Ventilation Scintigraphy of the Middle Ear

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In this study, an attempt was made to administer radioactive gas into the tympanic cavity to measure initial gas trappings as well as clearance from the middle ear to evaluate eustachian tube function. **Methods:** Twenty-eight patients were administered 50 MBq ^{133}Xe gas. Three different methods for gas application were tested: (a) direct injection through a tympanostomy tube in two patients, (b) administration through a nasopharyngeal catheter combined with Valsalva maneuvers in six subjects without middle ear dysfunction and (c) insufflation into the pharyngeal space through a nose olive performed in 12 patients with normal eustachian tube function and in eight patients with one-sided tube dysfunction. **Results:** All three approaches were successful in visualizing middle ear ventilation, demonstrating tracer trapping within the tympanic cavities in 20 of 28 patients. Semiquantitative evaluation by region of interest techniques revealed a left-to-right uptake ratio of 48.4%-51.6% in 13 patients without tube dysfunction. Five patients with one-sided tube dysfunction showed a significantly lower median uptake of 31.6% ($p = 0.01$). The clearance half-lives ranged from 9 to 283 min in normal subjects and 37–64 min in patients with one-sided tube malfunction, demonstrating no statistically significant difference between the two groups and a trend towards increased washout in patients with tympanic dysfunction. **Conclusion:** Middle ear ventilation scintigraphy with ^{133}Xe through a nose olive is an easy-to-perform test to evaluate eustachian tube function and has a success rate of about 70%, thus, reflecting the complex physiological mechanisms involved.

Key Words: middle ear ventilation; eustachian tube function; ventilation scintigraphy; xenon-133

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The application of radioactive gas or aerosol for diagnostic purposes in medicine is mainly used for lung ventilation scintigraphy, although many cavities in the ear, nose and throat regions are physiologically subject to air ventilation to maintain their function. In particular, the middle ear space reacts pathologically when eustachian tube ventilation fails or is insufficient (*1*). In current clinical settings, tympanometry is the most commonly used test in patients with intact tympanic membrane. In this test, the impedance of the middle ear system is obtained as an indirect and qualitative measure for tube function. However, there has been no quantitative test for clinical practicability to quantitate tube function for both diagnosis and follow-up in patients with middle ear affections, although numerous studies of direct and indirect quantification methods have been published (*2–6*).

The application of radioactive gas for measuring middle ear ventilation by puncturing the cellular system was suggested in 1970 by Elner and Nilsen (*7*). The first scintigram of pneumatic spaces of the ear and the paranasal sinuses with ^{133}Xe was obtained by Kirchner in 1974 (*8*). There have been few attempts to use nuclear medicine procedures to evaluate tympanic cavity ventilation or to measure uptake and clearance half-life of ventilated radioactive gas in the middle ear (*9–12*).

In this study, several methodological approaches for invasive and especially noninvasive administration of ^{133}Xe gas into the tympanic cavity were attempted to investigate middle ear ventilation.

MATERIALS AND METHODS

Patients

Studies were performed on 28 patients (13 women, 15 men; age range 23–74 yr; mean age 43 yr). Prior to scintigraphy, standard ENT tests including otoscopy, endonasal examination by rigid Hopkins endoscopes, tympanometry, audiometry and standard radiograph of middle ear and paranasal sinuses were performed on all 28 patients. Due to this workup, 18 patients with normal tympanometry were considered normal concerning eustachian tube function. In the remaining 10 patients, one-sided tube dysfunction was stated with normal contralateral tube function (Table 1).

Tracer

Xenon-133 with a gamma radiation of 81 keV and a physical half-life of 5.3 days was used. The gas was supplied in a multidose container holding 925 MBq ^{133}Xe in 10 ml volume. Throughout this study, a patient dose of 50 MBq ^{133}Xe dissolved in 50 ml air volume was administered in a 50-ml, lead-shielded syringe.

Administration Procedures

The tracer was injected directly through a tympanostomy tube by flushing the middle ear with 50 ml gas in Patients 1 and 2 (Table 1, Procedure A). The external ear channel was then closed with a wax plug allowing the measurement of the clearance from the middle ear.

Radioactive gas was injected through a flexible nasal tube placed into the nasopharynx in six patients without tube dysfunction. Gas uptake in the middle ear was increased with the patients performing three Valsalva maneuvers (Procedure B).

In 12 patients with normal tube function and eight with one-sided tube malfunction (Table 1), ^{133}Xe was applied into the nasopharyngeal space through a tube connected to a tightly fitting nasal olive in the right nostril while the other nostril was closed. Immediately after insufflation, patients were asked to perform three Valsalva maneuvers (Procedure C).

Data Acquisition and Processing

Sequential gamma camera imaging was performed obtaining images initially at 60-sec intervals for 10 min. Imaging was then continued in 5-min intervals up to 30 min. A double-headed camera system with high-resolution, low-energy collimators was used for simultaneously recording of the anterior and posterior views. Visual interpretation of the images was completed by calculating the side-related uptake in the tympanum after 3 and 4 min from

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TABLE 1
Clinical Data*

Patient no.	Sex	Age	Diagnosis	Imaging
1	F	46	Chronic inflammation of the right middle ear	Possible
2	M	59	Carcinoma of the left epipharynx (T4)	Possible
3	M	47	Recurrent inflammation after tympanoplasty	Possible
4	M	23	Acute inflammation of the right middle ear	Negative
5	F	53	Carcinoma of the right palatinal tonsil (T3)	Possible
6	M	39	Acute inflammation of the left middle ear	Possible
7	F	47	Cholesteatoma of the right middle ear	Possible
8	F	52	Chronic tonsillitis and left-sided otitis	Negative
9	M	61	Carcinoma of the right palatinal tonsil (T3)	Negative
10	M	33	Left-sided peritonsillitis	Possible

*In three patients, scintigraphic imaging of the middle ears was not successful.

posterior projections as well as by plotting time-activity curves of the middle ear using region of interest (ROI) techniques. For the time-activity curves, background correction was necessary because of contaminations by exhaled ^{133}Xe gas, in particular, on the early images. Irregular ROIs for the middle ear regions and a rectangular ROI over the brain for background measurement were used. Exponential curve fitting revealed the clearance half-life of the tracer from the tympanic cavity starting 3 min after gas insufflation in order to reduce the influence of scattered radiation from the initial high activity in the nose and pharyngeal cavity.

Normal Ranges

The subset of 18 patients with normal eustachian tube function was used for determination of a normal range of the xenon clearance from the middle ear and for the evaluation of a left-to-right uptake ratio. The data given in the Results Section are median and range as well as mean $\pm$ 1 s.d. To evaluate statistical differences considering $p < 0.05$ significant both Wilcoxon-Mann-Whitney test and two-tailed Student's t-test for unpaired data were used.

RESULTS

The main finding of this study was that visualization of the middle ear is feasible by ventilation scintigraphy with surprisingly high contrast in most patients and by all three approaches, yielding an overall success rate of 69%.

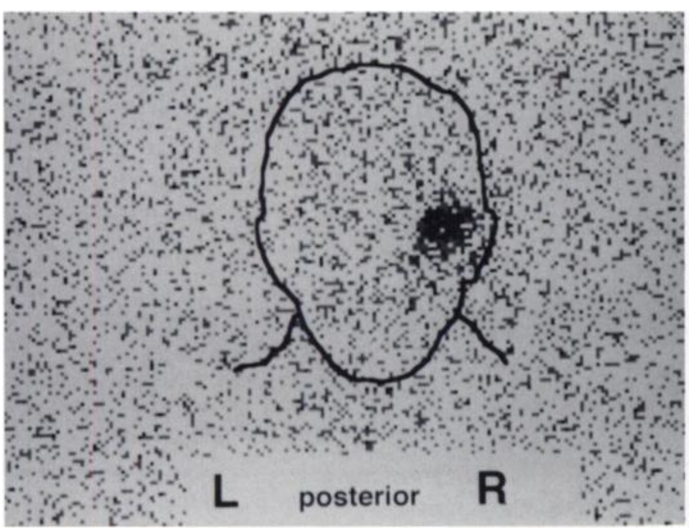

FIGURE 1. Posterior view of head 15 min postinjection of 50 MBq ^{133}Xe gas into the right tympanic cavity through a tympanostomy tube in Patient 1 shows tracer accumulation in the right middle ear region.

In both patients to whom ^{133}Xe was administered directly into the tympanic cavity, the middle ear could be clearly seen (Fig. 1) on the posterior view. In these two patients, clearance half-lives were 53 and 163 min, respectively. Tracer application through a tympanostomy tube needs skillful experience because touching the ear channel or the tympanic membrane is extremely painful and can hardly be avoided when pushing a tiny needle through the tympanostomy tube for gas insufflation.

Procedure B was not painful, but use of a nasal catheter was rather inconvenient for the patients. By this method of indirect and noninvasive tracer application supported by three Valsalva maneuvers, visualization of the tympanum was possible in four of six patients. The clearance half-lives of these four patients, without middle ear dysfunction, ranged from 32 to 237 min (mean 115 min). Median side-related tracer uptake was 45.4% for the left side and 54.6% for the right side. An example demonstrating the whole sequence of images from anterior and posterior views is shown in Figure 2.

Procedure C—insufflation of the gas through a nasal olive—proved to be the easiest to perform and the most comfortable procedure for the patients. When using this method, ventilation of the maxillary sinuses could be observed in all patients. A representative example is shown in Figure 3. Visualization of the tympanum was possible in 14 of 20 patients (70%). In nine patients with normal middle ear function, the median clearance half-life was 55 min, ranging from 9 to 283 min, and the side-related uptake was 49.8% for the left side and 50.2% for the right. In five patients with one-sided tube malfunction, the median uptake was 31.6% and clearance half-lives ranged from 37 to 64 min (mean 55 min) for the side of dysfunction. The corresponding clearance values of the contralateral, i.e., normal side ranged from 31 to 210 min (mean 104 min). Figure 4 demonstrates decreased uptake in the left middle ear region in a patient with proven left-sided malfunction of the eustachian tube.

According to Procedure B or C, the time-activity curves usually showed an initial fast decrease of activity during the first 2 or 3 min followed by a slow washout phase, while the two patients with direct insufflation of the tracer gas into the tympanic cavity revealed only a slow washout similar to the second phase of the curves in patients with indirect xenon application. An example is given in Figure 5.

The results of quantitative evaluation of middle ear ventilation are summarized in Table 2. First, there were significant differences ($p = 0.01$) of initial tracer uptake in the middle ear between patients with normal and patients with one-sided tube malfunction. In the latter subset, tracer uptake of the corre-

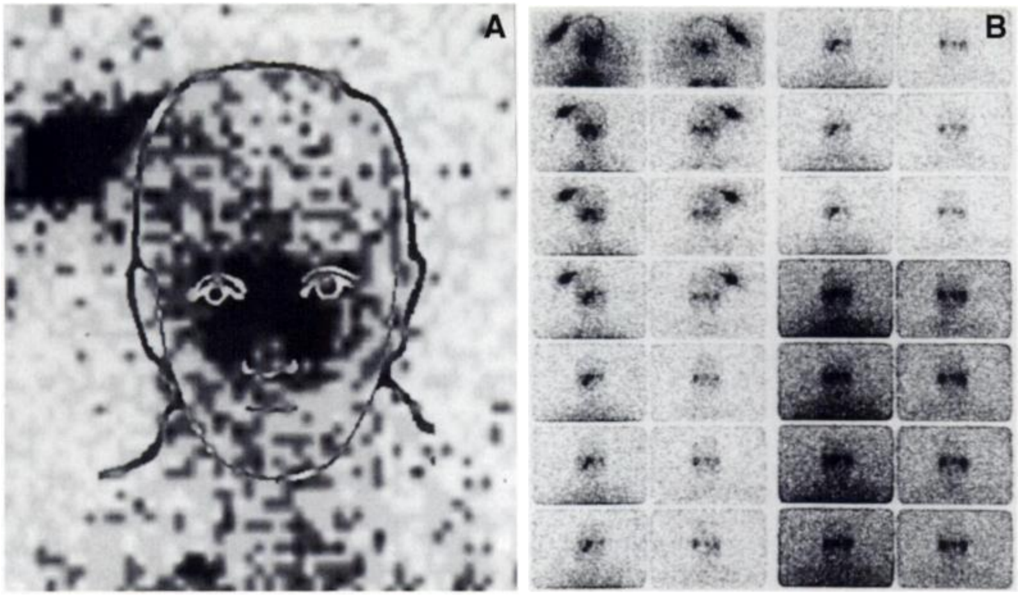

FIGURE 2. Images after administration of 50 MBq ^{133}Xe through a nasal catheter in accordance with Procedure B. Anterior view (A) 2 min after insufflation shows activity in the nose and pharynx, paranasal sinuses and in the syringe on top right of the patient. (B) Image sequence from anterior and posterior views beginning with the left upper images (10 $\times$ 1 min, 4 $\times$ 5 min). From posterior view, both middle ear regions can be seen on all images 2–30 min after tracer insufflation.

sponding side was less than 32% in each case, but overlapping of normal and pathological values occurred in only one patient. Second, there were no significant differences in the widely scattering clearance half-lives between patients with normal function and patients with one-sided tube malfunction. However, patients with one-sided malfunction had tracer half-lives ranging from 37 to 64 min, while about 40% (9 of 23 values) of the values of patients without tube dysfunction were higher than 100 min. Third, there were no significant differences between Procedures B and C for successful visualization of the tympanic cavities, tracer uptake and clearance half-life.

DISCUSSION

We have presented a new approach for noninvasive investigation of ventilation in the ear, nose and throat region using ^{133}Xe. Among the few reports dealing with scintigraphic ventilation studies of the tympanum (*7–12*), there are data on direct and invasive tracer application by puncturing the cellular system (*7*) or application through a tube inserted into the pharyngeal orifice of the eustachian tube (*11*). Paulsson et al. (*12*) mentioned xenon uptake in the middle ear when studying ventilation of paranasal sinuses by SPECT without presenting data on tympanum ventilation, and the reports of Kirchner et al. (*8,9*) focused mainly on imaging technique. Our study focused on different ventilation procedures of the middle ear to finally develop a semiquantitative test to evaluate eustachian tube function.

Technical Aspects

The major result of this study is the successful scintigraphic imaging of the middle ear under nearly physiological conditions with the patients performing only Valsalva maneuvers. The concentration of radioactivity in the pharyngeal space as used in this study, i.e., 50 MBq ^{133}Xe per 50 ml air flushed into the nasopharynx, is sufficient for imaging middle ear ventilation using conventional nuclear medicine equipment.

Based on our experience, most of the subjects studied were able to perform correct Valsalva maneuvers. Therefore, radioactive gas can be administered simply through a nose olive according to Procedure C, which is a convenient method for the patients and has a 70% success rate for visualizing the tympanum. For some patients, it was difficult to perform effective Valsalva maneuvers or to keep their breath between gas insufflation and Valsalva's actions. However, in four patients, no tracer trapping in the tympanic cavities was observed, although the patients seemed to perform well. In these subjects, physiological conditions of middle ear ventilation were most probably responsible for the lack of tracer trapping. When performing Valsalva maneuvers, the tubes do not open in all patients to let air into the tympanum (*1*). In particular, when overpressure becomes too high in the nasopharynx, a locking of the tubes can occur, and then they do not open without swallowing (*13*). Furthermore, the opening of the tube depends on the patient's position: In an upright position the opening

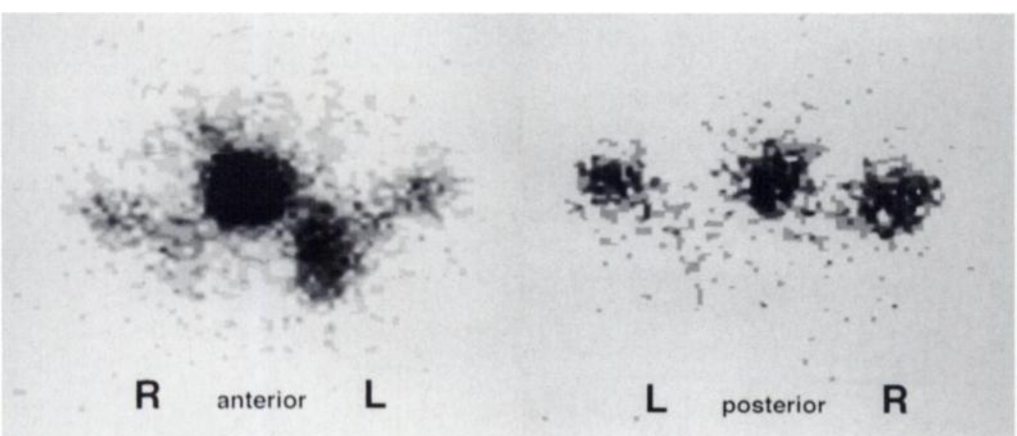

FIGURE 3. Images 15 min after 50 MBq ^{133}Xe administration through a nose olive according to Procedure C. From the anterior view, there is marked tracer uptake in the nasopharynx, ethmoidal and sphenoidal sinuses and in the left maxillary sinus, while accumulation of ^{133}Xe in the tympanic cavities is only faint due to skull attenuation. Corresponding posterior view clearly shows activity in both tympanic cavities.

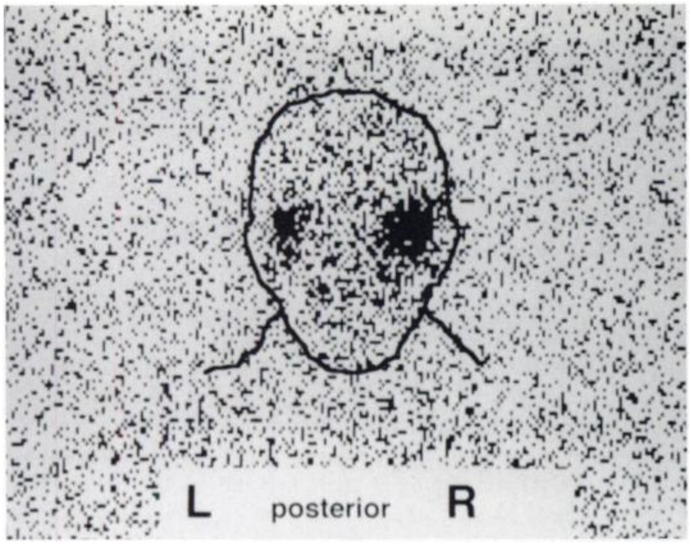

FIGURE 4. After 50 MBq ^{133}Xe insufflation through a nasal olive, scintigram demonstrates decreased uptake of only 31.6% in the left middle ear region in a patient with proven left-sided tube malfunction (Patient 6).

occurs more regularly than in a supine position (*1*). Therefore, after air displacement with ^{133}Xe, Valsalva maneuvers in combination with swallowing should be performed to improve imaging as suggested by Kirchner et al. (*9*). Xenon should be administered in an upright position to support the tube opening and not in the supine position on the camera table as done in this study.

Finally, there is a principal technical problem due to tracer application supported by Valsalva maneuvers: The gas is forced with pressure into the tympanic cavities through the eustachian tubes. It is not known whether tube function is influenced by this partially nonphysiological method, but it seems possible that minor disease-caused differences in tube function and, thus, in side-related uptake may be missed when using Valsalva maneuvers.

Quantification

One measure of tube function might be a simple left-to-right comparison assuming that one tube has normal function. In this study, the side-related uptake was calculated by 3- and 4-min images from the posterior view. In the anterior view, nose, pharynx, paranasal cavities and middle ear space are hardly separated by ROI techniques, so that cross-contamination of the tympanum will occur in almost every case. In the posterior view, the middle ear region could be separated from nasal and sinusoidal activity because of the dorsal position of the tympanum and the rather high photon attenuation of ^{133}Xe by the skull. However, even in the posterior view on the first images, accurate separation of the middle ear region was difficult. On later images, however, the uptake ratio might change because of different tracer clearance. Therefore, 3- and 4-min posterior view images were considered to best reflect tracer uptake. As shown in Table 2, the uptake ranged from 32.4% to 67.6% in normal subjects, while the results in patients with one-sided tube dysfunction ranged from 15.3% to 31.7%. Only one patient had an uptake of 44.9% on the side with dysfunction. Thus, uptake values were significantly different in normals and patients with one-sided tube dysfunction, a finding that confirms the results of Yamashita et al. (*11*), who reported reduced xenon inflation into the middle ear in patients with occluded tubes when using direct tracer application into the orifice of the eustachian tube.

Another parameter for tube function might be tracer clearance. Because of cross-contamination of the middle ear ROI during the first minutes, clearance half-lives were calculated by exponential curve fitting using the time-activity curves from 4 to 30 min postinjection. As shown in Figure 5, the initial fast decrease of activity was observed only when there was high activity in the nose and pharyngeal cavity during the first minutes according to Procedure B or C. Paulsson et al. (*12*) have already mentioned the possibility of underestimating half-times due to the influence of scattered radiation, especially in sinuses with low activity as represented by the tympanic cavities. To calculate clearance half-life, the first 3 min of data were not considered in this study. As shown in Table 2, clearance values were widely scattered, ranging from 9 to 283 min in patients with normal eustachian tube function. The tube normally opens only during swallowing and not necessarily during each act of swallowing (*1*). Therefore, there is no continuous and free gas exchange between the middle ear and the nasopharynx.

Furthermore, most gases, including xenon, are continuously absorbed (*7,11,14*) and diffuse into the blood vessels. Consequently, activity was found in the expired air of patients after direct inflation of ^{133}Xe into the tympanum (*7*). According to these physiological facts, the xenon clearance is primarily a function of resorption into the bloodstream and not middle ear ventilation. Therefore, the clearance should be faster in patients with inflammatory middle ear disease according to increased blood flow. This hypothesis is supported by the results of Yamashita et al. (*11*) showing a higher clearance rate from the tympanum in patients with pathologic middle ear mucosa. Our findings also suggest a trend to increased washout from the affected tympanum, but there was no significant difference in patients with normal middle ear function. Thus, the initial tracer uptake as a measure of eustachian tube function seems to be of greater clinical significance than clearance half-life.

Further Applications

As shown in Figure 3, the tracer is also ventilated into the paranasal cavities when administered through a nose olive. In all of these patients, the maxillary sinuses were clearly seen from anterior view. The clearance half-life was 17 ± 9 min for both the right and left maxillary sinuses. These consistent clearance data with a small range of clearance half-life and quick washout compared to the tympanum are due to the

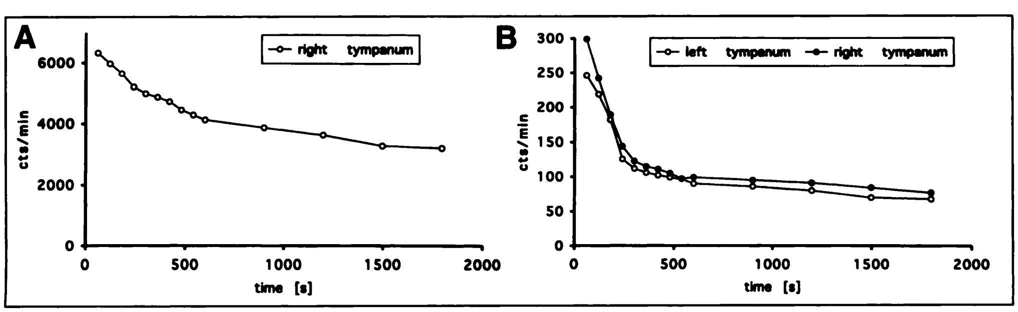

FIGURE 5. Time-activity curves of the tympanum over 30 min. (A) There is only a phase of slow washout after direct insufflation of ^{133}Xe into the tympanum through a tympanostomy tube. (B) After indirect tracer application through a nose olive, Procedure C, initial fast decrease of activity due to cross-contamination from the nose and paranasal sinuses is observed followed by a slower phase of declining activity corresponding to the washout of the patient shown in (A).

TABLE 2
Middle Ear Uptake and Washout of Xenon-133 for Administration Procedures A–C in Normal Subjects and Patients with One-Sided Tube Malfunction

	Uptake (%)	CHL (min)
Subjects (Procedure B) (n = 4)		
Median	45.4:54.6	115
Mean ± s.d.	48.6 ± 8.6:51.4 ± 8.6	100 ± 75
Range	38.7–61.3	32–237
Subjects (Procedure C) (n = 9)		
Median	49.8:50.2	55
Mean ± s.d.	48.3 ± 8.5:51.7 ± 8.5	79 ± 72
Range	32.4–67.6	9–283
Subject (Procedure B + C) (n = 13)		
Median	46.0:54.0*	59†
Mean ± s.d.	48.4 ± 8.1:51.6 ± 8.1*	86 ± 72†
Range	32.4–67.6	9–283
Patients (n = 5)		
Median	31.6*	55†; 104‡
Mean ± s.d.	30.4 ± 10.5*	50 ± 12†; 102 ± 70‡
Range	15.3–44.9	37–64; 31–210‡

*Significantly different uptake values in patients with normal eustachian tube function and patients with one-sided tube malfunction ($p = 0.01$).
†No significant differences ($p > 0.05$).
‡Values of the contralateral side with normal tube function.
CHL = clearance half-life; uptake = left-to-right uptake.

constantly open airway passage of the maxillary sinuses, which clearly represents the involved physiological mechanisms. Thus, the use of ^{133}Xe might also serve as a functional test to estimate maxillary sinus ventilation.

Radiation Load

The radiation recieved can be estimated according to the doses reported for lung ventilation scintigraphy with ^{133}Xe. For a 5-min rebreathing ventilation study with ^{133}Xe, the following dosimetric data are given in mGy/MBq: total body 2.7E-3, gonade 8.1E-4, lungs 6.8E-3 and trachea 2.7E-2 (*15*). The effective dose equivalent is 7.3E-4 mSv/MBq (*16*). In comparison with lung ventilation scintigraphy, usually performed with about 500 MBq ^{133}Xe over a rebreathing time of 5 min, the received radiation for tympanic ventilation scintigraphy with 50 MBq and an exposure time of full activity of about 0.5 min ought to be approximately 100 times lower. Since tracer trapping in the middle ear occurs with a half-life of approximately 100 min, the middle ear space and its mucosa will be the critical organs. However, only a fraction of the 50 MBq administered are finally trapped, and no radiation-sensitive structures are to be considered next to the tympanic cavity. Thus, tympanic ventilation scintigraphy using 50 MBq ^{133}Xe can be considered as a nuclear medicine procedure with very low radiation exposure.

CONCLUSION

Tympanum ventilation scintigraphy with ^{133}Xe—simply applied through a nose olive in combination with Valsalva maneuvers—is an easy-to-perform, low radiation-burden test for middle ear ventilation. Moreover, the 70% rate of successful visualization of tympanic ventilation stresses the importance of patient compliance and the complex physiological mechanisms of middle ear ventilation. In quantifying tube function, initial tracer uptake seems to be of greater clinical significance than measuring washout clearance. Although the number of patients in this study is limited, the test may be suggested for clinical evaluation of larger patient groups. Furthermore, this test seems applicable for ventilation studies of the paranasal cavities.

REFERENCES

1. Thullen A. Prüfung von Tubenfunktion und Paukendruck In: Berende J, Link R, Zöllner F, eds. *Hals-Nasen-Ohren-Heilkunde in Praxis und Klinik. Band 5: Ohr I.* Thieme, Stuttgart; 1979;15.1–15.36.
2. Perlmann HB. Physiological basis of tubal function tests. *Arch Otolaryng* 1960;71: 384–385.
3. Ingelstedt S, Örtegren U. Qualitative testing of the eustachian tube function. *Acta Otolaryngol (Stockholm)* 1963;182(suppl):7–23.
4. Flisberg K, Ingelstedt S, Örtegren U. Controlled ear aspiration of air. A physiological test of the tubal function. *Acta Otolaryngol (Stockholm)* 1963;182(suppl):35–38.
5. Guillerm R, Riu R, Badre R, Le Den R, Le Mouel C. Une nouvelle technique d'exploration fonctionelle de la trompe d'eustache. La sonomanometrie tubaire. *Ann Oto-Laryngol* 1966;83:523–542.
6. Münker G, Pedersen P, Grundmann S. Tubenfunktionsprüfung in der Druckkammer: registrierung mittels eines differentialmanometres. *Arch klin exp Ohr Nas Kehlk Heilk* 1972;201:249–257.
7. Elner A, Nilsen R. Preliminary studies of gas resorption from the middle ear. *Acta Otolaryngol (Stockholm)* 1970;70:197–202.
8. Kirchner FR. Radio scanning studies of ear and sinuses. *Laryngoscope* 1974;84:1894–1904.
9. Kirchner FR, Robinson R, Smith RF. Study of the ventilation of middle ear using radioactive xenon. *Ann Otol Rhinol Laryngol* 1976;25(suppl):165–168
10. Dressler J, Heiden C, Lichte H. Untersuchungen zur Ventilation der pneumatisierten Räume des Schädels mit Radioxenon. In: Schmidt HAE, ed. *Nuclear Medicine: quality factors in nuclear medicine.* New York: Schattauer, Stuttgart; 1977: 823–826.
11. Yamashita T, Maeda N, Tomoda K, Kumazawa T. Middle ear ventilation mechanism. *Acta Otolaryngol (Stockholm)* 1990;471(suppl):33–38.
12. Paulsson B, Bende M, Larsson I, Ohlin P. Ventilation of the paranasal sinuses studied with dynamic emission computer tomography. *Laryngoscope* 1992;102: 451–457.
13. Flisberg K. Ventilatory studies on the eustachian tube. *Acta Otolaryngol (Stockholm)* 1966;219(suppl):1–82.
14. Ingelstedt S, Jonson B. Mechanism of the gas exchange in the normal human middle ear. *Acta Otolaryngol (Stockholm)* 1967;224(suppl):452–461.
15. Moses DC. Pulmonary ventilation scanning. In: Keyes JW, ed. *CRC manual of nuclear medicine procedures.* West Palm Beach, FL: CRC Press; 1978:121–123.
16. Johansson L, Mattsson S, Nosslin B, Leide-Svegborn S. Effective dose from radiopharmaceuticals. *Eur J Nucl Med* 1992;19:933–938.