Radionuclide Hysterosalpingography with Technetium-99m-Pertechnetate: Application and Radiation Dose to the Ovaries

Kuang Tao A. Yang, Jung-Hsiang Chiang, Biau-Shione Chen, Chi-Hao Liang, Shing Fang Lee, and Sheuh-Chun Liao

Departments of Nuclear Medicine, Obstetrics, and Gynecology, Changhua Christian Hospital, Changhua, Taiwan, Republic of China

Although radionuclide hysterosalpingography (RNHSG) has been suggested as an efficient procedure for assessing function of fallopian tubes, the radiation dose to the ovaries was addressed as an important issue to be taken into consideration. We describe a modified method of RNHSG, calculating the radiation dose to the ovaries. A small dose of approximately 18.5 MBq (0.5 mCi) of [^{99m}Tc]pertechnetate was administered directly into the uterine cavity without overpressure. The accuracy of the method was 84.5% as compared with the contrast hysterosalpingography. The estimated average dose to the ovaries was 0.057 mGy/MBq (0.21 rad/mCi) or 1.08 mGy (108 mrad) per study. RNHSG is an accurate method for functional study of fallopian tube patency with low radiation dose.

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Iturralde and Venter first described how ^{99m}Tc-labeled albumin spheres were transported from the vagina to the peritoneal cavity and ovaries (*1*). Since then, radionuclide hysterosalpingography (RNHSG) has been tried in a few medical centers (*2–4*). However, the procedure has not become widely used. Compared with contrast hysterosalpingography (HSG), RNHSG was reported to deliver a higher dose of radiation to the ovaries. Some authors have reservations about the use of radionuclide hysterosalpingography (*5*). In this study, we describe a modified method for RNHSG, and compare the results to contrast hysterosalpingography, both for detection of tubal patency and for estimated radiation burden.

MATERIALS AND METHODS

Twenty-eight of 29 patients (aged 26–36) included in this study were investigated by contrast HSG and RNHSG for infertility. An additional patient underwent RNHSG only. Images of the RNHSG of this patient were used only for estimation of the radiation dose to the ovaries and not for comparison with the contrast HSG.

Contrast HSG was performed using the conventional method with 10–20 ml Angiografin (Schering). The RNHSG was performed in the late follicular phase within 1 mo of the contrast HSG. After signing an approved consent, the patient was placed in the lithotomy position for the RNHSG. About 18.5 MBq (0.5 mCi) of [^{99m}Tc]pertechnetate in a small volume of less than 1 ml was injected slowly into the uterine cavity through a Frayman's tube. Injection was undertaken carefully to avoid overpressure. It took approximately 10 sec to complete the injection. The patient was then placed in a slight Trendelenberg position under a gamma camera (Apex 609, Elscint) equipped with a low-energy general-purpose collimator. A series of anterior 1-min images was obtained immediately and every 5 min up to 1 hr.

The normal pattern of the image obtained was an area (in most cases triangular in shape) with high activity representing the uterus. There were two smaller areas lateral and superior to the uterus on both sides corresponding to the activities in the regions of fimbria and ovaries. The two areas usually began to be visualized in the immediate or 5-min image. The activity in these areas cleared more rapidly than that in the uterus (Fig. 1). If a fallopian tube was not patent, there was no significant activity seen around the region of ovary (Fig. 2) and the diagnosis of an obstructed tube was made. There was usually some activity noted in the vagina.

Images from 18 to 29 patients who completed the RNHSG at 1 hr were used for radiation dose estimation. A region of interest (ROI) was placed circumscribing the regions of right and left ovaries (if present) and uterus and vagina, respectively. A count was obtained for each ROI in each image. In two cases, there was spillage of radiotracer into the peritoneum. The activity in the peritoneum was included in the activity of the ovary adjacent to it. The total injected activity was expressed as the sum of counts from the ROIs of ovaries, uterus and vagina in the immediate image. As pertechnetate might diffuse into tissues, we assumed that the administered activity was distributed uniformly in the source organs immediately after the injection. The percentage of activity reaching the ovary was calculated as the ratio of count of the ovary with maximal ovarian count in the series of images to the total injected activity. Decay correction was made. The percentages of activity reaching the uterus and vagina were calculated in the same manner. A time-activity curve was plotted for the ovaries, uterus and vagina, respectively. Each time-activity curve approximated a monoexponential curve. Following curve fitting

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For reprints contact: Kuang Tao A. Yang, MD, MS, Department of Nuclear Medicine, Changhua Christian Hospital, Changhua, Taiwan 500, R.O.C.

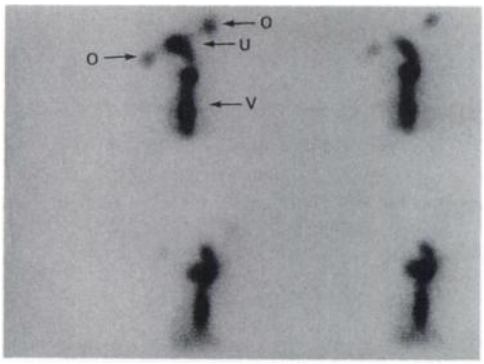

FIGURE 1. Representative images from a patient with patent fallopian tubes at 1 min (upper left), 10 min (upper right), 30 min (lower left), and 50 min (lower right). The activities around the ovaries (O) cleared more rapidly than the activities in the uterus (U) and vagina (V).

with the least-squares method, the effective half-time for the ovaries, uterus, and vagina could be measured, respectively.

Mean organ dose ($\bar{D}$) to ovaries from free pertechnetate activity ^{H_2O}were calculated based on the basic MIRD formula:

$$\bar{D} = \tilde{A}_h \times S,$$

where $\tilde{A}_h$ is the accumulated activity in the source organ (h) and S is the mean absorbed dose in the target organ per unit accumulated activity in the source. $\tilde{A}_h$ = A × 1.44 × effective half-time; A is the initial activity in the source organ. The S values are tabulated in MIRD Pamphlet No. 11 (*6*). The S value is 4.2 × 10^{-3} rad/μCi-hr for the ovaries as both target and source organs. This S value gives total energy absorbed in both ovaries from activity in both ovaries. S value for right (or left) ovary to both ovaries was derived using the concept of "the remainder of the body". The concept was used for calculating the S value for the remainder of the body (RB). The method was described by Coffey and Watson (*7*). The S values from the MIRD Pamphlet No. 11 may be modified according to the following expression:

$$S(r_k \leftarrow RB) = S(r_k \leftarrow TB)(mTB/mRB) - S(r_k \leftarrow r_h)(mh/mRB)$$

where r_k is the region of target organ, r_h is the region of source organ, mTB is the mass of the total body (TB), mRB is the mass of the remainder of the body (i.e., mass of the total body minus the mass of the source organs), and mh is the mass of the source organ h. In this study, the total body was substituted by both ovaries, the source organ by the right ovary and the remainder of the body by the left ovary. Both ovaries were treated together as the target organ. Assuming that the right and left ovary were equal in shape and mass, $S(r_k \leftarrow r_h)$ was equal to $S(r_k \leftarrow RB)$, mTB was equal to 2mRB, and mh was equal to mRB. The above equation could be expressed as:

$$S(r_k \leftarrow r_h) = S(r_k \leftarrow TB) \times 2 - S(r_k \leftarrow r_h),$$

and

$$S(r_k \leftarrow r_h) = S(r_k \leftarrow TB).$$

The S value tabulated for both ovaries to both ovaries could thus be used as the S value for right (or left) ovary to both ovaries. This value was used for calculation in this study.

Another approach to calculate the S value for the right (or left) ovary to both ovaries was to consider separately the penetrating and nonpenetrating component. The nonpenetrating component was calculated as 4.0 × 10^{-3} rad/μCi-hr using the nuclear data (*8*) and the mass of the ovaries tabulated (*9*). The photon component was estimated using the absorbed fraction for a uniformly distributed source in an ellipsoid in MIRD Pamphlet No. 8 (*10*) and the mass of the ovaries, which was 4.4 × 10^{-4} rad/μCi-hr. The S value was 4.4 × 10^{-3} rad/μCi-hr, which was close to the S value tabulated for both ovaries in MIRD Pamphlet No. 11.

The MIRD phantom has no source region representing the uterus or vagina. Some approximations made by Stabin (*11*) to estimate the radiation dose to the ovaries from activity in the uterus were also used in this study. Reciprocity was used to obtain the dose to the ovaries from activity in the uterus, which was 2.1 × 10^{-5} rad/μCi-hr. Because of the similarity in position, the S value for the urinary bladder was used to represent that for the vagina. The S value is 7.3 × 10^{-6} rad/μCi-hr for the urinary bladder as a source organ. For convenience, the activities in the uterus and vagina were summed and counted as the activity in the uterus and the S value for the uterus was used for calculation. The effective half-time of free pertechnetate in these two regions was also estimated as the effective half-time in the uterus. The mean radiation doses to the ovaries from the ovaries and uterus (including the vagina) as source organs were then derived from these values.

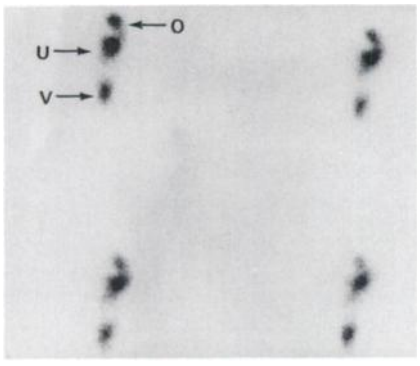

FIGURE 2. Representative images from a patient with obstructed right fallopian tube at 1 min (upper left), 10 min (upper right), 30 min (lower left), and 50 min (lower right). There was ^{99m}Tc activity around the left ovary (O) only. U = uterus; V = vagina.

RESULTS

A comparison of results between contrast HSG and RNHSG was made for 28 patients. The right and left fallopian tubes were estimated independently. In the contrast HSG examinations, there were 44 patent fallopian tubes and 12 obstructed fallopian tubes. Of the 44 patent tubes, 37 were diagnosed as patent in the RNHSG. Of the 12 obstructed tubes, 10 were interpreted as obstructed in the RNHSG based on no significant activity being noted around the ovary. Two of the 12 obstructed fallopian tubes were diagnosed as having hydrosalpinx in the contrast HSG. It was interesting to note that one of these two tubes was diagnosed as patent while the other one was diagnosed as obstructed in RNHSG. The latter might represent a fallopian tube with hydrosalpinx but retaining its epithelial function. Using the contrast HSG as the standard, the sensitivity, specificity, and accuracy for detection of fallopian tube patency was 81.3%, 83.3%, and 84.5%, respectively (Table 1).

TABLE 1
Comparison of Results of RNHSG and Contrast HSG

RNHSG	Contrast HSG: Patent	Contrast HSG: Obstructed
Patent	37	2
Obstructed	7	10

Sensitivity = 81.3%; Specificity = 83.3%; Accuracy = 84.5%.

In the 18 studies for estimation of dose to the ovaries, 24 fallopian tubes were patent in the RNHSG. The percentage of the injected activity reaching these ovaries was 12.5% ± 14.3%. The remaining activity was assumed to be the activity in the uterus and vagina. The effective half-time of free pertechnetate in the ovaries was 0.26 ± 0.23 hr (n = 24). It was 0.86 ± 0.12 hr (n = 18) for the uterus (including the vagina).

The radiation dose to the ovaries was calculated for each of the 18 patients. The mean ± 1 s.d. was 0.057 ± 0.047 mGy/MBq or 0.21 ± 0.18 rad/mCi (Table 2). This ranged from 0.0028 mGy/MBq (0.010 rad/mCi) to 0.18 mGy/MBq (0.67 rad/mCi). The least radiation doses of 0.0028 mGy/MBq (0.010 rad/mCi) (patient 18) and 0.012 mGy/MBq (0.043 rad/mCi) (patient 13) were noted in the two patients who had obstructed tubes on both sides. For patients with one obstructed tube, the dose was 0.069 ± 0.056 mGy/MBq or 0.26 ± 0.21 rad/mCi (n = 8). It was 0.061 ± 0.033 mGy/MBq or 0.23 ± 0.12 rad/mCi (n = 8) for patients with both tubes patent. There was no significant difference between these two groups ($p > 0.05$). The percentage of activity reaching the ovaries in the patients with one obstructed tube was 12.7% ± 11.7% (n = 8). The effective half-time was 0.33 ± 0.32 hr. It was 8.84% ± 6.32% for the activity reaching the ovaries and was 0.20 ± 0.16 hr for the effective half-time in the patients with both tubes patent (n = 16). The percentages of uptake and effective half-times did not differ significantly between the two groups ($p > 0.05$).

Most of the radiation dose to the ovaries was from self-irradiation. The activity in the uterus and vagina contributed about 15% of the radiation dose to the ovaries as estimated in the patients with both fallopian tubes patent.

DISCUSSION

The RNHSG is a simple, accurate, and relatively non-invasive method for evaluation of patency of fallopian tubes. Its ability to detect functional tube obstruction renders it a promising procedure in the field of infertility. Lack of pre-ovulatory transportation would transfer the patient to the category of in vitro fertilization (IVF) and egg transfer (ET), excluding the possibility of gammete

TABLE 2
Effective Half-times (T), Percentages (%) of Injected Activity Reaching the Ovaries and Uterus (Including the Vagina) and Doses to the Ovaries from the Ovaries and Uterus as Source Organs

	Source organ: Right ovary			Left ovary			Uterus				
No.	T (hr)	%	Dose (rad/mCi)	T (hr)	%	Dose (rad/mCi)	T (hr)	%	Dose (rad/mCi)	Total (rad/mCi)	Dose (mGy/MBq)
1	0.082	16.6	0.083	0.117	6.8	0.048	0.686	76.6	0.016	0.15	0.040
2	0.492	8.0	0.24	0.043	6.7	0.16	1.810	25.2	0.045	0.42	0.11
3	0	0	0	0.084	40.4	0.21	0.711	59.6	0.013	0.22	0.059
4	0	0	0	0.993	7.2	0.43	1.228	92.8	0.035	0.47	0.13
5	0.094	26.0	0.15	0.203	16.5	0.20	1.133	57.5	0.020	0.19	0.051
6	0	0	0	0.599	6.8	0.24	3.167	93.2	0.089	0.34	0.091
7	0.092	4.2	0.023	0	0	0	2.743	95.8	0.080	0.10	0.028
8	0.251	7.0	0.11	0	0	0	1.505	93.0	0.042	0.15	0.040
9	0.272	5.1	0.082	0.482	5.3	0.15	1.126	89.6	0.030	0.26	0.070
10	0.034	3.2	0.0063	0	0	0	0.897	97.0	0.026	0.033	0.088
11	0.098	9.2	0.053	0.276	3.7	0.05	0.233	87.1	0.0062	0.11	0.030
12	0	0	0	0.514	20.6	0.64	1.239	79.4	0.030	0.67	0.18
13	0	0	0	0	0	0	1.417	100.0	0.043	0.043	0.012
14	0.079	7.3	0.035	0.045	4.1	0.011	1.351	88.6	0.036	0.083	0.022
15	0	0	0	0.079	12.9	0.062	0.155	87.1	0.0041	0.066	0.018
16	0.176	15.4	0.16	0.208	1.2	0.015	0.438	83.4	0.011	0.19	0.052
17	0.638	5.9	0.23	0.336	3.6	0.073	3.174	90.5	0.087	0.39	0.11
18	0	0	0	0	0	0	0.340	100.0	0.010	0	0.0028
Mean ± s.d.									0.034 ± 0.026	0.21 ± 0.18	0.057 ± 0.047

Mean ± s.d. of the percentages of the injected activity reaching the ovaries with patent fallopian tubes was 12.5% ± 14.3% (n = 24); Mean ± s.d. of the effective half-times for the ovaries with patent fallopian tubes was 0.26 ± 0.23 hr (n = 24).

intrafallopian transfer (GIFT) or zygote intrafallopian transfer (ZIFT) (*3*).

In the original work of Iturralde and Venter, 10 mCi of ^{99m}Tc-human albumin microspheres (HAM) with a parallel all-purpose collimator were used. Such doses have never been used in recent clinical practice. McCalley et al. used 1 mCi of ^{99m}Tc-HAM with a pinhole collimator (*2*). The efficiency of RNHSG for evaluation of fallopian tube patency was over 94%. In Brundin's study, about 11–51 MBq (0.3–1.4 mCi) of ^{99m}Tc-HAM were administered and a pinhole collimator was used. The congruent findings between contrast HSG and RNHSG were observed in 49% (*3*). A later study using only 3–5 MBq (0.08–0.13 mCi) of ^{99m}Tc-HAM with a planar collimator resulted in 41% efficiency (*4*). In only one study was [^{99m}Tc]pertechnetate used (*12*).

Human serum albumin microspheres measure about 20 μm in mean diameter. After administration, in the posterior fornix of the vagina, about 15% of the activity went to the ovaries, 65% went to the uterus, and the remaining 20% remained in the vagina. The activity was assumed to be removed by physical decay only (effective half-time = 6.03 hr) as HAM could not penetrate the blood capillary due to its large size of particle. The total dose to the ovaries was 1.5 mGy/MBq (*11*). This dose was erroneously quoted as 0.75 mGy/MBq to each ovary by McCalley (*2,11*) and was reported to be 25 times higher than contrast HSG by van der Weiden & van Ziji (*5*). In contrast to this, Hyznar et al. used free [^{99m}Tc]pertechnetate resulting in an estimated dose of 0.048 mGy/MBq, which is a factor of 30 lower than the value for ^{99m}Tc-HAM (*12*). They assumed that only 3% of the injected activity reached the ovary. The measured effective half-time was 50 min. It is apparent that pertechnetate can diffuse into blood capillaries and be removed from the entire region.

We used free pertechnetate for RNHSG. As little as 18.5 MBq of [^{99m}Tc]pertechnetate was administered. About 13% of the injected activity was estimated to reach the ovaries. The average of effective half-times of [^{99m}Tc]pertechnetate in the ovaries was 0.26 hr. The radiation dose to the ovaries was 0.057 ± 0.047 mGy/MBq. It was comparable with the dose of 0.048 mGy/MBq in Hyznar's study. Even if the free pertechnetate that crossed into the bloodstream was taken into consideration, the dose to the ovaries from it was neglectable. It should be less than 0.0081 mGy/MBq which is the mean dose to the ovaries from [^{99m}Tc]pertechnetate injected intravenously (*13*). The short effective half-time in the ovaries suggested that a significant fraction of the injected activity would reach the peritoneum. We assumed that the effective half-time of the pertechnetate in the peritoneal cavity was the same as that in the uterine cavity (it was 0.86 hr for this study). We further assumed that all the activity reaching the ovaries (about 12.5% in this study) ultimately drained into the peritoneum. The dose to the ovaries from the activity in the peritoneum could be estimated using the S value of 4.0×10^{-7} mGy/MBq-sec calculated by Watson et al. (*14*). The dose was 1.0×10^{-4} mGy/MBq or 3.8×10^{-7} rad/μCi. It was about a factor of 600 lower than the self-dose from the ovaries.

Direct intrauterine injection may facilitate migration of radiotracer into the fallopian tubes as compared with administration of radiotracer in the posterior fornix of vagina or external orifice of cervix. The dose injected could be reduced without deterioration of the image quality. About 18.5 MBq of [^{99m}Tc]pertechnetate was used in this study, which resulted in an average dose to the ovaries to be about 1.08 mGy (108 mrad) per study. The intrauterine injection might be more uncomfortable for the patient and possibly less physiologic as compared with the vaginal instillation in other studies. In this study, the procedure was well tolerated by all the patients. Efforts were made to avoid overpressure during injection in order to acquire physiologic migration of ^{99m}Tc into fallopian tubes. The mean dose per unit administered activity to the ovaries using this method was 0.057 ± 0.047 mGy/MBq. It was 0.048 mGy/MBq in Hyznar's study. In that study, pertechnetate was used. As much as 12.5% of the injected activity reached the ovaries in our study, while only 3% was assumed to reach the ovaries in Hyznar's study. This might account for the fact that images with quality sufficient for interpretation could be obtained using a very small amount of pertechnetate (18.5 MBq or 0.5 mCi) in our study. The total radiation dose thus might be reduced. However, comparison between intrauterine injection and vaginal instillation using pertechnetate awaits further study.

A parallel-hole general-purpose collimator instead of a pinhole collimator was used in our study. However, use of a pinhole collimator would be helpful. Unfortunately, the low energy pinhole collimator has not been available from the manufacturer for the type of gamma camera we used. Although resolution may be theoretically decreased, the results of our study revealed an accuracy of 84.5%. The results were obtained when contrast HSG was used as the gold standard. If it is correct that the anatomically patent but functionally obstructed fallopian tube can be differentiated by RNHSG (*1*), only 2 out of 56 fallopian tubes studied were incorrectly classified by RNHSG in this report. This would increase the accuracy of RNHSG from 84.5% to 96.4%.

The mean diameter of 20 μm of HAM, approximates the size of human sperm. The size of free [^{99m}Tc]pertechnetate is smaller than this. There is the possibility that the fallopian tubes are patent for [^{99m}Tc]pertechnetate, but obstructed for HAM or human sperm. In our study, the predictive value of a positive test was 95% (37/39). This was close to the positive predictive value of 97% (34/35) in McCalley's study and comparable with 87% (13/15) in Kennedy's study (HAM was used in both of these studies). Based on these figures, we believe that this possibility is low but further studies with comparison between [^{99m}Tc]

pertechnetate and ^{99m}Tc-HAM are needed to confirm this. On the other hand, if the fallopian tubes are obstructed with [^{99m}Tc]pertechnetate, there is only a very low possibility that the tubes may be patent with ^{99m}Tc-HAM. RNHSG with [^{99m}Tc]pertechnetate is thus very helpful to identify tubal obstruction. It is especially helpful for infertile patients. For functionally obstructed fallopian tubes, GIFT or ZIFT may be less successful.

Van der Weiden and van Ziji quoted a mean dose of 1.28 mGy for contrast HSG (*5*). Freedmen et al. reported a mean dose of 1.1 mGy using electronic fluorography (*15*). Higher mean doses for HSG have been reported: 33.66 mGy (*16*) and 5.25 mGy (*17*) for fluoroscopy and three spot films, and 6.75 mGy (*2*) for three spot films alone. The National Council of Radiation Protection and Measurement quoted a high dose of 67 mGy not including the dose due to fluoroscopy (*18*). In this study with the use of as small as 18.5 MBq (0.5 mCi) of [^{99m}Tc]pertechnetate, functional patency of fallopian tubes could be investigated. The radiation dose estimated was about 1.08 mGy per study. It was comparable to or, in most cases, lower than the reported doses for contrast HSG.

RNHSG with slow intrauterine administration of a small dose of [^{99m}Tc]pertechnetate may represent an accurate test of tubal function and it is as safe as contrast HSG considering the low radiation dose.

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