

Joint ADS/ANZSNM guideline for FDG PET/CT imaging in patients with type 1 and type 2 diabetes

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Introduction

Purpose

To assist medical, nursing and nuclear medicine staff to prepare and manage people living with diabetes undergoing a PET scan. This guideline is for the provision of advice only and does not replace clinical decision making in individual patients or specific protocols adapted for individual centres.

Background

FDG-PET/CT is a commonly utilised imaging modality, particularly for the evaluation of tumours, including the initial staging, restaging, treatment monitoring and treatment planning. Appropriate patient preparation is important to optimise the image quality necessary for accurate interpretation of the PET/CT studies. There are several considerations in the preparation of patients with diabetes that can influence image quality, including carbohydrate restriction, management of blood glucose levels and insulin administration.

^{18}F -FDG is a radiolabelled glucose analogue that is actively transported into cells by glucose transporting proteins (GLUTs). In tumours and processes, such as inflammation, in which there is an increase in metabolic rate, cells increase the number of GLUT receptors. This results in an increase in ^{18}F -FDG uptake.

Glucose competes with FDG for uptake into tumours or sites of inflammation, potentially reducing the sensitivity of the PET scan. Similarly, hyperinsulinaemia promotes uptake of FDG into non-target tissues such as muscles, resulting in altered biodistribution of radiotracer with high background FDG uptake, commonly referred to as a “muscle scan”.

Different centres have introduced various fasting recommendations and insulin protocols based on local experience, noting the scarcity of evidence. Whilst some centres require patients to fast from midnight for a morning scan, others may opt to allow the patient to consume an early breakfast with the patient’s usual insulin, ensuring a minimum of 4-hour delay to FDG injection. The most recent European Association of Nuclear Medicine procedure guideline published in 2015 outlines a preference for a subcutaneous short-acting insulin injection to manage hyperglycaemia. FDG injection should be delayed for a minimum of 4 hours following administration of subcutaneous short-acting insulin. As it may not be practical to delay the scan for the minimum 4 hours required after subcutaneous insulin administration, some centres may elect to use intravenous insulin to correct hyperglycaemia. There is some concern about the risk of hypoglycaemia and hypokalaemia with the administration of intravenous insulin, particularly in centres where staff experience and availability for glucose monitoring are limited.

Outlined below is a guideline for managing patients with diabetes scheduled for FDG PET scans. If there is concern regarding the type of diabetes that the patient has, please consult the patient’s treating physician.

References:

1. Boellaard R et al. FDG PET/CT: EANM procedure guidelines for tumour imaging: version 2.0. *Eur J Nucl Med Mol Imaging* 42:328–354 (2015).
2. Surasi DS et al. ^{18}F -FDG PET and PET/CT Patient Preparation: A Review of the Literature. *J Nucl Med Technol* 42:5–13 (2014).
3. Pattison DA, MacFarlane LL, Callahan J et al. Personalised insulin calculator enables safe and effective correction of hyperglycaemia prior to FDG PET/CT. *EJNMMI Res* 9, 15 (2019).
4. Krause B, Barrington S & Cranston I. Scan preparation for patients with type I diabetes treated with continuous subcutaneous insulin infusion (CSII) pumps. *Eur J Nucl Med Mol Imaging* 46, 2217 (2019).

General principles

- Ensure that the glucometer used to monitor glucose levels in the Nuclear Medicine Department is calibrated regularly.
- Advise the patient to avoid vigorous exercise for 24 hours before the scan.
- GLP-1 and GLP-1/GIP receptor agonists should be continued as prescribed, but consider fasting the patient from midnight due to the potential for effects on gastric emptying.
- For insulin-treated patients, a preference should be given for morning appointments.
- For evaluation of gastrointestinal tumours/lesions, or if there has been prominent gastrointestinal uptake interfering with interpretation on prior PET studies, consider ceasing metformin for 48 hours before the scan.
- For evaluation of cardiac sarcoidosis/inflammation, it is recommended that the patient consumes a high fat/protein and very low-carbohydrate diet for 24 hours and that they fast from midnight to suppress background physiologic myocardial FDG uptake. Departmental protocols should be followed in this regard where available. Consider Endocrinology input for complicated patients (especially those treated with insulin).
- A blood glucose target of ≤ 12.0 mmol/L (or ≤ 10.0 mmol/L for brain imaging) is recommended. This is a guide only. Some centres may elect to use a slightly lower or higher target for individual patients.
- If hyperglycaemia is not successfully managed in the PET suite, consider contacting the patient's Endocrinologist or the local endocrine service for advice.
- If a patient not known to have diabetes has a fasting glucose level of ≥ 7.0 mmol/L and/or a post-prandial glucose of ≥ 11.1 mmol/L, a new diagnosis of diabetes is likely and should be communicated to the referring doctor.
- If a patient presents to the PET suite with a glucose level > 16.0 mmol/L, consider rescheduling the scan and recommending that the patient be referred to their Endocrinologist or the local endocrine service for advice.
- Some PET studies (e.g. neurofibromatosis or with bladder protocol) may require two acquisitions – the first acquisition immediately after the FDG uptake period and a second delayed acquisition at about 4 hours post FDG injection. If the patient has been fasting throughout the morning and has omitted their morning insulin, they should be advised that they can eat and have their usual morning insulin after they have had their first acquisition/scan (i.e. following the FDG uptake period).

Type 2 diabetes not treated with insulin

Patients on oral diabetes medication and/or injectable GLP-1 or dual GLP-1/GIP receptor agonists

Preparation for PET scan

When to schedule scan	Any time
Evening prior to scan	Patients can take their usual oral diabetes medication.
Morning of PET scan	If fasting from midnight, withhold usual morning oral diabetes medications for a morning scan. If having breakfast, take usual morning oral diabetes medications for an afternoon scan, noting that a minimum of a 4-hour fast is required.

On arrival to the PET suite

Check the glucose level		
Glucose level < 4.0 mmol/L	Glucose level 4.0-12.0 mmol/L	Glucose level > 12.0 mmol/L
Administer clear apple juice or lemonade (150 ml) and repeat glucose levels in 15 mins. Repeat this process until glucose levels > 4.0 mmol/L. ¹	Proceed with PET scan. (Target glucose ≤ 10.0 mmol/L for brain PET scans)	Consider insulin administration as suggested below OR reschedule scan. Please note: the cut-off of 12.0 mmol/L is a guide only.

¹In the event of hypoglycaemia, consider rescheduling the scan to another day and allow the patient to eat. The PET scan is likely to be technically suboptimal in the setting of very recent hypoglycaemia. Some centres may elect to proceed with the scan 6 hours after the patient is treated for hypoglycaemia.

If glucose level > 12.0 mmol/L (> 10.0 mmol/L for brain scan) – consider one of two options below:

Option 1: Use intravenous insulin

Administer intravenous insulin via a local protocol. Intravenous insulin should be used with caution in patients with known renal impairment or BMI <25 kg/m² due to the risk of hypoglycaemia.

Once intravenous insulin has been administered, a Medical Officer should be present until the PET scan is undertaken. The capillary glucose level should be monitored regularly (at least every 15 minutes) to ensure that capillary glucose level has started rising again, before the FDG is injected. If there is uncertainty, wait another 15 minutes and check again. Should symptomatic hypoglycaemia occur after insulin administration, it should be reversed by glucose administration in accordance with local hypoglycaemia management guidelines.

Option 2: Use subcutaneous insulin (see suggested doses below)

	Weight < 60 kg	Weight 60-100 kg	Weight > 100 kg
Glucose levels	Subcutaneous NovoRAPID, HumALOG or Apidra (units)		
10.1-12.0 mmol/L*	2 **	2**	4**
12.1-14.0 mmol/L	2	4	6
14.1-16.0 mmol/L	3	6	8
>16 mmol/L***	4	8	Contact Endocrinology
Glucose monitoring: 2 hours and 4 hours post subcutaneous insulin injection or if patient unwell.			
* Use for brain PET scan where target glucose ≤ 10.0 mmol/L.			
** Alternatively, encourage hydration and walking if glucose level 10.1-11.0 mmol/L.			
*** Some centres may reschedule scan if glucose > 16 mmol/L.			

4 hours following subcutaneous insulin injection	
Glucose level 4.0-12.0 mmol/L	Glucose level > 12.0 mmol/L
Proceed with PET scan. (Target glucose ≤ 10.0 mmol/L for brain PET scans)	Consider rescheduling the scan. Depending on the circumstances, the Nuclear Medicine Specialist may proceed with scanning. Please note: the cut-off of 12.0 mmol/L is a guide only.

After PET scan

If fasted from midnight, the patient should test their glucose levels, eat breakfast if omitted and administer their usual morning oral diabetes medications. Patients should recommence glucose monitoring.
Glucose levels must be > 5 mmol/L prior to leaving the units, especially if patient is driving.

Type 2 diabetes treated with insulin

Patients treated with insulin, including those treated with oral diabetes agents and/or injectable GLP-1 or dual GLP-1/GIP receptor agonists

Preparation for PET scan

When to schedule scan	At approximately 8 am if fasting from midnight OR following a minimum of a 4-hour fast, if having breakfast.	
Evening prior to scan	Patients should take their usual insulin the night before their PET scan.	
Morning of PET scan	<p>If fasting from midnight: Withhold usual morning short-acting and mixed insulin.</p> <p>Examples: NovoRAPID, Actrapid, HumALOG, HumULIN R, Apidra, NovoMIX 30, Humalog MIX25, Humalog MIX50, Ryzodeg 70/30, Mixtard 30/70</p> <p>Patients may administer their usual morning long-acting insulin.</p> <p>Examples: Toujeo, Levemir, Protaphane, Optisulin</p>	<p>If having breakfast: Have usual morning insulin with early breakfast if morning scan OR at the usual time if afternoon scan.</p> <p>Ensure administration of insulin > 4 hours prior to arrival time for PET scan.</p>

On arrival to the PET suite

Check the glucose level		
Glucose level < 4.0 mmol/L	Glucose level 4.0-12.0 mmol/L	Glucose level > 12.0 mmol/L
Administer clear apple juice or lemonade (150 ml) and repeat glucose level in 15 mins. Repeat this process until glucose levels > 4.0 mmol/L. ¹	Proceed with PET scan. (Target glucose ≤ 10 mmol/L for brain PET scans)	Consider insulin administration as suggested below OR reschedule scan. Please note: the cut-off of 12.0 mmol/L is a guide only.

¹In the event of a hypoglycaemia, consider rescheduling the scan to another day and allow the patient to eat. The PET scan is likely to be technically suboptimal in the setting of very recent hypoglycaemia. Some centres may elect to proceed with the scan 6 hours after the patient is treated for hypoglycaemia.

If glucose level > 12.0 mmol/L (> 10.0 mmol/L for brain scan) – consider one of two options below:

Option 1: Use intravenous insulin

Administer intravenous insulin via a local protocol. Intravenous insulin should be used with caution in patients with known renal impairment or BMI <25 kg/m² due to the risk of hypoglycaemia.

Once intravenous insulin has been administered, a Medical Officer should be present until the PET scan is undertaken. The capillary glucose level should be monitored regularly (at least every 15 minutes) to ensure that capillary glucose level has started rising again, before the FDG is injected. If there is uncertainty, wait another 15 minutes and check again. Should symptomatic hypoglycaemia occur after insulin administration, it should be reversed by glucose administration in accordance with local hypoglycaemia management guidelines.

Option 2: Use subcutaneous insulin (see suggested doses below)

	Weight < 60 kg	Weight 60-100 kg	Weight > 100 kg
Glucose levels	Subcutaneous NovoRAPID, HumALOG or Apidra (units)		
10.1-12.0 mmol/L*	2 **	2**	4**
12.1-14.0 mmol/L	2	4	6
14.1-16.0 mmol/L	3	6	8
>16 mmol/L***	4	8	Contact Endocrinology
Glucose monitoring: 2 hours and 4 hours post subcutaneous insulin injection or if patient unwell.			
* Use for brain PET scan where target glucose ≤ 10.0 mmol/L.			
** Alternatively, encourage hydration and walking if glucose level 10.1-11.0 mmol/L.			
*** Some centres may elect to reschedule scan if glucose > 16 mmol/L.			

4 hours following subcutaneous insulin injection	
Glucose level 4.0-12.0 mmol/L	Glucose level > 12.0 mmol/L
Proceed with PET scan. (Target glucose ≤ 10.0 mmol/L for brain PET scans)	Consider rescheduling the scan. Depending on the circumstances, the Nuclear Medicine Specialist may choose to proceed with scan. Please note: the cut-off of 12.0 mmol/L is a guide only.

After PET scan

If fasted from midnight, patient should test their glucose levels, eat breakfast if omitted and administer their usual morning insulin and oral diabetes medications. Patients should recommence glucose monitoring.
Glucose levels must be > 5 mmol/L prior to leaving, especially if patient is driving.

Type 1 diabetes treated with multiple daily insulin injections

Preparation for PET scan

<p>Long-acting insulin should NEVER be withheld. Inappropriate cessation of insulin can result in diabetic ketoacidosis.</p>		
24 hours prior	<ul style="list-style-type: none"> Advise patients using Flash Libre or continuous glucose monitoring systems that these devices will need to be removed just before their PET scan. Advise patients to bring a new Flash Libre or continuous glucose monitoring system for reinsertion after the PET scan. 	
When to schedule scan	At approximately 8 am if fasting from midnight OR following a minimum of a 4-hour fast, if having breakfast.	
Evening prior to scan	Patients should take their usual insulin the night before their PET scan.	
Morning of PET scan	<p><u>If fasting from midnight:</u> Withhold usual morning short-acting insulin.</p> <p>Examples of short acting-acting insulin: NovoRAPID, Fiasp, Actrapid, HumALOG, Apidra.</p> <p>Patients should administer their usual morning long-acting insulin at around 6 am.</p> <p>Examples: Toujeo, Levemir, Proptaphane, Optisulin</p>	<p><u>If having breakfast:</u> Have usual morning insulin with early breakfast if morning scan OR at the usual time if afternoon scan.</p> <p>Ensure administration of insulin > 4 hours prior to arrival time for PET scan.</p>

On arrival to the PET suite

Check the glucose level		
Glucose level < 4.0 mmol/L	Glucose level 4.0-12.0 mmol/L	Glucose level > 12.0 mmol/L
Administer clear apple juice or lemonade (150 ml) and repeat glucose level in 15 mins. Repeat this process until glucose level > 4 mmol/L. ¹	Proceed with PET scan. (Target glucose ≤ 10.0 mmol/L for brain PET scans)	Consider insulin administration as suggested below <u>PROVIDING NO CORRECTION DOSE GIVEN IN LAST 2 HOURS</u> (if it has, repeat glucose after one hour) OR reschedule scan. Please note: the cut-off of 12.0 mmol/L is a guide only.

¹In the event of hypoglycaemia, consider rescheduling the scan to another day and allow the patient to eat. The PET scan is likely to be technically suboptimal in the setting of very recent hypoglycaemia. Some centres may elect to proceed with the scan 6 hours after the patient is treated for hypoglycaemia.

If glucose level > 12 mmol/L (> 10 mmol/L for brain scan) – consider one of two options below:

Option 1: Use intravenous insulin

Administer intravenous insulin via a local protocol. Intravenous insulin should be used with caution in patients with known renal impairment or BMI <25 kg/m² due to the risk of hypoglycaemia.

Once intravenous insulin has been administered, a Medical Officer should be present until the PET scan is undertaken. The capillary glucose level should be monitored regularly (at least every 15 minutes) to ensure that capillary glucose level has started rising again, before the FDG is injected. If there is uncertainty, wait another 15 minutes and check again. Should symptomatic hypoglycaemia occur after insulin administration, it should be reversed by glucose administration in accordance with local hypoglycaemia management guidelines.

Option 2: Use subcutaneous insulin (see suggested doses below)

	Calculate the patient's total daily dose of insulin (the total amount of insulin a patient uses in 24 hours)			
Total daily insulin	< 30 units	31-50 units	51-100 units	>100 units
Glucose levels	Subcutaneous NovoRAPID, HumALOG or Apidra (units)			
10.1-12.0 mmol/L*	1**	2**	3**	4**
12.1-14.0 mmol/L	1	3	4	6
14.1-16.0 mmol/L	2	3	5	8
>16 mmol/L***	2	4	6	Contact Endocrinology
Glucose monitoring: 2 hours and 4 hours post subcutaneous insulin injection or if patient unwell.				
Ketones to be checked if glucose levels > 15.0 mmol/L. A medical officer should be notified if ketone levels are > 1.5 mmol/L.				
* Use for brain PET scan where target glucose ≤10.0 mmol/L.				
** Alternatively, encourage hydration and walking if glucose level 10.1-11.0 mmol/L.				
*** Some centres may elect to reschedule scan if glucose > 16 mmol/L.				

4 hours following subcutaneous insulin injection	
Glucose level 4.0-12.0 mmol/L	Glucose level > 12.0 mmol/L
Remove any glucose monitoring devices and proceed with PET scan. (Target glucose ≤ 10.0 mmol/L for brain PET scans)	Consider rescheduling the scan. Depending on the circumstances, the Nuclear Medicine Specialist may choose to proceed with scan. Please note: the cut-off of 12.0 mmol/L is a guide only.

After PET scan

Patients should test their glucose levels, eat breakfast if omitted, and administer their usual short acting insulin. A new Flash Libre or continuous glucose monitoring system can be reapplied.
Glucose must be > 5 mmol/L prior to leaving, especially if the patient is driving.

Type 1 diabetes using an insulin pump

Preparation for PET scan

Insulin pumps should NEVER be removed until the time of the PET scan. Insulin pumps should not be removed for > 3 hours. Inappropriate cessation of insulin can result in ketoacidosis.			
24 hours prior	<ul style="list-style-type: none"> ▪ Patients using an insulin pump should undergo a pump set change if not undertaken in the past 72 hours. ▪ Advise patients using Flash Libre or continuous glucose monitoring systems that these devices will need to be removed just before their PET scan. ▪ Advise patients to bring a new Flash Libre or continuous glucose monitoring equipment for reinsertion after the PET scan. 		
When to schedule scan	At approximately 8 am if fasting from midnight OR following a minimum of a 4-hour fast, if having breakfast.		
Evening prior to scan	Patients should bolus through their pump with dinner as per usual until midnight. Patients are to keep the insulin pump and glucose monitoring devices (Flash Libre or continuous glucose monitoring system) running in their usual mode.		
Morning of PET scan	<table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 50%; vertical-align: top;"> <p><u>If fasting from midnight:</u> Patient can check glucose level and give a correction dose through the pump if glucose > 12.0 mmol/L, but ensure administration of insulin > 4 hours prior to their arrival time for PET scan.</p> </td> <td style="width: 50%; vertical-align: top;"> <p><u>If eating breakfast:</u> Have early breakfast and bolus using the insulin pump in the usual way if morning scan OR at the usual time if afternoon scan.</p> <p>Ensure administration of insulin > 4 hours prior to arrival time for PET scan.</p> <p>Patient can check glucose level and give a correction dose through the pump if glucose > 12.0 mmol/L, but ensure administration of insulin > 4 hours prior to their arrival time for PET scan.</p> </td> </tr> </table>	<p><u>If fasting from midnight:</u> Patient can check glucose level and give a correction dose through the pump if glucose > 12.0 mmol/L, but ensure administration of insulin > 4 hours prior to their arrival time for PET scan.</p>	<p><u>If eating breakfast:</u> Have early breakfast and bolus using the insulin pump in the usual way if morning scan OR at the usual time if afternoon scan.</p> <p>Ensure administration of insulin > 4 hours prior to arrival time for PET scan.</p> <p>Patient can check glucose level and give a correction dose through the pump if glucose > 12.0 mmol/L, but ensure administration of insulin > 4 hours prior to their arrival time for PET scan.</p>
<p><u>If fasting from midnight:</u> Patient can check glucose level and give a correction dose through the pump if glucose > 12.0 mmol/L, but ensure administration of insulin > 4 hours prior to their arrival time for PET scan.</p>	<p><u>If eating breakfast:</u> Have early breakfast and bolus using the insulin pump in the usual way if morning scan OR at the usual time if afternoon scan.</p> <p>Ensure administration of insulin > 4 hours prior to arrival time for PET scan.</p> <p>Patient can check glucose level and give a correction dose through the pump if glucose > 12.0 mmol/L, but ensure administration of insulin > 4 hours prior to their arrival time for PET scan.</p>		
Important note	<u>Patients should remove their pump and glucose monitoring devices (Flash Libre or continuous glucose monitoring system) just before their PET scan as radiation can damage these devices. These devices should be detached just before FDG is injected. The pump and a new sensor should be reattached immediately after patient leaves the camera room. Insulin pumps should not be removed for > 3 hours. Inappropriate cessation of insulin can result in diabetic ketoacidosis.</u>		

On arrival to the PET suite

Check the glucose level		
Glucose level < 4.0 mmol/L	Glucose level 4.0-12.0 mmol/L	Glucose level > 12.0 mmol/L
Administer clear apple juice or lemonade (150 ml) and repeat glucose level in 15 mins. Repeat this process until glucose levels > 4.0 mmol/L. ¹	Proceed with PET scan. (Target glucose ≤ 10.0 mmol/L for brain PET scans)	Consider insulin administration as suggested below PROVIDING NO CORRECTION DOSE HAS BEEN ADMINISTERED IN THE LAST 2 HOURS (if it has, repeat glucose level after one hour) OR reschedule the scan. Please note: the cut-off of 12.0 mmol/L is a guide.

¹In the event of a hypoglycaemia, consider rescheduling the scan to another day and allow the patient to eat. The PET scan is likely to be technically suboptimal in this setting. Some centres may elect to proceed with the scan 6 hours after the patient is treated for hypoglycaemia.

If glucose level > 12.0 mmol/L (> 10.0 mmol/L for brain scan):

Option 1: Patient to use their insulin pump

If glucose level > 12.0 mmol/L, patient should administer a correction dose via their insulin pump.
Glucose monitoring: 2 hours and 4 hours post subcutaneous insulin injection or if patient unwell
Check ketones if glucose > 15.0 mmol/L. A medical officer should be notified if ketone > 1.5 mmol/L.

Option 2: Use intravenous or subcutaneous insulin

For patients unable to administer a correction dose through their pump, intravenous or subcutaneous insulin could be used as per the guide for type 1 diabetes treated with multiple daily insulin injections, provided there is appropriate expertise on site.

4 hours following pump or subcutaneous correction dose

Glucose level 4.0-12.0 mmol/L	Glucose level > 12.0 mmol/L
Remove the insulin pump and glucose monitoring device and proceed with PET scan. (Target glucose ≤ 10 mmol/L for brain PET scans).	Consider rescheduling the scan. Depending on the circumstances, the Nuclear Medicine Specialist may proceed with scanning. Please note: the cut-off of 12.0 mmol/L is a guide only.

After PET Scan

Glucose must be > 5.0 mmol/L prior to leaving, especially if the patient is driving.
The patient should reattach their pump and a new Flash Libre or continuous glucose monitoring system, and bolus as usual with breakfast if omitted.