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Some aspects of measuring levels of potassium in the brain

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Abstract

The general aim of this work is to measure brain potassium (K) levels as a marker of intracellular water content and to test the hypothesis of whether edema in multiple sclerosis (MS) is associated with increased intracellular brain water. For that purpose, a system to measure K in brain is being developed. Our specific aim is to assess the potential contribution to the K photopeak from cranial K located outside the brain. For this, a simplified spherical phantom to represent the brain, a square box to represent the cranium, and a K point source to assess the contributions due to K outside the brain were used. It is estimated that only about 1–2% of the K photopeak might be attributable to K outside the brain.

Keywords

Potassium; Brain; In vivo; Multiple sclerosis; Edema

Introduction

Multiple sclerosis (MS) is a major acquired neurologic disease of young adults and involves CNS edema and inflammation as the earliest detectable changes within the brain. Recent studies suggest that MS brain regions with the highest water content are at an increased risk for future MS lesion development [1]. Although CNS edema is known to occur in MS and reflects new disease activity, the proportion of intracellular to extracellular edema is entirely unknown. The determination of this ratio would provide new insight into the MS disease processes. Brain parenchyma has three obvious spaces: a vascular space (blood vessels), an interstitial space, and an intracellular space. About 80% by weight of the normal brain is water, of which only about 20% is extracellular. The most abundant aqueous cations in the brain are sodium and potassium, which are distributed asymmetrically across the cell membrane; sodium is excluded from the intracellular spaces, whereas potassium (K) is concentrated. When cerebral edema occurs, it is very difficult to assess the proportions of extracellular (vasogenic) and intracellular (cytotoxic) edema. It is hypothesized that, in the case of intracellular edema, increased intracellular water content should result in a corresponding increase in the brain K in order to maintain cell membrane potential. The total brain volume can be determined using MRI; however, since K is found within the cell, a normalized change in K signal intensity might be indicative of an increase in intracellular water, thus indicating cytotoxic edema. This working hypothesis assumes that there are no changes in the dynamic K equilibrium in the brain.

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Since conventional neuroimaging methods cannot assess intracellular water, an approach used in whole body composition studies [2,3] was adapted for this purpose. In this method changes in the total body potassium (TBK) were very successfully related to the whole body cell mass (BCM). Furthermore, K, being about 97% intracellular, is recognized as the best estimate of BCM [3]. In contrast, the determination of the serum K levels in blood samples has been shown to be an unreliable index of the changes in the TBK concentration [4].

In this short report, we present the initial estimate of the contribution of the intracranial K located outside the brain to the measured K photopeak.

Methods

The approach to measure K is based on the measurement of the natural radioactive ^{40}K , which because of its long half-life of 1.28×10^9 years is in equilibrium at a 0.012% level with the stable isotopes of K [5]. Furthermore, a person of standard 70-kg mass contains about 140 g of K in the entire body, of which the brain contains about 4.2 g and 3.7 g is located in the cerebrum [6]. Thus, measurement of the 1.46 MeV gamma ray from ^{40}K provides the direct measure of the amount of K in the inspected volume. The branching ratio of the 1.46 MeV gamma ray is 10.7% per disintegration. A K spectrum measured with a 3"×3" NaI detector from a brain water phantom is shown in Fig. 1.

The contribution of the K located outside the brain was assessed using a spherical water phantom (WP) 14 cm in diameter with a volume of 1437 cc, which is similar to that of a human brain, 1,400 cc. A second WP 24 cm in diameter and volume of 7,238 cc was used to simulate larger distances from the brain. Two WPs were filled with distilled water and one small WP was filled with a KCl solution containing 10 g K. A K point source was placed at various points on the circumferences of the WP and measurements were taken in air and with WP in place. In addition, using a K point source, measurements were taken inside a large water bath placed adjacent to the detector.

Results

Initially a calibration line was determined using small WP with various K concentrations. The resulting sensitivity and the minimum detection limit (MDL), defined as three standard deviations of the background, for the current system and 1-h measurement are 60 counts/gK per hour and 0.6 gK, respectively. The projected values for a clinical system using four detectors, two 3"×3" and two 3"×5", are 600 counts/gK per hour and 0.2 gK, respectively.

The ratio, 0.49, in the net K counts from a point source placed behind a small WP to that from the same place without a WP was in a close agreement with the calculated attenuation of 0.48, using a water linear attenuation coefficient of 0.0574cm^2 per gram at 1.5 MeV.

The total K content in the cranium from the skin, muscle, and the skeleton, excluding the brain, is about 1.9 g. It was also determined that a point source with the same activity as a WP filled with 10 g KCl solution and placed at the back of small WP filled with distilled water yields only 23% of the counts. However, such a high concentration of K in one point is highly unrealistic. Since 1.9 g K is estimated to be in a total mass of 1420 g, diluting by a factor of 100 shows the contribution to the K photopeak outside of the brain to yield less than 1%.

Discussion

Measurement of K in the brain may offer new insights into the pathophysiology of MS. Since K is found almost entirely (97%) within the cell, it provides the best estimate of the BCM, defined as $\text{BCM(g)} = 8.33 \times \text{TBK(mEq)}$ [3]. Although this relationship was derived for whole

body, isolating the brain K component (about 4 g out of the whole body of 140 g) provides information on brain cell mass. Combined with a measurement of intracranial water, this technique would allow one to test the hypothesis of whether cytotoxic edema (reflecting cell injury) is a component of the CNS injury process in MS patients. Variations in the K content in the white matter of MS patients have been documented postmortem [7].

From these and previous measurements, it is apparent that these experiments demonstrate the feasibility of measuring K levels typically encountered in an adult brain at the level of about 4 g. It was also pointed out that, with a clinical system using four detectors, there would be an improvement in the signal by about a factor of 10. Accounting for the six muscles in the head region above the quadratus labii muscle, the skin, and the bone, the total K outside the brain is about 1.9 g. Thus, a conservative estimate of the contribution of the outside K to the photopeak counts is about $(1.9/4.2/100 \times 0.23)$ or less than 1%. It is estimated that the use of additional detectors and a proper shielding design, the K contribution from outside the brain will be reduced to below 2% of the total K contribution.

It was pointed out that an improved system with more detectors, covering the head area would improve the detection efficiency resulting in an increased number of counts in the K photopeak. This improvement in the counting statistics can be further augmented by reducing the error propagation during the analysis using the Library Least-Squares method [8].

In short, this communication reports the feasibility of measuring K in brain and estimates the possible contribution to the photopeak from K outside the brain to be about 1% or less.

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References

1. Richert N, Ostuni J, Bash C, et al. Interferon β -1b and intravenous methylprednisolone enhance lesion recovery in relapsing remitting multiple sclerosis (RRMS) patients. *Proc Int Soc Magn Reson Med* 2000;233:79.
2. Wielopolski. Brookhaven National Laboratory Report-52630. 2000. Workshop on body composition in basic and clinical research and the emerging technologies.
3. Pierson, RN, Jr. Quality of the body cell mass, body composition in the third millennium. Springer; New York: 2000.
4. Miller CE, Remenchik AP. Problems involved in accurately measuring the K content of the human body. *Ann NY Acad Sci* 1963;110:175. [PubMed: 14062381]
5. Bin Samat S, Green S, Beddoe AH. The activity of one gram of potassium. *Phys Med Biol* 1997;42:407–413. [PubMed: 9044422]
6. Snyder, WS.; Cook, MJ.; Nasset, ES., et al. Report of the Task Group on Reference Man, ICRP 23. Pergamon; Oxford, UK: 1975.
7. Tourtellotte, WW.; Parker, JA. Some spaces and barriers in postmortem multiple sclerosis. In: Lajtha, A.; Ford, DH., editors. *Brain barrier systems*. Elsevier; Amsterdam: 1968. p. 493-525.
8. Wielopolski L, Cohn SH. Application of the library least squares analysis to whole body counter spectra derived from an array of detectors. *Med Phys* 1984;11:528–533. [PubMed: 6482847]

Fig 1.
Typical potassium spectrum with a single K peak. Potassium spectrum basically contains one photopeak; other peaks belong to the background