Continuing Education Series

Pediatric Nuclear Cardiology

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This is the third of a four-part continuing education series on pediatric nuclear medicine. After reading and studying the article, the nuclear medicine technologist will be able to: (1) identify important clinical indications for performing nuclear cardiology procedures in children, (2) identify the radiopharmaceuticals that are used to perform myocardial imaging, first pass angiocardiography, and gated blood pool imaging, (3) discuss important technical considerations for performing these procedures in children, and (4) describe the information derived from computer analysis of data gathered during these procedures. Information about CEU(VOICE) credit appears immediately following this article.

Progress in nuclear medicine instrumentation and radiopharmaceuticals has greatly expanded the scope and acceptance of pediatric nuclear cardiology. This article will discuss first pass radionuclide angiocardiography, myocardial scintigraphy, and gated blood pool scintigraphy as they apply to children.

First Pass Radionuclide Angiocardiography

This method relies on the initial passage of a bolus of radiotracer through the central circulation; therefore, patient position and cooperation are essential.

The most common indications for first pass radionuclide angiocardiography are:

(1) Detection, localization, and quantification of left-to-right shunts and right-to-left shunts

(2) Determination of cardiac output, left and right ventricular ejection fraction, stroke volume, and end-diastolic volume

(3) Evaluation of the cyanotic newborn

(4) Postoperative evaluation of patients undergoing cardiovascular surgery

(5) Assessment of function and patency of palliative shunts, and

(6) Assessment of patency, deviation, dilatation, and congenital abnormalities of large vessels.

The assessment of right and left ventricular ejection fractions during rest and exercise has also become important in the pediatric patient. Causes for right and left ventricular dysfunction in children are anomalous coronary artery, myocarditis, long-term transfusion myocardiopathy, left ventricular outflow abnormality, and cystic fibrosis. First pass radionuclide angiocardiography is also helpful in evaluating children with congenital and acquired valvular heart disease.

Method

Patient Preparation: Oral potassium perchlorate is given in a dose of 3-6 mg/kg of body weight about 15 min before the study. Sodium perchlorate may be given intravenously in the same dose with Tc-99m pertechnetate.

Radiopharmaceuticals and Injection Technique: The radiopharmaceutical most commonly used for first pass radionuclide angiocardiography is technetium-99m as sodium pertechnetate ($200\ \mu$Ci/kg with a minimum total dose of 2-3 mCi) (Table 1). The Tc-99m is administered in a small volume (< 1 ml) and in a high specific activity. The preferred injection site is the external jugular vein. In premature babies and infants, an antecubital or even a scalp vein often, but not always, results in an acceptable compact bolus.

The patient is placed in the supine position on the examining table. It is very important that the child be as relaxed as possible at the time of injection. If the child is very tense or crying, a Valsalva maneuver can result, and this will adversely affect the study. With some children, careful restraining may be indicated. When this is necessary, we use additional help to restrain the child. In our institution, the overwhelming majority of pediatric studies are carried out without sedation, which can affect the quantitative results of the examination.

We use a butterfly type needle (21,23, or 25 gauge) to enter the vein; then we secure the needle to the skin with adhesive tape. The intravenous line is flushed with a small volume of saline to ascertain patency and to prevent extravasation of the radiotracer.

It is imperative to inject the radiopharmaceutical so that it reaches the right atrium as a single bolus. We use a specially

TABLE 1. Radiopharmaceuticals for Pediatric Nuclear Cardiology

Radiopharmaceutical	mCi/kg	Minimum activity (mCi)	Radiation absorbed dose (rad)*		
			Whole body	Critical organ	
Tc-99m sodium pertechnetate	0.200	2.0	0.110–0.182	Intestine	1.3–2.8
Tc-99m human serum albumin	0.200	2.0	0.124–0.210	Blood	0.48–0.70
Tc-99m red blood cells	0.200	2.0	0.124–0.210	Blood	0.48–0.70
Tc-99m pyrophosphate	0.050	2.0			
Tl-201 thallous chloride†	0.030	0.150	0.25–0.36	Kidney	1.1–2.4

*Absorbed doses per imaging dose and in a range from one-year-old to adult.
†Maximum 2 mCi.

designed disposable injector with a one-way valve (valve check injection unit, Paramedical, Inc., Watertown, MA). A saline flush is started and the radiopharmaceutical is rapidly injected into the small chamber of the injector without interrupting the saline flush. Retrograde flow is prevented by the one-way valve (1).

At our institution, work has been done with iridium-191m for first pass radionuclide angiocardiography. An osmium-191 → iridium-191m generator has been developed from which it is possible to produce multiple doses of iridium-191m (2,3). Iridium-191m emits x-rays at about 65 keV and a 129 keV gamma photon. Because of the short physical half-life (5.0 sec) of iridium-191m, relatively large amounts of activity can be administered with much lower radiation exposure than with relatively smaller activities of Tc-99m. Iridium-191m provides a high photon flux that permits rapid imaging with high information density. Serial studies in the same patient within short periods of time without background interference are also possible using iridium-191m. This conveniently allows examination of the heart and great vessels under a variety of conditions such as rest and exercise (4).

Imaging: A high sensitivity, parallel hole collimator is used for imaging most children and adolescents, while a converging collimator of high sensitivity is used for premature neonates and infants. The patient is imaged in the anterior projection. For qualitative radionuclide angiography and for detection and quantification of shunts, a computer recording at 4 frames/sec for premature infants and term neonates and at 2 frames/sec for older children is recommended. For determining ejection fractions a frame rate of at least 20 frames/sec or list mode recording is used. The collimator of choice for ejection fraction measurements is a slant-hole collimator positioned anteriorly over the patient with the slant in the right anterior oblique position.

The quality of the bolus should always be checked using a time activity curve obtained over the superior vena cava. The curve should have a single, sharp peak of 3 sec or less in duration. Once it is established that the bolus is acceptable, the intravenous line is removed. When selecting the region of interest over the superior vena cava, it is important to exclude the lung fields and pulmonary arteries. If the bolus through the superior vena cava takes more than 3 sec or if evidence of a double bolus exists, the examination should be repeated. The only exceptions are if one can establish that a study is otherwise normal despite a poor bolus, or if a deconvolution analysis can be satisfactorily applied.

Shunt Quantification: Quantification of left-to-right shunting is possible by numerical analysis of pulmonary time-activity curves. It has been shown that a gamma variate function well describes a single transit of indicator (without recirculation) (5,6). If only a portion of an indicator curve is available, the gamma variate can be used to construct a single transit curve.

The gamma variate function is fitted to the initial portion of the pulmonary transit curve, that is, from a point at 5–10% of the peak activity on the upslope to a point where the downslope decreases uniformly and before recirculation begins. The area under the curve (A_1) is proportional to the pulmonary blood flow = Qp (Fig. 1). If the gamma variate curve (A_1) is subtracted from the pulmonary curve, another curve results—which represents the first early pulmonary recirculation due to left-to-right shunt plus subsequent shunt and systemic recirculation.

A second gamma variate function is fitted to the initial segment of the subtracted curve and another curve representing a single pulmonary transit it described. The area under this new curve (A_2) is proportional to the shunt flow. If the shunt flow area (A_2) is subtracted from the pulmonary flow area (A_1), the value that results represents the systemic flow $(Qs = A_1 - A_2)$. If A_1 is then divided by $A_1 - A_2$, a pulmonary (Qp)-to-systemic flow (Qs) ratio results.

$$Qp{:}Qs = A_1/(A_1 - A_2).$$

The method described above can quantify left-to-right shunts when the pulmonary-to-systemic flow ratio is between 1.2 and 3.0. Shunts greater than 3.0 generally produce pulmonary curves that are difficult to analyze (7,8) (Figs. 1 and 2).

Ejection Fraction (EF) Determination: A major assumption of this method involves homogeneous mixing of the tracer with blood, so that changes in count rate are proportional to changes in chamber volume.

Computer analysis is applied to time-activity curves produced for each ventricle: points are selected on the histogram representing end-diastolic and end-systolic frames. Selected frames are added together and images produced of the right and left ventricles at diastole and systole. Regions of interest are drawn around the respective images and counts recorded are applied to the formula:

$$EF = \frac{\text{end diastolic counts} - \text{end systolic counts}}{\text{end diastolic counts}}.$$

No background-subtraction technique is applied (Fig. 3).

First pass ejection fraction techniques used at different institutions may be validated by comparing the radionuclide data with data obtained by cardiac catheterization.
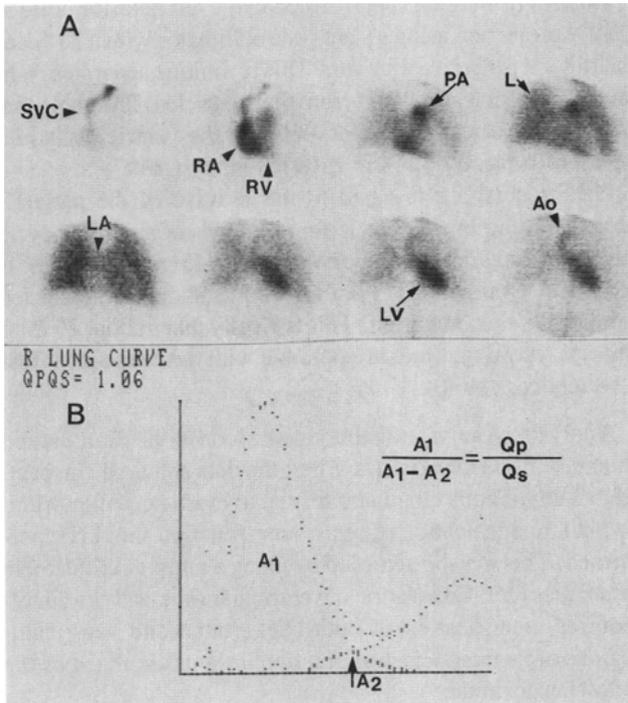
FIG. 1. Normal first pass radionuclide angiocardiogram (Tc-99m pertechnetate anterior view). (A). Each frame represents 1 sec. Radiotracer circulates through superior vena cava (SVC), right atrium (RA), right ventricle (RV), pulmonary artery (PA), lungs (L), left atrium (LA), left ventricle (LV), and aorta (Ao). (B). Pulmonary time-activity curve and calculation of pulmonary-to-systemic flow ratio, Qp:Qs = 1.06 (see text).

$$\frac{A1}{A1-A2} = \frac{Qp}{Qs}$$
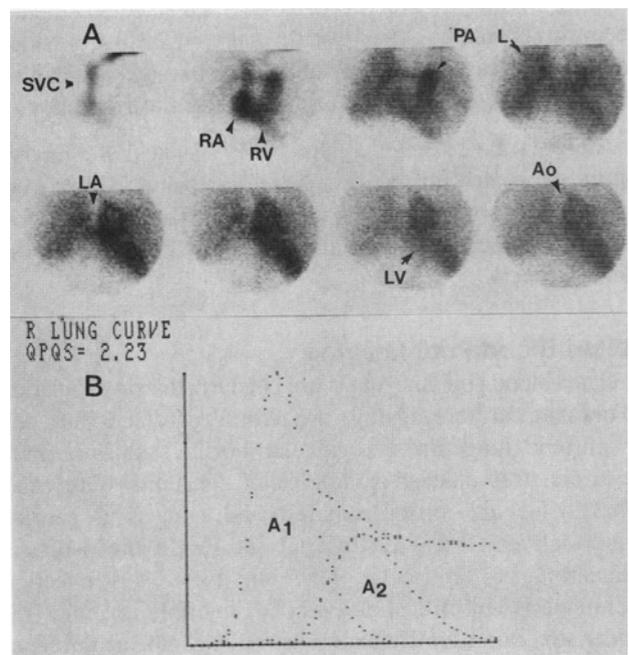
FIG. 2. Left-to-right shunt. (A). Tc-99m radionuclide angiogram shows tracer in superior vena cava (SVC), right atrium and ventricle (RA and RV), pulmonary artery (PA), and lungs (L). The heart's left side is not clearly visible and lungs do not seem to clear activity because of the left-to-right shunt. (B). Pulmonary time-activity curve showing premature tracer recirculation that is due to a left-to-right shunt. (Qp:Qs = 2.23).

Myocardial Scintigraphy

Myocardial imaging is used to evaluate regional distribution of myocardial blood flow. In children, Tl-201 is used to evaluate the following: myocardial ischemia or infarction caused by anomalous coronary artery disease, right ventricular hypertrophy, idiopathic hypertrophic subaortic stenosis, and other congenital abnormalities. It is also used to evaluate asphyxiated newborns. While Tc-99m pyrophosphate myocardial imaging has been used extensively for the diagnosis and localization of myocardial infarctions in adults, it has been used infrequently in pediatric patients.

Patient Preparation: The patient should fast for at least 4 hr before the study to reduce blood flow to the abdominal organs.

Radiopharmaceutical: Thallium-201 in biological systems behaves similarly to potassium in terms of its body distribution. Thallium-201 decays by electron capture to mercury-201 with a physical half-life of 73.1 hr. The photons are emitted by excited states of mercury-201. The principal radiation emissions are x-rays in the range of 68–80 keV (9–12). The patient is injected intravenously with 30 μCi/kg with a minimum dose of 150 μCi and a maximum dose of 2 mCi 5 min before imaging.

Imaging: Imaging is performed with a low energy, high resolution collimator. Magnification scintigraphy with the pinhole collimator is recommended in the newborn. Imaging
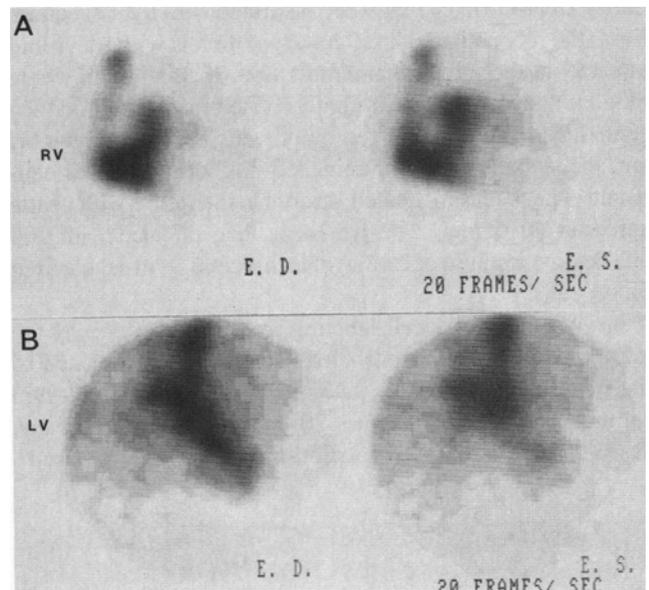
FIG. 3. First pass radionuclide angiocardiogram for measurement of ejection fraction. (A). End-diastolic and end-systolic images of right ventricle. Right ventricular ejection fraction was calculated as 0.46. (B). End-diastolic and end-systolic images of left ventricle. Left ventricular ejection fraction was calculated as 0.65.

includes these views: anterior, 30°, 45°, 60° left anterior oblique, and left lateral. Shielding is placed around the heart to minimize background. Images are acquired for 250,000 to 500,000 counts with the parallel hole collimator or 150,000 to 200,000 counts with the pinhole collimator. Each image

takes approximately 5–15 min (Fig. 4). Simultaneous computer recording should be done for static images with an acquisition matrix of at least 64 × 64 pixels. Greater matrix acquisition if available should be used to improve spatial resolution.

Analysis: Processing thallium-201 images with a computer optimizes evaluation of myocardial perfusion. Subtracting background, smoothing, and interpolating facilitate interpretation and enhance the physician's ability to detect small perfusion defects.

Gated Blood Pool Imaging

Gated blood pool imaging is used in the pediatric population to evaluate cardiomyopathy, myocarditis, cardiac failure due to chronic lung disease, valvular aortic stenosis, single ventricle, drug-induced cardiotoxicity, congenital ventricular diverticula, and other acquired and congenital cardiac abnormalities. It has distinct advantages in the pediatric evaluation of ventricular function. First, the injection technique is not critical and second, multiple imaging (13) under stress or after drug administration can be achieved up to 6 hr after a single injection of radiotracer.

Patient Preparation: The patient is placed in the supine position and an intravenous line is started. Blood is drawn for labeling. Electrocardiographic leads are attached to the patient.

Radiopharmaceutical: In our institution we label red blood cells using a modification of the Brookhaven National Laboratory kit (14,15). The kit is reconstituted with 8 ml of saline. From the reconstituted kit, 2 ml of solution is withdrawn and injected into a 3-ml vacutainer test tube. To this 1 ml of whole blood is added. The tube is gently rotated for 10 min and then centrifuged. The packed red blood cells are then drawn off and added to the tube containing 0.5–1 ml of sodium pertechnetate. The tube is incubated at room temperature with gentle agitation for 5 min. The patient is then injected with 200 μCi/kg (a minimum of 2 mCi) of technetium-99m-labeled red blood cells.

In vivo red blood cell labeling may also be done by the intravenous injection of unlabeled stannous pyrophosphate (0.5 mg of stannous chloride) followed by 1–15 mCi of Tc-99m sodium pertechnetate 15 to 20 min later. Alternatively, Tc-99-labeled human serum albumin (HSA) may be used.
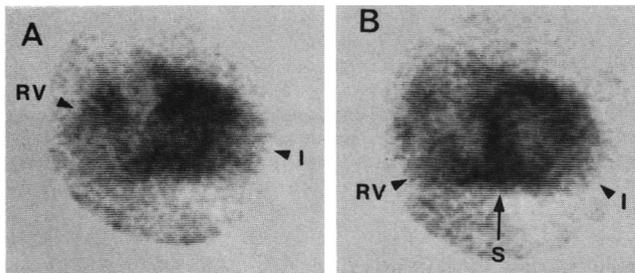
Imaging: Imaging is performed in the left anterior oblique (LAO) projection using a slant-hole collimator with a 30° caudal tilt or a pinhole collimator. This technique separates right and left ventricles and atria from the ventricles. The angle that offers the greatest separation between the ventricles should be used (typically 35–40° LAO) (Fig. 5) (16).

Data acquisition is gated to the R wave of the patient's electrocardiogram. From 16 to 64 images of a cardiac cycle each representing one short phase (5–15 msec/image) is recorded. Optimally, ten million counts should be recorded for the entire examination. This typically takes about 20 min. Shorter recording times are possible with the consequent loss of statistical counts.

Analysis: Analysis of the gated blood pool examination should be done in two parts. First, the data should be inspected in a continuous cinematic format to evaluate wall motion. Second, quantification of ventricular function should be performed. This may be achieved by using a number of different techniques (16). Calculation of ventricular time-activity curves requires identification of both background and ventricular regions of interest. Ejection fraction is then calculated by the following formula:

$$EF = \frac{\text{end diastolic counts} - \text{end systolic counts}}{\text{end diastolic counts} - \text{background}}.$$
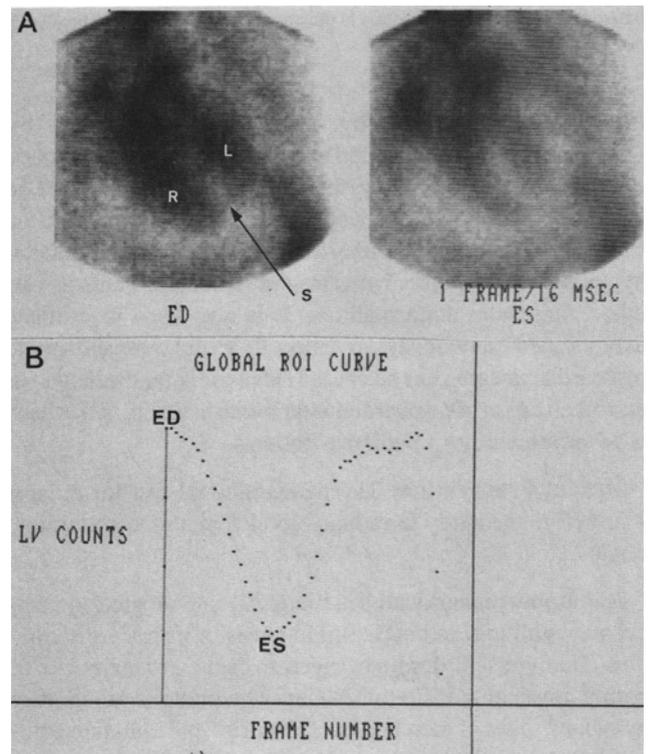
FIG. 5. Gated blood pool scan using Tc-99m labeled red blood cells. (A). End-diastolic (ED) and end-systolic (ES) images in left anterior oblique projection, slant hole collimator, caudally tilted. Both ventricles contract, but not completely. There is a "halo" of decreased perfusion around the cardiac blood pool, which corresponds to a pericardial effusion. RV = right ventricle; S = septum; LV = left ventricle. (B). Time-activity curve for left ventricle corresponding to average cardiac cycle. ED = end diastole; ES = end systole. Left ventricular ejection fraction was 0.7.


FIG. 4. Myocardial infarction in 4-month-old boy. (A) Anterior and (B) 30° left anterior oblique projections (thallium-201). There is focal myocardial perfusion deficit (I); interventricular septum (S) is clearly defined; and right ventricular (RV) wall is hypertrophic.

Conclusion

Radionuclide angiocardiography is a relatively noninvasive procedure that is both reproducible and safe to perform on the pediatric patient. Reliable quantification of left-to-right shunting is possible using radionuclide techniques. Ventricular function is being evaluated with increasing validity. Finally, there is much potential for further interventional testing and more specific evaluation of the myocardium.

Acknowledgment

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