Equilibrium Radionuclide Angiography/ Multigated Acquisition

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1. Introduction

Equilibrium radionuclide angiography (ERNA), also known as radionuclide ventriculography (ERNV), gated synchronized angiography (GSA), blood pool scintigraphy or multi gated acquisition (MUGA), is a well-validated technique to accurately determine cardiac function. In oncology its high reproducibility and low inter observer variability allow for surveillance of cardiac function in patients receiving potentially cardiotoxic anti-cancer treatment. In cardiology it is mostly used for diagnosis and prognosis of patients with heart failure and other heart diseases.

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

Several Class I (conditions for which there is evidence and/or general agreement that a given procedure or treatment is useful and effective) indications exist:

- Evaluation of left ventricular function in cardiac disease:
- Coronary artery disease
- Valvular heart disease
- Congenital heart disease
- Congestive heart failure
- Evaluation of left ventricular function in non-cardiac disease:
- Monitoring potential cardiotoxic side effects of (chemo)therapy
- Pre-operative risk stratification in high risk surgery
- Evaluation of right ventricular function:
- Congenital heart disease
- Mitral valve insufficiency
- Heart-lung transplantation

4. Contraindications

None

5. Medical information necessary for planning

- Clear description of the indication (left and/or right ventricle)
- Previous history of cardiac disease
- Previous or current use of cardiotoxic medication

6. Radiopharmaceutical

Two intravascular tracers can be used: ^{99m}Tc-labelled erythrocytes (red blood cells, RBC) and ^{99m}Tc-labelled human serum albumin (HSA).

^{99m}Tc-labelled erythrocytes:

Erythrocytes can be labelled via an in vivo, an in vitro or a combined vivo/vitro technique. All three methods require pre-tinning of the red blood cells. A stannous agent is administered 10-30 min before ^{99m}Tc pertechnetate to allow Sn_{2+} ions to diffuse into the red blood cells. In presence of these Sn_{2+} ions, pertechnetate is reduced and is subsequently bound to haemoglobin.

In vivo labelling is the simplest and safest technique as it does not require handling of blood, however the labelling efficiency is generally lower and more variable.

In vitro labelling requires strict procedures as blood products are handled in the hotlab, it does provide the highest labelling efficiency.

In vivo / in vitro is a good compromise as it requires less cumbersome procedures regarding the blood products and it does provide sufficient labelling efficiency.

Activity: Administered activity ranges from 500 to 1050 MBq for adult patients. Paediatric dosage is calculated according to body weight with a minimum of 80 MBq.

Interactions: Several drugs (e.g. anthracyclines, heparin) have been reported to interfere with the stannous agent limiting the labelling efficiency leading to increased background activity.

^{99m}Tc-HSA:

^{99m}Tc-HSA can be used as an alternative to labelled RBCs. The main advantage is an easy and fast injection without the handling of blood products. The lesser stability of ^{99m}Tc binding to HSA, which does not allow scanning over a longer period of time, can be a disadvantage. Also HSA does not fully remain in the intravascular space which leads to slightly higher background activity.

Activity: Administered activity ranges from 370 to 925 MBq for adult patients. Paediatric dosage is calculated according to body weight with a minimum of 80 MBq.

Interactions: No drug interactions have been reported

7. Radiation safety

The effective doses are 0,007 mSv/MBq for ^{99m}Tc-labeled erythrocytes and 0,006125 mSv/MBq for ^{99m}Tc-HSA.

Pregnancy is a relative contraindication for both tracers.

According to ICRP 106 there is no need to interrupt breastfeeding, but due to possible free ^{99m}Tc pertechnetate it is advisable to interrupt the feeding for 4 h.

Only when using in vivo labelling a temporary interruption for 12 h according to IRCP 106 is advised

8. Patient preparation/essentials for procedure

No specific patient preparation is required

9. Acquisition and processing

Images are acquired using a standard gamma camera equipped with a low energy

collimator using ^{99m}Tc isotope settings, a matrix size of 64x64 with the heart occupying at least 50% of the field of view.
A minimum of 16 frames per R-R interval is required for an accurate measurement of the ejection fraction (EF) with a R-R interval tolerance window set to 10-20%. Measuring diastolic functional parameters requires a higher frame rate (32 or 64 frames / R-R).
The R-R interval tolerance is set to 20%, which means beats with a R-R interval 90 to 110% of a predefined or average heart rate are accepted. A higher tolerance leads to a less accurate study.
Images can be gated in several ways. In forward gating the R peak is used as the starting point to register counts into frames predefined as the mean heart cycle length (R-R interval) divided by the number of frames. As a result the first frames (systole) are more exact than the later frames (diastole) due to the changing cycle length during acquisition. In backward gating the R peak is used as the end point to register counts into frames preceding this R peak. In contrast to forward gating this results in more accurate diastolic frames than systolic frames.
The patient is imaged in a supine position. Images are most commonly acquired at a 45° camera angle which is known as the left anterior oblique (LAO) view or 'best septal' view as it usually allows the best separation of the left and right ventricles. The angle can be varied individually to provide optimal separation.
In order to asses regional function additional views can be used e.g. anterior view (45° less than the best septal view) or lateral view (45° greater than the best septal view). A caudal tilt may help separate the left ventricle and left atrium.
Several software packages are available to calculate different ventricular functional parameters and to generate a time activity curve and parametric images such as phase or amplitude images. These functional parameters are calculated using ventricular and background ROI's which can either be drawn manually or (semi-)automatically. The phase image can help discriminate valve planes when drawing ventricular ROI's. The background ROI should not be placed over the spleen, the stomach or the aorta.
A cine loop should be used to make a subjective visual assessment of left ventricular function. Discrepancies between the visually estimated and computer generated values should be resolved by reprocessing of the images. Inspection of the cine loop, the time activity curve, ROI placement and R-R histogram are necessary to ensure the quantitative results are consistent with the acquired data.

10. Interpretation

The most important goal of this technique is the measurement of the left ventricular ejection fraction (LVEF). It is calculated using background corrected counts and the following formula: EF = (ED-ES) / ED. Normal values vary from 50 to 80%.
LVEF accuracy can be compromised by several factors:

- Low ^{99m}Tc-RBC labelling efficiency
- Poor patient/camera positioning
- Gating errors: R peak not correctly triggering, > 20% R-R interval tolerance, high number rejected beats, heart rate variability
- Insufficient image statistics
- Processing errors

Regional wall motion can be assessed reviewing cine loop images combined with inspection of phase and amplitude images. Several software packages also provide regional ejection fraction calculation.
The cine loop can also be reviewed to assess chamber size, the pericardial space, the size of the pulmonary artery the aorta and any unusual extracardiac activity or artefacts.
Arrhythmias such as atrial fibrillation or frequent premature ventricular contractions can be assessed on the R-R interval histogram. The phase image can provide information on conduction abnormalities such as a left or right bundle branch block.
Several quantitative parameters (e.g. volumes and filling and emptying rates) can be extracted from the time activity curve.

11. Report

The report should summarize the test result as either normal or abnormal and provide the LVEF, most commonly presented as a percentage value.
A further description may be provided about:

- Possible technical problems during the test which may influence the result
- Cardiac morphology such as size and orientation, presence of extra cardiac abnormalities
- Global and regional contraction patterns
- Right ventricular function
- Quantitative parameters
- Comparison to previous studies, especially in oncology patients receiving cardiotoxic chemotherapy

12. Literature

- Society of nuclear medicine procedure guideline for gated equilibrium radionuclide ventriculography, 2002.
- ACR/SNM/SPR Practice guideline for the performance of cardiac scintigraphy, 2009.
- ACC/AHA/ASNC Guidelines for the Clinical Use of Cardiac Radionuclide Imaging-Executive Summary, 2002.
- EANM/ESC guidelines for radionuclide imaging of cardiac function, 2008.
- Aanbevelingen NVNG, Hoofdstuk Hartfunctiescintigrafie, 2007.
- Scintigraphic techniques for early detection of cancer treatment induced cardiotoxicity, J Nucl Med 2011; 52:560-71.