Radionuclide Generators

RADIONUCLIDE GENERATORS & EQUILIBRIUM

Overview

After studying this tutorial, one should be able to

- describe the two different types of equilibrium
- explain the relationship between radionuclide generators and equilibrium
- define the term “generator”
- give examples of each type of generator
- explain the principles of separation of daughter from parent
- list the properties of the ideal generator system;
- identify the parts of the Mo-99/Tc-99m generator
- explain the elution process
- identify the three clinically useful generators sold in the US:

Topics to Be Covered

- Definition of Parent-Daughter Equilibrium
    - Secular Equilibrium
    - Transient Equilibrium
- Definition of a Generator
- Properties of the Ideal Generator System
- Design of a Mo/Tc Generator Column
- Principles of Operation of a Radionuclide Generator
- Clinically Useful Radionuclide Generators
- Genealogy of Mo-99
- Miscellaneous Information

EQUILIBRIUM

Definition: Equilibrium is a condition established in a parent/daughter mixture when both parent and daughter are radioactive and when the daughter's half-life is shorter than that of the parent. If the daughter's half-life exceeds that of the parent, equilibrium will never be reached.

There are two types of equilibrium:

- Secular Equilibrium
- Transient Equilibrium

The basic difference between these two types of equilibrium is the following: during 10 half-lives of the daughter, essentially no parent decay takes place during secular equilibrium, but significant decay takes place during transient equilibrium.

There is a rule of thumb regarding how long it takes to reach equilibrium:

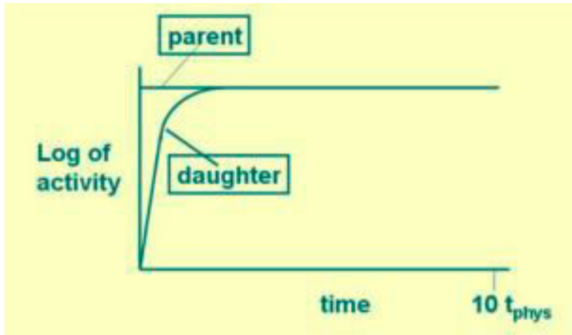
- Transient equilibrium is reached in ~4 daughter half-lives. For Tc-99m, predicted length of time is 24 hours; actual time to equilibrium is 23 hr.
- Secular equilibrium is reached in ~6 half-lives of daughter.

Secular Equilibrium

Secular Equilibrium is a condition reached when the t_{phys} of the parent is many times greater than the t_{phys} of the daughter, e.g., 100-1000 times greater or more. For example:

$$\underset{1620\text{ years}}{\text{Ra-226}} \longrightarrow \underset{3.8\text{ days}}{\text{Rn-222}}$$

In this case, the ratio of half-life of parent to half-life of the daughter is >155,600. To keep things in perspective, during 10 half-lives of the daughter (38 days in the example above), decay of the parent is negligible. Decay of the parent is represented by the flat line in the diagram below.



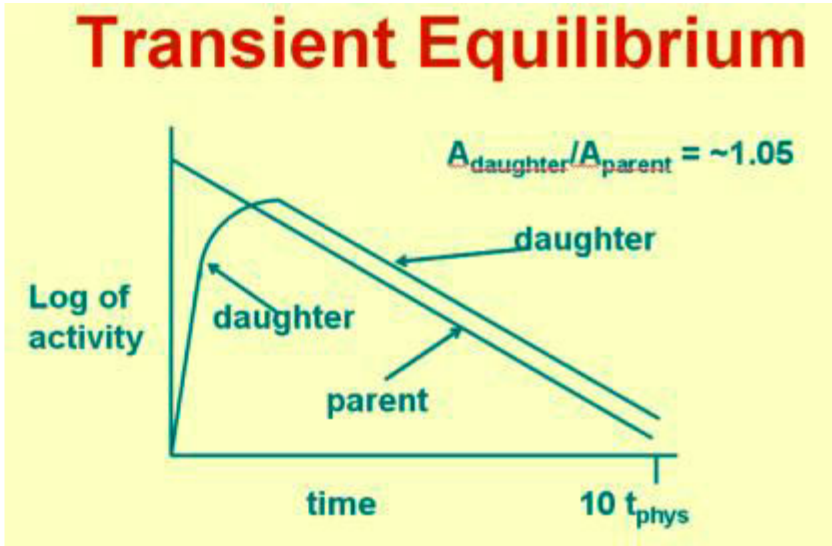
At the point at which activity of the parent and activity of the daughter become equal, equilibrium has been reached and the lines become parallel (as well as superimposed). The relationship between half-lives in secular equilibrium is:

$$t^{\text{apparent}}_{\text{daughter}} = t^{\text{physical}}_{\text{parent}}$$

This means that in the equilibrium mixture, the daughter **appears** to decay with the half-life of the parent. When the daughter is isolated from the mixture, it has its expected half-life. Perhaps the simplest explanation for their appearing to be equal is that the daughter can't decay until it is formed, and so the rate of formation of the daughter equals the rate of decay of the parent, which is very slow. Therefore the parent and daughter appear to have the same half-lives. In the case of the decay of Ra-226 to Rn-222, the decay constant of the parent is 0.000001171day-1 (only 1 millionth decays per day).

Transient Equilibrium

Transient Equilibrium is a condition reached when the t_{phys} of the parent is approximately 10 times greater than the t_{phys} of the daughter. A classic example is the Mo-99/Tc-99m Generator, where the ratio of the half-lives is 67 hr/6 hr = 11:1. During the 60 hr period representing 10 half-lives of Tc-99m, almost 50% of the Mo-99 has disappeared, as noted in diagram. This represents a very significant amount, unlike the negligible amount in secular equilibrium.

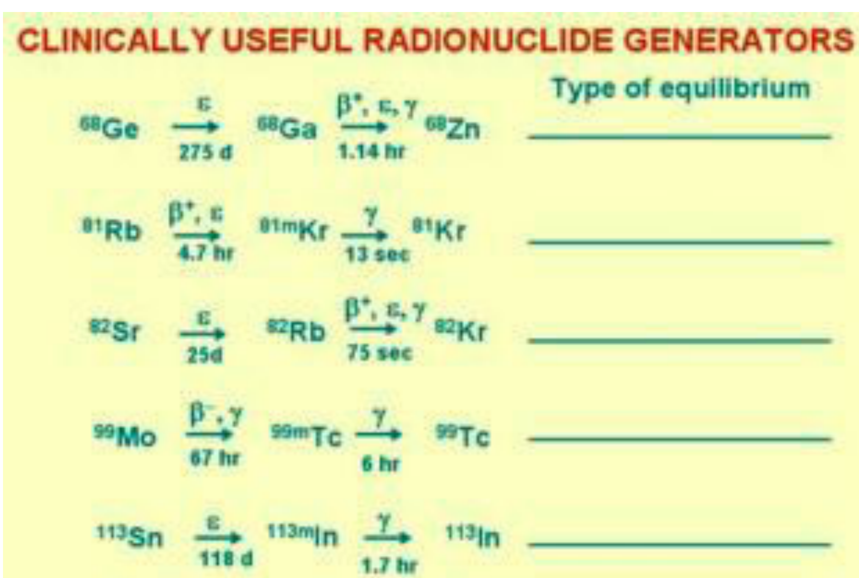


The relationship between half-lives in transient equilibrium is the same as that in secular equilibrium:

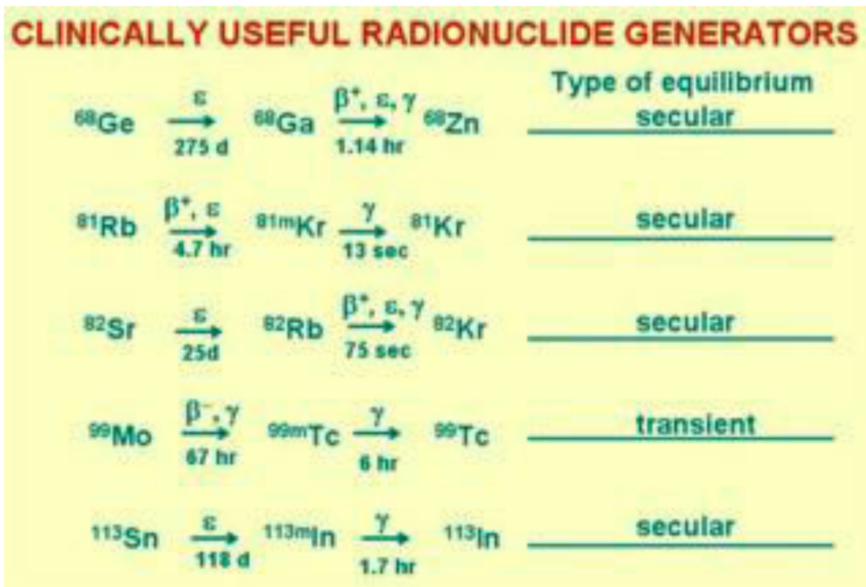
$$t^{\text{apparent}}_{\text{daughter}} = t^{\text{physical}}_{\text{parent}}$$

CLINICALLY USEFUL GENERATORS

Indicate whether each generator listed below is in transient or secular equilibrium (check your answers using the answer key below)



ANSWER KEY



Definition of a Generator

- A radionuclide generator is a self-contained device housing a parent/daughter mixture in equilibrium.
- There must be a method of removing the daughter and leaving the parent behind to regenerate more daughter activity.
- It is designed to produce the daughter for some purpose separate from the parent.
- Generators produce certain short-lived radioisotopes on-site which cannot be shipped by commercial sources. To be useful, the parent's half-life must be long compared to the travel time required to transport the generator to recipient.
- The typical shelf-life of a Mo/Tc generator is 2 weeks, as is the expiration date.
- The process of removing the daughter from the generator is referred to as **elution**; the solution used to remove the daughter is called the **eluent**; and the solution collected from the generator containing the daughter radioisotope is called the **eluate**.
- A photograph of the Lantheus generator is shown below.

When radiochemists design generators for medical use, there are certain properties generic to all generators:

Properties of an Ideal Generator

1. If intended for clinical use, output of the generator must be sterile and pyrogen-free. There is no compromise on either of these requirements.

2. The chemical properties of the daughter must be different than those of the parent to permit separation of daughter from parent. Separations are usually performed by affinity or ion exchange chromatography.

3. Generator should be eluted with 0.9% saline solution and should involve no violent chemical reactions. Human intervention should be minimal to minimize radiation dose. Eluents other than 0.9% NaCl may require tedious pH adjustment, associated with a significant radiation dose, and are therefore undesirable.

4. Daughter isotope for diagnostic studies should be short-lived gamma-emitting nuclide (t_{phys} = hrs-days). Beta particles are undesirable as they confer a high radiation dose and are not imageable.

5. Physical half-life of parent should be short enough so daughter in-growth after elution is rapid, but long enough for practicality. The Mo/Tc generator is a perfect example- in-growth of Tc-99m is very rapid, but the shelf-life of the generator is two weeks.

6. Daughter chemistry should be amenable to the preparation of a wide variety of compounds, especially those in kit form. In the case of the Mo/Tc generator, there are cold kits for imaging essentially any organ or system in the human body.

7. Very long-lived or stable granddaughter so no radiation dose is conferred to patient by decay of subsequent generations. In the case of Tc-99 ground state, the granddaughter of Mo-99, the half-life of 220,000 yr guarantees a minimal radiation dose to the patient, regardless of the effective half-life.

8. Inexpensive, effective shielding of generator, minimizing radiation dose to those using it. This is easy to accomplish since lead is very dense and therefore a good attenuator of radiation. In addition, it is a very inexpensive metal and can be easily molded into almost any shape desired.

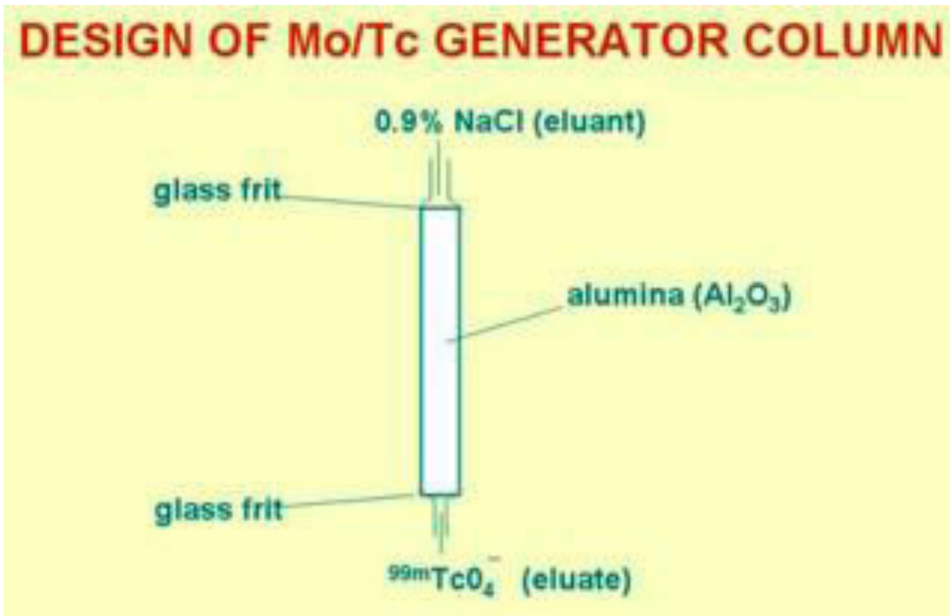
9. Generator is easily recharged (we do NOT recharge Mo/Tc generators- radiation dose associated with this procedure would be excessive). After their useful life is over, we store them in a decay area until a background reading is obtained at the surface of the generator.

Mo/Tc GENERATOR: PRINCIPLES OF OPERATION

- Prior to shipping the generator to the Nuclear Medicine Department, Mo-99 sodium molybdate is immobilized on a column of alumina (Al_2O_3; aluminum oxide) due to its very high affinity for alumina. This step must be performed very carefully using remote control equipment to minimize radiation dose to the workers manufacturing the generator.
- 0.9% saline solution (the eluent) is passed through the column and Na pertechnetate, the daughter of Mo-99 decay, is eluted from the column with high efficiency due to its almost total lack of affinity for alumina. The driving force is the evacuated vial that creates a very significant pressure differential on the two sides of the generator since the saline side of the generator is always at 1 atm of pressure.
- The pertechnetate is collected in a shielded, evacuated sterile vial and must undergo quality control testing, then must be calibrated prior to use. It is referred to as the eluate.
- Quantitative removal of pertechnetate from the alumina column is attributed to the lack of affinity of pertechnetate for alumina, whereas

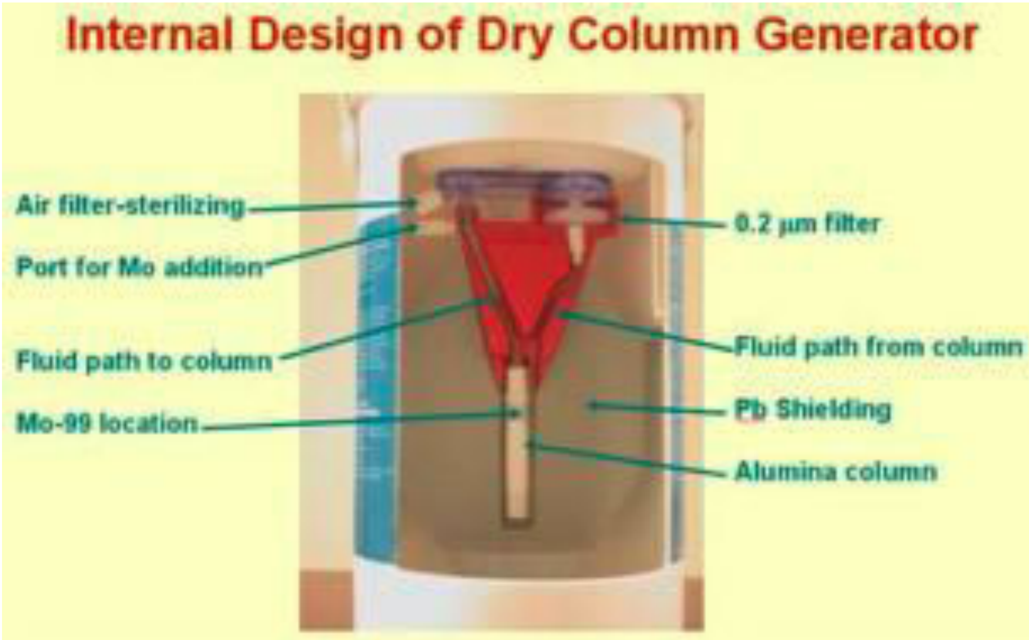
molybdate is essentially completely and irreversibly bound to the alumina (quantitative retention) and cannot be removed, regardless of the volume of saline passing through the column.

Mo/Tc Generator: Design of the Generator Column



Mo/Tc Generator: Schematic of A Dry Column Generator-Internal Construction

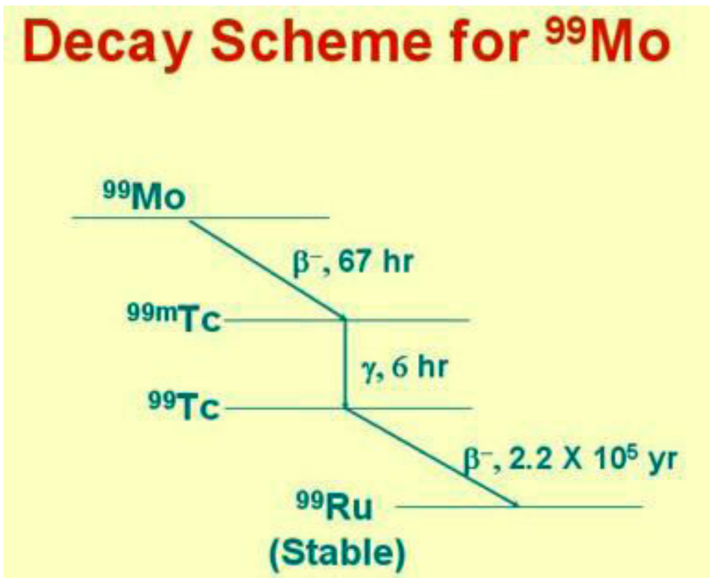
Mo/Tc Generator: Photograph of A Dry Column Generator-Internal Construction



Bar III Box Label for Generator

Genealogy of Mo-99

The complex decay scheme shown below indicates that Mo-99 decays by β- emission to Tc-99m, the metastable (excited) state of Tc. The half-life of the Mo-99 is 67 hr and the half-life of Tc-99m is 6.02 hr. From there it decays by isomeric transition to the ground state, Tc-99, which has a half-life of 220,000 yr. The final step is decay of Tc-99 by β– emission to Ru-99, which is not radioactive.



Question # 1

Why does a Mo/Tc generator contain almost **50 lb** of lead shielding?

a. To shield Mo-99 parent

b. To shield Tc-99m daughter

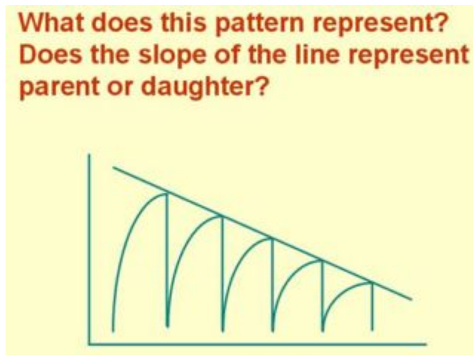
c. To shield Tc-99g granddaughter

d. To shield Ru-99 great granddaughter

Question # 2

Why are you not concerned for your patients' safety if 10 mCi of 99mTc sulfur colloid is injected into a patient? 99mTc-sulfur colloid never clears the liver. All of it will ultimately decay into 99Tc, which has a t_{phys} of 2.2×10^5 yr.

Question # 3:



Answer Question 1:

a. To shield the high energy photons of Mo-99 (740 and 780 KeV). It takes much less lead to shield the 140 KeV photons of Tc-99m.

Answer Question 2:

Since the t_{phys} is 2.2×10^5 yr, the rate of decay is only 0.000003 per year (3 millionths/year). During the patient's lifetime, the number of decays is negligible compared to background radiation.

Answer Question 3:

This pattern represents 5 sequential elutions equally spaced in time. Parent and daughter are in transient equilibrium and the slope of the line represents parent's half-life. The time interval between elutions could be almost any time unit (min, hr, da, wk, etc)

Consultants In Nuclear Medicine
Nucmedconsultants@comcast.net
Stephen Karesh, PhD
Phone: 773-802-7617
Fax: 773-304-2545
2910 W. Estes Ave. Chicago, IL 60645-2394