

Procedure Guideline for Planar Radionuclide Cardiac Ventriculogram for the Assessment of Left Ventricular Systolic Function

Version 2 2016
Review date 2021



Alice Nicol^a, Mike Avison^b, Mark Harbinson^c, Steve Jeans^d, Wendy Waddington^e, Simon Woldman^e (on behalf of BNCS, BNMS, IPEM).

^a Southern General Hospital, NHS Greater Glasgow & Clyde, Glasgow, UK ^b Bradford Royal Infirmary, Bradford, UK ^c Queens University, Belfast, UK ^d Christie Hospital NHS Foundation Trust, Manchester, UK ^e University College London Hospitals NHS Foundation Trust, London, UK

1. Introduction

The purpose of this guideline is to assist specialists in nuclear medicine in recommending, performing, interpreting and reporting radionuclide cardiac ventriculograms (RNVG), also commonly known as multiple gated acquisition (MUGA) scans. It will assist individual departments in the development and formulation of their own local protocols.

RNVG is a reliable and robust method of assessing cardiac function [1-5]. The basis of the study is the acquisition of a nuclear medicine procedure with multiple frames, gated by the R wave of the electrocardiogram (ECG) signal. The tracer is a blood pool agent, usually red blood cells labelled with technetium-99m (^{99m}Tc).

One aim of this guideline is to foster a more uniform method of performing RNVG scans throughout the United Kingdom. This is particularly desirable since the National Institute for Health and Clinical Excellence (NICE) has mandated national protocols for the pre-assessment and monitoring of patients undergoing certain chemotherapy regimes [6, 7], based on specific left ventricular ejection fraction (LVEF) criteria.

This guideline will focus on planar equilibrium RNVG scans performed for the assessment of left ventricular systolic function at rest, using data acquired in the left anterior oblique (LAO) projection by means of a frame mode, ECG-gated acquisition method. Guidance will be provided for the following data analysis and evaluation methods: quantitative estimation of global and regional LVEF, visual assessment of cine images (e.g. evaluation of the presence and extent of regional dysfunction) and visual assessment of amplitude & phase parametric images. The guideline is suitable for several referral criteria, including the evaluation of cardiac function in patients undergoing cardiotoxic drug therapy (e.g. chemotherapy).

There will not be detailed coverage of the following aspects of gated cardiac blood pool imaging: first pass acquisition, list mode acquisition and reframing, assessment of right ventricular function, quantitative indices of diastolic function, quantitative volume measurements, peak filling & ejection times and rates, acquisition for patients with significant disturbance of cardiac rhythm, studies performed at stress (exercise), tomographic RNVG.

RNVG allows the quantitative assessment of left ventricle (LV) dynamics and qualitative observation of wall motion. Because the LV overlies other dynamic

2. Methods of Guideline Development

vascular structures in some projections, quantitative analysis can only be carried out in an LAO projection. However, other projections may be acquired for qualitative assessment of motion on walls which are not observable on the LAO view.

The writing group consisted of medical and scientific staff experienced in radionuclide cardiac ventriculograms. Members of the British Nuclear Cardiology Society (BNCS) committee, British Nuclear Medicine Society (BNMS) Professional Standards & Education committee, Institute of Physics and Engineering in Medicine (IPEM) Nuclear Medicine Special Interest Group, and UK Radiopharmacy Group provided comments on drafts of the guideline. The final document was endorsed by BNCS, BNMS and IPEM.

A systematic literature search of Pub Med / MEDLINE from January 1970 to February 2008 was performed. The following search was undertaken: radionuclide ventriculography OR {(gated blood-pool imaging OR ventricular ejection fraction OR ventricular function) AND (radionuclide imaging OR nuclear medicine OR radioisotope OR scintillation counting)}. The following terms were excluded: stress, exercise, right, first pass, tomography, emission-computed, tomography x- ray, echocardiography, MRI, perfusion, hypertension, cardiomyopathies, heart valves, Diabetes Mellitus, infarc*, coronary artery bypass, heart failure, transplants, surgery, clinical trial. Only literature on human subjects written in English were considered. A total of 510 references were obtained using this search. In addition, previous published guidelines were reviewed (American Society of Nuclear Cardiology (ASNC) guideline on equilibrium radionuclide angiocardiology [8], Society of Nuclear Medicine (SNM) Procedure Guideline for Gated Equilibrium Radionuclide Ventriculography [9]). The papers considered to be most representative from the literature search and additional relevant papers identified from published guidelines & the writing group are included in this document.

Relevant data were reviewed by members of the writing group and discrepancies were reconciled by consensus. All recommendations are therefore based on either evidence from clinical studies, previous published guidelines or expert opinion of the writing group and comments received from members of professional organisations.

3. Guideline Indications

Many indications for RNVG have appeared in the literature, though some are used predominantly in specialist settings and several have not been adopted into routine clinical practice. The most common reason for requesting a RNVG scan is routine assessment of left ventricular systolic function. This section lists the common, and some less frequently used indications for RNVG scans and briefly comments on some of the most important aspects.

3.1 Standard indications for RNVG

3.1.1 Measurement of left ventricular systolic function

This has been performed in several clinical scenarios, all of which have an evidence base. The indications below have generally been endorsed in guideline statements for RNVG use [8, 9].

- Coronary artery disease (stable coronary artery disease for prognosis [10-12], after myocardial infarction [13, 14]). Left ventricular function, most frequently assessed by left ventricular ejection fraction, is one of the strongest prognosticators in coronary disease. Hence LVEF derived from RNVG carries important information in both stable disease (such as angina), and in patients with myocardial infarction.
- Suspected heart failure (e.g. selection of patients for ACE inhibitor) [15, 16]
- Patients receiving cardiotoxic chemotherapy (e.g. anthracyclines, trastuzumab) [17-19]. Various chemotherapeutic agents are known to be associated with a risk of developing left ventricular systolic dysfunction and heart failure. One such agent is herceptin (trastuzumab), used for the treatment of breast cancer. It is directed against cancers which express the HER2 (Human EGF-like Receptor No. 2) protein and in such cases reduces mortality and recurrence [20]. However, large trials have shown that the drug may be cardiotoxic. Left ventricular systolic impairment, and eventually heart failure, occurred in between 2% to 27% of patients, depending on clinical profile [21]. NICE has approved the use of herceptin [6, 7], but with cardiac monitoring. Given its accuracy and reproducibility, RNVG is well placed to undertake this monitoring.

- Valvular heart disease [22]. Resting or exercise induced changes in LVEF in patients with valvular disease may help in decision making regarding the timing of cardiac surgery.

The RNVG study may be performed initially for baseline assessment and for prognosis. The technique is also particularly suitable for repeated follow up studies (due to its good reproducibility and repeatability) which are particularly indicated in some of the above populations, for example to monitor LVEF during potentially cardiotoxic chemotherapy [3, 23].

3.1.2 Measurement of right ventricular (RV) systolic function

The assessment of right ventricular systolic function is beyond the scope of these guidelines and is becoming more infrequent with the advent of alternative imaging techniques. However, studies for this indication are still performed in specialist centres e.g. in patients with congenital heart disease or valvular heart disease. RNVG has also been used to assess RV function in patients with possible right ventricular cardiomyopathy, though this is being superseded by cardiac magnetic resonance imaging [24, 25].

3.2 Infrequent indications for RNVG

There have been many other uses for RNVG but, in general, these have been superseded by other imaging techniques or have not been reproducible in clinical practice and hence are not in routine clinical use. Many are based on evidence, and some are still used in a specialist setting e.g. assessment of patients with cardiac transplantation. However, these specialist applications are beyond the scope of these guidelines.

3.3 Relative contra-indications for RNVG

3.3.1 Pregnancy

3.3.2 Breast feeding – advice regarding patients who are breast feeding may be obtained from the ARSAC Notes for Guidance on the Clinical Administration of Radiopharmaceuticals and

3.3.3 Significant disturbance of cardiac rhythm, e.g. atrial fibrillation, is a relative contraindication for frame mode RNVG as it can compromise the accuracy of the test.

4. Radiopharmaceutical and administration

4.1 Labelling of red blood cells

In vivo, modified in-vivo [26] or in vitro methods may be used for the labelling of red blood cells with ^{99m}Tc for gated blood pool imaging. The superiority order of labelling is reported to be: in vitro method, modified in-vivo, in vivo method [27]. However, the in-vivo method has gained widespread use in UK due to its convenience and provision of satisfactory image quality in most instances.

4.1.1 In-vivo labelling

The first stage of in-vivo labelling is the intravenous administration of a stannous agent (a reducing agent), generally pyrophosphate or medronate. Information on the dose and method of administration may be obtained from the SPC (summary of product characteristics). This first administration results in stannous loading of red blood cells, facilitating the accumulation of ^{99m}Tc pertechnetate, which is administered approximately 20 minutes later (time interval as per SPC).

4.2 Administration—practical aspects

4.2.1 The ARSAC diagnostic reference level for ^{99m}Tc normal erythrocytes for gated cardiac blood pool imaging in adult studies is 800MBq [28]. The corresponding effective dose in healthy subjects is 6mSv. Further information on dosimetry may be obtained from ICRP 80 [29].

4.2.2 The use of ^{99m}Tc pertechnetate produced from a generator without excessive ingrowth time should be considered [30]. However, this is not generally seen as a practical problem in most departments.

4.2.3 The stannous agent and ^{99m}Tc pertechnetate are administered intravenously. If possible, avoid the use of

intravenous (i.v.) lines for either injection as these may contain large volumes of heparin and may have a teflon coating which may interfere with the cell labelling.

- 4.2.4** For patients with difficult venous access, consider giving both injections using an intravenous cannula. For patients who have had unilateral breast surgery, it is recommended that i.v. administrations are into an arm vein on the opposite side.

4.3 Interaction with other medicinal products

Certain medications are known to interfere with red blood cell labeling. A list of the patient's medications should be available. Medicinal products to consider include: heparin, beta blockers (e.g. propranolol), anthracycline antibiotic, digitalis related compounds, dextran, penicillin and iodinated contrast media [31]. Further information on interaction with other medicinal products should be obtained from the SPC.

4.4 Contra-indications

See SPC of stannous agent e.g. stannous pyrophosphate, stannous medronate.

5. Data acquisition and analysis

- 5.1** Serial acquisitions for an individual patient should be performed using the same data acquisition and analysis processes.

5.2 Equipment Quality Assurance (QA)

- 5.2.1** The gamma camera should be subject to a routine QA program in accordance with national guidelines.

- 5.2.2** The adequacy of the R-wave trigger should be assessed prior to gated acquisitions.

5.3 Preparation

- 5.3.1** The procedure should be explained to the patient.

- 5.3.2** It should be suggested that the patient goes to the toilet before the procedure in order to maximise compliance during acquisition.

- 5.3.3** The patient should be positioned supine on the imaging couch. After preparing the skin, place electrodes on the patient's chest as follows: RA (right arm) – right shoulder, just below the clavicle, LA (left arm) – left shoulder just below the clavicle, LL (left leg) – lower left chest. Best quality of signal is achieved with the leads placed over the bony prominences, taking care to avoid areas where muscle movement may occur.
- 5.3.4** The ECG trace should be observed to check for an adequate signal. The trace should show clear R waves at regular intervals which provide a trigger to the gamma camera. Care should be taken to ensure that triggering is occurring on the R wave and not the T wave of the ECG. If this is not the case, adjustment may be required of the gating signal on the ECG monitor. If this fails to provide a suitable ECG signal, it may be necessary to reposition the ECG electrodes. Ideally, the adequacy of the ECG trace should be checked prior to administration of the stannous agent and ^{99m}Tc pertechnetate.
- 5.3.5** The optimal LAO position for imaging is that in which the left ventricle is seen separate from the other structures of the heart. This may be determined using the persistence mode or by acquiring a series of short scout views at a range of different imaging positions (see section 5.3.8). Best separation is usually seen with a LAO projection in the range of 30 to 45 degrees and 10 to 15 degrees of caudal tilt. A caudal tilt may be achieved by tilting the camera if this movement is allowed, using a slant hole collimator, or else by adjusting the patients position to produce a 10 to 15 degree incline.
- 5.3.6** The acquisition should be set up with the left ventricle centred in the field of view. Images should be acquired, with a zoom applied if necessary, so that the heart occupies ~50% of the usable field

of view [9].

5.3.7 The patient should be relaxed before starting the acquisition. During the acquisition, the atmosphere in the camera room should be kept calm and quiet so that the patient is relaxed and there are no stimuli which may modify their heart rate.

5.3.8 Scout views to determine the optimal LAO position for imaging:

5.3.8.1 If performing scout views, typically, four views should be acquired at LAO 45°, 40°, 35° and 30°, with 10 to 15 degrees of caudal tilt. These should be inspected to determine the camera angle showing the best separation between the left ventricle and other structures in the heart.

5.3.8.2 The acquisition parameters should be adjusted according to local preference e.g. reduced no. of frames per cycle and counts acquired. Indeed, some centres may prefer to use un-gated images, and may prefer to acquire for a fixed length of time. The only requirement is that images produced are of sufficient quality to judge the optimum angle for LV separation.

5.3.8.3 When performing repeat investigations, it is still advisable to carry out the scout views, in case there has been any gross change in cardiac anatomy. The best view for left ventricular separation should be selected, which will usually be the same as for previous investigations.

5.3.9 The angle at which the LAO image is acquired should be recorded so it is available if the patient is referred for repeat investigations.

5.3.10 For determination of LVEF, no views other than LAO are necessary. However, if further investigation of wall motion is

required, images should be acquired in approximate anterior and left lateral projections. The angles for these images should be rotated +/-45° from the optimum LAO angle.

5.4 Data Acquisition

5.4.1 Acquisition parameters

For determination of LVEF, the following acquisition parameters produce satisfactory image quality in most instances [8, 9, 32-36]

Collimator	A LEGP collimator is generally utilised, although a LEHR collimator may be suitable, depending on sensitivity and spatial resolution [8,9]
Energy window	15-20% at 140keV (^{99m} Tc)
Pixel size	of the order of 2 - 4 mm [8]
Beat rejection window	± 10% to ±15% [8]
Gating	Frame mode gating (forward framing) with a fixed time per frame is the usual method [8].
Counts	Of the order of 500k to 1M total counts in the LV. (total acquisition times are typically 10 to 15 minutes)
No. of frames/cycle	A frame rate of ≥ 24 frames per cycle is preferred [8, 9, 32]

5.4.2 Termination of the study may be based on counts acquired or acquisition time. Written protocols must include advice on modifying the acquisition parameters in the event of low count rates.

5.4.3 During the acquisition, it is important to monitor the number of beats

rejected. If a large number is being rejected (e.g. > 20%), consider repeating the study after the patients heart rate has settled or widening the R-R interval tolerance in cases of arrhythmia. Consideration may be given to list mode acquisition with subsequent reformatting of the data (outwith the scope of these guidelines).

5.4.4 Before the patient leaves the department, a preliminary review of the acquisition in cine mode should be performed to ensure the image data is satisfactory. Review positioning of the heart, adequacy of radiopharmaceutical labelling (e.g. checking stomach / thyroid uptake) and count statistics. If uncertain, the data should be analysed at this point to check the software analysis of LVEF. Additionally, a check of the injection site may be helpful if extravasation is suspected.

5.5 Data Analysis

5.5.1 The data should be reviewed to determine the percentage of rejected beats. If a significant number were rejected (e.g. > 20%), this should be noted and made available to the operators undertaking the data review and clinical evaluation. A local decision will have to be made as to whether the LVEF determined from the data will be reliable.

5.5.2 A subjective visual assessment of left ventricular systolic function should be performed before calculation of LVEF.

5.5.3 Determination of LVEF will normally be carried out using software packages. These packages should be validated locally e.g. using a standard set of data [37, 38] or a cardiac phantom [39, 40].

5.5.4 Software to smooth the image data, both spatially and temporally, may be applied as required. The smoothing applied may affect quantification [41], and centres should consider consistent filters for all studies.

5.5.5 Region of interest definition

- 5.5.5.1** Regions of interest (ROI) are determined around the left ventricle. These are defined at end diastole (ED) and end systole (ES) as a minimum and may be drawn manually or automatically. All the counts from the radiopharmaceutical in the LV should be included in each ventricular ROI.
- 5.5.5.2** The frame for drawing the ED ROI should correspond to maximum counts in the LV. This is often the first frame. The use of the final frames for ED ROI counts may be sub-optimal as a result of “drop off” due to heart rate variability.
- 5.5.5.3** When delineating LV ROIs, it is often useful to view the regions on the phase and amplitude parametric images (the phase image shows the relative timing at which each pixel in the gated image contracts, whilst the amplitude image shows the magnitude of these contractions).
- 5.5.5.4** A small number of centres estimate LVEF using a single ROI drawn around the LV at ED. This usually results in a different normal range for LVEF relative to the use of ROI's defined at both ED and ES. Careful consideration must be given to this variation in technique as referrals and follow up studies may move between centres.
- 5.5.5.5** A background (BG) ROI is also defined, normally adjacent to the infero-lateral wall of the LV. This ROI should be representative of the background counts within the LV and should not include any vessels, organs or other areas of high radiopharmaceutical uptake. Avoid overlapping with the ED ROI. Consistent placement of the BG ROI is important.
- 5.5.5.6** If ROI's are defined automatically, they should be available for the operator to review and adjust, if necessary. Automatic ROI definition should work for the majority of studies and should give

reproducible results on all studies [42-44]. However, there may be occasions when inappropriate ROIs are generated and an incorrect value for LVEF calculated. Manual ROI adjustment should be performed in these circumstances. Fully automatic software usually refers to software in which no operator intervention is possible, and semi-automatic methods are preferred.

5.5.6 The LVEF is determined from the BG corrected counts within the LV at ED and ES using the formula:

$$EF (\%) = \left(\frac{EDcounts_{BG\ corrected} - EScounts_{BG\ corrected}}{ED\ counts_{BG\ corrected}} \right) \times 100$$

5.5.7 The EF obtained should be compared with the subjective visual assessment (section 5.5.2), and discrepancies resolved (e.g. re-processing study, taking advice from experienced operators as required).

5.5.8 A curve is produced to represent the counts in the ROI through the LV cycle. This curve may be produced using (i) LV ROI's defined on each frame of the gated image or (ii) a single LV ROI defined at ED. It is preferable that the former method is utilised.

5.5.9 There are variations on the above analysis methods which may produce satisfactory results. For example, some software packages have curve-fitting algorithms to fit a curve to the individual LV ROI counts for each frame to better determine the ED and ES counts, and thereby the LVEF. This is acceptable if the results are validated against the other methods [45].

5.5.10 When processing RNVG studies, it is useful to have available the results of any previous studies for the patient. This will help to ensure consistency in the drawing of ROIs and hence the reproducibility of the method.

5.5.11 It is important that detailed work instructions for performing data analysis are available. Processing must only be carried out by staff who have received adequate training in the technique and have training records to demonstrate this.

5.5.12 It is recommended that two members of staff process each study and their results should agree to within locally defined limits. If there is a discrepancy between the results, a further opinion may be obtained. Inter-operator variability standard deviation values for analysis of the order of three percentage points, and certainly less than five percentage points, should be attainable [38, 46]. The inter-operator variability may depend on whether automated, semi-automated or manual analyses are performed.

5.5.13 The computer monitors used to analyse, review and clinically evaluate data should be of sufficient quality to permit these operations to be performed.

6. Data review

A review of each study should be performed prior to clinical evaluation as a quality assurance procedure. In some centres, this review may be performed by the operator undertaking the clinical evaluation, whilst in other centres it may be undertaken by a different operator in which case any findings noted at review should be communicated to the operator responsible for the clinical evaluation.

6.1 Data acquisition: Any deviations from the acquisition protocol in terms of radiopharmaceutical preparation and administration, patient preparation, data acquisition must be checked for and noted

6.2 An assessment of the adequacy of the acquired counts should be made. This may be visual or quantitative in the first instance. If required, quantitative information (e.g. number of counts present in LV ED ROI in the first gated frame) should be available.

6.3 The cine image display should be critically reviewed with respect to the

adequacy of ECG gating and labelling efficiency [8]. Uptake in the stomach and / or thyroid may indicate suboptimal labeling efficiency.

6.4 The accuracy of the ROI delineation should be assessed:

6.4.1 The LV ROI's should be reviewed to ensure that they include all the counts from the radiopharmaceutical in the LV and no extraneous activity (e.g. left atrium, right ventricle, spleen, descending aorta) [8, 9]. However, it is acknowledged that some overlap with the left atrium is frequently unavoidable.

6.4.2 The background ROI should be reviewed to ensure that it is representative of the background counts within the LV and does not contain any vessels, organs or other areas of high radiopharmaceutical uptake (e.g. atria, left ventricle, aorta, spleen or stomach) [8].

7. Data to be available for operator undertaking clinical evaluation

The following information should be available to the operator performing the clinical evaluation of the gated blood pool scan.

7.1 Any aspects of the study that deviate from the protocol

7.2 Any matters raised in the review process of section 6 above.

7.3 Key details of the procedure: administered activity, radiolabelling agent and labelling technique (in vitro, modified in vivo, in vivo), patient positioning (e.g. rest 45° LAO, with 15° caudal tilt).

7.4 LVEF:

7.4.1 this should preferably be stated as an integer percentage value to reflect the attainable level of accuracy of this estimation.

7.4.2 The validated normal range for LVEF should be clearly stated where

this is as determined by the institution, and for the protocol that has been used to acquire the study.

7.5 QA of gating data:

7.5.1 mean R-R interval

7.5.2 total number of beats accepted

7.5.3 total number of beats rejected / percentage of beats accepted

7.6 R-R histogram should also be displayed (if possible)

7.7 Continuous cine loop display of gated dataset [8, 9], with the spatial and/or temporal filtering applied by the processing software. A linear gray scale should be used [8], taking care to ensure that the display is normalised to the hottest pixel within the heart if significant extracardiac activity is seen [8]. Cine display may not be available if reporting is performed on a PACS workstation. If this is the case, the cine display may need to be reviewed separately on a nuclear medicine workstation. It may be useful for the operator undertaking clinical evaluation to be told whether any end-cycle frames have been 'dropped' due to low count statistics by the processing software to remove visual 'flicker'.

7.8 ROI's: These should be displayed on the image; preferably either as an operator removable overlay or on an adjacent copy of the dataset.

7.9 The ED frame number should be stated and the frame displayed. The ES frame number should be stated and the frame may be displayed.

7.10 Phase and amplitude parametric images should be displayed, together with a phase histogram. An appropriate colour map should

be used – i.e. one suitable for the display of parametric data with discrete intervals, rather than subtle colour gradations across a continuous spectrum. These can be used to evaluate regional variations in timing and magnitude of contraction, identifying valve planes and conduction abnormalities [9].

7.11 If determined, regional LVEF values should be displayed within a graphic segmented LV overlay.

7.12 Resultant LVEF curve should be displayed, with clearly annotated X and Y axes. It should be known to the interpreter whether the displayed curve is fitted to the individual frame data points, or not, and whether these data points have been scaled.

8. Interpretation of gated blood pool scan

8.1 General

8.1.1 In interpreting the result of a gated blood pool scan, it is essential to incorporate the reported result, the known clinical details and the reason for request. Analysis and reporting of the phase, amplitude, and cine images are often just as essential as the reporting and interpretation of the ejection fraction.

8.2 Left ventricula rejection fraction

8.2.1 The normal range for ejection fraction varies by the radionuclide acquisition technique and analysis method used. It is thus essential that the LVEF is interpreted with reference to a previously validated normal range for that institution.

8.2.2 Furthermore, the LVEF may vary quite considerably between different techniques of measuring it. For example, results may not be directly comparable between radionuclide techniques and echocardiography, and it is important for the reporting operator to highlight this in the

report as required. For repeatability, serial scans for an individual patient should ideally be performed using the same technique (e.g. during a course of chemotherapy).

8.2.3 Assuming a normal institutional value of > 50% for LVEF, an LVEF of 40-50% represents mildly impaired LV function, 30-40% moderately impaired LVEF, and 20-30% severely impaired LVEF and <20% very severely impaired LVEF.

8.2.4 Equilibrium radionuclide ventriculography is a highly reproducible technique. The significance of changes in left ventricular function should be assessed using local measurements of intra- and inter- operator variability.

8.3 Amplitude, phase, and cineanalysis

8.3.1 The LAO cine image display should be critically reviewed with respect to the position and presentation of the heart and the presence of significant arrhythmia or rhythm abnormalities [8]. Where acquired, the anterior and lateral cine views should also be assessed for regional wall motion abnormalities indicating the possibility of ischaemic heart disease as a cause for any deterioration in LV function. However it is to be noted that other causes of LV dysfunction. e.g. dilated cardiomyopathy, can also cause apparent regional wall motion abnormality, even in the absence of left bundle branch block (LBBB).

8.3.2 If the LVEF is impaired, it is important to look for clues as to the possible cause. For example regional, as opposed to global wall motion abnormality may represent ischaemic heart disease. This can be quantified if necessary, by the measurement of regional ejection fraction, although this remains a useful research tool, rather than a clinical one.

8.3.3 A careful examination of the amplitude, phase and cine images is thus mandatory for detection of akinetic or dyskinetic function. It may be possible to comment on likely size of the left ventricle from the raw data cine images. Caution is required for patients with LBBB. This pattern of ventricular activation represents disease of the His-Purkinje electrical conduction system. Whilst LBBB is commonly associated with major left ventricular contractile dysfunction, it is sometimes associated with normal or near normal global LV systolic function.

8.3.4 In either event, LBBB is associated with a characteristic pattern on the phase and amplitude images, where the ventricle contracts dyssynchronously. This should not be confused with regional dysfunction caused by ischaemic heart disease, but it may be impossible to differentiate the cause of the regional dysfunction, purely on the basis of the radionuclide ventriculogram.

9. Controversies/ Issues requiring further clarification

9.1 Time interval between repeat scans (toxicity of stannous salts)

9.2 LVEF analysis using a single LV ROI.

9.3 Standardisation of LVEF values and normal ranges [47]

9.4 There is some evidence that early detection of diastolic dysfunction may indicate subsequent systolic dysfunction in patients treated with chemotherapy [48]. This lies outside the scope of this guidance, but such judgements should only be made in centres experienced in this regard, as inappropriate cessation of chemotherapy may follow.

10. Acknowledgements

Thank you to the following who contributed comments during development of the guidelines: UK Radiopharmacy Group, BNMS PSE committee, IPEM Nuclear Medicine SIG, BNCS committee, Sarah Hiscock.

11. Notes

This guideline must be read in conjunction with the BNMS Generic Guidelines.

Abbreviations used:

ARSAC	Administration of Radioactive Substances Advisory Committee
LEGP	low energy general purpose
LEHR	low energy high resolution
PACS	picture archiving and communication system

References

1. Marshall RC, Berger HJ, Reduto LA, Gottschalk A, Zaret BL. Variability in sequential measures of left ventricular performance assessed with radionuclide angiocardiology. *Am J Cardiol* 1978; 41: 531-536.
2. Bacharach SL, Green MV, Borer JS. Instrumentation and data processing in cardiovascular nuclear medicine: Evaluation of ventricular function. *Semin Nucl Med* 1979; 9: 257-274
3. Wackers FJ, Berger HJ, Johnstone DE, Goldman L, Reduto LA, Langou RA et al. Multiple gated cardiac blood pool imaging for left ventricular ejection fraction: validation of the technique and assessment of variability. *Am J Cardiol* 1979; 43:1159-66.
4. Brodin LA, Bone DE. Effect of acquisition and analysis routines on gated blood pool measurements. *Clin Physiol* 1990; 10: 439-450.
5. Zaret BL, Wackers FJ. Nuclear cardiology – Second of two parts. *N Engl J Med* 1993; 329: 855-863.
6. National Institute for Health and Clinical Excellence, March 2002, Technology Appraisal 34 "Guidance on the use of trastuzumab for the treatment of advanced breast cancer". Available from <http://www.nice.org.uk>. (accessed 10.10.08)

7. National Institute for Health and Clinical Excellence, August 2006, Technology Appraisal 107 "Trastuzumab for the adjuvant treatment of early stage HER2-positive breast cancer". Available from <http://www.nice.org.uk> (accessed 10.10.08)
8. Corbett JR, Akinboboye OO, Bacharach SL, Borer JS, Botvinick EH, DePuey EG et al. Quality Assurance committee of the American Society of Nuclear Cardiology. Equilibrium radionuclide angiocardiology. *J Nucl Cardiol* 2006; 13: e56-79
9. Scheiner J, Sinusas A, Wittry MD, Royal HD, Machac J, Balon HR et al. Society of Nuclear Medicine Procedure Guideline for Gated Equilibrium Radionuclide Ventriculography. SNM Procedure Guidelines Manual, June 2002. Available from <http://www.snm.org> (accessed 10.10.08)
10. Bonow RO, Bacharach SL, Green MV, Kent KM, Rosing DR, Lipson LC, et al. Impaired left ventricular diastolic filling in patients with coronary artery disease: assessment with radionuclide angiography. *Circulation* 1981; 64:315-23.
11. Mancini GB, Slutsky RA, Norris SL, Bhargava V, Ashburn WL, Higgins CB. Radionuclide analysis of peak filling rate, filling fraction, and time to peak filling rate. Response to supine bicycle exercise in normal subjects and patients with coronary disease. *Am J Cardiol* 1983; 51:43-51.
12. Pryor DB, Harrell FE, Lee KL, Rosati RA, Coleman RE, Cobb FR, et al. Prognostic indicators from radionuclide angiography in medically treated patients with coronary artery disease. *Am J Cardiol* 1984; 53:18-22.
13. Ritchie JL, Cerqueira M, Maynard C, Davis K, Kennedy JW. Ventricular function and infarct size: the Western Washington Intravenous Streptokinase in Myocardial Infarction Trial. *J Am Coll Cardiol*. 1988; 11: 689-697.
14. Morgan CD, Roberts RS, Haq A, Baigrie RS, Daly PA, Gent M, Armstrong PW. Coronary patency, infarct size and left ventricular function after thrombolytic therapy for acute myocardial infarction: results from the tissue plasminogen activator: Toronto (TPAT) placebo-controlled trial. TPAT Study Group. *J Am Coll Cardiol*. 1991; 17: 1451-1457.
15. Pfeffer MA, Braunwald E, Moyer LA, Basta L, Brown EJ, Cuddy TE. et al. Effect of captopril on mortality and morbidity in patients with left ventricular dysfunction after myocardial infarction: Results of the Survival and Ventricular Enlargement Trial. The SAVE Investigators. *N Engl J Med*. 1992; 327: 669-677.

16. Waagstein F, Bristow MR, Swedberg K, Camerini F, Fowler MB, Silver MA. et al. Beneficial effects of metoprolol in idiopathic dilated cardiomyopathy: Metoprolol in Dilated Cardiomyopathy (MDC) Trial Study Group. *Lancet*. 1993; 342: 1441-1446.
17. Schwartz RG, McKenzie WB, Alexander J, Sager P, D'Souza A, Manatunga A, et al. Congestive heart failure and left ventricular dysfunction complicating doxorubicin therapy. Seven- year experience using serial radionuclide angiocardiology. *Am J Med* 1987; 82: 1109 – 1118.
18. Shureiqi I, Cantor SB, Lippman SM, Brenner DE, Chernew DE, Fendrick AM. Cinical and economic impact of multiple gated acquisition scan monitoring during anthracycline therapy. *Br J Cancer* 2002; 86: 226-232.
19. Mitani I, Jain D, Joska TM, Burtness B, Zaret BL. Doxorubicin cardiotoxicity: prevention of congestive heart failure with serial cardiac function monitoring with equilibrium radionuclide angiocardiology in the current era. *J Nucl Cardiol*. 2003; 10:132-9.
20. Piccart-Gebhart MJ, Procter M, Leyland-Jones B, Goldhirsch A, Untch M, Smith I et al.. Trastuzumab after adjuvant chemotherapy in HER2-positive breast cancer. *N Engl J Med* 2005;353:1659-72
21. Routledge HC, Rea DW and Steeds RP. Monitoring the introduction of new drugs – Herceptin to cardiotoxicity *Clin Med* 2006;6:478–81
22. Borer JS, Hochreiter C, Herrold EM, Supino P, Aschermann M, Wencker D, et al. Prediction of indications for valve replacement among asymptomatic or minimally symptomatic patients with chronic aortic regurgitation and normal left ventricular performance. *Circulation* 1998; 97:525-34.
23. Palmeri ST, Bonow RO, Myers CE, Seipp C, Jenkins J, Green MV, et al. Prospective evaluation of doxorubicin cardiotoxicity by rest and exercise radionuclide angiography. *Am J Cardiol*. 1986; 58:607-13.
24. Le Guludec D, Slama MS, Frank R, Faraggi M, Grimon G, Bourguignon MH, et al. Evaluation of radionuclide angiography in diagnosis of arrhythmogenic right ventricular cardiomyopathy. *J Am Coll Cardiol* 1995; 26:1476-83.
25. Le Guludec D, Gauthier H, Porcher R, Frank R, Daou D, Benelhadj S, et al. Prognostic value of radionuclide angiography in patients with right ventricular arrhythmias. *Circulation* 2001; 103:1972-6.
26. Callahan RJ, Froelich JW, McKusick KA, Leppo J, Strauss HW. A modified method for the in vivo labeling of red blood cells with Tc-99m: concise communication. *J Nucl Med* 1982; 23: 315- 318.

27. Armstrong LK, Ruel JM, Christian PE, Taylor A . Variation in gated blood pool image quality using in vivo, modified in vivo, and invitro red blood cell labeling techniques. J Nucl Med Technol 1986; 14: 63-65.
28. Administration of Radioactive Substances Advisory Committee. Notes for Guidance on the Clinical Administration of Radiopharmaceuticals and Use of Sealed Radioactive Sources. From <http://www.arsac.org.uk> (accessed 10.10.08)
29. International Commission on Radiological Protection. ICRP Publication 80: Radiation dose to patients from radiopharmaceuticals. Annals of the ICRP, vol 28, 1998.
30. Kelly MJ, Cowie AR, Antonino A, Barton H and Kalf V. An assessment of factors which influence the effectiveness of the modified in vivo technetium-99m-erythrocyte labeling technique in clinical use. J Nucl Med 1992; 33:2222-2225
31. Saha GB Fundamentals of Nuclear Pharmacy. Springer, 2003
32. Bacharach SL, Green MV, Borer JS, Hyde JE, Parkas SP, Johnston GS. Left-ventricular peak ejection rate, filling rate, and ejection fraction – Frame rate requirements at rest and exercise: Concise communication. J Nucl Med 1979; 20:189-193
33. Bacharach SL, Green MV, Bonow RO, Findley SL, Daube-Witherspoon ME, Larson SM. The effect of energy window on cardiac ejection fraction. J Nucl Med 1988; 29: 385-391.
34. Juni JE, Chen CC. Effects of gating modes on the analysis of left ventricular function in the presence of heart rate variation. J Nucl Med 1988; 29: 1272-1278.
35. Bacharach SL, Bonow RO, Green MV. Comparison of fixed and variable temporal resolution methods for creating gated cardiac blood-pool image sequences. J Nucl Med 1990; 31: 38-42.
36. Pennell DJ, Prvulovich E. Clinicians Guide to Nuclear Medicine: Nuclear Cardiology. London UK: BNMS, 1995.
37. Skrypniuk JV, Bailey D, Cosgriff PS, Fleming JS, Houston AS, Jarritt PH et al. UK audit of left ventricular ejection fraction estimation from equilibrium ECG gated blood pool images. Nucl Med Commun 2005; 26: 205-215
38. Hiscock SC, Evans MJ, Morton RJ, Hall DO. Investigation of normal ranges for left ventricular ejection fraction in cardiac gated blood pool imaging studies using different processing workstations. Nucl Med Commun 2008; 29: 103-109

39. De Bondt P, Vandenberghe S, De Mey S, Segers P, De Winter O, De Sutter J et al. Validation of planar and tomographic radionuclide ventriculography by a dynamic ventricular phantom. *Nucl Med Commun* 2003; 24:771-777.
40. De Bondt P, De Winter O, Vandenberghe S, Vandevijver F, Segers P, Bleukx A et al. Accuracy of commercially available processing algorithms for planar radionuclide ventriculography using data for a dynamic left ventricular phantom. *Nucl Med Commun* 2004; 25: 1197-1202
41. Bonow RO, Bacharach SL, Crawford-Green C, Green MV. Influence of temporal smoothing on quantitation of left ventricular function by gated blood pool scintigraphy. *Am J Cardiol*. 1989; 64:921-5.
42. Bourguignon MH, Douglass KH, Links JM, Wagner HN. Fully automated data acquisition, processing, and display in equilibrium radioventriculography. *Eur J Nucl Med* 1981; 6: 343-347.
43. Douglass KH, Tibbits P, Kasecamp W, Han ST, Koller D, Links JM et al . Performance of a fully automated program for measurement of left ventricular ejection fraction. *Eur J Nucl Med* 1982; 7: 564-566
44. Reiber JHC, Lie SP, Simoons ML, Hoek C, Gerbrands JJ, Wijns W, et al. Clinical validation of fully automated computation of ejection fraction from gated equilibrium blood-pool scintigrams. *J Nucl Med* 1983; 24: 1099-1107.
45. Wagner RH, Halama JR, Henkin RE, Dillehay GL, Sobotka PA. Errors in the determination of left ventricular functional parameters. *J Nucl Med* 1989; 30: 1870-1874
46. Hains AD, Al-Khawaja I, Hinge DA, Lahiri A, Raftery EB. Radionuclide left ventricular ejection fraction: a comparison of three methods. *Br Heart J* 1987; 57: 242-6.
47. Fleming JS. Standardisation of LVEF values from MUGA scanning. *Nucl Med Commun*. 2008; 29: 91.
48. Dorup I, Levitt G, Sullivan I, Sorensen K. Prospective longitudinal assessment of late anthracycline cardiotoxicity after childhood cancer: the role of diastolic function. *Heart* 2004; 90; 1214-1216

Whilst every effort has been made to ensure the BNMS provides accurate and expert information and guidance, it is impossible to predict all the circumstances in which it may be used. Accordingly the BNMS shall not be liable to any person or entity with respect to any loss or damage caused or allege to be caused directly or indirectly by what is contained in or left out of this guidance.

Reviewed: Dr Kshama Wechalekar 2016

Date for review: 2021