18F-DOPA PET Scan for Diagnosis of Congenital Hyperinsulinism

Practice Guideline ©

DOCUMENT SUMMARY/KEY POINTS

This document is intended for use within Sydney Children's Hospital Randwick and The Children's Hospital at Westmead in conjunction with Endocrine team consultation.

The following guidelines may also be useful to inform aspects of management not covered in this document: Hypoglycaemia Management for Non-Diabetic Patients

- ^{18}F-DOPA PET scan is the gold standard investigation for diagnosis of a focal lesion associated with congenital hyperinsulinism.
- The Endocrinology team is responsible for liaison with relevant teams and coordination of timing on the day of the scan.
- Medications used in the treatment of hyperinsulinism (including diazoxide, octreotide and glucagon) may be continued at clinician discretion if required for glycaemic control during the scan.
- The scan requires patients to be fasted and occurs under general anaesthesia.
- Blood glucose monitoring must be performed throughout the scan, for which a subcutaneous continuous glucose monitor (CGM) may be used.
- IV glucose infusion must continue throughout the scan to maintain BGL 4 – 8 mmol/L.

CHANGE SUMMARY

- N/A – New Document

Approved by:	SCHN Policy, Procedure and Guideline Committee	
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READ ACKNOWLEDGEMENT

- Medical and nursing staff responsible for the care of patients undergoing ^{18}F-DOPA PET scan within SCHN are to read and acknowledge (sign-off) having read this guideline.

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1 Background

1.1 What is congenital hyperinsulinism?

- Congenital hyperinsulinism (CHI) is the most common cause of persistent hypoglycaemia in infants and children and carries the risk of severe neurological disability if treatment is delayed.
- It is caused by the dysregulation of insulin secretion by pancreatic beta-cells, which results in recurrent episodes of hyperinsulinaemic hypoglycaemia.
- Hyperinsulinism occurring in the neonatal period is more commonly acquired than genetic in aetiology. Acquired hyperinsulinism is usually a transient condition with identifiable risk factors such as low birthweight, perinatal asphyxia, or maternal diabetes mellitus. Genetic hyperinsulinism is a beta-cell disorder and thus usually chronic, unless surgically curable.
- Genetic CHI can be classified as focal, diffuse, or atypical – infants with focal lesions may be curable by surgical resection.
- Rapid genetic testing should be undertaken to identify infants with genetic variants likely to result in focal lesions, who will then be candidates for diagnostic imaging with ^{18}F-DOPA PET scan, in combination with a CT scan.
- Presence of a paternally inherited pathogenic variant (*KCNJ11* or *ABCC8*) predicts a focal lesion with a sensitivity of 97%, thus rapid testing of the *KCNJ11* and *ABCC8* genes should be performed in diazoxide unresponsive CHI patients.
- If genetic testing suggests focal disease, an ^{18}F-DOPA PET scan is required to localise the lesion.

1.2 What is an ^{18}F-DOPA PET scan?

- ^{18}F-L 3,4-dihydroxyphenylalanine (^{18}F-DOPA) PET scan is the gold standard imaging technique for diagnosis of a focal CHI lesion.
- ^{18}F-DOPA is a radiolabelled version of dopamine, which is taken up by neuroendocrine cells including pancreatic beta-cells.
- CHI focal lesions show increased uptake of the radiotracer, compared to the surrounding normal pancreatic tissue.
- A low dose non-contrast enhanced CT scan is acquired concurrently for attenuation correction and to assist with anatomical localisation of the lesion
- If a focal lesion is identified, accuracy of localisation is approximately 90%. ^{18}F-DOPA PET scan may not detect very small focal lesions, therefore a negative study does not rule out focal CHI.
- The criteria for referral for ^{18}F-DOPA scan are included below:

Criteria for referral for ^{18}F-DOPA PET scan:

The patient must satisfy **ALL** of the following criteria:

1. Evidence of congenital hyperinsulinism (CHI), during an episode of hypoglycaemia:
    a. Detectable serum insulin

    AND

    b. Inappropriate suppression of serum ketones and free fatty acids

AND

2. Persistent hyperinsulinaemic hypoglycaemia unresponsive to diazoxide

AND

3. Genotyping suggestive of focal disease, or inconclusive:
    a. Paternally inherited pathogenic variant of *KCNJ11* or *ABCC8*

    OR

- Pathogenic variant documented in the literature to be associated with focal CHI, and/or not to be associated with diffuse disease

2 Coordination of ^{18}F-DOPA PET scan

2.1 For patients off-site – transfer and admission to SCH

- For patients requiring inter-hospital transfer to SCH to facilitate ^{18}F-DOPA PET scan, the transferring team must organise the following:
    - Early clinical handover to the SCH Endocrinology On Call, who will in turn notify all other relevant teams (see ***Teams involved at SCH 2.2***) for coordination of a multidisciplinary planning meeting.
    - Follow the standard procedure for inter-hospital transfer. In most instances this will be with Newborn and Paediatric Emergency Transport Service (NETS).
    - Ensure the Bed Manager is aware that the patient will require SCH CICU admission.
    - CICU admission is required as CHI patients require strict glycaemic control involving higher concentration IV glucose infusions.
    - At least two points of secure IV access must be established. In most cases, central access will be required, thus care must be taken to avoid central femoral access due to interference with imaging.

2.2 Teams involved at SCH

Due to the complexity of the scan, a multidisciplinary meeting should be considered to assist in planning. The SCH Endocrine Team will be responsible for liaising with the relevant teams listed below and ensuring the following considerations are addressed:

2.2.1 Nuclear Medicine Department (POWH)

- Initial discussion should occur following the scan request from the treating team.
- Coordination of scan booking date and time must include specific consideration of ^{18}F-DOPA radiotracer production and expiry time in accordance with Department of Nuclear Medicine protocols.

2.2.2 Anaesthetics team

- An Anaesthetist and an Anaesthetic nurse are required for the scan.
- As the scan may not be performed as part of a routine list, contact should be made with the Anaesthetics department well in advance to confirm availability of staff
- Special considerations for ^{18}F-DOPA PET/CT scan should be discussed with the Anaesthetist including choice of the anaesthetic agent (see ***Anaesthetic Agent 3.5***) and any specific fasting requirements pertaining to anaesthesia.

2.2.3 SCH CICU team

- For planned transfers, a Request For Admission (RFA) form must be completed and the admission booking approved by the CICU NUM.
- The plan for fasting and glucose infusion should be clarified by the SCH Endocrine Team once the date and time of the scan are confirmed.
- Placement of a Continuous Glucose Monitor (CGM) should be facilitated, if not already being used and education provided regarding calibration.

2.2.4 SCH Executive

- Consideration should be given to the cost of the tracer and any additional *ad hoc* costs, including the Anaesthetist if the scan is performed outside of a routine general anaesthesia Nuclear Medicine list, or if the patient requires transfer to SCH. Responsibility for additional costs should be discussed with hospital executive prior to approval of the scan.

3 Considerations prior to the scan:

3.1 Consent

- The SCH Endocrine team are responsible for obtaining consent from the parents/carers for the scan to be performed under general anaesthesia, prior to the day of the scan to avoid unnecessary delays.
- ^{18}F-DOPA PET scan has an excellent safety profile and there are no adverse effects attributable to the radiotracer, including from the small amount of radiation exposure. The theoretical risk of exposure to radiation is vastly outweighed by the clinical benefits of achieving a diagnosis.

3.2 Fasting

- Patient should be fasted for at least 6 hours prior to the scan, with the recommendation to gradually titrate down any feeds (rather than stop immediately) whilst titrating up the IV glucose infusion to maintain a stable glucose level.
- Any nasogastric tube present must be removed prior to the scan, as it will result in a significant imaging artefact and obscure the area of interest. Additionally, a nasogastric tube must not be inserted at the time of induction.

3.3 IV access

- To avoid interruption of the IV glucose infusion, patients require a separate intravenous line for injection of radiotracer. In most cases, this will need to be a double lumen central line due to:
  - the difficulty of securing two stable peripheral lines
  - the likely need for infusion of high concentration glucose
  - the risk of severe hypoglycaemia if IV fluids and/or glucagon infusions are interrupted.

3.4 Glucose monitoring

Normoglycaemia should be maintained during the scan i.e. blood glucose level 4 – 8mmol/L, ideally aiming for a higher normal blood glucose level of 6 – 8 mmol/L.

- Blood glucose level must be stable for a minimum of 3 – 4 hours prior to the scan, with minimal fluctuation.
- This should be achieved in ICU by weaning off feeds and transitioning to IV fluids on the night leading up to the scan, with individualised titration of IV glucose concentration and (if necessary) glucagon infusion, as required.

A continuous glucose monitor (CGM) is safe and appropriate to be used during the scan:

- The CGM should be calibrated prior to the scan to ensure readings are within the accepted 20% discrepancy (when compared with blood glucose levels).
- The CGM should be placed below the lower pelvis, for example on the lower thigh, to remain outside the field of view during scanning and thus prevent imaging artefact.
- If the CGM discrepancy exceeds 20%, or fails to read during the scan, glucose level monitoring should continue with regular finger or heel-prick sampling 30 minutely to hourly.
- If the CGM reading is trending high or low, or changing rapidly, finger-prick samples should be collected to confirm a true reading prior to intervention

3.5 Medications

- Glucose infusion must be continued throughout the scan
- Glucagon, diazoxide and octreotide are safe to continue if required for glycaemic control and do not interfere with radiotracer uptake, however in some situations it may be advisable to cease or alter medications
    - For example, intermittent IV octreotide injections are associated with tachyphylaxis and significant fluctuations in BGL, including a risk of rebound hypoglycaemia. Preferably, intermittent injections should be replaced by an increased glucose infusion rate and glucagon infusion OR a continuous subcutaneous infusion of octreotide via an insulin pump.

3.6 Anaesthetic agent

- Most patients will require general anaesthesia and intubation – the usual anaesthetic agent of choice is propofol and/or fentanyl
- Halogenated anaesthetic agents should be avoided as they may cause hyperglycaemia.

3.7 Manufacturing the radiotracer

- ^{18}F-DOPA radiotracer is manufactured on the day of the scan and verification of quality control confirmed by Radiopharmaceutical Science Specialist
- The aim should be to administer the radiotracer as soon as practical, ideally within 2 to 3 hours of production as it has a short shelf-life.

4 Considerations during the scan:

- A CT scan is performed first
- Following the CT, with the patient in an unchanged position on the scanner, a 60 min dynamic PET acquisition is commenced immediately prior to administration of the radiotracer. Additional images are acquired as per the instructions from the supervising Nuclear Medicine Specialist.
- IV glucose is required to maintain normoglycaemia i.e. BGL 4 – 8mmol/L

Blood glucose fluctuations during scan:

- During the scan, aim for a higher normal blood glucose level of 6 – 8 mmol/L and ideally maintain tight control as this may impact accuracy of the scan.
- All patients should have an individualised glucose management plan however general principles are as below:
  - Hypoglycaemia during scan:
    - If blood glucose level is 3.0 – 3.9 mmol/L, increase glucose infusion rate by 10%.
    - If blood glucose level is < 3.0mmol/L, give 2mL/kg 10% glucose bolus over 5 minutes and then increase glucose infusion rate by 10%.
  - Hyperglycaemia during scan:
    - If blood glucose level is > 8.0mmol/L, decrease glucose infusion rate by 10%.
- Further changes in rate should be tailored to the observed effect on BGL.

5 Considerations after the scan:

- As anaesthesia wears off, IV glucose should be titrated carefully to aim for high normal blood glucose levels as the stress of anaesthesia, as well as the inherent effects of anaesthetic agents, can transiently increase plasma glucose concentration. This may result in a hypoglycaemic episode if IV glucose is weaned too quickly
- Upon recommencement of feeds, the IV glucose infusion rate may also need to be increased as there is an added risk of hypoglycaemia due to the resultant transient increase in insulin secretion

6 Example: Process of Events for ^{18}F-DOPA PET scan

TIME*	EVENT
DAYS PRIOR	Coordination of scan, including consultation with POWH Nuclear Medicine and Anaesthetics Admission to SCH CICU
NIGHT PRIOR	Overnight slow weaning of feeds to nil IV glucose to be titrated to maintain BGL 4 – 8 mmol/L CGM in situ
06:00	Patient nil by mouth by 6am Nasogastric tube to be removed once feeds ceased
11:00	Following confirmation that the patient is stable and the scan will proceed, tracer production will commence
11:30	Patient transferred to Nuclear Medicine Department in POWH CICU nurse to accompany patient for transfer Anaesthetics review and commencement of general anaesthesia
12:30	Tracer passes quality control and is released by the Radiopharmaceutical Scientist
12:45	Scan commences Tracer injection 1-hour dynamic image acquisition, followed by any additional image acquisition as required
14:00 – 15:00	Scan completed Recovery from anaesthesia Patient transferred back to CICU with CICU nurse

*NB: times are included as a guide only and may vary significantly

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