^{82}Rb PET/CT of Myocardial Perfusion

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1. Introduction

Myocardial perfusion imaging is performed to identify are as of reduced or absent blood flow as a result of coronary artery disease (CAD).
Rubidium-82-PET/CT (^{82}Rb-PET/CT) is one of the non-invasive techniques used to evaluate myocardial perfusion, indicate possible ischaemia or even infarction. It can help to determine whether there is a cardiac cause for symptoms and if so,whether invasive coronaryangiography is indicated or if medical therapy should suffice.
Provided adequate PET equipment and processing software is used, myocardial perfusion can be quantified which is of value when assessing 3 vessel disease with balanced ischemia or with endothelial dysfunction.
Through analysis of myocardial perfusion and left ventricular function this investigation also provides prognostic information on the risk of cardiac related events.
Hybrid techniques such as PET/CT make quantification possible. They can be supplemented with calcium score CT (CaCS) and diagnostic coronary CT (CCT) thus combining physiology with anatomical imaging to identify the culprit lesion(s).

2. Methodology

This guideline is based on available scientific literature on the subject, the previous guideline (Aanbevelingen Nucleaire Geneeskunde 2007), international guidelines from EANM and/or SNMMI if available and applicable to the Dutch situation.

3. Indications

Diagnosis of

- Presence
- Location (coronary territory)
- Severity of coronary artery disease

- Assessment of the impact of known coronary stenosis on regional perfusion
- Aid in distinguishing between viable ischaemic myocardium and scar tissue
- Risk assessment and stratification
  - Post-myocardial infarction
  - Pre-operatively for major surgery in patients at risk of coronaryevents
- Monitoring of treatment effect
  - After coronary revascularization
  - Medical therapy for congestive heart failure or angina

Myocardial perfusion test should be performed in patients

- in the intermediate risk group for CAD
- with cardiac symptoms who are unable to perform bicycle or treadmill tests.
- with cardiac symptoms and an uninterpretable ECG e.g. LBBB

4. Relation to other diagnostic procedures

Cardiac perfusion imaging is usually done through myocardial perfusion SPECT (MPS). MPS has a good predictive value and correlates well coronary angiography.

The results of ^{82}Rb myocardial PET can be compared to PET with ^{15}O or $^{13}NH_3$. However, an on-site cyclotron is required for the latter two.
The extraction and uptake of ^{82}Rb in myocardial tissue is not as linear as with O_2 but adequate software can correct for this non-linear extraction which its reproducible.
Another difference is the longer positron range for ^{82}Rb, about 7,5 mm mean range, which results in blurrier pictures. As compared to ^{15}O, 3,0 mm mean range, and $^{13}NH_3$, 1,7 mm mean range. Still, the resolution of ^{82}Rb -PET is better than SPECT.
It is important to distinguish the functional imaging of perfusion from the anatomical imaging with CCTA. The hybrid technique has advantages in certain groups of patients, especially the intermediate risk group.
Myocardial blood flow quantification allows for calculation of the myocardial perfusion reserve (MBFR). This is not possible with SPECT.
In contrast to stress cardiac echo, myocardial PET is a robust and reproducible technique.

Fractional Flow FFR Reserve is measured during invasive coronary angiography and gives us a pressure derived from relative flow reserve. It does not reflect the absolute flow or coronary flow reserve. The discordance between CFR and FFR is as high as 40%.

Myocardial perfusion imaging with PET is only possible with pharmacological stress (either vasodilation with adenosine/regadenoson or inotropic effect with dobutamine) while other perfusion imaging can (also) be done with bicycle or treadmill ergometry.

In summary the advantages of myocardial PET above SPECT are:
- More economical
- Improved efficiency
- Lower radiation exposure
- Fewer attenuation artefacts
- Improved resolution
- Improved accuracy, among others due to absolute MBF measurements

5. Medical information necessary for planning

It is important to know the medical history of a patient. Previous cardiac intervention, pacemaker placement, cardiac implants and a full list of patients' medication are essential information.
Certain medication should be interrupted due to interaction with pharmacological stress agents. Also, the cardiologist may be interested in the perfusion without medical treatment.
Patients with a history of respiratory disease (e.g. COPD) may develop bronchoconstriction under Adenosine, determine whether or not pharmacological stress with Regadenoson or Dobutamine is a better option. The agent of pharmacological stress can make a difference in logistics and should be taken into account when scheduling patients.
Some patients need strict rhythm observation which is available during scanning but not always possible in the waiting room.

6. Radiopharmaceutical

Tracer

^{82}Rb is a positron emitting cationic analogue of potassium.
^{82}Rb is produced in a generator with an elution column with Strontium-82. ^{82}Sr has a half-life of 25,5 days and decays to ^{82}Rb by electron capture.
Therefore, the generator becomes weaker within a couple of weeks and the column must be replaced or 'refilled'.

Nuclide

^{82}Rb has a physical half-life of 75 sec and decays to stable ^{82}Kr after emitting several positrons with a relatively high energy.

Activity

The tracer dose is dependent on the scanner (2D/3D) and detector material used:

	BGO detector	LSO detector
2D scanner	1480-2220 MBq	
3D scanner	370-740 MBq	1110-1480 MBq

Administration

The short half-life makes it necessary to have the generator near the patient and infusion lines should be as short as possible. Acquisition starts during infusion of ^{82}Rb and continues for several minutes after administration.
A computer-controlled elution pump, injection system with remote facilities and automatic stopping of the tracer infusion result in reduced radiation dose to staff.
Administration of the ^{82}Rb takes about 30-60 sec.

7. Radiation safety

No long-term studies have been performed to determine the carcinogenic or mutagenic potential of ^{82}Rb. As with all radioisotopes it should only be used in pregnant women if the benefits outweigh the potential risk.
Although it is not known whether ^{82}Rb is excreted in breast milk the theoretical likelihood is low.
Breast feeding within 5 half-lives of the administration of ^{82}Rb is practically impossible, because of the short half-life of 75 sec and an acquisition duration of about 4 minutes from last Rb inflow.
There are also no known recommendations for with holding breast feeding after ^{82}Rb tests.

One (stress or rest) test with a 'standard' dose of 1110 MBq ^{82}Rb gives a radiationdose of 1,26 E-3 * 1110 = 1,40mSv.
Including two low dose attenuation correction CT 's a complete (stress and rest) study would give less than 3,5 mSv.
As reference: a complete ^{99m}Tc Myoview study with both rest and stress testing (without attenuation CT) gives a dose of about 10 mSv.

8. Patient preparation/essentials for procedure

Patients must be instructed to abstain from caffeine for 12 h (tea, coffee, chocolate and energy drinks with caffeine and chocolate containing food products) or longacting theophylline containing medication.

As mentioned under (5), a list of patients' medication is required as it may be of great importance to instruct a patient not to take certain medication before the test. E.g. if vasodilator stress with adenosine is performed, interference with Dipyridamol will give a higher intravascular adenosine concentration and raise the risk of adverse events. Dipyridamol and Theophylline containing medication should be stopped 24 h (or 48 h in case of longacting ('retard') medication) prior to the day of the test.

Patients with COPD GOLD I/II can be stressed with adenosine when prepared adequately e.g. with bronchodilators (Ventolin/Atrovent) just before stress. During the scan O_2 (1 liter) can be given through nasal prongs.

In patients with COPD GOLD III/IV Regadenoson or Dobutamine can be used. Dobutamine can also be used when 'bridging' coronary arteries are suspected.

Regadenoson is given in a bolus of 400 mcg just before starting ^{82}Rb infusion.

Patients must be able to lie in the scanner for 30-45 min.

When using adenosine it is preferable to have two intravenous lines so the administration of Adenosine does not interfere with the Rubidium infusion.

This is also the case with Dobutamine. Regadenoson is injected as a bolus with the Rubidium infusion following about 30 sec later, thus a single i.v. line is required.

During the investigation a 12 lead ECG and blood pressure (measured on arm or ankle)must be monitored.

For ECG gating the PET/CT camera requires a cardiac trigger.

9. Acquisition and processing

During acquisition the patient is in supine position on the camera table and as comfortable as possible with arms above the head. Two intravenous lines are present, onefor the stress pharmaceutical and one for Rubidium.

ECG and trigger leads are necessary as is a bloodpressure cuff. In most cases the bloodpressure is measured at the ankle due to the presence of an i.v. line in each arm.

Scanning protocol can be done in stress-rest or rest-stress order.

This depends on the stress protocol used. As the effect of Dobutamine is relatively long-lasting a rest-stress protocol is preferred.

The patient is left alone as soon as the Rubidium infusion is started. This is usually between the 3rd and 4th min of a 6-min Adenosine infusion (140 mcg/kg/min) or at the maximum dose of Dobutamine infusion or shortly after the Regadenoson bolus is given.

The blood pressure, heart rhythm and ECG are monitored from the operators' room.

Acquisition is started manually in list mode when the activity monitoring window on the acquisition station shows the first activity in the gantry.

Shortly before or after the acquisition a low dose CT is acquired for attenuation correction.

Acquisition time is about 7 min from the start of the ^{82}Rb infusion. The infusion time of ^{82}Rb will vary between 30-60 sec, depending on the generator used, the activity in the generator and the tubing used.

The list mode data are reconstructed into static rest and stress images both with and without attenuation correction, gated SPECT rest and stress images without attenuation

correction and dynamic stress and rest images with attenuation correction.
The dynamic images are reconstructed with a certain framing dependent upon the camera and software package used.
There are different software packages in use for ^{82}Rb (FlowQuant (Ottawa), Corridor4DM (Michigan), *Syngo*MBF (Siemens), QPET (Cedars-Sinai), PCARD (PMOD), Carimas or Cardiac VUIer).
Studies to date have not found great differences in results of calculated myocardial bloodflow. However,the different software packages are not fully interchangeable for gated results.
Follow up scans should be assessed using the same software as the initial investigation.
Correction for rate-pressure product can be used (not available in all packages) for correction of a high rest flow.

10. Interpretation

Measured CFR should always be interpreted in combination with other findings and bearing in mind what tracer is used. Using ^{82}Rb and pharmacological stress with Dipyridamol, a CFR of about 1,7 identified the ischemic group in the largest report known.
For Adenosine and ^{82}Rb a cut off of 2,0 or just below is accepted.
For optimal interpretation of the scans it is necessary to look at both the attenuation corrected and the uncorrected reconstructions.
Attenuation artefacts due to misalignment with the low dose CT is usually seen in the anterolateral wall and apex.
The myocardial perfusion images and the gated images with LV wall motion and thickening as well as the LVEF are interpreted as other MPI studies.
Using a 17 segment model is helpful in determining the summed stress, rest and difference scores (SSS, SRS and SDS).
The ECG triggered functional images result in LVEF and possibly a difference in LVEF during stress and rest. Ventricle dilation during stress relative to rest on the static images as well as a lower LVEF during stress are predictors of worse prognosis.

11. Report

Standardized reporting is suggested in the ASNC guideline.
A ^{82}Rb myocardial perfusion PET/CT report should contain information on patient preparation, the protocol and type of pharmacological stress used as well as the ^{82}Rb dose.
Symptoms prior to and during stress, ECG changes, heart rate and blood pressureduring rest and stress must be reported.
The perfusion images are described as other MPI studies. A 17 segments model with summed stress and rest scores are used.
Left ventricular function and ejection fraction during stress and rest are mentioned.
When a (low dose) CT scan for attenuation correction is available this is screened for abnormalities which are mentioned in the report.
When available a coronary calcium score is given.
The quantification values can be integrated in the report when applicable.

12. Literature

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