SCOTTISH EXECUTIVE

Health Department

Dear Colleague

POSITRON EMISSION TOMOGRAPHY (PET) SCANNING: IMPLEMENTATION WITHIN NHSSCOTLAND

Background

1. In November 2002 the then Health Technology Board for Scotland (HTBS) published its Health Technology Assessment (HTA) Report 2: Positron emission tomography (PET) imaging in cancer management. It recommended, *inter alia,* that a PET imaging facility including a cyclotron for both clinical use and for specific health services research applications, should be set up in Scotland as rapidly as possible to allow Scottish patients and researchers to realise the potential benefits of FDG-PET imaging in cancer management. It was further recommended that such facility(ies) should be linked to an existing cancer centre and have functional links to the existing PET facility in Aberdeen.

2. The Minister for Health and Community Care set up a working group to consider the recommendations and to propose how they should be implemented. The Group was also asked to provide advice on education and training of staff to support a PET service. The working group's full report and recommendations is attached.

3. Implementing the recommendations of the PET working group offers one of the first challenges for the new regional planning arrangements being put in place. Regional Cancer Advisory Groups and Regional Planning Groups should work together, and on an all-Scotland basis as recommended, to develop sustainable plans for the delivery of PET services for Scottish patients.

4. This HDL and Report is available on the Scottish Health on the Web (SHOW) website – www.show.scot.nhs.uk.

Yours sincerely

TREVOR JONES **DR E M ARMSTRONG**

16th December 2003

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ANNEX

POSITRON EMISSION TOMOGRAPHY (PET) SCANNING: IMPLEMENTATION WITHIN NHSSCOTLAND

Background

1. In November 2002 the then Health Technology Board for Scotland (HTBS) published its Health Technology Assessment Report 2: Positron emission tomography (PET) imaging in cancer management.

2. It recommended, *inter alia,* that a PET imaging facility including a cyclotron, for both clinical use and for specific health services research applications, should be set up in Scotland as rapidly as possible to allow Scottish patients and researchers to realise the potential benefits of FDG-PET imaging in cancer management. It was further recommended that this should be linked to an existing cancer centre with functional links to the existing PET facility in Aberdeen.

3. The Minister for Health and Community Care decided that a working group should be set up to consider the implications for NHSScotland and to recommend on how best these should be implemented. The Group was also asked to provide advice on education and training of staff to support the planned PET service.

4. The working group's full report and recommendations are attached. This HDL sets out the actions which should be taken by NHSScotland to secure access to PET services with immediate effect and to plan for the medium and longer term. As evidence to support the use of PET is growing rapidly, the report does not rule out the possibility of further PET facilities being introduced over time and RCAGs/Regional Planning Groups (RCAGs/RPGs) should keep the situation under review and plan accordingly to meet emergent patient need. Commercial activity due to become available both for radio-pharmaceuticals production and for clinical imaging provide further options for consideration. These are all matters for RCAGs/RPGs as they develop plans and business cases to support the delivery of PET services.

Actions required

5. Implementing the recommendations of the PET working group offers one of the first challenges for the new regional planning arrangements being put in place. RCAGs and RPGs should work together, regionally and on an all-Scotland basis as recommended, to develop sustainable plans for the delivery of PET services for Scottish patients.

Immediate

6. RCAGs/RPGs should assess the numbers of patients who under current recommendations benefit from PET scanning and make appropriate arrangements to secure that access, either through the existing PET facility in Aberdeen, use of a commercial mobile facility which may become available and/or through referral to NHS PET facilities in England.

7. In particular, and if appropriate arrangements are not already in place, immediate steps should be taken to implement the HTBS advice on the importance of using PET scanning in restaging Hodgkin's disease. The PET imaging facility already in place in Aberdeen has sufficient spare capacity to be able to meet the needs of all patients in Scotland with Hodgkin's Disease (HD). There are approximately 90

patients with HD per year who may benefit clinically from PET scanning. The cost per scan will need to be agreed through negotiation with NHS Grampian but are likely to be in the region of £600-£700 per scan. (The HTBS economic modelling indicated a cost per scan of c. £677 assuming 1500 patients per year). For patients with other types of cancer where there is evidence of benefit from PET imaging, e.g. lung, similar arrangements should be made.

8. In all cases it is essential that the use of PET is subject to audit and subsequent evaluation. A suggested dataset was prepared by HTBS and is reproduced at Annex D of the Working Group's report. Regional cancer networks should ensure that the findings of PET audit are incorporated within their overall quality improvement/clinical governance framework. It is important that central analysis and reporting functions are set up, supported by the ISD Cancer Group. In the first instance this will be taken forward by the Cancer Branch who will also keep RCAGs informed of and involved with developments. Over time, as the PET service develops, it will be necessary to assess its utility for all Scottish patients with cancer or other diseases.

9. For consistency of information and efficiency of administration, all referrals for PET imaging must be made using the template attached at Annex E of the Working Group's report. This is available electronically for downloading from the SHOW website at www.show.scot.nhs.uk and *Cancer in Scotland* website at www.cancerinscotland.scot.nhs.uk.

10. Service level agreements or contracts as appropriate with preferred PET service providers should be agreed through regional commissioning arrangements already in place or developed through the RCAGs/RPGs. Where services in Aberdeen are selected we have been asked to make clear that it would be very helpful indeed if three (regional) host NHS Boards could act as formal channels for paying invoices.

Medium and Longer term options for provision of PET

11. RCAGs/RPGs should consider their longer term requirements for PET scanning and plan provision accordingly. In particular they will wish to consider whether there is a need to plan in the longer term for the development of PET facilities in Scotland over and above the 2002 HTBS recommendation, especially as the indications for the use of PET are rapidly increasing supported by evidence of benefit across the range of cancers and in conditions other than cancer.

12. HTBS indicated that the estimated capital costs of a fully equipped PET unit (imager, cyclotron, chemistry) integrated with nuclear medicine and radiology departments would involve a capital outlay of approximately £4.2m (2002 prices). Commercial developments currently underway will see the establishment of a cyclotron/radiopharmaceuticals production facility in central Scotland which could supply FDG (or other radiopharmaceuticals) to any new NHS PET facility(ies). Such a partnership would reduce the NHSS capital costs to around £2m for a single facility. In that case, and over time as evidence supporting the use of PET emerges, it might be possible to establish further NHS PET facility(ies) in Scotland. Because of the need for close inter-relationships with nuclear medicine and radiology departments, and to support and strengthen existing cancers in Scotland, NHS PET facilities in Scotland in future will be linked with existing cancer centres.

13. A PET advisory group will be set up led by the Clinical Strategies: Cancer Branch in Health Planning and Quality Division. It will include Finance Directorate input and will work in a similar way to the Department's radiotherapy equipment strategic planning group. Business cases for the development of PET facilities will require to be submitted to the SEHD and will be subject to scrutiny by the Capital Investment Group (CIG) in the normal way.

14. HTBS estimated annual running costs of a PET facility at around £1.2m per annum (2002), dependent on the preferred service delivery model. RCAGs/RPGs should ensure that projected costs are built into planning for future years, probably beginning in 2005-06. The level of running costs required will depend on the finally agreed configuration of services proposed nationally and in particular the use (or not) of a commercial cyclotron/FDG production facility. RCAGs/RPGs will also want to consider the economic case/value for money of lease arrangements vs purchase of PET or PET/CT equipment and/or the use of commercial clinical imaging facility(ies). In the interim period RCAGs/RPGs should consider how best to provide for revenue cost implications of using PET services.

15. Following CIG approval of relevant business case(s), Scottish Healthcare Supplies (SHS) will as required work with RCAGs/RPGs to draw up tender documentation and will facilitate contract negotiations with commercial companies re the provision of FDG. They will also advise on and assist with providing or securing the provision of capital assets including buildings and PET or PET/CT equipment. SHS will also advise on contract arrangements with commercial companies for the use of their clinical imaging facilities, whether fixed or mobile PET and/or PET/CT.

Training of Staff

16. A national (UK) approach to training is recommended in which National Education Scotland (NES) will be closely involved and, indeed, may wish to take the lead. RCAGs/RPGs will require to ensure appropriate provision is made for training of relevant staff. Details of the range of training required and options for its delivery are set out in Annex H to the Working Group's report. The range and numbers of staff that will require to be trained and the type of training needed will be dependent on regional (national) decisions on the preferred option(s) for the provision of PET services, i.e. whether the HTBS recommendation of a dedicated cyclotron for the production of FDG and imaging facility or commercial production facility and provision of FDG coupled with NHSS imaging facility(ies) or commercial imaging or a combination of any or all of the above.

Next Steps

RCAGs/RPGs

- Review and/or set up SLAs with Aberdeen NHS Board/Grampian University Hospitals NHS Trust or other provider for the provision of PET services until such time as any new NHSScotland facility is available
- Set in place robust clinical audit arrangements to support qualitative assessment of the provision of PET services using the minimum dataset attached at Annex D of the Working Group's report.
- Agree standard referral documentation based on Annex E of the Working Group's report.
- RCAGs/RPGs to plan for medium and longer term provision of PET services whether in NHSS facility(ies) linked with cancer centre(s) and/or by contract with commercial imaging companies, involving SHS as required for tender/contract negotiations. RCAGs/RPGs must ensure that patients' and carers' views are taken into account and that their involvement is integral to the planning process.
- RCAGs/RPGs will also wish to consider the information needs of patients' and carers' before, during and after a scan in line with the recommendations of HTBS HTA 2 PET Report Chapter 8 – *Patient Issues*.
- Where NHSS PET facility(ies) are to be set up, standard Business case(s) to be drawn up for submission to SEHD Finance Department for consideration by CIG. RCAGs should nominate a lead body through which funding will be channelled. If a nationwide consortium approach is agreed then one lead NHS Board will need to be nominated (see below).

- The three RCAGs and their RPGs will wish to consider the benefits of an all-Scotland consortium arrangement for the provision of PET services, especially if a phased approach to provision is the preferred option.
- Outline Implementation Plan(s) to be submitted to Scottish Executive Health Department (Cancer Branch) by end May 2004.

Scottish Executive

- Set up PET Advisory Group to provide advice both to SEHD and RCAGs/RPGs on planning for PET provision and in particular the development of business case(s).

National Education Scotland

- Work with RCAGs/RPGs to develop an agreed national training programme to fit with the needs of the Scottish PET development programme so that appropriately trained staff are in place to deliver the range and type of services required in time for the commissioning of dedicated NHSS PET facility(ies).

Clinical Strategies: Cancer
Health Planning & Quality Division
SEHD

November 2003

SCOTTISH EXECUTIVE

NHS SCOTLAND

Implementation of HTBS' Health Technology Assessment of Positron-Emission Tomography In Scotland

Report and Recommendations

October 2003

CONTENTS

Executive Summary

In November 2002, the Health Technology Board for Scotland, as it then was, published a Health Technology Assessment on positron-emission tomography (PET) imaging in cancer management. It recommended that a PET imaging facility including a cyclotron, dedicated to clinical use and specific health service research applications should be established in Scotland. It should be linked to an existing cancer centre and have functional links to the existing PET facility in Aberdeen.

In accepting the report, the Minister for Health and Community Care established a Working Group to plan implementation of the HTA.

In the interim, the clinical and commercial issues surrounding PET have continued to develop, and the Working Group has looked again at some of the options considered by the HTA group. In particular, the issue of sourcing the radiopharmaceuticals was reviewed in the light of the public intent of a number of companies to develop commercial radiopharmaceutical production facilities within Scotland.

In the light of these discussions, the Working Group recommends that:

1) NHSScotland should provide a PET service for appropriate patients

2) because of the emerging availability of alternative commercial sources in Scotland, manufacture of radiopharmaceuticals need not be undertaken within an NHS-funded facility. This will be taken account of by Scottish Healthcare Supplies in the tendering process.

3) as per option 3 in the HTBS report, if it is the wish of NHS Boards/regional planning to do so, the nationally available capital resource can be utilised to provide additional scanning facilities. The HTA recognised that this option would be quicker to set up as no cyclotron or radiochemical laboratories are required which substantially reduces the capital outlay in comparison with a fully equipped PET unit. The overall time taken to construct a cyclotron requires to be taken into consideration in the planning processes for scanning facilities.

4) the Regional Cancer Advisory Groups (RCAGs) and NHS Boards should be asked to indicate their preference for the development of the provision of services and for their preference between PET and PET/CT within a defined timescale. Relevant business plans will be required to support stated preferences which will need to be submitted to the Scottish Executive Health Department in the normal way.

5) in the interim, the capacity available in Aberdeen should be used and, if not already in place, arrangements rapidly put in hand for the scanning of patients requiring restaging for Hodgkin's Disease and those under consideration for surgery for apparently localised lung cancer

6) the three RCAGs and their constituent NHS Boards should consider whether it may be appropriate to develop a national consortium approach to both the interim use of a mobile service and for the provision of PET services, especially if a phased development is the preferred option.

7) a Scotland-wide workforce planning and training needs analysis requires to be undertaken to support the provision of PET across the country. If commercially produced radiopharmaceuticals is not the preferred option the training needs analysis will need to encompass radiopharmaceutical production

8) Scottish Healthcare Supplies will lead the procurement for capital equipment and the provision of the Radiopharmaceutical service

9) Regional Cancer Advisory Groups will prospectively monitor the use of PET in Scotland and report annually through the Quality Improvement sub-group to the SCG and thereby to the Chief Medical Officer.

Background

1. Positron-emission tomography (PET) is a non-invasive imaging procedure that is increasingly being used in the USA and Europe to provide functional rather than purely anatomical information. The technique requires the intravenous injection of a radiolabelled tracer that is then taken up by tissues. For studies in cancer patients, the most commonly used tracer is FDG, which is glucose labelled with ^{18}Fluorine (2-[^{18}F]-fluoro-2-deoxy-D-glucose).

2. PET imaging provides information about the level of metabolic activity in a suspect area, and can detect tumours due to their differential rate of glucose utilisation. It is thus a functional image, in contrast to other techniques such as magnetic resonance imaging (MRI) or computed tomography (CT), although the latter is increasingly combined with PET in a single machine to provide both functional and anatomical information in a single study.

3. The two requirements for a PET facility are therefore the provision of FDG and the availability of an appropriate imaging device. FDG production requires a radiopharmaceutical facility based around a cyclotron that is within two hours travel time from the scanner. This is because the half-life of the ^{18}Fluorine is 110 minutes, ie the activity drops by 50% approximately every two hours. FDG is not suitable for imaging organs such as the brain (which has a high normal utilisation of glucose), and other isotopes of potential clinical significance have even shorter half-lives[1]. If these prove to be of clear value, the implication is that the cyclotron and scanner will have to be co-located.

4. PET imaging has thus many potential roles in the management of cancer: in diagnosis and staging, in determining the response to treatment, in determining the nature of any residual mass after chemotherapy and/or radiotherapy and in the diagnosis of recurrence of the disease.

5. In Scotland the only available PET facility is located in the John Mallard Centre in Aberdeen. This scanner is a dedicated PET facility with cyclotron and scanner co-located. It has been primarily a research facility, but has undertaken some scans for the NHSS including patients from outwith Aberdeen.

6. In November 2002, the then Health Technology Board for Scotland (now part of NHS Quality Improvement Scotland (NHSQIS)), published a Health Technology Assessment (HTA) report (Ref. 1). It recommended, amongst other things, that:

   - a PET imaging facility including a cyclotron, dedicated to clinical use and specific health services research, should be set up in Scotland. It should be linked to an existing cancer centre, with functional links to the existing PET facility in Aberdeen

[1] ^{15}Oxygen has a short half-life of only two minutes.

- during the approximately two years it will take to build and commission such a facility, interim solutions for the provision of PET imaging should be considered. Possible options are the use of the John Mallard Scottish PET Centre in Aberdeen, and/or the use of a mobile PET facility in a fixed location and/or other UK facilities

- all patients who require restaging of Hodgkin's Disease should be sent for a FDG-PET scan. Extension to the restaging of all patients with lymphoma should be investigated by further research.

- all patients undergoing FDG-PET should have booking information and outcomes recorded according to a common agreed format to allow prospective audit, economic modelling and research. A template data set was included in Appendix 27 of the HTBS report.

RECOMMENDATION:
As recommended by HTBS, NHSScotland should provide a PET service for appropriate patients.

7. In accepting the HTBS report, the Minister for Health and Community Care announced the establishment of a Working Group to recommend the most appropriate way(s) of implementing the HTA recommendations.

8. In March 2003, the Minister for Health and Community Care announced £5m capital funding available in 2004-05 to support the development of PET services.

Remit and Methods of Working

9. The remit of the Working Group is attached at **Annex A**

10. Membership is attached at **Annex B**.

11. In the interval between the HTA report publication and the establishment of the Working Group and subsequently, significant developments occurred in both the clinical and commercial environments that potentially affect both the configuration and use of PET in Scotland. The Working Group therefore decided it was necessary to review each of the four options presented in the HTA report:
    - Option 1 – a fully equipped PET unit (imager, cyclotron, radiochemical facility) located within a hospital, purchasing support services from the Trust but with dedicated staff

    - Option 2 – a fully equipped PET unit integrated with and drawing staff skill from other relevant hospital departments

    - Option 3 – a PET imager receiving its radiopharmaceuticals from another source

    - Option 4 – a mobile PET imager receiving its radiopharmaceuticals from another source

12. As well as a vigorous internal debate, the Working Group received presentations from several commercial companies and a variety of potential clinical users. (One company did not present to the whole of the Working Group but to a core representation of the group).

13. Clinical algorithms and protocols for both Lung and Haematology PET indications have been prepared by clinicians on the Working Group and these are attached at **Annex C**.

Findings

Capacity

14. The clinical indications for PET scanning considered in the HTBS report were confined largely to Hodgkin's Disease, non-Hodgkin's lymphomas (NHL) and early stage non-small cell lung cancers (NSCLC) being evaluated for suitability for surgery. Only in the restaging of Hodgkin's Disease after chemotherapy (to confirm complete remission and avoid potentially toxic radiotherapy if not needed) was the clinical and cost-effectiveness case considered proven. For patients with lung cancer considered as candidates for potentially curative surgery, the evidence was clinically convincing but overall there was insufficient evidence with regard to cost-effectiveness. Only one scan per patient was provided for. On this basis, some 1500 scans per year would be required in Scotland, effectively the capacity of one dedicated PET scanner.

15. The role of PET in other tumour types, such as head and neck cancer, melanoma, teratoma and colorectal was not considered to have a sufficient evidence base at the time of the HTA report but is being actively developed and has become more established in the interim.

16. The use of PET to monitor response to treatment in chemo-sensitive tumours such as lymphoma and breast cancer (allowing treatment to be stopped or changed at the earliest evidence of non-response) has also become more firmly established.

17. For these reasons, the Working Group felt that the HTBS estimate of capacity required was very likely to be outdated by the time any facility could enter clinical use and a substantial upgrading of the earlier estimate was required. (The current reimburseable conditions for PET by USA Medicare are attached at **Annex F** for information.)

18. The revenue implications of providing capacity at this level are recognised. However as this capacity will not become available for at least three years, time is available for the revenue costs to be planned for within the 2005-06 Comprehensive Spending Review. In the interim period, NHS Boards will wish to consider how best to secure these costs as capacity becomes available and clinical indications are refined. Revenue considerations may also dictate the phasing of the development of new facilities, which may require a degree of central co-ordination. Monitoring of the implications of PET scans for decisions on patient care (see paras 42 and 43 below) should show some offsetting savings in treatments avoided (surgery, radiotherapy and chemotherapy). However the reality of what will be required for modern, effective cancer care will inevitably require that these facilities are available to patients.

Source of FDG

19. FDG must be produced in a licensed radiopharmaceutical facility with the appropriate quality assurance within 2 hours travel time because of the half-life of the isotope (road, rail or air travel have all been approved for radioactive materials of this type). Transportation of FDG, as required in future, will be subject to the normal Radiation Protection Act requirements and the relevant rules and regulations as applicable to travel by chosen mode of transport. In Aberdeen, FDG is produced on site in a suite co-located with the scanner. The production of radiopharmaceuticals is subject to the Medicines Act 1968 and the Medicines (Administration of Radioactive Substances) Regulations 1978 (see **Annex G)**.

20. The preferred HTBS solution would provide a similar facility on a single site in Scotland located with a designated cancer centre. Cancer Centres are based in Inverness, Aberdeen, Dundee, Edinburgh and Glasgow.

21. This single site model greatly increases patient travel and inconvenience. For some patients, this might also involve overnight stays, either in hospital or nearby hotel/hostel, with a concomitant increase in costs. The capital outlay required for the purchase and siting of the cyclotron is considerable, as well as significant implications for training and staffing with the necessary technical and radiochemical expertise. Reliance on a single site facility is considered inherently vulnerable to major disruptions for patients in the event of machine failure.

22. The Working Group is aware that several companies are looking to create commercial radiopharmaceutical facilities capable of meeting Scottish needs. After a recent hesitation, at least one of these is now preparing to commence building in Livingston[2], West Lothian, with an anticipated date of starting production in the third quarter of 2004. This company has a production licence from the Department of Health, and has charges capped to a maximum of £400 per dose, subject to negotiation.

23. In the light of these representations, the Working Group felt that, at this time, it would be an inappropriate use of NHS capital resource to purchase a dedicated cyclotron for the semi-commercial production of FDG.

24. There was a recognition however that any future developments requiring the use of tracers with much shorter half-lives could not be catered for from a distant cyclotron and that the installation of a cyclotron co-located to at least one of the Scottish cancer centres would then need to be considered.

25. To ensure the most cost-effective provision of FDG to NHSScotland Scottish Healthcare Supplies has offered to work with RCAGs/NHS Boards to assist with tender/contract negotiations with potential commercial suppliers.

[2] Schering Health Care announced on 29 October a new Scottish venture to manufacture FDG in Scotland.

RECOMMENDATION:

- Manufacture of radiopharmaceuticals need not be undertaken within an NHS-funded facility because alternative commercial sources will be available in Scotland.
- Scottish Healthcare Supplies will lead the procurement for the provision of the radiopharmaceutical service

Location(s) of PET scanning facility

26. At present, the only PET scanning facility available within Scotland is the John Mallard PET Centre in Aberdeen. The Working Group is aware of patients currently travelling to London and elsewhere for PET scans.

27. Four of the five cancer centres in Scotland have expressed an interest in these deliberations and in hosting a PET facility.

28. If not required for the purchase of the cyclotron and associated capital works, the £5m capital made available might be sufficient for the provision of 2 and possibly more scanners, but dependent on the choice between PET and PET/CT and possibilities of advantageous terms being negotiated by Scottish Healthcare Supplies. Detailed costing of these options was beyond the remit of the Group as it relies on decisions required by NHSScotland through Regional Cancer Advisory Groups/regional planning arrangements.

29. Business cases for the development of PET facilities will require to be submitted to the SEHD and in the normal way will be subject to scrutiny by the Capital Investment Group (CIG). An SEHD Working group, led by the Cancer Branch, should be set up and include representation from Finance and Analytical services to support the development of strategic planning for the introduction of PET. This will operate in a similar way to the strategic review group for Radiotherapy Equipment, to review and advise on developing equipment plans (s) and provide links with Finance Department for business case development etc.

30. The view of the Working Group was that, if funding permits and there are viable regional or national business plan(s) to support it, a scanning facility could be located within a cancer centre in each of the three Regional Cancer Group areas. It may be that this will require to be phased over time as demand grows.

RECOMMENDATION:

- If it is the wish of NHS Boards/regional planning to do so, as per option 3 in the HTBS report, the nationally available capital resource can, be utilised to provide two or more scanning facilities within the regional cancer advisory group areas simultaneously or phased over time as required, subject to the caveats in paragraph 28 above. The HTA recognised that the last option would be quicker to set up as no cyclotron or radiochemical laboratories are required which substantially reduces the capital outlay in comparison with a fully equipped PET Unit.

PET v. PET/CT

31. The Working Group heard some of the technical debate as to the relative merits of the two approaches – stand alone PET or combined PET/CT.

32. The functional image produced by PET scanning can be combined with the more precise anatomical information provided by computed tomography (CT) scanning in the latest generation of combined scanners.

33. Combined machines, as well as providing the anatomical definition required for radiotherapy planning, include a more rapid throughput and consequent increase in capacity. The potential problems include a more claustrophobic environment and a higher radiation exposure.

34. The Group was also aware of a recent publication suggesting that integrated PET-CT improves the diagnostic accuracy of staging of the most common form of lung cancer (Ref 2).

35. The Working Group view was that the Regional Cancer Advisory Groups (RCAGs) should be asked to consult their constituent NHS Boards and clinicians (radiological, nuclear medicine and oncological) and advise as to their requirements/preferences within a defined timetable and in line with the needs of patients.

RECOMMENDATION:

- RCAGs and NHS Boards should be asked to indicate their preference for development of the provision of services and for their preference between PET and PET/CT within a defined timescale. Relevant business plans will be required to support stated preferences which will need to be submitted to the Scottish Executive Health Department in the normal way.

- Scottish Healthcare Supplies will lead the procurement for capital equipment.

36. None of the proposals above will provide any additional PET scanning capacity in Scotland for at least two years.

37. In recognising this, the HTA report recommended that interim solutions for the provision of PET scanning should be considered.

38. The options available include:

- The John Mallard PET Centre in Aberdeen where between 500 and 700 scanning slots could be made available to NHSScotland at a cost of approximately £600-£700 per scan.

- One company described for the Working Group their mobile PET facility. This could be made available in a relatively short time, subject to agreeing a source of FDG from Aberdeen and local agreement as to appropriate locations within Scottish hospital sites hosting a cancer centre that can provide a suitable pad to site mobile machine. This

costs approximately £10k to construct (power supply and lead safe are also required). At present, the company operates a number of mobile PET facilities capable of scanning up to 8 patients/day. They may shortly announce a mobile PET/CT facility capable of scanning 12-15 patients/day, as is available currently in America. However, even if this was to become available in the UK, there may be problems with weight distribution and suitability for British roads that will require clarification.

- PET facilities are available elsewhere in the UK, both within the NHS and private facilities. The same company that can provide mobile capacity has a facility in London with spare capacity. This would cost approximately £850/scan including radiopharmaceuticals, excluding travel and reporting costs.

39. The Working Group recommends, in line with HTBS' advice, that in the first instance the capacity available in Aberdeen should be utilised. In particular, and if not already in place, arrangements should be made urgently for patients requiring restaging for Hodgkin's Disease and those under consideration for surgery for apparently localised lung cancer to have PET scans in Aberdeen.

40. A consortium approach by SHS for the provision of a mobile service on behalf of all NHS should be further considered by RCAGs in the first instance.

RECOMMENDATION:

- In the interim, the capacity available in Aberdeen should be used and if not already in place arrangements rapidly put in hand for the scanning of patients requiring restaging for Hodgkin's Disease and those under consideration for surgery for apparently localised lung cancer.
- The three RCAGs and their constituent NHS Boards should consider whether it may be appropriate to develop a national consortium approach to both the interim use of a mobile service and for the provision of PET services, especially if a phased development is the preferred option.

Monitoring

41. The HTBS report recognised the need to monitor the impact that PET scanning had on clinical decisions and outcomes in order to derive more directly relevant research and cost-effectiveness data for NHSScotland.

42. The Working Group felt that a consistent data set relevant to each clinical indication should be designed by the appropriate clinical community and collected for every scan commissioned by NHSScotland. A generic template for the data set was helpfully provided in appendix 27 of the HTBS report (**Annex D**) and a suggested referral template prepared by a member of the PET working group (**Annex E**) and algorithms for the use of PET in haematology and a proposed economic evaluation in lung cancer are attached at **Annex C1** and **C2**.

43. As part of the Quality Assurance (QA) process a mechanism will be required for the collection and collation of the data sets with the intention of producing an annual report on activity outcomes and audit. Regional Cancer Advisory Groups will monitor the

use of PET in Scotland and report annually through the Quality Improvement sub-group to the SCG and thereby to the Chief Medical Officer. Ideally, data collection should be incorporated within the ongoing cancer clinical audit programmes but it is recognised that because of its highly specialised nature it may not lend itself to doing so.

RECOMMENDATION:

- Regional Cancer Advisory Groups will prospectively monitor the use of PET in Scotland and report annually through the QI sub-group to the SCG and thereby to the Chief Medical Officer.

Training

44. The training implications of providing PET facilities are not confined to Scotland, and need to be addressed UK-wide.

45. A paper outlining the training requirements of medical staff, physicists and technologists/radiographers prepared by Professor Sharp on behalf of the Group is attached at **Annex H**.

46. The Working Party suggested that a Scotland-wide workforce planning and training needs analysis requires to be undertaken to support the provision of PET across the country; including:-

- Current numbers and expertise available in Scotland to include level of training for all staff involved in PET Centres eg medical, technical, allied health professionals, nursing

- Future staffing requirements in order to make PET available to Scottish patients (dependent on required configuration and phasing of PET service facilities).

- Numbers likely to require ARSAC certification training e.g. one trained Medical Director per PET site or one appropriately trained person covering the whole of Scotland?

- Whether second reading expertise is required given that commercial companies can offer a second reading service.

- Whether PET or PET/CT combined is the preferred option and the impact this decision will have on training requirements.

- If commercially produced radiopharmaceuticals is not the preferred option the training needs analysis will need to encompass requirements for radiopharmaceutical production.

47. Workforce planning and training requirements will take time to set in place and will need to be phased so that the relevant specialist experts receive appropriate enhanced training in the first instance. The timescale and funding for such initial and subsequent cascade training amongst all relevant professions/disciplines therefore needs to be

factored in to regional or national business plans for the provision of PET services and will therefore also affect the timescale within which facility(ies) can be commissioned. As noted above, if commercially produced radiopharmaceuticals is not the preferred option the training needs analysis will need to encompass requirements for radiopharmaceutical production.

RECOMMENDATION:

- A Scotland-wide workforce planning and training needs analysis requires to be undertaken to support the provision of PET across the country.

- The relevant professional groups, in conjunction with NHS Education for Scotland (NES) and together with colleagues elsewhere in the UK, develop a training strategy to ensure the availability of the necessary expertise both initially and as needs/capacity expand. However if a commercial collaboration for the provision of radiopharmaceuticals is the preferred option the responsibility for staffing and training in this area would fall to the commercial company.

REFERENCES

1. Positron emission tomography (PET) imaging in cancer management. Bradbury I, Bonnell E, Boynton J, Cummins E, Facey K. Iqbal K, Laking G, McDonald C, Parpia T, Sharp P, Single A, Walker A, Health Technology Assessment Report 2: Glasgow: Health Technology Board for Scotland

2. Lardinois D, Weder W, Haby TF et al
Staging of non-small cell lung cancer with integrated positron-emission tomography and computed tomography NEngJ Med (2003) 348:2500-2507

ANNEX A

SCOTTISH EXECUTIVE HEALTH DEPARTMENT

SCOTTISH CANCER GROUP

PET WORKING GROUP

REMIT

To develop an implementation/action plan to secure access to PET imaging in Scotland and to provide advice on education and training requirements.

Health Planning and Quality Division
January 2003

ANNEX B

Membership of Working Group

Dr M A Cornbleet, SMO, SEHD (Chair)

Mr M Baxter, Finance Directorate, SEHD

Mr M Clancy, Patient representative

Mr Steve Ebdon-Jackson, Diagnostic Imaging and Radiation Protection, DoH, London

Dr T Fitzsimons, Consultant Haematologist, Glasgow

Mr G Gillespie, Finance Directorate, SEHD

Dr J Hannan, Head of Medical Physics, Edinburgh

Mr T Haswell, Patient representative

Mr R Hemsley, Scottish Healthcare Supplies

Mr G Marr, Chief Executive, Tayside University Hospitals NHS Trust

Dr N MacMillan, Consultant Radiologist, North Glasgow Trust, Western Infirmary

Professor J McKillop, Muirhead Professor of Medicine, University of Glasgow

Professor G Needham, NES representative

Professor A Price, Professor of Clinical Oncology, University of Edinburgh

Professor P Sharp, Professor of Medical Physics, Grampian University Hospitals NHS Trust

Ms J Whelan, CancerBacup

Mrs E Porterfield, Head, Clinical Strategies: Cancer, SEHD

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ANNEX C1

A Health Economic evaluation of PET in Non-small Cell Lung Cancer (NSCLC)

Sara C. Erridge and Allan Price, Division of Oncology, University of Edinburgh, Edinburgh.

Background

PET has been demonstrated in a large number of studies and three meta-analyses[1-3], to be superior to CT scanning in the staging of the mediastinum in lung cancer. In addition, in up to 20% of patients, previously unsuspected distant metastases are detected. In one series of 167 patients in whom radical radiotherapy was the proposed treatment, 7.5% of Stage 1, 18% of Stage II and 24% of Stage III patients had unsuspected distant metastases detected on PET scan[4].

Though PET appears to be superior to CT in the staging of lung cancer, whether this has an impact on patients' survival or quality of life is unproven. The summary statement of the HTBS report of PET imaging in cancer states that 'research should be undertaken to inform economic modelling in order to produce a robust assessment of the value of PET imaging in the staging of patients with NSCLC who are CT negative in the regional lymph nodes'. However, the HTBS report concentrated on the surgical management of lung cancer and did not address the potential impact of PET on patients managed with radical radiotherapy. Patients receiving radiotherapy often have disease at a more advanced stage (Stage III), so it is possible that the savings, both economic and quality of life, from avoiding futile radical radiotherapy in the presence of distant metastases, could be substantial. We therefore propose to conduct a study of all patients (both CT node positive and node negative) who lack clear evidence of distant metastases on standard imaging and who are medically fit for potentially curative therapy (surgery or radical radiotherapy +/- chemotherapy). The rationale for including 'all patients without metastases' is that in many series there are a substantial number of patients[5] who are down-staged by PET and may currently be denied potentially curative therapy.

In order to fully assess the cost-effectiveness of the use of PET scanning in this group of patients, a randomised controlled trial must be performed. To date there have been two randomised controlled trials of PET in patients managed with resection[6, 7], with conflicting results. The PLUS study[6] reported PET as effective, but the Australian study suggested PET was ineffective[7]. It is therefore reasonable to randomise patients to either undergo a PET or not, in addition to their standard staging investigations.

OUTLINE OF DESIGN

Randomised-controlled trial to assess the quality-adjusted cost-utility of PET scanning in NSCLC. A cost-utility analysis balances improvements seen in health-related quality of life against costs with the purpose of aiding decision-making[8].

Inclusion criteria

1) All patients with histologically or cytologically proven NSCLC without clear evidence of metastatic disease on conventional investigations.

2) Must be medically fit for potentially curative therapy (surgery or radiotherapy with or without chemotherapy).

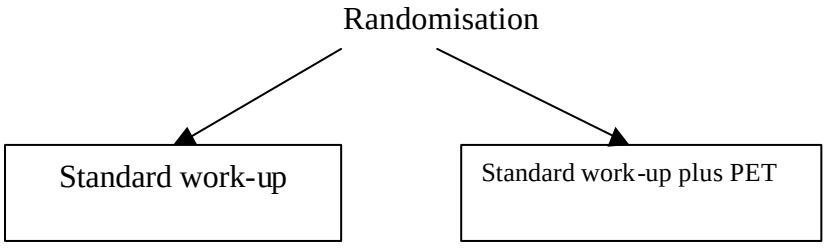
3) Able to give written informed consent

Exclusion criteria

1) Inability to fast for six hours pre-PET scan – diabetic patients can be included but require special information regarding diet and blood glucose levels.
2) Claustrophobia or other condition, which could result in inability to lie still for 40 minutes.

Randomisation

Stratified by
1) CT nodal stage – N0-1 *vs* N2
2) Proposed therapy – surgery v radiotherapy
3) Surgeons who perform mediastinoscopy on radiologically normal mediastinum or not.



'Standard work-up' would ordinarily consist of
a) History and examination
b) CXR
c) CT chest and upper abdomen
d) Bronchoscopy for proximal lesions or CT-guided FNA for peripheral lesions.
e) Pulmonary function tests (FEV_1, FVC and measures of gas transfer)
f) Bone scans and CT scan brain will only be performed if symptoms suggest metastases (SIGN guidelines).

Patients randomised to 'standard work-up' will receive the proposed therapy according to usual departmental guidelines. Mediastinoscopy will be performed as per local practice. To avoid bias from varying practices across Scotland, this will be stratified in the randomisation.

Patients who are randomised to 'standard work-up plus PET'

1)PET is negative (mediastinum and distant) will proceed with proposed therapy. A mediastinoscopy will be performed at the discretion of the surgeon.

2) PET positive for nodal metastases. The PET positive nodal station should be biopsied prior to the patient being declined potentially curative therapy, as up to 10% of cases are false positive.

3) PET positive for distant metastases. Wherever safe, a biospy should be performed to exclude a false positive result.

4)PET positive for both distant and nodal metastases. A biopsy should be performed at the safest location.

Data collection

All events from randomisation should be collected for 24 months. Up to 90% of events will occur within 2 years of initial treatment (in a series from British Columbia (personal communication) 80% of events had occurred by 2 years).

1) Economic
a) Costs of initial anti-cancer management – surgery, radiotherapy, chemotherapy.

b) Costs of in-patient stays – hospital and hospice

c) Costs of primary care contact e.g. visits to GP, home visits, district nurse visits

d) Costs of medications –both symptom control and for general medical conditions

e) Costs to patient e.g. travel expenses

f) Costs to society – the economic contribution from employment

2) Quality of life

Data collection on

Day of randomisation	6* weeks	12 weeks	18 weeks	24 weeks	36 weeks	52 weeks	78 weeks	104 weeks

EuroQoL EQ-5D (the most validated health economic questionnaire-see Appendix A)

EORTC QLC Q30 with LC 13 (the most widely used QOL questionnaires in lung cancer trials – see Appendix B)

End-points

Primary

1) Two-year overall survival
1) Cost utility of the addition of PET to standard work-up

Secondary

1) Overall two-year cause specific survival
2) The number of unnecessary mediastinoscopies performed in PET mediastinum negative patients
3) Percentage of patients whose stage and management changed because of PET

Statistics

In the 1995 audit[9] 47% of patients with confirmed NSCLC presented with local or regional disease which could be amenable to potentially curative therapy. However, this audit was unable to establish either disease configuration (identifying cases not be suitable for such an approach), nor collected data on co-morbidity. Therefore, it is difficult to estimate the number of potentially eligible cases for this study. However, using the estimates from the Cancer Scenarios document from the Scottish Executive[10], if 60% of patients with localised disease and 30% of patients with regional disease were suitable for potentially curative therapy, then 1200 patients (25.5% of total cases) would be eligible per annum. However, in the 1995 audit[9] only 16.3% of all lung cancer cases received potentially curative therapy. This is much lower than other areas of the world, for example, for the same year in British Columbia this figure was 25% and 28% in 1993 in Victoria, Australia[11].

This study will be powered to detect two endpoints:

a) To detect a 25% reduction in deaths occurring within two years of potentially curative therapy. In the 1995 audit the two-year overall survival for patients undergoing PCT was 40% therefore, with 80% power at the 5% significance level, this study will require 400 patients to detect an improvement in 2 year survival from from 40% to 55% (reduction in mortality from 60% to 45%).

b) To detect whether PET meets standard cost-effectiveness criteria (1QALY=£20,000). Currently a retrospective analysis of patient pathways for a group receiving PCT from November 2000 to October 2001 is being performed, to provide an estimate of the treatment related costs. From this, the power of the study to assess the economic impact of PET will be determined.

APPENDIX A

EOROQOL EQ-5D

By placing a tick in each group below, please indicate which statement best describes your own health state today

Mobility

I have no problems in walking about ☐

I have some problems in walking about ☐

I am confined to bed ☐

Self-care

I have no problems with self-care ☐

I have some problems washing and dressing myself ☐

I am unable to wash or dress myself ☐

Usual Activities (e.g. work, study, housework, family or leisure activities)

I have no problems in performing my usual activities ☐

I have some problems in performing my usual activities ☐

I am unable to perform my usual activities ☐

Pain/Discomfort

I have no pain or discomfort ☐

I have moderate pain or discomfort ☐

I have extreme pain or discomfort ☐

Anxiety / Depression

I am not anxious or depressed ☐

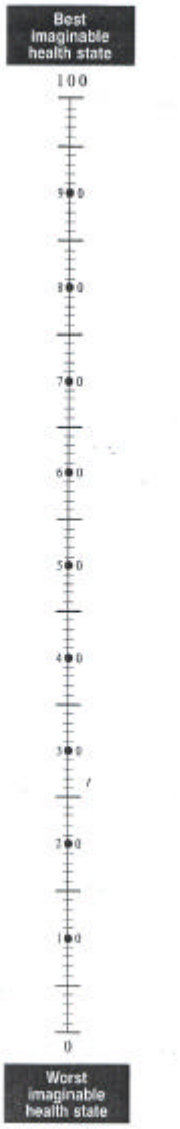
I am moderately anxious or depressed ☐

I am extremely anxious or depressed ☐

To help people say how good or bad a state of health is we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst you can imagine is marked 0.

We would like you to indicate on this scale how good or bad your health is today, in your opinion.

Please do this by drawing a line from the box below to whichever point on the scale indicates how good or bad your state of health is.



Your own health state today

APPENDIX B

EORTC QLQ-C30 (version 3)

We are interested in some things about you and your health. Please answer all of the questions yourself by circling the number that best applies to you. There are no "right" or "wrong" answers. The information that you provide will remain strictly confidential.

Please fill in your initials: ____
Your birthdate (Day, Month, Year): __ __ __ __ __ __
Today's date (Day, Month, Year): __ __ __ __ __ __

	Not at all	A little	Quite a bit	Very much
1. Do you have any trouble doing strenuous activities, like carrying a heavy shopping bag or a suitcase?	1	2	3	4
2. Do you have any trouble taking a long walk?	1	2	3	4
3. Do you have any trouble taking a short walk outside of the house?	1	2	3	4
4. Do you need to stay in bed or a chair during the day?	1	2	3	4
5. Do you need help with eating, dressing, washing yourself or using the toilet?	1	2	3	4

During the past week:	Not at All	A little	Quite a bit	Very much
6. Were you limited in doing either your work or other daily activities?	1	2	3	4
7. Were you limited in pursuing your hobbies or other leisure time activities?	1	2	3	4
8. Were you short of breath?	1	2	3	4
9. Have you had pain?	1	2	3	4
10. Did you need to rest?	1	2	3	4
11. Have you had trouble sleeping?	1	2	3	4
12. Have you felt weak?	1	2	3	4
13. Have you lacked appetite?	1	2	3	4
14. Have you felt nauseated?	1	2	3	4
15. Have you vomited?	1	2	3	4
16. Have you been constipated?	1	2	3	4

Please go on to the next page

During the past week:	Not at all	A little	Quite a bit	Very much
17. Have you had diarrhea?	1	2	3	4
18. Were you tired?	1	2	3	4
19. Did pain interfere with your daily activities?	1	2	3	4
20. Have you had difficulty in concentrating on things, like reading a newspaper or watching television?	1	2	3	4
21. Did you feel tense?	1	2	3	4
22. Did you worry?	1	2	3	4
23. Did you feel irritable?	1	2	3	4
24. Did you feel depressed?	1	2	3	4
25. Have you had difficulty remembering things?	1	2	3	4
26. Has your physical condition or medical treatment interfered with your family life?	1	2	3	4
27. Has your physical condition or medical treatment interfered with your social activities?	1	2	3	4
28. Has your physical condition or medical treatment caused you financial difficulties?	1	2	3	4

For the following questions please circle the number between 1 and 7 that best applies to you

29. How would you rate your overall health during the past week?

1	2	3	4	5	6	7
Very poor						Excellent

30. How would you rate your overall quality of life during the past week?

1	2	3	4	5	6	7
Very poor						Excellent

EORTC QLQ-LC13

Patients sometimes report that they have the following symptoms or problems. Please indicate the extent to which you have experienced these symptoms or problems during the past week. Please answer by circling the number that best applies to you.

During the past week:	Not at all	A little	Quite a bit	Very much
1. How much did you cough?	1	2	3	4
2. Did you cough blood?	1	2	3	4
3. Were you short of breath when you rested?	1	2	3	4
4. Were you short of breath when you walked?	1	2	3	4
5. Were you short of breath when you climbed stairs?	1	2	3	4
6. Have you had a sore mouth or tongue?	1	2	3	4
7. Have you had trouble swallowing?	1	2	3	4
8. Have you had tingling hands or feet?	1	2	3	4
9. Have you had hair loss?	1	2	3	4
10. Have you had pain in your chest?	1	2	3	4
11. Have you had pain in your arm or shoulder?	1	2	3	4
12. Have you had pain in other parts of your body?	1	2	3	4
If yes, where?				
13. Did you take any medicine for pain? Yes No				
If yes, did it help?	1	2	3	4

References

1. Hellwig D, Ukena D, Paulsen F, *et al.* [Meta-analysis of the efficacy of positron emission tomography with F-18-fluorodeoxyglucose in lung tumors. Basis for discussion of the German Consensus Conference on PET in Oncology 2000].[comment]. *Pneumologie.* 2001;55:367-377.
2. Fischer BM, Mortensen J, Hojgaard L. Positron emission tomography in the diagnosis and staging of lung cancer: a systematic, quantitative review. *Lancet Oncology.* 2001;2:659-666.
3. Dwamena BA, Sonnad SS, Angobaldo JO, *et al.* Metastases from non-small cell lung cancer: mediastinal staging in the 1990s--meta-analytic comparison of PET and CT. *Radiology.* 1999;213:530-536.
4. MacManus MP, Hicks RJ, Matthews JP, *et al.* High rate of detection of unsuspected distant metastases by pet in apparent stage III non-small-cell lung cancer: implications for radical radiation therapy. *International Journal of Radiation Oncology, Biology, Physics* 2001;50:287-293.
5. Kalff V, Hicks RJP, MacManus M, *et al.* Clinical Impact of (18)F Fluorodeoxyglucose Positron Emission Tomography in Patients With Non-Small-Cell Lung Cancer: A Prospective Study. *Journal of Clinical Oncology* 2001;19:111-118.
6. van Tinteren H, Hoekstra OS, Smit EF, *et al.* Effectiveness of positron emission tomography in the preoperative assessment of patients with suspected non-small-cell lung cancer: the PLUS multicentre randomised trial.[comment]. *Lancet.* 2002;359:1388-1393.
7. Boyer MJ, Viney R, Fulham M, *et al.* A Randomised Trial of Conventional Staging (CS) With or Without Positron Emission Tomography (PET) in Patients (Pts) with Stage 1 or 2 Non-Small Cell Lung Cancer (NSCLC). *Proceedings of ASCO* 2001:abstract 1233.
8. Oliver A, Healey A, Donaldson C. Choosing the method to match the perspective: economic assessment and its implications for health-services efficiency. *Lancet.* 2002;359:1771-1774.
9. Gregor A, Thomson CS, Brewster DH, *et al.* Management and survival of patients with lung cancer in Scotland diagnosed in 1995: results of a national population based study. *Thorax* 2001;56:212-217.
10. Gregor A, Milroy R. Cancer Scenarios: An aid to planning cancer services in Scotland in the next decade. Edinburgh: Scottish Executive Health Department, The Scottish Executive; 2001. p. Chapter 4.
11. Richardson GE, Thursfield VJ, Giles GG. Reported management of lung cancer in Victoria in 1993: comparison with best practice. Anti-Cancer Council of Victoria Lung Cancer Study Group. *Medical Journal of Australia* 2000;172:321-324.

ANNEX C2

CLINICAL ALGORITHMS FOR THE USE OF FDG-PET SCANNING IN HAEMATOLOGICAL MALIGNANCY

OCTOBER 2003

SUMMARY

Current PDG-PET guidance in Hodgkin's disease (HD) should be adopted. Haematological cancer however now represents the 4th most frequent adult cancer in Scotland and this guidance underestimates the demand for more widespread use of FDG-PET scanning to minimise treatment toxicity and maximise cure rates for these patients.

Unlike many other cancers the blood cancers do not lend themselves to either preventive measures or screening procedures. The only advances then available for these illnesses can come from the use of more effective and less toxic treatments. FDG-PET scanning offers the opportunity for these treatment improvements and should be recommended for patients with potentially curable forms of lymphoma.

RECOMMENDATIONS FOR USE OF FDG-PET SCANNING IN HD

1 HTBS guidance on the use of FDG-PET scanning in HD should be adopted.

2 Patient entry to the forthcoming NCRI study in early HD should be considered.

RECOMMENDATION FOR FUTURE USE OF FDG-PET SCANNING IN HD

1 Staging FDG-PET scan be performed in patients with early stage HD for whom radiotherapy alone is the preferred treatment.

RECOMMENDATIONS FOR FUTURE USE OF FDG-PET SCANNING IN DIFFUSE LARGE B CELL NON HODGKIN'S LYMPHOMA (DLBC NHL)

1 FDG-PET scanning be used to stage disease prior to treatment

2 FDG-PET scanning should be repeated at 6 weeks for patients with extensive disease to assess response to treatment.

3 FDG-PET scanning should be carried out at the completion of chemotherapy to assess the need for consolidation XRT.

Current Status

Current guidance issued by HTBS (October 2002) recommends that FDG-PET be used to restage all patients with Hodgkin's Disease (HD) with either PR or CR after initial therapy. This guidance is aimed particularly at those patients who complete firstline chemotherapy to select those for either:

a) no further treatment
b) additional consolidation/involved field radiotherapy (IFXRT)

At the end of initial therapy FDG-PET has absolute positive predictive value for relapse (100% of cases will relapse if restaging PDG-PET scan is positive after initial therapy) and a negative predictive value of 82% (82% will remain in remission when restaging PGD-PET is negative). Bulky mediastinal disease (more than 10cm) may still be considered an absolute indication for consolidation XRT even with a negative restaging FDG-PET scan.

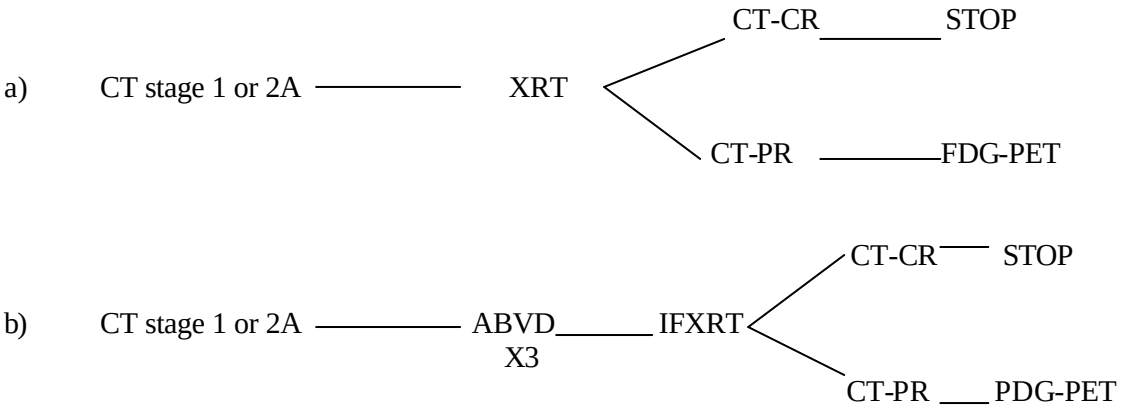
Radiologically detectable residual abnormalities post chemotherapy are not uncommon. In view of difficulties in both obtaining and interpreting repeat biopsies FDG-PET scanning provides the best means of assessing residual masses for the presence of active lymphoma.

EARLY STAGE HD

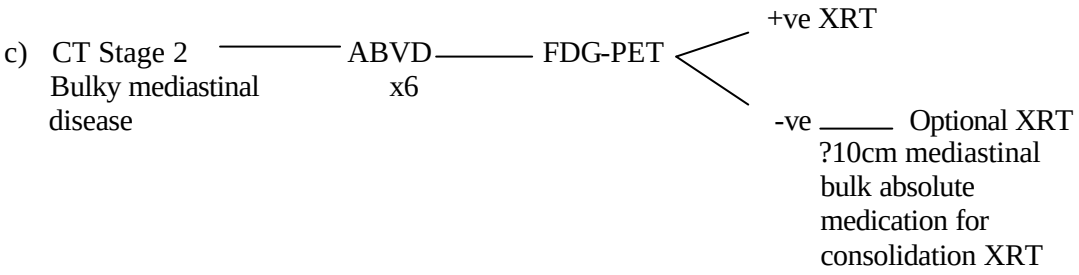
TREATMENT PLANS (to include HTBS guidance on PDG-PET)

Current FDG-PET guidance has not been given to influence the choice of firstline treatment modality in early stage HD (stages 1 and 2a). In early stage HD limited chemotherapy followed by IFXRT offers significantly better disease free survival than XRT treatment alone following which 20-30% relapse occurs (survival is unaffected). In Scotland alone 109 cases of HD were diagnosed in 2001 and 10 received XRT. Optimum treatment of early stage HD in Scotland (to include HTBS guidance) should for the most part follow one of three clinical algorithms (Fig 1).

Figure 1 Treatment Options for Early HD (2003)



Early HD continued



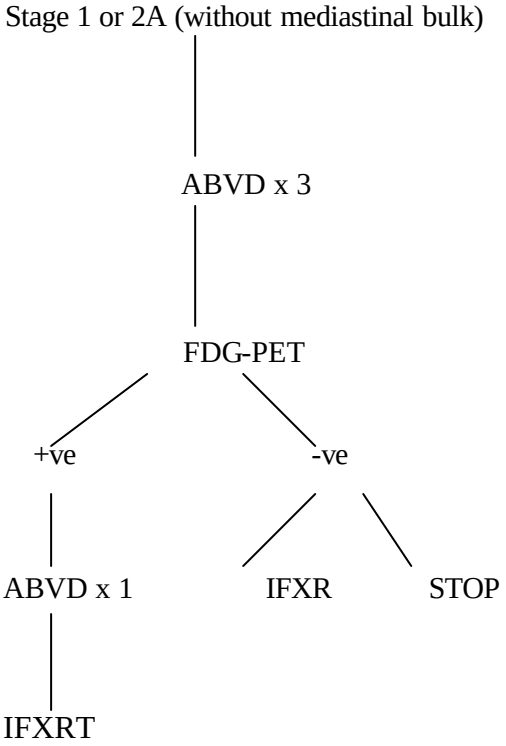
NOTE: At present the majority of Scottish patients with HD do not receive a FDG-PET scan at any time in their treatment.

FORTHCOMING TREATMENT PLAN

NCRI Trial in early HD

With improved availability of FDG-PET scanning in the UK the forthcoming NCRI Study has adopted the following treatment algorithm (Fig 2) to test the need for IFXRT in patients with early stage HD who become FDG-PET negative after 3 courses of ABVD. Support for this trial is recommended.

Figure 2 Forthcoming NCRI Study in Early HD

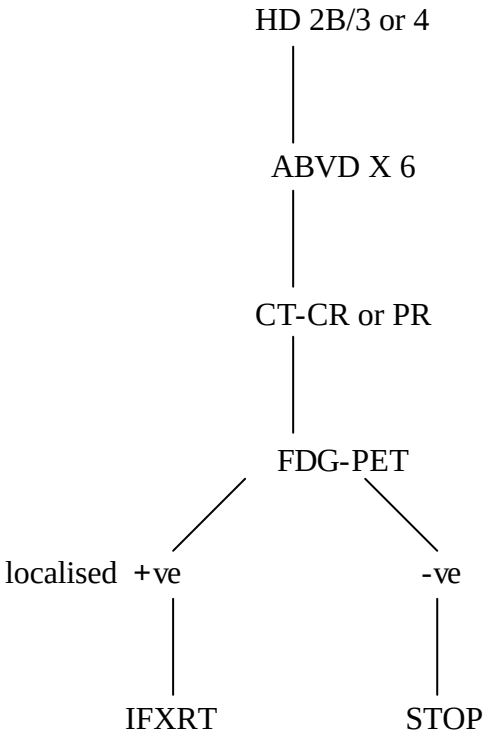


ADVANCED HODGKIN'S DISEASE (Stage 2b/3 or 4)

Current Treatment Plan (to include HTBS guidance)

The majority of patients should follow the illustrated algorithm (Fig 3)

Figure 3 Treatment Plan for Advanced HD (2003)



RECOMMENDATIONS FOR USE OF FDG-PET SCANNING IN HD

1 HTBS guidance on the use of FDG-PET scanning in HD should be adopted.

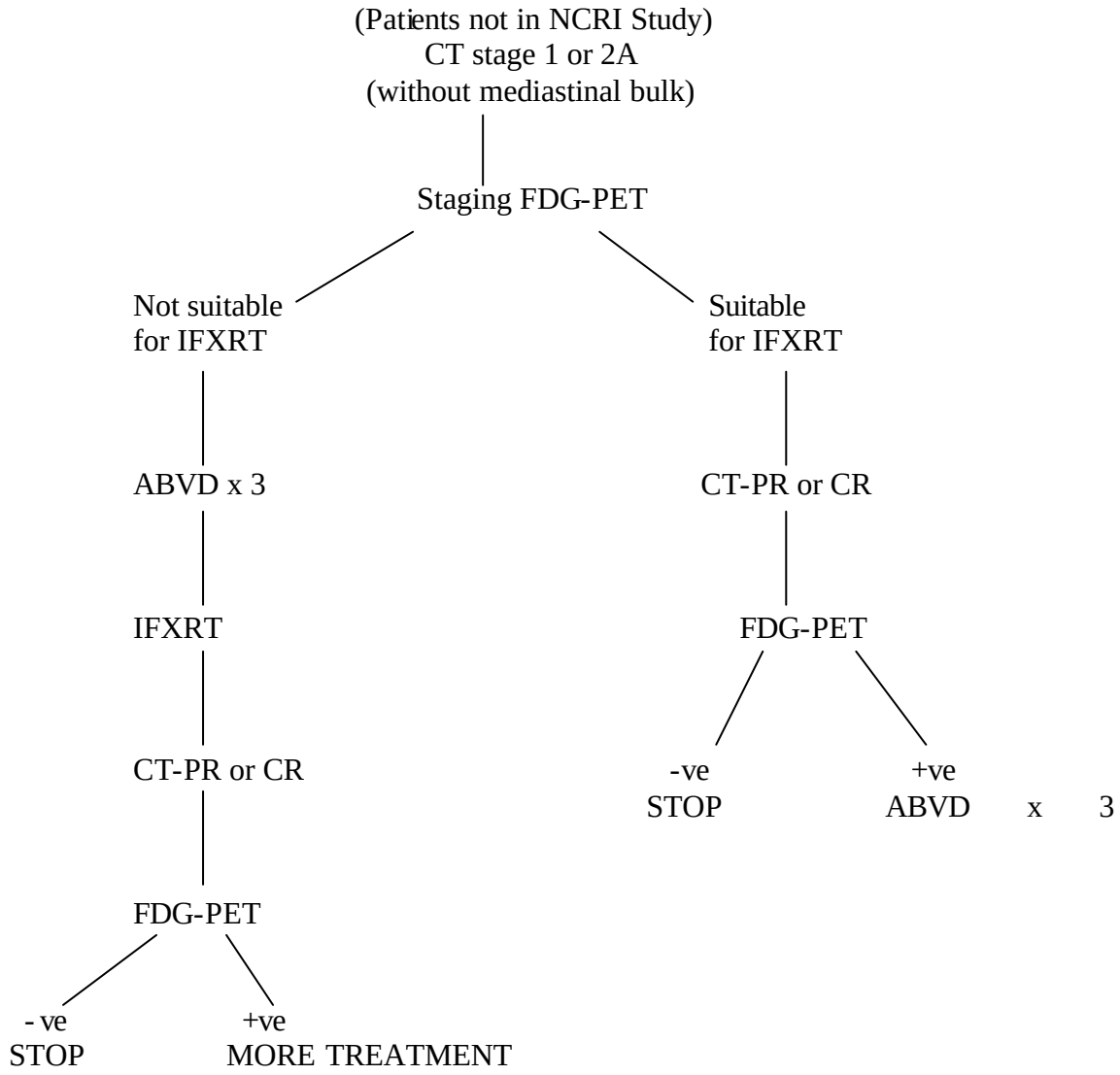
2 Patient entry to the forthcoming NCRI study in early HD should be considered.

FUTURE STUDIES FOR FDG-PET SCANNING IN HD

Current FDG-PET guidance has not been issued to influence the choice of treatment modality for firstline treatment of early stage HD. Although relapse rate is significantly reduced by the use of chemotherapy (ABVD x 3) plus IFXRT, radiotherapy alone does provide highly effective treatment within the radiotherapy field. Indeed virtually all relapses following radiotherapy alone occur outwith the treatment field. Relapse following radiotherapy alone then is more likely to reflect the failure of CT scanning to provide accurate stage in early HD rather than any primary radiotherapy resistance.

Initial staging FDG-PET scanning is recommended in early stage HD for patients not suitable for the NCRI study or in whom even limited chemotherapy should be avoided. A total of 10 patients of 109 Scottish patients with HD received XRT treatment alone in 2001. The following treatment algorithm is proposed for such patients (Fig 4).

Figure 4 Future Treatment Plan for Early HD



The aim of this algorithm is to identify the 70% of patients with early stage HD who should be cured with IFXRT alone thereby eliminating the need for

a) more extensive radiotherapy (extended field or mantle)

b) chemotherapy prior to XRT

RECOMMENDATION FOR FUTURE USE OF FDG-PET SCANNING IN HD

1 Staging FDG-PET scan be performed in patients with early stage HD for whom radiotherapy alone is the preferred treatment.

THE FUTURE OF FDG-PET SCANNING IN HAEMATOLOGICAL MALIGNANCY: THE ROLE IN NON HODGKIN'S LYMPHOMA

Blood cancer is now the 4^{h} most frequent adult cancer in Scotland. The cause of these disorders is not known and they do not lend themselves to either:

a) preventive measures or
b) screening programmes.

Emphasis must then be directed to define the optimum treatment to maximise cure for patients but at the same time avoid:

a) unnecessary toxicity resulting from excessive treatment
b) disease progression resulting from inadequate treatment.

In the assessment exercise conducted by HTBS the majority of studies examined included patients with Non Hodgkin's Lymphoma (NHL) as well as HD The incidence of NHL in Scotland has increased at approximately 4% pa over the past 2 decades. The cost effective modelling carried out by HTBS however was confined to HD. The limitations of the current HTBS Guideline are that it applies:

a) only to HD (150-180 HD cases per annum as compared to 900-100 NHL cases per annum). Information taken from SNLG database, population 8million.
b) only to restaging after initial therapy.

The majority of these NHL patients will have low grade lymphoma which is generally accepted to be incurable. From the SNLG database however approximately 300 new patients will be diagnosed with Diffuse Large B Cell (DLBC) NHL pa. These 300 patients share with the 180 HD patients the opportunity for curative treatment. However the cure rate for DLBC NHL is only about 40% and significantly less for that seen with HD. FDG-PET scanning provides an opportunity to improve these cure rates for DLBC NHL by:

a) providing accurate disease staging pre-treatment
b) early assessment of response to treatment.

Staging FDG-PET scan in NHL

FDG-PET scanning is at least as sensitive as CT but substantially more specific than CT for the detection of lymphoma. Approximately 40% of new lymphoma patients will be upstaged by FDG-PET scanning when compared to CT scanning. Improved accuracy of staging achieved by FDG-PET is likely to lead to change in treatment in approximately 25% of lymphoma patients.

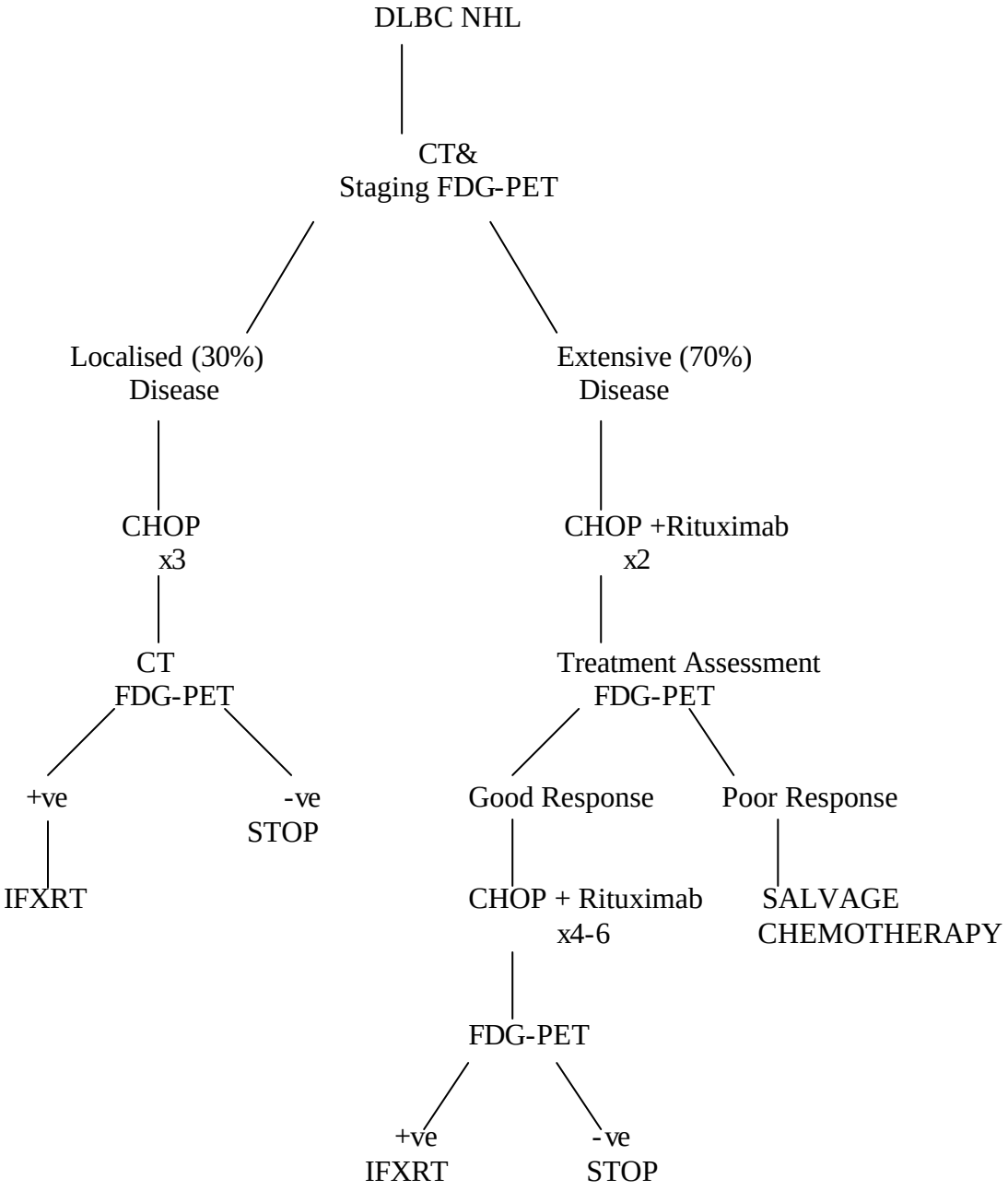
FDG-PET scanning during treatment

FDG-PET scanning at 6 weeks after the start of firstline chemotherapy is strongly predictive for outcome in lymphoma. We would then recommend the following treatment plan and algorithm for all patients with DLBC NHL (Fig 5)

PROPOSED FUTURE TREATMENT PLAN FOR DLBC NHL

We would recommend that all patients with potentially curable DLBC NHL should have staging FDG-PET scan to identify localised and extensive disease. Patients with localised disease (approximately 30% of cases) should receive 3 coures of chemotherapy (CHOP). Thereafter a FDG-PET scan should be carried out to assess the need for IFXRT.
Patients with extensive disease (approximately 70% of cases) should have FDG-PET to assess response 6 weeks after the start of chemotherapy (CHOP + Rituximab). Those patients with inadequate response should be considered for salvage chemotherapy. Those patients who show a good response to treatment should continue conventional chemotherapy and receive a restaging FDG-PET scan at the completion of treatment to decide on the need for IFXRT. (Fig 5)

Fig 5 DLBC NHL: Proposal for Future Treatment Plan



RECOMMENDATIONS FOR FUTURE USE OF FDG-PET SCANNING IN DIFFUSE LARGE B CELL NON HODGKIN'S LYMPHOMA (DLBC NHL)

1 **FDG-PET scanning be used to stage disease prior to treatment**

2 **FDG-PET scanning should be repeated at 6 weeks for patients with extensive disease to assess response to treatment.**

3 **FDG-PET scanning should be carried out at the completion of chemotherapy to assess the need for consolidation XRT.**

ABBREVIATIONS

ABVD	Adriamycin Bleomycin Vinblastine Dacarbazine
CHOP	Cyclophosphamide Adriamycin Vincristine Prednisolone
DLBC	Diffuse large B cell
HD	Hodgkin's disease
IFXRT	Involved field radiotherapy
NHL	Non Hodgkin's lymphoma
XRT	Radiotherapy

ANNEX D

Appendix 27 from HTBS Report

DATA FOR EVALUATION OF PET SCANNING

It is recommended that the following data be routinely collected from all cancer patients undergoing FDG-PET scanning within NHSScotland, to allow thorough evaluation of the clinical and economic value of FDG-PET. Clearly, such data will be collected routinely in patients undergoing FDG-PET scanning as part of a formal clinical trial, but it will also be important to ensure that data collected in trials are compatible with those collected on patients undergoing FDG-PET scanning for 'clinical use'.

Since both follow-up data and measurements of 'subjective experience' will form an important part of the dataset, full informed consent is needed from patients before the data are collected. The information given should stress that data will only be used and reported in an anonymised form – personal identifiers are needed only to facilitate data collection and linkage.

- Patient identifiers (CHI number in Scotland, NHS number, name, Date of Birth, address)
- Sex
- Current diagnosis (what and when and how made)
- Co-morbidities (disease and date of onset)
- Anti-cancer treatments before FDG-PET (date and description)
- Other investigations for the cancer
- Results of previous FDG-PET scans for this disease
- Indication for FDG-PET scan
- Time to FDG-PET scan after it was ordered
- Patient satisfaction and comments on the experience
- Results from FDG-PET scan
- Changes to treatment plan resulting from the FDG-PET scan
- Anti-cancer treatments given post-PET
- Follow-up exam results (full results for each scheduled follow-up point)
- Final outcome (perhaps at 5 years)

ANNEX E

PREFERRED REFERRAL TEMPLATE –

INFORMATION REQUIRED FOR PET IMAGING, JOHN MALLARD CENTRE, ABERDEEN

1. **Clinical Indication**

- This should include provisional diagnosis and justification for PET imaging.
- Dates of previous treatment, e.g. surgery, Radiotherapy or Chemotherapy should be included.
- Whether or not the patient is diabetic and if so, the severity of the disease.
- Patient name, full address, telephone number and date of birth.
- State of mobility if disabled in any way.
- Any other special requirements.

2. **CT scan**

The patient's most recent CT scan is required for reporting with the PET images.

3. **Funding**

The contact name and number of the person to whom the invoice should be sent (unless part of agreed service level agreement).

4. **General Practitioner**

The name and address of the patient's GP are required to obtain a hospital number for Aberdeen.

5. **Next of Kin**

The name, address and relationship of the next of kin.

ANNEX F

Potential PET scanning requirement currently reimburseable by US Medicare in the USA

Patient category

Lung cancer dx NSC
Lung cancer restaging

Colorectal dx
Colorectal staging
Colorectal restaging

Melanoma dx

Lymphoma dx
Lymphoma staging
Lymphoma restaging

Head/neck dx
Head/neck restaging

Oesophageal dx
Oesophageal staging
Oesophageal restaging

Breast restaging post tx
Breast tx evaluation

ANNEX G

RADIOPHARMACY CONSIDERATIONS

As with conventional radiopharmaceuticals, those used in PET are classed as prescription only medicines and are subject to the Medicines Act 1968. In addition, under the Medicines (Administration of Radioactive Substances) Regulations 1978, radiopharmaceuticals for administration to humans may be supplied only to a doctor or dentist holding a certificate issued by Health Ministers on the advice of the Administration of Radioactive Substances Advisory Committee (ARSAC).

It should be noted that ARSAC research authorisations are specific to a particular trial; multiple trials require multiple authorisations.

For the routine supply of radiopharmaceuticals within a NHS Trust (or other such responsible legally constituted NHS body once NHS Trusts are dissolved), the Radiopharmacy may hold a manufacturer's "specials" licence or operate under the exemption for hospitals or registered pharmacies in section 10 of the Medicines Act. The former is a requirement if a Trust is supplying outwith its boundaries. To operate under a section 10 exemption, procedures must be under the supervision of a pharmacist; this mode of operation is used for relatively small scale preparation.

As with conventional medicines, radiopharmaceuticals marketed commercially are required to have a product licence. Where a material carrying a valid product licence is available, it must be used in preference to any unlicensed alternative. In the case of PET, were a licenced source of ^{18}FDG to become available from (say) a commercial source, use of an unlicensed locally-produced material on a routine basis would not be acceptable.

At present, this would not apply for purely research use or in rare cases where an application for administration to "a particular patient" could be made. Widespread use of the latter exemption would not fall within current guidelines. From April 2004, all clinical trials will require a Clinical Trial Authorisation from the Medicines and Healthcare products Regulatory Agency.

Transport of radiopharmaceuticals must comply with the Radioactive Materials Road Transport Regulations. These require packaging in approved containers, traceable documentation and driver training.

ANNEX H

Training Requirements for PET Facilities

Training needs vary with the type of facility being provided, i.e. whether it is an imager alone or a full PET centre with cyclotron and radiopharmacy. The latter case is not considered here, but for this there would be additional training required for a cyclotron engineer and radiochemists. It is also assumed that, as recommended in the HTBS Report, the PET facility is linked to a nuclear medicine department.

Medical Staff

Details of training for specialist registrars in nuclear medicine are available on the British Nuclear Medicine Society website (www.bnms.org.uk). It requires 4 years training in a recognised centre of which Glasgow Royal Infirmary is the only one in Scotland. Applicants with an FRCR get 2 years exemption. Completion of the training leads to the award of a CCST. However it should be noted that not all consultants practising nuclear medicine in Scotland hold a CCST. There is a national shortage of qualified staff and so the main training route in Scotland might be in providing additional training to existing consultants in nuclear medicine.

Nuclear medicine training, while giving a good general background to PET, does not provide sufficient detailed training for the clinical management of a PET centre. Training courses in PET are available from the St Thomas's Clinical PET Centre. This course lasts for 3 days and is usually held annually. Just this year a PET Learning Facility has been set up in Vienna by the European Association for Nuclear Medicine (EANM). It held its first course in March 2003 and a further 7 are scheduled for 2003. They are 2 day courses and a course programme is attached as Appendix 1. Both these courses have a registration fee in the region of £400-500.

All PET studies on patients or volunteers conducted in the UK must be under the supervision of a consultant who holds an ARSAC certificate for PET issued by the Department of Health in London on behalf of UK Health Ministers. The requirements for PET certification are under discussion but are likely to be around 3 months training and experience of around 300 studies in a recognised PET centre.

It should be noted that if regional/national preference is for a combined PET/CT facility then there may be additional training required in cross-sectional anatomy.

Physicists

The NHS funds basic training for 4 medical physicists annually in Scotland. This is done through National Services Division (NSD) and administered by the Aberdeen department on behalf of a consortium of all medical physics departments in Scotland. This covers an initial 2 years of training for physicists, who must hold an Honours degree in Physics or similar subject, consisting of an MSc in Medical Physics (done at either Aberdeen or Glasgow University and accredited by the Institute of Physics and Engineering in Medicine (IPEM)) and a year of competency based training in 3 areas of medical physics. At the completion of training trainees are assessed on submitted portfolios of work and undergo an oral exam held

centrally across the UK by the IPEM. On completion of this training they can apply for a specific post in the NHS.

They must then undergo a further two years on a Programme of Advanced Training and Responsibility before they are eligible to apply for State Registration as a Clinical Scientist through the Health Professions Council. An additional 2 years of PATR entitles them to Corporate membership of IPEM. During this time, and for the rest of their career, they are expected to follow a CPD programme administered by IPEM.

While the initial training is broad, physicists will have some training in PET as part of their MSc, and have some practical experience if they are at Aberdeen,. If they choose to do nuclear medicine as one of their competency areas then they will also do some PET.

However, across the UK we are not training sufficient physicists for the vacancies available, particularly in radiotherapy where there has already been an expansion in facilities.

It would be possible to offer short training courses for physicists at Aberdeen.

Technologists/Radiographers

Technical support for nuclear medicine services, including PET in Aberdeen, is provided by either medical physics technologists, employed by the NHS as Medical Technical Officers, or radiographers. There is no difference between them in terms of quality and proficiency. However, when a combined PET/CT is being use the operator would clearly need to have had appropriate radiography training.

Currently the training of MTOs has been less structured than that of radiographers and they only have access to a voluntary register, whereas radiographers are state registered under HPC.

An MTO training scheme has recently been set-up by the IPEM, which has technologists as part of its membership. One route is via an IPEM approved vocational degree, but at present no such degree course is available in Scotland although Paisley University are developing one such course. This permits the applicant entry to the voluntary register. The technologist then undertakes a further year of "orientation and experienced training" which entitles them to receive the IPEM Diploma in Clinical Technology. Three years advanced training follows the diploma.

Medical Physics departments in Scotland are registered for the training. It is not thought there should be difficulty in recruiting additional staff as MTOs although there is a recognised UK-wide shortage of radiographers. Consideration needs to be given to the time taken to train any new staff.

Alternatively PET training courses are becoming available for technologists and radiographers already experienced in nuclear medicine.