NCRI
PET Research Network

NCRI
National Cancer
Research Institute

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Final Report of the NCRI PET Research Initiative 2008–2012

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Executive summary

This report summarises the achievements and outputs of the NCRI PET Research Initiative, which ran from 2008 to 2012. Its three workstreams and steering committee took on activities to support early and late phase PET research, and to reduce the technological and QA challenges of delivering PET trials.

A series of summary messages is captured below to help researchers, funders and other stakeholders to identify resources available, opportunities that have been identified or created, and areas of ongoing need.

The many resources produced by the NCRI PET Research Initiative are available on the website www.ncri-pet.org.uk for ongoing reference.

► This includes guidance on PET in radiotherapy planning, databases of radiotracer availability and PET facilities across the UK, advice on finding information on ongoing PET trials, and tips on navigating treatment costs.

The NCRI PET Core Lab and network of accredited PET sites is ongoing, and can help researchers to plan and deliver PET QC for multicentre trials (email: pet-trials@kcl.ac.uk).

► Researchers: Costs need to be built into funding applications to cover the use of this service. The Core Lab team should be contacted early in trial development to help with QA planning and costing.

► Funders: Some short-term core funding has been put forward by NCRI partners through to 2015 for the Core Lab to transition to a funding model where costs of the Core Lab are built into funding applications for new trials that use the service. New applications for PET trials from 2012 onwards should be prompted at application stage if these costs are not included.

It remains difficult to identify research that includes PET (or other types of imaging) within portfolios of ongoing trials, both on an organisational and national level, because it is not always the primary purpose of a study.

► Funders: Driving improvements in data capture on imaging in clinical trials would help to identify gaps in research, avoid overlapping funding applications being made by different groups, and could prompt collaborations.

► Researchers: Including an explicit reference to use of PET (or other imaging) in study abstracts will help to make this information accessible through current databases.

Clinical questions of high priority for PET research in cancer have been identified through the Delphi process, and will be submitted for publication in 2012.

► Funders: Briefing funding panels accordingly, or considering a highlight call or other process to encourage applications in these areas, could help to channel resources towards the areas that have been identified as having the greatest need/potential.

► Researchers: This assessment should inform decisions about new trials to be developed.

Patient information on the use of FDG-PET within cancer clinical trials is available in video format online (www.ncri.org.uk/pet/video).

► Clinicians and researchers: This resource will help patients if they are considering taking part in a trial that involves the use of PET. A flyer can be downloaded from the website to pass on the link or advertise this resource.

Access to novel radiotracers is expensive and bulk purchase of novel radiotracers such as FLT is one way that has been identified to lower the cost per dose.

► Funders: To limit the overall costs of PET research, there may be economies of scale from funding parallel studies with the same tracer, or making pre-purchase commitments of quantity directly with tracer suppliers.

► Researchers: Joint or parallel applications with other groups wishing to use the same tracer in a similar timeframe should be considered. There is now a precedent for being able to negotiate bulk purchase of FLT, and discussions with the prospective research funder and tracer suppliers would be the first step.

The MRC-MHRA PET Expert Group provides a source of advice and guidance on regulatory aspects of PET research, acting as a bridge to the MHRA.

► Researchers: Information and resources from the Group can be accessed at http://www.mrc.ac.uk/Ourresearch/Ethicsresearchguidance/MHRA-PET/index.htm

PET clinical trials often incur high excess treatment costs, and it is uncertain how new commissioning and research funding arrangements may affect the delivery of PET research.

► All stakeholders are encouraged to keep this issue under watch during the transition of commissioning arrangements.

With the PET Research Initiative having ended, there is no longer a single point of contact for advice and support on clinical/translational aspects of using PET in cancer trials.

► Researchers: The key groups in which both clinical/translational cancer research and PET research are represented are now the ECMC Imaging Network Group and the Biomarkers and Imaging Clinical Studies Group. Either can be approached for advice.

► Funders: It would be prudent to review these arrangements in the medium term to determine whether they are sufficient to sustain PET trial development.

1. Background

Between 2005 and 2007, a Positron Emission Tomography (PET) Strategic Planning Group was convened by NCRI to review the opportunities and needs for PET scanning research in cancer, and a final report was published in 2007.[1] Amongst other findings from the group, it was determined that a coordination function was needed to provide national leadership and act as a focal point to facilitate research.

The NCRI PET Research Initiative was set up in 2008 to stimulate and support the build-up of a UK research programme in PET that is internationally competitive, novel in approach and relevant to the eventual uses of PET in the clinic. It was funded collaboratively by Cancer Research UK, the Medical Research Council, and the four Government health departments in England, Scotland, Wales and Northern Ireland, with a total budget of £208k/year for 3 years. This paper summarises how the initiative was run, its collective achievements, and the lessons to take forward into future work within and beyond cancer imaging.

2. Group setup and aims

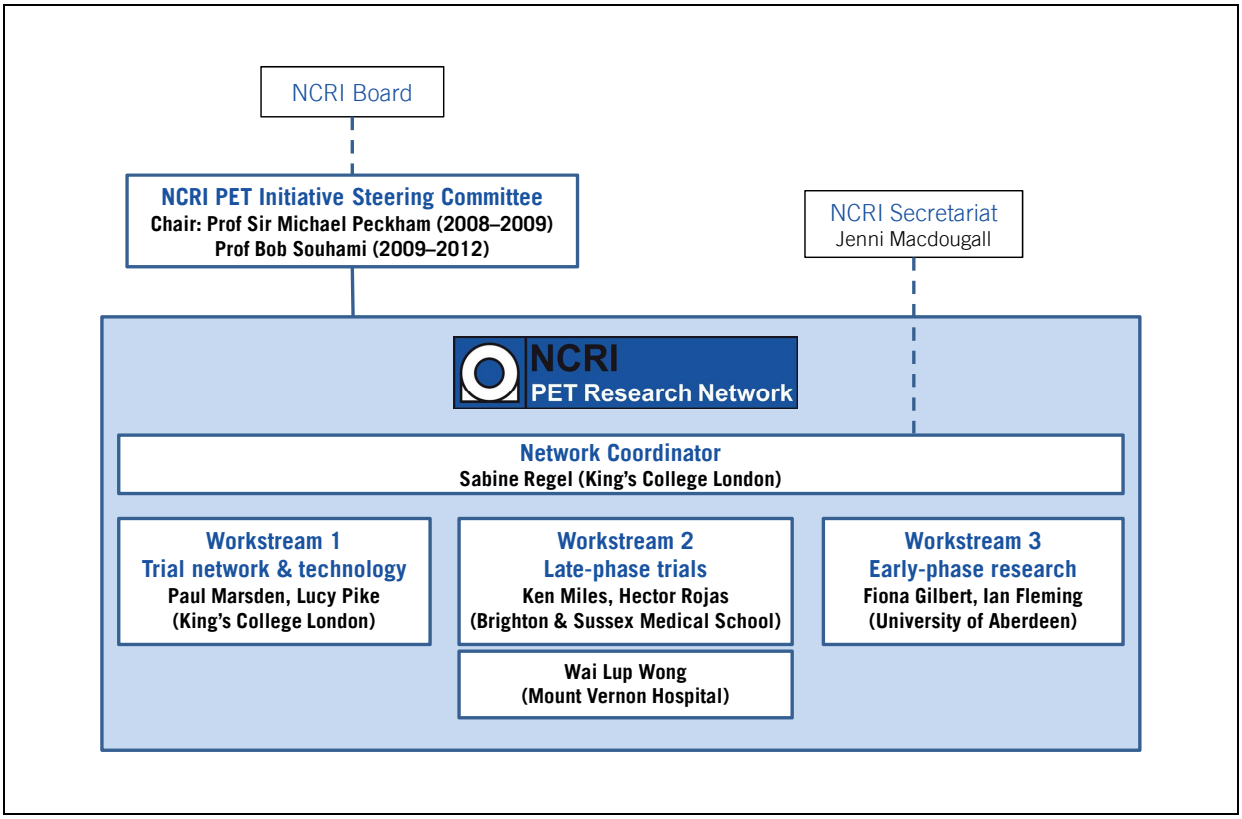
A PET Research Steering Committee was put in place to provide a cross-disciplinary overview of PET research challenges, and to set the broad strategy within which work was taken forward. The first chair was Professor Sir Michael Peckham, succeeded in 2009 by Professor Robert Souhami who had chaired the original Strategic Planning Group.

To provide the executive function of the Committee, applications were sought competitively from across the UK from centres with PET expertise and a willingness to lead work in this area. Having originally planned a model where one centre would be selected, after shortlisting and interview it was considered necessary to instead split the funding across three centres to provide a balance of expertise in technology and quality assurance (QA), late phase trials and early phase trials. These three centres were collectively known as the PET Research Network (PRN).

The three PRN workstreams had a staggered start as staff members were recruited or freed up from other responsibilities, and the full initiative spanned the time period from September 2008 to July 2012. Each centre had a PET Research Network Lead, appointed on a part-time basis, supported by a further part time post. Workstream 2 also received support from Dr Wai Lup Wong, the Department of Health Clinical Guardian for PET-CT, from 2010 onwards. A network coordinator role was created to unite activities across the three workstreams, to provide scientific and administrative support to the workstream leads, and to manage the steering committee meetings. Additional project support and guidance was also provided by the NCRI Secretariat.

Two to three steering committee meetings were held each year to provide guidance and oversight for the PET Research Network; the steering committee Chair reported in to the NCRI Board, providing accountability to the funders by this route. Cross-workstream communication was centred on monthly teleconferences.

Structure and governance of the NCRI PET Research Initiative



Each workstream's remit was broken down into a number of objectives (Appendix 1), which were set and refined in collaboration with the Steering Committee as the project evolved. Many of the outputs (Appendix 2) had input from more than one workstream, and the Network Coordinator, NCRI Secretariat and Steering Committee Chair also contributed to the delivery of a number of the individual projects. External expertise was drawn upon through the setup of a number of groups and panels (Appendix 3), making this a truly collaborative enterprise.

This paper has therefore been structured in a way that reflects the collective achievements of the Initiative across several key themes. It also offers reflection on what research funders, PET researchers and NHS research delivery structures can take away from this experience, in terms of resources available, lessons learned, and areas of ongoing need.

3. Outputs and achievements

Sourcing information on PET in research

At the outset when planning objectives for the Workstreams, a fundamental challenge was accessing information on existing PET research infrastructure and activity. This was necessary for establishing the areas of need, and providing a baseline against which progress could be assessed.

In terms of infrastructure, data was gathered through a combination of personal contact with centres and survey data collection. Workstream 1 developed a catalogue of the capabilities of facilities for PET research around the UK, including the type and number of PET scanners, the

availability of cyclotrons for onsite radiotracer production, and contact details for centre leads. Workstream 3 also evaluated aspects of PET infrastructure such as the number and type of hot cells, and created two resources summarising novel radiotracer availability in the UK and funding stream options for PET research. These items are hosted on the PRN website, www.ncri-pet.org.uk and the findings were analysed and reported in a summary paper.[2]

It was essential for future planning to determine not only the extent of PET infrastructure but also the range of existing studies, the opportunities for collaboration and the areas where new projects were desirable. However, the use of technologies such as PET cannot be readily identified within most online trial summaries, as they are often not the primary focus of the research. Online sources of clinical information in cancer such as the UKCRN portfolio database, clinicaltrials.gov website and others are usually categorised by disease or treatment type, and neither the search functionality nor title/summary text tend to give details of the technologies used.

Workstream 3 took on the task of gathering information on current trials in PET, and through a combination of extensive manual searching of online research databases and phone/email contact with individual centres, put together a database of ongoing and recently completed trials. This identified 114 current trials using PET, both commercially and publically funded, across the UK. Of these 76 were phase I/II or pilot studies, and 28 were phase II/III trials (the phase of the remaining ten entries was not known).

The database is hosted on the website and creates a snapshot of PET research in 2010/2011. However, while information on facilities and capabilities changes fairly slowly over time and is amenable to a single analysis with periodic updates, information on current research and trials using PET still lacks a real-time solution. Workstream 3 and the NCRI Secretariat raised this issue with NCRN and the ECMCs in the hope that data capture might be improved and made more accessible via improved search functionality – an issue not just for PET, but for technologies in general.

In response to the PRN raising this issue, there have been stepwise improvements in data capture, for example ECMCs are now requesting data in their annual reporting on whether trials have an imaging substudy or include imaging biomarkers. However, larger publicly accessible databases such as the UKCRN portfolio have many competing demands placed upon them, and have not yet been able to accommodate this kind of change. As a pragmatic step, Workstream 3 produced a guide on how to retrieve information on PET trials most efficiently from the multiplicity of online sources, so that researchers can perform more focused internet searches.

Establishing the NCRI PET Trials Network and Core Lab

Clinical trials involving PET face specific technical and logistical issues associated with standardisation of protocols and the rapid turn-around times necessary for clinical decision making. This is particularly true for multicentre trials where standardisation of all aspects of the procedure is necessary if meaningful and publishable data is to be obtained. The primary purpose of Workstream 1 was to focus on technical areas of PET scanning within research, to enable delivery of high quality multicentre trials using PET in centres across the UK.

An informal network of PET centres that grew out of five multicentre trials coordinated by the PET centre at St Thomas' prior to 2008 was re-badged as the NCRI PET Clinical Trials Network under the management of Workstream 1. Formal accreditation requirements and standards were put in place for sites to join the Trials Network and participate in multicentre trials, and the number of

accredited PET Centres in the UK grew from 14 in 2008 to 32 in 2012, covering a total of 37 scanners. In addition, two mobile scanners have also been accredited in this period. A PET Scanning Methodology Expert Panel was established by Workstream 1 to help with setting standards and to advise on issues such as the use of mobile scanners in research.

The collation of PET scanning data across multiple sites requires harmonised methods to be used for acquisition and analysis at each participating centre, which can be a considerable burden for local teams. With the PET Trial Network now in place, Workstream 1 moved on to set up what is referred to as a 'Core Lab'. In this model, a central team provides a service that delivers independent quality control (QC) and audit of scans from each PET centre participating in a particular trial, central management of image data and assessment of all acquired images to verify adherence to the trial protocol and assess image quality. The Core Lab team acts upon any issues identified and provide expert feedback directly to sites, thus improving overall compliance to trial protocols.

The NCRI PET Core Lab at St Thomas' Hospital has managed the PET QA for eight multicentre PET trials since its inception in 2008, one of which has now completed patient recruitment. In addition the Core Lab is providing the PET QA for a further eight trials due to open in late 2012/early 2013 and three trials that are in the process of setup. Workstream 1 has also helped several overseas centres to set up Core Labs for the UK-led RATHL trial, allowing large international studies to be performed using the same level of standardisation.

Both the NCRI PET Trials Network and Core Lab have received a further three years of funding from NCRI Partners (CR-UK, DH, MRC, Wales and Scotland) for 2012–2015, during which time they are moving towards a model where costs are covered by individual research grants. Details on how to access Core Lab services, as well as a range of documents to underpin the function of the PET Trials Network and Core Lab, are available on the PRN website. The website as a whole will transfer to the NCRI PET Core Lab team at St Thomas' for ongoing management, and be adapted to suit the purposes of the Core Lab and Network.

Cost as a barrier to late-phase PET research

Workstream 2 undertook a user survey to identify factors that influence the use of PET in phase III oncology trials in the UK, and what barriers are perceived.[3] Despite 81% of the 116 respondents considering that PET research would be beneficial, only 31% were satisfied with the availability of PET for use in late-phase research. Three-quarters of respondents agreed that obtaining funding for excess treatment costs (ETCs) in oncology is difficult and constitutes a barrier to PET research.

Under the steering committee's advice, Workstream 2 focused its attention on ways to smooth the process of accessing NHS funding for late phase trials. A series of meetings was held with specialist commissioners, to unpick the detail of the processes and communication channels needed to make this work. This was supplemented by a survey to explore the experiences and perceptions of NHS R&D Managers when implementing DH guidance on excess treatment costs.

In this survey, 47 responses were received from Trusts throughout England, Scotland and Wales; the degree of knowledge amongst managers was variable, with University Teaching Trusts being the most likely to have both processes for negotiating ETCs with commissioners and a readily identifiable budget. Only 55% of R&D Managers felt that they routinely received sufficient notice of studies that would incur ETCs, with most approaches from researchers made after the study

had been set up rather than early in development of the protocol. Low levels of awareness and lack of explicit procedures were found to be key issues. The survey findings were submitted as evidence to the Academy of Medical Sciences' 2010 regulation and governance review.

At the time this work was undertaken, the DH guidance in place was the 2005 ARCO document.[4] Following discussions with DH about the survey outcomes, it became clear that ARCO was due to be replaced, culminating in the publication of the ACoRD guidance[5] that will be in effect from October 2012. As the principles of cost attribution would remain the same, it was seen as more pragmatic to seek ways to support the research community than to focus on trying to modify central processes at that time, particularly as the wider government plans for NHS changes were still under consultation. The mainstay of interaction was therefore to advise investigators on undertaking cost attribution and promoting earlier interaction with local R&D departments and research networks. A guidance flowchart was produced, to help researchers determine which scans fall under which cost attribution categories under the ARCO guidance, and this has been promoted at educational workshops as well as on the PRN website.

When recently contacted, most investigators of several ongoing phase III PET trials reported that they had managed to resolve any ETC issues that had arisen though it is not known how many other studies, and study sites, have fallen by the wayside. With commissioning processes currently changing across England, it is not clear who will keep a watch on how research that incurs substantial ETCs will fare within the new system. The challenges of implementation remain, and in the absence of a central imaging group tasked with focusing on this, it is likely to fall to PET researchers themselves to flag problem areas.

Strategic considerations for PET in late-phase trials

Given the funding challenges of PET research and the limited capacity of scanners and staff to undertake research as well as clinical scans, Workstream 2 undertook two projects to explore ways in which resources could be used more strategically to further research.

The first was a Delphi study to prioritise phase III research questions on the clinical application of PET in oncology, such that investments could be directed towards areas of greatest need; this has recently been submitted for publication. This included consideration of the potential to change health outcomes, potential to change health care costs and the burden of illness imposed by the condition. Ten priority questions were identified as reported in the full paper, which was submitted for publication in 2012 and will be put forward to the CSGs for consideration once published. The top three priorities were:

1. Does the addition of ^{18}FDG PET-CT to the *preoperative staging of oesophageal cancer* improve clinical effectiveness and/or cost-effectiveness as compared to conventional staging methods?
2. In patients with *high grade non-Hodgkin's lymphoma*, does the addition of ^{18}FDG PET-CT to the evaluation of *treatment response on completion of treatment* improve clinical effectiveness and/or cost-effectiveness as compared to conventional methods of assessing response?
3. In patients with *diffuse large B-cell non-Hodgkin's lymphoma*, does the addition of ^{18}FDG PET-CT to the assessment of *treatment response at an early stage of treatment* improve clinical effectiveness and/or cost-effectiveness as compared to the addition of ^{18}FDG PET-CT to the assessment of treatment response on completion of therapy?

The second piece of work was intended to demonstrate the potential for PET to be used in patient selection, and how this could have economic advantages in certain situations. For example, in a treatment trial, using PET as a staging tool to determine patient eligibility incurs a cost and means screening more patients to reach target recruitment levels – but this may be offset by costs saved on treatment and follow-up, with a smaller number of patients needing to be included if the improved staging information increases the statistical power. Some exploratory modelling work was undertaken by Workstream 2 in this area but was not able to be completed within the timeframe of the PRN.

Collaborative working to support and develop PET clinical trials

Having a group such as the PRN with a remit to promote the use of PET in research gave a focal point for people to make contact when seeking advice. For instance, Workstream 2 was approached to advise on the brief for work commissioned by NICE on PET-CT. They also provided guidance to chief investigators on a number of late-phase trials during their development phase, of which three are now funded and in progress (CONVERT, FOxTROT, PET-PANC). Members of Workstreams 2 and 3 attended Brain CSG (Imaging Sub-Group), Gynaecological CSG and Breast meetings to explain the PRN's work, the QA service offered via the core lab, and the ways in which PET can be incorporated into trials.

To expand the capacity to provide such advice, the concept of a PET-CT expert group was proposed by the steering committee and set up by Workstream 2. This group brought together 16 experts with cancer expertise and an interest in ensuring that high quality proposals are put forward to advance the use of PET across all tumour types (Appendix 3). In defining the group's remit, there was a collective interest in providing advice and stimulus for PET-CT research in clinical trials, with a vision for oncologists and PET researchers to work alongside each other.

With the group up and running, a practical challenge was noted: a group comprised of PET experts alone risks its members being seen to have a subordinate role in trial development if they act solely as an advisory service, for example by supporting oncologist-led imaging trials delivered by tumour-specific CSGs. And yet the alternative of creating a standalone structure outside the CSGs that includes both clinical as well as imaging members would create a disconnect from the national trials portfolio.

Accordingly, towards the end of its funding period, Workstream 2 put forward a proposition that PET be given a greater share of voice within the CSG structures, for example by embedding the current group within the Biomarkers and Imaging group or as a separate group in its own right. This request coincided with the CSG strategic review led by NCRN in 2011/2012, and with no decision able to be made while the review was ongoing, the PET-CT group came to an end with the closure of Workstream 2 in late 2011.

The Biomarkers and Imaging CSG (BI CSG) has meanwhile been looking at ways to increase the share of voice for imaging, which is currently under-represented in its membership. The BI CSG has existed in its present form only since April 2010, and Prof Gilbert joined the group at this time to provide a connection with the PET Research Initiative. In the BI CSG's 2012 progress review, the panel was supportive of taking forward a proposal for an imaging subgroup (including but not limited to PET) with a larger number of members than usual due to the multidisciplinary nature of imaging and the number of modalities to be covered. If this is successful, it is likely that some of the former members of the PET-CT expert group will apply for a position on this subgroup to continue their original goals of stimulating and advising on PET-CT research.

An international approach to collaborative working was also explored by Workstream 3, who opened a dialogue with the American College of Radiology Imaging Network (ACRIN). Based in the USA, ACRIN was set up in 1999 and receives substantial core funding from the NCI Cancer Imaging Program. There are 100+ sites worldwide that take part in ACRIN studies, and if UK sites could overcome the logistical and regulatory processes required to take part, they would also benefit from funding provided by ACRIN to cover recruitment and scan costs; to date this has not been achieved but it remains a desirable channel to explore.

Defining the needs for early phase PET research

One task of Workstream 3 was to determine capabilities, aspirations and research needs that might be supported by the PRN. A survey of ECMCs was conducted, and followed up with site visits, teleconferences and a workshop. This showed that most centres had access to static PET/CT scanners to carry out early phase PET research, though the range of makes and models underlined the need for strong QA/QC processes.

At the time of the survey in 2009, 10/19 ECMCs either had cyclotrons or were in the process of installing them, and 9/19 had or were setting up GMP radiochemistry facilities. Most centres performed 1–10 research scans per week, compared with >30 clinical scans.

This scoping work confirmed a strong interest in PET within the ECMCs, and respondents saw a role for the PRN in facilitating collaboration and sharing between UK centres on common themes such as protocol design, ethical approvals, regulatory issues, access to PET radiotracers, and training. As a result of this survey, the PRN and ECMC Imaging Network worked more closely, for example by collaborating on the ECMC vascular imaging consensus conference in 2010.

Improving access to non-FDG radiotracers

In the ECMC survey, 14/19 centres were keen to work with non-FDG radiotracers, and 16 were interested in participating in multicentre trials to validate or to help understand the clinical utility of novel tracers. However, one of the difficulties in early phase PET research has been gaining access to experimental radiotracers. Unless investigators have a local academic supply available to them, they are reliant on commercial radiotracer manufacturers for supply, and companies need to sell a certain volume to make production financially viable. The small sample sizes in early phase work often make the price per dose unaffordable.

A series of workshops was held to bring academic researchers, industry researchers and radiotracer manufacturers together to find a way forward. This began with a workshop in 2010 to open dialogue with commercial and academic manufacturers of radiotracers, and to seek ways to reduce or manage the costs of access. Suggestions put forward included the formation of researcher-led purchasing consortia to negotiate bulk purchase at a lower rate, the upfront purchase of a number of doses by a research funder with a subsequent highlight call, and investment at academic sites to allow more frequent production of experimental tracers in larger quantities.[6] In 2011, a further workshop focused on tumour hypoxia and cell proliferation as areas with potential for collaboration; the discussion in each area led to further work which is outlined below.

FLT, a novel tracer that can be used to image cell proliferation, was the radiotracer most often listed by ECMCs as desirable to access, and this provided a focus to look at real world examples of how multicentre studies with novel tracers can be delivered. An FLT sub-study of the POETIC trial was designed by Workstream 3 and funded by Cancer Research UK, whereby patients with

oestrogen receptor-positive breast cancer will have an FLT-PET scan before and after 2 weeks of aromatase inhibitor treatment. The design allows FLT-PET to be compared against Ki67, the current gold standard biomarker for proliferation, and is currently in setup. Workstream 3 was also successful at negotiating a joint purchasing arrangement with one manufacturer (Siemens) that allows researchers to group together and commit to >30 FLT doses at a much reduced cost, and at the time of workstream closure was pursuing models of funding consortia or upfront bulk purchase of radiotracer by funders.

For hypoxia tracers, discussion at the collaboration workshop and in the ECMC survey feedback showed interest in this area but where some centres had selected a tracer of interest, others were unsure which to use and how this choice would fit in with work being done elsewhere in the UK. (This reinforces the need for a better central register of ongoing PET research, particularly for early phase work where studies may be single centre and not publicised externally.) The hypoxia tracers under investigation in the UK include ^{18}F-FMISO, ^{64}Cu-ATSM, ^{18}F-AZA, ^{18}F-HX4, each of which has different strengths and weaknesses, and a further meeting was convened in late 2011 to determine how their development can be strategically taken forward. The general conclusion was that limited data on the individual tracers and a lack of head-to-head comparison studies between hypoxia tracers makes it too early to recommend a single 'lead candidate', but that a review of tracers would be produced as a first step. Participants also had the vision of putting together a loose consortium of centres with access to hypoxia tracers to attempt a comparison study in a single tumour type, with each centre leading on each particular tracer.

Smoother navigation of the regulatory environment

The survey and workshops held with ECMCs showed that the complexity of regulation and the burden of paperwork associated with the use of PET in clinical trials are considered to be a barrier to research. A meeting was held in September 2010 to look at regulations in the UK with reference to PET imaging in academia and industry, organised jointly by Workstream 3, the MHRA and the MRC. It was agreed that a mechanism was needed to increase dialogue between the MHRA and PET researchers and an MHRA PET Expert Panel was set up accordingly, with representation from members of the PET community with expertise in areas such as GMP, QA, or industry studies, and from key members of the MHRA. Dr Franklin Aigbirhio (PET Research Initiative Steering Committee member) became the first Chairperson in February 2011, working closely with Dr Elaine Godfrey as the principal MHRA lead.

The panel's main roles are to provide advice and guidance to researchers, and to highlight problem areas back to the MHRA on behalf of the PET community, thus acting as a facilitator. Workstream 3 led a publication summarising information on PET regulations for academic researchers,[7] and educational resources produced by the MHRA PET Expert Group are hosted on the MRC website (http://www.mrc.ac.uk/Ourresearch/Ethicsresearchguidance/MHRA-PET/index.htm), including case studies exemplifying how to deal with different situations, a decision tree to determine whether an IMP dossier and manufacturer's license are needed for a particular tracer, and FAQs. Following the completion of NCRI funding for the PET Research Initiative, the group is receiving funding and administrative support from the MRC to continue its work and to encompass a cross-disease remit.

As part of its work to reduce the burden of regulatory processes in PET research, Workstream 3 also encouraged the sharing of IMP dossiers between groups, with contacts provided on the PRN website to individual researchers and to the European Association of Nuclear Medicine radiopharmacy committee.

Patient perspectives on PET

Little was known about patients' views on taking part in trials involving PET. A focus group that included former patients who had undergone PET scans, or carers thereof, was run by Workstream 2 in 2010. When explained clearly, the inclusion of PET within a trial was generally seen as positive, but patients were concerned that the information around the radiation risks of PET scans is often poorly described, and that paper-based information should be supplemented with clear, detailed information in more engaging formats.

In response to this need, a video was produced created to show the patient journey through a PET-CT scan within a research setting. This can be accessed on YouTube (http://bit.ly/ncri-pet-video) and is in the process of being publicised through the NCRI Consumer Liaison Group and other channels.

4. Summary

To ensure that the progress made by the NCRI PET Research Initiative is carried forward, this paper has summarised the opportunities that have been identified or created as a result of this work, as well as documenting ongoing challenges. The PET Research Initiative took on a number of broad and complicated topic areas during its three years of funded activity, and its legacy includes the ongoing work of the NCRI PET Core Lab and network of accredited sites, an expert group to help researchers navigate MHRA processes, and an extensive portfolio of publications and resources.

The PET Research Initiative also fulfilled the important functions of promoting the research use of PET, providing centralised expertise, and building relationships across sectors and countries (notably Europe and the USA). The NCRI PET Core Lab at St Thomas' provides an ongoing entry point for those seeking help on technical matters, which is a significant advance since before the PET Research Initiative. Contact points for policy makers, funders or individual research groups to gain broader advice on the use of PET in research and raise PET-specific research issues now revert to groups with a cross-modality imaging remit, such as the Biomarkers and Imaging CSG and the ECMC Imaging Network Group. NCRI will keep a watching brief on these arrangements, in the context of its current exploratory work that is looking at the challenges of coordination across all modalities in cancer imaging.

References

1. National Cancer Research Institute. A Framework for PET Research in the UK: Report of the NCRI PET Strategic Planning Group, 2007:http://www.ncri.org.uk/includes/Publications/reports/petreport_low.pdf.
2. Fleming IN, Regel SJ, Pike LC, Marsden PK, Gilbert FJ. Positron emission tomography oncology research in the UK: a comparison with USA and Europe. *Nucl Med Commun* 2012;33(4):341-8.
3. Rojas-Anaya H, Skogen K, Miles KA. Stakeholder perspectives on the use of positron emission tomography in phase III oncology trials in the UK. *Nucl Med Commun* 2012;33(6):626-32.
4. Department of Health. Attributing revenue costs of externally-funded non-commercial research in the NHS (ARCO), 2005:http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_4125282.pdf.
5. Department of Health. Attributing the cost of health and social care Research & Development (AcoRD), 2012:http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_133882.
6. Gilbert FJ, Fleming IN, Marsden PK. Beyond 18F-fluorodeoxyglucose: making the next generation of PET radiotracers available for oncology research in the UK. *Nucl Med Commun* 2011;32(1):1-3.
7. Fleming IN, Whelan M, Baxendale R, Gilbert FJ, Matthews PP, Aigbirhio FI. Positron emission tomography radiopharmaceutical studies in humans: a guide to regulations for academic researchers. *Nucl Med Commun* 2012;33(9):899-906.

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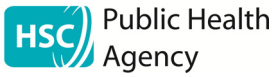

Appendix 1. PET Research Network workstream aims

Trials network and technology workstream

1. Establish a network for performing high quality clinical trials using PET
2. Determine technology development and research needs

Late phase workstream

1. Identify areas of intervention to increase the research use of PET in phase III oncology clinical trials
2. Streamline the funding of PET research in the NHS, and perform a strategic analysis of the value of PET
3. Disseminate information and advice on the potential roles and protocols for PET
4. Provide information and stimulate new research on non-randomised controlled trials methods for PET evaluation
5. Conduct research into the patient perspective of PET

Early phase workstream

1. Stimulate early phase PET research
2. Work with MHRA and MRC to try to reduce regulatory burden
3. Increase availability of radiotracers

Appendix 2. PET Research Network informational and educational outputs

Information resources

Cross-workstream

- www.ncri-pet.org.uk website, which hosts or links to many of the other outputs listed here

Workstream 1

- NCRI PET Site Accreditation Standards
- NCRI PET Core Lab QC Procedures
- NCRI PET Core Lab Electronic Transfer Procedures: FTP Server
- NCRI PET Core Lab Electronic Transfer Procedures: NHS N3 Network
- Spreadsheet of UK PET Facilities
- Statement on the Use of Mobile PET/CT Scanners in Multicentre Trials

Workstream 2

- Scan cost guidance flowchart
- Video: PET-CT scans in cancer research: Information for patients

Workstream 3

- Spreadsheet of UK Radiotracer Availability
- Spreadsheet of Funding Opportunities
- How to Find UK PET Trials: Guidance for Researchers
- Spreadsheet of UK PET Trials

Publications

Cross-workstream

- Fleming IN, Regel SJ, Pike LC, et al. Positron emission tomography oncology research in the UK: a comparison with USA and Europe. *Nucl Med Commun* 2012;33:341–8
- Aboagye EO, Gilbert FJ, Fleming IN, et al. Recommendations for measurement of tumour vascularity with positron emission tomography in early phase clinical trials. *Eur Radiol* 2012;22:1465–78
- Fleming IN, Gilbert FJ, Miles KA, et al. Opportunities for PET to deliver clinical benefit in cancer: breast cancer as a paradigm. *Cancer Imaging* 2010;10:144–52
- Picture Perfect [feature article on opportunities for PET in UK drug development]. *World Pharmaceutical Frontiers*, Sept 2010, 91–93

Workstream 1

- Somer E, Pike LC, Marsden PK. Recommendations for the use of positron emission tomography and positron emission tomography-CT for radiotherapy planning in research projects. *Br J Radiol* 2012 [epub]

Workstream 2

- Rojas-Anaya H, Skogen K, Miles KA. Stakeholder perspectives on the use of positron emission tomography in phase III oncology trials in the UK. *Nucl Med Commun* 2012;33:626–32
- Rojas-Anaya H, Lord J, Cameron D, et al. Establishing research priorities for the use of Positron Emission Tomography in Oncology in the National Health Service. [In progress, 2012]

Workstream 3

- Gilbert FJ, Fleming IN, Marsden PK. Beyond ^{18}F-fluorodeoxyglucose: making the next generation of PET radiotracers available for oncology research in the UK. *Nucl Med Commun* 2011;32:1–3
- Fleming IN, Gilbert FJ, Blower PJ. Building PET research collaborations. *Nucl Med Commun* 2011;33:1–3
- Fleming IN, Whelan M, Baxendale R, et al. Positron emission tomography radiopharmaceuticals studies in humans: A guide to regulations for academic researchers. Nucl Med Commun 2012;33:899–906
- Chia K, Fleming IN, Blower PJ. Hypoxia imaging with PET: which tracers & why? *Nucl Med Commun* 2012;33:217–22

Abstracts, posters and presentations

Cross-workstream

- Regel SJ. NCRI PET Core Lab – An update. Royal Society of Medicine 15th Annual PET-CT Meeting, 19 Mar 2012, London
- Pike LC, Rojas-Anaya H. NCRI PET Research Network: An update. Royal Society of Medicine 14th Annual PET-CT meeting, 15 Mar 2011, London
- Fleming I, Gilbert FJ, Regel S, Marsden PK, Pike LC. Facilitating Early Phase PET Research in the UK. PET Meeting, Oct 2010, Cambridge

Workstream 1

- Marsden PK. The NCRI PET Research Network. British Nuclear Medicine Society Autumn Meeting, 17–18 Sep 2009, Guildford
- Marsden PK. NCRI PET Clinical Trials Network: Standards for multicentre PET trials. Royal Society of Medicine 13th Annual PET-CT Meeting, 23 Mar 2010, London
- Marsden, PK. The NCRI PET Research Network. CR-UK/EPRSR/MRC/NIHR Cancer Imaging Conference, 24 Mar 2010, Oxford
- Pike LC, Marsden PK. Use of the NHS N3 Network for PET Multicentre Trials. British Nuclear Medicine Society Spring Meeting, 26–28 Apr 2010, Harrogate
- Pike, LC. NCRI PET Clinical Trials Network. British Nuclear Medicine Society Spring Meeting, 9 May 2011, Brighton
- Pike LC, Marsden PK. Update on Mobile PET/CT in Research. PET/CT Governance Board Meeting, 7 Sep 2010, London
- Pike LC. An Overview of the NCRI PET Research Network. RTTQA meeting, 19 Jan 2011, London
- Pike LC. Technical Issues in Clinical Trials: PET/CT Clinical Trials Network. Institute of Nuclear Medicine Physics Seminars, UCL, London
- Pike, LC. The NCRI PET Clinical Trials Network. PET Research Network workshop on Building PET Research Collaborations, 16 May 2011, London
- Pike LC. NCRI PET Clinical Trials Network. Institute of Physics and Engineering in Medicine Special Interest Group (IPEM SIG) meeting, 25 May 2011, London
- Pike LC. Quantitative PET applied to monitoring cancer therapy. KCL PET Physics Seminar, 31 May 2011, London
- Pike LC. Quantitative imaging for the future: Quantitative PET. UK Radiological Congress, 8 Jun 2011, Manchester
- Pike, LC. NCRI PET Core Lab and Clinical Trials Network. Biomarkers and Imaging CSG/PET Research Network workshop: Expanding the Use of PET in Clinical Cancer Research, 30 Sep 2011, London
- Marsden, PK. Supporting PET QA in clinical trials: The NCRI PET Core Lab. CTRad workshop on Biomarkers for Future RT Trials, 23 Apr 2012, Leicester

Workstream 2

- Rojas-Anaya H, Miles KA. Utilisation of PET in late phase clinical trials in oncology: a review of research databases in the UK and abroad. British Nuclear Medicine Society Autumn Meeting, 17–18 Sep 2009, Guildford
- Rojas-Anaya H. Stakeholder perspectives on the use of PET in phase III oncology trials in the UK. British Nuclear Medicine Society Spring Meeting, 9 May 2011, Brighton

Appendix 3. Participants in PET Research Initiative activities

PET Initiative Steering Committee members

Membership at close of initiative:

- Robert Souhami (Chair), Former Chair of NCRI PET Strategic Planning Group
- Eric Aboagye, Imperial College London
- Franklin Aigbirhio, University of Cambridge
- David Ardron, NCRI Consumer Liaison Group
- Jane Cope, NCRI
- Erika Denton, Norfolk and Norwich University Hospital, Norwich
- Myrna Gray, consumer representative
- Otto Hoekstra, University of Amsterdam, Netherlands
- Peter Johnson, Cancer Research UK
- Maria Lioumi, Cancer Research UK
- Paul Matthews, GSK, Hammersmith London
- Herbie Newell, Northern Institute for Cancer Research, Newcastle
- Chris Nutting, Royal Marsden NHS Foundation Trust
- Mike O'Doherty, King's College London
- Matt Seymour, NIHR Cancer Research Network
- Daniel Sullivan, Duke University Medical Centre, USA
- Helen Young, AstraZeneca

Former members:

- Sir Michael Peckham (Chair)
- David Cameron, National Cancer Research Network
- Andrew Farmer, NIHR Health Technology Assessment Commissioning Board
- Roger Wilson, consumer representative

Scanning Methodology Panel members

- Ronald Boellaard, VU Medical Center, Amsterdam, Netherlands
- Kathryn Carson, Royal Victoria Hospital, Belfast
- John Dickson, University College London Hospitals NHS Trust
- Tim Fryer, Addenbrooke's Hospital/University of Cambridge
- William Hallett, Hammersmith Hospital/Imperial College London
- Brian Hutton (CIC representative), University College London Hospitals NHS Trust
- Peter Jarritt, University of Cambridge
- Peter Julyan, University of Manchester
- Paul Kinahan (International representative), University of Washington, Seattle, USA
- Paul Marsden, King's College London
- Julian Matthews, University of Manchester
- Daniel McGowan, Oxford University Hospitals NHS Trust
- Iain Murray, Royal Marsden NHS Trust
- Lucy Pike (ex-officio member), King's College London
- Bal Sanghera, Mount Vernon Hospital
- Kris Thielemans, King's College London
- Federico Turkheimer (CIC representative), Imperial College London
- Wendy Waddington (IPEM rep), University College London
- Andy Welch, University of Aberdeen

PET-CT Expert Group members

- Sally Barrington, St Thomas' Hospital, London
- Tara Barwick, Imperial College Healthcare NHS Trust, London
- Jamshed Bomanji, University College Hospital, London
- Kevin Bradley, John Radcliffe Hospital, Oxford
- Sue Chua, Royal Marsden NHS Foundation Trust, Sutton
- Gary Cook, Royal Marsden NHS Foundation Trust, Sutton
- Fiona Gilbert, University of Aberdeen, Aberdeen
- Fergus Gleeson, Churchill Hospital NHS Trust, Oxford
- Peter Guest, Queen Elizabeth Hospital, Birmingham
- Sharon Hain, University College Hospitals, London
- Simon Hughes, Royal Victoria Hospital, Belfast
- Irfan Kayani, University College Hospital, London
- Russell Moule, Mount Vernon Cancer Centre, Northwood
- Mike O'Doherty, St Thomas' Hospital, London
- Andrew Scarsbrook, St James' University Hospital, Leeds
- Wai Lup Wong, Mount Vernon, Northwood

MHRA PET Expert Panel members

PET researcher representatives:

- Dr Franklin Aigbirhio (Chair), Cambridge
- Prof Eric Aboagye, Imperial College, London
- Dr Colin Archer, GE
- Prof Norbert Avril, Bart's
- Dr Jim Ballinger, KCL/St Thomas' Hospital, London
- Dr Ron Barrack, Erigal
- Dr Roy Baxendale, GSK
- Dr István Boros, Cambridge
- Dr Kevin Bradley, Oxford
- Prof David Brooks, Imperial
- Prof John Clark, Edinburgh
- Dr Gary Cook, KCL / St Thomas' Hospital, London
- Dr Bev Ellis, Manchester
- Prof Tony Gee, KCL/St Thomas' Hospital, London
- Dr Ralph Harris, IBA Molecular UK Ltd
- Dr Craig Hughes, PETNET Solutions
- Dr Sajinder Luthra, GE
- Dr Chris Marshall, Cardiff
- Prof Paul Matthews, GSK
- Dr Adam McMahon, Manchester
- Prof David Newby, Edinburgh
- Dr Hanna Nicholas, Bart's
- Prof Mike O'Doherty, KCL/St Thomas' Hospital, London
- Dr Jan Passchier, Imanova
- Mr Bimal Patel, GE
- Dr Lutz Schweiger, Aberdeen
- Mr Shankar Seetharaman, Pharmanswers
- Dr Dmitri Soloviev, Cambridge
- Dr Pauline Squibb, Imanova
- Dr Joanna Jenkinson, MRC

MHRA representatives:

- Dr Elaine Godfrey, Pharmaceutical Assessor, Clinical Trials Unit
- Mr Ian Thrussell, GMP Inspector Inspection, Enforcement & Standards
- Mr Martin O'Kane Pharmaceutical Assessor, Clinical Trials Unit
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