Quality Control In The Hot Lab

After reviewing this tutorial, the user should be able to

- list the various types of impurities found in the eluate collected from the Mo-99/Tc-99m generator and give an example of each
- identify the various classes of impurities found in radiopharmaceuticals and give an example of each
- describe in detail how QC testing is performed on the eluate and on Tc-99m radiopharmaceuticals
- state the specifications for each of these tests and what action is required if there is a test failure
- list the 4 QC tests performed on a dose calibrator and required frequency of performance
- describe how each test is performed, state the legal specification, and describe the action required if there is a test failure
- state the difference between agreement states and non-agreement states
- know the basics of licensure by the NRC and State regulatory agencies
- list the various requirements for maintaining log books in the lab and the required frequency of entry
- be familiar with basic rules of radiation safety, e.g., to describe what precautions and action must be taken when there is a spill or contamination is found on a technologist's hands define "reportable event" according to the new rules, and to state what one must do to document and report the occurrence.

Topics to be covered

- Rationale for Performing Quality Control: Criterion
- Description of a Non-Diagnostic Study and how to avoid it
- Impurities in Generators and Radiopharmaceuticals: Classification and Detection
- QC Testing of a Mo/Tc Generator
- QC Testing in Radiopharmaceuticals
- Quality Control of Dose Calibrators

Classification of Impurities in the Hot Lab

TYPE	EXAMPLE	EFFECT
Radionuclidic	Mo-99	High Radiation dose; Poor Image Quality
Radiochemical	HR Tc	Poor Image Quality, Altered Radiation Dose
Chemical	Al^{3+}	Altered Radiation Dose Image Quality

Method of Quantification of Impurities in the Hot Lab

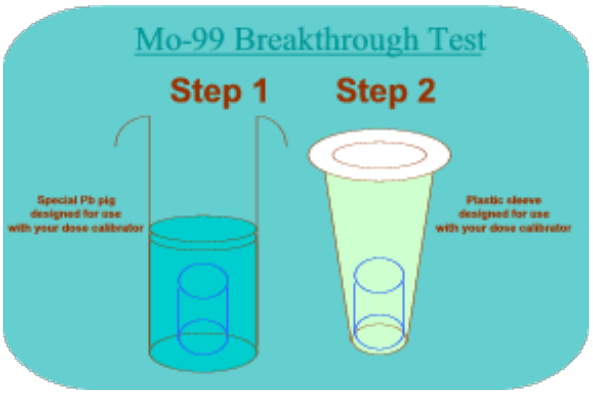
TYPE	EXAMPLE	METHOD
Radionuclidic	Mo-99	Dose Calibrator or Multi-Channel Analyzer
Radiochemical	HR Tc	Thin Layer Chromatography
Chemical	Al^{3+}	Colorimetric or other methods

Required Quality Control Testing of a Mo/Tc Generator

TEST	FREQUENCY	SPECIFICATIONS
Mo Breakthrough	First Elution	<0.15 μCi Mo/mCi Tc at $t_{administration}$
Al^{3+} Breakthrough	Not Required	<10 ppm of Al^{3+}; may be expressed as μg/ml
Hydrolyzed Reduced Tc	Optional, but recommended	< 5% recommended

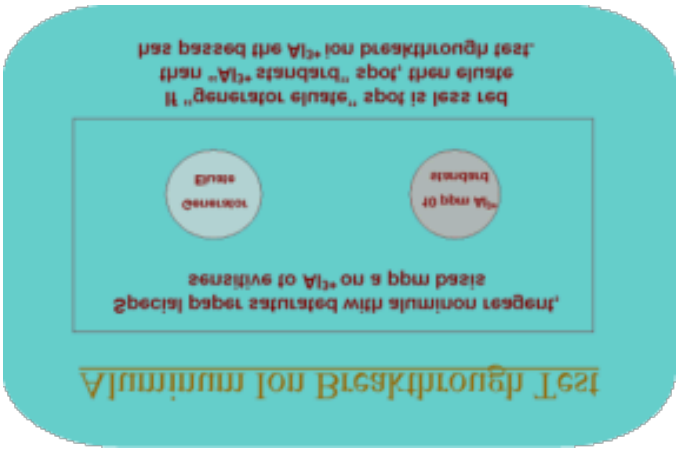
Performance of the Mo-99 Breakthrough Test

- Mo-99 is assayed directly in the special lead pig supplied by manufacturer of your dose calibrator. Tc-99m is then assayed directly in the plastic sleeve. Activity (uCi) of Mo-99 is divided by activity (mCi) of Tc-99m to obtain a ratio. If this ratio is <0.15 uCi Mo-99 per mCi of Tc-99m at time of administration, the generator eluate has passed the Mo-99 Breakthrough Test. As a rule of thumb, if the ratio is <0.038 at time of elution, the material will be suitable for injection for at least 12 hours.



Aluminum Ion Breakthrough

- Al^{3+} ion is measured colorimetrically. A drop of the eluate is placed on one end of a special test paper; a drop of a standard solution of Al^{3+}, concentration 10 ppm, is placed on the other end of the test strip. If the color at the center of the drop of eluate is less red than that of the standard solution, the eluate has passed the
- Al^{3+} Ion Breakthrough Test. Units may be also be expressed as µg/ml.



Radiopharmaceuticals: Quality Control

Radiochemical Impurity	Chemical Form
Free Tc	Pertechnetate, TcO_4^{-1}
Hydrolyzed Reduced Tc	probably $TcO(OH)_2.H_2O$, a hydrated Tc-oxide
99mTc MAG3	Possible impurity is 99mTc tartrate
99mTc HMPAO	Stereochemical impurities

Thin Layer Chromatography Systems of Tc-99m Compounds

For Tc-99m DTPA, MDP, GH, PYP, HDP, MAA, MIAA, SC:

CHROMATOGRAPHY SYSTEM	IMPURITY MEASURED
Silica Gel/0.9% saline	Hydrolyzed Reduced Tc
Paper/acetone or paper/MEK	Free Tc (Pertechnetate)

Tc-99m Thin Layer Chromatography: Separation on Strip

CHROMATOGRAPHY SYSTEM	SEPARATION OF RADIOCHEMICAL SPECIES
Silica Gel/ Saline	HR Tc in bottom half; all other species in top half
Paper/acetone or paper /MEK	Free Tc in top half; all other species in bottom half.
ITLC-SA/20% saline	HR Tc in bottom half; all other species in top half
ITLC-SG/water	Free Tc in top half; all other species in bottom half

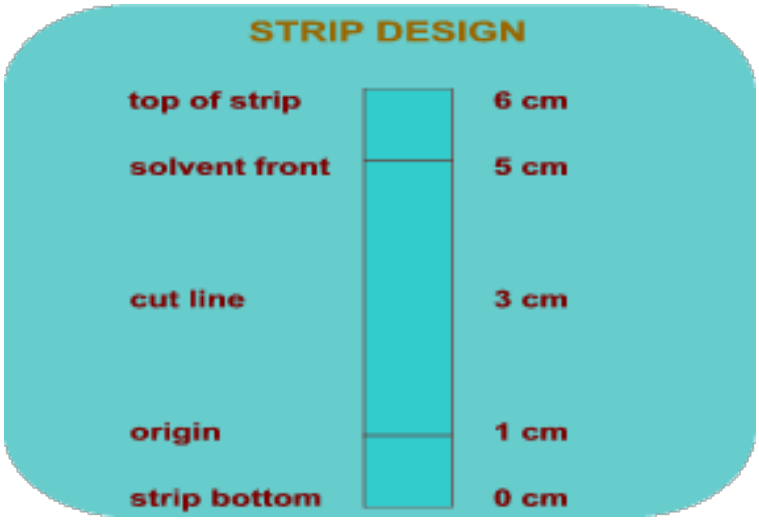
Thin Layer Chromatography Systems Tc-99m Hepatobiliary Agents

CHROMATOGRAPHY SYSTEM	IMPURITY MEASURED
ITLC-SA/20% saline	Free Tc (Pertechnetate)
ITLC-SG/water	Hydrolyzed Reduced Tc

Exception to the Rule

- For insoluble Tc-99m Radiopharmaceuticals (e.g., Tc-MAA, Tc-SC), it is only necessary to test for the presence of free Tc. No simple system can effectively separate colloidal HR Tc from an insoluble product, so HR Tc cannot be measured in these products. We therefore ignore its presence.

Strip Design

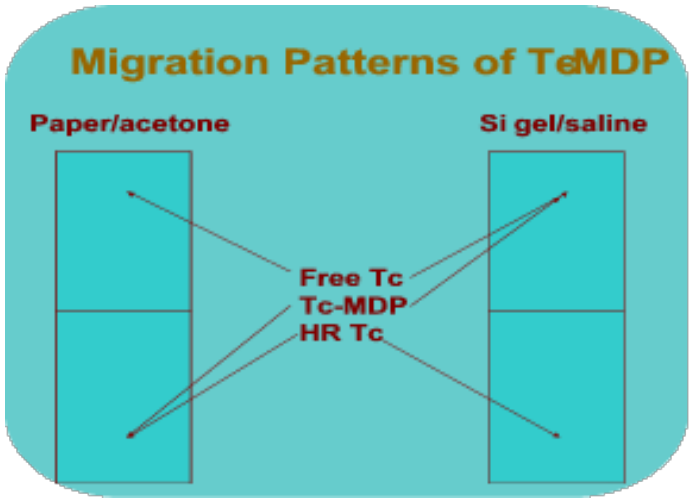


Calculations

$$\% \text{ Impurity} = \frac{\text{CPM in Half of Strip X 100}}{\text{CPM in Whole Strip}}$$

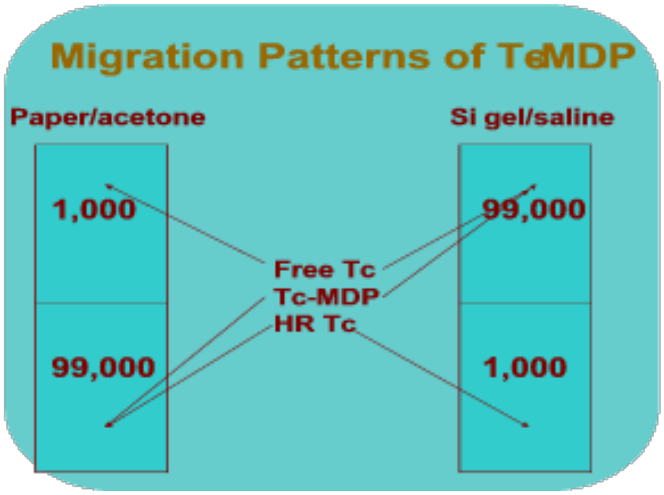
Labeling Efficiency = 100% - % HR Tc - % Free Tc

Migration Patterns



What is the radiochemical purity of Tc-MDP for strips below?

Numbers represent "Counts per Minute" for each half of strip.



Answer:

Migration Patterns of Tc-MDP Results:

% free Tc = 1,000/(1,000 + 99,000) = 1 %

% HR Tc = 1,000/(1,000 + 99,000) = 1 %

Therefore, radiochemical purity of Tc-99m MDP is 98% since

% Tc-MDP = 100 % - 2 % = 98%

DOSE CALIBRATORS: MANDATORY QUALITY CONTROL TESTS

TEST	FREQUENCY	REGULATORY AGENCY
Accuracy	Annually	NRC/State Dept Of Nuclear Safety
Constancy	Daily	NRC/State Dept Of Nuclear Safety
Linearity	Quarterly	NRC/State Dept Of Nuclear Safety
Geometry	At installation	NRC/State Dept Of Nuclear Safety

Accuracy Test

- This test is designed to show that the calibrator is giving correct readings throughout the entire energy scale that we are likely to encounter. Low, medium, and high energy standards (usually Co-57, Ba-133 or Cs-137, and Co-60, respectively), are measured in the dose calibrator using appropriate settings. Standard and measured values are compared.

Standard	Energy (keV)	expected value (mCi)	measured value (mCi)
Co-57	122	2.48	2.48
Cs-137	662	3.38	3.29
Co-60	1,332	1.55	1.52

Constancy Test

- This test measures precision and is designed to show that a long-lived source, usually 30 y Cs-137, yields reproducible readings on a daily basis on all isotope settings we are likely to use. The Cs-137 source is placed in the dose calibrator. Activity is then measured on the Cs-137 setting and all other settings used on a daily basis. Values are recorded in the dose calibrator logbook and are compared with recent values to determine if instrument is maintaining constancy on a daily basis

Reading (μCi)

Isotope	Monday	Tuesday	Wednesday	Thursday	Friday
Cs-137	123	124	122	126	124
Ga67	223	224	222	224	226
Tl201	163	164	162	166	164
Tc99m	243	242	244	246	244
I131	313	314	312	316	314
I123	193	192	194	196	194
In111	283	284	282	286	284
Xe133	433	434	432	436	434

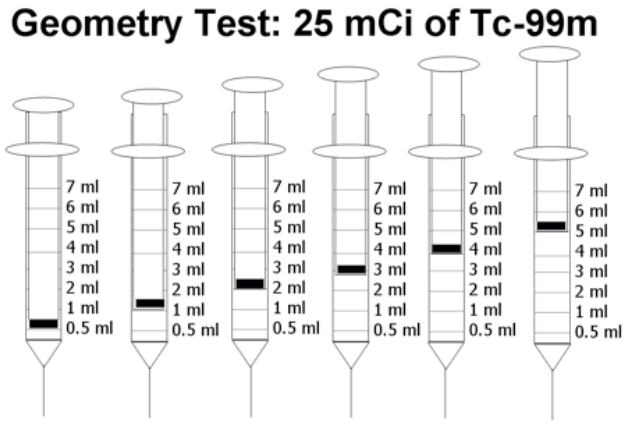
Linearity Test

- This test is designed to prove that the dose calibrator readout is linear for sources varying from the mCi range through the mCi range. A high activity Tc-99m source (50-300 mCi) is measured at T_0 and at predetermined time intervals up to 72 hours. Expected and actual measurements are compared (and may be analyzed graphically) to determine if the instrument is linear throughout the activity range we are likely to encounter.

Elapsed time	**Expected reading**	**Measured reading**
(hr)	(mCi)	(mCi)
0	300	300
1	267	272
2	238	241
3	212	209
6	150	148
12	75	72.4
24	18.75	19.1
48	1.17	1.19
72	0.073	0.074
78	0.036	0.037

Geometry Test

- This test is designed to show that correct readings can be obtained regardless of the sample size or geometry. One ml of Tc-99m in a 10 ml syringe (activity 25 mCi) is measured in the dose calibrator and the value obtained is recorded. The activity is then diluted with water to 2 ml, 3 ml, 5 ml, and 10 ml. At each of these points a reading is taken and the value recorded. Data are then evaluated to determine the effect of sample geometry on the dose calibrator reading. If instrument is geometry-dependent, it may be necessary to routinely correct readings obtained when using calibrator.
- This test must also be performed after repair, recalibration or after moving instrument.



The following table displays the data collected during a Geometry Test. The dose calibrator has passed the test.

Sample Volume	Activity (mCi)
0.5	25.5
1.0	25.3
2.0	25
3.0	24.8
4.0	24.7
5.0	24.5
6.0	24.4

Specifications for All Dose Calibrator QC Tests

- Deviation from standard or expected values must be within ± 10%.
- If Deviation > 10%, then obligation is to record value, note repair or recalibration of instrument, retest, and record new values.
- In addition to the above steps, every dose must be corrected mathematically until the instrument is repaired. There is NO LONGER a reporting requirement.

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