Lacrimal Gland Dosimetry for the Brain Imaging Agent Technetium-99m-HMPAO

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We calculated lacrimal gland dosimetry for the brain imaging agent ^{99m}Tc-HMPAO. One hundred thirty-eight patients were studied using a dedicated brain imaging device. Only 11% of the patients showed lacrimal gland uptake. For a 740-MBq (20 mCi) injected dose of ^{99m}Tc-HMPAO, the radiation exposure to the lacrimal glands is 10.2 mGy (1.02 rad), or 0.0138 mGy/MBq (0.051 rad/mCi). These values are five times lower than the ones reported by the manufacturer of HMPAO. As the dosimetry calculation is only for subjects showing ^{99m}Tc-HMPAO uptake in the lacrimal gland, the average radiation dose to all subjects is considerably lower, 1/10 of the estimated value.

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Technetium-99m d,l, hexamethylpropylene amine oxime (^{99m}Tc-HMPAO, exametazime, Ceretec™, Amersham, Arlington Heights, IL), is a cerebral perfusion imaging tracer (*1–5*). It is a lipophilic molecule that crosses the blood-brain barrier (BBB), where it is transformed to a hydrophilic form. The brain retention time is prolonged and single-photon emission tomography (SPECT) can be performed several hours later.

Technetium-99m-HMPAO has many characteristics which make it suitable for brain SPECT imaging. Technetium-99m-HMPAO in its d,l, optical configuration has a high first-pass extraction by the brain. Three and one-half to seven percent of the injected dose is taken up by the brain and equilibrium is reached within 2 min. Only 15% of the amount taken up by the brain may diffuse back (*3*). Once in the brain, ^{99m}Tc-HMPAO is converted to a meso-optical hydrophilic form that is trapped and cannot cross the BBB. After this period, the brain concentration does not change significantly for 24 hr. The biologic half-life in the brain is estimated to be 71 hr (*4,5*).

Dosimetry for ^{99m}Tc-HMPAO has been calculated by its manufacturer (Amersham, Arlington Heights, IL). The target organs are the lacrimal glands which receive 57 mGy (5.7 rad) from a 740-MBq (20 mCi) dose (*6*). This relatively high value limits the administered dose of ^{99m}Tc-HMPAO. We have calculated lacrimal gland dosimetry with a larger number of patients than originally studied by Amersham.

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MATERIALS AND METHODS

Study Population

We analyzed a total of 154 brain ^{99m}Tc-HMPAO SPECT studies. The reason for performing a brain SPECT scan were multiple: normal volunteers, evaluation of dementia, stroke, seizure, and psychiatric disorders. All were adult subjects. One hundred thirty-eight patient studies were selected because the whole volume of the orbit including the lacrimal gland region was included in the transaxial slices. The dosimetry calculations that follow derive from 15 patients who showed uptake in the lacrimal glands (11% of the studied group).

Procedure

HMPAO is available as a lyophilized kit. Freshly eluted technetium pertechnetate is added and in the presence of a stannous reductant a lipophilic compound is formed, the d,l diastereoisomer. A yield of >90% of d,l ^{99m}Tc-HMPAO is obtained by using freshly eluted sodium pertechnetate ^{99m}Tc and using the preparation within 20 min after reconstitution (*1,5*). The patient dose was 740 MBq (20 mCi) of ^{99m}Tc-HMPAO, injected intravenously, and SPECT acquisition was begun 60 min later.

Imaging of ^{99m}Tc-HMPAO distribution in cerebral cortex can be optimally achieved with a brain-dedicated imaging device and by using high resolution collimation (Shimadzu Headtome Set 031, Kyoto, Japan) (*7,8*). Resolution of 8 mm in the brain cortex and 9.6 mm at the level of the basal ganglia is achieved, comparing favorably to the 15-mm resolution of the rotating gamma camera. Relatively high sensitivity is also maintained and typically the total number of counts in the series of transaxial slices is 20 million, which is 6 times more than the counts obtained with a rotating gamma camera. Nine 1.6-cm thick transaxial slices cover the whole brain volume. The attenuation correction factor for ^{99m}Tc was obtained from a pool phantom filled with water. All calculations were done on images corrected for uniformity and attenuation.

Radiation Dose Calculation

Lacrimal gland uptake was present in 15 patients (11%) and was quantified as follows. We assumed that 5% of the injected dose (37 MBq, 1 mCi) was retained by the brain

(*3,5*). Areas of interest were drawn over the two lacrimal glands and also over the whole brain volume (nine transaxial slices), and counts were obtained. The lacrimal gland uptake was calculated from the ratio to the brain uptake (37 MBq, 1 mCi) and ranged from 185 to 296 Bq (5 to 8 μCi) with a mean of 222 ± 37 Bq (6 ± 1 μCi), mean ± s.d. The measurements were done 1 hr after administering ^{99m}Tc-HMPAO and the values corrected for decay are 259 ± 37 Bq (7 ± 1 μCi).

As the normal tear production averages 1.7–9.4 ml/24 hr and the tear volume is 6 μl/eye with a turnover rate of 1.2 μl/min (*9,10*), the residence time in the gland in normal conditions may follow an exponential washout. But we estimated the worst possible situation, where ^{99m}Tc-HMPAO is retained without removal. Other investigators used the same approach where the lacrimal gland uptake was considered to be constant over a 24-hr period (*11,12*).

Dose (D) was calculated using the MIRD format. The following parameters and definitions were used: Activity at time 0 (A_0) = 259 Bq (7 μCi) for the lacrimal glands and 37 MBq (1,000 μCi) for the brain, physical half-life of ^{99m}Tc ($T_{½}$ (eff)) = 6 hr, S values from (*11*).

a) D 1 = lacrimal gland → lacrimal gland
$= A_0 * (1.44 * T_{½}(\text{eff})) * S\ 1$
$= 7 * (1.44 * 6) * 0.0147$
= 0.889 rad (8.89 mGy)

b) D 2 = brain → lacrimal gland
$= A_0 * (1.44 * T_{½}(\text{eff})) * S\ 2$
$= 1000 * (1.44 * 6) * (6.65 * 10^{-6})$
= 0.057 rad (0.57 mGy)

c) D 3 = total body → lacrimal gland
was substituted for
= total body → thyroid as described in (*11*)
$= \tilde{A}S = (2436) * (20) * (1.5 * 10^{-6})$
=0.073 rad (0.73 mGy)

Total dose to lacrimal gland:
= 1.02 rad / 20 mCi
= 10.2 mGy / 740 MBq
= 0.051 rad / mCi
= 0.0138 mGy / MBq.

As the brain uptake of ^{99m}Tc-HMPAO ranges from 3.5% to 7% (*1,3,5*), we may over- or underestimate lacrimal gland dosimetry by ~30%, a range acceptable for most dosimetry calculations.

CONCLUSION

Our results show that the radiation absorbed dose to the lacrimal glands from a diagnostic dose of ^{99m}Tc-HMPAO is acceptably low. Only 11% of our patient population had significant lacrimal gland uptake, and for a 740-MBq (20 mCi) injected dose they receive 10.2 mGy (1.02 rad). The original series of Amersham includes 22 patients from four centers in Europe and only a few of those patients had lacrimal gland uptake (*11*). Our study is probably more reliable because of the large number of patients studied and the use of a device that is six times more sensitive than the gamma camera and has better resolution. The composition of the lacrimal gland uptake after injection of ^{99m}Tc-HMPAO is not known, and may be related to the primary d,l lipophilic form, to the secondary hydrophilic complex, to free pertechnetate, and/or to reduced hydrolyzed technetium. If the uptake is due to an anion such as free pertechnetate, it might be blocked with a competing anion such as perchlorate (ClO_4^-). This mechanism is possible as the lacrimal gland is the only epithelial tissue of the orbit with characteristics similar to the salivary glands.

Soon after the injection of ^{99m}Tc-HMPAO, 30% of the dose is found in the gastrointestinal tract. Over 48 hr, 50% of the dose is excreted through the gastrointestinal tract and 40% through the kidneys and urine (*2,5,6*). The organs that receive the highest radiation dose are the gallbladder wall (0.054 mGy/MBq, 0.20 rad/mCi), kidneys (0.038 mGy/MBq, 0.14 rad/mCi), and the upper larger intestine (0.027 mGy/MBq, 0.10 rad/mCi) (*11,12*). These values are comparable to those received in diagnostic procedures such as biliary scanning with ^{99m}Tc-HIDA and myocardial perfusion imaging with thallium-201 and gallium-67 imaging.

Since lacrimal gland uptake has been thought to be quite high, it is considered to be a limiting factor in determining the administered dose of ^{99m}Tc-HMPAO. Our results suggest that the dose could be increased to 1,100 MBq (30 mCi), thus improving counting statistics for SPECT while maintaining acceptable lacrimal gland dosimetry.

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A Comparative Study of Contrast Dacryocystogram and Nuclear Dacryocystogram

Tapan K. Chaudhuri, Gerald R. Saparoff, Kenneth D. Dolan, and Tuhin K. Chaudhuri

The technique of choice for evaluating obstruction in the lacrimal drainage apparatus is, at present, contrast dacryocystography (DCG). In this study, we compare contrast DCG with nuclear DCG in order to assess the accuracy of the latter procedure.

Twenty-one patients having symptoms of blockage were studied using both contrast and nuclear DCG. Approximately 200 mCi of pertechnetate in 0.01–0.05 ml sterile saline solution was used as an eye drop for each eye. Following instillation of the radioisotope in the conjunctival sac, the patients' eyes were scanned sequentially at 0, 5, 10, and 15 min. Both polaroid and conventional X-ray films were exposed. Physicians were only allowed to evaluate one of the two studies.

Twelve studies demonstrated obstruction in the lacrimal drainage system in both contrast and nuclear DCG. Seven had unilateral obstruction; five had bilateral obstruction. Five patients underwent dacryocystorhinostomy, and a postoperative scan also was obtained in this group of patients. Two studies were normal in contrast DCG and irrigation but abnormal in nuclear DCG (functional block). Two studies demonstrated anatomic discontinuity of canaliculus.

The procedure commonly employed at present to diagnose blockage in the lacrimal drainage apparatus is radiographic contrast DCG. The major disadvantage of this technique is the requirement of catheterization of the canaliculi, thus, traumatizing the patient.

We observed a good correlation between these two techniques in all studies. In none of our cases did we observe abnormal constrast DCG but normal nuclear DCG. In two studies, there was a discrepancy, namely, normal contrast DCG but abnormal nuclear DCG. The reason for this discrepancy is that the contrast DCG is performed under manual injection pressure while nuclear DCG is a physiologic study mimicking the normal state of tear drainage. With contrast DCG, normal and extreme pathologic obstruction can be demonstrated. In functional block, however, such as in abnormal lacrimal pump or partial stenosis of the nasolacrimal duct, the nuclear DCG would be abnormal whereas the contrast DCG would be normal. Thus, contrast DCG, which employs direct catheterization of the canaliculi and injection under pressure, could create a false passage or open up physiologic or anatomic blocks—thus erroneously implying normality.

We therefore think nuclear DCG is superior to contrast DCG because it is an atraumatic procedure, provides better diagnosis of functional and anatomic block, and delivers a smaller radiation dose to the lens and anterior chambers. ■

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Half-Life

Tapan K. Chaudhuri

Fifteen years ago, my brother and I were working separately on what were arguably the world's largest and smallest hole collimators. My elder brother, Dr. Tuhin K. Chaudhuri, and his colleague, Dr. James H. Christie, were working with a 44-mm diameter collimator, scanning the whole body with only 10 μCi of ^{59}Fe. Their success was reported by the *Journal* in 1974. At the same time, I was busy trying to build the world's smallest pinhole collimator, featuring a 1-mm diameter hole, in order to scan the tiny nasolacrimal duct system.

After initial skepticism, the members of the ophthalmology community became very supportive of my efforts and began to utilize this new procedure, called nuclear dacryocystography (DCG), in patients. Diagnostic radiologists soon came to see that this method was superior to conventional contract DCG, which was a relatively cumbersome procedure for the physician to undertake, and painful for the patient.

Fifteen years later, nuclear DCG remains an FDA-approved procedure for the evaluation of obstruction in the lacrimal drainage apparatus, and I believe that in the medical diagnostic armamentarium, nuclear DCG has not yet reached its half-life. ■