

Robust PET/CT Research in Practice

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Introduction

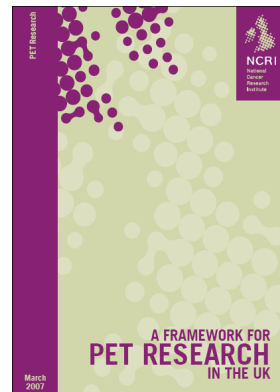
- **Background**
- **Before we have even started**
- **OK so now we can start**
 - Referrals
 - Patient Preparation
 - Imaging
 - Reconstruction
 - Reporting
 - Quality Control
- **Where are we now**

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Background

March 2007

NCRI Framework for PET
Research in the UK



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NCRI Framework for PET Research

Research Questions and Priorities in PET Clinical Research

The Need for Research

- Validate new uses of PET
- Staging cancer particularly relating to the impact on patient outcomes
- Monitor therapy and change both drug and radiotherapy treatment regimens
- Evidence of value for money

Prioritisation

It will be important to prioritise large-scale, potentially practice changing, trials to ensure the major research questions are addressed without deleterious impact on service delivery

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NCRI Framework for PET Research

Barriers to PET Research

Funding

There is an historic reluctance or inability of PCrTs to meet the costs of those scans defined as treatment costs in clinical research protocols. There is a need for funding mechanisms for the R&D to convert complex PET methods into simplified but effective assays for use in multi-centre research.

Regulation

Regulation of the production and licensing of PET radiotracers is perceived to be disproportionate to risk.

Workforce

There is a national shortage of radiochemists... *(and the rest)* Provision of training needs to be closely linked to infrastructure, in terms of facilities for training and the requirement to coordinate staff training with future skill and capacity requirements.

Technology

The lack of standardisation of the methods used to acquire and analyse PET data impedes multicentre research and collation of research findings. There is a need for leadership and mechanisms for forward planning and prioritisation of the technology developments required to underpin research.

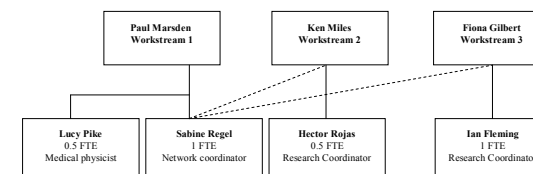
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NCRI PET Research Initiative



- **Funded and set up by the NCRI**
- **Aim is to stimulate and support the use of Positron Emission Tomography (PET) in cancer research**

UK PET Research Steering Committee



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1. Trial Network & Technology



Paul Marsden & Lucy Pike, King's College London

- **Establish network for high quality clinical trials**
 - NCRI PET Clinical Trials Network
 - Site accreditation and QC procedures
 - Data analysis methods across sites
 - Develop audit process
 - Expand to new tracers and more complex studies, consider options for core lab
- **Technology development and research needs**
 - Guidance on consensus statements and standardisation of software
 - PET Scanning Methodology Panel
 - Guidance on use of mobile PET scanners in research
 - Discussions regarding international alignment

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2. Late Phase Clinical Trials



Ken Miles & Hector Rojas, Brighton & Sussex Medical School

- **Identify areas of intervention to increase research use of PET in late phase trials**
- **Streamlining funding of PET research in the NHS**
 - Periodic meetings with Specialised Commissioners; Excess Treatment Costs
- **Delphi study to identify UK PET research priorities**
 - To inform HTA commissioned research
- **Promoting potential roles for PET in oncological research**
 - PET-CT expert panel; provide information and advice to NCRI Clinical Studies Groups (CSGs) and PET researchers

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3. Early Phase Clinical Trials

Fiona Gilbert & Ian Fleming, University of Aberdeen

Stimulate early phase PET research

- Survey/ visits of ECMC PET centres and workshop on early phase research priorities (report on website)
- Workshop on how to increase PET radiotracer availability for research in the UK (report on website)
- Ongoing dialogue with academia and industry regarding increase of non-FDG tracers in the UK

Understanding and progressing regulatory issues

- Working with MRC & MHRA to organise workshop to guide PET research community on regulatory issues (September 2010)
- Support developing PET-specific algorithm to help researchers decide if study is clinical trial or not

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All Workstreams

Resources for the PET community

- Register of UK PET sites
- UK PET research funding routes
- UK oncology PET radiotracer directory
- UK PET clinical trials database

www.ncri-pet.org.uk

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NCRI PET Core Lab

To allow the collation of research data across multiple sites there needs to be harmonisation of the methods used for acquisition and analysis of PET data at the participating scanning centres thus ensuring consistent results.

Currently the NCRI PET Core Lab provides the following:

Primary roles:-

- Co-ordination of imaging studies in liaison with relevant clinical trials unit or local coordinator
- Data transfer, QC and collation processes
- Ongoing QC and audit of PET centres in the NCRI PET Clinical Trials Network

Secondary roles:-

- Advice on regulatory approvals that need to be obtained and how to obtain them
- Contact with UK PET facilities that have completed an accreditation process for PET clinical trials/accreditation of new sites
- Advice on protocols for PET/CT acquisition and processing


The accreditation requirements and standards for sites to join the Trials Network and participate in multicentre trials have been posted on the NCRI PET Research Network (PRN) website.

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NCRI PET Clinical Trials Network

- Total number of fixed sites in the UK: 35 (39 PET/CT, 2 PET & 1 brain only)
- Number of NCRI accredited PET Centres: 21 (24 PET/CT fixed scanners);

- Aberdeen
- AMICL (Bulstrode Place)
- Barts
- Belfast
- Birmingham
- Cambridge (Addenbrookes)
- Cheltenham
- Christie
- CISC (Brighton)
- Coventry
- Glasgow
- Guildford
- Guys and St Thomas'
- Mount Vernon
- Newcastle
- Nottingham
- Oxford
- Preston
- Royal Marsden
- UCLH
- WMIC




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Before we have even started


Or how can we join the club?

NCRI Statement on use of mobile PET/CT scanners in multi-centre trials
Jan 2010



Statement on the use of mobile PET/CT scanners in multi-centre trials

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Statement on the use of mobile PET/CT scanners in multi-centre trials

Before a scanning site can take part in a multi-centre trial it must undergo accreditation by the NCRI PET Clinical Trials Network.

If a mobile scanner is to be used in multi-centre trials it must conform to the same standards as expected for a fixed scanner site.

Each site will be subject to ongoing audit to ensure compliance with these standards and trial protocols. This applies equally to fixed and mobile scanners.





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Statement on the use of mobile PET/CT scanners in multi-centre trials


Particular issues that may impact on the feasibility of using mobile scanners in multi-centre trials are:

- It is a condition of trials involving multiple scans on a patient that the same scanner is used for all scans.

PETCT2 PETCT2 ✓ PETCT1 ✗ PETCT3 ?

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Statement on the use of mobile PET/CT scanners in multi-centre trials

Particular issues that may impact on the feasibility of using mobile scanners in multi-centre trials are:

- Sites are required to ensure the same mobile scanner is available on a particular day to comply with complex patient scheduling with respect to therapy.

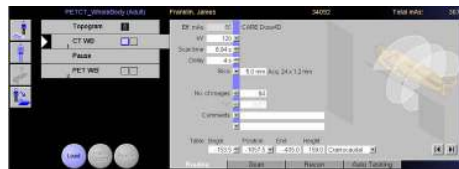
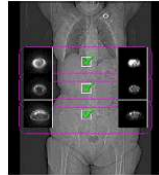
| PETCT2 | | |
|------------|-----------|-------------------|
| 19/07/2010 | Monday | Leicester |
| 20/07/2010 | Tuesday | Norfolk & Norwich |
| 21/07/2010 | Wednesday | |
| 22/07/2010 | Thursday | |
| 23/07/2010 | Friday | Northampton |
| 24/07/2010 | Saturday | |
| 25/07/2010 | Sunday | |
| 26/07/2010 | Monday | Leicester |
| 27/07/2010 | Tuesday | Norfolk & Norwich |
| 28/07/2010 | Wednesday | |
| 29/07/2010 | Thursday | |
| 30/07/2010 | Friday | Northampton |

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Guidelines - Imaging

Time delay
Usually 60 min (+/-) 5 min

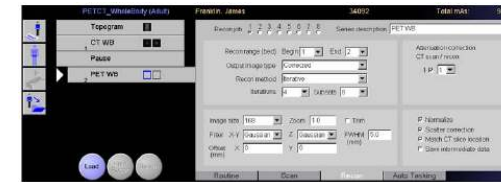
Imaging Parameters
CT protocol
Scan length
Arms up



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Guidelines - Reconstruction

Reconstruction Parameters
3D OSEM, 4 iterations, 8 subsets
5 mm Gaussian filter in all directions
256 x 256 matrix
1 x zoom



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Guidelines - Reporting

Clinical Report

Clinical Information

Indication and relevant patient history

Quality of examination

Motion artefacts, muscular uptake, CT related artefacts

Description of localisation

Extent and intensity of pathologic uptake (mild, moderate, intense)
SUV relative to background (liver parenchyma)

Limitations

Sensitivity/specificity of PET
Small lesions

Summary

Diagnosis, differential diagnoses, repeat/additional examinations

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Guidelines - Reporting - SUV

Quantification is key for high quality PET research

$SUV = \frac{\text{Average concentration (kBq/ml)}}{\text{FDG dose (MBq)/ BW (kg)}}$

Technical Errors

Scanner to calibrator calibration
Residual activity in syringe

Biological Factors

Glucose level
Uptake period
Inflammation

Physical Factors

Acquisition/Reconstruction
ROI (size and type)
Contrast agents

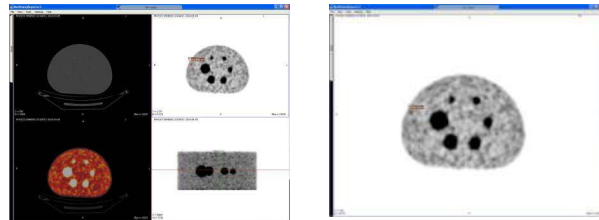
See R Boellard
JNM May 2009; 50 11S-20S

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Guidelines - Reporting - SUV

Quantification is key for high quality PET research

Physical Factors
ROI (size and type)



Medstamp Reporter 2.1

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Guidelines - Quality Control

Daily QC

Two bed position scan of Ge-68 cylinder with SUV

Other QC

Periodic scanner/calibrator cross calibrations

Recovery Coefficients with Image Quality Phantom

Hot spheres (5:1) concentration, no lung insert

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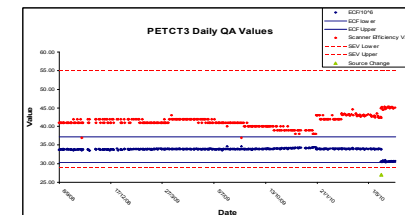
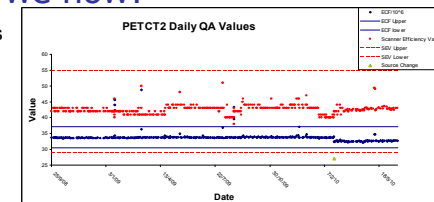
Where are we now?

- Stability of mobiles
- Radionuclide Calibrator Calibration/ Cross Calibration
- Interchangeability of similar mobile scanners
- Software validation

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Where are we now?

Stability of mobiles



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Where are we now?

Radionuclide Calibrator Calibration/ Cross Calibration



Secondary Standard



PETCT2



PETCT3



PETCT4



PETCT5

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Where are we now?

Must Do

- Cross calibrations
- Change Ge-68 sources on all scanners

Like To

- Investigate interchangeability of similar mobile scanners
- Validate / improve software for SUV calculations

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Thanks to

- Lucy Pike of NCRI PET Research Network for slides 6-12

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