Positron emission tomography

A strategy for provision in the UK

A report of the Intercollegiate Standing Committee on Nuclear Medicine

Representing the Royal College of Physicians of London, the Royal College of Physicians and Surgeons of Glasgow, the Royal College of Physicians of Edinburgh, the Royal College of Pathologists, the Royal College of Radiologists and the British Nuclear Medicine Society

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Contents

Foreword v
Executive summary and recommendations vii

PART 1: A STRATEGY FOR THE PROVISION OF POSITRON EMISSION TOMOGRAPHY IN THE UK

1 Introduction 3
   Background 3

2 Clinical PET: areas of use 5
   The role of PET in oncology 5
   The role of PET in cardiology and cardiac surgery 7
   The role of PET in neurology and neuropsychiatry 7
   Cost effectiveness 7

3 The requirements of a national PET service 9
   Equipment and personnel 10

4 Current problems and their solutions 11
   Problems with service provision 11
   Problems with establishing PET in the UK 12

5 Suggested strategy for the provision of a PET service 13

6 Conclusion 16

PART 2: CLINICAL INDICATIONS FOR POSITRON EMISSION TOMOGRAPHY IMAGING: CURRENT ICSCNM SUGGESTIONS

Introduction 19
   Radiation hazards 19
   Breast feeding 20
   Pregnancy and protection of the foetus 20
   The clinical indications table 20

Clinical indications for positron emission tomography 21
<table>
<thead>
<tr>
<th>APPENDICES</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1: Imaging with a distant supply of tracer: the minimum establishment</td>
<td>29</td>
</tr>
<tr>
<td>2: Imaging with full production of tracer: the minimum establishment</td>
<td>32</td>
</tr>
<tr>
<td>3: Training issues</td>
<td>38</td>
</tr>
<tr>
<td>References</td>
<td>39</td>
</tr>
<tr>
<td>Bibliography</td>
<td>41</td>
</tr>
</tbody>
</table>
Foreword

The Intercollegiate Standing Committee on Nuclear Medicine (ICSCNM) is committed to the maintenance of standards in, and the development of, nuclear medicine and radionuclide radiology in a way which contributes to the care of patients.

Nuclear medicine technologies are developing at a great pace and, in keeping with the molecular developments in medicine, positron emission tomography (PET) is now capable of providing molecular imaging. Clinical PET’s contribution to the management of patients with cancer is growing in terms of diagnosis, staging, restaging and the monitoring of response to therapy. The new combination technology of PET-CT scanners will impact on radiotherapy planning as well as on assessing gene therapy and early tumour response. Although oncology is the major area of PET usage, applications in neurology and cardiology are apparent and will develop in the future.

As with all new technologies, setting up a service can be difficult both in terms of capital cost and staff training. Currently the access to PET services for UK patients is extremely limited and inequitable in geographical location. For PET to be developed and used appropriately and to a high standard, the constituent bodies of the ICSCNM felt that a strategic view should be available to allow decisions to be made for a rational implementation of a service.

This document is therefore intended to provide a clear indication of the potential value and practical implications of the development of a PET service. It should also act as a stimulus to those in relevant patient care to press for the provision of such a service.

A working party of the ICSCNM (consisting of Dr MJ O’Doherty (Chairman), Prof I McCall and Dr TO Nunan) produced this document, which has since been reviewed and modified by all members of the committee. It has therefore been endorsed by the Royal College of Physicians of London, the Royal College of Physicians and Surgeons of Glasgow, the Royal College of Physicians of Edinburgh, the Royal College of Pathologists, the Royal College of Radiologists and the British Nuclear Medicine Society. The document will be available on the websites of the Royal College of Physicians, the Royal College of Radiologists and the British Nuclear Medicine Society.

Special thanks are extended to Ms M Dakin (of Guy’s and St Thomas’ Clinical PET Centre) for the financial information.

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PROFESSOR IAIN McCALL
Chairman, ICSCNM
SUMMARY

Positron emission tomography (PET) has been in use for over 20 years as a research tool, and over the last decade in a clinical role. The major clinical applications of PET are in the areas of oncology, cardiology and neurology, with over 85–90% of the workload in oncology. There have been around 15,000 publications related to PET, and although the majority of these have been small retrospective studies, all major studies have had similar findings. The literature lacks randomised controlled trials (with the exception of lung cancer) and large prospective series or cost-effectiveness analyses (other than modelling studies). Despite this, PET scanning has been adopted throughout the USA and Europe, gaining Centers for Medicare and Medicaid Services (CMS, previously known as the Health Care Financing Administration or HCFA) approval for reimbursement in patients with certain cancers and cardiac conditions in the US. There are over 160 sites in the USA and over 120 sites in Europe (80 of these are in Germany).

PET is a technology that uses short-lived radionuclides (with half-lives currently ranging from 2 to 110 minutes) attached to tracers to examine metabolic processes associated with health and disease. These functions are often altered by disease and precede changes that can be visualised by cross-sectional imaging (eg computed tomography (CT) or magnetic resonance imaging (MRI)). PET radionuclides are produced in cyclotrons which are available in a variety of sizes and energies. The most commonly produced radionuclide is fluorine-18 (F-18), but others include nitrogen-13 (N-13), carbon-11 (C-11) and oxygen-15 (O-15). F-18 has the advantage of having a longer half-life (110 minutes) and can be attached to a molecule that mimics glucose metabolism, fluorodeoxyglucose, to produce 18F-FDG. Cancer cells have altered glucose metabolism and therefore FDG is a major tracer used in the assessment of cancer.

Evidence of the diagnostic accuracy of PET scanning is based on traditional full-ring dedicated PET, with very few publications using gamma camera coincidence imaging (GCI). The technology for GCI is currently inferior to dedicated PET scanners and is unlikely to have the same versatility. Health technology assessment is notoriously difficult to undertake since the technology is advancing so rapidly. The studies that have been performed demonstrate that PET is more accurate in detecting malignant disease than conventional imaging, but is often best used in combination with conventional cross-sectional imaging in the assessment of cancer patients. Modelling studies in pulmonary nodules and lung cancer have been carried out using published sensitivities and specificities. The points of interest are that the predications of these studies appear to support the findings from recent prospective research and a recent randomised controlled trial of lung cancer and PET. There are a number of studies in different cancer groups demonstrating change in management as a result of PET scanning. In one study, 62 out of 102 patients with lung cancer being assessed for surgery had their management changed, having been staged by conventional means.
PET in the UK has been severely restricted by the lack of availability of scanners and cyclotrons. Clinical PET was introduced into the UK at Guy’s and St Thomas’ Hospitals in 1992; the unit now has two scanners and has rapidly become inundated with work, such that 2,000 patient studies are being performed per annum on patients travelling from Scotland, Wales and all corners of England. Since 1992 only three other dedicated clinical PET facilities have developed, all of which are in London. Research scanners have been established in London, Manchester, Cambridge and Aberdeen. All of these have access to a cyclotron and radiotracer production facilities.

PET scanning has been limited by the lack of positron-emitting tracers caused by the small number of cyclotrons. The present cyclotrons can supply 18F-FDG to hospitals within an approximate two-hour travel-time radius. However, radionuclides currently used for vascular flow measurements all have a very short half-life and can only be used in scanners immediately adjacent to the cyclotron. The key to delivering a service lies in deciding how many centres and which studies are required.

PET should be available to all cancer centres for early diagnosis, staging and the identification of tumour recurrences. These tasks will constitute approximately 85–90% of a PET centre’s work. It should also be available to tertiary referral centres where there is substantial work being undertaken on neuropsychiatric conditions (eg epilepsy), and possibly dementing illnesses (eg Alzheimer’s disease) and also the evaluation of cardiac muscle viability prior to coronary artery surgery (see Part 2). These latter uses will only make up the remaining 10–15% of the workload.

A dedicated PET camera could perform between 1,000 and 1,600 patient studies per year, depending on the complexity and type of study. With new technologies, such as PET-CT cameras, their number may increase. Therefore a knowledge of the population base which is likely to provide at least that number is required. It is estimated that a population of approximately 1–1.5 million people would have 700–750 patients per annum falling in to the cancer types which from the body of evidence available would benefit from PET scanning, ie lung cancer, metastatic or recurrent colorectal cancer and lymphoma. In addition to these groups the evidence for the role of PET in a larger range of cancers is becoming established (see Part 2). Most cancer centres in the UK subserve this population of patients. The establishment of a PET centre in each cancer network would be a useful start to the process.

PET centre options

There would need to be two types of PET centre developed in the UK: dedicated full-ring PET scanners in conjunction with a cyclotron and radiochemistry production facility, and stand-alone PET scanners. The staffing of these centres is outlined in Part 1 of this document and in the appendix. The delivery of a PET service is expensive; however, the calculated incremental cost-effectiveness ratios (ICERs) are low. The location of each type of centre would need to be carefully considered to give optimum access for the patient population. The likely capital cost of a PET scanner facility is £1,285,050 and the cyclotron/radiochemistry facility is an additional £1,469,700. Revenue consequences will vary depending on the service offered, but for the scanner alone the estimate based on 1,000 patients is £585,900 (see the appendices for a more detailed analysis of costs).
Staffing issues

The staffing requirements of a PET centre will vary depending on the type of centre (scanner and cyclotron, or scanner alone) and also on whether the centre is predominantly clinical, or both research and clinical. Whatever the service offered, there are issues relating to training for all staff members. There are few trained clinicians, radiochemists, cyclotron engineers, physicists and radiographers/medical technologists. Staff training in the UK needs to be addressed with funding and the establishment of formal training courses. The funding may come partly from the industry and partly from the government. A curriculum for medical training has been established within the nuclear medicine training programme.

Findings

- The committee accepts that the accumulating evidence indicates that with regard to patients with lung cancer, solitary pulmonary nodules and colorectal cancer and lymphoma, the addition of PET is likely to be cost effective in their management.
- Evidence suggesting that PET will be beneficial in the management of patients with other tumour types is accumulating.
- Currently PET is used in addition to other imaging techniques and in most cancers FDG PET has a higher sensitivity than other forms of imaging.
- FDG PET is safe to perform.
- The method of imaging should be dedicated full-ring PET. The crystal type remains to be evaluated and depends on recent developments with germanium oxyorthosilicate (GSO) and lutetium oxyorthosilicate (LSO) rings. Most available data uses bismuth germanate (BGO) systems.
- PET services performed using GCI should be discouraged. This should only be reviewed:
  - when these systems can demonstrate performance that is equivalent to or better than the full-ring PET systems; or
  - if their clinical utility can be demonstrated by adequate clinical studies to indicate an incremental value to patient management compared with other imaging methods.
- The establishment of clinical PET in the UK should be centrally controlled and financed to allow the optimum provision of service throughout the UK whilst maintaining a high clinical standard. A public-private partnership may be appropriate for the provision of cyclotron facilities and tracer supply.
- The established cancer networks, cancer centres and appropriate tertiary referral centres should provide the structure upon which the introduction of PET centres is based. The exact siting of such centres will depend on the availability of tracer in the short term, and the development of cyclotrons either by using or upgrading existing facilities. There will be a need to develop new facilities particularly in those areas
without access. These include the North East and South West of England, the central corridor of Scotland and Northern Ireland.

RECOMMENDATIONS

1. A national policy for the development of PET facilities should be established as soon as possible.

2. State-of-the-art dedicated PET camera facilities should be established in at least 15 sites within the UK in the next 3–5 years, and in at least 40–60 sites in the next 10 years.

3. The majority of the initial sites should include cyclotron and radiotracer production facilities or be sited where there are existing production facilities within two hours' journey time.

4. Each cancer network should have access to a dedicated PET facility attached to a radiotracer production facility. This is to enable the full range of PET tracers to be available on at least one site within the network.

5. Cyclotron provision may be government funded, privately funded or a combination of both. The cyclotrons should either be 10–13 or 13–18 MeV, depending on the proposed size of the unit and the research potential.

6. PET scanners should be funded by the government, or a combination of private and government funding. Operating costs should be included in the budgets of the cancer networks and the cardiac and neurology services as appropriate.

7. Government funding is required in training programmes for PET radiochemists and cyclotron engineers.

8. The number of trained personnel and the expense may be reduced by siting several cameras on one site, providing patients have ready access to the facility.

PET imaging is developing rapidly elsewhere in the world. Health technology reviews performed one or two years ago are already dated. The time is ripe to press on with providing an organised national service for PET. This technology development should be regarded as a necessary part of the NHS Plan and the NHS Cancer Plan.
PART I
A strategy for the provision of positron emission tomography in the UK
Introduction

1.1 Clinical positron emission tomography (PET) is now a reality. The transition from the research environment, where it has been in use for over 25 years, to the clinical environment has been made successfully over the last ten years. The major problem is that the UK has fallen behind the rest of Europe and the USA in the provision of this service. The need for the service will increase over the next five to ten years, particularly in relation to the management of patients with malignancy such that a PET service is likely to be regarded as a mandatory part of staging and restaging disease as well as monitoring therapy. It is therefore essential that the issue of the provision of PET services is addressed. The NHS Plan has identified cancer, heart disease and mental health as current clinical priorities. The NHS Cancer Plan outlines a series of objectives aimed at reducing times from referral to diagnosis and appropriate treatment. PET has a role in selecting patients for appropriate treatment, in diagnosis and in monitoring the patient's response to treatment. Decades of underinvestment in people and equipment have taken their toll and it is possible this mistake will continue if the opportunity to develop clinical PET is not taken.

Background

1.2 PET is a nuclear medicine technology that uses short-lived radionuclides (carbon-11, oxygen-15, nitrogen-13 and fluorine-18) attached to biological molecules to allow the visualisation of metabolic processes in the body by producing an image of the distribution. Using these tracers to visualise the biochemistry of a human, it is possible to view perturbations of the system caused by disease processes such as cancer, coronary artery disease and neurological disease. Biochemical or functional changes in the body often occur before any structural change, so these functional images can show disease before anatomical images (computed tomography (CT), magnetic resonance imaging (MRI) or ultra-sound scans (USS)) in some circumstances.

1.3 The most commonly used tracer is F-18 fluorodeoxyglucose (FDG) which allows the examination of alterations in glucose metabolism which are known to occur in cancer cells. It can also demonstrate abnormalities in areas of the body that use glucose preferentially as their energy source, for example the brain and the myocardium. Other molecules which have a role in evaluating disease (eg aminoacids, purines and pyrimidines as well as tracers that show blood flow, hypoxia etc) can also be labelled. These short-lived radionuclides are made using cyclotrons and then attached to the biological molecules using rapid chemistry techniques.

1.4 Clinical PET was introduced in the UK in 1992 through a self-funding unit based at Guy's and St Thomas' Hospital. This unit has two dedicated PET cameras and is currently working at capacity, accepting patients from around the UK. The use of PET, however, is now established and its role becoming known to a wide variety of clinicians. There are three other clinical PET imaging centres in the UK, two based in London, at University College London and Harley
Street, and a further one at the Paul Strickland Scanner Centre at Mount Vernon Hospital in Middlesex. There are also two research units in London, based at Imaging Research Solutions Limited (IRSL, formerly the Medical Research Council Cyclotron Unit) at the Hammersmith Hospital and the Functional Imaging Laboratory at Queen Square. Outside of London there are the Wolfson Brain Imaging Centre at Addenbrooke’s Hospital in Cambridge, the Manchester PET Centre at Christie Hospital and the PET Imaging Research Group at the University of Aberdeen. These research units do not offer a comprehensive clinical scanning service, but some do produce and distribute PET radiotracers. The above centres all have dedicated PET scanners. There are also a number of other trusts that have acquired gamma camera coincidence imaging (GCI), and these provide a limited PET service. The capabilities of such cameras are in their infancy; whether they will mature remains to be seen, and their role is not established. The technology is unlikely to have the same capabilities as dedicated PET and there may be other drawbacks to providing a quality service. In line with clinical governance and evidence-based practice this document considers the establishment of dedicated PET centres.

1.5 There are also private initiatives including mobile PET scanners, which may have a role in the establishment of PET scanning in other regions of the country. Careful supervision would be required to establish a quality service and the provision for adequate training of the reporting clinicians. The costs of such an initiative would need to be explored with the private sector. Similarly there are already commercial companies with expertise gained in the USA and Europe who are establishing radiotracer production facilities in the UK.
2 Clinical PET: areas of use

2.1 There are three areas of use in the clinical arena. The largest area is within the field of oncology, with cardiology and neuropsychiatry as the other predominant areas. A list of the committee’s views on the current indications for PET are identified in Part 2 of this document.

The role of PET in oncology

2.2 The principal role of PET in oncology can be thought of either in generic terms or in terms of the systems affected by cancer.

Generic indications

2.3 The generic use of PET in the assessment of malignant disease can be summarised as:

- distinguishing benign from malignant disease, eg lung nodules, brain lesions etc;
- establishing the grade of malignancy, eg brain tumours, soft tissue masses;
- establishing the stage of disease, eg lung cancer, lymphoma;
- establishing whether there is recurrent or residual disease, eg lymphoma, teratoma, seminoma;
- establishing the site of disease in the face of rising tumour markers, eg colorectal, germ cell tumours;
- establishing the response to therapy before, during and after therapy imaging; and
- identifying the primary site of a tumour for biopsy either when site is unknown but clinical indications are strongly pointing to a tumour (eg paraneoplastic syndrome) or for therapeutic purposes.

Tumour-specific indications

2.4 PET is changing the way in which cancer is managed and is forcing a reassessment of conventional staging with CT and MRI in certain cancer groups. It can be used to plan the delivery of, and rapidly assess response to, therapy, allowing the treatment regimens to be modified without delay if the response is inadequate. The largest influence of PET has been in the management of lung tumours, colorectal tumours and lymphoma (see the appropriate sections in the bibliography). The management of many other tumours is also affected. This is evidenced by an increasing number of publications (particularly head and neck cancer recurrence, testicular tumours, oesophageal cancer and melanoma (see bibliography)). These roles although less well evaluated have been shown with anecdotal evidence to be beneficial to patients.
2.5 FDG PET has been shown to be cost effective in the assessment of pulmonary nodules and in the staging of lung cancer. In the assessment of pulmonary nodules FDG PET has a reported sensitivity of 82–100% and a specificity of 60–100%, with the majority of studies suggesting a sensitivity of approximately 90% and a specificity of approximately 85%. The use of PET, either in combination with CT or on its own, has been shown through the use of decision-tree modelling to be cost effective. Ghambir et al demonstrated that a CT and PET strategy produced savings of $1,154 per patient without loss of life expectancy. Dietlein et al showed that compared to a watch-and-wait strategy the PET incremental cost-effectiveness ratio (ICER) was €3,218 per life year saved, whereas if exploratory surgery were the norm then PET would be €6,912 per life year saved. In lung cancer staging the sensitivity in the detection of metastatic disease has varied between 66% and 100% with the majority of the literature suggesting 75% and the specificity ranging between 80% and 100% with the majority in the region of 95%. Ghambir et al have shown cost savings of between $91 and $2,200 per patient using both CT and PET to stage patients with lung cancer. Dietlein et al showed that FDG PET was most cost effective in those patients with normal sized mediastinal nodes on CT, with the ICER per life year saved costing only €143. Recently a prospective study has demonstrated the superiority of PET over CT in the assessment of patients with lung cancer referred for surgery. Management changes have been observed in 20–60% of patients in various studies. These changes have been in both up- and down-staging of patients; either promoting patients to surgery or preventing ineffective surgical intervention. A recent randomised controlled study demonstrated that conventional workup and FDG PET resulted in a 51% relative reduction in futile thoracotomy compared to conventional workup alone. The use of FDG PET in radiotherapy treatment planning and for down-staging assessment after chemotherapy is still to be evaluated. If PET is found to be valuable in these areas as well as in surgical assessment then its role will expand within lung cancer.

2.6 Patients with recurrent colorectal carcinoma present a number of problems to the clinician. Conventional imaging assessments have a poor record, with only 25% of patients with apparently limited disease curable at surgery. With hepatic recurrence, over 50% are found to be unresectable at surgery. A meta-analysis of the literature available on recurrent colorectal cancer demonstrates an overall sensitivity of 97% (95% confidence levels 95–99%) and specificity of 76% (95% confidence levels, 64–88%) for detecting disease sites, with management changes in 29% (95% confidence levels of 25–34%) when FDG PET is used.

2.7 CT is normally the modality used to stage lymphoma. FDG PET has been shown to change management in anything up to 40% of patients who have already been staged with CT. Furthermore, FDG PET appears to be useful in the assessment of residual masses found on CT. The other potential area of use is in early assessment of disease response to chemotherapy, since change of treatment regimes may be instigated earlier than normal if no response or a limited response is observed following two cycles of therapy. This may have long-term benefits in the reduction of second malignancies following initial chemotherapy.

2.8 The role of PET in other tumours cannot be underestimated. Significant evidence of utility has been demonstrated, for example in the management of oesophageal cancer, soft tissue sarcomas, testicular tumour recurrence (in residual masses or patients with rising markers), metastatic melanoma and many other tumours. As of January 2001, health insurers in the USA are funding FDG PET studies for solitary pulmonary nodules, staging of non-small cell lung
cancer, lymphoma staging and restaging as well as recurrent colorectal tumours and recurrent or metastatic melanoma. This list has expanded from its introduction in 1998, and in the USA Centers for Medicare and Medicaid Services (CMS, previously known as the Health Care Financing Administration or HCFA) proposed that ‘this science-based coverage decision provides important expanded coverage of dedicated full-circular ring PET scanners and some partial-ring systems for any clinically appropriate use for six types of cancer – lung, colorectal, lymphoma, melanoma, oesophageal, and head and neck (but not brain or thyroid) cancer – and new coverage of the neurologic and cardiac applications’. This list was further updated in November 2001 to stipulate that most of these indications were for full-ring or partial-ring PET cameras.

The role of PET in cardiology and cardiac surgery

2.9 The major role for PET imaging in this area is to establish whether there is sufficient viable myocardium in a patient with poor ventricular function to justify attempts at revascularisation. The predictive ability for contractile recovery is approximately 80% positive predictive value of mismatched perfusion and FDG uptake, and 85% negative predictive value for matched reduction in perfusion and FDG uptake. The other potential use is in patients with severe ischaemic cardiomyopathy who are being considered for cardiac transplantation. A survival benefit has been shown to be present in those that had mismatched perfusion and FDG, and underwent revascularisation, compared with those that had no mismatch and underwent medical treatment. Those patients who had no mismatch and underwent cardiac transplantation also had improved survival. Furthermore, the accuracy of PET for the detection of coronary artery disease is highly sensitive and specific of the order 82–100%. The indications would appear to be:

- diagnosis of hibernating myocardium in patients with poor left ventricular function prior to revascularisation procedure;
- distinguishing ischaemic from non-ischaemic cardiomyopathy;
- identifying patients with a fixed single photon emission computed tomography (SPECT) deficit who might benefit from revascularisation; and
- use prior to referral for cardiac transplantation.

The role of PET in neurology and neuropsychiatry

2.10 The principal applications for PET in neurology are for the pre-surgical workup of patients with partial epilepsy, assessment of dementias, and diagnosis and detection of recurrent primary brain tumours. The sensitivity and specificity for unilateral hypometabolism in temporal lobe epilepsy are approximately 70–85% and 86% respectively. The role in dementia imaging is at present limited, since although it has a high sensitivity and diagnostic accuracy is not a great deal better than single photon emission tomography (SPET) imaging techniques.

Cost effectiveness

2.11 There have been a number of reports by a variety of health technology assessments including, most recently, the Commonwealth report on PET,14 the United States Veterans Affairs Management
Clinical PET: areas of use

Decision and Research Center (MDRC) Technology Assessment Program in 1996 and 1998,15,16 and the United Kingdom National Coordinating Centre for Health Technology Assessment (NCCHTA).17 These reports all have their problems, not least the fact that they are now out of date and using literature that is at least two years old, and in some cases six or seven years old. The NCCHTA report had a number of other problems, particularly the Delphi study in which questions were asked of researchers or specialists who were hoping to generate funding for equipment and research. The areas of assessment of the technology raised in the report by Roberts and Milne are likely to be superseded since there is broad agreement that the GCI technology is inferior to dedicated PET cameras. Similarly, prospective studies have been performed in real clinical situations demonstrating the added value of dedicated PET over conventional CT imaging in lung cancer. Peter Valk has eloquently argued that randomised controlled trials are not appropriate for assessing imaging methods, and the use of modelling sensitivity and specificity data to assess the likely cost effectiveness is a more rapid way of providing such information, and one which does so in a way that can be applied to each country’s health circumstances.18 It is also of interest that the most recent review of PET in the Commonwealth document still used these dated HTA reports, and despite reaching the conclusion that there is little cost-effectiveness data available the report suggested that PET has a role in:

- differentiation of malignant from benign lesions in patients with a solitary pulmonary nodule;
- primary staging in patients with non-small cell lung cancer (NSCLC);
- primary staging in patients with suspected primary brain tumour;
- evaluation of residual structural lesions after definitive therapy for colorectal cancer (CRC);
- evaluation of residual structural lesions after definitive therapy for recurrent glioma;
- pre-operative assessment of metastatic disease in CRC;
- pre-operative assessment of apparently limited metastatic disease in malignant melanoma;
- localisation of epilepsy; and
- assessment of ischaemic heart disease.

2.12 The economic modelling has been performed in different health care settings and suggests that PET is cost effective, or even cost saving, based on the assumptions made. Whether PET affects long-term outcome remains to be fully tested in malignant conditions, however it is clear that it can affect the short-term management of patients with cancer. Outcome effects may take up to 20 years to evaluate; for example, whether changes in chemotherapy or radiotherapy regimens early in the course of disease treatment will reduce the occurrence of second cancers. If an imaging modality is superior to another imaging modality and provides different information allowing management changes, we should not wait a further 5–10 years to show long-term outcome effects; these changes have been modelled and prospective studies are showing these models to be true. Furthermore, the human costs of delay in the introduction of this modality may be large, since the management changes demonstrated suggest that unnecessary surgery can be avoided and necessary surgery expedited. There is consequently the potential to enable the appropriate treatment pathway.
3 The requirements of a national PET service

3.1 The major use of clinical PET is in oncology as discussed above. The recent publication of health statistics shows the number of cases of cancer in England and Wales.\textsuperscript{19} If the major cases of cancer are considered and compared with the current identified role of PET then the potential patient base can be identified. The number of new cases of cancer identified in 1994 was 224,320. The major cancers in men were lung, colorectal and prostate and in women they were lung, colorectal and breast. These tumour types constituted over half the registrations. For lung cancer and colorectal cancer there is meta-analysis evidence of the utility of PET. There is emerging evidence of probable use in breast cancer. Furthermore the cancer statistics for 1997 show over 6,000 new cases of oesophageal cancer, 1,400 cases of testicular cancer, 3,500 cases of brain tumour and 7,200 cases of non-Hodgkin’s lymphoma, 5,500 cases of lip, mouth and larynx cancer and 4,600 cases of melanoma in 1997.\textsuperscript{19} All of these tumour groups would benefit from PET examinations for staging and treatment response assessments. The prevalence of patients with cancer on the 1 January 1993 was almost 650,000. The patients who are still alive and have had cancer will be under surveillance and so may also contribute to the demand for PET (since a large portion of these will have colorectal cancer where the evidence for the role of PET scanning in the detection of recurrent disease is robust). The registration of new cancers for 1995–7 is very similar to the numbers for 1994 with 219,700 noted.

3.2 The statistics quoted can also be portrayed as new cases per million of the population. These figures show an overall cancer incidence of 8,690 p.a. per million with over half of these falling into groups where there is robust evidence of the benefits of clinical PET with the currently available tracer, FDG. Assuming the role of PET is confined to the tumour groups with either meta-analysis evidence or robust clinical data supporting its use, the new lung cancer cases are presently 1,390 p.a. per million, colorectal disease 1,120 p.a. per million and lymphoma cases 280 p.a. per million. Assuming that 15% of lung cancers are considered operable and a further 10% may be downstaged by chemotherapy, then PET has a potential role in approximately 25% of lung cancers, that is 208–347 p.a. per million of the population. Similarly for the colorectal cancers with this sort of incidence the prevalence of cases for assessment of residual or recurrent disease is likely to be 250 p.a. per million of the population. All lymphomas would benefit from staging with PET scanning in addition to either interim assessment during chemotherapy or post chemotherapy. Therefore within a population of a million a conservative estimate of the number of patients who would directly benefit from PET scans each year is 730. Other tumour types will also benefit under a variety of circumstances. Perhaps a more realistic estimate can be obtained by projecting that about 15–20% of the 8,000 patients p.a. per million of the population with cancer would benefit from PET imaging; this would amount to approximately 1,600 patients each year.

3.3 A dedicated clinical PET centre could be justified serving a population of 1–1.5 million people. This is approximately the number of people subserved by the current cancer centres.
Some of these PET centres would enable investigation of the other conditions for which PET can contribute to the treatment within cardiology and neurology. This would be particularly true if the PET facility was in a tertiary referral centre with a high workload in these areas.

**Equipment and personnel**

3.4 An editorial in *Lancet* has addressed the issue with regard to the equipment currently available and becoming available. The staffing issues will ultimately depend on the mix of clinical service provision and research and development undertaken by a centre. The presence of an on-site cyclotron would generally need a larger than normal scanning staff in addition to the production staff, due to the ability of the centre to perform more complex studies using a variety of shorter half-life radiotracers. Staffing of a clinical PET centre depends on the number of PET cameras and the variety and volume of work undertaken. A model can be established for a scanning facility supplied with fluorine-based radiotracers from a distant production facility. The work is likely to be less complex and may start later in the day.

3.5 For each of these models, costs for providing a service can be divided into fixed and variable costs. The costs for a centre which provides an imaging service with a distant supply of tracer are:

- **Capital costs:** £1,285,050
- **Operating costs:** £585,900 p.a.

The costs for a centre which undertakes imaging and full production are:

- **Capital costs:** £2,761,750
- **Operating costs:** £670,850 p.a.

These figures are discussed in more detail in the appendices.
4 Current problems and their solutions

Problems with service provision

Staffing
4.1 The problem with staffing PET units is that there is at present a shortage of suitably trained and experienced staff at all levels. Providing a full scanning service with radiotracer production requires a multidisciplinary team of scientific, medical, technical and support staff. The pressure of dealing with short half-life radiotracers can at times be challenging and requires flexibility, precision, commitment and the ability to work to stringent time pressures. Staff at a scanning site which is remote from the production facility can be subject to delays and the occasional production failure; this can be frustrating and disruptive to the working day.

Training issues
4.2 There are training issues associated with all the disciplines involved in PET scanning. There is a need to establish a comprehensive training programme. There are few trained PET radiochemists or cyclotron engineers/technicians in the world, let alone the UK. Training may be undertaken by private companies with experience in providing radiotracer production facilities. However it may also be provided through MSc courses, or vocational training on an approved university course which is sponsored by industry or the government. This needs to be established as a matter of urgency. Similarly there are few trained cyclotron engineers/technicians, but other disciplines such as radiotherapy workshop technologists do have some of the skills, which, with the appropriate training, could provide necessary trouble-shooting and first-line maintenance. Formal training and on-the-job experience is required for these key members of the production team. The current difficulties in recruiting nuclear medicine technologists and radiographers for general departments are exacerbated when attempting to recruit for PET centres. Experienced, trained staff are not readily available in the UK and training needs to be given on site. BSc courses now include some PET lectures and an annual course is now offered by Guy’s and St Thomas’ PET Centre, but on-the-job training is required. Arranging rotations or split posts with other cross-sectional imaging departments (such as CT or MRI) may make these positions more attractive to radiographers who have not trained in nuclear medicine. There are few trained PET clinicians. Training for clinicians is being addressed by including PET as part of the Certificate of Completion of Specialist Training (CCST) in nuclear medicine, but post-CCST experience is also required. Post-CCST modular training would also be appropriate for radionuclide radiologists but there is no mechanism to validate such training. There are few centres in the UK where this experience can be gained and consequently it has been necessary for clinicians to gain on-the-job experience or to spend short periods in non-UK centres. This will be a significant issue in the clinical staffing of PET centres.

4.3 The delivery and maintenance of the service needs to be consistent with the Ionising Radiation (Medical Exposure) Regulations 2000 and the relevant aspects of Ionising Radiations...
Regulations 1999,\textsuperscript{21} and the Administration of Radioactive Substances Advisory Committee (ARSAC).\textsuperscript{22} It also needs to comply with necessary standards of delivery of a high quality service as well as issues related to clinical governance.

\begin{boxedtext}{Action on staffing}
\begin{itemize}
\item The training of staff needs to be addressed with government support for training programmes, especially for the scientific staff.
\item For medical trainees the training has been addressed in the new curriculum of the RCP for the CCST in nuclear medicine.
\item Radiographers should be encouraged to embrace PET scanning as an additional skill, perhaps linking it with CT and MRI training to provide combined jobs in the future.
\end{itemize}
\end{boxedtext}

Problems with establishing PET in the UK

4.4 Currently there are few centres in the UK with PET scanning, and even fewer radiotracer production sites. There needs to be a large capital investment programme covering all regions of the UK to establish the technique and provide a service, especially for cancer patients. There is a golden opportunity at this time for the government to identify strategic geographical sites for the establishment of radiotracer production facilities and a subsequent positioning of scanning units. There are currently cyclotrons at St Thomas’ Hospital, Imaging Research Solutions Limited (IRSL) at the Hammersmith Hospital, the Wolfson Brain Imaging Centre at Addenbrooke’s Hospital Cambridge, Mount Vernon Hospital, and the PET Imaging Research Group at the University of Aberdeen. The cyclotron at Clatterbridge produces F-18 for FDG production at the Manchester PET Centre at the Christie Hospital. There is also a large cyclotron in Birmingham which could possibly be adapted to produce radiotracers for PET scanning. These centres could provide the starting point for a network of PET radiotracer production facilities, with PET scanning units being established within two to four hours’ travel from those sited in cancer centres. This has the advantage that the major capital outlay on cyclotrons and radiotracer production facilities could be deferred whilst ensuring access for a larger number of patients to PET scanning. Consideration should be given to funding for a cyclotron and production facilities associated with cancer centres and nuclear medicine facilities in the north east and south west of England and the central corridor of Scotland. This would establish a unit in regions of the country where access would otherwise be difficult and would involve travelling to London.

4.5 While these developments are occurring, staff could be trained in existing clinical PET institutions providing funding can be found.
5 Suggested strategy for the provision of a PET service

5.1 There is a proposal to develop approximately 37 cancer networks in England and Wales. These could form the basis for the provision of a high quality PET service. If Scotland and Northern Ireland follow the same model, it could be developed to cover the whole of the UK. There are currently around 60 cancer centres in the UK and even more cancer units. All cancer centres should have access to the full range of nuclear medicine services, and therefore have the services of one or more specialists in nuclear medicine.23

5.2 The case has been made in this document for a PET service to supply a population of about one million people. This number of people will allow a single camera facility to be utilised full-time, providing enough patients to maintain the throughput necessary to ensure the need for a high quality service and maintenance of clinical skills. Larger cancer centres which deal with a greater variety of tumours and provide advances in therapy would almost certainly need an additional camera to allow research and development alongside the monitoring of therapy. The introduction of PET can be phased in around the country, but individual trusts would need financial support to introduce a service and maintain it. An initial investment to provide a service in 15 areas of the country should be considered, along with the establishment of a PET radiotracer production facility in the North East and South West of England, the central corridor of Scotland, and Northern Ireland. There should then be a second phase introducing further scanners, either at new or established sites.

5.3 The expenditure on dual coincidence imaging should be curtailed. Even if the dual coincidence GCI has a limited role it will not compete with dedicated PET, and the previously quoted statement from the HCFA in the USA suggests that full-ring systems are the method they are willing to finance. Both technologies are advancing and the likelihood is that dedicated PET systems will have a high patient throughput in the next few years because of the advances in crystal design and nature, and the electronics of the cameras, which will allow larger numbers of patients to be scanned. The clinical utility is proven with dedicated PET and has yet to be proven with GCI. The UK has a history of not funding the optimum methods of imaging until much later than is necessary. There should be no delay in funding this imaging method with the optimum equipment.

5.4 The resource of PET has to be embraced as a national strategy to give patients the full benefit of the technology. Therefore a controlled introduction, judiciously positioned, needs to be considered. It will need to be funded either separately by the Government (both the capital outlay and the running of the service), or by private investment. This latter strategy is beyond the scope of this paper.
5.5 Macintyre et al recently discussed the use of evidence to inform health policy. The criteria suggested for use in the evaluation of policy recommendations have been applied to PET as follows:

1 **Support by systematic evidence, empirical evidence.** There is a wealth of data establishing the role of dedicated PET in oncology, and other data to support its role in specific areas of cardiology and neuropsychiatry (see bibliography). Accompanying these publications have been meta-analyses of the available data supporting the use in colorectal recurrence, lung malignancies and so on, and cost-effectiveness analyses supporting the use of PET in solitary pulmonary nodules and the staging of pulmonary malignancies.

2 **Support by cogent argument.** The case for development of a PET network throughout the UK is presented above.

3 **Scale of likely health benefits.** The cost-effectiveness data for lung cancer points the way to further cost-effectiveness studies which need to be performed. There is, however, substantial published evidence which demonstrates the effect on management of patients such that the US health insurers have accepted the role of PET in areas outlined above.

4 **Likelihood that policy would bring benefits other than health benefits.** Benefits would be in terms of employment of skilled personnel and contribution to research.

5 **Compatibility with existing or proposed government strategy.** The proposed introduction of PET facilities coincides with the government strategy on improving the management of patients with cancer and cardiac disorders.

6 **Possibility that the policy might do harm.** The introduction of a number of PET centres is unlikely to do harm. It is important to avoid the introduction of a system where the centres are not run by trained personnel and where misdiagnosis is therefore a potential problem.

7 **Ease of implementation.** The strategy would be possible to implement if the distribution of centres was determined by a central government edict. The siting of cyclotrons could be evaluated, depending on the populations to be subserved, transport links and the skills available. PET scanners could be installed through a rolling programme, initially in centres with access to existing cyclotrons and then

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**BOX 2 Action on the provision of a national PET service**

- The currently available clinical cyclotrons should be invested in to ensure they are capable of producing tracer for other units.
- The sites for clinical PET centres should be identified as a first phase for new scanners.
- PET should be associated with cancer centres, or at the least cancer networks.
- Private sector funding should be assessed.
rolled out when further cyclotrons are installed. Over this period funding for training individuals (as outlined above) would need to be started and trainees encouraged to take up posts.

8 Cost of implementation. PET is an expensive technology and therefore needs to be implemented in several phases and over many years. If an initial 10–15 centres were established around the UK an assessment could be made over one or two years as to the ultimate requirement. This is likely to be between 40 and 60 centres with between one and three scanners per centre.
6 Conclusion

6.1 The establishment of clinical PET in the UK should be controlled and financed centrally to allow the optimum provision of service throughout the UK whilst maintaining a high clinical standard.

6.2 The established cancer networks and cancer centres should provide the structure upon which the introduction of PET centres is based. The exact siting of the centres will depend on the availability of tracer in the short term, and the development of radiotracer production facilities around the country. These facilities already exist in certain areas and the feasibility of them providing tracer or being upgraded to increase tracer production needs to be investigated. The areas of the country which are without access include the North East and South West of England, the central corridor of Scotland and Northern Ireland, and investment in cyclotrons may need to be provided to establish these areas.
PART 2
Clinical indications for positron emission tomography imaging: current ICSCNM suggestions
Introduction

Positron emission tomography (PET) scanning is now available in the UK as a diagnostic imaging modality. This rapidly developing technique has been shown to be clinically useful in a range of specialties, and further assessment of its role in patient management is under way in a number of clinical studies worldwide. Although PET scanning is sometimes thought of as a separate and unique imaging specialty (like MRI) it should be regarded as an extension of nuclear medicine using specific radiopharmaceuticals (positron-labelled tracers) and a specialised detecting system optimised for the detection of the 511 KeV coincidence photons.

It is not possible at the current time to be dogmatic about the role of PET imaging in clinical medicine, partly because of the limited facility for PET imaging in the UK. However, based on clinical experience, coupled with the published data, there are now many clinical situations where it is the imaging method of choice. There will always be situations when more than one diagnostic technique can be used to provide similar although less accurate information and the choice will often depend on factors such as availability, cost, skills etc.

The common radiotracers used are FDG (F-18 Fluorodeoxyglucose), methionine (C-11 methionine), ammonia (N-13 ammonia), water (O-15 water) and flumazenil (C-11 flumazenil).

Table 1 Typical radiation doses for current practice. The administration of activity for paediatric studies are scaled down by the body weight as a proportion of a 70kg adult dose.

<table>
<thead>
<tr>
<th>Radionuclide</th>
<th>Radiopharmaceutical</th>
<th>Injected activity (MBq)</th>
<th>Target organ</th>
<th>Whole body dose (mSv)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbon-11</td>
<td>Methionine</td>
<td>370–740</td>
<td>Pancreas</td>
<td>1.7–3.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>370</td>
<td>Small intestine</td>
<td>1.32</td>
</tr>
<tr>
<td>Fluorine</td>
<td>Fluorodeoxyglucose</td>
<td>250–400</td>
<td>Bladder</td>
<td>6.8–10</td>
</tr>
<tr>
<td></td>
<td></td>
<td>222</td>
<td>Bladder</td>
<td>6.0</td>
</tr>
<tr>
<td>Nitrogen-13</td>
<td>Ammonia</td>
<td>550</td>
<td>Bladder</td>
<td>1.5</td>
</tr>
<tr>
<td>Oxygen-15</td>
<td>Water</td>
<td>2,300</td>
<td>Ovaries (female)</td>
<td>2.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Large intestine (male)</td>
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</tr>
</tbody>
</table>

Radiation hazards

The radiation dose to the patient, associated with PET investigations, will depend on the tracer used and the activity administered (Table 1).

Radiation doses received by accompanying persons are low because of the short half-lives of the tracers currently used. The doses to adults are below the current European recommended levels.
Children should not accompany parents who are having a PET scan, since close contact immediately following tracer administration will result in higher received radiation doses. The radiation dose rates are low when contact is resumed two hours after the injection.\(^{25}\)

**Breast feeding**

The patient is encouraged to express the next feed after the scan but does not need to reduce contact with children given the current injected activity of 350–400 MBq of FDG. Breast feeding may then be restarted normally. Whilst this advice applies to one-off exposures, patients who are likely to receive a number of PET or nuclear medicine scans may be advised to reduce close contact with small children for a longer period.

**Pregnancy and protection of the foetus**

Irradiation of a foetus is to be avoided whenever possible. If the scan is judged clinically essential then discussion with the patient with regard to the radiation dose and the risks associated with not performing the investigation should be undertaken.

**The clinical indications table**

The following table is divided into the four clinical sections which cover the main areas of PET imaging: oncology, cardiology, neuropsychiatry and miscellaneous applications. For each of these sections the indications will be classified into ‘indicated’, ‘not routinely indicated (but may be helpful)’, and ‘not indicated’.

The strength of the evidence for the various indications is identified using the NHS Executive clinical guidelines.\(^{26}\) This system of definitions is used in the *Making the best use of a department of clinical radiology* booklet published by the Royal College of Radiologists.

The strength of evidence is classified as:

A. Randomised controlled clinical trials, meta-analyses, systematic reviews.

B. Robust experimental or observational studies.

C. Other evidence where the advice relies on expert opinion and has the endorsement of respected authorities.

**Note about oncology applications**

Applications in oncology can be considered under a number of headings, which have different importance in different tumours. Areas of use may be considered by generic guidance or by the pathological system affected. The generic guidance considers the management issues for oncology patients. The list in paragraph 2.3 of Part 1 relates generally to all malignancies and forms a basis for which PET examinations may be useful. Indications organised by the pathological system affected are given in the table below.
Clinical indications for positron emission tomography

<table>
<thead>
<tr>
<th>Oncology applications</th>
<th>Indicated</th>
<th>Not indicated routinely (but may be helpful)</th>
<th>Not indicated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain and spinal cord</td>
<td>▶ Suspected tumour recurrence when anatomical imaging is difficult or equivocal and management will be affected. Often a combination of methionine and FDG PET scans will need to be performed. (B) ▶ Benign versus malignant lesions, where there is uncertainty on anatomical imaging and a relative contraindication to biopsy. (B) ▶ Investigation of the extent of tumour within the brain or spinal cord. (C)</td>
<td>▶ Secondary tumours in the brain. (C) ▶ Assess tumour response to therapy. (C)</td>
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</tr>
<tr>
<td>Parotid</td>
<td>▶ Identification of metastatic disease in the neck from a diagnosed malignancy. (C)</td>
<td>▶ Differentiation of Sjogrens Syndrome from malignancy in the salivary glands. (C) ▶ Primary tumour of the parotid to distinguish benign from malignant disease. (C)</td>
<td></td>
</tr>
<tr>
<td>Malignancies of the oropharynx</td>
<td>▶ Identify extent of the primary disease with or without image registration. (C) ▶ Identify tumour recurrence in previously treated carcinoma. (C)</td>
<td>▶ Preoperative staging of known oropharyngeal tumours. (C) ▶ Search for primary with nodal metastases. (C)</td>
<td></td>
</tr>
<tr>
<td>Larynx</td>
<td>▶ Identify tumour recurrence in previously treated carcinoma. (C)</td>
<td>▶ Staging known laryngeal tumours. (C) ▶ Identification of metastatic disease in the neck from a diagnosed malignancy. (C)</td>
<td></td>
</tr>
<tr>
<td>Thyroid</td>
<td>▶ Assessment of patients with elevated thyroglobulin and negative iodine scans for recurrent disease. (B)</td>
<td>▶ Assessment of tumour recurrence in medullary carcinoma of the thyroid. (C)</td>
<td>▶ Routine assessment of thyroglobulin positive recurrence with radioiodine uptake. (C)</td>
</tr>
</tbody>
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continued
<table>
<thead>
<tr>
<th>Clinical indications</th>
<th>Indicated</th>
<th>Not indicated routinely (but may be helpful)</th>
<th>Not indicated</th>
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</thead>
<tbody>
<tr>
<td><strong>Parathyroid</strong></td>
<td></td>
<td>▶ Localisation of parathyroid adenomas with methionine when other investigations are negative. (C)</td>
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<tr>
<td><strong>Lung</strong></td>
<td></td>
<td>▶ Assessment of response to treatment. (C)</td>
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<td></td>
<td>▶ Differentiation of benign versus malignant lesions where anatomical imaging or biopsy are inconclusive or there is a relative contraindication to biopsy. (A)</td>
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<tr>
<td></td>
<td>▶ Preoperative staging of non small cell primary lung tumours. (A)</td>
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<td></td>
<td>▶ Assessment of recurrent disease in previously treated areas where anatomical imaging is unhelpful. (C)</td>
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<tr>
<td><strong>Oesophagus</strong></td>
<td></td>
<td>▶ Assessment of neoadjuvant chemotherapy. (C)</td>
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<td></td>
<td>▶ Staging of primary cancer. (B)</td>
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<td></td>
<td>▶ Assessment of disease recurrence in previously treated cancers. (C)</td>
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<tr>
<td><strong>Stomach</strong></td>
<td></td>
<td>▶ Assessment of gastro-oesophageal malignancy and local metastases. (C)</td>
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<td></td>
<td>▶ No routine indication. (C)</td>
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<tr>
<td><strong>Small bowel</strong></td>
<td>▶ No routine indication. (C)</td>
<td>▶ Proven small bowel lymphoma to assess extent of disease. (C)</td>
<td></td>
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<tr>
<td><strong>Breast cancer</strong></td>
<td>▶ Assessment and localisation of brachial plexus lesions in breast cancer. (Radiation effects versus malignant infiltration.) (C)</td>
<td>▶ Routine assessment of primary breast cancer. (C)</td>
<td></td>
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<tr>
<td></td>
<td>▶ Assessment of the extent of disseminated breast cancer. (C)</td>
<td>▶ Axillary node status where there is a relative contraindication to axillary dissection. (C)</td>
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<td></td>
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<td>▶ Assessment of multifocal disease within the difficult breast (dense breast or equivocal radiology). (C)</td>
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<td></td>
<td>▶ Suspected local recurrence. (C)</td>
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<td></td>
<td></td>
<td>▶ Assessment of chemotherapy response. (C)</td>
<td></td>
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<tr>
<td><strong>Liver: primary lesion</strong></td>
<td></td>
<td>▶ Routine assessment of hepatoma. (C)</td>
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<thead>
<tr>
<th>Clinical indications</th>
<th>Indicated</th>
<th>Not indicated routinely (but may be helpful)</th>
<th>Not indicated</th>
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</thead>
<tbody>
<tr>
<td>Liver: secondary lesion</td>
<td>Equivocal diagnostic imaging (CT, MRI, ultrasound), (C)</td>
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<td></td>
<td>Assessment pre and post therapy intervention. (C)</td>
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<td></td>
<td>Exclude other metastatic disease prior to metastecomy. (C)</td>
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<tr>
<td>Pancreas</td>
<td>Staging a known primary. (C)</td>
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<td></td>
<td>Differentiation of chronic pancreatitis from pancreatic carcinoma. (C)</td>
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<td></td>
<td>Assessment of pancreatic masses to determine benign or malignant status. (C)</td>
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<tr>
<td>Colon and rectum</td>
<td>Assessment of recurrent disease. (A)</td>
<td>Assessment of tumour response. (C)</td>
<td>Assessment of polyps. (C)</td>
</tr>
<tr>
<td></td>
<td>Prior to metastectomy for colorectal cancer. (C)</td>
<td>Assessment of a mass that is difficult to biopsy. (C)</td>
<td>Staging a known primary. (C)</td>
</tr>
<tr>
<td>Renal and adrenal</td>
<td>Assessment of possible adrenal metastases. (C)</td>
<td>Paragangliomas or metastatic phaeochromocytoma to identify sites of disease. (C)</td>
<td>Assessment of renal carcinoma. (C)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Phaeochromocytoma – MIBG scanning is usually superior. (C)</td>
</tr>
<tr>
<td>Bladder</td>
<td>No routine indication. (C)</td>
<td>Staging a known primary in selected cases. (C)</td>
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<tr>
<td></td>
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<td>Recurrence with equivocal imaging. (C)</td>
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<tr>
<td>Prostate</td>
<td></td>
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<td>FDG in prostate cancer assessment. (C)</td>
</tr>
<tr>
<td>Testicle</td>
<td>Assessment of recurrent disease from seminomas and teratomas. (B)</td>
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<td></td>
<td>Assessment of residual masses. (B)</td>
<td></td>
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<tr>
<td>Ovary</td>
<td>In difficult management situations to assess local and distant spread (C)</td>
<td></td>
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<tr>
<td>Uterus: cervix</td>
<td>No routine indication. (C)</td>
<td>In difficult situations to define the extent of disease with accompanying image registration. (C)</td>
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<table>
<thead>
<tr>
<th>Clinical indications</th>
<th>Indicated</th>
<th>Not indicated routinely (but may be helpful)</th>
<th>Not indicated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uterus: body</td>
<td>► No routine indication. (C)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymphoma</td>
<td>► Staging of Hodgkin’s lymphoma. (B)</td>
<td>► Assessment of bowel lymphoma. (C)</td>
<td></td>
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<tr>
<td></td>
<td>► Staging of non-Hodgkin’s lymphoma. (B)</td>
<td>► Assessment of bone marrow to guide biopsy. (C)</td>
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<tr>
<td></td>
<td>► Assessment of residual masses for active disease. (B)</td>
<td>► Assessment of remission from lymphoma. (C)</td>
<td></td>
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<td></td>
<td>► Identification of disease sites when there is suspicion of relapse from clinical assessment. (C)</td>
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<td></td>
<td>► Response to chemotherapy. (C)</td>
<td></td>
<td></td>
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<tr>
<td>Musculoskeletal tumours</td>
<td>► Soft tissue primary mass assessment to distinguish high grade malignancy from low or benign disease. (B)</td>
<td>► Image registration of the primary mass to identify optimum biopsy site. (C)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>► Staging of primary soft tissue malignancy to assess nonskeletal metastases. (B)</td>
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<tr>
<td></td>
<td>► Assessment of recurrent abnormalities in operative sites. (B)</td>
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<td></td>
<td>► Assessment of osteogenic sarcomas for metastatic disease. (C)</td>
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<tr>
<td></td>
<td>► Follow up to detect recurrence or metastases. (B)</td>
<td></td>
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<tr>
<td>Skin tumours</td>
<td>► Malignant melanoma with known dissemination to assess extent of disease. (B)</td>
<td>► Staging of skin lymphomas. (C)</td>
<td>► Malignant melanoma with negative sentinel node biopsy. (B)</td>
</tr>
<tr>
<td></td>
<td>► Malignant melanoma in whom a sentinel node biopsy was not or can not be performed in stage II. (AJCC updated classification). (C)</td>
<td></td>
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</tr>
<tr>
<td>Metastases from unknown primary</td>
<td>► Determining the site of an unknown primary when this influences management. (C)</td>
<td>► Widespread metastatic disease when the determination of the site is only of interest. (C)</td>
<td></td>
</tr>
</tbody>
</table>

*continued*
**Cardiac applications**

<table>
<thead>
<tr>
<th>Indicated</th>
<th>Not indicated routinely (but may be helpful)</th>
<th>Not indicated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis of hibernating myocardium in patients with poor left ventricular function prior to revascularisation procedure. (A)</td>
<td>Diagnosis of coronary artery disease or assessment of known coronary stenosis where other investigations. (SPECT, ECG etc) remain equivocal. (B)</td>
<td>Patients with confirmed coronary artery disease in whom revascularisation is not contemplated or indicated. (C)</td>
</tr>
<tr>
<td>Patients with a fixed SPET deficit who might benefit from revascularisation. (B)</td>
<td>Differential diagnosis of cardiomyopathy (ischaemic versus other types of dilated cardiomyopathy). (C)</td>
<td>Routine screening for coronary artery disease. (C)</td>
</tr>
<tr>
<td>Prior to referral for cardiac transplantation. (B)</td>
<td>Medical treatment of ischaemic heart disease in high risk hyperlipidemic patients. (C)</td>
<td></td>
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</tbody>
</table>

**Neuropsychiatry applications**

<table>
<thead>
<tr>
<th>Indicated</th>
<th>Not indicated routinely (but may be helpful)</th>
<th>Not indicated</th>
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<tbody>
<tr>
<td>Presurgical evaluation of epilepsy. (B)</td>
<td>The grading of primary brain tumour. (B)</td>
<td>Diagnosis of dementia where MRI is clearly abnormal. (C)</td>
</tr>
<tr>
<td>Suspected recurrence or failed primary treatment of primary malignant brain tumours. (Most of these patients will have had MRI and CT with equivocal results). (B)</td>
<td>Localisation of optimal biopsy site (either primary or recurrent brain tumour). (C)</td>
<td>Most instances of stroke. (C)</td>
</tr>
<tr>
<td>Early diagnosis of dementia (especially younger patients and Alzheimer's disease) when MRI or CT is either normal, marginally abnormal or equivocally abnormal. (B)</td>
<td>Differentiating malignancy from infection in HIV subjects where MRI is equivocal. (C)</td>
<td>Most psychiatric disorders other than early dementia. (C)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pre-symptomatic or at risk Huntington's disease. (C)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Diagnosis of epilepsy. (C)</td>
</tr>
</tbody>
</table>

**Miscellaneous applications**

| Indicated                                                                 | Not indicated routinely (but may be helpful)                                                                 | Not indicated                                      |
| Disease assessment in HIV and other immunosuppressed patients            | Routine assessment of weight loss where malignancy is suspected. (C)                                       |                                                   |
| Identification of sites to biopsy in patients with pyrexia. (C)          |                                                                                                           |                                                   |
| Differentiating benign from malignant cerebral pathology. (B)            |                                                                                                           |                                                   |

| Indicated                                                                 | Not indicated routinely (but may be helpful)                                                                 | Not indicated                                      |
| Assessment of bone infection                                              | Assessment of bone infection associated with prostheses. (C)                                              |                                                   |
|                                                                            | Assessment of spinal infection or problematic cases of infection. (C)                                       |                                                   |

*continued*
<table>
<thead>
<tr>
<th>Clinical indications</th>
<th>Not indicated routinely (but may be helpful)</th>
<th>Not indicated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assessment of bone metastases</td>
<td>▶ When bone scan or other imaging is equivocal. (C)</td>
<td></td>
</tr>
<tr>
<td>Assessment of tumour recurrence in the pituitary</td>
<td>▶ Identifying recurrent functional pituitary tumours when anatomical imaging has not been successful. (C)</td>
<td></td>
</tr>
<tr>
<td>Fever of unknown origin</td>
<td>▶ Identifying source of the fever of unknown origin. (C)</td>
<td></td>
</tr>
</tbody>
</table>
APPENDICES
APPENDIX I
Imaging with a distant supply of tracer: the minimum establishment*

<table>
<thead>
<tr>
<th>Summary of costs</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Capital costs</td>
<td>£1,285,050</td>
</tr>
<tr>
<td>Operating costs</td>
<td>£585,900</td>
</tr>
<tr>
<td>Staff costs</td>
<td>£198,050</td>
</tr>
<tr>
<td>Fixed costs</td>
<td>£72,850</td>
</tr>
<tr>
<td>Variable costs</td>
<td>£315,000</td>
</tr>
</tbody>
</table>

**Capital costs**

Capital costs include the PET scanner, associated computer workstations and network equipment in addition to data storage media. A full resuscitation trolley, a pulse oximeter and blood glucose monitoring equipment for the scan room are included, as well as radiation protection and monitoring equipment. An allocation for basic office equipment and furniture is also listed. Building and space renovation costs have not been included.

**Operating costs**

It has been assumed that this facility would scan in the region of 1,000 patients per year. This assumes an average throughput of four patients per day if scanning is said to be five days per week for 48 weeks of the year with allowance made for maintenance, breakdown and bank holidays. London weighting and on-costs are included. It is assumed that the facility will be managed from an associated nuclear medicine or radiology department.

**Staff costs**

Two to three radiographers/nuclear medicine technologists would be required to perform radiotracer administration, patient scanning and image processing. The support of one WTE medical physicist would be necessary to provide cover for data processing, scanner quality control and the on-going development of image acquisition and processing protocols and radiation protection. The receptionist/secretary is required to book scans, send out appointments, type

* The figures in this appendix are based on the experience of the Guy’s and St Thomas’ Clinical PET Centre in 2001.
reports and provide general administrative support. In addition, two 0.5 WTE clinical appointments would provide scan reporting and medical support. This assumes that basic FDG imaging is being performed.

Table 1  Capital costs for imaging with a distant supply of tracer. VAT is not included.

<table>
<thead>
<tr>
<th>Item</th>
<th>Quantity</th>
<th>Costs (£)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PET scanner</td>
<td>1</td>
<td>1,200,000</td>
</tr>
<tr>
<td>Capintec</td>
<td>1</td>
<td>5,000</td>
</tr>
<tr>
<td>Protected bench</td>
<td>1</td>
<td>16,000</td>
</tr>
<tr>
<td>Lead safe</td>
<td>1</td>
<td>5,000</td>
</tr>
<tr>
<td>Protected injection devices</td>
<td>3</td>
<td>600</td>
</tr>
<tr>
<td>Hand/area radiation monitors</td>
<td>2</td>
<td>3,000</td>
</tr>
<tr>
<td>Emergency trolley</td>
<td>1</td>
<td>6,000</td>
</tr>
<tr>
<td>Pulse oximeter</td>
<td>1</td>
<td>2,000</td>
</tr>
<tr>
<td>Blood glucose monitor</td>
<td>1</td>
<td>500</td>
</tr>
<tr>
<td>Patient trolleys</td>
<td>2</td>
<td>1,850</td>
</tr>
<tr>
<td>Transportation pot</td>
<td>1</td>
<td>4,500</td>
</tr>
<tr>
<td>Workstations</td>
<td>2</td>
<td>10,000</td>
</tr>
<tr>
<td>Hard disks (36Gby)</td>
<td>2</td>
<td>1,000</td>
</tr>
<tr>
<td>Tape drives</td>
<td>2</td>
<td>1,000</td>
</tr>
<tr>
<td>Image printer</td>
<td>1</td>
<td>12,000</td>
</tr>
<tr>
<td>PCs (general use)</td>
<td>6</td>
<td>6,000</td>
</tr>
<tr>
<td>Text printer</td>
<td>1</td>
<td>600</td>
</tr>
<tr>
<td>Furniture</td>
<td>–</td>
<td>10,000</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td><strong>1,285,050</strong></td>
</tr>
</tbody>
</table>

Table 2  Staff costs per annum for imaging with a distant supply of tracer. These figures assume a throughput of 1,000 patients each year, and include London weighting and on-costs.

<table>
<thead>
<tr>
<th>Grade</th>
<th>WTEs</th>
<th>Total salary costs (£)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radiographer (senior 1/MTO 3)</td>
<td>1</td>
<td>29,200</td>
</tr>
<tr>
<td>Radiographer (senior II/MTO 2)</td>
<td>2</td>
<td>50,000</td>
</tr>
<tr>
<td>Clinical scientist (physicist)</td>
<td>1</td>
<td>30,800</td>
</tr>
<tr>
<td>Consultant physician</td>
<td>1 (0.5 + 0.5)</td>
<td>65,700</td>
</tr>
<tr>
<td>Receptionist/secretary (grade 4)</td>
<td>1</td>
<td>19,850</td>
</tr>
<tr>
<td>Training/uniforms etc</td>
<td>–</td>
<td>2,500</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td><strong>198,050</strong></td>
</tr>
</tbody>
</table>
**Fixed costs**

Fixed costs are itemised in Table 3 and include the cost of a fully comprehensive maintenance contract for the scanner and associated workstations. The cost of space allocation has not been included but contract cleaning is listed. Germanium rod sources need to be replaced yearly and are therefore included. Costs associated with the initial marketing of the service and educational sessions for potential referrers have also been included.

<table>
<thead>
<tr>
<th>Item</th>
<th>Costs (£)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scanner maintenance</td>
<td>50,000</td>
</tr>
<tr>
<td>Computer maintenance</td>
<td>750</td>
</tr>
<tr>
<td>Housekeeping contract</td>
<td>4,500</td>
</tr>
<tr>
<td>Marketing/education</td>
<td>5,000</td>
</tr>
<tr>
<td>Rod sources</td>
<td>6,000</td>
</tr>
<tr>
<td>Building maintenance</td>
<td>6,600</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>72,850</strong></td>
</tr>
</tbody>
</table>

**Variable costs**

Variable costs are identified at £315 per patient scan. This includes the delivery of tracer doses at £300 per patient dose (assuming that a dose is defined as 350MBq) of FDG. VAT has not been included. The cost of radiotracer supply will vary depending on the distance between the scanner and the production facility. For the purposes of this paper it has been assumed that there is a maximum time of one half-life between dispatch from the production site to the first patient administration. Doses for subsequent patients will need to be decay-corrected appropriately for timed administrations. It is usually possible for 3–4 patient doses to be included in one delivery but this will depend on activity available from each production run. Radiotracer and delivery costs will inevitably increase with distance from the production facility. The market for radiotracers is increasing rapidly and costs are likely to be subject to variations as commercial suppliers enter the market. Basic consumable costs per patient scan have also been included.

<table>
<thead>
<tr>
<th>Item</th>
<th>Costs (£)</th>
</tr>
</thead>
<tbody>
<tr>
<td>350MBq FDG and transport</td>
<td>300,000</td>
</tr>
<tr>
<td>Scanning supplies (needles, syringes, linen etc)</td>
<td>10,000</td>
</tr>
<tr>
<td>Data storage</td>
<td>1,000</td>
</tr>
<tr>
<td>Hard copy and stationery</td>
<td>4,000</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>315,000</strong></td>
</tr>
</tbody>
</table>
APPENDIX 2
Imaging with full production of tracer: the minimum establishment

Summary of costs

<table>
<thead>
<tr>
<th></th>
<th>Costs (£)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capital costs:</td>
<td>£2,761,750</td>
</tr>
<tr>
<td>Imaging facility:</td>
<td>£1,292,050</td>
</tr>
<tr>
<td>Radiotracer production:</td>
<td>£1,469,700</td>
</tr>
<tr>
<td>Operating costs:</td>
<td>£670,850</td>
</tr>
<tr>
<td>Staff costs:</td>
<td></td>
</tr>
<tr>
<td>Scanning:</td>
<td>£301,300</td>
</tr>
<tr>
<td>Radiotracer production:</td>
<td>£140,700</td>
</tr>
<tr>
<td>Fixed costs:</td>
<td></td>
</tr>
<tr>
<td>Scanning:</td>
<td>£72,850</td>
</tr>
<tr>
<td>Radiotracer production:</td>
<td>£74,000</td>
</tr>
<tr>
<td>Variable costs:</td>
<td></td>
</tr>
<tr>
<td>Scanning:</td>
<td>£18,000</td>
</tr>
<tr>
<td>Radiotracer production:</td>
<td>£64,000</td>
</tr>
</tbody>
</table>

Capital costs

Imaging Scanning costs are as per the remote site, but with the addition of a syringe pump and ECG monitoring to enable stress heart studies to be performed. If quantitative research studies are to be performed a gamma counter, fluid analyser and associated equipment for handling blood sampling would be required.

Table 5 Total capital scanning costs for imaging and radiotracer production facility.

<table>
<thead>
<tr>
<th>Item</th>
<th>Quantity</th>
<th>Costs (£)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scanning room (as per Table 1)</td>
<td>1,285,050</td>
<td></td>
</tr>
<tr>
<td>Syringe pump</td>
<td>1</td>
<td>2,000</td>
</tr>
<tr>
<td>12 lead ECG machine</td>
<td>1</td>
<td>5,000</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td><strong>1,292,050</strong></td>
</tr>
</tbody>
</table>

* The figures in this appendix are based on the experience of the Guy’s and St Thomas’ Clinical PET Centre in 2001.
Equipment to enable production of the main clinical tracers has been itemised. It is assumed that FDG will be produced for use internally and for distribution. Quality control equipment has therefore been included to enable the centre to perform rigorous analysis of FDG in particular in order to comply with present Medicines Control Agency (MCA) regulations and the European Pharmacopea entry.

Commercial chemistry modules for the production of FDG and C-11 Methionine have been included. It should be noted that the commercial market for these units is developing rapidly and pricing is competitive. As with the previous model, building costs or renovation of existing space have not been included.

Operating costs

This model assumes that the scanning and radiotracer production facility operates as an integrated unit within areas of shared expertise and resources. Internal cross-charging for FDG tracer doses has not therefore been itemised. The costs associated with FDG production are included in the operating costs of the cyclotron and radiotracer production.

It has been assumed that this facility would scan in the region of 1,200+ patients per year, giving an average throughput of five patients per day. Scanning is said to be five days per week for 48 weeks of the year, allowance being made for maintenance, breakdown and bank holidays. This level of throughput has been based on the experience of one centre performing oncological, cardiological and neurological scans as well as some research studies. This may be considered to be a fairly conservative estimate which will be affected by variations in patient mix and protocol design. Faster scanners coming on to the market should also improve the throughput of patients.

Staff costs

This model would require a staffing complement similar to the previous model. However with an on-site cyclotron and production facility it is likely that more complex clinical imaging and some research would be undertaken during a longer working day. The staff costs for the scanning facility therefore reflect this and anticipate some shift work to accommodate the longer scanning times and increased patient throughput. There is a requirement for two WTE physics and computing personnel to provide support for data processing and storage, scanner quality control, trouble-shooting and the development of image processing protocols for clinical and basic research studies. If complex quantitative research protocols are envisaged then additional physics and computing staff will be required. Secretarial/reception support of one WTE is listed. An additional 0.5–1 WTE SpR will be required for medical support, training and scan reporting. The complexity of the total operation requires a person in the position of manager/administrator who is able to co-ordinate the activities of the centre as a whole. This would include strategic planning, the setting and monitoring of budgets, marketing and arranging contracts for FDG supply and distribution, and day-to-day operational management. If the centre is under the management of nuclear medicine or radiology, some of these activities may be undertaken by personnel or departments already in existence. However it is likely that, having invested in a radiochemistry production facility, there will be a significant commercial component to the operation which will require careful planning and on-going management if the full potential is to be realised.
Table 6  Capital costs for full production of radiotracer within an imaging and full production of tracer facility.

<table>
<thead>
<tr>
<th>Item</th>
<th>Quantity</th>
<th>Costs (£)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclotron and laboratory infrastructure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cyclotron</td>
<td>1</td>
<td>1,000,000</td>
</tr>
<tr>
<td>Isolator cabinet</td>
<td>1</td>
<td>40,000</td>
</tr>
<tr>
<td>Dispenser</td>
<td>1</td>
<td>15,000</td>
</tr>
<tr>
<td>Dose meters (Mini-Inst)</td>
<td>2</td>
<td>2,000</td>
</tr>
<tr>
<td>Surface/hand monitors</td>
<td>2</td>
<td>4,500</td>
</tr>
<tr>
<td>Area monitors (Lab Impex)</td>
<td>6</td>
<td>9,000</td>
</tr>
<tr>
<td>Personal radiation monitors</td>
<td>6</td>
<td>1,200</td>
</tr>
<tr>
<td>Fume cupboards</td>
<td>2</td>
<td>6,000</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td><strong>1,077,700</strong></td>
</tr>
<tr>
<td>FDG production</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FDG box</td>
<td>1</td>
<td>50,000</td>
</tr>
<tr>
<td>Mini hot cell</td>
<td>1</td>
<td>30,000</td>
</tr>
<tr>
<td>Lead castles</td>
<td>–</td>
<td>15,000</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td><strong>95,000</strong></td>
</tr>
<tr>
<td>C-11 production</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C-11 chemistry module</td>
<td>1</td>
<td>60,000</td>
</tr>
<tr>
<td>Hot cell</td>
<td>1</td>
<td>50,000</td>
</tr>
<tr>
<td>Gradient pump</td>
<td>1</td>
<td>13,000</td>
</tr>
<tr>
<td>UV detector</td>
<td>1</td>
<td>6,000</td>
</tr>
<tr>
<td>Rad detector</td>
<td>1</td>
<td>8,000</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td><strong>137,000</strong></td>
</tr>
<tr>
<td>QC equipment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dionex PED detector</td>
<td>1</td>
<td>20,000</td>
</tr>
<tr>
<td>Isocratic pump</td>
<td>1</td>
<td>5,000</td>
</tr>
<tr>
<td>Rad detector</td>
<td>1</td>
<td>6,000</td>
</tr>
<tr>
<td>PC, software and printer</td>
<td>1</td>
<td>7,000</td>
</tr>
<tr>
<td>TLC scanner</td>
<td>1</td>
<td>25,000</td>
</tr>
<tr>
<td>Supressor</td>
<td>1</td>
<td>2,000</td>
</tr>
<tr>
<td>Injector</td>
<td>1</td>
<td>750</td>
</tr>
<tr>
<td>Gradient pump</td>
<td>1</td>
<td>12,000</td>
</tr>
<tr>
<td>UV detector</td>
<td>1</td>
<td>6,000</td>
</tr>
<tr>
<td>Rad detector</td>
<td>1</td>
<td>8,000</td>
</tr>
<tr>
<td>Injector</td>
<td>1</td>
<td>750</td>
</tr>
<tr>
<td>PC, software and printer</td>
<td>1</td>
<td>7,500</td>
</tr>
<tr>
<td>Gas chromatograph</td>
<td>1</td>
<td>16,000</td>
</tr>
<tr>
<td>Chart recorders</td>
<td>2</td>
<td>3,000</td>
</tr>
<tr>
<td>Oven</td>
<td>1</td>
<td>1,500</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td><strong>120,500</strong></td>
</tr>
</tbody>
</table>

*continued*
Table 6 continued.

<table>
<thead>
<tr>
<th>General laboratory equipment</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Refrigerator</td>
<td>1</td>
<td>400</td>
</tr>
<tr>
<td>Freezer</td>
<td>1</td>
<td>200</td>
</tr>
<tr>
<td>Assorted glassware</td>
<td></td>
<td>400</td>
</tr>
<tr>
<td>Assorted tweezers and tongs</td>
<td></td>
<td>500</td>
</tr>
<tr>
<td>Lead safe</td>
<td>1</td>
<td>3,000</td>
</tr>
<tr>
<td>Lead pots</td>
<td>20</td>
<td>1,000</td>
</tr>
<tr>
<td>Balances</td>
<td>2</td>
<td>5,000</td>
</tr>
<tr>
<td>Pipettes</td>
<td>3</td>
<td>400</td>
</tr>
<tr>
<td>Solvent cupboards</td>
<td>2</td>
<td>400</td>
</tr>
<tr>
<td>Internal transport trolley</td>
<td>1</td>
<td>2,000</td>
</tr>
<tr>
<td>Capintecs</td>
<td>2</td>
<td>10,000</td>
</tr>
<tr>
<td>Crimping tool</td>
<td>1</td>
<td>200</td>
</tr>
<tr>
<td>Decrimping tool</td>
<td>1</td>
<td>200</td>
</tr>
<tr>
<td>Rad detector (GM tube)</td>
<td>1</td>
<td>1,000</td>
</tr>
<tr>
<td>Lead syringe shields</td>
<td>8</td>
<td>1,000</td>
</tr>
<tr>
<td>Osmolality kit</td>
<td>1</td>
<td>2,000</td>
</tr>
<tr>
<td>Shielded delivery boxes</td>
<td>2</td>
<td>5,000</td>
</tr>
<tr>
<td>Ultrasonic bath</td>
<td>1</td>
<td>400</td>
</tr>
<tr>
<td>LAL test kit</td>
<td>1</td>
<td>400</td>
</tr>
<tr>
<td>Laboratory/office furniture</td>
<td></td>
<td>6,000</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td><strong>39,500</strong></td>
</tr>
</tbody>
</table>

**Total capital costs**  1,469,700

Table 7 Staff costs per annum for imaging within an imaging and full production of tracer facility. These figures assume a throughput of 1,200+ patients per year, and include London weighting and on-costs.

<table>
<thead>
<tr>
<th>Grade</th>
<th>WTE’s</th>
<th>Total salary costs (£)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radiographer (supt III/MTO 4)</td>
<td>1</td>
<td>31,800</td>
</tr>
<tr>
<td>Radiographer (senior I/MTO 3)</td>
<td>1</td>
<td>29,200</td>
</tr>
<tr>
<td>Radiographer (senior II/MTO 2)</td>
<td>1.5</td>
<td>37,500</td>
</tr>
<tr>
<td>Clinical scientist (physicist)</td>
<td>1</td>
<td>30,800</td>
</tr>
<tr>
<td>Systems administrator</td>
<td>1</td>
<td>26,500</td>
</tr>
<tr>
<td>Consultant physician</td>
<td>1 (0.5 + 0.5)</td>
<td>65,700</td>
</tr>
<tr>
<td>SpR</td>
<td>0.5</td>
<td>17,950</td>
</tr>
<tr>
<td>Receptionist/secretary (grade 4)</td>
<td>1</td>
<td>19,850</td>
</tr>
<tr>
<td>Manager/administrator</td>
<td>1</td>
<td>38,000</td>
</tr>
<tr>
<td>Training, uniforms etc</td>
<td></td>
<td>4,000</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td><strong>301,300</strong></td>
</tr>
</tbody>
</table>
To maintain a reliable daily production of 18F-fluoride based radiotracers for internal and external distribution, in addition to a variety of shorter half-life tracers, a minimum complement of two radiochemists and a laboratory technician working a flexible rota would be required. A minimum of two WTE cyclotron technicians with the experience and capability to trouble-shoot and provide first line maintenance is also necessary. It may be possible to cross-train cyclotron and chemistry staff to perform routine functions in the laboratory to increase flexibility, but this would not reduce the need for experienced and competent technicians and chemists.

Staffing for the cyclotron and radiotracer production facility has assumed that the following routine clinical radiotracers are available: $^{18}$FDG, $^{N13}$H$_3$, $^{C11}$ Methionine and $^{H2O15}$.

State-of-the-art FDG chemistry processing units are providing increasing yields and reduced turnaround times. This enables one production site to support a number of imaging units. Capital investment in additional imaging equipment will be required as patient numbers increase; however, placing these facilities strategically with respect to the production facility remains the most cost effective means of providing a comprehensive service for PET scanning. Extra staff would be required for extra production runs, to operate additional cameras and to perform more complex research studies, but optimum equipment usage can be achieved by flexible staffing and extended hours of operation. The configuration of the imaging sites in relation to the production facility is crucial to the optimum use of this expensive resource.

<table>
<thead>
<tr>
<th>Grade</th>
<th>WTEs</th>
<th>Total salary costs (£)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Senior radiochemist RA1A/MTO4</td>
<td>1</td>
<td>33,250</td>
</tr>
<tr>
<td>Radiochemist RA1A/MTO3</td>
<td>1</td>
<td>28,600</td>
</tr>
<tr>
<td>Chemistry technician MTO2</td>
<td>1</td>
<td>18,250</td>
</tr>
<tr>
<td>Cyclotron technologists</td>
<td>2</td>
<td>58,600</td>
</tr>
<tr>
<td>Training, uniforms etc</td>
<td>2,000</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>140,700</td>
<td></td>
</tr>
</tbody>
</table>

Fixed costs

The scanning component would not differ significantly from the remote site (£72,850 – see table 3).

Fixed costs for the production facility include contract maintenance for the cyclotron and items of laboratory equipment. It should however be noted that maintenance expertise from supplying companies may not be well developed in the UK. Trouble-shooting expertise and first-line maintenance provided on-site is invaluable and could be deemed essential if a reliable service of daily radiotracer production is to be supported (see section of staff training). General plant maintenance costs, power usage and housekeeping are also included.
Variable costs

Assuming that the cyclotron production facility supplies radiotracers to the scanning unit, costs associated with medical/injection supplies, data storage, stationery and hard copy production are included (assuming a throughput of 1,200 patients per annum).

<table>
<thead>
<tr>
<th>Item</th>
<th>Cost (£)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclotron maintenance</td>
<td>50,000</td>
</tr>
<tr>
<td>Laboratory equipment maintenance</td>
<td>5,000</td>
</tr>
<tr>
<td>Power/building maintenance</td>
<td>15,000</td>
</tr>
<tr>
<td>Housekeeping contract</td>
<td>4,000</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>74,000</strong></td>
</tr>
</tbody>
</table>

Imaging

Laboratory supplies and cyclotron gases are included in this sum in addition to the production chemicals and target materials. It should be noted that the target material for $^{18}$F-, O18 water is an expensive commodity which is presently in short supply worldwide.

<table>
<thead>
<tr>
<th>Item</th>
<th>Cost (£)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scanning supplies (needles, syringes, linen etc)</td>
<td>12,000</td>
</tr>
<tr>
<td>Data storage</td>
<td>1,200</td>
</tr>
<tr>
<td>Hard copy and stationery</td>
<td>4,800</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>18,000</strong></td>
</tr>
</tbody>
</table>

Radiotracer production

<table>
<thead>
<tr>
<th>Item</th>
<th>Cost (£)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laboratory supplies</td>
<td>25,000</td>
</tr>
<tr>
<td>Chemicals/target materials</td>
<td>30,000</td>
</tr>
<tr>
<td>Gases</td>
<td>9,000</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>64,000</strong></td>
</tr>
</tbody>
</table>

Replacement programme

When pricing scans and radiotracer doses the cost of replacement equipment must be considered. A PET scanner can be used for 8–10 yrs whilst computing equipment will generally need to be replaced in 2–3 yrs.

The cyclotron will be operational over a longer period, around 20 years, but provision will need to be made for replacement of some major parts depending on how the maintenance programme is structured.
APPENDIX 3

Training issues

There are training issues associated with all the disciplines involved in PET scanning. There are few trained PET radiochemists in the world let alone the UK. Consequently there is a need to establish a comprehensive training programme which could be organised either through MSc courses or vocational training by an approved university course. This needs to be established as a matter of urgency. Similarly there are few trained cyclotron engineers/technicians, and whilst other disciplines (ie radiotherapy workshop technologists) do have some of the skills, there is a need for experience in trouble shooting and first-line maintenance skills. Formal training and on the job experience is required for these key members of the production team. The current difficulties in recruiting nuclear medicine technologists and radiographers for general departments are exacerbated when attempting to recruit for PET centres. Experienced, trained staff are not readily available in the UK and training needs to be given on site. BSc courses now include some PET lectures and an annual course is now offered by Guy’s & St Thomas’ PET Centre but on the job training is required. Arranging rotations or split posts with other cross-sectional imaging departments such as CT or MRI may make these positions more attractive to radiographers who have not trained in nuclear medicine. There are few trained PET clinicians. Training for clinicians is being addressed by including PET as part of the CCST training in nuclear medicine but post-CCST experience is also required. There are few centres in the UK where this experience can be gained and consequently it has been necessary for clinicians to gain on the job experience or to spend short periods in overseas centres. This will be a significant issue in the clinical staffing of PET centres.

The delivery and maintenance of the service needs to be consistent with the Ionising Radiation (Medical Exposure) Regulations 2000\(^4\) and the relevant aspects of IRR 1999\(^2\) and ARSAC. It also needs to comply with necessary standards of delivery of a high quality service as well as issues related to clinical governance.
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**Colorectal**


### Lymphoma


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**Oropharynx**


Breast


**Testicle**


2. Cardiology

**Meta-analysis**


**Supporting papers**


### 3. Neuropsychiatry

#### Meta-analysis

None available

#### Supporting papers


