Thallous Chloride Tl 201 Injection

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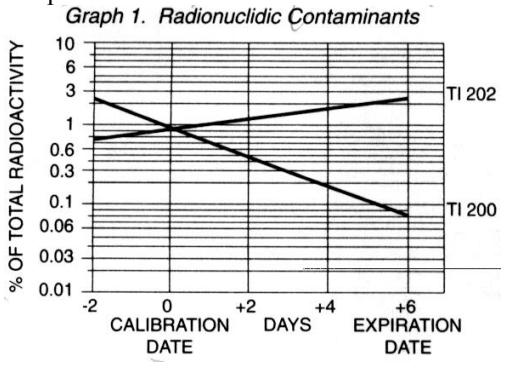
Diagnostic—For Intravenous Use
R7/95

DESCRIPTION

Thallous Chloride Tl 201 Injection is supplied in an isotonic solution as a sterile, non-pyrogenic diagnostic radiopharmaceutical for intravenous administration. Each milliliter contains 37 megabecquerels (1 millicurie) Thallous Chloride Tl 201 at calibration time, made isotonic with 9 milligrams sodium chloride and preserved with 0.9% (v/v) benzyl alcohol. The pH is adjusted to between 4.5 to 7.0 with hydrochloric acid and/or sodium hydroxide. Thallium TI 201 is cyclotron produced. At the time of calibration it contains no more than 1.0% Thallium Tl 200, no more than 1.0% Thallium Tl 202, no more than 0.25% Lead Pb 203, and no less than 98% Thallium Tl 201 as a percentage of total activity. No carrier has been added.

It is recommended that Thallous Chloride Tl 201 be administered close to calibration time to minimize the effect of higher levels of radionuclidic contaminants present at pre- and post-calibration dates. The concentration of each radionuclidic contaminant changes with time. Graph 1 shows maximum concentration of each radionuclidic contaminant as a function of time.

Graph 1. Radionuclidic Contaminants



PHYSICAL CHARACTERISTICS

Thallium Tl 201, with a physical half life of 73.1 hours, decays by electron capture to mercury Hg 201.[1] Photons that are useful for detection and imaging are listed in Table 1. The lower energy x-rays obtained from the mercury Hg 201 daughter of thallium Tl 201 are recommended for myocardial imaging, because the mean percent disintegration at 68.9 to 80.3 keV is much greater than the combination of gamma-4 and gamma-6 mean percent disintegration.

Table 1. Principal Radiation Emission Data[1]

Radiation	Mean % Per Disintegration	Energy (keV)
Gamma-4	2.7	135.3
Gamma-6	10.0	167.4
Mercury x-rays	94.4	68.9–80.3

EXTERNAL RADIATION

The specific gamma ray constant for thallium Tl 201 is 4.7 R/mCi-hr* at 1 cm. The first half-value thickness of lead (Pb) is 0.0006 cm. A range of values for the radiation emitted by this radionuclide with the corresponding exposure rate at 1 cm that results from interposition of various thicknesses of lead is shown in Table 2. For example, the use of 0.21 cm of lead will decrease the external radiation exposure by a factor of about 1,000.

Table 2. Radiation Attenuation by Lead Shielding

cm of Lead (Pb)	Coefficient of Attenuation
0.0006	0.5
0.015	10^{-1}
0.098	10^{-2}
0.21	10^{-3}
0.33	10^{-4}

*Includes 10 keV x-rays.

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

Table 3. Thallium Tl 201 Decay Chart;
Half-Life 73.1 Hours

Hours	Fraction Remaining	Hours	Fraction Remaining
0*	1.00	66	0.53
6	0.94	72	0.51
12	0.89	78	0.48
18	0.84	84	0.45
24	0.80	90	0.43
30	0.75	96	0.40
36	0.71	108	0.36
42	0.67	120	0.32
48	0.63	132	0.29
54	0.60	144	0.26
60	0. 57		

* Calibration Time

CLINICAL PHARMACOLOGY

Thallous Chloride Tl 201 with no carrier added has been found to accumulate in viable myocardium in a manner analogous to that of potassium. Experiments in human volunteers using labeled microspheres have shown that the myocardial distribution of Thallous Chloride Tl 201 correlates well with regional perfusion.

In clinical studies, Thallous Chloride Tl 201 images have been found to visualize areas of infarction as "cold" or nonlabeled regions which are confirmed by electrocardiographic and enzyme changes. When the "cold" or nonlabeled regions comprise a substantial portion of the left ventricle, the prognosis for survival is unfavorable. Regions of transient myocardial ischemia corresponding to areas perfused by coronary arteries with partial stenoses have been visualized when Thallous Chloride Tl 201 was administered in conjunction with an exercise stress test. Anatomic configurations may interfere with visualization of the right coronary artery.

After intravenous administration, Thallous Chloride Tl 201 clears rapidly from the blood with maximal concentration by normal myocardium occurring at about 10 minutes. It will, in addition, localize in parathyroid adenomas; it is not specific since it will localize to a lesser extent in sites of parathyroid

hyperplasia and other abnormal tissues such as thyroid adenoma, neoplasia (e.g., parathyroid carcinoma) and sarcoid. Biodistribution is generally proportional to organ blood flow at the time of injection. Blood clearance of Thallous Chloride Tl 201 is primarily by the myocardium, thyroid, liver, kidneys and stomach with the remainder distributing fairly uniformly throughout the body. The dosimetry data in Table 4 reflect this distribution pattern and are based on a biological half-life of 2.4 days. Thallous Chloride Tl 201 is excreted slowly and to an equal extent in both feces and urine.

Five minutes after intravenous administration only 5 to 8 percent of injected activity remained in the blood. A biexponential disappearance curve was obtained, with 91.5 percent of the blood radioactivity disappearing with a half-time of about 5 minutes. The remainder had a hall-time of about 40 hours.

Approximately 4 to 8 percent of the injected dose was excreted in the urine in the first 24 hours. The whole body disappearance half-time was 9.8 ± 2.5 days. Kidney concentration was found to be about 3 percent of the injected activity and the testicular content was 0.15 percent. Net thyroid activity was determined to be only 0.2 percent of the injected dose, and the activity disappeared in 24 hours. From anterior and posterior whole-body scans, it was determined that about 45 percent of the injected dose was in the large intestines and contiguous structures (liver, kidneys, abdominal musculature).[2]

INDICATIONS AND USAGE

Thallous Chloride Tl 201 may be useful in myocardial perfusion imaging using either planar or SPECT (Single Photon Emission Computed Tomography) techniques for the diagnosis and localization of myocardial infarction. It may also have prognostic value regarding survival, when used in the clinically stable patient following the onset of symptoms of an acute myocardial infarction, to assess the site and size of the perfusion defect.

Thallous Chloride Tl 201 may also be useful in conjunction with exercise stress testing as an adjunct to the diagnosis of ischemic heart disease (atherosclerotic coronary artery disease).

It is usually not possible to differentiate recent from old myocardial infarction, or to differentiate exactly between recent myocardial infarction and ischemia.

Thallous Chloride Tl 201 is indicated also for the localization of sites of parathyroid hyperactivity in patients with elevated serum calcium and parathyroid hormone levels. It may also be useful in pre-operative screening to localize extrathyroidal and mediastinal sites of parathyroid hyperactivity and for postsurgical reexamination. Thallous Chloride Tl 201 has not been adequately demonstrated to be effective for the localization of normal parathyroid glands.

CONTRAINDICATIONS

None known.

WARNINGS

When studying patients suspected or known to have myocardial infarction or ischemia, care should be taken to assure continuous clinical monitoring and treatment in accordance with safe, accepted procedures. Exercise stress testing should be performed only under the supervision of a qualified physician and in a laboratory equipped with appropriate resuscitation and support apparatus.

PRECAUTIONS

Data are not available concerning the effect on the quality of Thallous Chloride Tl 201 images of marked alterations in blood glucose, insulin or pH (such as is found in diabetes mellitus). Attention is directed to the fact that thallium is a potassium analog, and since the transport of potassium is affected by these factors, the possibility exists that the Thallous Chloride Tl 201 may likewise be affected.

General

This drug should not be used after six (6) days from the calibration date, or nine (9) days from date of manufacture, whichever comes first.

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.

Radiopharmaceuticals should be used only by physicians who are qualified by training and experience in the safe use and handling of radionuclides.

Carcinogenesis, Mutagenesis,
Impairment of Fertility
No tong-term animal studies have been performed to evaluate carcinogenic potential, mutagenic potential or whether this drug affects fertility in males or females.

Pregnancy Category C
Animal reproductive studies have not been conducted with Thallous Chloride Tl 201, It is also not known whether Thallous Chloride TI 201 can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Thallous Chloride Tl 201 should be given to a pregnant woman only if clearly needed.

Nursing Mothers
It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, as a general rule nursing should not be undertaken when a patient is administered radioactive material.

Pediatric Use
Safety and effectiveness in children below age 18 have not been established.

ADVERSE REACTIONS
Following the administration of Thallous Chloride T1 201, adverse anaphylactoid reactions have been reported (characterized by cardiovascular, respiratory, and cutaneous symptoms), some severe enough to require treatment. Hypotension, pruritus, flushing, and diffuse rash which responds to antihistamines have been reported. Other reported events include, itching, nausea/vomiting, mild diarrhea, tremor, shortness of breath, chills, fever, conjunctivitis, sweating, and blurred vision.

DOSAGE AND ADMINISTRATION
The recommended adult dose of intravenous Thallous Chloride T1 201 for planar myocardial imaging is 37 to 74 MBq (1-2mCi). The recommended intravenous doses for SPECT myocardial imaging are 74 to 111 MBq (2-3 mCi). The efficacy of a 1.0 mCi dose for SPECT imaging has not been well established.

For the localization of parathyroid hyperactivity, Thallous Chloride Tl 201 may be administered before, with or after a minimal dose of a thyroid imaging agent such as sodium pertechnetate Tc 99m or sodium iodide I 123 to enable thyroid subtraction imaging.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Do not use if contents are turbid.

Waterproof gloves should be worn during the handling procedures.

The patient dose should be measured by a suitable radioactivity calibration system immediately prior to administration.

With a shielded sterile syringe, aseptically withdraw the material for use.

For resting Thallous Chloride Tl 201 studies, imaging should begin 10 to 20 minutes after injection. Myocardial-to-background ratios are improved when patients are injected upright and in the fasting state; the upright position reduces the hepatic and gastric Thallium Tl 201 concentration.

When utilized in conjunction with exercise stress testing, Thallous Chloride Tl 201 should be administered at the inception of a period of maximum stress which is sustained for approximately 30 seconds after injection. Imaging should begin within ten minutes after administration to obtain maximum target-to-background ratios. Several investigators have reported that within two hours after the completion of stress testing the target-to-background ratios may decrease significantly in lesions that are attributable to transient ischemia.

RADIATION DOSIMETRY

The estimated absorbed radiation doses[3] at calibration time to an average patient (70 kg) from an intravenous injection of a maximum dose of 74 megabecquerels (2mCi) of Thallous Chloride Tl 201 are shown in Table 4.

Table 4. Radiation Dose Estimates for Tl 201 Chloride (plus contaminants)

	Estimated Radiation Dose	
Organ	mGy/MBq	rad/mCi
Adrenals	6.2E-02	2.3E-01
Brain	5.9E-02	2.2E-01
Breasts	3.6E-02	1.3E-01
GB Wall	8.3E-02	3.1E-01
LLI Wall	3.4E-01	1.2E+00
Small Intestine	4.5E-01	1.7E+00
Stomach	1.9E-01	6.9E-01
ULI Wall	3.3E-01	1.2E+00
Heart Wall	2.8E-01	1.0E+00
Kidneys	4.6E-01	1.7E+00
Liver	9.9E-02	3.7E-01
Lungs	4.7E-02	1.7E-01
Muscle	4.6E-02	1.7E-01
Ovaries	1.0E-01	3.7E-01
Pancreas	7.4E-02	2.7E-01
Red Marrow	5.5E-02	2.0E-01
Bone Surfaces	8.8E-02	3.3E-01
Skin	3.3E-01	1.2E-01
Spleen	1.8E-01	6.5E-01
Testes	8.2E-01	3.0E+00
Thymus	4.6E-02	1.7E-01
Thyroid	6.2E-01	2.3+00
Urinary Bladder Wall	5.2E-02	1.9E-01
Uterus	8.5E-02	3.1E-01
Effective Dose Equivalent	3.6E-01/ mSv/MBq	1.3E+00 rem/mCi

Based on data gathered in humans by Krahwinkel et al. (J Nucl Med 29 (9):1582-1586, 1988) and data gathered in humans by Gupta et al (Int J Nucl Med & Biol 8:211-213, 1981)

Table 5. Assumed Distribution and Retention

Brain	1.76% $T_{b=}\infty$	
LLI	3.6% T_b=191 hr	(Activity in Wall)
Small Intestine	14.4% T_b=191 hr	(Activity in Wall)
Stomach	2.8% T_b=205 hr	(Activity in Wall)
ULI	4.7% T_b=191 hr	(Activity in Wall)
Heart Wall	3.4% T_b=179 hr	
Kidneys	4.5% T_b=260 hr	0.97% Tb=27 hr
Liver	4.6% T_b=218 hr	
Spleen	0.74% T_b=640 hr	0.28% T_b=37 hr
Testes	1.0% T_b= ∞	
Thyroid	0.29% T_b=350 hr	0.24% T_b=166 hr
Total Body	31% T_b=146 hr	69% T_b=502 hr
Urinary Bladder Clearance	6.2% T_b=146 hr	13.8% T_b=502 hr

Bladder voiding interval 4.8 hr. Contaminants assumed: Tl 200 (1%), Tl 202 (0.33%), Pb 201 (.33%), Pb 203 (0.33%). Includes dose from Tl 201 Auger electrons. Estimate calculated using phantom of Cristy & Eckerman (Report ORNL/TM-8381/V1 & V7)
Radiation Internal Dose Information Center

HOW SUPPLIED

Catalog Number 120.

Thallous Chloride Tl 201 is supplied in a sterile, non-pyrogenic solution for intravenous administration. Each ml contains 37 MBq (1 mCi) Thallous Chloride Tl 201 at calibration time, 9 mg sodium chloride and 0.9 percent (v/v) benzyl alcohol. The pH is adjusted to between 4.5 to 7.0 with hydrochloric acid and/or sodium hydroxide solution. Vials are available in the following quantities of radioactivity: 74, 148, 296, and 333 megabecquerels (2, 4, 8 and 9 millicuries) of thallium Tl 201.

The contents of the vial are radioactive. Adequate shielding and handling precautions must be maintained.

STORAGE CONDITIONS

Store this drug at room temperature (below 86°F/30°C).

Storage and disposal of Thallous Chloride Tl 201 Injection should be controlled in a manner that is in compliance with the appropriate regulations of the government agency authorized to license the use of this radionuclide.

[1]Kocher, David C., "Radioactive Decay Data Tables," DOE/TIC- 11026, 181 (1981).

[2]Atkins, H. L., et al. Thallium-201 for Medical Use. Part 3: Human Distribution and Physical Imaging Properties. Journal of Nuclear Medicine, 18(2):133-140, Feb. 1977

[3]Values listed include an average maximum correction of 6 percent to the radiation doses from Thallium TI 201 due to the radiocontaminants Thallium TI 200 and Thallium TI 202 on calibration date.

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Mallinckrodt, Inc.
St. Louis, MO 63134

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Thallous Chloride
TI 201 Injection
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