Practical Generator Kinetics

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Equations describing the decay and buildup of nuclides in the ^{99}Mo–^{99m}Tc generator are presented and discussed. The three basic time functions which describe the quantities of ^{99}Mo, ^{99m}Tc, and ^{99}Tc are then manipulated to yield time-dependent factors which simplify the calculations of generator decay. These factors are (A) the fraction of maximum ^{99m}Tc radioactivity at t hr following prior elution, (B) ^{99m}Tc radioactivity as a fraction of ^{99}Mo radioactivity at time t following prior elution, and (C) The mole fraction of total technetium present in the generator as the metastable isomer at time t. These factors allow simple and accurate calculations of relative yields of ^{99m}Tc at different times following prior elution, expected yield in millicuries and generator elution efficiency, and total molar quantity of technetium eluted. Examples are presented. Solutions of the basic differential equations are described in detail in the Appendix.

The ^{99m}Tc ion-exchange generator is one of the primary reasons for the remarkable growth of nuclear medicine during the past decade. In addition to the steadily increasing capabilities of nuclear medical instrumentation, the ready clinical availability of ^{99m}Tc has reduced patient radiation exposures per microcurie by two to three orders of magnitude, increased the available photon flux in imaging studies, and produced a dramatic reduction in cost per study relative to the radionuclides used previously. The technetium generator has allowed even the smallest of institutions to maintain a continual supply of this short-lived radiopharmaceutical.

The decay kinetics of parent–daughter systems are well known, with one of the earliest descriptions by Rutherford in 1902 (*1*)! Even so, the complex exponential relationships needed to describe the decay and buildup of nuclides in the ^{99m}Tc generator are too cumbersome for routine clinical use. Transient equilibrium is not attained for two to three days; therefore, an estimate of ^{99m}Tc activity which assumes an equilibrium condition prior to this time is invalid. However, a close examination of the classical decay kinetics indicates certain simple and accurate methods for predicting such parameters as the activity of ^{99m}Tc to be eluted from the generator, the generator elution efficiency, and the total mass of technetium present in an eluate.

Theory

The following differential equations (Eqs. 1–3) describe the decay and buildup of nuclides in the radionuclide generator, where subscripts 1, 2, and 3 refer to ^{99}Mo, ^{99m}Tc, and ^{99}Tc, respectively:

$$dN_1/dt = -\lambda_1 N_1, \text{ where } N_1\,(0) = N_1^0, \quad (1)$$

$$dN_2/dt = \lambda_1 N_1 - \lambda_2 N_2, \text{ where } N_2\,(0) = N_2^0, \quad (2)$$

$$dN_3/dt = \lambda_2 N_2, \text{ where } N_3\,(0) = N_3^0. \quad (3)$$

The superscript ^{0} in these equations refers to the number of atoms present at time t = 0; the quantities N_1, N_2, and N_3 then refer to the numbers of atoms of each respective nuclide at time t. The differential dN/dt in each equation expresses the time rate of change of the number of atoms present, the equality being introduced by multiplying the number of atoms by a proportionality constant, or decay constant, λ. The minus sign in Eq. 1 indicates a decrease in the number of atoms of ^{99}Mo initially present, while the positive term in Eq. 3 indicates a buildup of ^{99}Tc (although ^{99}Tc is radioactive, its $T_{1/2}$ is so long relative to ^{99}Mo and ^{99m}Tc that it is considered stable). Equation 2 demonstrates a buildup of ^{99m}Tc equal to the decay of ^{99}Mo, in addition to its own decay, $-\lambda_2 N_2$. The methods for solving these equations, i.e., removing the differential terms by integration, are presented in Appendix A. The solutions of Eqs. 1–3 are indicated by Eqs. 4–6, respectively:

$$N_1 = N_1^0\, e^{-\lambda_1 t}, \quad (4)$$

$$N_2 = \frac{\lambda_1}{\lambda_2 - \lambda_1} N_1^0\,(e^{-\lambda_1 t} - e^{-\lambda_2 t}) + N_2^0\, e^{-\lambda_2 t}, \quad (5)$$

$$N_3 = N_3^0 + N_2^0\,(1 - e^{-\lambda_2 t}) + N_1^0\left(1 + \frac{\lambda_1}{\lambda_2 - \lambda_1} e^{-\lambda_2 t} - \frac{\lambda_2}{\lambda_2 - \lambda_1} e^{-\lambda_1 t}\right). \quad (6)$$

If only ^{99}Mo is present initially, then $N_2^0 = N_3^0 = 0$ and Eqs. 5 and 6 simplify to:

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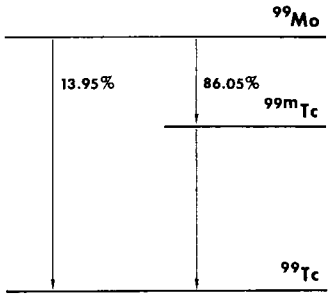

FIG 1. Branching decay of ^{99}Mo.

$$N_2 = \frac{\lambda_1}{\lambda_2 - \lambda_1} N_1^0 (e^{-\lambda_1 t} - e^{-\lambda_2 t}), \quad (7)$$

$$N_3 = N_1^0 \left(1 + \frac{\lambda_1}{\lambda_2 - \lambda_1} e^{-\lambda_2 t} - \frac{\lambda_2}{\lambda_2 - \lambda_1} e^{-\lambda_1 t}\right). \quad (8)$$

These equations assume that 100% of ^{99}Mo decays to ^{99m}Tc, which in turn decays to ^{99}Tc. However, from the ^{99}Mo decay scheme (Fig. 1), 13.95% of ^{99}Mo decays directly to ^{99}Tc, while only 86.05% decays to the metastable isomer, ^{99m}Tc (*2*). This fact must be considered in Eqs. 7 and 8 by replacing N_1^0 by 0.8605 N_1^0, and also in equation 8 by adding a buildup term to account for the accumulation of ^{99}Tc directly from the decay of ^{99} Mo. Thus the final equations representing the numbers of atoms of ^{99}Mo, ^{99m}Tc, and ^{99}Tc in the generator, at any time following prior elution, are

$$N_1 = N_1^0 e^{-\lambda_1 t} \quad (9)$$

$$N_2 = 0.8605\, N_1^0 \frac{\lambda_1}{\lambda_2 - \lambda_1} (e^{-\lambda_1 t} - e^{-\lambda_2 t}), \quad (10)$$

$$N_3 = 0.8605\, N_1^0 \left(1 + \frac{\lambda_1}{\lambda_2 - \lambda_1} e^{-\lambda_2 t} - \frac{\lambda_2}{\lambda_2 - \lambda_1} e^{-\lambda_1 t}\right) + 0.1395\, N_1^0 (1 - e^{-\lambda_1 t}), \quad (11)$$

where (*3*)

$$\lambda_1 = \frac{\ln 2}{66.48 \text{ hr}} = 0.01043 \text{ hr}^{-1},$$

$$\lambda_2 = \frac{\ln 2}{6.02 \text{ hr}} = 0.1151 \text{ hr}^{-1}.$$

The following applications use these equations to derive simple relationships and to develop tabulated data sufficient to determine basic stoichiometric information regarding the technetium generator. The calibration activity of ^{99}Mo and the time elapsed between generator elutions are the only input data needed for these calculations.

Applications

Three important questions about available technetium can be answered by manipulating these basic decay equations to yield time-dependent factors which then allow simple calculations. The first question is: "How long after a prior elution is the radioactivity of ^{99m}Tc in the generator maximized?" A related question is: "What is the ^{99m}Tc activity at various times as a fraction of this maximum activity?" The first step necessary to answer these questions is to multiply both sides of Eq. 10 by λ_2 to give units of disintegrations per second (A) rather than atoms (N):

$$\lambda_2 N_2 = 0.8605\, N_1^0 \frac{\lambda_1 \lambda_2}{\lambda_2 - \lambda_1} (e^{-\lambda_1 t} - e^{-\lambda_2 t}).$$

Since $A = \lambda N$,

$$A_2 = 0.8605\, A_1^0 \frac{\lambda_2}{\lambda_2 - \lambda_1} (e^{-\lambda_1 t} - e^{-\lambda_2 t}). \quad (12)$$

A graph of the decay of ^{99}Mo (Eq. 9) and the buildup and decay of ^{99m}Tc (Eq. 12) is shown in Fig. 2. Setting the first derivative with respect to time equal to zero and solving for t yields t_{max}:

$$\frac{dA_2}{dt} = \left(\frac{0.8605\, A_1^0 \lambda_2^2}{\lambda_2 - \lambda_1}\right) e^{-\lambda_2 t} - \left(\frac{0.8605\, A_1^0 \lambda_1 \lambda_2}{\lambda_2 - \lambda_1}\right) e^{-\lambda_1 t} = 0,$$

$$\left(\frac{0.8605\, A_1^0 \lambda_2^2}{\lambda_2 - \lambda_1}\right) e^{-\lambda_2 t} = \left(\frac{0.8605\, A_1^0 \lambda_1 \lambda_2}{\lambda_2 - \lambda_1}\right) e^{-\lambda_1 t},$$

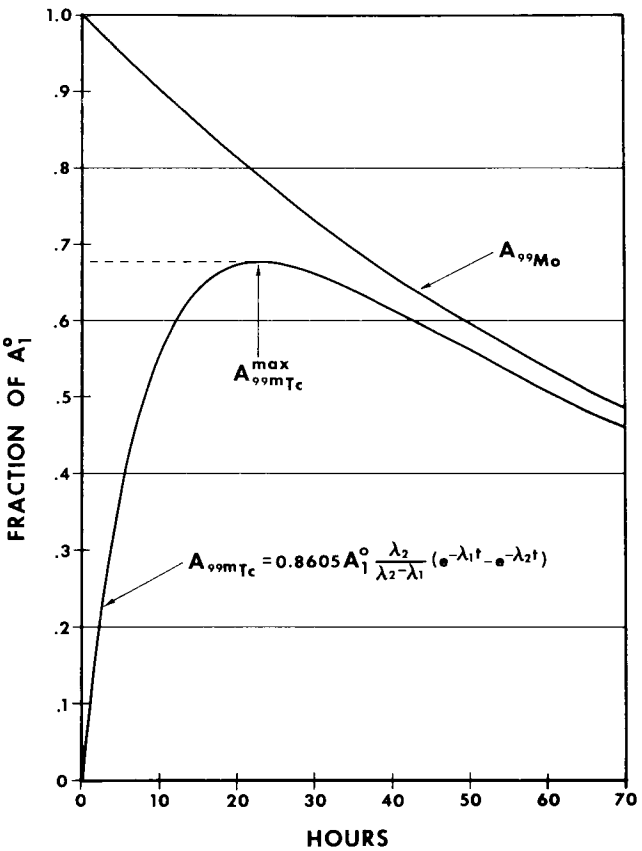

FIG. 2. Buildup and decay of ^{99m}Tc from ^{99}Mo. Maximum technetium radioactivity is 67.7% of activity of ^{99}Mo at t = 0 (time of previous elution).

$$e^{-\lambda_1 t}/e^{-\lambda_2 t} = \lambda_2/\lambda_1,$$

$$e^{t(\lambda_2 - \lambda_1)} = \lambda_2/\lambda_1,$$

$$t(\lambda_2 - \lambda_1) = \ln(\lambda_2/\lambda_1),$$

$$t_{max} = \frac{\ln(\lambda_2/\lambda_1)}{(\lambda_2 - \lambda_1)} = 22.9 \text{ hr.}$$

The maximum activity of ^{99m}Tc is present in the generator at 22.9 hr following prior elution. Using Eq. 12, if $t = t_{max} = 22.9$ hr, then solving for A_2 yields the maximum activity of ^{99m}Tc as a fraction of the initial activity of ^{99}Mo. A_2^{max} is thus equal to 0.677 A_1^0. By substituting various time intervals into Eq. 12 and dividing by A_2^{max}, the fraction of the maximum activity of ^{99m}Tc present at any time following prior elution is determined. This function is

$$f(t) = \frac{0.8605\, A_1^0 \lambda_2 (e^{-\lambda_1 t} - e^{-\lambda_2 t})}{A_2^{max} (\lambda_2 - \lambda_1)}. \qquad (13)$$

The equation was evaluated at several values of t and the resultant data are presented in Table 1 and Fig. 3. The f(t) factor allows one to determine relative activities of ^{99m}Tc on the column at various times (see Example 1 below). Note that within 2 hr after prior elution 25% of the maximum ^{99m}Tc radioactivity is regenerated.

A second question regarding the ^{99}Mo-^{99m}Tc system is: "What is the radioactivity of ^{99m}Tc as a fraction of ^{99}Mo radioactivity after any time t?" This information allows the calculation of elution efficiency as well as the expected yield of ^{99m}Tc based on the calibration activity of ^{99}Mo. The function g(t) is simply A_2 (Eq. 10 multiplied by λ_2) divided by A_1 (Eq. 9 multiplied by λ_1), and reduces to

$$g(t) = \frac{A_2}{A_1} = \frac{0.8605\, \lambda_2 (e^{-\lambda_1 t} - e^{-\lambda_2 t})}{(\lambda_2 - \lambda_1)(e^{-\lambda_1 t})}. \qquad (14)$$

The limit of this function as t becomes very large is

$$\lim_{t \to \infty} g(t) = \lim_{t \to \infty} \left[\frac{\lambda_2 (0.8605) - \lambda_2 (0.8605)(e^{-\lambda_2 t}/e^{-\lambda_1 t})}{\lambda_2 - \lambda_1} \right]$$

$$= \frac{\lambda_2 (0.8605)}{\lambda_2 - \lambda_1} = 0.946.$$

When t is large, e.g., greater than approximately two to three days, the radioactivity of ^{99m}Tc becomes a constant fraction of the ^{99}Mo radioactivity (0.946) and decreases with the half-life of ^{99}Mo; this is known as transient equilibrium. Function g(t) was evaluated versus time. The data are presented in Table 2 and displayed graphically in Fig. 4. With the radioactivity of ^{99}Mo from the stated calibration activity, this factor allows one to calculate the present radioactivity of ^{99m}Tc in the generator. Comparing this with the eluted radioactivity yields the elution efficiency (see Examples 2 and 3 below).

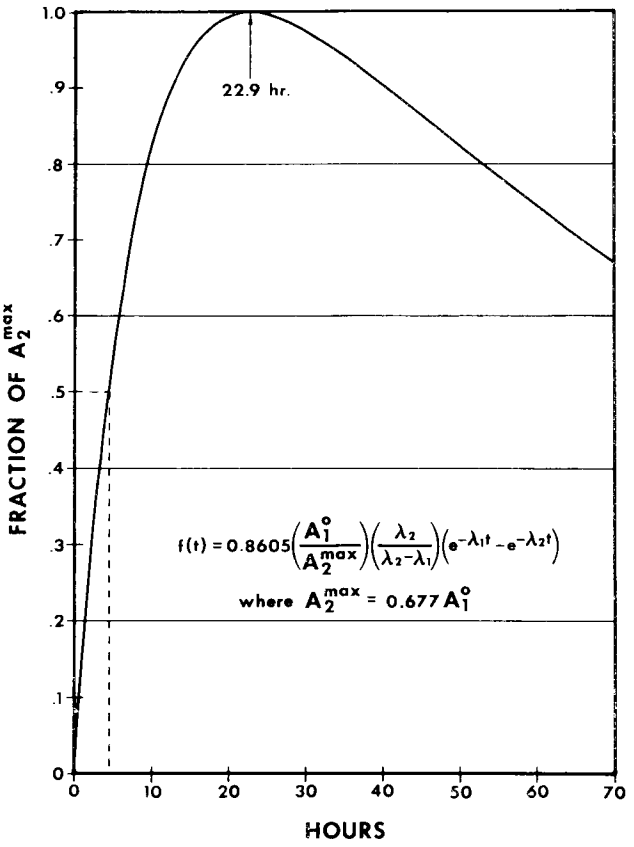

FIG. 3. Fraction of maximum ^{99m}Tc radioactivity. Technetium activity is 50% of maximum at 4.5 hr after prior elution; A_2^{max} occurs at 22.9 hr.

TABLE 1. Radioactivity of ^{99m}Tc in Generator as Fraction of Maximum ^{99m}Tc Radioactivity

$$f(t) = \frac{0.8605\, A_1^0 \lambda_2 (e^{-\lambda_1 t} - e^{-\lambda_2 t})}{A_2^{max} (\lambda_2 - \lambda_1)},$$

where $A_2^{max} = 0.677\, A_1^0$

Time (hr)	f (t)	Time (hr)	f (t)	Time (hr)	f (t)
0.5	0.071	10.0	0.817	27	0.992
1.0	0.137	10.5	0.836	28	0.987
1.5	0.200	11.0	0.852	29	0.983
2.0	0.258	11.5	0.868	30	0.977
2.5	0.314	12.0	0.882	32	0.965
3.0	0.365	13	0.907	34	0.952
3.5	0.414	14	0.928	36	0.937
4.0	0.458	15	0.946	38	0.922
4.5	0.501	16	0.961	40	0.906
5.0	0.540	17	0.973	44	0.874
5.5	0.578	18	0.982	48	0.841
6.0	0.612	19	0.989	54	0.793
6.5	0.645	20	0.994	60	0.746
7.0	0.675	21	0.998	66	0.701
7.5	0.703	22	0.999	72	0.659
8.0	0.729	23	1.000	78	0.619
8.5	0.754	24	0.999	84	0.582
9.0	0.776	25	0.998	90	0.546
9.5	0.798	26	0.995	96	0.513

TABLE 2. Radioactivity of ^{99m}Tc in Generator as Fraction of Present ^{99}Mo Radioactivity

$$g(t) = \frac{A_2}{A_1} = \frac{0.8605\,\lambda_2(e^{-\lambda_1 t} - e^{-\lambda_2 t})}{(\lambda_2 - \lambda_1)(e^{-\lambda_1 t})}$$

Time (hr)	g (t)	Time (hr)	g (t)	Time (hr)	g (t)
0.5	0.048	10.0	0.614	27	0.890
1.0	0.094	10.5	0.631	28	0.896
1.5	0.138	11.0	0.647	29	0.901
2.0	0.179	11.5	0.662	30	0.905
2.5	0.218	12.0	0.677	32	0.913
3.0	0.255	13	0.704	34	0.919
3.5	0.290	14	0.728	36	0.924
4.0	0.324	15	0.750	38	0.929
4.5	0.356	16	0.769	40	0.932
5.0	0.386	17	0.787	44	0.937
5.5	0.414	18	0.803	48	0.940
6.0	0.441	19	0.817	54	0.943
6.5	0.467	20	0.830	60	0.944
7.0	0.492	21	0.841	66	0.945
7.5	0.515	22	0.852	72	0.946
8.0	0.537	23	0.861	78	0.946
8.5	0.558	24	0.870	84	0.946
9.0	0.578	25	0.877	90	0.946
9.5	0.596	26	0.884	96	0.946

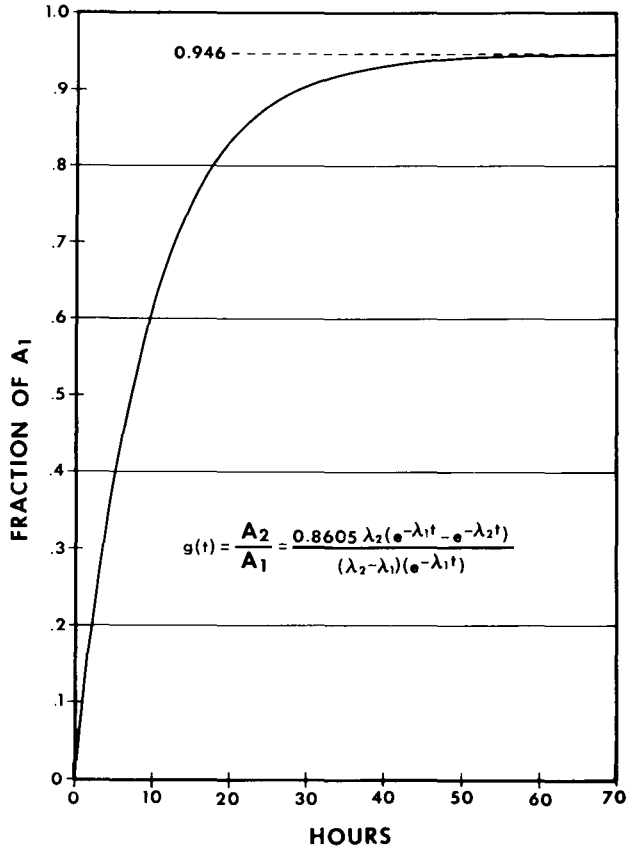

FIG 4. Radioactivity of ^{99m}Tc as fraction of ^{99}Mo radioactivity. Transient equilibrium is demonstrated as technetium activity approaches constant fraction of molybdenum activity (0.946), 2–3 days following previous elution.

A third question elaborated by the basic kinetic equations (Eqs. 9–11) allows one to prepare a table of 99m mole fractions at various times following prior elution; i.e., fraction of the total molar quantity of technetium that is present as the metastable isomer. Thus the total quantity of technetium can be calculated from a knowledge of 99m radioactivity in the eluate and the time elapsed between elutions (*4*). The function describing the mole fraction, h(t), is simply the number of atoms of ^{99m}Tc divided by the total number of atoms of technetium (both the metastable and ground-state isomers), and reduces to

$$h(t) = \frac{N_2}{N_{total}} = \frac{N_2}{N_2 + N_3} = \frac{\lambda_1\,(e^{-\lambda_1 t} - e^{-\lambda_2 t})}{1.162\,(\lambda_2 - \lambda_1)\,(1 - e^{-\lambda_1 t})}. \quad (15)$$

This function was also evaluated versus time and results are shown in Table 3 and Fig. 5. The mole fraction is undefined at t = 0 (the denominator is zero when t = 0), but by using l'Hôpital's rule it can be shown that the limit of h(t) as t approaches zero is 0.8605. This is another way of arriving at the branching ratio and restates the fact that the first ^{99}Mo nucleus to decay after t = 0 has an 86% probability of going to the metastable isomer. Since $N_{total} = N_{99m}/h(t)$, and $A_{99m} = \lambda_{99m} N_{99m}$, then

$$N_{total} = \frac{A_{99m}}{[h(t)]\,[\lambda_{99m}]}.$$

The total number of atoms of technetium in an eluate can be calculated from the activity of 99m and from the 99m mole fraction, which is based on time elapsed since prior elution. (An example of this calculation is shown in Example 4 below.) The number of moles (N_{total} divided by Avogadro's number) multiplied by

TABLE 3. Mole Fraction of Technetium in Generator as Metastable Isomer

$$h(t) = \frac{N_2}{N_{total}} = \frac{\lambda_1(e^{-\lambda_1 t} - e^{-\lambda_2 t})}{1.162\,(\lambda_2 - \lambda_1)(1 - e^{-\lambda_1 t})}$$

Time (hr)	h (t)	Time (hr)	h (t)	Time (hr)	h (t)
0.5	0.836	10.0	0.506	27	0.248
1.0	0.813	10.5	0.494	28	0.239
1.5	0.790	11.0	0.482	29	0.231
2.0	0.768	11.5	0.471	30	0.223
2.5	0.747	12.0	0.460	32	0.209
3.0	0.727	13	0.439	34	0.196
3.5	0.707	14	0.419	36	0.184
4.0	0.688	15	0.401	38	0.173
4.5	0.670	16	0.384	40	0.163
5.0	0.653	17	0.367	44	0.146
5.5	0.636	18	0.352	48	0.131
6.0	0.619	19	0.338	54	0.113
6.5	0.603	20	0.324	60	0.098
7.0	0.588	21	0.311	66	0.086
7.5	0.573	22	0.299	72	0.077
8.0	0.559	23	0.288	78	0.068
8.5	0.545	24	0.277	84	0.061
9.0	0.532	25	0.267	90	0.055
9.5	0.519	26	0.257	96	0.050

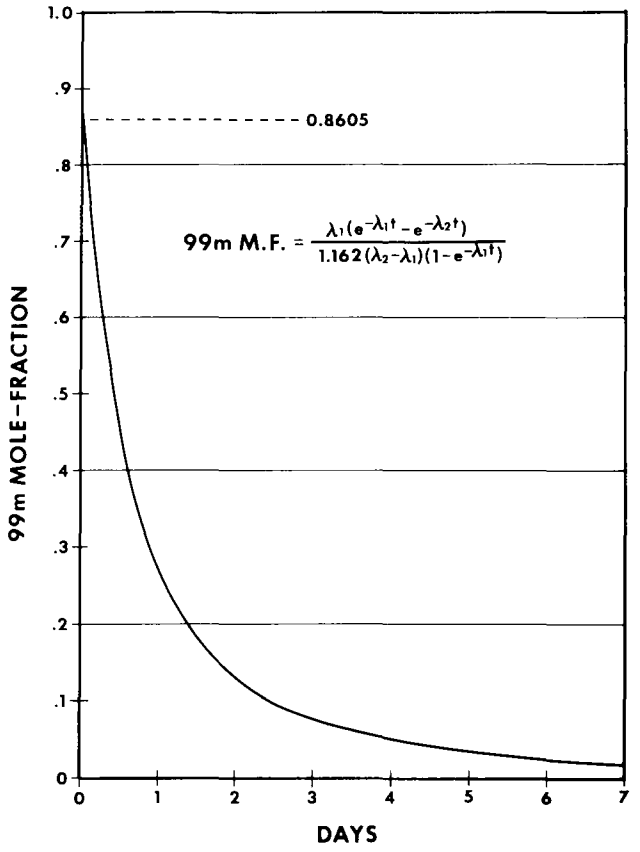

FIG. 5. 99m mole fraction as function of time. This allows calculation of total molar quantity of technetium in eluate based on A_2 and time since previous elution. Since first ^{99}Mo nucleus to decay after t = 0 has 86% probability of decaying to ^{99m}Tc, mole fraction approaches 0.8605 as t approaches zero.

the atomic weight gives the mass of technetium in solution.

Examples

1. On Friday night a technologist is called to do a lung scan and elutes the generator at 9 pm. There are several patients scheduled for studies on Saturday and as much radioactivity as possible is needed. If the technologist waited until 10 am to elute the generator, rather than eluting at 7 am, by what percentage would the yield be increased?

	f(t) from Table 1
9 pm- 7 am = 10 hr	0.817
9 pm-10 am = 13 hr	0.907

$$\frac{0.907 - 0.817}{0.817} \times 100 = 11\%.$$

The yield of a 10 am elution will be 11% greater than at 7 am. However, note in Table 1 that if it is eluted at 7 am the ^{99m}Tc in the generator will be back to 36% of maximum activity at 10 am, if more activity is needed.

2. How many millicuries of ^{99m}Tc will you expect to elute from the generator at 8 am Friday morning, assuming 95% elution efficiency, if the prior elution was at 8 am Thursday? The molybdenum is calibrated for 200 mCi at noon Friday. Friday, 8 am is 4 hr prior to calibration time, so, from Table 4 (^{99}Mo decay factors),

$$A_{^{99}Mo} = (200 \text{ mCi})(1.04) = 208 \text{ mCi}.$$

From Table 2, after 24 hr the ^{99m}Tc radioactivity is 0.870 of ^{99}Mo radioactivity:

$$(208 \text{ mCi})(0.870) = 181 \text{ mCi}.$$

With 95% elution efficiency the yield would be approximately 172 mCi eluted from the column.

3. A generator is eluted daily at 8 am. On Thursday morning 442 mCi are washed from the column. The molybdenum is calibrated for 400 mCi at noon Friday. What is the elution efficiency? Thursday, 8 am is 28 hr prior to calibration time of the molybdenum; therefore there are 536 mCi of molybdenum on the column:

$$A_{^{99}Mo} = (400 \text{ mCi})(1.34) = 536 \text{ mCi}.$$

The generator is being eluted at 24-hr intervals, so, from Table 2, g(t) = 0.870.

$$(536 \text{ mCi})(0.870) = 466 \text{ mCi } ^{99m}\text{Tc on the column.}$$

Therefore, elution efficiency = 442/466 × 100 = 95%. You should be aware, however, that there may be some inaccuracy in generator calibrations and dose calibrator readings (5).

4. Similarly, what is the total mass (grams) of tech-

TABLE 4. Molybdenum-99 Decay Factors

	Factor = $e^{-\lambda_1 t}$				
Time (hr)	Factor	Time (hr)	Factor	Time (hr)	Factor
-168	5.76	-48	1.65	36	0.687
-144	4.49	-44	1.58	40	0.659
-124	3.64	-40	1.52	44	0.632
-120	3.49	-36	1.46	48	0.606
-116	3.35	-32	1.40	52	0.581
-112	3.22	-28	1.34	56	0.558
-108	3.08	-24	1.28	60	0.535
-104	2.96	-20	1.23	64	0.513
-100	2.84	-16	1.18	68	0.492
-96	2.72	-12	1.13	72	0.472
-92	2.61	-8	1.09	96	0.368
-88	2.50	-4	1.04	120	0.286
-84	2.40	0	1.00	144	0.223
-80	2.30	4	0.959	168	0.174
-76	2.21	8	0.920	192	0.135
-72	2.12	12	0.882	216	0.105
-68	2.03	16	0.846	240	0.082
-64	1.95	20	0.812	264	0.064
-60	1.87	24	0.779	288	0.050
-56	1.79	28	0.747	312	0.039
-32	1.72	32	0.716	336	0.030

netium present in the eluate which contained 442 mCi of ^{99m}Tc at the time of elution?

$$h(t) \text{ at } 24 \text{ hr} = 0.277,$$

$$N_{total} = \frac{A_2}{[h(t)]\ [\lambda_2]}$$

$$= \frac{(442 \text{ mCi})\ (3.7 \times 10^7 \text{ dps/mCi})\ (3600 \text{ sec/hr})}{(0.277)\ (0.1151 \text{ hr}^{-1})}$$

$$= 1.85 \times 10^{15} \text{ atoms},$$

$$\frac{1.85 \times 10^{15} \text{ atoms}}{6.02 \times 10^{23} \text{ atoms/mole}} (99 \text{ gm/mole}) = 0.30\ \mu\text{g}.$$

Conclusion

As illustrated with the previous examples, the factors presented in Tables 1–4 allow simple and accurate calculation of various data in regard to the ^{99}Mo–^{99m}Tc generator. The information in these tables obviates the need to reproduce the cumbersome manipulation of kinetics equations, and yet provides the requisite accuracy necessary for nuclear medicine procedures.

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Appendix A. Solution of Differential Equations Describing Decay and Buildup of Nuclides in Radionuclide Generator

Equations 1–3 are linear first-order differential equations and are readily solved by multiplying by the appropriate integrating factor prior to integration or by separation of variables.

Equation 1.

$$dN_1/dt = -\lambda_1 N_1, \quad N_1(0) = N_1^0,$$

$$dN_1/dt + \lambda_1 N_1 = 0.$$

With the integrating factor $e^{\lambda_1 t}$:

$$(dN_1/dt)\, e^{\lambda_1 t} + \lambda_1 N_1 e^{\lambda_1 t} = 0.$$

The left hand side is now the derivative of $N_1 e^{\lambda_1 t}$:

$$D(N_1\, e^{\lambda_1 t}) = 0.$$

Integrating both sides gives

$$N_1\, e^{\lambda_1 t} = C. \tag{A1}$$

By the initial condition, when $t = 0$, $N_1 = N_1^0$. Solving for the constant of integration C,

$$C = N_1^0\, e^{\lambda_1 (0)} = N_1^0.$$

Substituting back into Eq. A1 and rearranging yields

$$N_1\, e^{\lambda_1 t} = N_1^0$$

or

$$N_1 = N_1^0\, e^{-\lambda_1 t}. \tag{4}$$

Equation 2.

$$dN_2/dt = \lambda_1 N_1 - \lambda_2 N_2, \quad N_2(0) = N_2^0.$$

Substituting in the expression derived for N_1 yields

$$dN_2/dt = \lambda_1 N_1^0\, e^{-\lambda_1 t} - \lambda_2 N_2.$$

By rearranging,

$$dN_2/dt + \lambda_2 N_2 = \lambda_1 N_1^0\, e^{-\lambda_1 t}.$$

Multiplying by the integrating factor $e^{\lambda_2 t}$ gives

$$(dN_2/dt)\, e^{\lambda_2 t} + \lambda_2 N_2\, e^{\lambda_2 t} = \lambda_1 N_1^0\, e^{-\lambda_1 t}\, e^{\lambda_2 t}.$$

The left hand side is now the derivative of $N_2 e^{\lambda_2 t}$:

$$D(N_2\, e^{\lambda_2 t}) = \lambda_1 N_1^0\, e^{t(\lambda_2 - \lambda_1)}.$$

Integrating both sides and rearranging yields

$$N_2\, e^{\lambda_2 t} = \lambda_1 N_1^0 \int^t e^{x(\lambda_2 - \lambda_1)}\, dx + C,$$

$$N_2\, e^{\lambda_2 t} = \lambda_1 N_1^0 \left(\frac{e^{t(\lambda_2 - \lambda_1)}}{\lambda_2 - \lambda_1}\right) + C,$$

$$N_2 = \lambda_1 N_1^0 \left(\frac{e^{t(\lambda_2 - \lambda_1)}}{\lambda_2 - \lambda_1}\right) e^{-\lambda_2 t} + C\, e^{-\lambda_2 t}. \tag{A2}$$

By the initial condition, when $t = 0$, $N_2 = N_2^0$. Solving for C,

$$N_2^0 = \lambda_1 N_1^0 \left(\frac{1}{\lambda_2 - \lambda_1}\right)(1) + C(1),$$

$$N_2^0 = N_1^0 \left(\frac{\lambda_1}{\lambda_2 - \lambda_1}\right) + C,$$

$$C = N_2^0 - N_1^0 \left(\frac{\lambda_1}{\lambda_2 - \lambda_1}\right).$$

By substituting the value of C back into Eq A2 and rearranging,

$$N_2 = \lambda_1 N_1^0 \left(\frac{e^{t(\lambda_2-\lambda_1)}}{\lambda_2 - \lambda_1}\right) e^{-\lambda_2 t} + \left[N_2^0 - N_1^0 \left(\frac{\lambda_1}{\lambda_2 - \lambda_1}\right)\right] e^{-\lambda_2 t},$$

$$N_2 = \frac{\lambda_1}{\lambda_2 - \lambda_1} N_1^0 e^{-\lambda_1 t} + N_2^0 e^{-\lambda_2 t} - \frac{\lambda_1}{\lambda_2 - \lambda_1} N_1^0 e^{-\lambda_2 t},$$

$$N_2 = \frac{\lambda_1}{\lambda_2 - \lambda_1} N_1^0 (e^{-\lambda_1 t} - e^{-\lambda_2 t}) + N_2^0 e^{-\lambda_2 t}. \quad (5)$$

Equation 3.

$$dN_3/dt = \lambda_2 N_2, \quad N_3(0) = N_3^0.$$

Substituting in the expression for N_2 gives

$$\frac{dN_3}{dt} = \lambda_2 \left[\frac{\lambda_1}{\lambda_2 - \lambda_1} N_1^0 (e^{-\lambda_1 t} - e^{-\lambda_2 t}) + N_2^0 e^{-\lambda_2 t}\right].$$

This equation is solved by separating variables:

$$dN_3 = \frac{\lambda_1 \lambda_2}{\lambda_2 - \lambda_1} N_1^0 (e^{-\lambda_1 t} - e^{-\lambda_2 t})\, dt + \lambda_2 N_2^0 e^{-\lambda_2 t}\, dt.$$

Integrating both sides yields

$$N_3 = \frac{\lambda_1 \lambda_2}{\lambda_2 - \lambda_1} N_1^0 \int^t (e^{-\lambda_1 x} - e^{-\lambda_2 x})\, dx + \lambda_2 N_2^0 \int^t e^{-\lambda_2 x}\, dx + C,$$

$$N_3 = \frac{\lambda_1 \lambda_2}{\lambda_2 - \lambda_1} N_1^0 \left(\frac{e^{-\lambda_2 t}}{\lambda_2} - \frac{e^{-\lambda_1 t}}{\lambda_1}\right) - \lambda_2 N_2^0 \left(\frac{e^{-\lambda_2 t}}{\lambda_2}\right) + C. \quad (A3)$$

By the initial conditions, when $t = 0$, $N_3 = N_3^0$. Solving for C,

$$N_3^0 = \frac{\lambda_1 \lambda_2}{\lambda_2 - \lambda_1} N_1^0 \left(\frac{1}{\lambda_2} - \frac{1}{\lambda_1}\right) - N_2^0 (1) + C,$$

$$C = N_1^0 + N_2^0 + N_3^0.$$

Substituting the value for C back into Eq. A3 and rearranging yields

$$N_3 = \frac{\lambda_1 \lambda_2}{\lambda_2 - \lambda_1} N_1^0 \left(\frac{e^{-\lambda_2 t}}{\lambda_2} - \frac{e^{-\lambda_1 t}}{\lambda_1}\right) - \lambda_2 N_2^0 \left(\frac{e^{-\lambda_2 t}}{\lambda_2}\right) + (N_1^0 + N_2^0 + N_3^0),$$

$$N_3 = \frac{\lambda_1}{\lambda_2 - \lambda_1} N_1^0 e^{-\lambda_2 t} - \frac{\lambda_2}{\lambda_2 - \lambda_1} N_1^0 e^{-\lambda_1 t} - N_2^0 e^{-\lambda_2 t} + (N_1^0 + N_2^0 + N_3^0),$$

$$N_3 = N_1^0 \left(1 + \frac{\lambda_1}{\lambda_2 - \lambda_1} e^{-\lambda_2 t} - \frac{\lambda_2}{\lambda_2 - \lambda_1} e^{-\lambda_1 t}\right) + N_2^0 (1 - e^{-\lambda_2 t}) + N_3^0. \quad (6)$$