedstage ovarian cancer. J Clin Oncol 2005;23:7445-53.

29. Borst GR, Belderbos JSA, Boellaard R, Comans EF, De Jaeger K, Lammertsma AA, et al. Standardised FDG uptake: a prognostic factor for inoperable non-small cell lung cancer. Eur J Cancer 2005;41:1533-41.

30. Boellaard R. Standards for PET image acquisition and quantitative data analysis. J Nucl Med 2009;50 Suppl 1:11S-20S.

31. Boellaard R, O'Doherty MJ, Weber WA, Mottaghy FM, Lonsdale MN, Stroobants SG, et al. FDG PET and PET-CT: EANM procedure guidelines for tumour PET imaging: version 1.0. Eur J Nucl Med Mol Imaging 2010;37:181-200.

32. Boellaard R, Oyen WJ, Hoekstra CJ, Hoekstra OS, Visser EP, Willemsen AT, et al. The Netherlands protocol for standardisation and quantification of FDG whole body PET studies in multi-centre trials. Eur J Nucl Med Mol Imaging 2008;35:2320-33.

33. Shankar LK, Hoffman JM, Bacharach S, Graham MM, Karp J, Lammertsma AA, et al. Consensus recommendations for the use of F-18-FDG PET as an indicator of therapeutic response in patients in national cancer institute trials. J Nucl Med 2006;47:1059-66. 34. Young H, Baum R, Cremerius U, Herholz K, Hoekstra O, Lammertsma AA, et al. Measurement of clinical and subclinical tumour response using [18F]-fluorodeoxyglucose and positron emission tomography: review and 1999 EORTC recommendations. European Organization for Research and Treatment of Cancer (EORTC) PET Study Group. Eur J Cancer 1999;35:1773-82.

35. Boellaard R, Krak NC, Hoekstra OS, Lammertsma AA. Effects of noise, image resolution, and ROI definition on the accuracy of standard uptake values: a simulation study. J Nucl Med 2004;45:1519-27.

36. Krak NC, Boellaard R, Hoekstra OS, Twisk JW, Hoekstra CJ, Lammertsma AA. Effects of ROI definition and reconstruction method on quantitative outcome and applicability in a response monitoring trial. Eur J Nucl Med MoI Imaging 2005;32:294-301.

37. Stahl A, Ott K, Schwaiger M, Weber WA. Comparison of different SUV-based methods for monitoring cytotoxic therapy with FDG PET. Eur J Nucl Med Mol Imaging 2004;31:1471-9.

38. Thie JA. Understanding the standardized uptake value, its methods, and implications for usage. J Nucl Med 2004;45:1431-4.

39. Weber WA. Use of PET for monitoring cancer therapy and for predicting outcome. J Nucl Med 2005;46:983-95.

40. Wahl RL, Jacene H, Kasamon Y, Lodge MA. From RECIST to PERCIST: evolving considerations for PET response criteria in solid tumors. J Nucl Med 2009;50 Suppl 1:122S-150S.

41. Jaskowiak CJ, Bianco JA, Perlman SB, Fine JP. Influence of reconstruction iterations on F-18-FDG PET-CT standardized uptake values. J Nucl Med 2005;46(3):424-428.

42. Visvikis D, Cheze-LeRest C, Costa DC, Bomanji J, Gacinovic S, Ell PJ. Influence of OSEM and segmented attenuation correction in the calculation of standardised uptake values for [18F]FDG PET. Eur J Nucl Med. 2001;28:1326-35.

43. Dai KS, Tai DY, Ho P, Chen CC, Peng WC, Chen ST, et al. Accuracy of the EasyTouch blood glucose self-monitoring system: a study of 516 cases. Clin Chim Acta. 2004;349:135-41.

Chapter 4: CT instrumentation and principles of CT protocol optimisation

Ann Heathcote, Amy Wareing, Angela Meadows

Introduction

This chapter commences with an overview of computed tomography (CT) development and an outline of the basic CT system configuration. Image production is then discussed, focussing on image acquisition, reconstruction and post-processing. Thereafter, general parameters and terminology for CT are highlighted to support the remainder of the chapter, which addresses CT protocol optimisation and attenuation correction in PET-CT. Kev relevant pitfalls are considered which can lead to degradation of the PET and CT image guality when best practice is not followed. It is recommended that if you have no prior knowledge of or background in CT, you should read the recommended literature and references to gain greater insight into the subject.

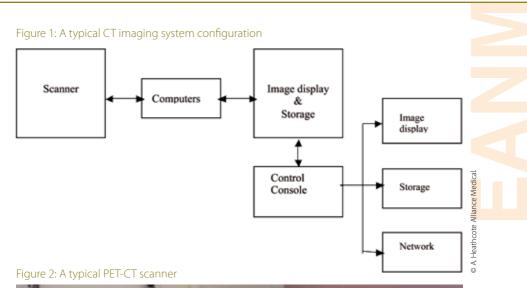
The development of CT and basic construction of a CT scanner

CT scanning was invented by Geoffrey Hounsfield in the 1970s. In the beginning only one image was produced per rotation of the x-ray tube and image quality was consequently very poor compared with the detail and resolution achievable today.

CT technology has developed significantly over the last 20 years, with the advent of spiral CT in the 1990s and the subsequent introduction first of dual-slice CT scanners and then of multi-slice scanners with the capability of generating 16, 64 and 128 slices per rotation. To help understand the fundamental principles of CT, knowledge of the basic CT imaging system configuration is required. Figure 1 identifies the three main components: the CT scanner, the computers that control the scanner and the image display/image archive aspects of the system.

Figure 2 demonstrates a typical PET-CT scanner. The two systems share the same housing, with the CT scanner to the front and PET to the rear. The central bore and surrounding structures within the housing are referred to as the gantry.

The gantry is a rotating framework that the patient moves through on the patient table during data acquisition. It holds the x-ray tube, x-ray generator, slip rings, detectors, collimators and digital acquisition system (DAS) [1]. The x-ray tube is responsible for the production of x-ray photons. The filters are responsible for removing low-energy x-ray photons, thereby reducing patient dose (to be detailed later in this chapter). The collimators are used to define the slice thickness and localise the x-ray field to the area of interest. The detectors capture the x-ray photons after they have passed through the patient and convert them ultimately into digital information via the DAS.





© A. Meadows Alliance Medical.

During the examination, the patient lays on the patient table. The table moves through the scanner gantry during the CT acquisition and subsequently moves further into position for the PET scan to the rear of the housing. There is a weight limit for the table to ensure that it will move reliably during image acquisition.

The computer system that 'controls' the scanner receives image data from the DAS and applies a series of reconstruction algorithms to produce a cross-sectional image.

Image acquisition, reconstruction and post-processing

The basic system configuration has been outlined above; we shall now focus on image production, sub-categorised as image acquisition, reconstruction and post-processing.

<u>Acquisition</u>

As the x-ray tube rotates around the patient, the detectors measure the radiation transmitted through the patient from various locations (Fig. 3). The attenuation measurements are calculated by the computer and stored as raw data files (also called projections). Modern scanners collect projections from 360° and typically measure 800-1500 projections per image.

Attenuation is the reduction of the intensity of a beam of radiation as it passes through an object – some photons are absorbed, others are scattered. In CT, attenuation depends on the effective atomic density (atoms/vol), the atomic number of the absorber and the photon energy (Fig. 3).

The computer system receives the digital data from the DAS and processes it to reconstruct the cross-sectional image. The computer system also enables general image techniques such as windowing, multi-planar reconstructions and 3D imaging [1].

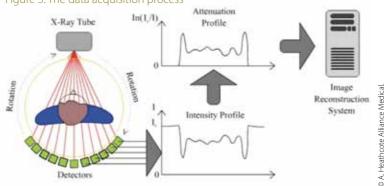


Figure 3: The data acquisition process

Reconstruction

The differential attenuation information is acquired by the detectors and converted to a digital signal. The computer processes involved in image reconstruction include algorithms, convolution and interpolation. An algorithm is basically a mathematical formula – in the CT scenario, algorithms are used to reconstruct the image. Convolution is a mathematical process applied to modify an image. Interpolation is specifically used in helical scanning and is a mathematical process to calculate or estimate information based on known values of adjacent information.

Interpolation

Linear interpolation (Fig. 4) also known as z-interpolation, allows the generation of a consistent data set from the volume using an arbitrary image position known as z_R . It enables the linear interpolation of data measured at a specified angular position just before and after a set table (slice) position (z_R).

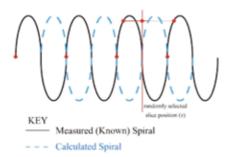


Figure 4: Diagram demonstrating interpolation

The interpolation process is required since the calculation of images from a 360° spiral results in image artefacts, as different areas of the object are measured at the start and end of the segment.

Convolution and back-projection

The interpolated data then undergo the convolution-back-projection procedure to produce the final CT image. In back-projection, each projection value that is produced is placed into the corresponding area in an imaging matrix. In simple back-projection, each projection value is added to all areas of the picture along the direction in which it has been acquired [2].

The back-projection method on its own results in an unsharp and inadequate image. To remove the unsharpness, each projection is 'convoluted' prior to back-projection being done. It is important to note that convolution and back-projection would warrant a chapter in their own right, and we therefore recommend further reading to study this concept in more depth if further clarification is required.

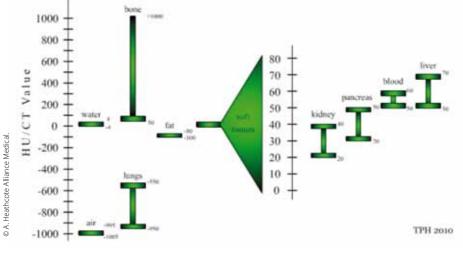
The CT image

CT is the measurement and 'demonstration' of the linear attenuation coefficients $\mu(x,y)$ of the structures that the x-ray beam passes through during the examination. The value μ is converted into a CT value relative to the attenuation of water; this is to make the value more user friendly. The CT value/number is displayed in Hounsfield units (HU). For a tissue (T) with an attenuation coefficient $\mu_{\rm tr}$ the CT value is defined as [2]:

CT value = ($\mu_T \ \mu_{water}$) / μ_{water} × 1000 HU



Therefore, each individual tissue type, e.g. fat or bone, is displayed with a different HU/CT value. Generally, the following CT values are accepted: water = 0, air = -1000 and dense bone = +1000. Figure 5 presents the Hounsfield scale and provides further example values for various tissue densities.



Post-processing

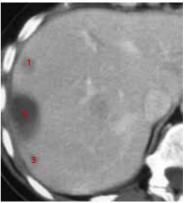
Post-processing is the term used to describe how the resultant CT image can be manipulated by the operator. A wide variety of post-processing functions are available to the CT operator:

- Windowing the manipulation of the contrast within the image to demonstrate certain structures or tissue types
- Multi-planar reconstructions (MPRs) generation of 2D images in the sagittal/coronal/axial plane

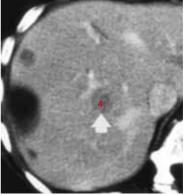
 3D imaging – the generation of 3D images such as surface-shaded (SSD) reconstructions used in orthopaedic imaging and maximum intensity projections (MIPs) Manipulation of the window width (WW) and window level (WL) is the most commonly used post-processing technique in CT [1]; WW is defined as the range of the CT numbers within the image and WL is defined as the number at the centre/mid point of the range. For example, when viewing the images, we select a WL setting to represent the density of the tissue of interest, e.g. WL 40 = kidney. The WW determines the amount of contrast within the image set, e.g. WW = 400. Therefore, in this example the range of levels demonstrated will be from -160 to +240. It is important to note that the narrower the WW. the greater will be the contrast within the image. Figure 6 provides an example of how the choice of settings can influence the imaging findings.

Upon completion of post-processing the CT data, the resultant images will be archived. For the purposes of PET, the data will have been used for attenuation correction of the PET data and subsequently the CT data will be presented as CT and fused PET-CT datasets to assist in anatomical localisation of pathologies (to be discussed later in the chapter). Ultimately, the image data can be archived onto either optical disc or CD or directly onto picture archiving communication systems (PACS).

Figure 6a,b: Images of liver metastases. Three liver metastasis (1-3) can be seen using standard abdominal window settings of 400 WW and 40 WL (a) but a fourth metastasis (4, arrow) can be clearly identified when using a narrow WW/WL setting of 250 WW and 40 WL (b)



A. Heathcote Alliance Medica



General parameters and terminology for CT Below is a list of the common parameters and terminology that are used in CT. Awareness of these will be required for the remainder of this chapter.

- Acquisition process in which a single continuous set of scan data is acquired without a pause
- kV penetrating power of x-ray
- mA tube current
- mAs mA × s
- s time (seconds)
- Pitch longitudinal distance (mm) that the table moves during one rotation of the tube
- Pitch ratio (PR) the pitch divided by the slice thickness, e.g. 1.5 or 1.5:1
- Image index (II) the distance (mm) between the centre of two consecutive slices
- Images per revolution pitch divided by image index
- Number of images total number of images reconstructed for one acquisition

CT protocol optimisation (dose reduction strategies)

A number of methods and techniques are available to minimise the radiation dose to a patient undergoing a CT examination, including Auto mA, Smart mA, mA range limitation and optimum patient positioning:

1. Auto mA – mA modulation per rotation based on the last acquired scout and noise index selected by the user. Auto mA modulates the patient dose in the z-direction and ensures consistent image quality independent of patient size.

The noise index value (NI) allows the user an absolute method to reproduce the same scan at a later date. The NI represents the number of x-ray photons per rotation and can be user defined; it is unique to the slice thickness and body part selected. Selection of the NI reflects the level of noise acceptable to the radiologist for a given CT examination. The CT scanner will then automatically select, within a preset range, the tube current (mA) required to maintain the level of noise under the NI, taking into account the patient's attenuation.

2. Smart mA – mA modulation as the tube rotates around the patient. The mA table per rotation is based on the last acquired scout and noise index selected. Smart mA can be used in conjunction with Auto mA to further reduce patient dose. When using Smart mA, the beam is modulated four times to minimise the dose (Fig. 7).

Figure 7: Dose modulation when using Smart mA Sector-1 © General Electric Company. Sector-2 Sector-4 All rights reserved.

Sector-3

3. mA range limitation – The mA exposure used can be 'capped' when a preset maximum level is

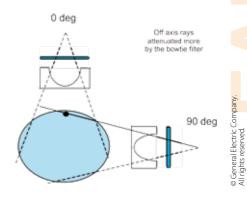
reached. This has its limitations, however, in that

when the maximum mA is reached, the resultant image quality is adversely affected as the noise within the image is greater than that of

the selected NI. As a result, consideration must be given to a compromise. For the purpose of PET-CT only a low-dose image acquisition is required as the intention is to acquire an image more specifically for the purpose of attenuation correction for the PET data (typically an mA of 80-110 is used as a capped value). As it is not intended to produce images of 'diagnostic' CT value unless specifically requested, some image degradation is to be expected on the CT.

4. Patient position - As PET-CT systems have the ability to vary the height of the table when the patient is within the gantry, it is essential that the technologist knows the importance of centralising the patient within the field of view and understands the impact this can have on subsequent image quality and patient surface dose, particularly as filters are used in CT in an effort to improve both factors. In CT, 'bowtie' filters are used to reduce the surface dose by attenuating the unwanted x-rays at the edge of the beam (Fig. 8).

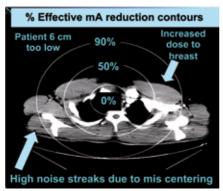




It is important to ensure that the correct scan field of view (SFOV), i.e. bowtie filter, is selected. For example, the head SFOV adds an extra algorithm to post-processing to reduce the beamhardening effect at the bone/brain interface. This is a factor which should be considered during imaging protocol management at the initial protocol set-up for PET. Nonetheless, the technologist must understand how filter selection and, more importantly, patient position within the gantry can impact on image guality and patient surface dose if the patient is not centered within the FOV. Figure 9 demonstrates how patient dose can be adversely affected if the patient is not correctly centered and how images are degraded. Subsequently, the poor quality CT data will in turn reduce the quality of the attenuation-corrected PET data, for which

the CT scan is initially acquired. Consequently, the noise within the image is also increased by mis-centering the patient (Fig. 10).

Figure 9: The effect of mis-centering on the patient dose

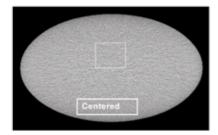


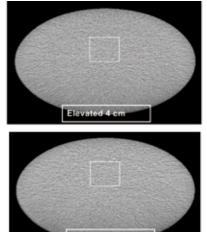
If the patient is off centre, with a fixed mA, too little dose will reach the centre of the patient as it will be filtered out, and the body surface will receive excessive dose. More importantly, when using Auto mA, if the patient is off centre, the calculations for Auto mA will be incorrect. Calculations for mA based on attenuation are taken at the isocentre of the scanner. Therefore, good positioning and use of positioning lasers is critical to make best use of the filters, thus improving image quality and reducing patient surface dose.

Figure 10: Effect of mis-centering on noise within the image

	σ	noise ir	nc. mA boost	
Cent	6.47	0 %	0%	
4 cm	8.40	30%	68%	
6 cm	9.22	43%	100%	

30 x 21.5 cm poly phantom Axial images scanned at 120 kv, 200 mA, 2.5 mm, 1 s





Elevated 6 cm

© General Electric Company All rights reserved.

Attenuation correction in PET-CT imaging

Presuming that an adequate low-dose CT acquisition for the purpose of PET has been acquired, we now need to consider how these data is used for the purpose of attenuation correction of the PET data.

The process of correcting images for attenuation artefacts in nuclear medicine has been widely utilised for many years. Attenuation in nuclear medicine imaging is described as the loss of detection of true gamma ray events due to either scattering out of the FOV of the detector or absorption within the body. Attenuation effects are more severe for coincidence imaging than for single-photon imaging (SPECT) [3]. Despite the photons being of a greater energy than those used in SPECT, PET relies on two photons simultaneously escaping across a greater mean photon path distance to be detected as a true event. The loss of true coincidence event detection in PET is known to range from 50% upwards to as high as 90% in large patients [4]. Loss of counts from attenuation correction (AC) increases image noise, image artefacts and image distortion (Fig. 11), and these problems are magnified when imaging larger patients (Fig. 12).

Figure 11: Comparison between non-AC and AC PET MIP images in a patient with an average BMI

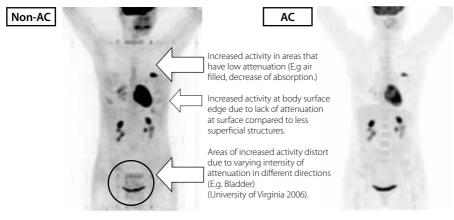
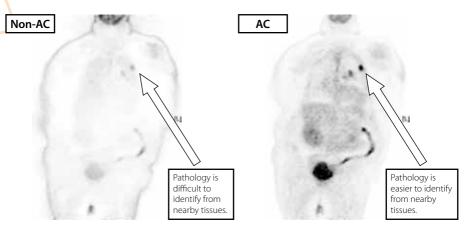


Figure 12: Comparison between non-AC and AC PET coronal images of a patient with a high BMI

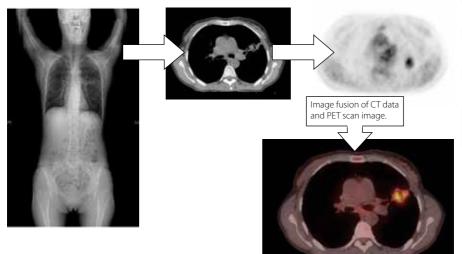
O A. Wareing Alliance Medical.



Attenuation correction may or may not improve lesion detection, depending upon body habitus, distribution of FDG and so on. Nonetheless, it will produce a more realistic radioactivity distribution which is essential for quantification of tracer uptake; the values produced are referred to as standardised uptake values (SUVs) [5].

Methods of attenuation correction in PET

Historically, prior to the use of CT, a transmission scan was used to correct for attenuation of emission data in PET imaging. Early generation scanners utilised germanium-68/gadolinium-68 rotation rod sources to produce transmission images. Later generation scanners combined PET and CT in a single housing. Almost all of the new sales for PET imaging are combined PET-CT scanners [6]. This is largely due to the practical and effective approach of acquiring co-registered anatomical and functional images in a single scanning session. Figure 13 demonstrates PET with CT attenuation correction. Much work has been conducted indicating that fusion of PET and CT image data significantly increases both sensitivity and specificity (see [7] for an early study). Figure 13: Example of PET with CT attenuation correction Top left: whole-body CT scout image; top middle: CT, axial slice showing lung pathology; top right: same axial slice, PET-only data. Below: fused axial slice demonstrating co-registration of functional and anatomical information



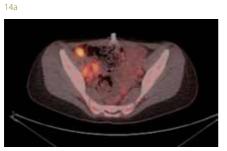
Attenuation correction and potential pitfalls At present, CT is the AC of choice. In addition to the advantages of CT-AC discussed above, it is however important to recognise the potential pitfalls of this method. Most oncology patients referred for a PET examination have undergone a diagnostic CT examination with or without intravenous or ingested contrast solutions. Therefore, PET-CT examinations are most commonly carried out using a low-dose CT technique, which is often labelled 'non-diagnostic'. As a result, the potential for bias in CT-AC can be high. This is because the measured CT Hounsfield unit (HU), related to the linear attenuation seen by the x-ray beam, must be transformed to the corresponding higher PET

photon energy (511 keV) [8]. The pixels are then segmented based on their HU and scaled accordingly by various algorithms. Although most applications using the very latest software can correct for discrepancies, there is a tendency for AC algorithms to 'over-correct' occasionally.

Much literature has been produced discussing CT-AC over-correction artefacts, including IV contrast agents, oral contrast preparations, chemotherapy ports and dense/metallic objects. A relatively simple and essential solution for any interpreting physician is to assess the non-AC PET images during the reporting review; it is therefore essential that non-AC data are always provided for interpretation [8]. Figure 14 provides two examples where image artefacts are apparent and streaking can be seen across the CT image, causing a potential for over-correction artefact. Clearly the pacemaker demonstrates a marked difference and is unavoidable. However, the metal button on a patient's trousers could have been avoided with better patient preparation.

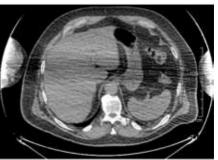
Figure 14a,b: CT-AC and potential for overcorrection. a A pacemaker causing streak artefact; b a metal button on a patient's trousers



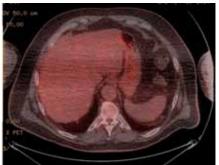


14b

Figure 15a,b: Patient arm position affecting AC when using low-dose CT



© A. Wareing Alliance Medical



15b

© A. Wareing Alliance Medical

Although artefacts from CT attenuation can occur due to poor positioning within the FOV (as previously discussed), equally scanning patients with their arms by their side can result in beamhardening/streak artefacts across the abdomen, where there is the greatest patient density (Fig. 15). Therefore, good practice requires that patients are scanned with their arms raised above their head if at all possible. If the patient can raise only one arm, then this is accepted as a compromise. If the arms are required in the FOV as part of a total body scan where the skin is the focus of the study, they should be appropriately immobilised over the anterior aspect of the abdomen; this ensures they are within the FOV and thus reduces the beam-hardening effect.

Conclusion

In summary, an overview has been provided of CT development, basic system configuration and the instrumentation and principles of CT. More specifically, potential pitfalls have been discussed, from patient position and preparation through to 'over-correction' complications. It is essential that the technologist is aware of the pitfalls to avoid prior to image acquisition, and that the image interpreter is also aware of the pitfalls and how they are presented when inevitable - particularly the importance of making reference to non-AC image data. In concluding, we would once again emphasise that if you have little prior knowledge of or background in CT, it would be advisable to read the suggested texts to gain a greater depth of knowledge on the subject.

References Chapter 4

References

 Seeram E. Computed tomography – physical principles, clinical applications and quality control. 3rd ed. St. Louis: Saunders; 2009.

2. Kalender WA. Computed tomography – fundamentals, system technology, image quality, applications. Erlangen: Publicis MCD Verlag; 2000.

3. Turkington TG. Attenuation correction in hybrid positron emission tomography. Semin Nucl Med 2000;30:2255-67.

4. University of Virginia. Attenuation correction. Published by the Rector and Visitors of the University of Virginia. 2006.

http://www.med-ed.virginia.edu/courses/rad/PETCT/Attenuation.html

5. Kamel E, <u>Hany TF, Burger C, Treyer V, Lonn AH, von</u> <u>Schulthess GK</u>, et al. CT vs 68Ge attenuation correction in a combined PET/CT system: evaluation of the effect of lowering the CT tube current. Eur J Nucl Med Mol Imaging 2002;29:346-50.

6. BIO-TECH Systems Inc. The market for PET radiopharmaceuticals and PET imaging. BIO-TECH Report # 300. Las Vegas: BIO-TECH Systems Inc; 2008.

7. Beyer T, Townsend DW, Brun T, Kinahan PE, Charron M, Roddy R, et al. A combined PET/CT scanner for clinical oncology. J Nucl Med 2000;41:1369-79.

8. Mehta A, Mehta A, Laymon C, Blodgett CM. Calcified lymph nodes causing clinically relevant attenuation correction artifacts on PET/CT imaging. J Radiol Case Reports 2010;4:31-7.

Suggested reading

Brink JA. PET/CT unplugged: the merging technologies of PET and CT imaging. AJR Am J Roentgenol 2005;184:S135-7.

Costa DC, Visvikis D, Crosdale I, Pigden I, Townsend C, Bomanji J, et al. Positron emission and computed X-ray tomography: a coming together. Nucl Med Commun 2003;24:351-8.

Kalender WA. Computed tomography – fundamentals, system technology, image quality, applications. Erlangen: Publicis MCD Verlag; 2000.

Kinahan P. CT-based attenuation correction for PET/CT scanners (ppt). Imaging Research Laboratory, Dept. of Radiology, University of Washington. USA. 2005.

http://depts.washington.edu/nucmed/IRL/ pims/2005_03_30/PETCTACv2r.pdf

Seeram E. Computed tomography – physical principles, clinical applications and quality control. 3rd ed. St. Louis: Saunders; 2009.

Wahl RL. Why nearly all PET of abdominal and pelvic cancers will be performed as PET/CT. J Nucl Med 2004;45 Suppl 1:82S-95S.

Chapter 5: Quality assurance and quality control for PET-CT

Peter Julyan

Introduction

As with all medical imaging equipment, when using PET-CT there is a legal requirement for a quality assurance (QA) programme to be in place which includes appropriate quality control (QC) procedures. A successful QA programme will reduce image artefacts by reducing the likelihood of scanning patients with malfunctioning equipment. Record keeping is a necessary part of any QA programme in that it demonstrates that appropriate tests have been performed and their results, monitored. Careful monitoring of results should increase system uptime and improve image guality by identifying faults promptly. For PET-CT systems, the general principles are the same as for any nuclear medicine imaging equipment, with two additional factors: firstly the inclusion of CT, and secondly the more quantitative nature of PET imaging.

This article outlines the requirements for instrumentation QA and QC with current PET-CT equipment, concentrating on the PET aspects. In doing so, it is recognised that virtually all current equipment combines a PET scanner with an x-ray CT scanner. In addition, most investigations involve imaging the trapped tracer of glucose metabolism, fluorine-18 fluorodeoxyglucose (FDG), usually in whole-body mode and predominantly in oncology.

It is to be noted that some aspects explicitly beyond the scope of this article, such as patient preparation, may be just as important for the overall quality of the diagnostic information obtained through the PET-CT investigation; information on these aspects can be obtained elsewhere [e.g. 1, 2].

QA programme

Any QA programme commences with the work done at installation to correctly set up the system and conduct a set of performance measures, which should follow the current NEMA NU 2-2007 standard [3]. The goal here is not generally to produce an exhaustive set of performance measure data to fully characterise the equipment (as may be suitable for a benchmark publication on that particular equipment) but to confirm the performance parameters from the tender process and act as a baseline for follow-up measurements.

The subsequent service programme will include periodic service visits and regular calibration. Fundamentally, calibration will set the gain of the photomultiplier tubes to give appropriate signals for 511-keV photons within an appropriate energy window. These signals are then used to correctly identify individual detector elements. For coincident events a timing calibration is then required. With the recent emergence of time-of-flight capable scanners from the major manufacturers, another level of calibration is necessary and there is potential for drift from optimal settings. As with gamma cameras, the uniformity of response will then be measured to high precision (typically with a long, low count-rate acquisition) and is used in data reconstruction – this is often termed the normalisation for PET systems.

A vital part of the calibration of a PET system is the absolute calibration such that results may be expressed quantitatively in terms of kBq/ ml. For this purpose, a known source generally of ¹⁸F is accurately measured in a dose calibrator. (For historical reasons this may be referred to as the well counter calibration.) This will be discussed in more detail later.

The frequency of repeat calibration should be guided by the manufacturer's recommendations and will vary from system to system.

Regardless of the mechanism of calibration, validation of the scanner must reflect the intended range of studies to be performed. Thus, if whole-body acquisitions are to be performed, whole-body acquisitions of ¹⁸F or ⁶⁸Ge phantom(s) must be carried out, checking for example that suitable overlap between bed positions has been set. Similarly, if dynamic acquisitions are to be performed, a representative dynamic validation should be carried out. Such validation can be done, for example, with a decaying source of ¹⁸F with dynamic framing typical of the intended frame durations; this enables one to check that, for example, the scatter correction is robust down to the shortest intended frame duration. Analysis of such acquisition will give the user either a decaying curve (which should be fitted to give the correct half-life) or a pre-corrected flat line. Either way, such a test enables the user to understand the data from the scanner. For a gated acquisition (whether cardiac or respiratory) it may sound redundant to perform a phantom scan of a static source, but this will check that equal sensitivity is given to each bin.

More extensive testing may be appropriate annually, when a full assessment of the CT performance should be undertaken and the user may wish to repeat some of the initial NEMA performance measures, perhaps most usefully the image quality phantom.

PET daily QC

The basis for PET scanner QC is the daily blank sinogram formed by irradiating the detectors approximately uniformly with 511-keV photons from a long-lived positron source, typically a rotating 68Ge rod source within the gantry or a ⁶⁸Ge cylinder placed within the field of view. This is analogous to a uniform ⁵⁷Co flood as would be used for gamma camera OC. As there is not a one-to-one relationship between the sinograms and the detector elements, the data are often re-sorted into fansums, as though the whole detector ring had been opened up and laid flat. This is illustrated in Fig. 1, where two sinograms are shown at the top with the fansum for the entire detector assembly at the bottom. Individual detector elements identified as yellow and green points correspond to lines in the sinograms.



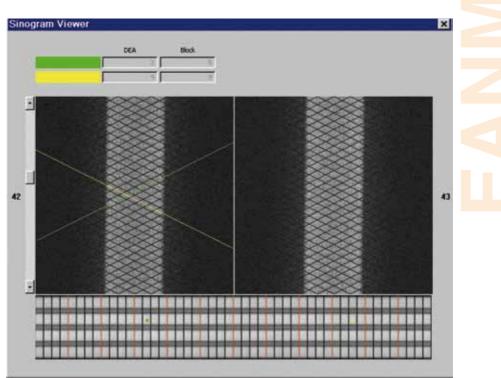
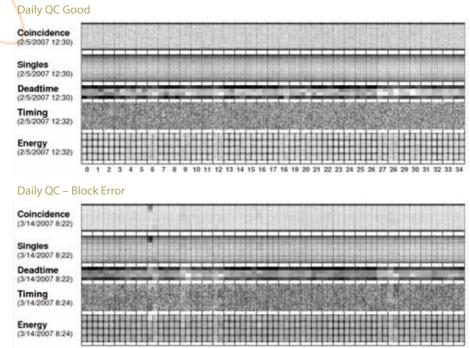


Figure 1: Daily QC sinogram and fansum images (resulting from irradiation with a ⁶⁸Ge cylinder in the centre of the field of view on a Siemens system)

In general the manufacturer's software will automatically compare the current readings with a reference set – typically acquired at the last service visit – but the user should be aware of how these are generated. In the example in Fig. 2, one of the detector blocks was giving very few counts and required attention. Exactly when errors seen in daily QC measurements give rise to significant problems is not easy to define, which is why users may prefer to study reconstructed images rather than the somewhat less direct sinogram or fansum.



Courtesy of The Christie NHS Foundation Trust

Figure 2: Daily QC fansum images for various detector parameters for good performance (above) and with a block error (below) (resulting from irradiation with an internal ⁶⁸Ge rod on a GE system)

When a central ⁶⁸Ge cylinder is used, this data set may be employed to reconstruct an image which may be analysed to give an image set of the appropriate activity level and uniformity in line with recent measurements. Indeed, such a daily check of quantitative accuracy can be very useful and such measurement (with either ⁶⁸Ge or ¹⁸F) may be required for clinical trials where quantification of the data is important.

Quantitative PET

There is the additional requirement in PET that the images produced should invariably be fully quantitative, with uptake in each voxel being expressed in terms of kBq/ml. On this basis, the standardised uptake value, SUV, is calculated by normalising for the administered activity and patient weight (or a variant there-of). This provides more refined diagnostic information but also requires additional quality

considerations. While the following may seem obvious, careful adherence is vital and sites have been found wanting in this respect [4, 5].

Ultimately the calibration of the scanner is tied (via the scanner calibration process) to the radioactive dose calibrator upon which injections are measured. There is guite rightly the requirement that this calibrator must be accurate and traceable to national primary standards so that patient injected activities and therefore effective doses are as intended. Nevertheless, in terms of calculating SUVs, a dose calibrator error would lead to a wrong scanner calibration and these errors would cancel each other out, leading to correct SUVs. It is important, though, to realise that the scanner is directly tied to a specific dose calibrator and there may be departments where small errors between calibrators (acceptable within 5% of the national standard, say) could introduce errors approaching 10% (with the calibrator off in different directions)

Just as important in the calculation of SUVs is the patient weight, and patient weighing scales must accordingly also be of suitable certified quality.

The final element in the calculation of SUVs lies in the relative timing of the injection measurement and scanning. Nowadays the ready availability of radio-controlled clocks at affordable prices offers a practical means of establishing the correct time although even here the periodic change between daylight saving times needs to be carefully observed.

Correction for the residual activity post injection must be applied, but this is complicated by the rapid decay of ¹⁸F, necessitating thoughtful application of decay corrections.

For repeat imaging in the same patient, as many factors as possible must be kept constant. On each occasion it must be ensured that the patient is in the fasting state by checking blood glucose levels. Consistency in the timing of the emission measurement is also important, as even at between 60 and 90 min after injection there can still be appreciable changes in the SUV.

The final and crucial part in the generation of results is the analysis software. It should also be recognised that for the calculation of SUVs this software should be checked to give correct results, using it in exactly the same way as is intended to be done for patients.

CT QA/QC

While the CT component of PET-CT is often used as fairly modest quality CT for the purpose of attenuation correction and anatomical localisation of PET abnormalities, the requirements for QA/QC are the same. It is necessary to have a QA programme in place that recognises the need to produce appropriate quality CT images at the intended patient effective dose [6]. An annual check by experts in diagnostic radiology equipment testing will assess the general radiation safety, CTDI (computed tomography dose index), slice width, absolute CT number, noise and resolution.

A useful and simple daily or weekly test of the CT should be undertaken to ensure that it gives the correct value (in Hounsfield Units, HU) for water, i.e. ~0 HU, with consistent noise levels.

Combined PET-CT QA/QC

The fundamental requirement of the combined PET-CT data sets is that they are correctly spatially aligned. The manufacturer will have procedures to set the physical alignment of the separate gantries to a certain tolerance together with acquisition of a specific test object to measure and correct for any residual misalignment. It is recommended that as well as having an awareness of these operations, users should consider independent tests. A combined PET-CT acquisition of an ¹⁸F or ⁶⁸Ge cylinder is a simple form of such a test. More sophisticated tests using small points filled with a mixture of radioactivity and contrast medium may also be undertaken and may include more extensive movement of a fully loaded bed

The inclusion of a full PET-CT acquisition in the daily or weekly QC has the advantage of testing the full patient acquisition including the database, table movement and alignment of the PET and CT data sets.

For clinical trials, there may be a requirement to send off data for pooled analysis across many sites. This should always be done with phantom data prior to imaging the first patient, and all the steps must be followed that would be performed on patient data. For example, if it is necessary to use a specific method to anonymise patient images, this method should be applied to the phantom data, too.

There are additional requirements if the PET-CT is to be used for radiotherapy planning. Firstly, patient positioning must aim to be as close as possible to that which will be used during the radiotherapy, with appropriate patient supports and an appropriate room laser alignment system. The integrity of the PET-CT in its transfer to the radiotherapy planning system is also vital. If the CT portion is to be used in the generation of radiotherapy plans, there will be additional and possibly more stringent requirements in terms of bed deflections and absolute calibration of the CT numbers. Most important is the close cooperation among various staff groups in nuclear medicine and radiotherapy departments.

References

1. Delbeke D, Coleman RE, Guiberteau MJ, Brown ML, Royal HD, Siegel BA, et al. Procedure guideline for tumor imaging with 18 F-FDG PET/CT 1.0. J Nucl Med 2006;47:885-95.

2. Boellaard R, O'Doherty MJ, Weber WA, Mottaghy FM, Lonsdale MN, Stroobants SG, et al. FDG PET and PET/CT: EANM procedure guidelines for tumour PET imaging: version 1.0. Eur J Nucl Med Mol Imaging 2010;37:181–200.

3. NEMA Standards Publication NU 2-2007. Performance measurements of positron emission tomographs.

4. Westerterp M, Pruim J, Oyen W, Hoekstra O, Paans A, Visser E, et al. Quantification of FDG PET studies using standardised uptake values in multi-centre trials: effects of image reconstruction, resolution and ROI definition parameters. Eur J Nucl Med MoI Imaging 2007;34:392–404.

 Scheuermann JS, Saffer JR, Karp JS, Levering AM, Siegel BA. Qualification of PET scanners for use in multicenter cancer clinical trials: the American College of Radiology imaging network experience. J Nucl Med 2009;50:1187-93.

6. IPEM Report 91. Recommended standards for routine performance testing of diagnostic x-ray systems. 2005

Suggested reading

Bailey DL, Townsend DW, Valk PE, Maisey MN, editors. Positron emission tomography: basic sciences. Berlin Heidelberg New York: Springer; 2005.

Saha GB. Basics of PET imaging: physics, chemistry, and regulations. Berlin Heidelberg New York: Springer; 2005.

Chapter 6: PET isotope production

Katy Szczepura

Introduction

Radioisotope production for PET is generally performed by means of a cyclotron that is used to accelerate charged particles. These accelerated particles then go on to interact with a target to produce radioisotopes suitable for use in PET imaging.

This chapter will introduce the general principles of operation of a cyclotron, explain how the particles interact in the target and discuss the production of some of the isotopes commonly used in clinical PET interactions. It will also look at the general safety considerations involved in the use of cyclotrons.

The cyclotron

A cyclotron is a type of particle accelerator that accelerates charged particles, such as protons and deuterons, to high energies. Before discussing how the cyclotron works, it is important to understand how these particles behave in the presence of electric and magnetic fields.

When a charged particle is in the presence of an electric field, it will feel a force that will accelerate it in the direction of the field. If this acceleration is in the direction that the particle is already travelling in, then it will cause the particle to gain energy.

When a charged particle is in the presence of a magnetic field, it feels a force that is perpendicular to its direction of motion. This force will make the particle change its direction, but not its speed. This means that when a charged particle enters a magnetic field, it will start to travel in a circle. The faster the particle is travelling, the bigger the circle it will travel in. A cyclotron takes advantage of these two phenomena and utilises them to accelerate positively charged particles.

A cyclotron consists of two semi-circular conducting structures known as dees, with an insulating gap between them. These dees are placed between two magnets with opposite poles facing each other, so there is a magnetic field travelling from top to bottom. As the charged particles enter the magnetic field, they will travel in a circular motion around the dees.

Once the charged particles are travelling in a circular motion, there needs to be a way of accelerating them. An electric field is placed between the surfaces of the two dees, such that when the charged ion exits one dee, it will be repelled by the oppositely charged surface of that dee and attracted to the surface of the second dee. This causes the particle to accelerate and gain energy. As the particle is now travelling at a faster speed, it will move in a larger circle within the second dee.

When the particle reaches the surface of the second dee, it needs to be accelerated again, and so the surface of the second dee needs to become oppositely charged while the other surface needs to become charged to attract the particle towards it, creating further accelera-

tion. This means that the direction of the electric field needs to change just as the particle emerges between the dees. This is achieved by applying a high-frequency alternating voltage across the dee electrodes. The dees themselves are isolated, and so the particles are not affected by the electric field once they are inside.

So, a summary of this process is:

- The particle moves in a circle when in a dee.
- When it reaches the surface of the dee, it is attracted into the opposite dee due to the electric field.

- This causes the particle to accelerate.
- The particle moves in a circle when in a dee (the circle is larger due to higher speed)

This process is repeated until the particle has accelerated sufficiently, and so is travelling in a large enough circle, to be released from the dees. As this particle is now accelerated, it has gained energy. This energy is then used to interact within a target to create radioisotopes (Fig. 1).

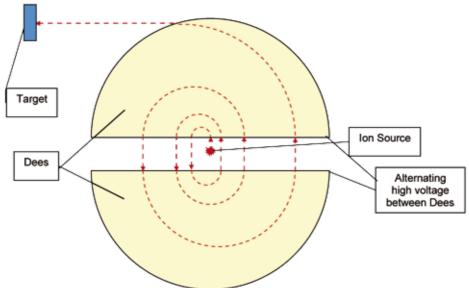


Figure 1: Diagram illustrating the operation of a cyclotron (magnetic field oriented perpendicular to the dees, not shown)

lon source

For these events to occur there has to be a source of ions, and the ion source is dependent on the isotope that is being produced, as different isotopes need different interactions between target and particle.

The ion source is a small chamber in the centre of the cyclotron that produces either negative or positive ions, depending on the configuration. These particles are attracted into the dees by electrostatic attraction.

Negative hydrogen ions (H⁻) are produced by using a tungsten filament to ionise hydrogen gas. These particles are attracted into the dees by electrostatic attraction. The electrons are stripped off the H⁻ particle using a carbon foil, leaving an accelerated proton to interact within the target.

The exiting charged particles are directed to the required target using a deviating electromagnet. This means that different isotopes can be produced using the same cyclotron depending on the target used.

Positron emitter production

Once charged particles exit the cyclotron, they can go on to produce positron emitters by interacting with a target. The isotope that is produced depends on the typed of charged particle that has been aceelerated and the material from which the target is made. While many different radioactive isotopes can be produced in the cyclotron, in order to be suitable for PET imaging they must have the following properties:

- Emit positrons when they decay
- Have an appropriate half-life
- Be capable of being synthesised into a pharmaceutical to produce a useful tracer for studies in humans

When targets of stable elements are irradiated by placing them in the beam of accelerated particles, the particles interact with the nuclei within the target and nuclear reactions take place.

A simple nuclear reaction induced by a proton p, on a target $\frac{A}{2}X$ can be given by:

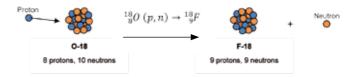
$^{A}_{Z}X\left(p,n\right)\rightarrow {}^{A}_{Z+1}Y$

A reaction induced by a deuteron d (a proton and a neutron), on a target ${}^{A}_{Z}X$ can be given by:

$_{Z}^{A}X(d,n) \rightarrow _{Z+1}^{A}Y$

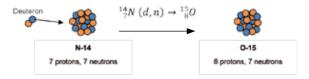
Fluorine-18

 ^{18}F is produced by proton bombardment of oxygen-18-enriched water. The proton interacts with the ^{18}O and produces a neutron and $^{18}\text{F}.$



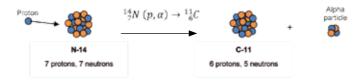
Oxygen-15

 ^{15}O is produced by deuteron bombardment of natural nitrogen. The deuteron interacts with the ^{14}N and produces $^{15}\text{O}.$



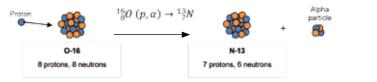
Carbon-11

 ^{11}C is produced by proton bombardment of natural nitrogen. The proton interacts with the ^{14}N and produces a neutron and $^{11}\text{C}.$



Nitrogen-13

 ^{13}N is produced by proton bombardment of distilled water. The proton interacts with the ^{16}O and produces an alpha particle and



Radiation protection issues when using a cyclotron

Due to the radiation protection issues involved in the production and disposal of radioactive materials, radiotracer production and cyclotron operation are mostly automated. This is normally achieved via a computer-controlled menu that the operator employs to select the isotope for use.

Cyclotrons also need a lot of internal shielding to protect staff from high radiation doses, not only from the positron emitters but also from the by-products that are produced, such as the alpha particle in ¹¹C production. There are two ways of providing this shielding. One is vault shielding, where the cyclotron is housed in a protected room with concrete walls. The second is incorporation of the shielding in the cyclotron, which is referred to as "selfshielded". In this option the steel frame of the cyclotron provides the primary shielding, with concrete blocks that are hydraulically driven providing complete radiation protection. The advantages of self-shielded cyclotrons are (a) they have a smaller footprint and so require less space and (b) there are fewer decommissioning implications. Currently, however, the cost of a self-shielded system is almost the same as the cost of building the concrete vault.

Introduction

Nuclear medicine technologists and radiographers find themselves in a unique position by virtue of having two quite different foci to their roles. On the one hand they have responsibilities that are technical in nature and on the other they must care appropriately for a broad range of patient types reflecting individual variations influenced by factors such as culture, religion, age and pathology. Whilst educational curricula vary between and within countries in terms of emphasis and outcome, a clear thread that exists among them is the requirement to include patient care and management competencies.

Nuclear medicine technologists and radiographers do not operate alone and this is particularly true within nuclear medicine and PET-CT. Here the multidisciplinary healthcare team in some centres can be guite large and include both clinical and non-clinical groups. Generally speaking, the non-clinical staff will not be required to have patient care skills (e.g. technical teams that operate cyclotrons) but invariably most of the clinical staff will be expected to have a range of patient care and management skills. Not all centres will have a nurse, but the inclusion of this professional engenders significant benefits because of their heightened ability in care and management. The medical practitioner, such as a radiologist or nuclear medicine physician, adds a different dimension to patient care and complements the nurse and others in looking after patients.

In this whole context sit the radiographer and the nuclear medicine technologist, and they bring their unique specific skill set to bear on patient care and management. Perhaps an important point to remind ourselves about at this stage is that patient care and management entail a team approach and that all clinical professionals should play their part. Regulatory requirements normally dictate that a suitably gualified medical practitioner will be responsible for the clinical radionuclide service but variations exist between countries regarding where the specific responsibilities lie for patient care and management outwith the PET-CT experience per se. For instance, some countries make it clear that the medical practitioner is in ultimate charge of a PET-CT unit, whilst in other countries, beyond the PET component, all healthcare professionals are personally and legally responsible for their actions and not accountable to that medical practitioner. Instead they are accountable to a nationally recognised legal body that assures professional conduct is to the correct standard Nonetheless, whichever of these alternatives is favoured, both have the same ambition: the appropriate care and management of patients.

PET-CT

There is a broad range of literature that concerns itself with the care of people in the context of health. It is not the purpose of this chapter to review that body of evidence and with that in mind we list three nursing texts under suggested reading that may be of value in this respect. Instead of giving a broad background to patient care and management, we shall focus purely on some matters that apply specifically to PET-CT.

Often, patients who attend for PET-CT examinations are worried about their health and this can manifest itself in anxiety that may be evident on their arrival at the PET-CT centre. Various novel and common strategies [1, 2] to minimise patient anxiety have been described in the literature, and emphasis is placed on the provision of information prior to, during and after clinical procedures [3]. Prior to the examination, letters, websites and information leaflets have proved helpful in explaining what the PET-CT procedure involves. Similarly, if post-procedure information is required then these written forms of information are helpful. When constructing such information sources, it is essential that the information is conveyed in a fashion that the majority of the population will understand, and for certain languages readability checks can be used to assess this. Obviously, all patients are individuals, but certain patient categories may require special materials just for them (e.g. children). Often each PET-CT centre has its own information booklet or set of leaflets: an example is shown in Fig. 1. On arrival at the PET-CT centre, the patient will be given a verbal explanation of the procedure: this will use vernacular that the patient will understand. Consequently each patient will be treated individually and the explanation will be tailored to his or her requirements. It is important to ask the patient whether they have understood the explanation and whether they are happy to proceed. Obtaining informed consent from the patient, however, may be a matter for the medical practitioner or another healthcare worker. Whichever is the case, national legislation and guidelines must be followed where they exist.

Figure 1: Patient information for PET-CT examinations: S.Maria Nuova Hospital's booklet, Reggio Emilia, Italy

Informazioni per Utenti che eseguono PET-TAC

SERVIZIO SANITARIO REGIONALE EMILIA-ROMAGNA



Courtesy of Department of Nuclear Medicine, S. Maria Nuovo Hospital, Reggio Emilia

The areas in which the radiographer or nuclear medicine technologist will have involvement with patient care and management are as follows:

- reception
- involvement of patients and/or other relevant people: patient empowerment
- communication and information
- comfort prior to, during and after the procedure
- safety
- privacy

Also they will have involvement with the following five phases:

- patient acceptance
- patient preparation
- explanation of the procedure to patients and relevant persons
- patient comfort, safety and privacy
- monitoring of patient's status during the PET-CT examination

Patient acceptance

Patient identity must be checked in accordance with any local policy that is in place. The patient is normally asked for three forms of identification, for example, name, date of birth and address. The request form must also be checked to ensure that information on it conforms with that given by the patient. This procedure is necessary to minimise the risk of identification error and misadministration of the radioactive substances and CT exposure. When guestioning the patient it is important to preserve their privacy and security. During this aspect of the patient experience it is quite appropriate to give some preliminary information about the PET-CT scan, including how long it will take and general details about the actual procedure.

Patient preparation

If there are no contraindications to the PET-CT procedure then the patient can be prepared. A simple but detailed explanation of the whole procedure should be given, making sure that the patient has understood what is required from them and what the procedure entails. Any relevant risks should be articulated, in accordance with local policy and to minimise clinical negligence claims. For the PET-CT examination the patient must stay in a quiet relaxing waiting room before and after the injection. In this rest room there should be comfortable waiting conditions with a suitable ambient temperature (Fig. 2). In certain instances, relaxing music might be played. The correct amount of PET radiopharmaceutical should be prepared, in line with any national or international guidelines that are being followed. Similarly, it should be administered in line with national or international guidelines. Finally, the administration should be documented appropriately. Further information about the patient and radiation risk can be found in Chap. 7 on radiation protection.

Figure 2: Hot waiting area where the patient relaxes post injection

Courtesy of Department of Nuclear Medicine, S. Maria Nuovo Hospital, Reggio Emilia



Explanation of the procedure to patients and relevant persons

Communication in this context may be defined as the transfer of information from the healthcare worker to the patient and vice versa with a view to changing understanding and perception in the recipient. Radiographers and nuclear medicine technologists should have well-developed communication abilities and these should be used effectively to alleviate patient anxiety whilst maximising patient compliance. Effective communication and patient education can increase patient motivation to comply; such upfront information can improve the patient experience and also improve the diagnostic quality of the scan (e.g. they may move less because they know what to expect). The nature of any interaction with the patient will depend on the patient's requirements: determinants for these requirements may include patient baseline knowledge and understanding and the quantity and type of information that needs to be imparted to them. The latter is an interesting point because it is well known that not all patients wish to have a detailed explanation; when patients indicate that they want only basic information then that request should be granted to them, thereby protecting their human rights. As noted earlier, any explanation should use terminology which is consistent with the patient's intellectual and subject-specific ability, and the use of technical terms may not always be appropriate.

Patient comfort, safety and privacy

<u>Comfort</u>

During the PET-CT examination it is important to use immobilization devices to avoid patient movement but it is also necessary to use devices to improve patient comfort. Devices that can be used to aid immobilisation and comfort include arm rests, knee rests and a warm blanket. Figure 3 gives an indication of how patients' arms and legs can be made more comfortable.

Figure 3a,b: Arm and leg placement to ensure comfort during a PET-CT examination



a

<u>Safety</u>

At all stages during the PET-CT procedure, the radiographer or nuclear medicine technologist must take responsibility for ensuring that the patient's physical well-being is optimal. Amongst other things this involves adhering to medicine management policies in the event of the patient requiring drugs and gasses (e.g. oxygen). Particular attention should be given to moving and handling of patients, and again it is important to adhere to local policies. Compliance with such policies heightens patient safety and also that of the healthcare team (e.g. by minimising the chance of a back injury). Patients should be observed at all times during the scan, whether through lead glass or video camera. Patients at a high risk of injuring themselves, perhaps through frailty, should be monitored closely prior to and after the scan. Risk assessment procedures should have been conducted and be up-todate, and policies arising from these assessments should be implemented in routine practice.



<u>Privacy</u>

Privacy of personal information is governed by national law and therein security of patient data must be maintained. Many hospitals have specific data protection policies and these should be followed to the letter. Some hospitals have a named individual who can be approached by staff for advice and information about local data protection policies and the law generally. In some countries, infringement of the local data protection policy (and therefore the law) may be deemed both a civil and a criminal offence and for the latter a jail sentence may be imposed. Aside from the legalities, the patient should be afforded an appropriate level of privacy, which is particularly important when they need to undress and during communication of information of a personal and intimate nature.

Monitoring the patient's clinical status during the PET-CT examination

Appropriate patient care will involve recognising and then responding appropriately to emergency situations. Various levels of emergency exist, from guite simple (e.g. faint) to severe (e.g. heart failure). For PET-CT the use of xray contrast media does give rise to reactions [4] and it is essential that the radiographer and the nuclear medicine technologist have a thorough understanding of contraindications and drug incompatibilities prior to their administration and also of reactions post administration. The radiographer and nuclear medicine technologist must be adequately trained to recognise and deal with a broad range of emergency situations, and their competence to practice should be updated in line with local policy. At the very least the training should involve a range of basic skills and also the ability to know when and how to call for help.

Summary

Patient care is a critical aspect of the radiographer's and nuclear medicine technologist's role. Patient care and management has been extensively studied and is well reported in the nursing literature and you are encouraged to access that material. Care and management of the patient is a team approach and understanding the role of other healthcare professionals in that team is important. Radiographers and nuclear medicine technologists have particular care and management responsibilities within their role and they should discharge them in a competent and professional manner.

Simona Cola would like to thank all the Nuclear Medicine team of S. Maria Nuova Hospital Reggio Emilia for their help towards this chapter.

References

1. Auerbach S, Martelli M, Mercuri L. Anxiety, information, interpersonal impacts, and adjustment to a stressful health care situation. J Pers Soc Psychol 1983;44:1284-6.

2. Chan Y, Lee P, Ng T, Ngan H, Wong L. The use of music to reduce anxiety for patients undergoing colposcopy: a randomized trial. Gynecol Oncol 2003;91:213-7.

3. Guennoc X, Samjee I, Jousse-Joulin S, Devauchelle V, Roudaut A, Saraux A. Quality and impact of information about interventional rheumatology: A study in 119 patients undergoing fluoroscopy-guided procedures, Joint Bone Spine 2007;74:353-7.

 Böhm I, Schild H. Immediate and non-immediate reaction after non-ionic X-ray contrast medium injection: case report and review of the literature. Eur J Radiol Extra 2007;61:129-33.

Suggested reading

General patient care

Parahoo K. Nursing research: principles, process and issues. 2nd ed. Basingstoke New York: Palgrave MacMillan; 2006.

Payne S, Seymore J, Ingleton C. Palliative care nursing: principles and evidence for practice. 2nd ed. Maidenhead New York: McGraw Hill; 2008.

Polit D, Beck C. Nursing research: principles and methods. 8th ed. Philadelphia: Lippincott, Williams & Wilkins; 2008.

PET-CT specific

Performance and responsibility guidelines for the nuclear medicine technologist (2003 revision). J Nucl Med Technol 2003;31:222-9.

PET-CT scanning competencies for clinical scientist and for clinical technologists/radiographers. Version 1.1 UK PET-CT Advisory Board Approved 26 September 2006 [06/04] http://www.bnms.org.uk/~bnms/images/stories/ downloads/documents/06 04 - pet-ct training requirements physis techs.pdf

Chapter 8: Radiographer and technologist competencies – education and training in PET-CT

Peter Hogg and Angela Meadows

Introduction

This chapter commences with consideration of where radiographer and nuclear medicine technologist PET-CT training and education might occur; it then progresses to the detail of which subjects might be learnt and the competencies that should be obtained. Emphasis is placed upon first post competence in PET-CT, and due regard will be paid to the requirements for practising to a level fit for purpose. To assist us in bringing together this chapter we have drawn upon national guidelines [1, 2] produced within the United States and also within the United Kingdom. We recommend both of these documents to you. At the end of the chapter we have indicated some suggested reading; these texts focus on the important areas of competence, accreditation of prior learning and curriculum development. If you are not familiar with educational processes then we strongly recommend that you consider reading a range of similar educational texts prior to engaging in the design of a PET-CT curriculum

When should PET-CT training occur?

Different countries have different models for training their radiographers and nuclear medicine technologists and even within the same country different models can exist between these professional groups. Whichever group is considered, it is important to have a rationale for when PET-CT training should occur. Two options presently exist: the first is within formative professional training; the second is after that training has occurred – this might be postgraduate or post-basic. One thing is certain – one size will not fit all, principally because of differences in the context of each country.

Formative professional training for radiographers and technologists varies considerably between countries. For instance, some countries offer 2-year hospital-based certificates, while others have 3- or 4-year university-based bachelor degrees and at least one offers a Masters of Science route. The decision to include PET-CT competencies within formative professional education should be well thought through, and this would likely be reflected in whether the first post of the professional would have a high probability of involving routine working within a PET-CT centre. If this is not the case (i.e. if, on qualification, professionals are likely not to work within PET-CT) then the inclusion of PET-CT within the formative professional curriculum may be of general interest but the required several weeks of clinical competence-based training might represent a poor investment. Of course, for radiographers this same argument could equally be applied to ultrasound, computed tomography, magnetic resonance imaging, gamma camera nuclear medicine, interventional procedures and so on. For the purpose of 'general interest', should there be a desire to include background information on PET-CT within formative professional education then this might be better done within the classroom with a small amount of time spent observing PET-CT in the clinical environment, so as to reinforce the theory. This latter option

would not be intended to imply competence to practice PET-CT. Should the requirement for PET-CT competence to practice be opted for within formative professional education then two quite different educational models exist for students to negotiate (Fig. 1) – mandatory and optional.

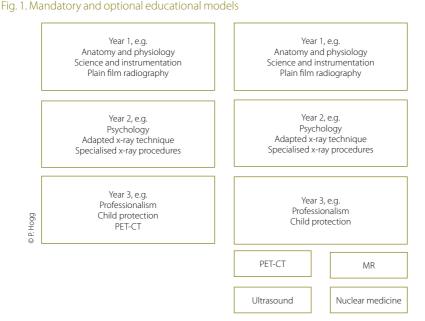
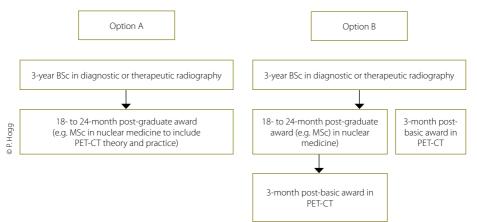


Figure 1 illustrates two fictitious models for radiographer training. If the mandatory model is selected then all students would have to take and also pass the PET-CT training and education within the third year. If the demand for trained professionals to work within PET-CT is relatively low on qualification, the optional approach might be preferred. By contrast, the optional model allows students to select the topic in which they would wish to gain competence upon qualification and the range of choices could include PET-CT, ultrasound, magnetic resonance and nuclear medicine. In the optional and mandatory models, the decision as to how much time is devoted to the training and education will be reflected in the range of competencies that are required to be achieved and also in the depth and level to which the theory is taken. Not all countries include PET-CT first post competencies within formative professional education, one example being the United Kingdom. In such cases PET-CT education and training would be provided within a post-graduate or post-basic framework. In this case those radiographers or technologists who wish to specialise within PET-CT would study either a non-degree award bearing qualification ('post-basic') or a higher degree award bearing qualification ('Post Graduate Diploma' / 'Masters of Science degree'). These options are illustrated in Fig. 2.

Fig. 2. Options for education and training in PET-CT



In option A (Fig. 2), PET-CT theory and practice would be included within the postgraduate nuclear medicine award. Option B would offer the opportunity to study either the 3-month non-degree-bearing post-basic programme in PET-CT or to select a post-graduate programme in nuclear medicine (which might not contain PET-CT, unlike option A). Those selecting the latter option would also subsequently take the post-basic award in PET-CT – should they wish to have specialist skills in PET-CT. Options A and B currently exist within the UK. The choice between these options may depend on what is available locally, the educational background of the radiographer (or technologist) and the clinical role requirements. Obviously, selecting the post-basic or postgraduate route into PET-CT would mean that a professional identity and knowledge base would have already been established and that generic matters such as ethics, patient care and management and 'the sciences' would have already been studied successfully within the formative professional training and education. The limiting factor in selecting this route would be the additional total time required to train somebody to be competent to practice PET-CT – around 5-6 years. Nonetheless, taking the lengthier route would add to the professional's skill and knowledge and this is already valued and recognised in the educational opportunities afforded to the medical profession, whose period of education and training can extend to around 10-12 years. Aside from the potential educational pathways already detailed, there are further complexities to consider[.]

- Radiographers and technologists who are already qualified with no PET or CT or PET-CT experience / knowledge
- Other professionals, such as nurses and physicists, who may also wish to gain competence in PET-CT imaging

Assuming that the PET-CT education and training experiences are well designed then the post-basic and post-graduate models should meet the needs of many professional groups, including qualified radiographers and

technologists. In the context of multi-professional education, certain factors require consideration if such well-designed experiences are to be achieved:

- Prior knowledge and skills of potential students
- Potential deficiencies in student knowledge and skill that are not covered within the PET-CT educational programme and the requirement for robust entry requirements

In some respects the first of these factors is easier to address than the second. Let us consider a scenario to illustrate the point – a newly qualified radiographer contrasted against a radiographer who gualified in 1985. The newly gualified radiographer is likely to have knowledge of and first post competence skills in using a CT scanner. This would be required to cope with the job demands of working as a radiographer in an accident centre at night and during the weekend. By contrast, the radiographer who gualified in 1985 and then guickly moved solely into nuclear medicine may not have obtained the CT competencies. If the PET-CT programme of study were to cover the fundamentals of CT, including matters like acquisition parameters, post processing and patient positioning then the newly qualified radiographer would likely not benefit from that education and time would be wasted. In such a case the robust application of Accreditation of Prior Learning would allow for knowledge and skill to be valued and accredited to that potential student so that they would only attend the required course elements. Obviously, this form of negotiated learning would become more complex as more professional groups participated.

The second factor is more complex. Let us consider two examples - nurses and physicists. We have not yet considered what the programme of study might include, so for the moment we need to make informed but simplistic assumptions to make the examples clearer. Let us assume that the PET-CT programme would cover (a) patient management and care with specific reference only to PET-CT and (b) science and technology of PET-CT specific only to PET-CT, without background information on radioactivity. These decisions could be easily justified in light of the professional groups most likely to enter the programme of study (i.e. radiographers and technologists), in that they should have already studied and been examined on generic matters of patient care and management and also background information on radioactivity. If nurse formative education does not include the background information on radioactivity that is required in order to develop a particular knowledge of PET and CT then this will present a problem. Similarly, if physicist formative education does not include the requisite aspects of generic patient care and management then this, too, will present a problem. The way to overcome both or similar problems is to make clear the entry requirements of the programme of study. These entry requirements could be articulated quite simply by stating nationally recognised qualifications and then Accreditation of Prior Learning could be included as a legitimate alternative to meet the requirement. For instance, the PET-CT programme entry requirement might be:

- 1. A recognised qualification in Radiography or Nuclear Medicine Technology or Medical Physics or Nursing
- School-level leaving certificate in physics or Accreditation in Prior Learning
- 3. School level certificate in human biology or Accreditation in Prior Learning
- Year 1 nursing skills and knowledge in patient care and management; a recognised Nuclear Medicine Technologist qualification; a recognised Radiography qualification; or Accreditation in Prior Learning

To illustrate, a radiographer who qualified one year ago would offer their nationally recognised certificate or BSc for entry to the PET-CT programme. This would satisfy point 1. They could demonstrate, using Accreditation of Prior Learning, that points 2-4 are also covered through their nationally recognised BSc or certificate by simply copying the learning outcomes from that BSc or certificate and enclosing them with the application form. In terms of economy of time and money it is essential that the curriculum takes into account what potential students already know and can do. This will avoid attendance at classes in which no new knowledge is acquired. In terms of being safe to practice, the entry requirements and assessment methods need to be robust to ensure that the clinical and theoretical learning outcomes are met.

What will be assessed in the programme of study?

Competence to practice must be assured on successful completion of a programme of study and to achieve this, clinical competency must be tested and the theory on which such competence is based must also be tested. Various approaches to testing theory and practice and their integration exist and an assessment strategy should be developed to ensure that the student is safe and fit to practice.

Theory can be assessed in different ways, for example:

- Examination
 - Seen
 - Unseen
 - Open book
 - Multiple choice questionnaire
- Objective structured examination
- Viva oral examination

- Written assignment
 - Individual
 - Group

It is worth noting that examinations are good for testing a wide breadth of knowledge but they are quite poor at assessing depth of understanding and also application of that knowledge. Written assignments are good at testing depth of understanding and application, but they are poor at testing breadth of knowledge. Clearly an appropriate blend of assignment types needs to be considered for assessing theory.

Clinical practice can be assessed in different ways, too, for example:

- Objective structured clinical examination
- Clinical assessment (Performing clinical practice whilst being observed and 'scored')
- Portfolio and case study compilation

The integration of theory and practice can also be assessed in different ways, for example:

- Reflective reports
- Portfolios and case study compilation
- Objective structured clinical examination

Each of the above has its value and limitations, and a well-designed programme of study would contain an appropriate range and balance of assessment methods within its assessment strategy.

What should be learnt and what competencies should be acquired?

There will be variation between countries and individuals in response to this question. For instance, in some countries only medically qualified staff may administer the PET radiopharmaceutical, whilst in others appropriately trained, qualified, competent and insured persons can do this task – clearly this will include medically qualified staff. However, for radiographers and technologists there would be a core set of competencies and principles that would be fairly well recognised internationally, and the final element of this chapter seeks to consider those aspects.

The first important principle is that the programme of PET-CT study should have external accreditation and be open for public and professional audit and accountability. This would involve at least one professional body approving the curriculum prior to it being delivered. If appropriate, a regulatory (legal) body might also need to accredit it. Public and professional scrutiny would come through an external quality inspection mechanism. Internal selfregulation would be discouraged as standards could not be assured or verified. Methods of achieving a robust educational quality assurance procedure could be through use of an external examiner system and delivery of the programme of study by an organisation that permits external educational audit and publication of the results ready for public access. An example of the latter would be a university. The ultimate aim of external accreditation and audit is to ensure that the programme of study and therefore the students are fit for purpose so as to protect patients from poor clinical practice.

It is likely that a PET-CT syllabus would attract significant debate, in terms of what should be included. Some are likely to argue that 'facts' and topics' are essential and that the student should rote learn a broad range of information. Such a list would include minute detail and be very wide in terms of the topics covered. The alternative approach would be to consider what knowledge is required to be competent and to what level that knowledge should be taken. This would require learning outcomes to be written and considerable thought would be required to link syllabus detail to those outcomes. This is a more thorough approach than simply listing syllabus content. Examples of topics that could be included are indicated below.

- Minimisation of dose to patients (PET and CT)
- Radiation protection of staff
- Maximisation of image quality

- Care of patient
- PET tracer production
- PET chemistry with respect to radiopharmaceuticals
- PET instrumentation construction and principles of operation
- Issues associated with PET and CT as a hybrid unit, including registration
- Quality control and assurance 'of the whole context'
- Diagnostic procedures
- Procedures for therapy planning
- PET tracers and their administration
- Non-radioactive medicines/drugs within the diagnostic procedures and therapy planning
- Computer processing

A comprehensive syllabus is provided by Society of Nuclear Medicine/American Society of Radiologic Technologists [1]. In light of the arguments already set out within this chapter, it would be advisable to consider prior knowledge and skill, which could call into question the need to 'teach' that curriculum. In contrast to the American approach is that offered by the Society and College of Radiographers [2] (UK). In their document they pay attention to competencies required by radiographers and technologists while leaving the detail of the syllabus to educational providers who would work in collaboration with clinical PET-CT centres. Table 1 [2] illustrates examples of the clinical competencies required for entry level PET-CT practice within the UK for radiographers and technologists (note that this is level 2 of a four-level structure: level 1 is assistant practitioner).

Table 1: Clinical competencies required by practitioners (level 2 of four levels) for PET-CT

Practitioners need to possess a current knowledge and understanding of:

- the risk-benefit philosophy as applied to nuclear medicine and hybrid imaging
- the scientific and legal basis for nuclear medicine and hybrid imaging examinations and interventions, including the legal basis and practical implementation of radiation protection laws
- the legal basis of supply, administration and prescribing of medicines
- drug interactions, pharmacology and adverse reactions of drugs commonly encountered within imaging settings, with a particular emphasis on radiopharmaceuticals and contrast agents
- the methods of administration of drugs, including the associated health, safety and legal issues
- developments and trends in the science and practice of nuclear medicine
- the safe practice of CT when used as an adjunct to a nuclear medicine service (i.e. PET-CT)
- the principles underpinning moving and handling, the principles underpinning emergency aid and the principles (including health, safety and legal considerations) underpinning assessment
- monitoring and care of the patient before, during and after examination

Practitioners' level of knowledge should be sufficient to enable them to:

- identify and respond to those situations that are beyond the scope of practice of the assistant practitioner
- select, plan, implement, manage and evaluate imaging procedures that are appropriate to, and take account of, individuals' health status, environment and needs and the legal framework of practice
- participate effectively within multi-professional health care and multi-agency teams and in health care environments both within and beyond clinical imaging services
- analyse systematically, evaluate and act upon all data and information relevant to the care and management of the patient
- be able to acquire and process CT images and data that have clinical relevance within nuclear medicine, observing the principles of exposure optimisation particularly with respect to attenuation correction and diagnostic CT
- assess patients' needs and, where necessary, refer to other relevant health care professionals
- be able to manipulate written and image data in differing formats for the benefit of the patient
- offer the highest standards of care in both physical and psychological respects in all aspects of nuclear medicine and hybrid imaging examinations and interventions in order to ensure effective procedures
- make informed, sensitive and ethically sound professional judgements in relation to imaging procedures in which they are involved
- ensure that consent given by patients to procedures is 'informed'
- apply safe and effective moving and handling skills in order to protect all individuals

Worthy of note are the competencies required for the highest grade of radiographer and technologist (consultant) within the UK for PET-CT, examples of which are shown in Table 2 [2]. Please note that there is one grade between Tables 1 and 2; this grade is called "advanced practitioner".

Table 2: Clinical competencies required by consultants (level 4 of four levels) for PET-CT

Consultants' depth and breadth of knowledge and expertise in nuclear medicine practice and hybrid imaging will enable them to:

- identify and respond to those situations that are beyond the scope of practice of the advanced practitioner, providing training, supervision and mentorship as part of the role
- effectively lead the clinical team in the delivery of the nuclear medicine service, including hybrid imaging
- exhibit expert clinical practice in managing complete episodes of care that lead to satisfactory patient outcomes and/or health gains, including determining the suitability of clinical requests
- deliver a whole-system, patient-focussed, approach rooted in a multi-professional perspective lead
 and/or represent the team at multidisciplinary meetings
- provide clinical leadership locally and across professional/organisational boundaries at a national and/or international level where appropriate
- manage personal case loads, including wide-ranging decision making and the provision of a clinical report
- engage in the development and advancement of innovative practice by means of active involvement in research
- be accountable for safety, legal and clinical governance issues for nuclear medicine and hybrid imaging practice
- evaluate, identify gaps in and integrate the research evidence base into practice such that expert professional judgements can be exercised routinely
- supply and administer medicines within the legal framework

The coverage of material by the syllabus needs to be balanced against the level to which the material is learnt and subsequently applied. As a rule of thumb, for the same programme length, the broader the syllabus coverage, the more superficial is the material learnt and applied. Conversely, the narrower the syllabus coverage, the greater can be the depth and application. When the programme is being designed, the depth versus breadth factor needs significant consideration and this will be driven by the level to which the radiographer or technologist will operate on qualification. Again, for similar programme lengths, a rule of thumb is that a broad syllabus range means a lower level of practice compared with a narrow syllabus range taken to a much greater depth. This trade off should be determined when a rationale for a PET-CT programme is proposed, and it is likely that this will result in differences between countries. Such differences are likely to be driven by political, legal and clinical factors.

Summary

Several philosophical educational debates need to be concluded prior to deciding on the fine detail of a PET-CT curriculum and syllabus. The broader curricular considerations encompass matters such as where PFT-CT will be learnt and applied within the professional's overall educational experience. Countryspecific issues will require due consideration. and these will inform the level of responsibility that could be held by radiographers and technologists. Such debates will drive the syllabus range and depth to engender the competencies that are to the required level for practice. Given the multi-professional nature of nuclear medicine and PET-CT, there is a need to design curricula that meet a range of professional needs. This means that an adaptive curriculum will be required that takes into account and also values prior knowledge and skill: but whatever the route that is taken, the educational outcomes must be assured. Perhaps the final and most important part of the educational provision concerns the need for public accountability through an open and robust quality assurance system.

References

1. Society of Nuclear Medicine and American Society of Radiologic Technologists. Positron emission tomography (PET)-computed tomography (CT) curriculum. https://www.asrt.org/media/Pdf/PETCTCurriculumAccepted021704.pdf. 2004

2. Society and College of Radiographers. Learning and development framework for hybrid nuclear medicine/ computed tomography practice (SPECT-CT/PET-CT). <u>www.sor.org</u>. 2009

Suggested Reading

Iwasiw CL. Curriculum development in nursing education. 2nd ed. Sudbury, Mass.: Jones and Bartlett; 2008.

Nyatanga L, Forman D, Fox J. Good practice in the accreditation of prior learning. London: Continuum International Publishing Group (Cassell Education); 1998.

Anema M, McCoy J. Competency based nursing education: guide to achieving outstanding learner outcomes. Berlin Heidelberg New York: Springer; 2009.

Imprint

ISBN: 978-3-902785-00-8 ISSN: 2079-3138

Publisher:

European Association of Nuclear Medicine EANM Technologist Committee Hollandstrasse 14, 1020 Vienna, Austria Tel: +43-(0)1-212 80 30, Fax: +43-(0)1-212 80 309 E-mail: info@eanm.org URL: www.eanm.org

Content:

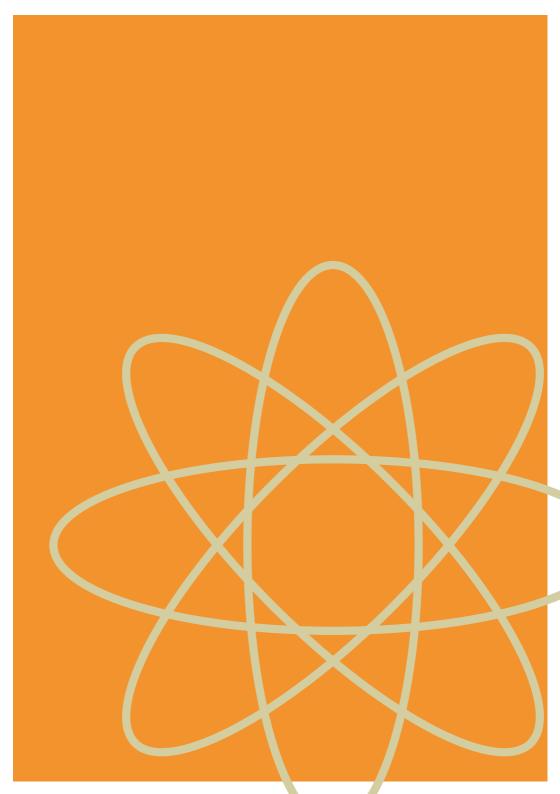
This copy is a reprint of the 2010 version. No responsibility is taken for the correctness of this information. Information as per date of preparation: August 2010

Layout and Design:

kreativ · Mag. Evelyne Sacher Linzer Straße 358a/1/7, 1140 Vienna, Austria Tel: +43-(0)1/416 52 27, Fax: +43-(0)1/416 85 26 E-mail: office@kreativ-sacher.at URL: www.kreativ-sacher.at

Printing:

Laber-Druck Ges.m.b.H. Michael-Rottmayr-Straße 46, 5110 Oberndorf, Austria Tel: +43-(0)62 72-71 35-426, Fax +43-(0)6272-7135-499 E-mail: hubert.jaud@laberdruck.at URL: www.laberdruck.at



Principles and Practice of PET/CT Part 1 A Technologist's Guide