Quantification of intracardiac shunts by gold-195m, a new radionuclide with a short half life

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SUMMARY Gold-195m, a radionuclide with a short half life (30.5 s) was used to quantify left to right intracardiac shunts. The results of this method were compared with those obtained with technetium-99m, a method that was validated against oximetry. In five patients the pulmonary to systemic flow ratio ($> 3:1$) obtained by both radionuclides indicated that the level of shunting was too high to be measured accurately. In one patient fragmentation of the bolus meant that no satisfactory gamma fit could be obtained. In the remaining 16 patients there was no significant difference between two successive ^{195m}Au studies. The agreement between ^{99m}Tc results and ^{195m}Au results was excellent. Oxygen administration, straight leg raising exercise, and the use of oblique projections did not affect the values of the pulmonary to systemic flow ratio. The technique of quantification of intracardiac shunts by ^{195m}Au gives reproducible and accurate results and the low radiation dose means that it is suitable for use in children with suspected left to right shunts.

In recent years the quantification of intracardiac left to right shunts by radionuclide techniques has been successfully applied to children and adults.¹⁻⁶ In this paper we compare the results obtained with gold-195m, a new radionuclide with a short half life (30.5 s) generated from mercury-195m,⁷ with those obtained with a technetium-99m sodium pertechnetate technique which we have validated against oximetry.

The low radiation dose of ^{195m}Au means that several studies may be performed in the same patient. We have determined the feasibility of using ^{195m}Au with a standard single crystal gamma camera and have assessed the effects of interventions on the results obtained.

Patients and methods

PATIENTS

We studied 22 patients aged 6-63 years (mean 22.5) (Table 1). In all left to right intracardiac shunts were suspected. Informed consent was obtained from every patient or their parents.

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METHODS

The patients were studied by means of a Technicare ON100 gamma camera. An intravenous cannula was inserted into the antecubital vein, preferably of the right arm. The detector head of the camera was positioned over the lung field. A bolus of radionuclide, volume < 1 ml, was injected, followed by a 10-20 ml saline flush. Immediately after injection we started data acquisition with a Nodecrest V77 computer. Seventy frames of 0.5 s duration were collected for subsequent processing. The mercury-195m/gold-195m generator was positioned in a shielded corner of the gamma camera room and injection therefore occurred almost immediately after elution of ^{195m}Au . Breakthrough of ^{195m}Hg was minimised by eluting the generator several times and discarding the eluates which contained higher quantities of ^{195m}Hg . This manoeuvre was also carried out if there was an interval of ≥ 2 minutes between consecutive elutions. At the time of injection the activity of ^{195m}Au was approximately 550 MBq. ^{99m}Tc was given on the basis of 5 MBq/kg body weight activity.

The data collected were recalled from disc and played back in cine film form. The frames of the pulmonary phase were then identified as was the frame in which the superior vena cava and right ventricle were well delineated. Two regions of inter-

Table 1 Pulmonary to systemic flow ratios in 22 patients with suspected left to right intracardiac shunts

Patient	Age	Au1	Au2	LAO	Oxygen	Exercise	^{99m} Tc	Diagnosis
1	11	>3	>3	>3	—	—	>3	ASD
2	20	>3	>3	>3	—	—	>3	ASD
3	8	2.1	2.2	3.0	3.2	—	2.2	ASD
4	7	1.6	1.6	1.6	—	—	1.5	VSD
5	7	1.1	1.1	1.1	—	—	1.0	ASD?
6	15	1.2	1.2	1.2	1.1	1.2	1.2	VSD
7	22	>3	>3	>3	—	—	>3	ASD
8	11	1.6	1.6	1.3	1.7	—	2.0	VSD
9	63	>3	>3	>3	—	—	>3	VSD and ASD
10	21	1.1	1.1	1.1	1.1	1.1	1.1	PS? ASD
11	26	Fragmented bolus			1.1	1.1	1.1	PDA?
12	35	1.1	1.1	1.1	1.1	1.1	1.1	VSD?
13	45	1.2	1.2	1.3	1.2	1.1	1.2	AV coronary fistula
14	7	1.8	1.8	1.7	1.9	1.8	1.7	ASD
15	35	1.2	1.2	1.2	1.1	1.1	1.4	VSD?
16	6	1.1	1.2	1.3	—	—	1.3	VSD
17	7	>3	>3	>3	—	—	>3	VSD
18	45	2.5	2.1	1.8	1.9	1.9	2.0	ASD
19	11	1.4	1.3	1.5	—	—	1.4	VSD
20	13	1.3	1.3	1.3	1.3	1.3	1.3	VSD
21	30	1.2	1.1	1.1	1.2	1.2	1.2	VSD
22	50	1.1	1.0	—	1.1	1.2	1.1	VSD?
Mean (SD)		1.4 (0.4)	1.38 (0.36)	1.44 (0.4)	1.44 (0.62)	1.3 (0.3)	1.42 (0.36)	

Au1, first gold-195m study; Au2, second gold-195m study; LAO, left anterior oblique; ASD, atrial septal defect; VSD, ventricular septal defect; AV arteriovenous; PS, pulmonary stenosis.

est were drawn: one over the superior vena cava avoiding the lung, and a second over the right lung avoiding the heart and superior vena cava. Activity-time curves were generated and the curve for the superior vena cava was examined to check the quality of the bolus. The lung curve was used to determine the pulmonary to systemic blood flow ratio (Qp:Qs) by means of a modification of the Maltz and Treves gamma variate fitting technique.⁵ If the bolus was fragmented or if its administration was unduly prolonged, and it was impossible to perform a satisfactory analysis, the study was rejected.

The method is designed to define a primary peak,

Fig. 1 Area under primary peak (A1) represents initial passage of radionuclide activity through lungs and area under secondary peak (A2) is attributable to premature recirculation caused by intracardiac shunting.

area A1, arising from the initial passage of activity through the lungs (Fig. 1) and a secondary peak, area A2, attributable to premature recirculation caused by shunting, which is superimposed on the descending slope of the primary peak. Activity arising from systemic recirculation appears towards the end of the curve.

The fitted primary peak is subtracted from the total curve and the operator may also fit the systemic recirculation curve which can also be subtracted. In our studies we only applied the recirculation correction if there was a clear recirculation peak. Finally A2 is obtained by fitting a curve to the shunt peak which has now been isolated. The ratio of pulmonary flow to systemic flow (Qp:Qs) is given by the formula:

$$A_2 \div (A_1 - A_2).$$

Statistics

All the results are expressed as mean (SD). Significant differences were assessed by the paired Student's *t* test and the Wilcoxon signed rank matched pairs test.

Validation

To validate our technique 20 patients who had previously undergone cardiac catheterisation were investigated by the ^{99m}Tc technique. The interval between the catheter and radionuclide studies ranged from two weeks to four months (mean 6.1 weeks). Ratio of pulmonary flow to systemic flow was calculated by oximetry (American Opical oximeter)

Fig. 2 Validation of flow ratios determined by ^{99m}Tc and oximetry in 15 patients with ratios of pulmonary flow to systemic flow of $< 3:1$.

Fig. 3 Agreement between two sequential ^{195m}Au studies without intervention. Au1, first ^{195m}Au study; Au2, second ^{195m}Au study. Results from 16 patients with ratios of pulmonary flow to systemic flow of $< 3:1$ are shown.

during the catheter study. The saturation run in each case took less than 10 minutes. Mixed venous oxygen content in patients with atrial septal defects was derived from the superior (SVC) and inferior vena caval (IVC) oxygen contents by the formula⁸:

$$(3 \times \text{SVC content} + \text{IVC content}) \div 4$$

The agreement between ^{99m}Tc values and oximetry values was excellent (Fig. 2). In five patients the ratio of pulmonary flow to systemic flow was $> 3:1$ by both the ^{99m}Tc technique and oximetry. These results are not included in any of the graphical comparisons since quantification is inaccurate at this level of shunting. The mean deviation from the line of identity for the remaining 15 patients was $-0.13 (0.22)$.

In addition, ^{99m}Tc studies were performed on a further 17 patients with clinically normal hearts who were receiving ^{99m}Tc for bone scans. All ratios of pulmonary to systemic flow were in the range of $1.0\text{--}1.2:1$ (mean (SD) $1.09 (0.06)$).

Results

In one patient a satisfactory gamma fit could not be obtained because of fragmentation of the bolus. In five of the patients the ratio of pulmonary flow to systemic flow was $> 3:1$ in both anterior and left anterior oblique ^{99m}Tc studies. In the 16 remaining patients the results of two successive anterior view ^{195m}Au studies were compared (Fig. 3). Mean (SD) deviation from the line of identity was $0.03 (0.12)$. Fig. 4 compares the mean of results obtained from

the two ^{195m}Au studies with the ^{99m}Tc result. Mean deviation from the line of identity was $-0.02 (0.15)$. The mean ratio of pulmonary flow to systemic flow derived from the two ^{195m}Au studies was $1.40 (0.19):1$.

The mean ratio of pulmonary flow to systemic flow was $1.44 (0.49)$ in the 15 patients in whom the ratio was $< 3:1$ from the left anterior oblique projection.

Fig. 4 A comparison between ratios of pulmonary flow to systemic flow measured by ^{195m}Au technique (mean of two studies) and ^{99m}Tc technique. Results from 16 patients with ratios of pulmonary flow to systemic flow of $< 3:1$ are shown.

Table 2 Dosimetry of typical injection of radionuclide derived from data given in MIRD 8¹² and Ackers and de Jong¹¹

	^{195m} Au (550 MBq)		^{195m} Hg (120 kBq)		^{99m} Tc (370 MBq)	
	μSv	mrem	μSv	mrem	μSv	mrem
Heart wall	117	11.7	—	—	—	—
Kidneys	24	2.4	402	40.2	—	—
Lungs	84	8.4	26	2.6	—	—
Liver	18	1.8	36	3.6	—	—
Spleen	5	0.5	45	4.5	—	—
Gonads	8	0.8	26	2.6	900	90
Bladder wall	—	—	—	—	8500	850
Stomach	—	—	—	—	5100	510
ULI	—	—	—	—	12000	1200
LLI	—	—	—	—	11000	1100
Red marrow	—	—	—	—	1700	170
Thyroid	—	—	—	—	13000	1300
Total body	6	0.6	19	1.9	1100	110
Effective whole body	27	2.7	58	5.8	4120	412

ULI, upper large intestine; LLI, lower large intestine.

This was not significantly different from the value found in the anterior projection. It was impossible to identify the site of shunting from the cine display.

Twelve patients were studied after oxygen administration and ten after exercise. The mean ratio of pulmonary flow to systemic flow was 1.49 (0.62) after oxygen and 1.3 (0.3) after exercise. These were not significantly different from the resting values.

DOSIMETRY

To assess the radiation risk arising from the use of ^{195m}Au the effective whole body dose equivalent (the dose to the uniformly irradiated whole body that carries the same risk as the observed non-uniform dose) was calculated using the weighting factors recommended by the International Commission on Radiological Protection.⁹ In our generator system, which resembles that described by Elliott *et al.*,⁷ we measured a mean (SD) ^{195m}Hg breakthrough of 96 (24) kBq ^{195m}Hg per injection (n = 6), with a maximum of 120 kBq. Data for the dosimetry of ^{195m}Au and ^{195m}Hg in animals have been published.^{10,11} The data we used were taken from Ackers and de Jong.¹¹ Table 2 compares the dose from a

single injection of ^{195m}Au with that from a typical injection of ^{99m}Tc labelled sodium pertechnetate.¹² Table 3 compares the effective whole body dose equivalent from five injections of ^{195m}Au with that from a single injection of 370 MBq ^{99m}Tc in adults and children. As a worst case estimate we assume that the volume of the eluate from the ^{195m}Au generator is not reduced for children, and that the maximum breakthrough dose of 120 kBq ^{195m}Hg is injected. The comparisons are made with ^{99m}Tc activities reduced according to body weight. Body weight factors were taken from Administration of Radioactive Substances Advisory Committee guidelines (appendix 1B).¹³

Discussion

For some years, radionuclide angiographic techniques have proved useful in the assessment of patients with left to right intracardiac shunts.^{1-3,6} The technique has been validated against oximetry and has proved valuable in the investigation of congenital heart disease in children.^{4,5} The radionuclide most widely used for shunt evaluation is ^{99m}Tc, which has a relatively long half life of six hours. ^{195m}Au, has a half life of 30.5 seconds and is available in generator systems⁷ from a ^{195m}Hg parent (half life 41.6 hours). The physical characteristics of ^{195m}Au ensure that the patient is subjected to minimal radiation dose. With all mercury-195m/gold-195m generators, however, the eluate is contaminated by ^{195m}Hg breakthrough. In our generator system the mean ^{195m}Hg breakthrough dose was 96 kBq per injection, with a maximum of 120 kBq. Mena *et al.*, using a different type of generator, quote a figure of 0.75 kBq ^{195m}Hg/^{195m}Au,¹⁴ implying a dose of 550 kBq of ^{195m}Hg per injection of 740 MBq of ^{195m}Au.

Because mercury accumulates in the kidneys radi-

Table 3 Whole body effective dose equivalents of radionuclides in adults and children calculated with weighting factors from Administration of Radioactive Substances Advisory Committee appendix 1B¹³

Age	^{195m} Au + ^{195m} Hg (5 injections)		^{99m} Tc (1 injection)	
	μSv	mrem	μSv	mrem
Adult	430	43	4120	412
10 years	860	86	4120	412
5 years	1400	140	4120	412
1 year	2580	258	4120	412
Newborn	7230	723	4120	412

ation doses from the breakthrough of $^{195\text{m}}\text{Hg}$ are important. But even in the case of a 1 year old child, the effective whole body dose equivalent from five $^{195\text{m}}\text{Au}$ studies is less than that from a single $^{99\text{m}}\text{Tc}$ study (Table 3). The dose to the kidneys of a 1 year old child when $^{195\text{m}}\text{Au}$ is used would be 12 mSv (1200 mrem), which, although it is high, is the same as the dose to the upper large intestine when 370 MBq $^{99\text{m}}\text{Tc}$ is given. In the newborn infant, kidney doses could be as high as 34 mSv (3400 mrem) if five studies are performed. In this study, however, multiple injections were given only to older children and adults and no child under the age of 6 years was studied. In routine clinical practice it is unlikely that more than two studies would be performed, and this would reduce the worse case estimates quoted here. We conclude that the radiation doses from eluates obtained from the type of $^{195\text{m}}\text{Au}$ generator used in this study are acceptable in all except the very young infant. Further, compared with existing techniques a significant reduction in radiation dose can be achieved in most patients, even when several $^{195\text{m}}\text{Au}$ studies are performed.

The $^{195\text{m}}\text{Au}$ is eluted immediately before use and an eluate may be collected sufficiently rapidly for repeat studies to be performed after an interval as short as 2 minutes.¹⁵

We compared the results of the $^{195\text{m}}\text{Au}$ studies with those obtained by a $^{99\text{m}}\text{Tc}$ technique that was validated against oximetry. We also assessed the effects of intervention on the results obtained. There was excellent agreement between the results obtained by the $^{195\text{m}}\text{Au}$ and $^{195\text{m}}\text{Tc}$ techniques (Fig. 4), and all five patients in whom the ratio (Qp:Qs) was calculated to be $>3:1$ with $^{99\text{m}}\text{Tc}$ had similar flow ratios calculated with $^{195\text{m}}\text{Au}$. The two successive $^{195\text{m}}\text{Au}$ studies without intervention also accorded well, demonstrating the reproducibility of the technique. These results confirm those of Treves *et al* who were able to quantify shunts with iridium-191m,¹⁶ another radionuclide with a short half life. They did not, however, perform sequential studies, and the very short half life of the $^{191\text{m}}\text{Ir}$ (4.96 s) and its relatively low energy, mean that it is less suitable for imaging than $^{195\text{m}}\text{Au}$.

The administration of oxygen might be expected to increase the ratio of pulmonary flow to systemic flow as a result of pulmonary artery vasodilatation, assuming that the pulmonary vascular bed is reactive. Fujii *et al* suggest that patients with high flow ratios have retained such reactivity, whereas in those with lower values the resistance is fixed.¹⁷ Unlike the eight patients studied by Fujii *et al* none of our patients with Qp:Qs values between 2 and 3:1 had end stage disease or Down's syndrome (6/8 in Fujii's study). There was little change in the ratio of pul-

monary flow to systemic flow after oxygen administration in our study, suggesting either that a longer period of administration was needed to change the flow ratio in this group, or that ratios did not change sufficiently to reflect alterations in pulmonary vascular reactivity. The latter assumption is supported by the lack of change on straight leg raising, an intervention which would be expected to cause a fall in ratio as a result of systemic vasodilatation.

The values obtained in the left anterior oblique view were no different from those obtained in the anterior view. We had hoped to identify the site of shunting in this projection but were unable to do so. The left anterior oblique projection is, therefore, of little use because it is more awkward to achieve than the anterior view and does not provide additional information.

In this study we applied a recirculation correction if we could identify a good recirculation curve.¹⁸ In most cases this correction was not essential, but occasionally it made fitting of the secondary curve easier. We found that use of intravenous cannula allowed excellent flushing of the bolus by saline without leakage and in only one case was it impossible to calculate the ratio of pulmonary flow to systemic flow. In this instance the bolus had become fragmented and even deconvolution of the curve would have proved fruitless.¹⁹

In summary, quantification of intracardiac shunts by means of the radionuclide $^{195\text{m}}\text{Au}$ is reproducible and accurate. The results are not affected by oxygen, exercise, or the choice of projection and the low radiation dose makes the radionuclide suitable for use in children with suspected left to right shunts. The combination of this technique with cross sectional echocardiography may obviate the need for cardiac catheterisation in children with simple congenital defects.

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