



Guidelines for the use of PET-CT in children, Second edition

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Introduction

This document has been updated by Dr Rosemary Allan and Dr Lorenzo Biassoni in October 2013, with the assistance of the Intercollegiate Standing Committee on Nuclear Medicine and the Royal College of Radiologists' Radionuclide Radiology Sub-Committee. In particular we would like to acknowledge and thank Mr Steve Ebdon-Jackson, Dr Andrew Scarsbrook, Dr Kevin Bradley and Dr Clare

Beadsmoore for their contributions. The previous edition, *Guidelines for the use of PET-CT in Children*, published in 2008 has now been withdrawn.

This is a companion document to *Evidence Based Indications for PET-CT in the United Kingdom*, which is updated annually by the Intercollegiate Standing Committee on Nuclear Medicine.

Background

The use of positron emission tomography co-registered with computed tomography (PET-CT) in adult oncology, neurology and cardiology is well established. The most common tracer used in clinical PET-CT is ¹⁸Fluorine fluorodeoxyglucose (FDG). However, experience with PET-CT in the field of paediatric imaging is limited.

Data can be extrapolated from adult studies for conditions which are found in adult and paediatric populations alike such as lymphoma, sarcoma and temporal lobe epilepsy. It would seem reasonable to use PET-CT for such indications where sufficient evidence exists to justify the use of PET-CT in adult patients. It is unlikely, however, that robust data will emerge for many conditions that are limited to childhood which are often rare diseases. Therefore, it is not possible to apply the same selection criteria for adult and paediatric imaging. In rare conditions, the routine use of PET-CT cannot be recommended but PET-CT may be able to assist in individual management by resolving clinical questions that are difficult to answer using anatomical imaging alone.

The optimal use of PET-CT in children relies on tailoring the scan acquisition and the scan environment to the needs of the child, with proper

attention to safety and appropriate risk management. As with any imaging modality, familiarity with the normal variation and appearances of pathological conditions experienced in childhood is important when interpreting scans which should be undertaken by individuals who are regularly reporting paediatric PET-CT studies.

In the face of this limited published data and experience, this report was compiled by individuals with experience in scanning children with PET-CT in the UK and paediatricians involved in clinical management of the type of conditions for which PET-CT is likely to be used. It represents a consensus reached between the authors of what is desirable 'best' practice. The guidance has been endorsed by the British Nuclear Medicine Society, The Royal College of Radiologists, Royal College of Physicians, Royal College of Surgeons and the British Society of Paediatric Radiology.

Issues specifically relating to children are discussed in this document. It is assumed that guidance relating to 'best practice' in scanning adults with PET-CT will also be applied in children.

Indications for PET-CT in children with known/suspected malignancy

Small studies have demonstrated many paediatric tumours to be FDG-avid; to date, no paediatric tumour has been identified as 'non-FDG-avid'.

With the exception of Hodgkin's lymphoma (where a clinical study involving the use of FDG-PET-CT is under way) no clear guidelines exist; however, data suggests FDG-PET-CT can be used to enhance the care of children with cancer.

The overall survival rate in paediatric malignancy is approximately 75%. For some cancers such as Wilms' tumour, this will be above 90%. However, for a significant number of patients (for example, those with stage 4 neuroblastoma), there remains a less than 50% chance of survival. When planning a child's care, it is important to consider the long-term effects of treatment that many children live with for the rest of their lives.

FDG-PET-CT is now used routinely in the management of Hodgkin's lymphoma and can significantly alter management. Much data have shown it has improved sensitivity and specificity when compared with conventional imaging (CT/MRI). When performed at staging and post-therapy, FDG-PET-CT allows a more accurate assessment of response to treatment. Current data demonstrate that PET-CT is a strong predictor of prognosis after initial chemotherapy and progression-free survival. There has been concern about late second malignancies in children who have received radiotherapy for Hodgkin's lymphoma and FDG-PET-CT may allow reduced treatment burden in those who have responded well to chemotherapy. Conversely, in poor responders, early treatment intensification may be beneficial.

Therapy modification based on FDG-PET-CT may be possible in other tumour types as more data are acquired. Currently PET-CT can be helpful in cases where additional information may assist in difficult clinical decisions; for example, giving radiotherapy to a growing child, planning minimally invasive surgery, withholding further cardiotoxic chemotherapy. To this end, PET-CT can be considered in many paediatric malignant conditions and the advice of physicians experienced in paediatric PET-CT may be valuable.

When a child or young person is diagnosed with an adult-type tumour such as malignant melanoma, relevant existing adult guidelines should apply. Magnetic resonance techniques are further developed in paediatric brain tumours and therefore the main functional imaging techniques employed for this tumour group. PET-CT with FDG and other tracers including ¹¹C-methionine may prove to have an additional role.

Other PET-CT tracers are becoming increasingly used in paediatric oncology, such as Ga-⁶⁸-DOTATATE in neuroblastoma (with the potential ability to administer Lu-177-DOTATATE as a therapeutic agent if there is uptake), F-¹⁸-DOPA in neuroblastic tumours and brain tumours, F-¹⁸-choline in brain tumours. Although these new tracers are still in the evaluation phase and no recommendation can be given based on the current experience, it is worth noting that they are being used by a number of groups.

Diagnosis/staging/restaging

The ability of PET-CT to answer clinical questions during a patient's treatment course may be greatly enhanced by the presence of a scan at the time of diagnosis, before treatment begins. However, it is clearly not appropriate for all children to have a pre-treatment scan.

Pre-treatment PET-CT scans should be considered in any child with:

- Hodgkin's lymphoma (on or off trial)
- Non-Hodgkin's lymphoma with unusual primary or metastatic sites
- Extra-medullary leukaemia
- Malignancy with unknown primary
- Soft tissue sarcoma – for staging
- Bony sarcoma with extra-pulmonary metastatic disease
- MIBG-negative neuroblastoma
- Opsoclonus myoclonus syndrome with no identified primary

- Germ cell tumours (especially when tumour marker negative, with retroperitoneal lymphadenopathy or mediastinal primary)
- Langerhans' cell histiocytosis (multisystem)
- Congenital hyperinsulinism of infancy (CHI)
- Relapsed disease (where data suggests the primary is FDG-avid as above)
 - Who may undergo radiotherapy
 - Where accurate biopsy is essential (such as heterogeneous tumours where treatment may be determined by highest grade of tumour; for example, ganglioneuroma vs ganglioblastoma, necrotic Wilms' tumour, brain tumours)
- Definite or equivocal stage 4 disease on other imaging, whose treatment may include mutilating or life-threatening surgery such as parameningeal rhabdomyosarcoma or hepatoblastoma requiring liver transplant.

Treatment-related scans

Before local therapy, FDG-PET scans should be considered in:

- Children who are candidates for radiotherapy (for conditions known to be FDG-avid)
- Hepatoblastoma requiring liver transplant
- Wilms' tumour considered for bilateral renal surgery (to assist nephron sparing)
- Stage 3 neuroblastoma after initial chemotherapy (if further chemotherapy is being considered to further reduce the tumour)
- Mutilating sarcoma surgery

- Limited stage lymphoma on conventional imaging to confirm the appropriateness of local treatment options.

Treatment response scans should be considered in any child with:

- Hodgkin's lymphoma (as per Euro-NET protocol, for children on and off trial)
- Non-Hodgkin's lymphoma with poor response on conventional imaging
- MIBG-negative neuroblastoma
- Langerhans' cell histiocytosis
- Soft tissue sarcoma.

Residual mass assessment may be appropriate in:

- Hodgkin's lymphoma
- Some soft tissue sarcomas
- Neuroblastoma.

Follow-up

Scans for follow-up are only advisable if prompt further life-saving treatment is planned in the event of relapse/progression.

Relapse

Scans may be considered in any child with confirmed or suspected relapse of above conditions.

Indications for PET-CT in children in neurology

In the investigation of epilepsy, FDG PET-CT scanning should be considered if the child has focal epilepsy that is potentially amenable to surgical intervention where MRI is negative or discordant with other investigations. Additional supportive evidence from FDG PET-CT may then justify more invasive procedures such as invasive electroencephalogram (EEG) monitoring to localise seizures with sufficient certainty to warrant surgical resection. In practice where the clinical, EEG and structural data are all concordant, FDG PET-CT is likely to be unnecessary.

Judicious use of PET-CT scans may be considered in the management of patients with neurofibromatosis 1 with symptoms suggestive of malignant transformation of a plexiform or subcutaneous neurofibroma. These include one or more of the following: persistent pain, rapid increase in size, change in texture or new or unexplained neurological deficit related to the lesion. Currently, there is no indication to use PET-CT to screen for malignant change in asymptomatic plexiform neurofibromas.

Indications for PET-CT in children with cardiac diseases

Rubidium-82 PET-CT may be useful to image myocardial perfusion and to assess the functional significance of anatomical abnormalities in coronary arteries or coronary flow reserve in selected cases including:

- Kawasaki disease with or without anatomical evidence of coronary artery involvement
- Children who have undergone coronary artery surgery for congenital malformations such as arterial switch operations, pulmonary valve autograft procedures or reimplantation of anomalous coronary arteries
- Congenital coronary artery anomalies with aberrant coronary artery anatomy or course of the coronary artery where impairment of perfusion is suspected or there is potential for impaired perfusion
- Post-cardiac transplantation where coronary artery disease continues to be a major contributor to graft failure.

PET-CT assessment of perfusion and glucose metabolism may be useful for cardiological risk assessment in patients with Duchenne's or Becker's muscular dystrophy undergoing spinal surgery.

Scan protocols in children

Scan planning and preparation

As soon as a request has been received and the indication for the scan is agreed, the procedure should be discussed with parents or carers verbally. A written explanation of the scan preparation and procedure should also be provided. Where a child is likely to require sedation or anaesthesia, the admitting paediatric physician and/or paediatric anaesthetist should be contacted. Further information may be requested at this stage including recent blood tests or imaging results.

Sedation is a continuum and in accordance with American College of Radiology Practice Guidelines and Scottish Intercollegiate Guidelines all paediatric patients requiring sedation for scanning, which includes patients receiving benzodiazepines orally should be monitored. This also includes children who are given diazepam for suppression of FDG uptake into brown fat. Some groups advise the use of premedication with propranolol to suppress FDG uptake in brown fat. In the Department of Nuclear Medicine of the University of Leipzig, Germany, oral propranolol (1 mg/kg, maximum 40 mg) 60–90 minutes before administration of FDG is standard premedication for all patients between the age of 15 and 30 years without contraindications for propranolol. Propranolol is also given routinely to children of ten years and above with lymphoma.

Consequently, scans involving with any form of sedation/anaesthesia should be performed at centres with facilities, personnel and equipment immediately available to manage paediatric emergency situations. It is often preferable to give a short duration anaesthetic than to administer sedation, as sedation can be unpredictable in children. In centres performing scans using anaesthesia, the scanning room should have access to piped gases. There should be adequate recovery facilities within the scanning centre and inpatient beds close by for children to be admitted into and return to. Following general anaesthetic, it is recommended that paediatric patients suitable for day-case anaesthesia should be admitted to a paediatric

ward for a minimum of three hours before being discharged home to ensure they have tolerated fluids or food without nausea or vomiting and are fully recovered from the general anaesthetic.

Sedation or anaesthesia should be administered to cover the period of the scan. Unless there are exceptional circumstances, children can be satisfactorily managed during the uptake period without the need for sedation or anaesthesia. Where sedation is administered, formulations including glucose should be avoided.

Scans in children who do not require sedation may be performed in hospitals without direct access to paediatric services. As a guide, it is recommended that children younger than 13 years should be imaged at static sites with access to full paediatric support services. This is based on requirements for paediatric resuscitation equipment in this age group but individual assessment is required on a case-by-case basis. Children older than 13 with special requirements, including children with developmental problems or behavioural difficulties and children with severe systemic illness, will also need to be imaged at a centre with direct access to paediatric services. If intravenous contrast is to be used during the scanning session as part of a separate contrast-enhanced CT examination, the examination should be done in centres with access to full paediatric support services due to the risk of contrast reaction.

Children aged between eight and 12 years old not requiring general anaesthetic or sedation or intravenous (IV) contrast could be imaged at sites without paediatric provision at the discretion of the referring paediatrician. In these circumstances, a suitably qualified person from the paediatric referring team trained in advanced paediatric life support (APLS) should be available within the vicinity where the scan is being performed. This responsibility could be transferred to a member of a local paediatric team by the referring paediatrician if desired. Full paediatric resuscitation equipment should be immediately available within the PET-CT scanning area and should include a paediatric

defibrillator, intubation equipment and resuscitation drugs. The individual trained in APLS and the resuscitation team should be aware of the exact location of the PET-CT scan department within the hospital.

If imaging is carried out in sites without paediatric services, staff should still be experienced in the care and imaging of children, including paediatric cannulation. The difficulties of paediatric imaging in environments not designed for imaging children should not be underestimated. A scan of good diagnostic quality relies on a co-operative child, which is more likely in a child-friendly environment where staff are imaging children on a regular basis. Advice and early involvement of a play specialist may be helpful. A sympathetic child-centred approach may render sedation unnecessary. Timing of scanning during a baby or infant's usual nap time during the day (especially after feeding the infant) may also help to avoid sedation.

Imaging should be performed in paediatric sessions separate from those used by adults. There should be a separate area where girls can be sensitively questioned about the possibility of pregnancy. All staff involved in the care of children should have criminal records bureau (CRB) checks and safeguarding children training appropriate for their level of involvement.

Written protocols should be in place for imaging children and the PET-CT parts of the examination should be optimised to reduce the radiation dose, including reducing the administered dose of radiotracer according to weight and the tube current according to the patient size and imaging requirements. Further guidance on dose reduction of the CT component can be found on the Image Gently® website (<http://www.pedrad.org/associations/5364/ig/>).

Independent of the site where the scan is performed, the scan should be reported by individuals skilled in reporting paediatric scans of the type requested (oncology, neurology or cardiology), with full knowledge of the clinical question being asked and of the result of the other previous investigations. Further guidance on training requirements are available in a document published by The Royal College of Radiologists entitled *Recent and future PET-CT developments: guidance on legislative and*

training aspects (Available at [http://rcr.ac.uk/docs/radiology/pdf/BFCR\(13\)3_PE_TCT.pdf](http://rcr.ac.uk/docs/radiology/pdf/BFCR(13)3_PE_TCT.pdf)).

Oncology studies

Prior to attendance, information relating to chemotherapy, radiotherapy and surgery should be obtained to ensure optimal timing of the visit to the PET-CT facility. Children should fast for four to six hours before being scanned. Children undergoing general anaesthetic or sedation should remain nil by mouth for six hours following an intake of solids, cow's milk or formula milk feeds; four hours following breast milk and two hours following clear fluids (water or any clear fluid that you can read print through). Opaque juices, sparkling water, soup, sucked (or swallowed) sweets and gum are regarded as solids.

Consideration should be given to administration of intravenous hydration during the uptake period with 0.9% normal saline *not* dextrose infusion. Children who are not having any anaesthesia or sedation should drink water to maintain good hydration and reduce the radiation dose to the bladder. Infants not having anaesthesia or sedation should be injected as close to the next milk feed as possible. A feed may be given from 30 minutes after the tracer injection. Blood glucose should be measured before the FDG injection and the doctor responsible for scan supervision informed if the level is >7 mM/l in a non-diabetic patient or >10 mM/l in a diabetic child. It is up to the supervising doctor to decide whether it is appropriate to continue with the tracer injection. Insulin should never be administered to reduce the glucose level as this can result in a non-diagnostic scan due to redistribution of tracer into skeletal and cardiac muscle.

The child should also be weighed so that a standardised uptake value (SUV) can be measured over a region of interest if required. Patients should be kept warm during the uptake period which can last one to two hours (or longer for soft tissue tumours). Oral diazepam may be required to reduce uptake in brown fat and if so this needs to be administered approximately one hour before the tracer injection. The use of music, DVDs, reading or electronic games may help. Electronic games should be avoided though if the disease involves or is likely to involve the

upper limbs. Most studies will involve scanning from below orbits to below the pelvis but in some tumour types total-body scans may be appropriate such as Ewing's sarcoma, MIBG-negative neuroblastoma or lymphoma with marrow involvement.

Neurology studies

Children should fast for four hours prior to scanning. Children with epilepsy should have electroencephalogram (EEG) monitoring during the uptake period. Studies involving children or young people with epilepsy should be performed in centres with paediatric neurology services, with a documented emergency management protocol for prolonged seizures. For brain oncology studies, the child or young person needs to be quiet and relaxed without stimulation during the uptake period.

Cardiology studies

For perfusion studies involving pharmacological stress, a person skilled in paediatric resuscitation and management of arrhythmias should supervise the stress part of the examination. The child's medication should be reviewed before attending to determine the stress agent. For studies with FDG, children should fast for four hours, prior to a glucose load given one hour before the FDG part of the scan. Additional insulin may be given before the FDG injection according to the blood glucose in line with individual departmental protocols. These studies should be performed in centres with access to full paediatric support services. Should an insulin clamp be required, patients should be observed in hospital for a minimum of six to eight hours post-procedure to ensure normalisation of the blood sugar.

Administration of radiotracer

Children should be offered local anaesthetic cream prior to the tracer injection. Problems can be experienced with the radioactive tracer sticking to a Hickmann line. However, use of a Hickmann line is reasonable in children, provided the line is flushed well after administration of the tracer, aseptic non-touch technique is employed and the site of suspected disease for assessment is away from the line. Port-a-caths should be accessed before attending the scanning centre.

The principle of as low as reasonably achievable (ALARA) with regards to radiation dose should always apply and the administered activity should be reduced in paediatric studies. Practitioners should refer to the position statement issued by Administration of Radioactive Substances Advisory Committee (ARSAC) in May 2013 (available at www.arsac.org.uk/newsletter/documents/May2013.pdf).

ARSAC recommends, until further research is available, continuing the use of the existing method of activity calculation published in the ARSAC Notes for Guidance for all investigations apart from 18F-FDG PET-CT. Centres using 18F-FDG in paediatric patients are encouraged to optimise the administered activity based on equipment settings and clinical reporting preferences. ARSAC holds the view that centres should ensure that image quality is maintained during this optimisation process. Centres using 3D or Time of Flight imaging should use the EANM 3D dosage card where appropriate (available at <http://www.eanm.org/docs/dosagecard.pdf?PHPSESSID=76pkrsed6fq5vti0klddf2cd46>).

Scan acquisition

All paediatric patients should be scanned according to the most recent evidence protocols whether routine clinical or research oriented. In accordance with the ALARA, dose optimisation procedures should be agreed, as discussed above. The tube current may be reasonably reduced to 25–35 mAs (pitch 1.5) in most children where the PET-CT is used for attenuation correction and localisation only. PET-CT scans acquired with imaging parameters typically used in separate 'diagnostic' PET-CT examinations should be performed only if this will avoid the need for a separate PET-CT scan. Until it is established whether there is an effect of intravenous contrast on attenuation correction and semi-quantitation of PET-CT data in children, if a diagnostic PET-CT scan with intravenous contrast is acquired at the same scanning session, consideration should be given to acquiring a separate low-dose (5 mAs) PET-CT scan prior to the injection of contrast for attenuation correction purposes. For response assessment scans where intravenous contrast may not be required, a PET-CT examination may

obviate the need for a separate 'diagnostic' PET-CT scan.

For brain and cardiac imaging, and where the CT is required for attenuation correcting the PET only, the tube current can be reduced to as low as 5 mAs (pitch 1.5). The minimum tube current on some cameras is higher than this and centres performing paediatric brain and cardiac imaging should ideally use a PET-CT camera which is capable of reducing the dose in accordance with the ALARA principle.

It is recommended that brain studies in children are acquired as dynamic studies or in list-mode (where available) so that frames with excessive movement can be rejected. Brain and cardiac images should be acquired in 3D. Other images should be acquired in 2D or 3D depending on patient size, according to local protocol.

Immobilisation aids may assist in positioning the patient and distraction with music or story tapes can be helpful. The nappy of infants should be changed immediately before the scan to reduce the amount of tracer seen in the nappy on the scan.

Scan interpretation

Interpretation of scans in children can be challenging. Reasons for this include the variety in the normal variation that occurs during development, including the variable distribution of FDG uptake in the brain at different ages, uptake in brown fat, thymus and lymphoid tissue in the head and neck. Paediatric conditions as discussed above may be rare conditions and experience may be built up by reporting these centrally. It is important that wherever a scan is acquired, a radiologist or nuclear physician who is regularly reporting paediatric PET-CT scans interprets the scan findings. This person should also be prepared to liaise with the referring clinician directly and provide scan data in a format that can easily be shown at multidisciplinary meetings. There should also be a mechanism for the referring clinician to liaise with the radiologist who will be demonstrating the scans at multidisciplinary team meetings (MDTM), if the primary reporter cannot attend the MDTM themselves.

Radiation protection aspects

It should be stressed that siblings or friends who are children should not be brought to the PET-CT facility where they may come into contact with injected patients. If the mother of a child to be scanned is pregnant, another member of the family should accompany the patient for the scan. Based on measurements of dose rates and models of behaviour if normal contact is resumed two hours after the injection, the dose to an individual should not exceed recommended dose constraints. Therefore, there is no requirement for restrictions to be placed on contact with family members after this time. The dose during the uptake period and the scan procedure received by a carer is unlikely to exceed the dose constraint of 3 mSv recommended by European guidance.

Audit and review

PET-CT facilities should have an agreed method of audit for scan procedures, scan interpretation and patient satisfaction. The number of scans aborted where patients were unable to comply with the scan procedure and the number of non-diagnostic scans should be reviewed regularly. Cases where patient motion required repeat CT scans and additional radiation exposure should also be monitored. It is recommended this data is collected as part of the national audit of PET-CT.

Service delivery

It is recognised that a balance needs to be achieved between providing local access for children and their families to PET-CT and the establishment of centres of excellence in paediatric imaging. Given the complexity of PET-CT scanning in children and the need to develop and maintain expertise in the reporting of sometimes rare conditions in children, it is recommended that specialist regional centres are established in the UK. Studies that require direct access to paediatric services as outlined above should be carried out at these centres. Other scans could be performed at sites more local to the patient including mobile scanners but should be performed according to protocols developed at the regional centre, with reporting being carried out at the regional centre with the specialist centre taking some responsibility for training and support of the centre where the

scans are performed (as detailed in the Department of Health document *Delivering Quality Imaging Services for Children* Point 38). Links should be forged between the regional centre and referring clinicians in paediatrics.

Networks

The direction of travel for children's imaging services is to be part of a network. Each cancer network should have access to PET-CT for children and ideally these should be co-located.

Transfer of images

Where a child has had different scans performed on different scanners, it is essential that all the images are available to all relevant clinicians involved in the care of the child.

Small children versus teenagers (young adults)

Practitioners should consider whether teenagers of a certain age/size should still be managed as children, while still taking into account the importance of dose reduction and, where applicable, the use of PET-MR. The potential benefits of PET-MR include reduced radiation exposure, superior soft tissue contrast and simultaneously acquired PET and MRI data. In the future, this technology may have an increasing role in the management of paediatric patients, but at present there is very limited clinical access to PET-MR scanners in the UK and the mainstay will be PET-CT for the medium term.

Summary

1. It is reasonable to scan children with conditions where there is good evidence for the use of PET-CT in adults.
2. In other conditions the use of PET-CT needs to be assessed on a case-by-case basis where it may be useful for individual management.
3. Liaison with parents/carers in advance of the scan is required.
4. Any examination requiring anaesthesia or sedation should be carried out in centres with personnel and equipment immediately available to manage paediatric emergency situations.
5. Neurology and cardiology examinations for children requiring monitoring need to be carried out in centres with paediatric services.
6. Examinations where a CT scan is performed with intravenous contrast at the same scanning session as the PET-CT scan should be carried out in centres with paediatric services.
7. Patients under the age of 13 should be scanned in specialist regional PET-CT units with experience in scanning children who have direct access to paediatric inpatient services ideally. Children older than this with developmental problems and children with severe systemic illness will also need to be scanned in specialist units.
8. Children aged between eight and 12 could be scanned in sites without paediatric services however at the discretion of the referring paediatrician, provided an individual trained in APLS is in the vicinity and paediatric resuscitation kit is available within the scanning facility.
9. Studies should always be performed by staff who are scanning children on a regular basis with experience in paediatric cannulation. All staff should be CRB checked and have appropriate safeguarding children training.
10. PET-CT protocols should be optimised in accordance with the ALARA principle.
11. Scans should be interpreted by nuclear physicians or radiologists who regularly report the type of paediatric study being performed.
12. Regular audit and review of scan procedure, quality and interpretation is mandatory.
13. Given the complexity of requirements for PET-CT scanning in children, and the need to develop and maintain expertise in the reporting of sometimes rare conditions in children, specialist regional centres should be established in the UK.
14. Scans could be performed at sites more local to the patient in circumstances outlined above but according to protocols developed at the regional centre with reporting carried out at the regional centre.

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Acknowledgements

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- M Brooks, Aberdeen Royal Infirmary
- SF Hain, University College London Hospitals NHS Trust

The authors also wish to acknowledge significant contributions to the document from the following:

- Caroline Davies, Consultant Anaesthetist, Guy's and St Thomas' NHS Trust.
- Rosalie E Ferner, Consultant Neurologist, Guy's and St Thomas' NHS Trust.
- Elaine Hughes, Consultant Paediatric Neurologist, King's College Hospital and Evelina Children's Hospital.
- Ruth Williams, Consultant Paediatric Neurologist, Evelina Children's Hospital.
- Robert Yates, Consultant Paediatric Cardiologist, Great Ormond Street Hospital for Sick Children.

Citation details

The Royal College of Radiologists.
Guidelines for the use of PET-CT in children, Second edition. London: The Royal College of Radiologists, 2014.

Ref No. BFCR(14)3
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