

TechneScan[®] MAA

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Diagnostic—For Intravenous Use

DESCRIPTION

The kit consists of five or thirty multidose reaction vials which contain the sterile, non-pyrogenic, non-radioactive ingredients necessary to produce Technetium Tc 99 Albumin Aggregated Injection for diagnostic use by intravenous injection.

Each 10-milliliter reaction vial contains 2 milligrams of aggregated albumin human, 0.5 milligram of albumin human, 120 micrograms of stannous chloride (SnCl₂•2H₂O), 80 milligrams of lactose, 24 milligrams of succinic acid and 1.4 milligrams of sodium acetate in lyophilized form under an atmosphere of nitrogen. Hydrochloric acid or sodium hydroxide has been added for pH adjustment. No bacteriostatic preservative is present.

TechneScan MAA is prepared from albumin that was non-reactive when tested for hepatitis B antigen (HB_sAg) by radioimmunoassay. Each vial contains approximately 8±4 x 10⁶ aggregated albumin particles. The particle size distribution of the aggregated albumin is such that not less than 90 percent are 10 to 90 microns in size. Typically, approximately 90 percent are within the 10 to 40 micron range. There are no aggregated albumin particles greater than 150 microns in size.

Technetium Tc 99m Albumin Aggregated Injection for intravenous use is in its final dosage form when sterile isotonic sodium pertechnetate Tc-99m solution is added to each vial. No less than 90% of the pertechnetate Tc-99m added to the reaction vial is bound to the aggregates at preparation time and remains bound throughout the 8-hour lifetime of the preparation.

The precise structure of the stannous-technetium-albumin complex is unknown at this time.

PHYSICAL CHARACTERISTICS

Technetium-99m decays by isomeric transition with a physical half-life of 6.02 hours.¹ The principal photon that is useful for detection and imaging is listed in Table 1

Table 1. Principal Radiation Emission Data 1

Radiation	Mean % per Disintegration	Energy (keV)
Gamma-2	89.07	140.5

EXTERNAL RADIATION

The specific gamma ray constant for technetium 99m is 0.78 R/mCi-hr at 1 cm. The first half-value thickness of lead (Pb) for technetium 99m is 0.017 cm. A range of values for the relative attenuation of the radiation emitted by this radionuclide that results from interposition of various thicknesses of Pb is shown in Table 2. For example, the use of 0.25 cm of Pb will decrease the external radiation exposure by a factor of about 1000.

Table 2. Radiation Attenuation by Lead Shielding

Shield Thickness (Pb) cm	Coefficient of Attenuation
0.017	0.5
0.08	10 ⁻¹
0.16	10 ⁻²
0.25	10 ⁻³
0.33	10 ⁻⁴

To correct for physical decay of this radionuclide, the fractions that remain at selected time intervals after the time of calibration are shown in Table 3.

Table 3. Physical Decay Chart: Technetium-99m
Half-Life 6.02 Hours

Hours	Fraction Remaining	Hours	Fraction Remaining
0*	1.000	7	0.447
1	0.891	8	0.398
2	0.794	9	0.355
3	0.708	10	0.316
4	0.631	11	0.282
5	0.562	12	0.251
6	0.501		

*Calibration Time

CLINICAL PHARMACOLOGY

Within 1 to 5 minutes of intravenous injection, over 90 percent of the technetium 99m albumin aggregated particles are trapped in the arterioles and capillaries of the lung.

Organ selectivity is a direct result of particle size. Below 1 to 10 microns, the albumin aggregates are taken up by the reticuloendothelial system. Above 10 to 15 microns, the aggregates become lodged in the lung capillaries by a purely mechanical process. Distribution of aggregated albumin in the lungs is a function of regional pulmonary blood flow.

The albumin aggregated is sufficiently fragile for the capillary microocclusion to be temporary. Erosion and fragmentation reduce the particle size, allowing passage of the aggregates through the pulmonary alveolar capillary bed. The fragments are then accumulated by the reticuloendothelial system.

In animal tissue distribution studies, measurements of retained activity showed a lung to liver ratio of about 70:1 within the first thirty minutes. Elimination of the technetium-99m albumin aggregated from the lungs occurs with a biological half-life of about 6.2 hours. Cumulative urinary excretion studies show an average of about 75% elimination of the injected technetium-99m dose 24 hours post administration.

Elimination of the technetium 99m albumin aggregates from the normal and abnormal human lungs occurs with a biological half-life of 10.8 hours. The effective half-life was estimated to be 3.8 hours for the lung.

Following administration of technetium Tc 99m albumin aggregated by intraperitoneal injection, the radiopharmaceutical mixes with the peritoneal fluid. Clearance from the peritoneal cavity varies from insignificant, which may occur with complete shunt blockage, to very rapid clearance with subsequent transfer into the systemic circulation when the shunt is patent.

Serial images should be obtained of both the shunt and lung (target organ). However, an adequate evaluation of the difference between total blockage of the shunt and partial blockage may not be feasible in all cases.

Toxicology data are available on request.

INDICATIONS AND USAGE

TechneScan MAA Tc 99m is indicated for scintigraphic imaging of the lungs as an adjunct to other diagnostic procedures whenever information about pulmonary circulation is desired.

Technetium Tc 99m albumin aggregated also may be used in adults as an imaging agent to aid in the evaluation of peritoneo-venous (LeVeen) shunt patency.

CONTRAINDICATIONS

TechneScan MAA Tc 99m should not be administered to patients with severe pulmonary hypertension.

The use of TechneScan MAA Tc 99m is contraindicated in persons with a history of hypersensitivity reactions to products containing human serum albumin.

WARNINGS

The possibility of allergic reactions should be considered in patients who receive multiple doses of TechneScan MAA Tc 99m.

Theoretically, the intravenous administration of particulate material such as aggregated albumin imposes a temporary small mechanical impediment to blood flow. While this effect is probably physiologically insignificant in most patients, the administration of aggregated albumin is possibly hazardous in acute cor pulmonale and other states of severely impaired pulmonary blood flow.

PRECAUTIONS

General

In cases of right-to-left cardiac shunt, additional risk may exist due to the rapid entry of aggregated albumin particles into the systemic circulation.

The contents of the TechneScan MAA reaction vial are not radioactive. However, after the sodium pertechnetate Tc 99m is added, adequate shielding of the final preparation must be maintained.

The labeling reactions involved in preparing TechneScan MAA Tc 99m depend upon maintaining tin in the reduced state. Any oxidants present in the sodium pertechnetate Tc 99m may thus adversely affect the quality of the preparation. Hence, sodium pertechnetate Tc-99m containing oxidizing agents are not suitable for preparation of TechneScan MAA Tc 99m.

The contents of the TechneScan MAA reaction vial are sterile and nonpyrogenic. It is essential that the user follow the directions carefully and adhere to strict aseptic procedures during preparation of the radiopharmaceutical.

Contents of the reaction vial are intended only for use in the preparation of Technetium Tc 99m Albumin Aggregated Injection and are not to be administered directly to the patient.

TechneScan MAA Tc 99m is a suspension and as such the particles will settle with time. Failure to mix the reaction vial contents adequately before use may result in a non-homogenous suspension with a resulting non-uniform distribution of radioactivity in the lung. If a dose is not administered immediately upon removal from the vial, the syringe should be agitated just prior to injection. A small air space in the syringe is needed to effect agitation.

It is also recommended that, because of the increasing probability of agglomeration with aging, TechneScan MAA Tc 99m not be used after eight hours from the time of reconstitution. If blood is withdrawn into the syringe any unnecessary delay prior to injection may result in clot formation in situ.

The contents of the reaction vial are under a nitrogen atmosphere and should be protected from air. On reconstitution with sodium pertechnetate Tc-99m, the contents of the vial should be thoroughly mixed by gentle swirling. Excessive agitation may produce changes in particle size. Do not use if clumping or foaming of the contents is observed.

As in the use of any radioactive material, care should be taken to minimize radiation exposure to the patient, consistent with proper management and to insure minimum radiation exposure to occupational workers.

TechneScan MAA contains no bacteriostatic preservative. TechneScan MAA Tc 99m should be stored at 2°C to 8°C and discarded eight (8) hours after reconstitution.

Radiopharmaceuticals should be used only by physicians who are qualified by training and experience in the safe use and handling of radionuclides and whose experience and training have been approved by the appropriate governmental agency authorized to license the use of radionuclides.

Carcinogenesis, Mutagenesis,
Impairment of Fertility

No long-term animal studies have been performed to evaluate carcinogenic or mutagenic potential or whether technetium Tc-99m albumin aggregated affects fertility in males or females.

Pregnancy Category C

Adequate reproduction studies have not been performed in animals to determine whether this drug affects fertility in males or females, has teratogenic potential, or has other adverse effects on the fetus.

Technetium Tc-99m albumin aggregated should be used in pregnant women only when clearly needed.

Ideally, examination using radiopharmaceuticals, especially those elective in nature, of women of childbearing capability should be performed during the first few (approximately 10) days following the onset of menses.

Nursing Mothers

Technetium 99m is excreted in human milk during lactation, therefore, formula feedings should be substituted for breast feedings.

Pediatric Use

Safety and effectiveness in children have not been established.

ADVERSE REACTIONS

The literature contains reports of deaths occurring after the administration of aggregated albumin to patients with pre-existing severe pulmonary hypertension. Instances of hemodynamic or idiosyncratic reactions to preparations of technetium Tc 99m albumin aggregated injection have been reported.

Hypersensitivity reactions are possible whenever protein-containing materials such as technetium Tc-99m albumin aggregated injection are used in man. Epinephrine, antihistamines and corticosteroid agents should be available for use.

DOSAGE AND ADMINISTRATION

Lung Imaging

The recommended intravenous dose range for the average patient (70 kg) is 37 to 148 megabecquerels (1 to 4 millicuries). The volume of the dose may vary from 0.4 to 1.0 milliliter.

The recommended number of aggregated albumin particles to be administered per dose is 200,000 to 1,200,000 with the suggested number being approximately 600,000.

While the number of particles available per millicurie dose of TechneScan[®] MAA Tc 99m will vary corresponding to the physical decay of technetium 99m which has occurred, the particles available in any specific dose may be estimated from Table 4.

In cases of right-to-left cardiac shunt the number of aggregated albumin particles administered per dose should be reduced to the minimum feasible.

The patient dose should be measured by a suitable radioactivity calibration system for total radioactivity immediately prior to administration. It is also recommended that the radiochemical purity be checked prior to administration. Resuspend particles by repeated inversion of the syringe immediately prior to injection. TechneScan MAA Tc 99m is injected intravenously, without aspirating, over a 20 to 30 second interval with the patient in the supine position. If blood is drawn into the syringe, any unnecessary delay prior to injection may lead to clot formation in the syringe. Do not back flush the syringe. For optimal results, lung imaging should begin as soon as possible. It is recommended the TechneScan MAA Tc 99m not be injected through intravenous tubing because of the occasional observation of "hot spots" in the lung.

LeVeen Shunt Patency

The suggested intraperitoneal dosage range used in the average patient (70 kg) for peritoneo-venous (LeVeen) shunt patency evaluation is 37 to 111 megabecquerels (1 to 3 millicuries). Adequate measures should be taken to assure uniform mixing with peritoneal fluid. Serial images of both the shunt and target organ should be obtained and correlated with other clinical findings. Alternatively, the drug may be administered by percutaneous transtubal injection. The suggested percutaneous transtubal (efferent limb) dosage range for the average patient (70 kg) is 12 to 37 megabecquerels (0.3 to 1.0 millicurie) in a volume not to exceed 0.5 mL.

RADIATION DOSIMETRY

The estimated absorbed radiation doses² to an average ADULT patient (70 kg) from an intravenous injection of 4 millicuries of Technetium Tc 99m Albumin Aggregated Injection are shown in Table 5.

Table 6 represents the absorbed radiation dose resulting from the intraperitoneal administration of 111 megabecquerels (3 millicuries) of technetium Tc 99m albumin aggregated.

HOW SUPPLIED

Catalog Number 093.

TechneScan MAA is supplied as a lyophilized powder packaged in vials. Each vial contains:

- 2 mg Aggregated Albumin Human
- 0.5 mg Albumin Human
- 120 µg Stannous Chloride (Dihydrate)
- 80 mg Lactose
- 24 mg Succinic Acid
- 1.4 mg Sodium Acetate

Hydrochloric Acid or Sodium Hydroxide is added for pH adjustment. The vial is sealed under an atmosphere of nitrogen. Each vial contains $8 \pm 4 \times 10^6$ aggregated albumin particles.

Kits containing 5 vials or 30 vials are available.

STORAGE

TechneScan MAA Kit should be stored at 2°C to 8°C before reconstitution.

TechneScan MAA contains no preservatives; after reconstitution, the shielded vial should be stored at 2°C to 8°C.

DIRECTIONS FOR USE

Procedural Precautions

SOLUTIONS OF SODIUM PERTECHNETATE Tc 99m WHICH CONTAIN OXIDIZING AGENTS (i.e., sodium hypochlorite or hydrogen peroxide) SHOULD NOT BE USED.

Solutions obtained from the following technetium-99m generators were tested and found to be acceptable for use with TechneScan MAA: Mallinckrodt's Ultra-TechneKow® FM Generators, New England Nuclear's Technetium-99m Generator and Squibb's Minitec® Generator. Other sources of technetium-99m can be used if the user has demonstrated that they are compatible with TechneScan MAA.

All transfer and vial stopper entries must be done using aseptic techniques.

Procedure

For the preparation of Technetium Tc 99m Albumin Aggregated.

Note 1: Wear waterproof gloves during the entire preparation procedure and during subsequent patient dose withdrawals from the Reaction Vial.

Note 2: Make all transfers of sodium pertechnetate Tc 99m solution during the preparation procedure with an adequately shielded syringe.

Note 3: Keep the Radioactive Preparation in the lead shield described below (with cap in place) during the useful life of the Radioactive Preparation. Make all withdrawals and injections of the Radioactive Preparation with an adequately shielded syringe.

1. A TechneScan MAA Reaction Vial is removed from the refrigerator and approximately 5 minutes are allowed for the contents to come to room temperature.
2. Attach radioassay information label with radiation warning symbol to the Reaction Vial and place the vial in a lead Dispensing Shield fitted with a lead cap and having a minimum wall thickness of 1/8 inch. Do not remove Reaction Vial from Dispensing Shield except to inspect contents prior to administration. Use proper shielding to perform the inspection.
3. Sodium pertechnetate Tc 99m solution (5 to 10 milliliters) is added to the Reaction Vial. In choosing the amount of technetium 99m radioactivity to be used in the preparation of Technetium Tc 99m Albumin Aggregated, the labeling efficiency, number of patients, administered radioactive dose, and radioactive decay must be taken into account. The recommended maximum amount of technetium-99m to be added to the TechneScan MAA Reaction Vial is 2.22 gigabecquerels (60 millicuries).

NOTE: When large millicurie size generators are used, the eluate (yield of technetium 99m) will be higher than 444 megabecquerels (12 millicuries) per milliliter. Before use, such eluates should be diluted with sterile, nonpyrogenic saline, containing no bacteriostatic preservative, to ensure that at least 5.0 milliliters of sodium pertechnetate Tc-99m solution is added to each reaction vial.

4. With the Reaction Vial in the Dispensing Shield (with cap in place) agitate for a few seconds and allow to stand for a minimum of 15 minutes at room temperature.
5. Assay the product in a suitable calibrator and record the time, date of preparation and the activity of the Tc 99m-MAA onto the radioassay information label.
6. Prior to withdrawing a dose, the contents of the Reaction Vial should be gently agitated sufficiently, to effect homogeneous suspension of the aggregated albumin. Withdrawals for administration must

be made aseptically using a sterile needle (18-21 gauge) and syringe. Since the vials contain nitrogen to prevent oxidation of the complex, the vials should not be vented. If repeated withdrawals are made from the vial, the contents should not be replaced with air.

7. Store the Reaction Vial in the Dispensing Shield at 2°C to 8°C when not in use and discard after 8 hours from the time of preparation.

This reagent kit is approved for distribution to persons licensed by the U.S. Nuclear Regulatory Commission to use byproduct material identified in Section 35.200 or under an equivalent license of an Agreement State.

Table 4. Particles x 10⁶/Dose*
(X = 8 x 10⁶ Particles/Vial)

To 99m added to vial gigabecquerels (mCi)	37 MBq (1mCi) Dose	74 MBq (2mCi) Dose	111 MBq (3mCi) Dose	148 MBq (4mCi) Dose
0.74 (20)	0.40	0.80	1.20	1.60
1.11 (30)	0.27	0.54	0.81	1.08
1.48 (40)	0.20	0.40	0.60	0.80
1.85 (50)	0.16	0.32	0.48	0.64
2.22 (60)	0.13	0.26	0.39	0.52

*The particles per millicurie dose will increase in relation to the physical decay of technetium 99m such that at six hours (one half-life) after preparation, the values in the table will increase by a factor of two.

Table 5. Absorbed Radiation Doses
Intravenous Injection

Tissue	Technetium Tc 99m Albumin Aggregated	
	mGy/148 MBq	rad/4 mCi
Total Body	0.60	0.060
Lungs	8.8	0.88
Liver	0.72	0.072
Spleen	0.68	0.068
Kidneys	0.44	0.044
Bladder Wall		
2-hr void	1.2	0.12
4.8-hr. void	2.2	0.22
Testes		
2-hr. void	0.24	0.024
4.8 hr. void	0.26	0.026
Ovaries		
2-hr. void	0.30	0.030
4.8-hr. void	0.34	0.034

Table 6. Absorbed Radiation Doses
Intraperitoneal Injection

Organ	Shunt Patency (open)		Shunt Patency (closed)	
	mGy	rads	mGy	rads
Lung	6.9	0.69	1.68	0.168
Ovaries and Testes	0.18 to 0.30	0.018 to 0.030	1.68	0.168
Organs in the Peritoneal Cavity	-----	-----	1.68	0.168
Total Body	0.36	0.036	0.57	0.057

ASSUMPTIONS:

Calculations for the absorbed radiation dose are based upon an effective half-time of 3 hours for the open shunt and 6.02 hours for the closed shunt and an even distribution of the radiopharmaceutical in the peritoneal cavity with no biological clearance.

¹ Kocher, David C., "Radioactive Decay Data Tables," DOE/TIC-11026, 108, (1981)

² Method of calculation: "S", Absorbed Dose per Unit Cumulated Activity for Selected Radionuclides and Organs, MIRD Pamphlet No. 11 (1975).

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