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Analysis of potassium spectra with low counting statistics using trapezoidal and library least-squares methods

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Abstract

Potassium spectra with low counting statistics were measured with a NaI detector from a water phantom, simulating a brain, and were analyzed for error propagation in determination of K employing either the Trapezoidal Method or the Library Least-Squares method. We demonstrate, using measured and synthetic spectra, that a smaller error is obtained in the analysis of potassium when using the Library Least-Squares method.

Keywords

Potassium; Library least-squares; Trapezoidal method; Low counting statistics; Brain; In vivo

1. Background

Potassium (K) is an essential element for sustaining life and is dominantly located as an intracellular cation in every living system. The amount of K in the extracellular fluid is negligible and there is none in the bone and other noncellular sites. Total body potassium in humans was demonstrated to be an excellent marker for the body cell mass and for intracellular water (Moore et al., 1963). Significant variations in total body potassium can be observed in some chronic diseases, e.g., diabetes, or in abnormal conditions, such as obesity, anorexia nervosa, or muscle atrophy due to immobilization.

Multiple sclerosis is a major acquired neurologic disease of young adults. Its earliest detectable manifestations are edema and inflammation in the brain and central nervous system. At present, the proportion of intracellular to extracellular edema in these patients is entirely unknown and determining this ratio might provide new insights into the multiple sclerosis disease processes. In patients with cytotoxic edema, increased intracellular water content might result in a concurrent increase in the level of K in the brain. Measuring K in the brain alone may reveal these changes assuming that the cell membrane potential, which is controlled by the intracellular K according to the Ernst equation, remains constant and is not affected by alternative or competing processes in the brain (Pierson, 2000). Thus, our working hypothesis assumes that there are no changes in the dynamic K equilibrium in the brain. Tourtellotte and Parker reported increases of 3–5% in the water content in the brain of multiple sclerosis patients (Tourtellotte and Parker, 1968).

To validate the hypothesis that edema of the brain in MS subjects occurs intracellularly, we proposed to estimate the changes in brain intracellular water content by measuring the natural radioactivity of ^{40}K with half-life of about 1.28×10^9 years that is in equilibrium with the stable ^{39}K and ^{41}K isotopes at 0.0012% abundance (Bin Samat et al., 1997). The normal

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adult brain, of a 70 kg man, has a volume of about 1400 mL and contains on average 4.2 gK out of the total body K of 140 g (Snyder et al., 1975). This low amount of K in the brain results in measured spectra that are weak with very poor counting statistics. K analysis is further exacerbated by the ever-present K photopeak due to the natural K background (Miller and Remenchik, 1963). To improve the assessment of K in the brain, we evaluated two approaches for spectral analysis, namely, the trapezoidal method (TM), and the library least-squares (LLS) method (Bevington, 1969; Wielopolski and Cohn, 1984; Gardner et al., 1978; Arinc, 1976).

2. Analysis

Spectral analysis consists of identifying the photo-peaks present in a spectrum and calculating their areas, which are proportional to the elemental concentrations in the sample. This proportionality is maintained as long as there are no spectral distortions due to nonlinear effects, e.g., pile-up during data acquisition, as is the case when spectra with low counting statistics are acquired. The conventional and simplest approach to evaluating the net number of counts (N) in an isolated photopeak, is the trapezoidal method. In this method the background under the photopeak is assumed to be linear. The net number of counts is expressed as the total number of counts (T) less the number of counts in the background (B) that are determined by the area of the trapezoid below the photopeak. This is simply expressed as

$$N = T - B, \quad (1)$$

and the error associated with the net counts is given by,

$$\sigma_N^2 = \sigma_T^2 + \sigma_B^2 \quad (2)$$

However, the error in the net number of counts in Eq. (1) is larger than that given by Eq. (2) because of the omnipresent K in the background that needs to be accounted for resulting in augmenting the error propagation in converting the measured K signal into the K signal from the brain.

An alternative to the TM method is the LLS method which relies on the fundamental assumption that an unknown measured spectrum, b_i , is a linear superposition of the contributions from all the elements present in a sample. Analytically, the sample's elements are expressed as reference standards, or library standards, a_{ij} , which contribute a fraction x_j to the measured spectrum. Thus, the LLS concept can be written as

$$b_i = \sum_{j=1}^m x_j a_{ij} + E_i \quad i = 1, 2, \dots, n, \quad (3)$$

where i is the channel number from 1 to n , m is the number of elements present in the sample, and E_i is the random error between the model and the measured spectrum in channel i . The objective of Eq. (3) is to find a set of x_j values that would minimize the error term E . Summing the squares of the error terms to avoid positive and negative values, and equating the first derivatives of the error term with regard to the x_j 's to zero accomplishes this. Very often, the error term is replaced with a Chi-square term and minimizing the χ^2 from which the x_j values are derived minimizes the error. Thus

$$\chi^2 = \sum_{i=1}^n \frac{E_i^2}{(n-m)\sigma_i^2}, \quad (4)$$

where σ_i is the standard deviation of E_i and the set of equations to be solved is

$$\frac{\partial(\chi^2)}{\partial x_j} = 0 \quad j = 1 \text{ to } m. \quad (5)$$

To minimize the error propagation in the calculated x_j values, the library standards a_{ij} are acquired with very high statistics allowing in the error matrix to discard their contributions to error propagation (Bevington, 1969; Wielopolski and Cohn, 1984; Gardner et al., 1978; Arinc, 1976).

3. Methods

3.1. Measurements

The preliminary measuring system consisted of a single standard 3" × 3" NaI detector with nuclear spectroscopy electronics and a multichannel analyzer (MCA). The detector was encased in a 2" thick Pb shielding and the ^{40}K spectra were derived from water phantoms with an approximate volume of 1400 ml. The water phantoms were filled with KCl solutions with concentrations between 0 and 10 gK and were placed adjacent to the front of the detector. In addition, variations in the Compton distribution due to the volumetric source were investigated using a point source consisting of 9.1 gK enriched with 5.2% ^{40}K encapsulated in a 4 cm³ molybdenum glass vial.

Due to the very low natural activity of ^{40}K in the human body, we envisioned that a measurement in a patient would take about 1 h. Therefore, we used 1 h for phantom measurements and subsequent analysis and simulations. However, the library reference spectra, background (Bckg) and 10 gK, were acquired for 18 h to obtain good statistics. The pure K reference library was derived using high statistics measurements in which the tail of the background spectrum, the part of the spectrum above the K peak, was least-squares fitted to the tail of the 10 gK spectrum. This fitted background then was subtracted in its entirety from the 10 gK spectrum, resulting in a pure source K library spectrum. The resulting Bckg and K library spectra, shown in Fig. 1, served as shape references for spectral deconvolution, as well as for quantitative analysis using the LLS method. Since normal statistics were imposed on the derived library spectra no correlation was observed in the residual spectra following analysis of the synthetically created spectra. Although here we discuss the use of two library spectra, application of the LLS method using thirty-four standard library spectra to analyze a complex X-ray spectrum from a tungsten standard has been successfully implemented (Wielopolski, 1981). There are additional approaches to spectral peak analysis that have not been included in the present work, for example a collection of numerical recipes is given in Press et al. (1986). Gamma-ray spectroscopy with particular reference to computer techniques is given in Quittner (1972).

3.2. Simulations

To demonstrate various aspects of the LLS method for analyzing the spectra, we employed simulated spectra, instead of measured ones, and scaled them down to be the equivalent of a 1 h measurement. The synthetic spectra were generated by adjusting the measured library standards by a desired factor x_j , then varying the number of counts in each channel according to a random normally distributed variation with a standard deviation corresponding to the square root of the number of counts in each channel (Arinc, 1976). Thus the two, background and K, library spectra were combined into one synthetic spectrum that was subsequently analyzed by the TM and the LLS methods. These simulated synthetic spectra with 0.1, 0.5, 1, 5, and 10 g K, shown in Fig. 2 with 0.5 g K omitted for clarity, were analyzed for error propagation. The effect of variations in the background counts for the same K concentration, the effect on error propagation of a missing library spectrum in the LLS analysis, and that of a shift in the spectrum also were investigated.

4. Results

The synthetic spectra for various K concentrations were analyzed first using the TM method, Eqs. (1) and (2). Thus, the calculated net K counts in the K peak had to be adjusted for the contribution of the K present in the background, $N_{KB} = 147 \pm 13\%$, thereby increasing error propagation. To convert the net number of counts in the K peak to g K, a calibration was drawn, $y = 59.56 x (\pm 0.26) + 0.89 (\pm 1.6)$, based on phantom measurements at 0, 4, and 10 g K. Table 1 summarizes the results of the TM analysis of the synthetic spectra. At concentrations equal to or greater than 1 g K, the errors varied from 8% to 57%. The total error in the net K counts is due to the error in the total counts, σ_T , the error in the background counts, σ_B , and also the error in the K determination from the background, σ_{KB} . The minimum detection limit (MDL) defined as $3\sqrt{B}$, using the TM method was 0.6 g K/h.

The same synthetic spectra were subsequently analyzed using the LLS method that employed two standard libraries; one for the background and one for K. Table 2 shows the fitted intensities, x_j , and the errors. The fitted values were converted to g K by multiplying them by 180 (18 h and 10 g K). The reduced χ^2 values, indicative of the goodness of fit, remained close to 1.0 for all cases. By evaluating the ratios between the calculated concentrations and the nominal values we then compared the methods; for all K concentrations, the error in the ratios was consistently smaller for the LLS method (Table 3).

The effect of increased background conditions on the spectral analysis and error propagation was investigated using 1 h 1, 5, and 10 g K synthetic spectra with a two- and ten-fold increased background. The spectra from 10 g K are shown in Fig. 3, and the results of the analysis using both the LLS and the TM methods are summarized in Tables 4 and 5. For all K concentrations, the LLS method yielded propagation errors that were consistently smaller than those resulting from the TM method; however, neither method satisfactorily resolved the spectrum for 1 g K with the ten-fold increased background. Nevertheless, the uncertainty of the LLS method was better, 16% error or less, for the 5 and 10 g K concentrations with the ten-fold increased background.

The positive attributes of the LLS method are that it offers the possibility to analyze the residual spectra and to perform iterative gain and zero shifts corrections in the measured spectra, where a residual spectrum is defined as the difference between the measured spectrum and the fitted library standards. When the fit is good, the residual spectrum in units of standard deviations (SD) will be randomly distributed between ± 3 to 4 SD, and the reduced χ^2 should approach a value of one. However, if one of the libraries is missing or there are any spectral distortions that cause the measured spectrum to differ from the linear superposition of the standard libraries, the residual spectrum will manifest a structure that is not randomly distributed; then, it should be further inspected. For example, Fig. 4 shows a residual spectrum of 5 g K in which the K library standard was omitted. The results of analysis of the previous spectra with a missing K standard are summarized in Table 6; note the changes in the χ^2 values.

Gain and zero shifts may occur due to electronic instabilities or other variations in the system. In these cases, the distorted spectrum can be iteratively corrected until the reduced χ^2 are minimized. Fig. 5 shows a spectrum that was acquired with a two-fold reduced gain relative to the libraries, and then was subsequently adjusted using gain and zero shift corrections. The correction is based on the fact that the total number of photons arriving at the detector is independent of the detection system and the associated electronics set-up. This can be expressed as an integral equating the areas under the curves before and after the gain and zero shifts

$$\int_a^b F(E) dE = \int_a^{b'} F'(E') dE' \quad (6)$$

where the standard spectrum is denoted by $F'(E')$, the shifted spectrum as $F(E)$, and E is the incident photon energy. Eq. (6) has to be expressed in terms of the measured pulse height instead of incident photon energy. Using Eq. (6) and substituting energy E and E' with the energy calibration lines for each spectrum (standard spectra of $E' = k'x' + A$, and shifted spectra of $E = kx + B$), the newly calculated spectrum f in channel i is given in terms of the measured spectrum f' as

$$f(i) = \left\{ f' \left[\left((i - B) / \beta \right) + A \right] \right\} / \beta, \quad (7)$$

where f is in counts per unit energy, and β is the ratio of the calibration line slopes. Although offset 'A' might be equal to offset 'B' or both might be 0 for zero intercept, in either case Eq. (7) remains the same.

The final corrected spectrum is shown together with an original spectrum in Fig. 5.

5. Discussion

The advantage of using the LLS method rather than the TM method is that the entire spectral information is used instead of the photopeak alone; this advantage is apparent from Tables 1–3. At the detection level of 1 g K, the LLS method gives greater accuracy in K determination, and lessens the error propagation. This benefit also is apparent when the K peak remains constant and there is an increase in the background; in the TM method the error increases faster than when using LLS. This situation is very relevant when considering an open system in a clinical set-up; the reduced shielding will increase the contribution from the background. Because of the compact configuration of the detector and subject's head position no large variations in the geometry are expected. Therefore, the Compton component in the library spectra that were acquired under similar conditions as that of the patient head will remain invariant. At present we did not identify any structure in the residual spectra that would indicate Compton variations.

Any spectral distortions due to instabilities in the system, in particular when multiple detectors are used, as is planned, will manifest themselves as a structure in the residual spectrum as shown in Fig. 4 when the analysis did not include a standard library. The resulting increase in the χ^2 value is shown in Table 6. At lower concentrations, this distortion is negligible.

In summary, despite the simplicity of the K spectra there are clear advantages in using the LLS method for potassium analysis as compared to the TM method. The advantage of the LLS method is even more pronounced when using a multiple detector system in which single detector fluctuations can be observed.

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Fig 1.
The background and K library spectra derived from 18 h measurements.

Fig 2.
1 h synthetic spectra for various K concentrations.

Fig 3.
Synthetic spectra of 10 g K with two- and 10-fold background library.

Fig 4.
Relative residuals from the analysis of a 5 g K synthetic spectrum lacking the K library.

Fig 5. Shifted and corrected 0 g K spectra for 1 h using gain shift correction. Background spectrum converted from 18 h to 1 h is shown for comparison.

Table 1
1 h Synthetic spectra analyzed using the TM method

Total g K in the synthetic spectra	K net counts±error (%) ^a	TM calculated g K±error (%)
10	641±8	10.7±8
5	338±13	5.6±13
1	69±57	1.1±57
0.5	~1±3926	~0±3926
0.1	~1±3834	~0±3834

^aRelative error calculated according to $\sigma_N^2 = (\sigma_T^2 + \sigma_B^2 + \sigma_{KB}^2)100 / N$.

Table 2

1 h Synthetic spectra analyzed using the LLS method with background and K standard libraries

Total g K in a synthetic spectrum	Standard x_j	Nominal x_j value	LLS calculated x_j value $\pm$ error %	Potassium (g) $\pm$ error %	Reduced χ^2
10	x_{Bckg}	0.0560	0.0550 ± 1^a	—	0.93
	x_{K}	0.0560	0.0530 ± 4	9.6 ± 4	
5	x_{Bckg}	0.0560	0.0560 ± 1	—	0.87
	x_{K}	0.0280	0.0260 ± 6	4.8 ± 6	
1	x_{Bckg}	0.0560	0.0560 ± 1	—	0.89
	x_{K}	0.0056	0.0056 ± 24	1.0 ± 24	
0.5	x_{Bckg}	0.0560	0.0550 ± 1	—	1.04
	x_{K}	0.0028	0.0011 ± 126	0.2 ± 126	
0.1	x_{Bckg}	0.0560	0.0550 ± 1	—	1.49
	x_{K}	0.00056	-0.0011 ± 141	-0.2 ± 141	

^aRelative error obtained from the least-squares fitting.

Table 3

Comparison of the ratios of the calculated to actual intensities for LLS and TM analysis methods

Total g K in a synthetic Spectrum	Standard x_j	LLS ratio of calculated/nominal $\pm$ error (%)	TM ratio of calculated/nominal $\pm$ error (%)
10	x_{Bckg}	0.99 $\pm$ 1	—
	x_{K}	0.96 $\pm$ 4	1.07 $\pm$ 8
5	x_{Bckg}	1.00 $\pm$ 1	—
	x_{K}	0.95 $\pm$ 6	1.13 $\pm$ 13
1	x_{Bckg}	1.00 $\pm$ 1	—
	x_{K}	1.01 $\pm$ 24	1.14 $\pm$ 57
0.5	x_{Bckg}	0.99 $\pm$ 1	—
	x_{K}	0.38 $\pm$ 126	-0.70 $\pm$ 3926
0.1	x_{Bckg}	0.98 $\pm$ 1	—
	x_{K}	-1.98 $\pm$ 141	-2.5 $\pm$ 3834

Table 4

Fitted background component from LLS analysis of 1, 5, and 10 g K/h synthesized with two- and 10-fold increased background

Background	Nominal g K	LLS	
		Nominal	Fitted $x_{\text{Bkg}} \pm \text{error} (\%)$
Normal	10	0.056	0.055±1.0
Two-fold		0.11	0.11±1.0
10-fold		0.56	0.55±0.3
Normal	5	0.056	0.056±1.0
Two-fold		0.11	0.11±1.0
10-fold		0.56	0.56±0.3
Normal	1	0.056	0.056±1.0
Two-fold		0.11	0.11±1.0
10-fold		0.56	0.56±0.3

Table 5

LLS and TM analysis of 1, 5, and 10 g K/h synthesized with two- and 10-fold increase in the background

Background	Nominal g K	LLS		TM	
		Fitted $x_K \pm \text{error}$ (%)	Calculated g K $\pm \text{error}$ (%)	Net K counts $\pm \text{error}$ (%)	Calculated g K $\pm \text{error}$ (%)
Normal	10	0.0530 $\pm$ 4	9.6 $\pm$ 4	641 $\pm$ 8	10.9 $\pm$ 8
Two-fold		0.0540 $\pm$ 4	9.7 $\pm$ 4	647 $\pm$ 10 ^a	11.0 $\pm$ 10
10-fold		0.0580 $\pm$ 8	10.4 $\pm$ 8	663 $\pm$ 19 ^b	11.3 $\pm$ 19
Normal	5	0.0260 $\pm$ 6	4.8 $\pm$ 6	337 $\pm$ 13	5.7 $\pm$ 13
Two-fold		0.0260 $\pm$ 9	4.6 $\pm$ 9	296 $\pm$ 20 ^c	5.0 $\pm$ 20
10-fold		0.0250 $\pm$ 16	4.6 $\pm$ 16	338 $\pm$ 36 ^d	5.8 $\pm$ 36
Normal	1	0.0056 $\pm$ 24	1.0 $\pm$ 24	69 $\pm$ 66	1.2 $\pm$ 66
Two-fold		0.0021 $\pm$ 91	0.4 $\pm$ 91	58 $\pm$ 94 ^e	1.0 $\pm$ 94
10-fold		-0.0016 $\pm$ 274	-0.3 $\pm$ 274	48 $\pm$ 254 ^f	0.8 $\pm$ 254

^a $N_{KBckg}=350 \pm 11\%$,^b $N_{KBckg}=1653 \pm 5\%$,^c $N_{KBckg}=274 \pm 14\%$,^d $N_{KBckg}=1488 \pm 6\%$,^e $N_{KBckg}=285 \pm 14\%$,^f $N_{KBckg}=1510 \pm 6\%$.

Table 6
LLS analysis on synthetic spectra with single (Bckg) library

Total g K in the synthetic spectra	Actual	Calculated±error (%)	Reduced χ^2	LLS ratio of calculated/actual
10	0.056	0.065±1.4	3.64	1.17
5	0.056	0.061±1.0	1.76	1.09
1	0.056	0.057±0.79	0.95	1.02
0.5	0.056	0.05±0.84	1.04	0.99
0.1	0.056	0.054±1.0	1.48	0.98