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Thallium ChlorideTl-201

פורמט עלון זה נבדק ותוכנו אושר על ידי משרד הבריאות

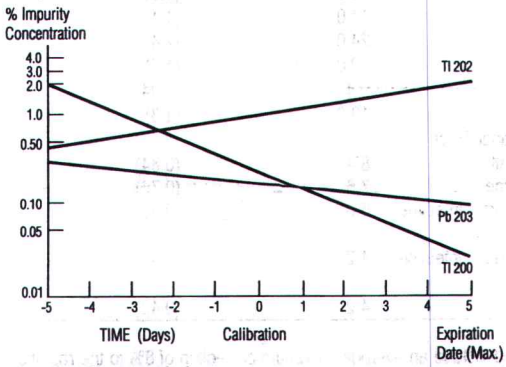
To be used in diagnostic institutes only

Description: Thallium Chloride Tl 201 is supplied in isotonic solution as a sterile, non-pyrogenic diagnostic radiopharmaceutical for intravenous administration. The aqueous solution at the time of calibration contains 37MBq/ml (1mCi/ml) Thallium Chloride Tl 201. The pH is adjusted with hydrochloric acid and/or sodium hydroxide solution. It is made isotonic with 9mg/ml sodium chloride.

Thallium Tl 201 is cyclotron produced with no carrier added and contains no less than 98% Thallium Tl 201 as a percentage of total activity with contaminants less than 0.3% Thallium Tl 200, 1.2% Thallium Tl 202, and 0.2% Lead Pb 203 expressed as a percentage of Tl 201 activity at calibration.

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

Graph 1. Radionuclidic Contaminants



Physical Characteristics:
Thallium Tl 201 decays by electron capture to Mercury Hg 201 with a physical half-life of 73.1 hours.[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 Tl 201 are recommended for myocardial imaging, because the mean %/disintegration at 68-80.3 KeV is much greater than the combination of gamma-4 and gamma-6 mean %/disintegration.

Table 1. Principal Radiation Emission Data

Radiation	Mean %/Disintegration	Mean Energy (KeV)
Gamma-4	2.7	135.3
Gamma-6	10.0	167.4
Mercury X-rays	94.4	68-80.3

[1]Martin, M.M., Nuclear Data Project, ORNL, January 1977.

EXTERNAL RADIATION
The specific gamma ray constant for Thallium Tl 201 is 33 microcoulombs/Kg-MBq-hr (4.7R/mCi-hr.) at 1cm. The first half-value layer is 0.0006cm of lead. A range of values for the relative attenuation of the radiation emitted by this radionuclide that results from the interposition of various thicknesses of lead (Pb) is shown in Table 2. For example, the use of 0.21cm of lead will decrease the external radiation exposure by a factor of about 1,000.

Table 2. Radiation Attenuation by Lead Shielding[2]

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}

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

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

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

Hours	Fraction Remaining	Hours	Fraction Remaining	Hours	Fraction Remaining
0*	1.00	42	0.67	84	0.45
6	0.95	48	0.63	90	0.43
12	0.89	54	0.60	96	0.40
18	0.84	60	0.57	108	0.36
24	0.80	66	0.54	120	0.32
30	0.75	72	0.51	132	0.29
36	0.71	78	0.48	144	0.26

*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, thallium images have been found to visualize areas of infarction as "cold" or non labeled regions which are confirmed by electro-cardiographic and enzyme changes. When the "cold" or non labeled 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 stenosis have been visualized when Thallium Chloride Tl 201 was administered in conjunction with an exercise stress test.

After intravenous administration, Thallous Chloride Tl 201 clears rapidly from the blood with maximal concentration by normal myocardium occurring at about ten 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, kidneys, thyroid, liver 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 11 days and an effective half-life of 2.4 days. Thallous Chloride Tl 201 is excreted slowly and to an equal extent in both feces and urine.
This technique has limited sensitivity for detecting parathyroid adenomas smaller than 5mm in diameter.

INDICATIONS AND USAGE: Thallous Chloride Tl 201 may be useful in myocardial perfusion imaging 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 in 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 post-surgical reexamination. Thallous Chloride Tl 201 has not been adequately demonstrated to be effective for the localization of normal parathyroid glands.

CONTRAINDICATIONS: None known.

WARNINGS: In studying patients in whom myocardial infarction or ischemia is known or suspected, care should be taken to assure continuous clinical monitoring and treatment in accordance with safe, accepted procedure. 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 of marked alterations in blood glucose, insulin, or pH (such as is found in diabetes mellitus) on the quality of Thallous Chloride Tl 201 scans. Attention is directed to the fact that thallium is potassium analog, and since the transport of potassium is affected by these factors, the possibility exists that the thallium may likewise be affected.

Diagnostic interference may occur due to postprandial state:
Increased accumulation of thallium in the abdominal viscera (postprandial stomach, liver, spleen, and intestines) may interfere with myocardial visualization during the resting, exercise, or pharmacologic stress thallium test).

GENERAL

Do not use after the expiration time and date (5 days maximum after calibration time) stated on the label.

Do not use if contents are turbid.

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

Thallium Chloride Tl 201, as all radioactive materials, must be handled with care and used with appropriate safety measures to minimize external radiation exposure to clinical personnel. Care should also be taken to minimize radiation exposure to patients in a manner consistent with proper patient management.

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 government agency authorized to license the use of radionuclides.

Carcinogenesis, Mutagenesis, impairment of Fertility

No long-term animal studies have been performed to evaluate carcinogenic potential, mutagenic potential, or whether Thallous Chloride Tl 201 affects fertility in males or females.

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

Pregnancy Category C

Adequate reproductive studies have not been conducted in animals with Thallous Chloride Tl 201. It is also not known whether Thallous Chloride Tl 201 can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Thallous Chloride Tl 201 should not be given to a pregnant woman except when benefits clearly outweigh the potential risks.

Nursing Mothers

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

Pediatric Use

Safety and effectiveness in children below the age of 18 have not been established.

ADVERSE REACTIONS: Exposure to ionizing radiation is linked with cancer induction and a potential for development of hereditary defects. For diagnostic nuclear medicine investigations the current evidence suggests that these adverse effects will occur low frequency because of the low radiation doses incurred.

Those indicating need for medical attention

Incidence less frequent of rare

Allergic reaction (skin rash, hives, or itching); *blurred vision hypotension*

Those indicating need for medical attention only if they continuous or are bothersome

Incidence less frequent or rare

Nausea; sweating

OVERDOSAGE: In the event of the administration of a radiation overdose with Thallous (Tl 201) chloride the absorbed dose to the patient should be reduced where possible by increasing the elimination of the radionuclide from the body by forced diuresis with frequent voiding and stimulation of the gastro-intestinal passage.

DOSAGE AND ADMINISTRATION: The recommended adult (70kg) dose of Thallous Chloride Tl 201 is (2-4mCi). Thallous Chloride Tl 201 is intended for intravenous administration only.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

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

For patients undergoing resting thallium studies, imaging is optimally begun within 10-20 minutes after inspection. Several investigators have reported improved myocardial-to-background ratios when patients are injected in the fasting state, in an upright posture, or after briefly ambulating. The upright position reduces the hepatic and gastric Thallium Tl 201 concentration.

Best results with thallium imaging performed in conjunction with exercise stress testing appear to be obtained if the thallium is administered when the patient reaches maximum stress and when the stress is continued for 30 seconds to one minute after injection. Imaging should begin within ten minutes post-injection since target-to-background ratio is optimum by that time. Several investigators have reported significant decreases in the target-to-background ratios of lesions attributable to transient ischemia by two hours after the completion of stress imaging.

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 Tc99m or sodium iodide I 123 to enable thyroid subtraction imaging.

RADIATION DOSIMETRY

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

Table 4. Radiation Dose Estimates of Thallous Chloride Tl 201 Absorbed Dose/74MBq (2mCi) Thallium Tl 201 Administered

Tissue	mGy/74MBq	(Rads/2mCi)
Heart Wall	10.0	(1.0)
Liver	11.0	(1.1)
Kidneys	24.0	(2.4)
Testes	10.0	(1.0)
Ovaries	9.4	(0.94)
Thyroid	13.0	(1.3)
Gastrointestinal Tract		
Stomach Wall	8.4	(0.84)
Small Intestine	7.6	(0.76)
Upper Large intestine Wall	5.0	(0.50)
Lower Large intestine Wall	4.2	(0.42)
Total Body	4.2	(0.42)

[3]Values listed include an average maximum correction of 8% to the radiation doses from Thallous Chloride Tl 201 due to the radio contaminants Thallium Tl 200 and Thallium Tl 202 on calibration date.

HOW SUPPLIED: Thallous Chloride Tl 201 for intravenous administration is supplied as a sterile, nonpyrogenic solution containing at calibration time, 37MBq/ml (1mCi/ml) of Thallous Chloride Tl 201, 9mg/ml sodium chloride, and 9mg/ml of benzyl alcohol. The pH is adjusted with hydrochloric acid and/or sodium hydroxide solution. Vials are available in the following quantities of radioactivity: 2, 4, 6, 8, 10 and 12mCi of Thallous Chloride Tl 201.

Preparation and Handling Procedures for Thallous Chloride Tl 201

a. Waterproof gloves should be worn during the handling and injection period.
b. Adequate shielding during the life of the radioactive drug should be maintained by using the lead shield and cover and by using a syringe shield for withdrawing and injecting Thallium Chloride T1 201.

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