**ACCELERATOR BASED RADIATION MEASUREMENTS OF IN VIVO TBN**

**ACCELERATOR BASED RADIATION MEASUREMENTS OF *IN VIVO* TOTAL BODY NITROGEN**

By

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A Thesis

Submitted to the School of Graduate Studies

in Partial Fulfillment of the Requirements

for the Degree of Philosophy

McMaster University

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## (Medical Physics) Hamilton, Ontario

## TITLE: Accelerator Based Radiation Measurements of *In Vivo* Total

## Body Nitrogen

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## NUMBER OF PAGES: xiii, 140

## 

*He did not understand that if he waited and listened and observed, another idea of some kind would probably occur to him some day, and that the development of this would in its turn suggest still further ones. He did not yet know that the very worst way of getting hold of ideas is to go hunting expressly after them. The way to get them is to study something of which one is fond, and to note down whatever crosses one's mind in reference to it, either during study or relaxation, in a little note-book kept always in the waistcoat pocket. Ernest has come to know all about this now, but it took him a long time to find it out, for this is not the kind of thing that is taught at schools and universities.*

Butler, Samuel (2000-02-01). The Way of All Flesh (Chapter XLVI). Public Domain Books. Kindle Edition.

##### **Abstract**

Accurate measurement of protein in the human body is essential to the management and maintenance of health in individuals when correct balance cannot be achieved without intervention. It can be measured in a number of ways but the least invasive method is by neutron activation analysis, in this case using the 14N(n,γ)15N reaction and measuring the prompt γ-rays in the region of 9 – 11 MeV, the single most prominent γ-ray being at 10.83 MeV. During the course of investigations, using phantoms containing different ratios of nitrogen to water, flux suppression was observed as the nitrogen content increased. This was attributed primarily to the 14N(n,p)14C reaction, which cannot be measured directly by the methods used in these investigations. The suppression of flux at 2.6% nitrogen content, typical of human body composition content, was found to be 7.0+/-1.0%, which should be taken into account when using hydrogen as an internal standard to quantify nitrogen. The optimum proton beam energy and current from the KN accelerator used to liberate neutrons from a thick lithium target was determined to be 2.5 MeV and 0.3 μA respectively. Over the course of the experiments, an overall improvement in precision was achieved by the addition of a fast pile-up rejector and pulsing of the proton beam. High energy γ-rays were observed, which can interfere with the counts in the nitrogen region via Compton scattering. The origin of these γ-rays was identified and then reduced by the effective use of beam pulsing. Investigations to achieve this reduction included shielding, filtering, and optimization of the pulsing parameters using a purpose-built multi-scalar unit, specifically designed to identify the timing of the arrival of the thermal neutrons.

##### **Acknowledgements**

I am deeply grateful to my supervisor, Dr David R Chettle for his encouragement in my pursuit of a PhD and his faith in my capabilities. His insight and knowledge have been invaluable to me during my studies at McMaster University. I would also like to express my thanks to my committee members, in particular Dr William V Prestwich for his encouragement and friendship and to Dr Soo-Hyun Byun for his patience and guidance.

I would like to thank the staff of the McMaster University Tandem Accelerator Laboratory, Scott McMaster, Jason Falladown and Justin Bennett and the professional help I received from Kenrick Chin.

My thanks also go to my friends and colleagues in the Medical Physics and Applied Radiation Department, particularly Jovica Atanackovic, Witold Matysiak, Elstan DeSouza, Phanisree Timmaraju, Sahar Darvish Molla, Hedieh Mohseni, Brandi-Lee McDonald, Andrei Hanu, Chitra Bhatia and Nancy Brand for their reassurances, encouragement and advice.

Finally, my deepest love and gratitude go to my partner, Jason Falladown and my daughter Charlotte for their love, support, patience and encouragement during the ups and downs of my pursuits.**Table of Contents**

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Chapter 1

##### **Nitrogen, Protein and Body Composition**

***1.1 Introduction***

Nitrogen makes up 78% of the earth’s atmosphere by volume. It is the fourth most abundant of the six essential elements that make up 98% of the total elements in the human body, after oxygen, carbon and hydrogen. It comprises about 3% of total body composition by mass in healthy individuals and 99% of it is found in protein, being an essential building block of DNA in nucleic and amino acids[1,2]. The nitrogen content of protein in all mammals is nearly constant at 16% mass[3]. Therefore, a direct assessment of protein content can be determined from an accurate measurement of nitrogen. Plants can synthesize nitrogen from the air and soil but animals must take in nitrogen from foods such as meat, fish, eggs, legumes, nuts and dairy products[4]. A healthy adult male requires approximately 105 mg of nitrogen/kg/day of body weight. Any excess is excreted from the body in the form of ammonia in urea and is thus returned to the environment as part of the nitrogen cycle.[5] Nitrogen deficiency symptoms include hair loss, muscle weakness, delayed wound healing, and brittle hair.[6] By accurately measuring nitrogen, and therefore protein, in the human body, information on body composition can be assessed, and assist in correcting imbalances so as to aid in the treatment of, for example, malnutrition in babies and cancer patients, diabetes, and patients undergoing surgery.

There is evidence that low protein levels in the human body can directly affect the survival rate of patients undergoing major surgery. In their 1989 paper, Kotler et al[7] reported that death occurs when body cell mass (protein plus intracellular water) is < 54% of normal and when body weight is 66% or less of ideal. The body cell mass (BCM) measurement here is more accurate than total body weight, indicating that the level of protein is the critical indicator. However, as BCM is a measure of both protein and intracellular water (ICW) (see Figure 1.1), fluctuations in it can affect the estimate of protein. The study was conducted on AIDS patients using total body potassium (TBK) as an indicator of BCM and by using anthropometric measurements for body fat content. Potassium makes up about 0.2% of the human body, which translates to about 120g in a 60kg adult[8] and is the main intracellular ion in human cells. By working with sodium, the main extracellular ion, potassium generates electrical potentials in cells, which is especially important in transmitting signals in nervous tissue. As one naturally occurring radioisotope of potassium is radioactive (40K), whole body counters can be used to measure the amount of potassium present and thus determine BCM. Anthropometric measurements usually include height and weight and can also include skinfold thickness measurements using calipers, bicep muscle measurements, hip to waist ratios in women and chest to abdomen ratios in men, which are a few of several examples. Anthropometric measurements are commonly used as they are quick and painless. However, they are subject to large errors, mainly due to non-uniformity in measurement techniques. The findings of studies such as the one carried out by Kotler are particularly relevant for patients whose body composition is already compromised, for example, cancer patients who need surgery to remove a tumour yet already have an imbalance in their body composition due to the effects of the cancer. To stress this point further, another example can be found in work carried out by Selberg et al[9] on liver transplant patients. They concluded that patients with a BCM of < 35% of body weight before liver transplantation had a lower likelihood of surviving for 5 years than those with BCM >35%. Malnutrition is a common finding in liver-diseased patients, and it is known that the malnutrition is of a protein-calorie nature. By monitoring nitrogen levels and assessing protein content, steps can be taken to redress the balance of body composition before a patient undergoes surgery.

In order to measure the different components that make up the human body, it would be logical to separate them into different compartments and attempt to isolate and measure the components of each compartment. This approach has evolved over time so a review of this evolution would assist in understanding current approaches.

***1.2 Body Composition***

***Two-compartment model***

The first and most simple model is the two-compartment model for body composition: fat mass (FM) and fat-free mass (FFM), developed by Behnke in 1942[10]. The disadvantage of having a simple model is that assumptions have to be made, which lead to errors. However, having a model that is too complex, also leads to errors due to the fact that each individual measurement will have associated errors that will be cumulative and propagate throughout the components. The two-compartment model assumes that water, protein and mineral proportions that make up FFM are constant and that their densities are fixed. Everything else that makes up body weight is assumed to be fat. This model does not take into account the changes that occur throughout the human life cycle, such as aging and pregnancy, nor changes that can happen such as weight loss in the obese, or the diseased. The principle for the two-compartment model was based on the Archimedes’ displacement model to assess body volume by hydrostatic weighing namely,

(1)

where *Vo* is the volume of water being displaced and *Vi* is the volume of the body being submerged.

The modern method for obtaining body density (Bd) by hydrostatic weighing involves fully submerging the subject in a tank of water and weighing them on a scale situated in the tank. This method is sensitive to the amount of air in the subject’s lung so it is imperative that the subject exhale as much as possible as they submerge; in addition, the residual lung volume is measured, usually using a closed-circuit oxygen dilution technique. Obviously, this method is not ideal for everyone; not only adults who are averse to being fully submerged in water, but it is also impractical for children, particularly babies.

There is now another method available to measure body volume, using air. The method of air displacement plethysmography works on the principle of measuring a volume of air in a chamber and calculating the displacement caused by the insertion of an object (ie a person). The commercially available BOD POD® is being widely used for university research, in sports clinics, military clinics and for health and wellness groups worldwide[11] . It is being touted as the “gold standard” of body composition measurement methods, mainly due to its ease of use and availability. Dempster and Aitkens[12] first reported on the introduction of the BOD POD® in their 1995 paper. Like other Bd measurement methods, the BOD POD® uses the Siri equation (see Equation 2) to estimate percentage body fat (%BF), which is independent of height and weight and therefore useful when monitoring changes in body fat, yet making it susceptible to the same errors of FM that all other Bd measurement methods have, in that it will inherently overestimate FM in population groups with lower bone mineral content (BMC).

However, extensive studies have shown that both hydrostatic weighing (HW) and air plethysmography (AP) can either underestimate or overestimate changes in %BF and FFM, particularly on an individual basis (as opposed to a study with an overall group change) and there is also disagreement between results from HW and AP when done in comparison. In particular, Collins et al[13] found that AP underestimated BF when compared to HW and dual-energy x-ray absorptiometry (DXA). DXA was used to determine %BF and BMC. Essentially, two x-rays of different energies are used, therefore having different absorption coefficients. The body fat will absorb one x-ray energy more than the other and the difference between the two can be determined to estimate the amount of body fat present, in relation to the surrounding tissue. By also determining BMC, a more accurate estimate of %BF can be made. Using a 4-component model (AP, HW, DXA, TBW) proved more accurate for adult subjects than for children, probably due to the larger ratio of empty chamber volume to subject volume. Fields et al[14] concluded that the BOD POD® underestimated BF when compared with the 4-compartment model (4C model explained later). Results were in agreement with HW but HW was not compared directly with the 4C model. Indications were that the 4C model is more accurate than BOD POD® or HW, both of which used the 2C model. In 2007, Mahon et al conducted a comparison study on the measurement of body composition changes with weight loss in postmenopausal women[15]. They found a bias in their results, which they attributed to the small population of subjects (27), using a single laboratory, and conducting each test in the same order for all subjects. However, they concluded that AP, when used in the 4C model, overestimated %BF and underestimated changes in FFM when compared to HW used in the 4C model. They recommended the use of regression equations to relate 4CAP to 4CHW in individual subjects (as opposed to group results).

As hinted at earlier, the fundamental problem with HW and AP inaccuracy is that neither method can possibly detect changes in bone mineral content, just by the nature of the method employed. This becomes particularly important when assessing body fat for older subjects. As the 2C model is based on data from young, healthy adults, the generally accepted Siri equation[16], used for estimating body fat, will consistently result in an overestimation of %BF in older subjects. The equation is:

(2)

Generally, the accepted density of FM is assumed to be 0.9007 g/cm3 (anhydrous density) and FFM to be 1.1000 g/cm3 at 36oC, according to Brozek et al[17]. However, these assumptions are based on measurements from three male cadavers only. %BF is then calculated using either the Siri formula above, or the Brozek formula:

(3)

which is derived from assuming that the body mass is unity, consisting of FM+FFM and therefore relates to body density, ρ, as follows:

(4)

In the study carried out by Behnke[10], it was found that the specific gravity for individuals with excess body fat is lower than that for individuals of the same body weight with lower body fat. However, the assumption is that body composition should be the same for all individuals, particularly that of muscle mass, and does not take into account any differences in gender, for example. The study subjects were all healthy, fit males from the naval service between the ages of 20 and 49. The model also relies on ratios of chest to abdomen and does not give any insight into the protein or mineral components of the FFM compartment.

***Three-compartment models***

The three-compartment model varies from the two-compartment model with the addition of total body water (TBW). Again, there is an assumption as to water content of 73.72%[17]. One way to measure TBW is via isotopic dilution, namely 2H2O dilution. The general method involves taking a saliva sample first to determine background concentration of 2H2O as documented by Withers et al[18] . An amount of 2H2O is then ingested and an equilibrium saliva sample is taken several hours later. The isotopic ratio is determined using a mass spectrometer. FFM can then be determined by assuming that 72% of FFM is water in a normally hydrated subject and using the formula:

(5)

FM can then be calculated by subtraction and represented as a percentage of total body mass.

With the addition of TBW, formula (4) can now be expanded to include TBW and again, with the substitution of densities and percentages, a formula can be derived to calculate compartments from the direct measurements made. However, once again, this method will not detect non-standard bone mineral content and will, therefore over- or underestimate %BF.

Another method for measuring TBW is bioelectrical impedance analysis (BIA), as reported by Kyle et al[19]. BIA is not a standardized technique. The basic principle is that the resistance, R, of a length of conductive material that is homogeneous and has a uniform cross-sectional area (ideally a cylinder) is proportional to the length, L, and inversely proportional to the cross-sectional area, A. Translating this to body measurements, where obviously the human body is not a uniform cylinder, can be done by using an empirical relationship between the impedance (L2/R) and the volume of water in the body. As the water in the human body contains electrolytes, it is conductive. By utilizing the relationship and the conductive properties of the water, a formula can be derived to measure TBW, correcting for real geometry by the use of a coefficient. Obviously, there are many areas where geometry must be matched, which give rise to large uncertainties in measurement. There are variations within the BIA measurement technique, single-frequency (SF-BIA), typically using a current of 800 μA and a frequency of 50 kHz, multi-frequency (MF-BIA) using a range from 0 to 500 kHz, bioelectrical spectroscopy (BIS), which uses mathematical modeling and mixture equations to generate relationships between resistance and body fluid compartments, and Segmental BIA. For both SF-BIA and MF-BIA, electrodes are attached to the hand and foot, on the same side of the body or hand-to-hand and Segmental BIA uses multiple sites. Localized BIA measures individual body segments, as the name implies, and vector BIA, which will not be discussed here. SF-BIA cannot directly measure TBW but rather a weighted sum of ICW and ECW, which means that although FFM can be determined, changes in ICW resulting from non-normal hydration cannot be detected with this method. MF-BIA, on the other hand, is more accurate for distinguishing ICW from ECW, which makes it useful for detecting edema or malnutrition, for example. As reported by Kyle et al, SF-BIA and BIS significantly overestimated TBW in healthy, normally hydrated subjects. MF-BIA was more suitable for measurements in obese subjects and those with renal failure. However, the method was not suitable for accurate measurements of BCM, as overestimation of ICW leads to underestimation of protein and vice versa. Also, in overhydrated subjects, there may be a significantly raised proportion of ECW. With this method, BCM and therefore protein cannot be measured directly, only estimated, based on a number of assumptions. For BIA to be as accurate as possible in predicting FFM, subjects must be normally hydrated and the empirically derived equations must be relevant to their age, gender and ethnicity. Electrolyte imbalance can affect readings and especially distort the ratios of ICW to ECW.

***Four-compartment model***

Similar to the expansion to a three-compartment model, the four-compartment model includes measurements for bone mineral density, taken using DXA. Figure 1.1 shows the components of the model. As was mentioned in the introduction, protein content is still determined by indirect methods, even in the 4C model.



*Figure 1.1 Diagram showing FFM, TBW, ICW, ECW and BCM and their relationship with assumed compartments (ie visceral protein)[19]*

DXA measurements usually report (BMC) as ashed bone. Therefore, a multiplication factor is used to convert the ashed bone to bone mineral mass (BMM). This conversion yields a bone density of 0.9935 g/cm3. However, difficulties surrounding DXA measurements for assessing FM and FFM arise from the fact that the attenuation coefficients for both are very similar, making it difficult to distinguish them. Another problem is that pixels must be differentiated for BM, FM and FFM; when they are adjacent, this makes for underestimation or overestimation of each compartment.

As can be seen throughout the additions to multiple compartment models, there are many assumptions made concerning absolute densities and it is clear that if any of the assumptions are erroneous, this will lead to an inaccurate measurement of body compartments. To test this understanding, Withers et al[18] conducted a study in the late 1990s tocompare two- three- and four- compartment models, using both active and sedentary men and women. They concluded that there was no significant difference between the three- and four-compartment models in terms of accuracy of measurements. They did find significant differences between each group however.

Baumgartner et al[20] conducted a study in 1991 on body composition in 98 elderly people, to determine if there were any significant differences in measurements using the 2C and 4C models. Subjects ranged in age from 65 to 94 years. %BF was estimated using anthropometric measurements and whole-body bioelectric resistance. Volume was derived from stature2/resistance and the %BF from resistance x weight/stature2. Db was determined by HW, TBW by tritium dilution and total-body bone ash (TBBA) was used to estimate BMM, using dual-photon absorptiometry (DPA), which is the forerunner to DXA and very similar in method. Protein is not measured directly and is derived from an equation for the 4C model:

(6)

where *F* is fat, *ρ* is density, M is aqueous body mass, *B* is bone mineral, and *P* is protein and glycerine. Note that the letters next to density in the denominator are all subscripts to denote the specific density.

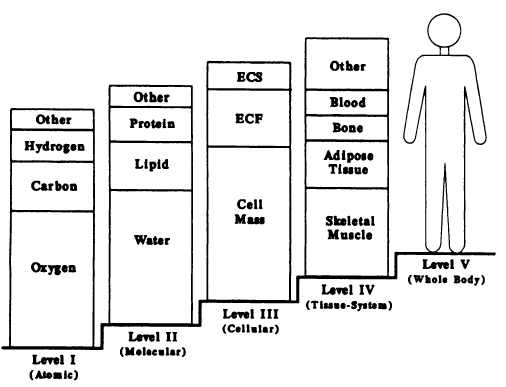
The overall emphasis of the study appears to be on estimates of %BF. The results of the study strongly point to ensuring that prediction equations when using bioelectric impedance and anthropometry in an elderly population are validated for body composition estimates, with a multi-compartment model. Baumgartner et al found that, when comparing the 2C model with the 4C model, the estimated differences were due to variation in hydration of FFM. They also found that, while testing the validity of using the Siri equation for the 2C model, it slightly overestimated %BF by 1-2% and underestimated FFM by 1-2 kg in their study population. The BMC fraction did not seem to affect either model, except for comparisons between sexes. However, they did concede that this may not be true for a population with significant differences in BMC; their population sample was small (n=98) and of the same ethnic origin.

***Five-level model***

Body mass can be assessed on five different levels that can interconnect and sometimes overlap[21]. The five levels are atomic, molecular, cellular, tissue-system, and whole body. The molecular level is the foundation on which the higher levels are built and also links to other areas, such as biochemistry. Nitrogen specifically belongs in the atomic level but nitrogen/protein is also included in the molecular level. Figure 1.2 illustrates the five levels and their major components.

From Figure 1.2, it can be seen that nitrogen falls under “Other” in the atomic level (Level I), along with calcium and phosphorus, and the six elements together constitute > 98% of body weight with the remaining 44 elements contributing the remaining < 2%. Total body weight is the sum of all atomic elements that comprise the atomic level.

In the molecular level (Level II) nitrogen comprises the “protein” compartment of the level. According to Wang et al, all compounds containing nitrogen are termed as protein, with the stoichiometric representation being C100H159N26O32S0.7 where the average molecular weight is 2257.4 and the density is 1.34g/cm3 at 37oC. Protein determination from nitrogen measurements is based on two assumptions: that all of body nitrogen is in protein, as mentioned above, and that 16% of total body protein is nitrogen.



*Figure 1.2 The five levels of human body composition[21]*

Body composition equations are presently constructed by estimating an unknown component from measurable components. For example, at the molecular level, body weight and the five major chemical components can be calculated from the six elements in the atomic level (carbon, nitrogen, sodium, chlorine and calcium) by in vivo neutron activation analysis. By studying body composition in healthy individuals a steady-state can be established whereby this steady-state exists during a specified time period, when there is no change between the various components. This can then be used as a benchmark for studying changes during growth, aging, disease and weight changes due to malnutrition or obesity, for example.

As previously mentioned, there are no practical methods to measure fat mass (FM) in vivo so it must be assessed by indirect methods. On the atomic level, this is done by measuring total body potassium and using the equation:

(7)

where Bwt = body weight and TBK = total body potassium. However, the dividing factor was derived from steady-state proportions in healthy individuals of sample populations. Another way to measure FM is to measure body density and derive fat from FFM by assuming the densities of 0.9007g/cm3 for FM and 1.100g/cm3 for FFM, as previously discussed.

Ryde et al[22] conducted a study of healthy subjects using a five-compartment (5C) model of body composition, consisting of protein, water, mineral, glycogen and fat. The only measurements made in their study of 31 healthy adults, ranging in age from 23.5 to 72 years and weight from 44.5 to 104.2 kg, were those of protein and water. Mineral and glycogen content were estimated as fixed fractions of FFM, and BF was calculated as body mass minus the sum of the other four components. Protein was measured by neutron activation analysis (NAA) of nitrogen x 6.25; water was measured by tritiated water analysis. Body fat estimates were compared to skinfold thickness values and calculations from tritiated water space. Agreement between different validation methods was low. However, if mineral and glycogen had been measured, instead of estimated, agreement may have been achieved. Glycogen plays the role of the secondary long-term energy storage mechanism in the body (fat being the primary storage), and is stored mainly in the liver and muscles. It can be measured by nuclear magnetic resonance of 13C *in vivo*. According to Heymsfield et al[23] the glycogen-protein ratio is assumed to be constant, at 0.044 and Beddoe (1984)[42] assumed that 0.91% of FFM is glycogen. Nitrogen measurements were tested for accuracy, by comparison with values from two prediction equations and returned high correlation coefficients, indicating that NAA of nitrogen is an accurate way to measure protein.

Body composition as a whole can be thought of as three inter-connecting areas: measuring individual components in the five different levels and determining components that cannot be measured directly; determining proportions of components in their steady-state; and studying how biological factors impact the proportions of body composition.

More and more complex models of body composition are continually being developed, such as 6- and 11- compartment chemical and elemental models. This chapter is not intended to be an exhaustive guide to the field of body composition, but rather an insight into important contributions to the field and the role that nitrogen plays.

In conclusion, the molecular level is ideally suited for incorporating nitrogen measurements by complementing them with measurements of TBW by deuterium or tritium labeled water, ECW by bromide or BIA, cellular protein by TBK of BCM, total lipid by MRI or CT and BMM by DXA. By directly measuring nitrogen *in vivo* using neutron activation analysis (NAA), an accurate measurement can be made which, when combined with reliable measurements of the other compartments, will lead to an accurate determination of body composition that is reproducible, which is especially important for dynamic studies following changes over time. With recent advancements in electronic equipment, better precision should be achievable, making NAA of *in vivo* nitrogen an even more attractive alternative to other methods.

Chapter 2

##### **Methods of Measuring Nitrogen**

***2.1 Nitrogen Balance***

One of the earliest methods used to measure nitrogen in vivo was that of nitrogen balance, also known as metabolic balance. In other words, *nitrogen in = nitrogen out* and there is a state of equilibrium. However, if *nitrogen in < nitrogen* *out* then problems arise, as discussed in Chapter 1. There are more unusual instances when the desired outcome is that *nitrogen in > nitrogen* *out* but these circumstances are in the extreme, such as protein levels required by body builders and high performance athletes who may need as much as 2.0-2.6 g/kg/day, compared to the recommended intake of 0.8 g/kg/day[24]. The general approach of determining if there is a net amount of nitrogen flowing into or out of the body seems logical, if a value for how much nitrogen is going into the body can be compared to how much nitrogen is coming out of the body, then the imbalance, if there is one, can be corrected. The nitrogen must first be isolated from other substances before the protein content can be determined. There are two accepted methods for this.

The Dumas method is based on a method developed by Jean-Baptiste Dumas in 1826, to measure protein by nitrogen content in chemical substances. The method involves heating the substance in a flask containing oxygen, thus releasing carbon dioxide, water and nitrogen. The nitrogen content is then converted to protein by using conversion factors for the particular amino acid sequence of the protein being measured.

The second method is called the Kjeldahl method, after Johan Kjeldahl who developed it in 1883. This method involves digesting the substance with sulphuric acid by heating, thus liberating any nitrogen as ammonium sulphate. After further chemical decomposition and distillation, ammonia is produced and, after back-titration, the amount of nitrogen present can be determined and thus the protein content, again by the use of conversion factors. The Kjeldahl method is the internationally accepted method for measuring protein in food. However, it cannot distinguish between true protein content and content falsified by the addition of nitrogen via, for example, melamine, which is rich in nitrogen[25]. The Dumas method is beginning to rival the Kjeldahl method as it is much faster and does not involve toxic chemicals.

One or other of the described methods for determining protein content is used when conducting nitrogen balance studies. According to Tomé and Bos[26], there are many difficulties surrounding these types of studies for determining accurate net content of body protein. The sampling methods are unpleasant, as they include the collection and analysis of faeces and urine, which also makes this a slow method. Determining true net protein balance is compounded by immeasurable losses due to, for example, sweating, hair loss and nail growth loss. Other uncertainties surround the precise timing of conducting measurements as the protein content of the human body fluctuates throughout the day, depending on whether the subject has just eaten, for example. The use of 15N-labelled proteins can help in determining the cycle that nitrogen takes through the body but it does not help to reveal the true protein content of the body.

Forbes[27] investigated errors in the metabolic balance method in 1973. It had already been known for quite some time that errors in collection of samples tend to lead to an overestimation of protein intake and an underestimation of output and rarely the reverse situation. Forbes pointed out that an additional error was apparent. The assumption was that the body will reach equilibrium after a change in protein intake. From reviewing the work of others, Forbes found that the level of protein increase in the diet (or decrease, depending on whether the new level was an increase or a decrease) followed an exponential curve and never actually reached a zero balance, if the new level was continued. Using an increase of protein as an example, a positive balance would be highest immediately after the start of the intake. This positive balance can be misinterpreted as malnutrition as the assumption is that if the body is protein-depleted, then an increase in the protein amount will immediately lead to a large positive increase in the nitrogen balance, if the subject is malnourished. This situation also appears to be true for well-nourished subjects. The reverse also appears to be true, that protein deficiency will show as a large negative balance initially, and gradually, logarithmically approach a zero balance (see Figure 2.1 for illustration).



*Figure 2.1 Plot of TBN and daily N increasing (left hand side) and*

*decreasing (right hand side)[29]*

Cheatham et al[28] reported on a study that they conducted in 2007 regarding additional protein losses from patients undergoing open abdominal surgery. Measurement of protein in hospitals is routinely performed by the nitrogen balance method. Protein catabolism (the breakdown of proteins into amino acids) occurs in the critically ill and loss of protein also occurs as a consequence of open abdominal surgery. Although nitrogen balance is performed both before and after surgery, it does not include a specific measurement or estimation of abdominal nitrogen losses in patients who undergo open abdominal surgery. This underestimation can lead to inadequate nutritional support post-operatively, causing delayed wound healing at best and death at worst. Recommendations are that an additional 2g of nitrogen per litre of abdominal fluid should be added to the diet as this will be lost as a consequence of open abdominal surgery. The study compared “open” and “closed” groups, matching age, weight and other factors so that the only major difference between the groups was whether or not they underwent open abdominal surgery. One difference noted during recovery was that feeding had to be interrupted on a number of the “open” group to perform further surgery, thus delaying increased protein delivery. The traditional nitrogen balance formula significantly overestimated actual nitrogen balance in the “open” group, indicating that protein requirements were lower than those actually needed by the patient.

***2.2 Neutron Activation Analysis***

Nitrogen balance studies were the traditional approach to assessing protein in body composition. A paradigm shift occurred with the introduction of neutron activation analysis as a direct, in vivo method to measure elements in the human body.

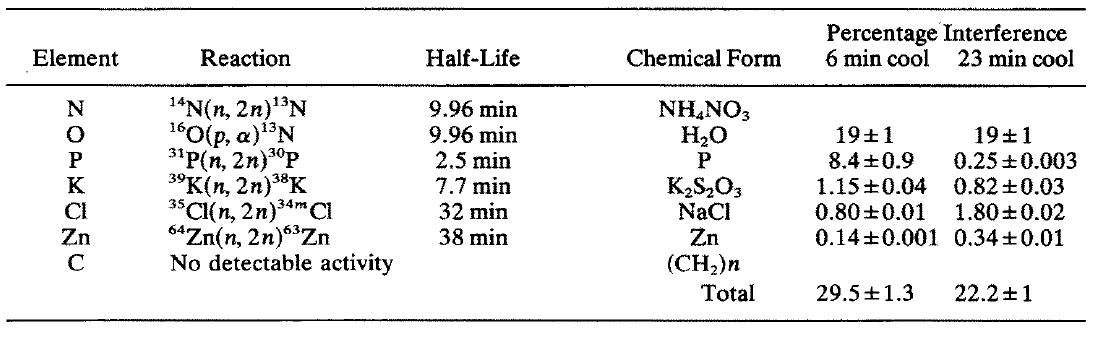
Neutron activation was discovered in 1936 by George de Hevesy and his assistant, Hilde Levi when they realized that certain rare earth elements became radioactive after being exposed to a source of neutrons. This led to Hevesy inventing the method of neutron activation analysis (NAA) as a method to identify and quantify trace elements[29]. However, it was not until the 1950s that neutron activation analysis was applied to investigate the nature of archaeological materials without destroying the original artefact.

The basic physics of neutron activation is as follows. Upon capturing a neutron, an atom is transformed to another nuclear isotope of the same chemical element. The new atom can either be stable or radioactive but it will have an excess of energy that must be released. This can occur either promptly (capture state of a stable atom) or be delayed (radioactive). The energy can be in the form of gamma rays (γ), protons (p), neutrons (n) or alpha (α) particles (He atoms). If the activation results in a prompt release, for example 14N(n,γ)15N where the prominent detectable γ-ray at 10.83 MeV is prompt (lifetime ~10-15s)[43] , then the γ-ray energy must be measured during irradiation. If the activation results in delayed release, the resulting radioactive isotope decays to another isotope, for example 23Na(n,γ)24Na. The new isotope 24Na has a half-life of 14.96 hours, where it decays to 24Mg by emission of a β- and two γ-rays.

In 1964, Anderson et al[30] successfully measured calcium, chlorine and sodium in vivo, by using NAA on two subjects, already knowing that it was possible to induce radioactivity in the human body, following studies in the 1950s on accidental exposure to neutrons. They suggested that it might be possible to measure nitrogen by using the 0.511 MeV positron emission that they observed in their spectrum and concluded that it originated from 13N.

***2.2.1 14N(n,2n)13N reaction***

In 1977, Leach et al[31] investigated interferences and spatial distribution while measuring the 14N(n,2n)13N reaction. They used 14 MeV neutrons produced by a neutron generator, as the reaction has a threshold of 11.3 MeV. As previously mentioned, the only emission to the decay of 13N is from the 0.511 MeV positron decay to 13C, which has a half-life of 9.96 m. As positron decay is not unique, other elements present can also emit γ-rays of 0.511 MeV, often at a lower threshold than for the nitrogen reaction. The high energy neutrons give rise to a secondary proton fluence, which can itself induce reactions such as the 16O(p,α)13N reaction, which causes interference. Table 2.1, taken from the paper, shows the percentage interferences measured when attempting to quantify nitrogen from the 14N(n, 2n)13N reaction.



*Table 2.1 Percentage interferences from competing reactions in a 14 MeV neutron field*[31]

From Table 2.1, it can be seen that the interference from 16O is the largest contributor. By varying nitrogen concentration in a phantom, it was deduced that the counts followed a linear relationship but had a non-zero intercept at zero nitrogen concentration, implying that the counts were from the 0.511 MeV photons from the 16O(p, α)13N reaction. Any corrections to separate interferences (for example, delayed counting to allow shorter-lived elements to decay, curve stripping based on known half-lives) resulted in loss of precision and up to 87% of counts from the 14N(n, 2n)13N reaction. In attempting to estimate oxygen content in the body in order to correct for it, further errors were introduced, due to the whole nature of using estimations.

While investigating spatial sensitivity (ie depth within the phantom), the counts dropped off very rapidly, indicating that only surface nitrogen was being measured. The skin of the human body is nitrogen-rich when compared to the rest of the body (4.7% and 2.6% respectively) so the measurement would not be representative of total body nitrogen. Introducing a medium to scatter neutrons into the body in an attempt to produce a more uniform flux would not improve the measurement because the neutrons would fall below the 11.3 MeV threshold required for the 14N(n, 2n)13N reaction.

Spinks[32] responded to Leach’s study by reporting on measurements of nitrogen using the same method with the neutrons being produced in a cyclotron. He agreed with Leach’s observations on the interferences and added to them, noting that electron-positron pairs (0.511 MeV) would also be produced by 49Ca and 24Na, both elements of which are present in the human body. He reported that the contribution from these interferences amounted to 5-10% of total counts and that the counts from 13N only constituted 50% of the total counts. His conclusion was that it was not possible to measure nitrogen accurately using this method.

The only advantage to measuring nitrogen via the 14N(n,2n)13N reaction is that the method produces a delayed reaction, which eliminates the complication of shielding the counting equipment from neutrons when counting prompt γ-ray reactions. However, this advantage seems to be far outweighed by the disadvantages of using the method.

***2.2.2 14N(γ,n)13N reaction***

In 1977, Brune et al[33] reported measuring the 14N(γ,n)13N reaction using a betratron to produce high energy electrons. They delivered 16 MeV Bremsstrahlung energy to a 150g sample of beef. The dose delivered was 5 rad (0.05 Gy), which is 25 times greater than the dose administered in a chest x-ray. Clearly, this is not a very safe way to obtain nitrogen measurements in living subjects.

***2.2.3 Gamma-ray nuclear resonance absorption of 14N***

Vartsky et al[34] successfully measured nitrogen using the gamma-ray nuclear resonance absorption technique (γ-NRA) and reported on it in 2000. The technique of γ-NRA was originally developed for detecting explosives and is described thus. 14N absorbs a γ-ray of specific energy (in this case, 9.17 MeV) and is raised to an excited state. The specific energy causes the excited state to exhibit resonance behaviour and a peak value of 2.6 barns. 93% of the time, the excited nucleus will decay to 13C by emission of a proton of 1.5 MeV and 4.6% of the time, it will decay directly to the ground state, emitting a γ-ray of 9.17 MeV. The source of the 9.17 MeV γ-rays comes from the same reaction just described, but obviously in reverse:

p + 13C → 14N\*→14N + γ (9.17 MeV) (4.6%)

→13C + p (93%)

This reaction requires a source of protons on a 13C target and the experiments were carried out here at McMaster University using the 3MV KN Van de Graaff accelerator.

The resonance of the 9.17 MeV γ-ray in the excited state of the 14N can be detected by means of a special resonant-response detector using liquid scintillation techniques. Only a narrow sampling angle is needed, as the 9.17 MeV γ-rays produced from the reaction on the target are emitted when the 14N isin flight and are therefore angle dependent (and Doppler-shifted). The γ-rays that can be resonantly absorbed are emitted at the same specific polar angle (80.6o, which is known as the resonant angle) so therefore, only that angle from the beam need be sampled.

The transmission profile can be imaged and also quantified as a percentage of nitrogen. Results were in good agreement with phantom content, including measurements where a layer of fat equivalent had been added. The dose was determined by Monte Carlo and by experiment and was deemed to be 17.6 μGy/h for a 100μA beam current at a distance of 55 cm. This is significantly less than that recorded by Brune et al[33]. Clearly, this technique needs to be developed further and should be the focus of future work for those interested in this field of study.

***2.2.4 Measurements using the 14N(n,γ)15N reaction***

The prompt gamma 14N(n,γ)15N reaction is by far the most popular for researchers to investigate, even given the additional task of shielding detectors, as they need to be present in the neutron field to simultaneously collect data while the reaction is taking place.

In 1972, Biggin et al[35] wrote a short article in *Nature New Biology* describing a new technique for measuring nitrogen in living patients during the period of irradiation. In vivo activation analysis had already been used for total body calcium, sodium and chlorine, as demonstrated by Anderson[30]. The article documented the first attempts at measuring nitrogen in vivo using the 14N(n,γ)15N reaction. The source of neutrons was 10 MeV protons produced in a cyclotron using a 7Li target via the 7Li(p,n)7Be reaction. The authors discuss the feasibility of the online measurement approach and describe their experiments using liquid phantoms to measure the characteristic 10.83 MeV γ-rays that decay from the capture state of 15N. About 15% of the excited nuclei decay directly to the ground state. Even though this is a low percentage, with a small cross-section (σ=80 mbarn), there are no other elements that would be present in the sample and activated by neutron capture that emit γ-rays anywhere near this energy level. The next nearest level is < 7MeV. However, as the NaI(Tl) detectors used for measurements needed to be large for the required sensitivity, and the fact that they were measuring in a neutron field, made them subject to high background interference, which caused problems with pulse pile-up. The detectors needed to be shielded from neutrons scattered from the phantom and were also placed outside of the collimated neutron ‘beam’ so as to be out of reach of the neutrons produced by the target. To further reduce unwanted signals, the cyclotron beam was pulsed and the collection was set up so that the unwanted interactions from fast neutrons would not be counted in the detectors. This means that most of the counts came from the γ-rays produced by thermal neutron captures in the phantom.

A dose of 0.1 rem is mentioned, for a 70 kg man, extrapolated from the 16,000 counts collected in the detectors. However, there is no mention of the length of time for irradiation, or the neutron energy resultant from 10 MeV protons on a 7Li target, which would be typically from 3.5 MeV to 8.5 MeV[36]. As the irradiation took place at 90o from the incident neutrons, their energy would be expected to fall towards the lower end of this range.

As mentioned earlier, although nitrogen could be detected, quantification was not possible and the group recognized the need for further investigation into counting rate variations due to differing body shapes and sizes, which cause non-uniform thermal flux, and the fact that the distribution of nitrogen is non-uniform.

In 1975, the same group from Birmingham, led by Ettinger[37] conducted further studies into the technique. They pointed out that a thermal neutron reaction, such as 14N(n, γ)15N, is more suitable for measuring total body nitrogen than a fast reaction, such as 14N(n,2n)13N, as it produces a more thermal neutron flux density in the body; they maintained that this must be produced by a fast neutron beam. Table 2.2 shows the migration lengths of fast neutrons of different energies as they thermalize in the soft tissue of the body. Migration length is defined as the root mean square distance between the point of entry and the capture point of the fast neutron.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Incident neutron energy | | | Migration length | |
| MeV |  |  | cm |  |
| 2 |  |  | 13.9 |  |
| 4 |  |  | 17.9 |  |
| 6 |  |  | 23.6 |  |
| 10 |  |  | 28.6 |  |
| 14 |  |  | 32.9 |  |
| 20 |  |  | 37.9 |  |

*Table 2.2 Migration lengths in soft tissue[37]*

It was noted that the body can be approximated to an 80 cm cylinder because the head, lower legs and feet only contribute 20% to the total nitrogen counts and increase the background by 40% due to scattering and poor moderation of the neutrons (very little soft tissue). The skeleton and internal organs do little to affect the overall thermal neutron flux, due to moderation and diffusion in the body as a whole. Water-based phantoms are a good approximation for human tissue, as the thermal neutron diffusion length is about 2.70 cm for soft tissue and about 2.88 cm for water. Also, the time taken for a neutron to thermalize in water is about 10 μs, when the initial energy of the neutron is a few MeV, which is not appreciably different for the time taken in soft tissue. To this end, a pulsed beam can be used effectively and a count started 10 μs after the beam has been turned off will ensure that the counts are coming from thermal neutron reactions. In short, optimization consisted of a 10 μs beam pulse, a 10 μs pause followed by a 136 μs count. This optimization was based on considerations for patient comfort and low dose (short irradiation time) and the need to reduce pulse pile-up (low beam intensity).

An alternative to measuring nitrogen via the 14N(n, γ)15N reaction using neutrons produced in a cyclotron, is to measure the same reaction with neutrons produced by a neutron source. The most common are the radioisotope (α,n) sources of Pu-Be and Am-Be, and 252Cf, produced by spontaneous fission. Although these sources are not mono-energetic (which is the advantage of using a cyclotron or accelerator with a thin target) they do have the advantage of being somewhat portable, relatively inexpensive when compared to a cyclotron or accelerator, and can be placed around the subject or phantom to achieve a more uniform neutron flux within the body or object.

Mernagh et al[38] used four collimated Pu-Be sources of 5 Ci (185 GBq) each, two above and two below the subject or phantom (y-axis). Two NaI(Tl) detectors placed on the x-axis, either side of the subject, needed to be heavily shielded from neutron capture by the iodine in the detector crystals and γ-rays from the source. Obviously, pulsing is not an option here but the combination of wax, lead and boron collimators served well to reduce the problem.

Using water-based phantoms, one containing nitrogen and one not, they were able to detect nitrogen from 10 minute irradiations and consistently reproduce the results to 1 SD of +/- 2.5%, consistent with statistical error. They went on successfully to detect nitrogen in three living subjects of different weights and heights, ranging from 48.5-86.4 kg and 159.5-183.0 cm respectively, using 10 minute irradiations for a dose of 50 mrem (0.05mGy). The resulting nitrogen counts reflected the difference in size of the three subjects, thus demonstrating the possibility of measuring nitrogen using neutron sources. If a method could be determined for extracting a quantitative measure of nitrogen from the data, for all methods of measuring nitrogen thus far, regardless of the neutron source, then this would become a powerful tool for the determination of protein in the body.

In 1979, Vartsky et al[39] described a method for determining the absolute value of nitrogen by using hydrogen data from the subject as an internal standard. This method had been demonstrated previously by the Birmingham group, using their cyclotron but will only be described in the context of this paper, for brevity. Vartsky used a single Pu-Be source of 85 Ci (3145 GBq) and similar shielding arrangements to Mernagh[38]. The group measured the 2.22 MeV γ-rays from hydrogen, emitted from the subject during irradiation following thermal neutron capture in the 1H(n, γ)D reaction. The neutron source was located under a motorized bed, permitting the subject to be moved through the neutron beam for a whole body scan. The source was collimated into a rectangular shape, allowing the full width of the subject to be scanned at once. The two NaI(Tl) detectors used for data collection were positioned above the subject, to measure γ-rays exiting the subject from the opposite side to irradiation entry. A method of fractional charge collection was employed[40] to handle the high count rates in the detectors and reduce pulse pile-up. The overall accuracy using this method of charge collection was improved by a factor of 1.7 over conventional (voltage) collection methods for nitrogen count collection.

Using hydrogen as an internal standard requires a uniform number of counts from the body per unit mass of the detected element, and the factors influencing this composite sensitivity are the neutron fluence, self-absorption of the escaping photons, and the subsequent detector efficiency of recording them. Upon investigation of counts in a phantom, it was observed that there was a build-up of slow neutrons initially, to a maximum at 4 cm and then a gradual tail-off through the phantom. A pre-moderator can eliminate build-up, and placement of the detectors on the opposite side of the body from the entrance of the neutrons, as mentioned earlier, can compensate for tail-off.

Tests were also carried out to determine if the presence of a subject in the neutron beam affected the background counts in the nitrogen region of interest, as the mere presence of an object can cause neutrons to scatter into the detectors. It was found that the thickness and shape of the subject do affect background levels but the shape of the background spectrum does not change. It was also found that the hydrogen background is not altered in the presence of a phantom, and contributes about 20% of the hydrogen peak. The nitrogen to hydrogen ratio (N/H) for different areas of the body had a coefficient of variance of +/- 3%, indicating that only thickness of the subject and not the overall shape needed to be taken into consideration when correcting for different geometries. Total body nitrogen was determined using the formula:

(1)

where k is a calibration constant, determined from phantom measurements, and TBH is determined from measurements of TBW, fat and weight (discussed in Chapter 1). The dose was determined to be 26 mrem (0.026 mGy) from 20 minutes of irradiation (10 minutes prone, 10 minutes supine). The determined nitrogen mass from measurements of 14 young, healthy volunteers was (2.7+/-0.2)% body weight and (3.38+/-0.15)% lean body mass, correlating highly with TBK measurements.

In 1984, the same group led by Vartsky[41], reported an improvement of the calibration for in vivo determination of nitrogen, necessitated by the requirement to be able to measure ‘non-normal’ subjects, for example obese or diseased subjects, which is where the highest demand for accurate measurements of body composition lies in the field of medicine. The improvement in the accuracy of the technique was applied to three different groups: normal, obese and cancer patients, still using hydrogen as an internal standard. The addition of information regarding subject thickness and width was introduced to the data analysis and improved the accuracy of the results. This improvement was tested on a much larger cohort than in the previous Vartsky study: 134 normal, 55 obese, and 29 cancer patients.

Total body nitrogen, hydrogen and fat can all be calculated simultaneously using this technique, coupled with measurements of body parameters. The group found that hydration is not fixed for non-normal subjects as was previously assumed, and set at 73% (see Chapter 1) but was different between the three groups in the study. The method of determining total body nitrogen but using body fat measured from weight proved more accurate for the obese subjects and cancer patients than previous methods.

Beddoe[42] took a similar approach to Vartsky for measuring nitrogen in the critically ill. One notable difference is that his group describes body habitus corrections, which are necessary to correct for the different attenuation coefficients of the 10.83 MeV γ-rays from nitrogen and the 2.22 MeV γ-rays from hydrogen in the body.

Baur et al[43] used a 27 mCi (1 GBq) 252Cf fission source as their source of neutrons and investigated total body nitrogen in children, with the emphasis on malnutrition. The set-up was similar to that of Mernagh[38] but with only one source (below the subject). From the results, there is very little difference to the other 14N(n,γ)15N results in that the technique is the same and, especially when using hydrogen as an internal standard and using body habitus corrections, the results are consistent between the groups, demonstrating reproducibility and robustness.

In 1993, Stamatelatos et al[44] used the same procedure for calibration as Vartsky[41] but, instead of using one ‘average’ sized phantom, they used three, to account for a range of body sizes. Preliminary tests were conducted using box phantoms and the group observed that width and thickness of the phantoms affected the N/H ratio, depending on the irradiation/detector geometry. Width was more strongly dependent when there was an “irradiation below/detector to the side” geometry and thickness was more strongly dependent in an “irradiation below/detector above” arrangement. To have both thickness and width dependence, the geometry arrangement used was an average of the “to the side/above” detector geometries ( ie 30o to the horizontal and 60o off-axis).

A second set of phantoms was used that was a distinct improvement over the box phantoms, as their shape was a more accurate representation of the human body. The phantoms are called bottle mannequin absorber phantoms (BOMAB) and are described in detail by Bush[45] who developed them in 1946. Figure 2.2 shows the phantom, with overlays for adding different materials. Using these phantoms produced N/H ratios that were more accurate as a ‘per section’ of the body approach could be used, which is more representative of human body measurements, such as those conducted by Vartsky[41]. Tests were conducted to determine the effect of a 5 cm layer of fat on the N/H ratio, by filling the overlays of the phantom with water, as the hydrogen content of water and fat are similar. The results showed a 50% reduction in the N/H count ratio. This occurs because the fat contains no nitrogen and also serves as a premoderator for the neutrons. This effect would lead to an underestimation of TBN in obese subjects if only width and thickness corrections are applied. A correction factor per section of an obese subject would need to be applied and would be based on thickness of adipose tissue, possibly measured using ultrasound for each subject.



*Figure 2.2 Diagram of BOMAB phantom and overlays[45]*

In 1998, the same group, led by Dilmanian[46] conducted a series of experiments to improve the TBN facility at Brookhaven, mainly guided by Monte Carlo simulations. Their goals were to decrease the background counts in the nitrogen region of interest (ROI) and to achieve uniform composite sensitivity for differing body sizes and shapes. They achieved this by improving shielding around the neutron source and detectors and by discovering the optimum angle for detector placement through computer simulations. The results in the paper serve to demonstrate that there is always room for improvement in the detection and quantification of nitrogen in the body and, with the continuing advances in electronic equipment and detectors, this improvement is set to continue.

Chapter 3

##### **Beam Optimization**

***3.1 Introduction***

Green[47] conducted studies into nitrogen detection using the McMaster Accelerator Laboratory (MAL) 238Pu-Be source as the subject of her Masters project. The current work is a continuation of Green’s work. After establishing continuity, by reproducing results obtained by Green with the 238Pu-Be source, investigation shifted to using the neutron source provided by the KN 3MV Van de Graaff accelerator, located in the MAL. During continuity investigations with the 238Pu-Be source, it was noted that there are a great number of peaks in the spectrum from the prompt γ-rays in Fe, as the structure of the box containing the source has a large Fe content. However, none of the activation peaks interfere with the nitrogen region of interest, at 9-11 MeV, the highest peak being ~9.30 MeV. A typical spectrum recorded using a HpGe detector and the 238Pu-Be source is shown as Figure 3.1, the nitrogen region of interest area has been enlarged and is shown as Figure 3.2. The prominent peaks in Figure 3.1 are all from activation of Fe, with the exception of the part-peak showing at 2.23 MeV, which is the full energy peak from the 1H(n,γ)2H reaction. The full peak is not shown in Figure 3.1 as the scale will not allow for prominent display of the other peaks. Suffice to say that the hydrogen peak channel contained over 70,000 counts. The phantom used in the acquisition of this spectrum was one prepared by Green and is presumed to contain 9% nitrogen. The phantom was placed between the source and the HpGe detector and counts were recorded for 2000 s.

*Figure 3.1 HpGe spectrum from 2.2-11.0 MeV recorded with a HpGe detector of 9% nitrogen phantom activated using the 238Pu-Be source*

The prominent peak in Figure 3.2 at 9.3 MeV is once again a result of activation of Fe in the construction materials of the source box containing the 238Pu-Be source. The smallest peaks at 9.8 MeV, 10.3 MeV and 10.8 MeV are the double escape peak, the single escape peak and the full energy peak respectively from the 14N(n,γ)15N reaction.

*Figure 3.2 Nitrogen Region of Interest from the full spectrum shown as Figure 3.1*

The main reasons for shifting investigations from the 238Pu-Be source to the KN accelerator is that (a) the neutron energy range can be varied, (b) the current can be varied which means that irradiation times can be optimized, and (c) the neutrons are mainly forward directed, making collimation easier, especially as patient measurements are the ultimate goal, whereby the desired direction of incoming neutrons would be vertical. This is because the patient would be most comfortable in a supine position. A HpGe detector was used for experiments with the 238Pu-Be. However, with the switch to using the accelerator as the source of neutrons, NaI(Tl) detectors became the detectors of choice. Although HpGe has a much better resolution than NaI(Tl), its efficiency is much lower at the energies required for the detection of nitrogen[48]. In order to gain the same counts as NaI(Tl) detectors, the dose to the patient would be far higher, either from having to count for much longer (low dose rate with prolonged time) or from having to increase the neutron flux (high dose rate with shorter time). Either way, the dose would be greater than that for NaI(Tl) detector use. Also, HpGe crystals are susceptible to neutron damage, even if the more resistant n-type detector is used, causing degradation in the resolution and a finite lifespan of the detector. A solution to the dose problem would be to use multiple HpGe detectors but this would make the setup very expensive and the problem of neutron damage would still be present. NaI(Tl) on the other hand suffers from activation by neutrons in the crystal but this is reversible with time (ie allowing the activation to decay over one or two days). Multiple NaI(Tl) detectors can be used, with advanced electronics, to improve resolution and recover more of the cascade γ-rays from the 14N(n,γ)15N reaction and will be mentioned further in Chapter 7.

The KN accelerator has an analyzing magnet which filters the protons through a 50o bend in the beam line to ensure that only protons of the same energy reach the target and, because this enables selection by charge-mass ratio, any deuterons are also removed. The target is constructed of lithium with a copper backing and coolant. Neutrons are produced via the 7Li(p,n)7Be reaction, which has a threshold of Ep=1.88 MeV, where Ep is the proton energy. Lee and Zhou[49] calculated the maximum neutron energy from the incident proton energy, which is shown in graphical form as Figure 3.3.

*Figure 3.3 Relationship between incident proton energy and maximum neutron energy for the 7Li(p,n)7Be reaction*

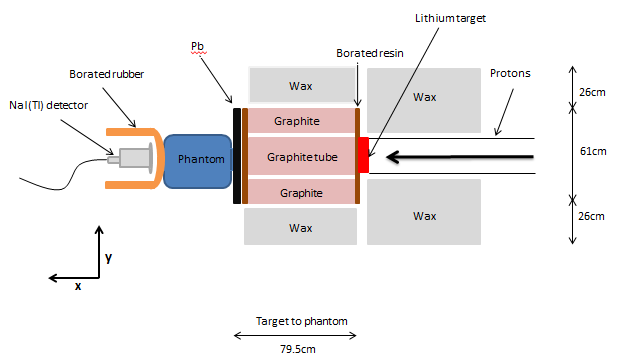
By using a phantom, not only as a substitute for a human body, but also as a neutron moderator, it should be possible to slow down the neutrons to thermal energies and detect the γ-rays from the reactions of interest on the far side of the phantom. This method was first demonstrated by Vartsky, Thomas and Prestwich[50] and labeled in their figure as “Symmetrised unilateral irradiation and counting procedure” whereby the patient was turned from supine to prone mid-way through the irradiation.

To determine the number of collisions that the neutrons will undergo in the phantom (moderator), the elastic scattering properties of the moderator should be considered. The parameter, ζ, which is the average logarithmic energy decrement per collision, is used in reactor theory for thermal reactors to determine the effectiveness of the moderator that will be used in the reactor design. The formula for this is , where Eo is the incoming neutron energy and E is the thermal neutron energy. Substituting Eo=786.7 keV, for the maximum neutron energy from an incident proton energy of 2.5 MeV, as shown in Figure 3.3, and a thermal neutron energy of E=0.025 eV, the number of collisions to thermalize the incoming neutron is 17.26/ζ. The logarithmic energy decrement, ζ for H2O is 0.927 m. Therefore, the average straight line distance travelled by a neutron after 17.26 collisions will be 0.05m, or 5 cm[51]. This implies that the majority of the neutrons are thermalized in the phantom in a forward-scattered direction, which means that the 14N(n,γ)15N reaction γ-rays should be detectable on the far side of the phantom, as the average distance travelled by a thermal neutron from formation to capture (the mean diffusion length) is 0.0276m, or 2.76 cm[52].

It was also necessary to determine the probable dose using different proton energies and currents. This will be described following the experimental set-up section where beam optimization, shielding and collimation are described.

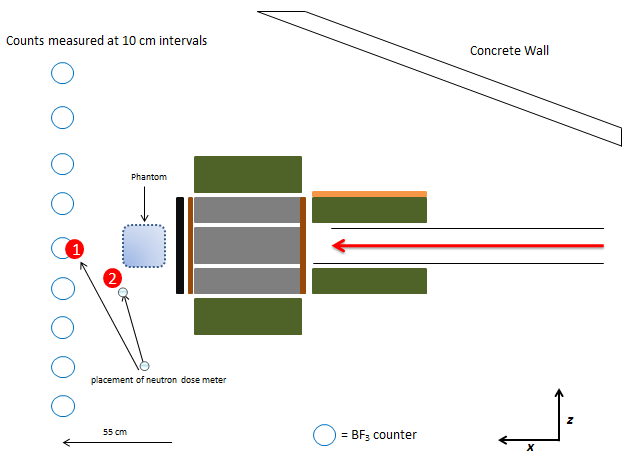
***3.2 Experimental set-up***

In order to gain optimum neutron activation, beam mapping and optimization experiments were conducted. Due to the fact that the protons hitting the lithium target are mono-energetic and entering from one direction, the flight of the neutrons is somewhat forward-directed and, therefore, has some degree of collimation. However, the lithium target is thick so the protons end up having a range of energies from the maximum to zero, capable of producing neutrons from their maximum energy down to the threshold energy. A graphite cylinder was used as a reflector to improve collimation of the neutron field. Additional graphite was placed around the cylinder, followed by layers of wax for shielding. The lead at the exit point of the beam line had a 10.16 cm (4”) hole in the centre, which lined up with the 62 cm long cylindrical graphite column placed between the end of the beam line and this sheet of lead and served to reduce the γ-rays coming from the interaction of neutrons in the graphite and wax. Additional lead was positioned around the exit hole for a thickness of 10 cm. The final distance between the target and the phantom was 74.5 cm. Borated rubber, with its high thermal neutron absorption cross-section (attributable to 10B), was placed around the detector to absorb neutrons scattering off the surroundings, preventing them from entering the detector. A schematic of the collimation and shielding set-up is shown in Figure 3.4. The detector is centred on the beam line axis.

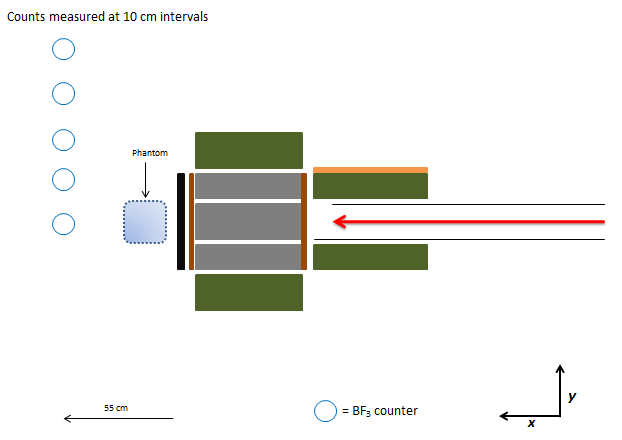
**

*Figure 3.4 Experimental set-up showing placement of the NAI(Tl) detector*

In order to map the neutron field around the beam line, a BF3 counter was used at various positions, as shown in Figures 3.5 and 3.6, and the counts recorded.

**

*Figure 3.5 Placement of BF3 counter and neutron dose meter in the x-z (horizontal) plane*



*Figure 3.6 Placement of BF3 counter in the x-y (vertical) plane*

Figures 3.7 and 3.8 show the variation in neutron counts with position, both for phantom present and absent. This also demonstrates that the presence of the phantom is an effective moderator for the neutrons. The rise in counts in the –*x* direction in Figure 3.7, with a phantom present, can be explained by room returns of neutrons, scattering off the concrete wall shown in Figure 3.5

*Figure 3.7 Effectiveness of shielding in the x-y plane: the blue line represents counts with no phantom present, the red line represents counts with a phantom placed in front of the opening in the graphite column*

*Figure 3.8 Effectiveness of shielding in the y-z plane: the blue line represents counts with no phantom present, the red line represents counts with a phantom placed in front of the opening in the graphite column*

***3.3 Dose calculations***

A neutron dose meter (“Snoopy”) was used to detect neutron counts in order to estimate the expected dose from the neutron flux. The meter is sensitive to neutrons from thermal energies to about 12 MeV[53] and was placed directly in front of the opening (position 1) at a distance of 50 cm and also to the side of the opening (position 2), at a distance of 30 cm from the beam line axis, in the negative z-direction, as shown in Figure 3.5. A nitrogen-free phantom was placed at the end of the beam line, between the beam line and the meter. Table 3.1 shows the recorded doses from the counter using different proton beam energies and currents.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Position | Current (μA) | Energy (MeV) | Dose rate (mrem/hr) | Dose rate (mSv/hr) |
| 1 | 5 | 1.95 | 120 | 1.2 |
| 1 | 0.5 | 2.1 | 100 | 1 |
| 1 | 1 | 2.3 | 500 | 5 |
| 2 | 5 | 1.95 | 100 | 1 |
| 2 | 4 | 2.1 | 800 | 8 |
| 2 | 1 | 2.3 | 810 | 8.1 |

*Table 3.1 Dose readings*

The highest recorded dose occurred at a proton energy of 2.3 MeV and a current of 1 μA, at position 2. These preliminary tests are inconclusive and circumstances beyond the author’s control did not allow for further investigations to be carried out. However, from these observations, it would appear that the dose is more sensitive to increases in proton energy and, therefore neutron energy, rather than current increase. Although it is important to keep the dose as low as possible, optimum detection of γ-rays is the ultimate goal; therefore, it would be wise to work within the premise that keeping the energy as low as possible is more important than keeping the current as low as possible.

***3.4 Beam Optimization***

In order to determine the best beam energy and current combination for maximum nitrogen detection, a series of experiments was conducted, varying both the proton energy and current. The higher the current, the higher the neutron flux.

Using the experimental set-up in Figure 3.2, a 5”diameter NaI(Tl) detector was used, placed behind a water phantom containing 16% nitrogen. The proton energy and current configurations were set as 2.1 MeV and 2.2 μA, 2.3 MeV and 1 μA, and 2.5 MeV and 0.7 μA. The results are shown in Figure 3.9.

*Figure 3.9 Beam Optimization*

The proton energy and current combinations were chosen to span a sensible range of proton energies available while keeping the dead time in the detectors reasonably constant. Each run lasted 60 minutes. The optimum combination from this experiment was determined to be Ep=2.5 MeV and I= 0.7 μA, as demonstrated by the blue data points in Figure 3.9. In particular, both the full energy (10.83 MeV) and single escape peaks from nitrogen are clearly seen with this combination, albeit with a high nitrogen concentration of 16%. The current was later adjusted to 0.3 μA, which still provided enough counts during a 30-60 minute run to determine nitrogen quantitatively, and reduced the amount of dead time in the detector.

Chapter 4

##### **Flux Suppression**

***4.1 Introduction***

Green[47] observed that the number of detected events in the hydrogen peak, when using a nitrogen-free phantom, was higher than for a phantom containing nitrogen. This observation had also been made by Kasviki et al[54] but only in passing, with no convincing explanation, because the emphasis of their work was on nitrogen concentrations in living tissue and the observation was only significant at higher concentrations (typically around 10% for both suppression amount and concentration level).

The next section of this chapter has been submitted as a paper to Applied Radiation and Isotopes for publication. The paper was written by me and revised by the co-authors. The introduction has been removed to avoid redundancy and the references changed to fit with the bibliography at the end of this thesis.

**Evidence of Neutron Flux Suppression while Measuring Nitrogen Using the 14N(n,γ)15N Reaction**

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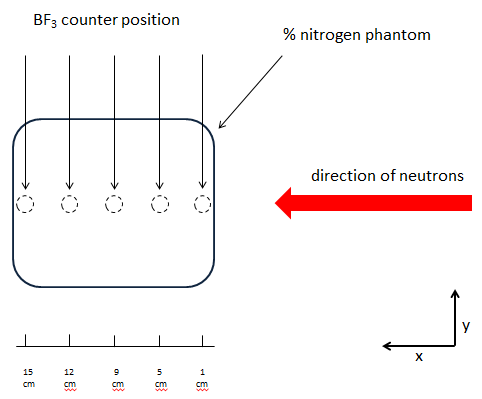
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Submitted for publication in *Applied Radiation and Isotopes*, 26 May 2014. Latest update: with journal for approval of changes suggested by reviewers, 9 January 2015.

The hypothesis is that both the 14N(n,p)14C reaction, and the 14N(n,γ)15N reaction, take incident neutrons away from the fluence, leaving less neutrons available for interaction with hydrogen nuclei. The 14 N(n,p)14C reaction could be measured, in principle, using a proton recoil scintillator or other similar detector, but it is beyond the scope of this paper. The suppression of neutron flux would be significant enough to alter the ratio of hydrogen to measured nitrogen counts, which is commonly used to quantify nitrogen in vivo. In order to investigate if the apparent flux suppression is significant, further experiments to measure the neutron counts in the nitrogen medium and Monte Carlo simulations were conducted. If quantification of nitrogen is to be determined using the hydrogen peak counts then the amount of suppression should be taken into consideration and therefore needs to be determined. Therefore, the primary objective of this work was to investigate neutron (self)absorption by nitrogen and to assess the extent to which it affects the measurement of the N/H ratio for the measurement of nitrogen in vivo, using hydrogen as an internal standard, and to derive appropriate corrections.

***4.2 Materials and Methods***

In order to quantify the suppression effect, a series of experiments was designed. A cylindrical BF3 counter, suitably waterproofed, was placed directly in one of five containers, which comprised water containing urea to give a specific percentage of nitrogen. Neutron counts were recorded at a set position within the container, the counter was moved to a new position in the *x* direction, as shown in Figure 4.1 and the counts recorded again. The counts were normalized to current via the proton charge incident on the lithium target. Any counts arising from γ-rays were excluded by setting the low level discriminator (LLD) above the energy region for these counts as demonstrated in Chapter 9 of the Med Phys 6R03 graduate course taught at McMaster University[55].



*Figure 4.1 Positioning of BF3 counter within phantom*

This procedure was repeated with the remaining four containers, of which the concentrations of nitrogen are detailed in Table 4.1.

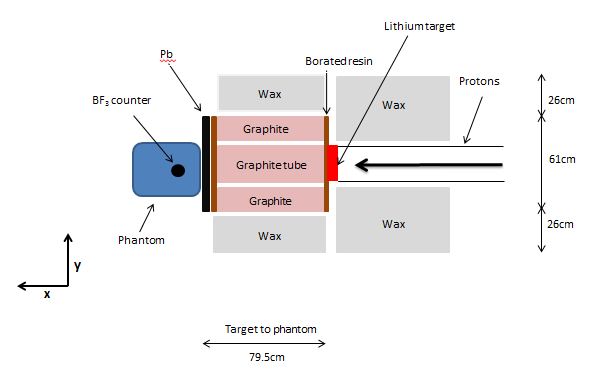
|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Nitrogen mass fraction (%) | 0.0 | 2.6 | 6.0 | 9.0 | 16.0 |
| Hydrogen mass fraction (%) | 11.2 | 10.9 | 10.6 | 10.3 | 9.7 |
| N/H mass fraction | 0 | 0.238 | 0.566 | 0.872 | 1.658 |
| Mass of urea (g) | 0 | 565 | 1329 | 2027 | 3749 |
| Mass of water (g) | 10000 | 9566 | 9000 | 8479 | 7182 |
| Mass of hydrogen (g) | 1119 | 1108 | 1096 | 1085 | 1055 |
| Mass of nitrogen (g) | 0 | 264 | 620 | 946 | 1749 |
| Proportional reduction of H | 0.00 | 0.01 | 0.02 | 0.03 | 0.06 |

*Table 4.1 Nitrogen concentrations for the tissue-equivalent phantoms*

Water phantoms are a good approximation for soft tissue, and can be used to determine penetration of neutrons by submerging a BF3 counter at various lateral depths within the phantom. The dimensions of each phantom container used in this study are 31.2 cm x 23.6 cm x 19.6 cm, and the capacity is 10L. The width of the tank is intended to represent a malnourished human torso. Urea dissolved in water, in differing amounts, yielded the following nitrogen concentrations: 2.6%, 6%, 9%, 16% (see Table 4.1) and water only, ie 0%. Since the mass fraction of hydrogen in urea (6.7%) is less than that in water (11.2%), there was a decline in the mass of hydrogen from 1119g in the 0.0% nitrogen phantom to 1055g in the 16% nitrogen phantom. These figures are also expressed as the proportional reduction of hydrogen in the nitrogen phantoms compared to the nitrogen-free phantom, in Table 4.1, the values of which can be used later to determine the absolute flux suppression value. Although 2.6% is the most realistic of these levels of nitrogen expected to be found in the human body and the fact that higher concentrations are extremely unlikely, it was necessary to include these amounts for detection and calibration purposes.

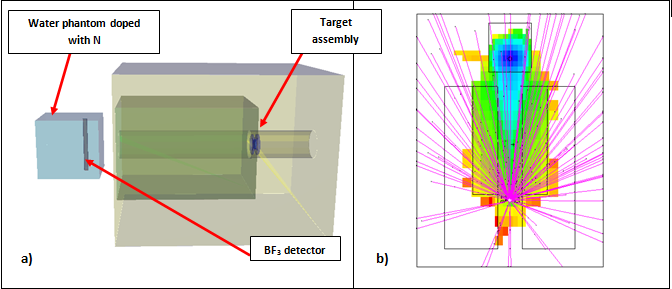
The KN Van de Graaff accelerator in the Tandem Accelerator Laboratory at McMaster University was used as the neutron source for the experiments. The optimal beam energy and current configuration for the experiments was found to be 2.5 MeV protons with a current of 0.3 µA on a thick 7Li target, producing < 800 keV neutrons via the 7Li(p,n)7Be reaction. This configuration was determined by positioning a 5” diameter NaI(Tl) detector on the opposite side to the neutron entry side and comparing spectra at different proton energies and currents, ranging from 2.1 MeV and 1μA to 2.5 MeV and 0.3μA. The energy and current combinations were determined by using the criterion that the dead time in the NaI(Tl) detector remains constant. Only the 2.5 MeV combination exhibited clear γ-ray peaks at 10.83 MeV and 10.32 MeV, which are the full energy peak from nitrogen and its single escape peak. This demonstrated that the neutrons were sufficiently energetic to penetrate the phantom deeply enough before thermalizing and interacting with the material, ensuring that the resulting γ-rays could be detected on the far side.

Figure 4.2 shows the experimental set up and dimensions. Wax was used for shielding the neutrons and graphite was used as a reflector to collimate the neutron field. Some collimation is inherent, since the momentum of the incident protons means that the resulting neutron emission is biased in the forward (0 degree) direction. The lead at the exit point of the beam line had a 10.16 cm (4”) hole in the centre, which lined up with the cylindrical 62 cm long graphite column, placed between the end of the beam line and this thin sheet of lead. Additional lead was added around the exit hole for a thickness of 10 cm, in order to stop any γ-rays from the graphite and wax from reaching the NaI(Tl) detector. The final distance between the target and the front edge of the phantom was 79.5 cm. Acquisitions of 300s were recorded with the BF3 counter, which was used bare (ie without cadmium shielding). The acquisition time was chosen to acquire at least 1x104 counts in the 15 cm position, which was the most distant position that the BF3 counter could be placed, away from the incident neutrons, within the phantom. This was done in order to gain as much difference in counts between the closest and farthest positions as was reasonable, without acquiring for an unnecessary length of time. After normalizing the counts to accommodate differences in current between runs, the results were plotted graphically and will be discussed in the results section.



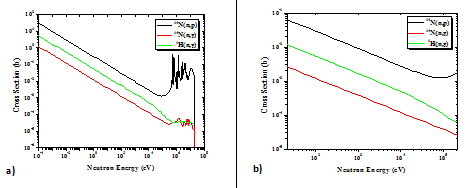
*Figure 4.2 Experimental set up showing placement of BF3 counter*

For the simulations, MCNP5 (v. 1.60) was used and the input deck was written to reproduce the experimental set up. The main body of the code is given in the Appendix. The 3D MCNP geometry and source tracks are presented in Figure 4.3.



*Figure 4.3 a) MCNP modeled experimental geometry set-up shown in 3D, b) Neutron source tracks were generated by VISual EDitor (Vised) 24J. Geometry weight windows are also presented, with the most important set coloured in dark blue around the tally area (BF3 detector)*

The volume-averaged flux tally (f4) was used with an appropriate reaction rate multiplier in order to calculate relative detector response for the different experiments. In particular, the 10B(n,α) reaction rate was tallied inside the active gas volume of the BF3 detector, using the MCNP reaction value of 107, as the third entry on the tally multiplier (fm) card. Setting this value to 107, a volume-averaged flux tally yields a relative (n,α) reaction rate inside the tallied volume per one source neutron per second. The BF3 counter was moved in steps of 3 cm, with the first position being 0.65 cm from the closest wall of the water phantom. Nine simulations were performed for each of the five nitrogen concentrations, accounting for 45 simulations in total. Only the measurements up to 15.65 cm are shown for comparison with the experimental measurements. In order to achieve better statistics and faster convergence of the MCNP runs, a variance reduction technique was used, based on geometry splitting using a rectangular weight windows generation. In this way, a more realistic tally can be recorded in the ‘detector’ and this technique effectively reduces computation time required for the simulations. The tally was designed to reflect both fast and thermal neutrons, as these were not separated in the experiments and the simulation was designed to mimic the experiments as closely as possible.



*Figure 4.4 Log-log plot of the 14N(n,p)14C, 14N(n,γ)15N and 1H(n,γ)2H reaction cross-sections. a) Full energy scale cross section, b) Cross sections from ~20eV to ~200 keV*

Figure 4.4 shows a comparison of the variation of cross-section with increasing neutron energy for the 14N(n,p)14C, the 14N(n,γ)15N and the 1H(n,γ)2H reaction. Figure 4.4a) depicts full-scale cross-sections, while Figure 4.4b) depicts the cross-sections from ~20 eV to ~200 keV. The data are taken from ENDF/B-VII libraries, stored online at the Brookhaven National Nuclear Data Center (NNDC) (http://www.nndc.bnl.gov/exfor/endf00.jsp). According to ENDF-6 tables from NNDC, the thermal neutron absorption cross sections (n,γ) for H, O and N are 0.332, 0.0019, and 0.075 barns, respectively, scattering cross sections are 20.44, 3.85  and 9.91 barns respectively and total cross sections are 20.77, 3.85 and 11.81 barns, respectively (the discrepancy for N total is 1.134 b from the (n,p) reaction).  For H and O and to some degree N, the total cross section (at a thermal energy of 0.0253 eV) is essentially the sum of scattering and absorption, suggesting that only these two mechanisms are important.  For 100 keV neutrons about 14 collisions in water are required to bring them to thermal energy, for 10 keV neutrons, 12 such collisions are required, and so on.  It is clear that the source neutron will become thermal after only a few collisions.  The neutron keeps interacting and can either be absorbed, or can scatter until it is absorbed, or until it escapes the body of water.  Eventually it has to be absorbed by “something”.  Using the above total cross section values, the mean free path of thermal neutrons in water is 6.6 mm.  This means that for every 6.6 mm of travel in water, the thermal neutron will interact, either by elastic scatter or absorption.  Indeed, looking at the hydrogen cross sections, it is 62 times more likely for a thermal neutron to be scattered than absorbed by a hydrogen nucleus.  However, comparing the size of the phantom (in 3D) with the mean free path of thermal neutrons, we can conclude that it will eventually be absorbed inside the phantom (either by hydrogen or nitrogen).  There might be some neutrons that escape the phantom via a multiple elastic scattering mechanism, but these would be the neutrons that enter the phantom close to the phantom boundaries.  Furthermore, the experimental setup contains graphite reflectors, implying that the reflectors “scoop up” these escaped neutrons and “push them back” inside the phantom, where they will be absorbed eventually. The highlights from the graphs are that the highest cross-section for the 14N(n,p)14C is 1.1340 b and occurs at a neutron energy of 6.18x10-8 MeV decreasing steadily down to 0.0013 b at 0.067 MeV neutron energy, where it increases to 0.051 b at about 0.7 MeV (approximate highest incident energy of neutrons at 2.5 MeV proton energy). In contrast, the cross section for the 14N(n,γ)15N reaction is only 0.0484 b at an incident neutron energy of 6.08x10-8 MeV and 3.52x10-5 b at 0.7827 MeV with the 1H(n,γ)2H cross-section being comparable to that of the 14N(n,γ)15N.

From Figure 4.4, it is obvious that more neutrons are interacting in the 14N(n,p)14C reaction than in the 14N(n,γ)15N reaction as the cross-section is consistently higher for this reaction to occur.

***4.3 Results***

Experimental and simulated data are shown in Tables 4.2 and 4.3. It should be noted that the experimental counts (shown in Table 4.2) were divided by the integrated current (charge) to make them comparable with the simulated data, and also for easier reading. For these measurements, the average charge was approximately 100 μC, making each count 100 times smaller than actual. By comparison, a relative level of neutron flux suppression with increasing nitrogen concentration in the phantom can be observed in tabular or graphical form.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  |  | Distance (cm) | | | | |
|  |  | 1 | 5 | 9 | 12 | 15 |
| Nitrogen | 0 | 18490±14 | 13148±12 | 4982±7 | 2145±5 | 650±3 |
| Concentration | 2.6 | 16818±13 | 11484±11 | 4454±7 | 1894±5 | 616±3 |
| (%) | 6 | 15679±13 | 10022±10 | 3934±7 | 1447±4 | 478±2 |
|  | 9 | 14992±12 | 9896±10 | 3670±6 | 1417±4 | 487±2 |
|  | 16 | 14996±13 | 8824±10 | 3048±6 | 1127±4 | 353±2 |

*Table 4.2 Experimentally measured number of counts in the BF3 counter per incident proton charge (counts/μC) for different positions of the counter and nitrogen concentrations in the phantom*

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Distance (cm) | | | | | |
|  |  | 0.65 | 6.65 | 9.65 | 12.65 | 15.65 |
| Nitrogen | 0 | 18658 | 11955 | 4631 | 2213 | 827 |
| Concentration | 2.6 | 18172 | 11320 | 4319 | 2092 | 779 |
| (%) | 6 | 17031 | 10582 | 3956 | 1949 | 732 |
|  | 9 | 16214 | 9971 | 3714 | 1872 | 701 |
|  | 16 | 14167 | 8773 | 3216 | 1699 | 649 |

*Table 4.3 Monte Carlo simulated BF3 counts/μC for different positions and phantom nitrogen concentrations (uncertainties have been omitted due to them being very small)*

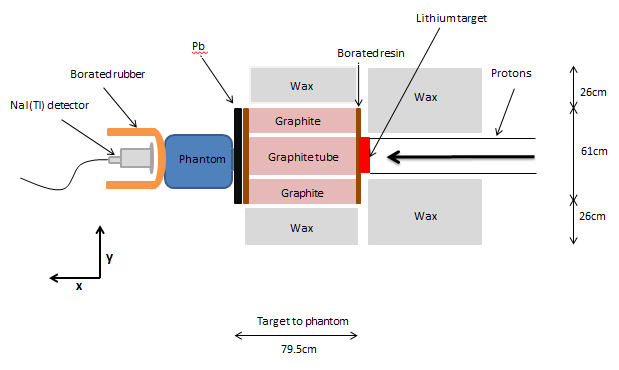
Figure 4.5 shows the experimental and simulation results in graph form. The simulations show less suppression at 2.6%, 6% and 9% nitrogen concentration at 0.65 cm and less suppression at 2.6% and 6% nitrogen concentration at 6.65 cm than the experiments. Distances are the position of the BF3 counter placement.

*Figure 4.5 Experimental (normalized to current) and simulated data of neutron counts in various nitrogen concentrations at increasing depth*

***4.4 Quantification of flux suppression***

A 5” NaI(Tl) detector was positioned behind the phantom in order to analyze the hydrogen peak area and compare it to the nitrogen ROI in all five phantoms. The placement of the detector is shown in Figure 4.6. The measurements were performed at 2.5 MeV proton energy and 0.3 μA current for 3600s. The counts were normalized to the 0% concentration phantom current, to eliminate fluence fluctuations between runs. For example, the current for the 0% nitrogen run at 1 cm was 332 nA (designated as *a* in the following formula) and the current for the 2.6% nitrogen run at 1 cm was 324 nA (designated as *b* in the formula). In order to have a consistent fluence, the counts (designated as *d*) for the 2.6% run were adjusted as follows:

where *c* is the number of counts for the run with current *b* that requires adjusting for consistent fluence. This procedure was applied to all of the experimental runs, where *a* was kept as the current for the 0% nitrogen run at 1 cm, and *b* was the current for the run requiring. Incidentally, the current was converted from the integrated current by dividing by the run length in seconds, thus converting coulombs (integrated current) to coulombs per second (current in amperes).



*Figure 4.6 Experimental set up showing placement of NaI(Tl) detector*

The NaI(Tl) detector is subject to activation by neutrons in the Na and I contained in the detector crystals, as investigated by Gardner *et al*[56]. However, the activation was insufficient to affect the results in that the added counts were low and the resulting γ-rays in the detector were far enough away in energy not to affect either the hydrogen peak at 2.22 MeV or the nitrogen region of interest at roughly 9 – 11 MeV.

Table 4.4 shows the number of experimentally measured net counts in the hydrogen peak at 2.22 MeV for each of the phantom concentrations. The hydrogen counts were determined in each spectrum by a simple trapezoidal subtraction in the energy region of the hydrogen peak. Since the mass of hydrogen in each phantom was decreasing as the % nitrogen was increasing (as shown in Table 4.1), Table 4.4 also shows the proportional reduction of hydrogen for the phantoms containing nitrogen, compared to the nitrogen-free phantom as the baseline, or denominator, taken from data in Table 4.1. This makes it easier to derive the origin of the total hydrogen count reduction in nitrogen phantoms, which is a combination of the hydrogen peak count ratio and the hydrogen mass ratio. The figures demonstrate the drop in neutron flux as the concentration increases. If there were no suppression, the actual counts for each concentration should be relatively equal, within uncertainty. However, even at 2.6% concentration, there is a drop of 7.03%, increasing to 14.53% at 16% concentration. For the BF3 and MCNP counts, the ratios of neutron counts for the different nitrogen phantoms to the neutron counts for the nitrogen-free phantom was calculated for each depth and then the mean of the ratios and its standard deviation across all depths were taken. These can then be compared to the single measurement of the nitrogen difference to the hydrogen counts for each concentration. It should be noted that the MCNP counts decline somewhat more rapidly with increasing N concentration, but the BF3 count ratios decline more sharply still. One contribution to these slightly different patterns is likely to be the fact that not all of the observed hydrogen counts come from the urea (or water) solution; a few counts must come from the walls of the phantom container. The mass of the container was 359 g, which can be assumed to have a composition close to (CH2)n and therefore to contain a mass of hydrogen of 52 g. Consequently, this would add a baseline level of hydrogen counts, independent of the actual urea solution, which would tend to reduce the apparent effect of flux suppression. However, this factor would only increase the suppression with 16% nitrogen from 14.53% to just over 15%. Another factor tending to increase the baseline hydrogen counts would be counts from surrounding materials, particularly hydrogenous materials such as wax used in shielding. As these materials are close to the beam line, but not very close to the detector, this too will be a minor effect. The further difference between MCNP and the measured BF3 counts could be due to systematic errors with the BF3 counter and the fact that, particularly at high nitrogen concentrations and greater distances, the statistics are much poorer than at closer distances with less nitrogen (higher count rates).

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| %N in phantom | Experimentally | Ratio of N to  N-free | SD | Proportional loss  of H | Total H count | Mean of ratio of | SD | Mean of ratio of | SD |
|  | measured  H counts | H peak counts |  | compared to 0% N | reduction (%) | MCNP counts |  | BF3 counts |  |
| 0 | (4642±3)x103 | 0 |  |  |  |  |  |  |  |
| 2.6 | (4270±3)x103 | 0.9199 | 0.00092 | 0.0098 | 7.03 | 0.9481 | 0.0154 | 0.9013 | 0.0286 |
| 6 | (4239±3)x103 | 0.9132 | 0.00092 | 0.0206 | 6.62 | 0.8836 | 0.0208 | 0.7619 | 0.0643 |
| 9 | (4157±3)x103 | 0.8955 | 0.00091 | 0.0304 | 7.41 | 0.8397 | 0.0246 | 0.7419 | 0.0538 |
| 16 | (3702±3)x103 | 0.7975 | 0.00085 | 0.0572 | 14.53 | 0.7480 | 0.0351 | 0.6324 | 0.1154 |

*Table 4.4 Variation of hydrogen counts with different nitrogen concentrations and comparison of MCNP simulated and measured BF3 counts with varying nitrogen concentrations*

***4.5 Discussion and Conclusion***

The most probable explanation for the observed suppression of neutron flux with increasing nitrogen is that both the 14N(n,p)14C reaction and the 14N(n,γ)15N reaction take incident neutrons away from the fluence, leaving less neutrons available for interaction with hydrogen nuclei. The first reaction can only be estimated from the cross section as it cannot be directly measured by the techniques used here.

From the estimates in Table 4.4, the data for 2.6% nitrogen, ie typical levels of nitrogen expected to be found in the human body, show a decrease in neutron flux of 7.0 ±0.1%. Therefore, if the nitrogen to hydrogen ratio is to be used to calculate total body nitrogen, this decrease should be incorporated into calculations using this method. How this effect will impact the analysis will depend on the approach followed. For example, the ratio of nitrogen counts to hydrogen counts should not be affected, but the hydrogen counts per gram of hydrogen will be directly affected by this neutron flux suppression.

***4.6 Simulation of neutron collisions***

This section was not included in the paper submitted for publication. The data were retrieved from the same simulations used to determine the flux suppression as described in section 4.2 *Material and Methods*. Information on neutron collisions is available in MCNP as a tally (f14), which was invoked in the program. This tally differs from the flux-over-volume (f4) tally used in that the information concerns the neutron collisions in the phantom at specific points, rather than the detector response at those points, which was the purpose for simulating the experimental results for the flux suppression.

Figure 4.7 shows the results of the Monte Carlo simulation for neutron collisions from 0 – 24 cm, which effectively spans the distance from the entrance point into the phantom of the neutrons exiting the beam line to the neutrons exiting the phantom at the point farthest from the beam line (ie horizontal depth). The simulations were conducted for the same concentrations of nitrogen used in the experiments, namely 0 (nitrogen-free), 2.6, 6, 9 and 16%.

*Figure 4.7 Neutron collisions as a function of depth and nitrogen concentration*

Observations of Figure 4.7 reveal that neutron collisions are fewest at greater depths for the highest concentration phantom. The depth at which the fewest collisions occur reduces as the concentration decreases. As the nitrogen content in the phantom is increased, the water content is decreased because the volume is fixed. Subsequently, the number of hydrogen atoms, and therefore the number of protons, is decreased. Collisions of neutrons with the protons dominates in this medium, which is why hydrogen is a good moderator and useful for thermalizing neutrons. This means that the probability of collisions increases as the energy of the neutrons decreases. As there are fewer protons in the highest concentration phantom, the depth taken to reduce the average energy of the neutrons increases, thus allowing the neutrons to penetrate further into the phantom before the maximum number of collisions takes place and the neutrons are fully thermalized. It can be seen that the neutrons reach thermal energies when the curve flattens out and occurs at different depths for the different concentrations. The nitrogen-free phantom obviously thermalizes the neutrons in the shortest depth and they appear to stay constant until they reach ~20 cm depth, at which point the collision rate decreases, implying that the neutrons are slowing down further. As this behaviour is not obvious in the higher concentration phantoms, it could be that the distances for slowing down are greater than those modeled, ie if the phantom had been of greater depth, the higher concentration phantoms would possibly begin to exhibit this same behaviour, having taken a greater depth to begin slowing down initially.

The evidence from the neutron collision simulation strengthens the claim made in the flux suppression paper that the alteration in the composition of the phantoms adds to the effect caused by the suppression itself.

***4.7 Fast Neutron Contribution***

Although also not included in the paper, earlier experiments were conducted using the same BF3 counter as that used for the flux suppression counts, but using a different, earlier set of phantoms. The experiments were conducted with the counter bare and cadmium-wrapped to determine the fast neutron component of the total counts.

There are two things to consider when attempting a determination of the fast neutron component. Firstly, the cross-section for cadmium is very large for neutron energies < 0.4 eV. By wrapping the BF3 counter in cadmium, the thermal neutrons are absorbed by the cadmium and do not reach the counter. The counts recorded should be from the fast neutron component only. However, by placing cadmium around the counter, some of the faster neutrons that would contribute as fast neutrons without the cadmium present, may be slowed sufficiently by the cadmium and not reach the counter. This is mentioned by Knoll[57] on page 748, when he states:

*The method* [of separating fast and thermal neutrons]  *does require some corrections for the nonideality of the cadmium filter, in that cadmium thicknesses that are large enough to fully stop all neutrons below 0.4 eV can also have a measurable effect on neutrons with higher energies.*

For the purposes of these experiments, it is sufficient to be aware of this change, as the contribution from fast neutrons is small enough to be negligible to the results.

Secondly, the efficiency of the counter can be calculated for neutrons of different energies using the following formula[57]:

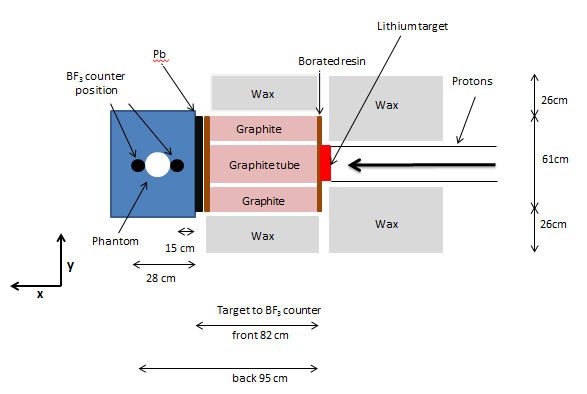
(1)

where Σa = macroscopic absorption cross-section of 10B at neutron energy E

L = active length of tube (ie diameter)

The example of a 30 cm tube with 96% enriched 10B at 600 torr has 91.5% efficiency for thermal neutrons (E = 0.025eV) and only 3.8% for 100 eV neutrons. Therefore, even if the fast neutrons can be separated from the thermal neutrons by comparing bare and cadmium-wrapped measurements, the drop in efficiency of the counter should be considered when estimating the number of fast neutrons.

The phantoms being used were cylindrical bottles, with a diameter of 13 cm and a height of 28.8 cm, placed inside a tank of water. Measurements were taken at 82 cm from the target, with the BF3 counter between the neutron ‘beam’ and the phantom, approximately 15 cm lateral depth from the front of the tank, and at 95 cm from the target, ie behind the phantom, at a lateral depth of approximately 28 cm from the front of the tank. Distances and positioning of the BF3 counter are shown in Figure 4.8.



*Figure 4.8 Positioning of BF3 counter relative to phantom and target*

Results from the experiments are shown in Table 4.5.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | 95cm (behind) | | | | 82cm (in front) | | | |
| %N | Bare | +/- | Cd wrapped | +/- | Bare | +/- | Cd wrapped | +/- |
| 0 | 318271 | 9954 | 6818 | 362 | 16575405 | 4774 | 1386600 | 618 |
| 9 | 280251 | 8008 | 6904 | 496 | 16467957 | 8978 | 1472102 | 1519 |
| 12 | 260314 | 7339 | 7386 | 308 | 16510784 | 5324 | 1441770 | 1381 |
| 16 | 228000 | 13881 | 7391 | 262 | 16551061 | 3822 | 1391944 | 1804 |

*Table 4.5 Bare and cadmium wrapped BF3 counts for positions in front of (82 cm) and behind (95 cm) phantoms of 0%, 9%, 12% and 16% nitrogen concentration*

The contribution from fast neutrons was found to be approximately 9% of the total neutrons as the neutrons entered the tank, and approximately 3% of the total neutrons after the neutrons had been moderated through a distance of 13 cm, ie at the far side of the phantom. This would indicate that the vast majority of the neutrons have thermalized and can interact with the contents of the phantom.

Chapter 5

##### **Instrumentation**

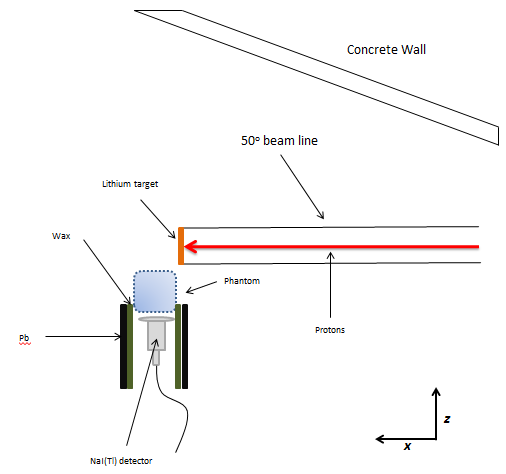
***5.1 Introduction***

While checking the feasibility of detecting γ-rays from nitrogen when the phantom was placed at 90o to the beam line, γ-rays of 17 MeV were detected. Although they were present in the 0o configuration, they had gone unnoticed as the gain had previously been set to limit the spectrum up to 14 MeV. It is important to identify the origin of these high energy γ-rays and eliminate them, as they will interfere with the signals from the nitrogen ROI due to their Compton scattering contribution.

Proton beam pulsing is one way to reduce unwanted contributions into detectors from direct and prompt interactions with the beam target, if this is where the high energy is coming from. The investigation and early attempts at solving the problem shall be described, before the use of the proton chopper for beam pulsing is introduced.

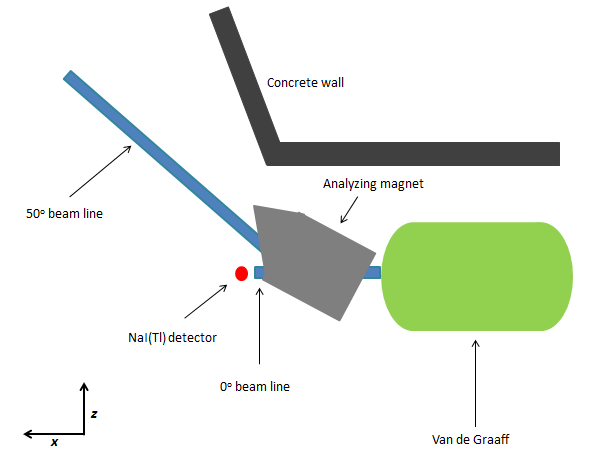
***5.2 Identification of high energy γ-rays***

Figure 5.1 shows the setup to test the feasibility of measuring γ-rays from the 14N(n, γ)15N reaction in the nitrogen sample at 90o from the direction of the beam line. As mentioned in the introduction, γ-rays of around 17 MeV were detected. In order to narrow down where they were coming from, the proton energy was dropped to 1.7 MeV (below the threshold for the 7Li(n, p)7Be of 1.88 MeV in the target). The high energy γ-rays were still being detected.



*Figure 5.1 90o configuration using the 50o beam line*

The first thought was that perhaps the γ-rays were coming from the end of the 0o beam line, which is not operational. Even though the protons are accelerated through the tank and bent into the 50o beam line by the analyzing magnet, not all of them reach the 50o beam line. The two stable isotopes of natural hydrogen are 1H and 2H (deuterium), which has an abundance of 0.015%, and this natural hydrogen makes up the plasma in the accelerator. The electrons are stripped from the plasma and the protons are accelerated. There are now protons (1H) and deuterons (2H). The analyzing magnet is tuned to allow only 1H protons to be bent into the 50o beam line, in order to have a mostly single energy beam impacting the target. The deuterons are mass 2 and do not make it around the bend. These deuterons can interact with each other in the DD reaction, creating 3He + n and emitting a γ-ray of around 14 MeV, which may possibly be detected at the 0o beam line port. The beam line currently in use is at 50o, as described in Chapter 3.

**

*Figure 5.2 Schematic of KN accelerator showing beam lines*

Figure 5.2 shows the location of the 0o beam line with respect to the 50o beam line. A NaI(Tl) detector was placed at the end of the 0o beam line, which is only a short stub beyond the analyzing magnet, as indicated, to test the hypothesis that the high energy γ-rays were coming from DD reactions. There is no threshold for the DD reaction, only the Coulomb barrier, so as the speed of the protons is increased, they will overcome the Coulomb barrier exponentially. In other words, the cross-section for the reaction increases with increasing proton energy. The test to detect these failed; no high energy γ-rays were detected when the detector was placed at the end of the 0o beam line. Figure 5.3 shows the spectrum with high energy γ-rays present, recorded using the NaI(Tl) detector in the position shown in Figure 5.1, along with the spectrum at the 0o beam line as shown in Figure 5.2. The counts in the region from 12 MeV to 18 MeV should not be present under normal conditions. The spectrum was recorded with the 2.6% nitrogen phantom in position. The 0o beam line spectrum shows no evidence of high energy γ-rays.

*Figure 5.3 Contrast between spectra taken at 90o to the 50o beam line and at the 0o beam port*

The next step was to revert back to the 50o beam line and place the detector at the 0o beam direction, ie directly at the end of the beam line, and observe the spectrum up to 20 MeV. The reasoning here was that maybe the high energy γ-rays were coming from the target itself. Protons on lithium release γ-rays from beryllium, with no energy threshold ie 7Li + p → 8Be + γ

where the reaction has a Q-value of 17.2543 MeV[58], all of which energy could, in principle, be available to the γ. Cross-sections for the reaction vary with proton energy, ranging from 1x10-5 b at Ep=230 keV to 5x10-4 b at Ep=2.5 MeV[59] , increasing by a factor of 50 over a proton energy increase of 11. With a proton energy of 1.7 MeV (below the neutron threshold energy), γ-rays of ~17 MeV were detected, indicating that the source is indeed the lithium target.

Figure 5.4 shows the effect of placing Pb between the target and phantom, in reducing the transmission of the γ-rays. Data for the attenuation coefficients were taken from NIST tables[60]. The two lines on the graph represent pair production attenuation γ-rays only and total attenuation excluding coherent scattering. By using the formula:

(1)

where I is γ-ray transmission, μ/ρ is mass attenuation coefficient, and d is area density, measured in g.cm-2, it can be seen that a thickness of 10 cm reduces transmission of the 17.3 MeV γ-rays to <0.004 for pair production attenuation only and <0.002 transmission for total attenuation, thus practically eliminating the high energy γ-rays.

*Figure 5.4 Log-normal plot of the effect of Pb thickness on high energy* *γ-rays*

By placing 10 cm of Pb bricks between the target and the phantom, no high energy γ-rays were detected when protons were directed at the target. The recommended maximum thickness of the Pb is 10 cm; beyond this thickness, the build-up of secondary radiations occurs due to external cosmic-ray interactions within the lead[61]. Attenuation of neutrons within 10 cm of Pb is insignificant due to the kinematics of neutron elastic scattering. Conservation of momentum and energy in the centre-of-mass system for neutrons with non-relativistic energy can be expressed as a formula showing the relationship for the energy of the incoming neutron’s recoil:

(2)

where ER is the energy of the recoiling neutron in the laboratory system, A is the mass of the target nucleus, θ is the scattering angle of the neutron in the centre-of-mass system and En is the kinetic energy of the incoming neutron in the laboratory system. By using the formula:

(3)

to translate from a mixed laboratory/centre of mass system to purely laboratory, equation (2) becomes:

(4)

From equation (4), it is clear to see that the scattering angle determines the energy given to the recoil nucleus so, for a grazing encounter, the recoil will be emitted almost perpendicular to the direction of the incoming neutron ie, θ = 90o, so equation (4) predicts that the recoil energy is almost zero. For a head-on collision, nearly all of the energy will be transferred to the recoil nucleus as the angle will be 0o. Therefore, equation (4) can be simplified in the case of maximum recoil energy to:

(5)

For a target nucleus of A = 82 (Pb), the maximum energy transferred from an incoming neutron, according to equation (5) is 328/6889 = 0.048. By also looking at the mean free path of neutrons in Pb, a determination of how far they will travel through the thickness of 10 cm is another indication of how much the Pb will attenuate the neutrons. Taking the macroscopic cross section of Pb to be crudely the product of its microscopic cross section (5.1 x 10-24 cm) and atomic density (3.29 x 1022 atoms), the mean free path for the neutrons is 5.96 cm. To determine the number of unscattered neutrons is simply where *x* is the thickness of the Pb and *l* is the mean free path of the neutrons, which yields 0.19, implying that the majority of the neutrons will be scattered. Considering these results together, implies that the effect of the Pb on neutrons is insignificant.

***5.3 Materials and Method for comparison of the effect of Pb vs no Pb***

A single 4”x4”x4” cubic, or square cross-section, NaI(Tl) detector was used in the experiments.

Figure 5.5 shows three spectra taken at the 0o orientation for the 0% nitrogen concentration phantom with 10 cm Pb present and for the 16% nitrogen concentration phantom with and without the Pb present. The only available data do not extend to 20 MeV yet still serve to illustrate the effect of Pb on the reduction of high energy γ-rays from the target.

*Figure 5.5 High energy region, with and without Pb shielding*

Measurements were taken for 30 minutes, with a proton energy of 2.3 MeV and a current of 0.3 μA. The phantom was placed between the target and detector, as described in Chapter 4. The counts were scaled because, even though the energy and current were the same for each run, the counts per second differed significantly, as shown in Table 5.1. The hydrogen peak was used to normalize the counts in the spectra and is illustrated in the table, along with the integral for each spectrum.

|  |  |  |  |
| --- | --- | --- | --- |
|  | 0%N | 16%N | 16%N |
|  | 10 cm Pb | 10 cm Pb | No Pb |
| H peak cps | 19044 | 829 | 1064 |
| Scaling factor | 0 | 1.3 | 1.7 |
| Integral (9.5- 11.5 MeV) | 8792 | 59476 | 118149 |
| Integral (11.5- 15.5 MeV) | 2098 | 6983 | 50715 |

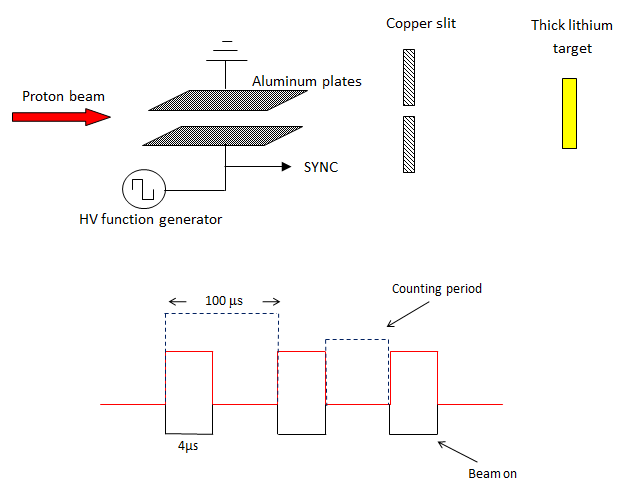
*Table 5.1 Normalization and integrals for comparison spectra*

It is clear to see from Figure 5.5 that the high energy γ-rays are not present when the Pb is in place. The few counts that are visible in the two spectra with Pb present have been attributed to pulse pileup during acquisition with a typical total count rate above 11 MeV of 1.45 cps and a dead time of 23.35% for the 0% nitrogen phantom and 2.04 cps and a dead time of 27.49% for the 16% nitrogen phantom. Additional experiments will show that the replacement of the shaping amplifier by one that has a pileup reject (PUR) feature contributes to the reduction of unwanted signals. The integrals in Table 5.1 serve to illustrate further the difference in counts for the nitrogen ROI (9.5 – 11.5 MeV) and beyond; the difference between the 16% nitrogen spectra, with and without Pb is almost a factor of 2 in the nitrogen ROI. However, another approach to solving this problem is to introduce a proton pulser into the path of the protons before they reach the target. Timing and coordination of counting should improve the resulting spectra by eliminating the high energy γ-rays, assuming that they are coming directly from the target and are emitted promptly after the 7Li(p,γ) reaction takes place. A description of the proton chopper, used for pulsing is given next, followed by a description of the system used to optimize the timing parameters for the pulses.

***5.4 Proton Chopper***

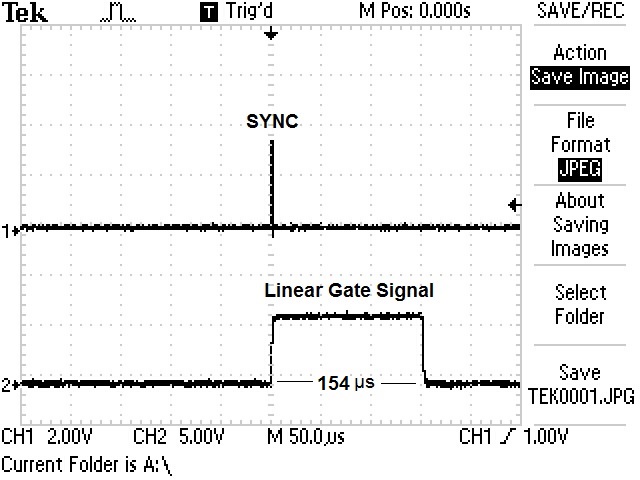
The proton chopper at McMaster University was developed by Witold Matysiak as part of his PhD thesis work[62] and was originally designed to use the time-of-flight technique for measuring the energy spectrum of neutrons produced by the 7Li(p,n) reaction.

The proton chopper consists of two 120 cm aluminium plates, separated by 2 cm, inserted into the beam line of the KN accelerator, between the analyzing magnet and the target. One plate is powered by 300V AC pulses and the other plate is grounded. This allows the proton beam to be deflected away from the positive plate when the power is on, and to be passed through an analyzing slit before hitting the target, when the power is off. A diagram of the chopper is shown as Figure 5.6. The diagram also shows how the pulses and subsequent counting are achieved, by using the system in anticoincidence ie only counting when the beam is off.



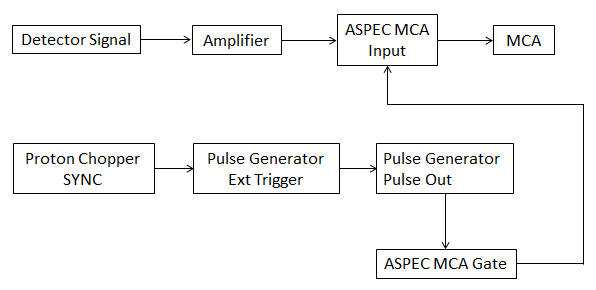
*Figure 5.6 Diagram of proton chopper; lower part of figure not to scale*

For these experiments, the proton chopper was set with a 4μs pulse, a 10 μs timed delay from when the pulse begins, and a frequency of 10 kHz. These initial settings were to account for the time it takes for neutrons of energy <500 keV to slow down to thermal energies, which is around 1 μs[63] so the 4 μs pulse was chosen to give some leeway. It is necessary to count only when the beam is off so that counts from the γ-rays produced by the target are ignored, which is why the MCA is set to anticoincidence. A sync pulse is used to set up timing parameters, to enable synchronization of measurements. Figure 5.7 shows a time variation of the sync signal and the pulse from the proton chopper.



*Figure 5.7 Time variation of sync signal and proton chopper pulse*

As demonstrated in Figure 5.7, the sync pulse arrives from the proton chopper when the power to the plate is off, meaning that the beam is not deflected and will impact the target. A short delay in the acquisition system (in this example 4 μs) ensures that counting cannot begin while the beam is on target if, for example, there is a delay between the beam being on and the sync pulse arriving. Here, the beam ‘on’ is set to 150 μs, different from the previous setting of 100 μs purely as a trial, using a pulse generator set in external trigger mode, in order to coincide with the length of time the 300 V to the proton chopper plate is applied, thus deflecting the beam away from the target and onto the analyzing slit. With the acquisition system set to anticoincidence, counting will take place 154 μs after the sync pulse arrives and continue until the next sync pulse arrives. A block diagram of the electronics is shown in Figure 5.8.

**

*Figure 5.8 Block diagram of proton chopper electronics set up*

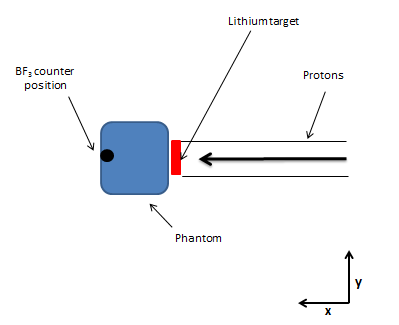
When the sync signal from the proton chopper has been received, the external trigger in the pulse generator starts the gate, which is set to be open for the same length of time as the proton chopper voltage is off, effectively synchronizing the two. This means that the multichannel analyzer, which has anticoincidence capabilities, receives the signal from the detector, via the amplifier and analogue-to-digital converter (ADC) and the counts when the beam is off can be recorded, using ORTEC Maestro software.

***5.5 Multi-scalar***

Early attempts were made to determine the best timing window to use with the proton chopper by varying the beam width and duty cycle and comparing the region of interest with the background in the region of the high energy γ-rays, the results of which will be discussed in Chapter 6. A more straightforward method to determine the time window is by using a multi-scalar, which was designed by Kenrick Chin at McMaster University and was incorporated into the system, thereby enabling the identification of optimum timing parameters to be established for use with the proton chopper. The rationale for this was three-fold. Firstly, if an estimate can be made of when the thermal neutrons peak, then the window for collecting data can be identified. Secondly, there should be an obvious cessation of data collection when the beam is on-target, coinciding with the timing parameters of the proton chopper, which will act as verification that the system is working properly. Thirdly, the shape of the spectrum may tell us something about the beam profile, for example, whether or not it is focused into a tight beam or has a definite halo. The shape of the beam can affect the pulse width, in that some protons can still impact the target even during deflection if the proton optics setting is not properly tuned, resulting in an excessively large beam-spread.

***5.5.1 Timing window***

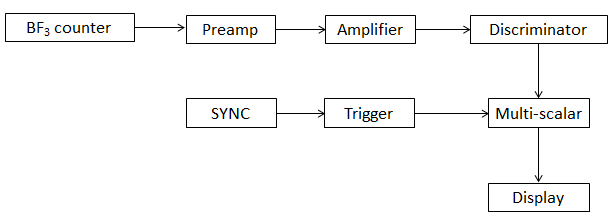
A BF3 counter was suspended inside the 0% nitrogen phantom, as shown in Figure 5.9.



*Figure 5.9 BF3 counter position for time window optimization experiments*

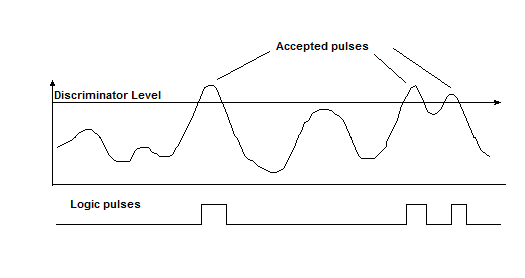
The counter has an overall length of ~ 14 cm and an effective length of ~ 5 cm. It was suspended in the phantom container far enough down for the effective length to be at the same height as the beam line, and was enclosed in a Lucite tube to keep it dry.

The proton chopper was set to a beam width of 150 μs and a total period of 2 ms (500 Hz frequency). The settings were arbitrary in order to have a starting point to determine the best window from the results. A block diagram of the set up for the multi-scalar is shown in Figure 5.10.



*Figure 5.10 Block diagram of multi-scalar system*

The discriminator in the system converts all detector pulses that are above a set threshold to logic pulses, thereby discriminating against low energy background and noise, as shown in Figure 5.11. Only those pulses above the discrimination level are converted to logic pulses and sent to the multi-scalar. The sync pulse from the proton chopper triggers the multi-scalar to begin its cycle, which is the beam on start-time as shown in Figure 5.7.

**

*Figure 5.11 Example of how a discriminator works*

The BF3 counter is sensitive primarily to thermal neutrons, as discussed in Chapter 4. By recording the time that pulses arrive in the multi-scalar, a time spectrum can be generated. The shape of the time spectrum for the thermal neutrons will provide the information of how long the beam pulse width should be. Figure 5.12 shows the raw spectrum from the multi-scalar, indicating the end of the beam pulse. Each time division is 5 μs, with a total counting period of 2 ms. All pulses are counted, which clearly shows that the peak of the thermal neutrons is around 200 μs, in this time spectrum. The proton energy was 2 MeV and the effective current 0.4 μA.

*Figure 5.12 Time spectrum from the multi-scalar*

Optimization consists of finding the longest beam ‘on’ time coupled with the shortest cycle period that encompasses the thermal neutrons, in order to have as many thermal neutron reactions with the nitrogen as possible, while minimizing the unwanted γ-rays from the 7Li(p,γ) reaction of the target. As mentioned earlier, the time taken for neutrons of <500 keV from the 7Li(p,n) reaction in the target to slow down to thermal energies is ~1 μs. However, there will be a build-up of thermal neutrons from cycles produced by the proton chopper, which will reach a maximum. By collecting a time spectrum using the multi-scalar, with arbitrary but reasonable estimates of the starting parameters for beam ‘on’ and period, it should be possible to determine the optimum combination of the two.

To confirm the optimum beam-width setting, the integral of the curve multiplied by the ratio of two time intervals can be calculated thus:

(6)

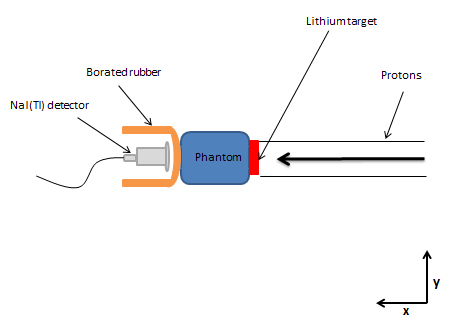
where *A* is the sum of the counts between the two time intervals τ1 and τ2. This gives an un-normalized efficiency, or duty cycle, which is the ratio that the beam is on to the total cycle time (2 ms). By increasing τ2 in successive increments of 5 μs (the smallest time interval recorded by the multi-scalar) and keeping τ1 fixed, a curve can be plotted, which shows how the counts vary with increasing time intervals. For example, starting with τ1 fixed at 100 μs and counts of 789, the first time interval, 105 μs has 842 counts. Using formula (6) above, this gives an integrated count of 1553. The next calculation will be τ2 at 110 μs and the counts for that time added to the previous two, and so on, until all counts up to the end of the time period recorded by the multi-scalar have been integrated. The highest count should indicate the point at which the time interval is maximized to allow the most thermal neutrons to interact with the phantom. Figure 5.13 shows four different time interval calculations performed using this method, from one data set.

*Figure 5.13 Calculation of optimal beam-width setting*

It can be seen from Figure 5.13 that the optimal beam-width is 150 μs, as the highest point in the graph occurs at 365 μs after the beam hits the target. The length of time for counting is thus around 400 μs, the time just after the peak reaches its maximum.

***5.5.2 High energy gamma ray elimination***

To determine if the proton chopper can be used to eliminate the high energy γ-rays from being counted, the same system as in Figure 5.10 was used but the BF3 counter was replaced with a 4”x4”x4” cubic NaI(Tl) detector, placed behind the 0% nitrogen phantom, as shown in Figure 5.14. This detector is one of a set of 6, which will be discussed again in Chapter 6.



*Figure 5.14 Experimental set-up using a NaI (Tl) detector*

The proton energy was set to 1.6 MeV (below the lithium neutron activation threshold of 1.88 MeV) with an effective current of 0.4 μA. The proton chopper had a beam-width of 150 μs and a frequency of 0.5 kHz (ie 2 ms period). Figure 5.15 shows the spectrum acquired with these settings.

*Figure 5.15 Time spectrum of gamma counts below lithium neutron threshold energy*

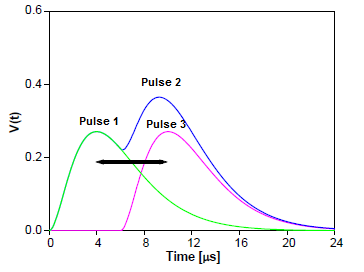
The peak of the γ-rays occurs at 30 μs. The counts in the first 20 μs are below 300 counts per channel, similar to the counts when the beam is off, which would imply that there is a ~20 μs delay between the sync pulse trigger to start the count and the beam being on target. The counts increase to a second maximum at 165 μs, beyond the time that the beam is supposed to be off and drop to a minimum at 185 μs. Therefore, the time scale can be shifted 20 μs to the right but this does not explain why there are higher counts at what would be 165 μs if the true start time is at 20 μs, unless the beam is skipping off the sides of the beam line and reaching the target, due to a non-uniform shape, and only truly off where there is a dip at 185 μs in the spectrum as shown. The expected beam shape would be a square wave for the duration of the beam on time. Comparison with a second spectrum, which had the same energy and current settings, and also the same proton chopper parameters, showed a different spectrum shape, which could be caused by a different beam-shape after focusing and steering. If the beam is not focused into a tight, uniform shape, the asymmetry and, possibly, a halo could cause protons to reach the target as the beam is deflected, much the same way as a lawn sprinkler with a wide setting splashes on the concrete as well as the lawn. This explanation could account for both peaks in Figure 5.15. For future experiments where the proton chopper is required, this would be a good method to check the beam profile in order to ensure that the beam is properly focused. It would be a much more efficient method and be less time-consuming than the alternative method of replacing the lithium target with a quartz window to observe the beam directly.

The use of the multi-scalar as a method to identify the optimum timing window when thermal neutrons peak, in order to maximize the counts recorded from interaction with nitrogen, is one of the unique features of this research. It has proved to be an effective method for this purpose and can be used for different proton energies, thereby identifying the correct timing window, depending on the desired proton energy. The second unique feature is its use in reducing the number of counts recorded from the unwanted high energy γ rays, which can interfere with the counts recorded from nitrogen and thus reduce the precision of the counting system.

***5.5.3 Pulse Pileup***

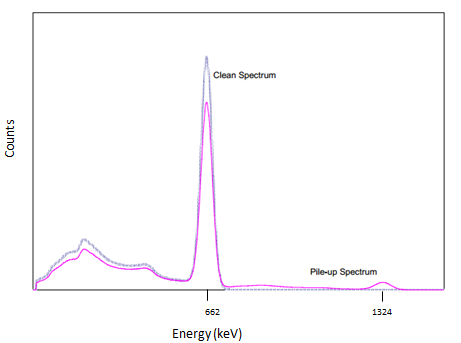
One of the main concerns with the acquisition system is pulse pileup. When investigations were taking place to determine the origin of the high energy γ-rays interfering with the nitrogen ROI, the question of pileup arose. If the high energy γ-rays were eliminated by using either Pb or by pulsing, and counts were still being measured in that region, could they be due to pileup?

Pileup occurs when pulses arriving in the amplifier are too close together to be analyzed separately (separated by a shorter time than the pulse resolution time for the system) and they overlap. An example of this is given in Figure 5.16.



*Figure 5.16 Situation where pulse pileup occurs[64]*

When this happens, pulses 2 and 3 are incorporated into one pulse so that there will only be two pulses: pulse 1 and pulse 2+3, which will be deposited in a channel that corresponds to their combined energy, effectively shifted up in energy. If the pulses are further apart, they may be deposited in separate channels, as two separate events, but still corresponding to an incorrect energy as they cannot be fully resolved (referred to as tail pileup). The above is an example of second order pileup, where the count rate is only slightly higher than the time resolution of the system. As the count rate increases, third and fourth order pileup occurs, involving the same situation but with additional pulses. Figure 5.17 shows the effects of first order pileup on a 137Cs spectrum, purely as an illustration of the differences in the two spectra.



*Figure 5.17 137Cs spectrum showing first order pileup[65]*

The photopeak at 662 keV is clearly visible with the pileup area showing at 1324 keV (2 x 662). If there are third and fourth order pileup, these will occur at 3 and 4 times the photopeak energy. Tail pileup will also contribute and show as a ‘smearing out’ of the spectrum at higher energies than the photopeak. The blue line shows the effect of eliminating pulse pileup, resulting in a higher photopeak and no counts in the 2 x photopeak energy area.

In an effort to eliminate pulse pileup, an amplifier with a pileup reject (PUR) feature can be used. If the gap between two pulses occurs in a time interval of τo to τmax, where τo is the time the first pulse arrives and τmax is the time interval by which the amplifier will recognize that both pulses cannot be resolved, then both events will be detected by the system and rejected. Obviously, if the pulses arrive too close together for the amplifier to distinguish them as two separate but close events then pileup will still occur, so efficiency will depend on how good the pileup rejection is for the expected count rates.

The amplifier used in the system is an ORTEC 671 Spectroscopy Amplifier. It features an automatic noise discriminator and an LED light that will turn from green at low count rates through yellow at moderate count rates to red when losses from pulse pileup are greater than 70%. Pulse pair resolution is typically 500 ns.

Figure 5.18 demonstrates the effectiveness of using pileup rejection by contrasting two spectra, one recorded with no pulse PUR and the other with pulse PUR.

*Figure 5.18 Comparison of spectra with and without pulse pileup rejection*

The overall counts are lower in the spectrum where PUR is in effect and the nitrogen ROI is more clearly defined than in the spectrum without PUR. The higher energy peak is the 10.83 MeV full energy peak and the lower is the 10.32 MeV single escape peak. Both spectra were taken with a proton energy of 2.3 MeV and an effective beam current of 0.4 μA, using the 16% nitrogen concentration phantom. The proton chopper was used at the optimum beam width of 150 μs, as established earlier, and both spectra were recorded in anticoincidence, ie when the beam was off. There are clearly more counts in the high energy region of the non PUR spectrum and very little in the PUR spectrum, demonstrating the effectiveness of the proton chopper combined with an efficient pulse pileup rejector.

Chapter 6

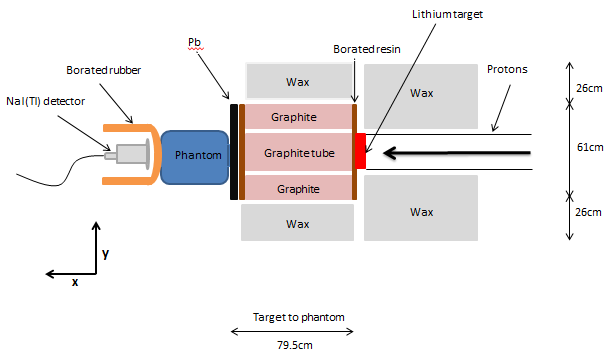
##### **Results**

***6.1 Introduction***

Apart from the flux suppression investigation that was large enough to warrant its own chapter and accompanying paper, an attempt will be made to set out the results chronologically, beginning with the acquisitions made using the original 5” NaI(Tl) detector, as described in Chapter 4, whereby data were collected for the full complement of nitrogen phantoms. In this way, the precision of measurements can be ascertained from those data, collected in 2011, and used as a comparison to the precision calculated after the system was improved by the replacement of the detectors, the addition of the proton chopper, and the use of the amplifier with pile up reject capability, where the data were collected in 2014, as described in Chapter 5. It is the precision that requires improvement, rather than the minimum detection limit, which is more common for systems requiring detection of trace elements. For the purposes of this work, however, it is already known that the human body should contain 2-3% nitrogen, as detailed in Chapter 1; therefore, it is more important to be able to detect small changes in the nitrogen, rather than being able to detect a small amount. This makes it more important to determine the precision of the system, rather than the minimum detection limit, as long as 2% nitrogen can be detected using this method. The goal for the level of precision should be 2% on the measurement, making an uncertainty of +/- 4x10-4 of the total sample.

***6.2 Experimental Set-up for Precision Calculations***

In order to determine the precision of the system, a complete set of phantom measurements was taken in 2011, henceforth referred to as (2011) and uncertainty calculations performed. Figure 6.1 shows the experimental set-up, which is the same as that used in Chapter 4 for the γ-ray part of the flux suppression investigation, (as shown in Figure 4.6 and described in section *4.4* *Quantification of flux suppression*).



*Figure 6.1 Set up for acquisitions used in precision calculations*

The NaI(Tl) detector used for the experiments has dimension of 5” diameter x 5” thick, and there was no PUR used, as indicated for these earlier experiments. The proton chopper was also not used in this particular set of experiments.

***6.2.1 Precision Calculations***

For the purposes of determining the nitrogen content from the 2.6% nitrogen phantom, in terms of counts, the background was subtracted by using the counts recorded from the 0%N phantom, assuming that the difference between the two is purely the counts from nitrogen. In addition, the area of the hydrogen peak at 2.22 MeV from the 0% nitrogen phantom was used to scale each of the nitrogen phantoms in turn, effectively eliminating the need to normalize to current while also accounting for any fluctuations in neutron flux, including flux suppression by the added nitrogen. Figure 6.2 shows the nitrogen region of the 16% nitrogen phantom, clearly showing that the full energy peak at 10.83 MeV can be fully resolved from the single escape peak at 10.32 MeV. There is also a hint that the double escape peak at 9.81 MeV is also visible. The feature at around 9.3 MeV is probably the 54Fe(n,γ)55Fe reaction at 9.295 MeV coming from iron in structural materials around the beam line and experimental arrangement. From the observation of the full energy and single escape peaks, the peak-to-peak energy difference is 0.511 MeV, which is equivalent to the full energy base width, indicated by the dotted lines on the graph. Therefore twice the full width at half maximum (FWHM) must be no more than 0.511 MeV, implying that the FWHM is no more than 0.256 MeV. Using this assumption, the nitrogen region of interest (ROI) can be extended to one FWHM beyond the full energy peak ,ie 10.83 + 0.256 = 11.086 MeV, and one FWHM below the double escape peak, ie 9.808 – 0.256 = 9.552 MeV, thereby defining the nitrogen ROI as 9.6 – 11.1 MeV.

*Figure 6.2 Nitrogen regions for the 16% nitrogen phantom*

The background beyond the nitrogen region, both higher and lower in energy should be included in the interrogation to determine precision. These areas extend to 3 σ, or approximately 3 x 0.256 MeV, which yields a ‘low’ energy ROI range of 8.7 to 9.5 MeV and a ‘high’ energy ROI range of 11.1 to 11.9 MeV.

The experimental configuration for data collected in 2014, henceforth referred to as (2014), was similar to that used for the (2011) data. However, the 5” NaI(Tl) detector, with an active volume of ~ 98 cubic inches, was replaced by a new cubic 4” x 4” x4” NaI(Tl) detector, with an active volume of ~ 64 cubic inches, as described in Chapter 5, section 5.5, and included the proton chopper and an amplifier with pileup rejection (PUR), described in Chapter 5, section 5.5.3.

Table 6.1 shows the results of the precision determination for the amount of net nitrogen (N2) from the full set of phantoms, for both (2011) and (2014) data, using standard uncertainty calculations. The 2014 data utilized both the proton chopper and pile up rejection. There are fewer counts in the 2014 data, which can be partly accounted for by the smaller active volume of the detector, as described above. The second reason is that the 2014 data were collected for a shorter physical time and at a lower proton energy (60 minutes at 2.5 MeV for 2011, 30 minutes at 2.3 MeV for 2014); the reason for both of these differences will be explained in section 6.2.2.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | 2011 | | | 2014 | | |
| Phantom | Net N2 counts | +/- | Precision | Net N2 counts | +/- | Precision |
| 0% | N/A | N/A | N/A | N/A | N/A | N/A |
| 2.6% | 2478 | 284 | 11% | 266 | 116 | 44% |
| 6% | 4223 | 314 | 7% | 764 | 127 | 17% |
| 9% | 5569 | 310 | 6% | 342 | 133 | 39% |
| 16% | 7310 | 356 | 5% | 1658 | 149 | 9% |

*Table 6.1 Precision calculations for 2011 and 2014 data*

***6.2.2 Experimental challenges***

In 2011, the KN accelerator was running reliably and the experimental requirements for proton energy and current could be routinely achieved and maintained for the duration of the experiments. However, a major water leak into the beam line occurred during 2012, which caused a series of major issues including contamination of the beam line, vacuum problems, gas depletion and a number of electrical problems, all of which took a long time to address.

In the running of the accelerator, insulating gas (sulphur hexafluoride, otherwise known as SF6) must be used in the van de Graaff tank in order to insulate against the negative charge generated in the tank, that is used to accelerate protons, from discharging to ground (arcing) randomly to places such as the walls of the tank, the accelerator column, the accelerator tube, the belt, and components inside the terminal, before they can be steered into the beam line. As the protons are accelerated to increasing energies, the gas pressure requirement increases as it is needed to support the higher charge state to increase this acceleration of the protons, which means that, for each energy required, a minimum volume of gas must be available as the insulator, to prevent discharge. Every time the tank is opened to address an issue, not only is some of the gas lost, but also the machine must be ‘conditioned’ slowly to reach the required proton energy again, otherwise discharges occur when the electrons find a path to ground. Once this happens, the ‘arc’ needs to be erased by careful running of the machine, bringing the energy up very slowly. A combination of depleted SF6, and a new technician/operator caused even further delays in attempting to reach the 2.5 MeV proton energy achieved in 2011. Eventually, more SF6 gas was purchased but, as time was now of the essence, the experiments of 2014 were conducted with the highest proton energy that could be maintained (2.3 MeV), even for a short period of time. Another ongoing issue with the accelerator is that it will overheat after a period of time, mainly due to the cooling water not being cold enough, and the cooling system needing a major overhaul. This issue has worsened over the years. The water temperature regulation is beyond the control of accelerator staff as it is maintained by facility services on the McMaster campus. The result of this is that the experimental running time for each run was severely compromised due to the need to complete full sets of phantom experiments in the short time available during each day before the accelerator had to be switched off in order to cool down.

***6.2.3 Uncertainty calculations***

The uncertainty calculations, resulting in the precision values shown in Table 6.1, were performed by taking the square root of the measured number, ie the raw counts. Subsequent propagation of uncertainties was calculated, depending on the manipulation of the raw counts. For example, when calculating the net N2 counts, there is a sequence of summations that needs to be performed and it begins with the raw counts in the three energy regions, ‘low’ ‘ROI’ and ‘high’. The uncertainty for each of these regions’ counts is just the square root of the counts. The next step is to scale the counts in each of the three regions to the corresponding counts in the 0% nitrogen phantom, as mentioned in section 6.2.1. Propagation of uncertainties is less straightforward here because the scaling factor involves the gross hydrogen counts in both the 0% nitrogen phantom and the % nitrogen phantom for which the calculations are being performed. Calculating the relative uncertainty in the scaling factor makes propagation easier later on and this is done as follows:

(2)

where *H* is the gross counts in the hydrogen peak of the 0% nitrogen phantom and *N* is the gross counts in the % nitrogen phantom. Now the absolute uncertainty in the scaled number of counts can be performed thus:

(3)

where *N* are the counts in either the ‘low’, ‘ROI’ or ‘high’ energy region of the %N in question, *∆N*  is the result of equation (2) and *s* is the result of multiplying the %N counts in question by the scaling factor.

Propagation of the uncertainties now requires the square root of the sum of the squares as follows:

(4)

where *∆A* is the uncertainty in the 0% nitrogen phantom and *∆B* is the uncertainty in the nitrogen phantom being summed.

Next, the net N2 calculation is performed by subtracting the ‘low’ and ‘high’ energy region counts from the ‘ROI’ counts. The associated uncertainties are calculated in the same way as equation (4). The precision was calculated by dividing the uncertainty in net N2 by net N2 and is therefore expressed as a percentage.

Superficially, it would appear that the precision is better overall for 2011. However, an examination of the strength of the relationship between counts, corrected only by scaling to hydrogen, provides further information. Correlation between counts in the five different phantoms and nitrogen content were performed for the three energy regions. So, by the use of statistics, specifically the Pearson product-moment correlation, r, and ‘Student’s’ t-test, t(3), a more in-depth analysis of the data can be achieved.

Table 6.2 shows the results of the Pearson product-moment correlation, and ‘Student’s’ t-test.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | 2011 | | | 2014 | | |
| Range (MeV) | r | p | t(3) | r | p | t(3) |
| 8.7-9.5 | 0.931 | ~0.02 | 4.415 | 0.975 | ~0.005 | 7.640 |
| 9.5-11.1 | 0.983 | <0.005 | 9.368 | 0.982 | <0.005 | 8.994 |
| 11.1-11.9 | 0.545 | >0.2 | 1.126 | 0.863 | >0.05 | 2.958 |

*Table 6.2 Statistical analysis results for 2011 and 2014 data*

The Pearson product-moment correlation measures the linear correlation between *x* and *y*, which are the nitrogen concentrations in the phantoms (*x*) and the net nitrogen counts (*y*). The calculated value falls between +1 and -1, where +1 is a total positive correlation, 0 is no correlation, and -1 is a total negative correlation. From Table 6.2 it can be seen that the results for the 2014 data correlate more positively overall, with the nitrogen region for both 2011 and 2014 being the same. This means that the improvements made to the system between 2011 and 2014 resulted in an overall improvement of being able to match the content of nitrogen in the phantoms to the number of counts recorded that correspond to the nitrogen content *in a consistent manner*. In other words, as the nitrogen content in the phantom being measured increases linearly, then so do the counts corresponding to that increase. However, in order to assess whether or not the correlation is statistically significant, the p-value should be interpreted along with the Pearson coefficient, which then determines if the correlation is real or not. If the p-value is low (generally <0.05) then the correlation is statistically significant and the Pearson coefficient has real meaning. Anything above this is generally interpreted as insufficient evidence of correlation, particularly if the sample size is small. The p-value can also be found from r, by looking it up in established tables. Table 6.3 is an excerpt from Bevington’s *Data Reduction and Error Analysis for the Physical Sciences*[66] of corresponding p-values for a known value of the Pearson correlation coefficient r, when n=5, the number of data points in each set, ie the counts each for 0%, 2.6%, 6%, 9% and 16% nitrogen phantoms. The p-value gives the probability of exceeding a value of r in a random sample, thereby testing the null hypothesis for no correlation, ie for a value of r, this is the probability of getting it purely by chance. This means that the smaller the probability, p, the less likely is the chance of getting it by accident, the more likely it is that there is some correlation (null hypothesis rejected).

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| p | 0.500 | 0.200 | 0.100 | 0.050 | 0.020 | 0.010 | 0.005 | 0.002 | 0.001 |
| r | 0.404 | 0.687 | 0.805 | 0.878 | 0.934 | 0.959 | 0.974 | 0.986 | 0.991 |

*Table 6.3 Excerpt of look-up table of p-values for n=5[66]*

The Student’s t-test is a measure of how well two sets of data can be compared and takes the form of:

(6)

where n is the number of observations, in this case 5 data points and (n-2) is the number of degrees of freedom, that is the total number of observations minus one degree of freedom for estimating the slope and minus one degree of freedom for estimating the intercept. Although it is generally accepted that *n* ≥ 6, J C F deWinter, in his 2013 paper[67] concluded that there are no principle objections for n < 5 but it should be noted that there is a greater risk of a false positive result with a small sample size. Other measures should be considered to add weight to the claim of an extraordinary result being true and the likelihood of a remarkable finding would need to be followed up by remarkable evidence. However, for the purposes of this test, the findings are not particularly remarkable and serve to suggest that the improvement in the 2014 data is a result of an improvement in the detection system. If t=0 then the two sets of data are indistinguishable with this null hypothesis being broken at t>2. For small numbers (n<30), t needs to be larger (>2) in order to reject the null hypothesis (p<0.05). Therefore, from the t-test results in Table 6.2 it can be seen that the two sets of data are indeed different, with the greatest difference being in the nitrogen ROI of the 2011 data. This test is difficult to interpret, other than the sets of data are different. The null hypothesis was that there was no correlation between the counts in a particular region and the nitrogen concentration. The null hypothesis is rejected (there *is* a correlation) for the 8.7 – 9.5 MeV and the 9.5 – 11.1 MeV regions for both the 2011 and 2014 data. It is accepted (there is *no* correlation) for the 11.1 – 11.9 MeV region for the 2011 data and it is marginal (p>0.05) in that region for the 2014 data.

Another way of looking at the data is to graph the non-zero nitrogen points and look at the slope and intercept, shown in Figure 6.3

*Figure 6.3 Net Nitrogen Counts vs % Nitrogen Concentration for 2011 and 2014 data*

Trend lines have been added to the graph, in order to estimate the slopes and intercepts for both sets of data. Using the equation for a straight line the slope and intercept for the 2011 data were found to be 358 and 1869 respectively and for the 2014 data 97 and -52 respectively, indicating that the smaller intercept for the 2014 data is probably due to pile up reduction and fewer high energy γ-rays being present. By taking the ratio of the intercept to the slope, in order to express the non-nitrogen counts as equivalent % nitrogen, 2011 yields 5.22 and 2014 yields -0.54, which could also be interpreted as a reduction in pulse pile up.

As was previously mentioned, another approach to demonstrate whether or not the 2014 data is an improvement on the 2011 data, despite the fact that there are fewer counts, would be to compare the ratios of nitrogen counts to gross counts. Table 6.4 (a), (b) and (c) are summaries of the counts for proportionality comparisons for each of the three regions of interest, respectively.

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| 1. **8.7-9.5 MeV Region of Interest** | | | | | | | | |
|  | 2011 | | | | 2014 | | | |
| % N | Gross | Net | Net/Gross | Gross-Net | Gross | Net | Net/Gross | Gross-Net |
| 2.6 | 26384 | -578 | -0.0219 | 26962 | 4677 | 630 | 0.1348 | 4047 |
| 6 | 30131 | 3169 | 0.1052 | 26962 | 5617 | 1570 | 0.2795 | 4047 |
| 9 | 29071 | 2109 | 0.0725 | 26962 | 5952 | 1905 | 0.3201 | 4047 |
| 16 | 36851 | 9889 | 0.2684 | 26962 | 6779 | 2732 | 0.4030 | 4047 |
|  |  |  |  |  |  |  |  |  |
| 1. **9.5-11.1 MeV Region of Interest** | | | | | | | | |
|  | 2011 | | | | 2014 | | | |
| % N | Gross | Net | Net/Gross | Gross-Net | Gross | Net | Net/Gross | Gross-Net |
| 2.6 | 9331 | 1291 | 0.1384 | 8040 | 2426 | 920 | 0.3793 | 1506 |
| 6 | 15147 | 7107 | 0.4692 | 8040 | 3868 | 2362 | 0.6106 | 1506 |
| 9 | 15424 | 7384 | 0.4787 | 8040 | 3857 | 2351 | 0.6096 | 1506 |
| 16 | 25499 | 17459 | 0.6847 | 8040 | 5983 | 4477 | 0.7483 | 1506 |
|  |  |  |  |  |  |  |  |  |
| **(c) 11.1-11.9 MeV Region of Interest** | | | | | | | | |
|  | 2011 | | | | 2014 | | | |
| % N | Gross | Net | Net/Gross | Gross-Net | Gross | Net | Net/Gross | Gross-Net |
| 2.6 | 1184 | -609 | -0.5138 | 1793 | 281 | 24 | 0.0862 | 257 |
| 6 | 1508 | -285 | -0.1891 | 1793 | 285 | 28 | 0.0980 | 257 |
| 9 | 1499 | -294 | -0.1965 | 1793 | 361 | 104 | 0.2878 | 257 |
| 16 | 2053 | 260 | 0.1266 | 1793 | 344 | 87 | 0.2528 | 257 |

*Table 6.4 Comparison of nitrogen proportional counts for 2011 and 2014 in each of the three energy regions of interest: (a) 8.7 – 9.5 MeV, (b) 9.5 – 11.1 MeV, (c) 11.1 – 11.9 MeV*

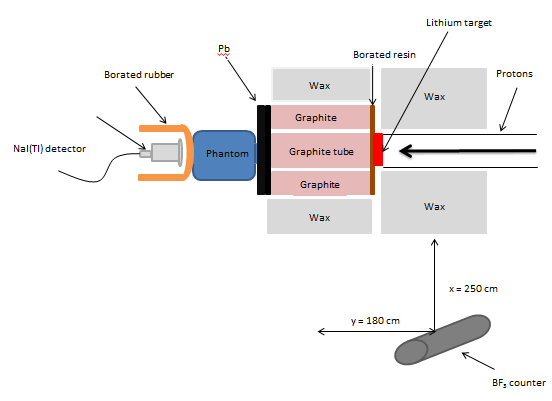
The *Gross* column represents the counts from each of the phantoms in that particular region of interest after being scaled to the 0% phantom counts for that region, effectively normalizing the counts. The *Net* column represents the gross counts from each of the phantoms in that particular region of interest, minus the 0% phantom counts, effectively removing the background counts. The *Gross-Net* column shows those counts just described, ie the 0% counts for 2014, which contribute a difference of 15.0% for the (a) region, 18.7% for the (b) region and 14.3% for the (c) region and, as they are lower for the 11.1 11.9 MeV region of interest, this could be further evidence of the effect of pile up rejection and elimination of high energy γ-rays in this region. It can be seen that the proportion of nitrogen counts (Net/Gross columns) for the 2014 data are consistently higher than those for the 2011 data, supporting the claim for improved collection technique in the 2014 data.

***6.3 Target performance monitoring***

As mentioned elsewhere in this thesis, the target used in the KN accelerator consists of lithium, as the threshold for neutrons occurs at a proton energy of 1.88 MeV, making it easily achievable for the range of energy available to the accelerator. The target is constructed of a brass holder, whereupon lithium is melted onto the surface; the target assembly is then very quickly removed from an air environment in order to reduce oxidation on the surface of the lithium, which can occur in a very short period of time. It is necessary to prevent or, at least, reduce oxidation in order to reduce contaminants, which interfere with the yield of neutrons from the target. Once the target is in use, degradation occurs over time; the higher the current intensity the faster the target will degrade as the lithium vaporizes. Carbonization from pump oil in the beam line causes target degradation, as well as oxidation from an imperfect vacuum and vaporization of the lithium. If the beam spot occurs in the same place on the target over a period of time, carbonization, oxidation and vaporization will intensify in that spot, making the surface lithium uneven, which may cause fluctuations in neutron flux. In order to monitor the combined effects of these processes, it is wise to be able to record the number of neutrons being generated by the 7Li(p, n) reaction on the target in order to determine if the yield is decreasing over time. This is useful for corrections in experiments and also gives an indication of when the target needs to be replaced.

***6.3.1 Experimental Set Up***

The experimental set up is exactly the same as for the beam optimization investigation in Chapter 3, Section 3.2 where the NaI(Tl) detector was used during different combinations of proton energy and beam current to determine the optimum neutron penetration into the phantom for maximum nitrogen detection. Figure 6.4 shows the full set up, including the positioning of a BF3 counter, placed to monitor neutron counts during experiments.



*Figure 6.4 Experimental set up showing positioning of BF3 counter*

By recording the counts from the BF3 counter, during the length of each experimental run and comparing them with the integrated current on the target, any fluctuation in counts/μcoulomb should indicate a change in neutron flux. Figure 6.5 shows how the counts/μcoulomb fluctuates from run to run, over a period of 3 days. The visible rise in counts/μcoulomb at time points 5 and 6 could be attributed to a variation in the beam spot on the target, yielding a higher neutron flux due to the reaction of the protons in a ‘fresh’ area of the target. Similarly, the dip at time point 13 could be due to a tight beam spot in an already used point on the target. However, there is no documented explanation for why these fluctuations occur and all yields are within the accepted range of fluctuations for the target, ie between 440,000 and 670,000 counts/μcoulomb, where fluctuations are expected between 400,000 and 700,000. This indicates that there was no serious degradation of the target during the runs.

*\*

*Figure 6.5 Counts/μcoulomb shown sequentially for each individual run*

Table 6.5 shows the data with uncertainties used in constructing Figure 6.5. The uncertainties are too small to show in the graph, as they amount to 0.3 – 0.5% of the counts/μcoulomb.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Date | count/μC | +/- | Date | count/μC | +/- |
| 5/7/11 | 529466 | 2470 | 6/7/11 | 567556 | 1801 |
| 5/7/11 | 509717 | 3382 | 6/7/11 | 566785 | 1775 |
| 5/7/11 | 527890 | 2479 | 6/7/11 | 566911 | 1771 |
| 5/7/11 | 528491 | 2477 | 6/7/11 | 567209 | 1775 |
| 5/7/11 | 595335 | 2648 | 8/7/11 | 579784 | 2631 |
| 6/7/11 | 665373 | 2884 | 8/7/11 | 437783 | 1484 |
| 6/7/11 | 547530 | 1737 | 8/7/11 | 549146 | 2542 |

*Table 6.5 Data used in Figure 6.5*

Calculating the mean of the individual counts in Table 6.5 and the standard deviation gives

(5.52 +/- 0.50) x 105 . The standard deviation is ~10%, which is more than an order of magnitude higher than the highest uncertainty in an individual count, meaning that there is an additional uncertainty in the results, most likely due to the variation in counts arising from the beam on target. Although this uncertainty cannot be quantified, it should not affect any nitrogen measurements, provided that the N/H ratio is taken.

***6.4 Timing window identification – the early days***

When the proton chopper, described in detail in Chapter 5, Section 5.4, was first set up to be used in these experiments, a method to identify the optimum timing window was devised for the system that was currently in place. This was before the multi-scalar, described in Chapter 5, was available, so the method was constrained by the electronics available at the time.

***6.4.1 Detector array***

Six 4” x 4” x 4” cubic NaI(Tl) detectors were used for this series of experiments. A schematic for the system is shown in Figure 5.8 and a description given in Chapter 5, Section 5.4.

***6.4.2 Rationale***

In order to determine the best timing window available, using the proton chopper to maximize the number of thermal neutrons and minimize the number of unwanted high energy γ-rays from the target, a number of experiments was conducted simply to vary the time interval and pulse width of the chopper and compare the results. By comparing the nitrogen ROI to the high energy region, the ratio from the counts in the two regions should indicate the best timing parameters. This seemed to be a logical approach, as there were no other means available at that time to determine the window.

***6.4.3 Experimental Set up***

All six detectors were used for the experiments, stacked two high, three across at the far side of the 16% nitrogen phantom, similar to Figure 6.4, without the BF3 counter. The detectors were gain-matched by inspecting the 1.33 MeV energy peak from a 60Co source and ensuring that each detector used the same channel on the MCA spectrum for the peak counts.

***6.4.4 Method***

The initial parameters for the proton chopper were a 4 μs pulse and a sweep interval of 60 μs, purely as a place to begin. An external trigger was placed in the system (see Figure 5.8) to control the start time for counting, after the beam was effectively ‘off’. There is a known delay between the sync pulse from the proton chopper and the beam actually impacting the target, estimated to be roughly 3 μs. Therefore, anything less than an 8 μs delay will result in counting γ-rays from the 7Li(p,n) reaction on the target. The delay time for the external trigger was varied from 5 μs to 8 μs to determine if the delay from the sync pulse was indeed around 3 μs. If this was truly the case, then the high energy γ-rays would be recorded in the spectra for a delay time less than 8 μs. The sweep interval was varied from 60 – 190 μs to allow counting for longer periods between pulses and to determine the maximum collection time. Figure 6.6 shows spectra of continuous beam, 7μs delay and 8 μs delay.

*Figure 6.6 Spectra acquired using the proton chopper in different configurations*

Each run was scaled to the gross hydrogen peak area of the 7μs/85μs run, purely because it had the highest area and all runs were corrected for variations in dead time. Additional run data were discarded when the count rate in the hydrogen peak became excessively high for the expected count rate for beam pulsing. The reason for this is that, during the later runs it became evident that a loose electrical connection had caused the proton chopper to malfunction and it was not obvious when this had occurred, indicating that at least some of the data may have been recorded during the malfunction. The count rate threshold was set to 774 ± 60 cps retrospectively as, once the proton chopper was working properly, subsequent runs confirmed the typical expected count rate during pulsing. On inspection of Figure 6.6, the 8 μs delay run appears to cut off the high energy γ-rays, while the 7 μs runs still have counts in the high energy region, with the exception of the 7 μs/70 μs run. The 8 μs/60 μs run appears to show a reduction in counts at energies below and above the nitrogen region. In conclusion, inspection of the spectra is not a sufficient method to determine the best beam window.

Another way of looking at the data is to determine the ratio of the nitrogen region to the high energy region. As the nitrogen content is consistent, any variation in counts in the high energy region will be reflected in the ratio. Figure 6.7 shows the results of comparing these two regions as a ratio.

*Figure 6.7 Ratio of nitrogen to high energy γ-rays*

The energy region for the nitrogen ROI was set as 9.5 – 11.1 MeV and the high energy region as 11.1 – 22.69 MeV, which is where the counts for all runs drop to zero. By using this method, it is clear that the 8 μs delay and 60 μs interval shows the best nitrogen to high energy γ-ray ratio. This method is tedious to perform and, as was described in Chapter 5, a better method was determined for optimizing the beam window. In comparison, the configuration determined to be the optimal beam window was 150 μs and 2 ms. However, the proton energy and current used were different to those used in this set of experiments. It was not possible to investigate further using this configuration as problems occurred with the KN accelerator, as described in 6.2.2 earlier, taking it offline for seven months, by which time the scalar and new electronics were available.

Chapter 7

##### **Conclusions and Future Work**

***7.1 Conclusions***

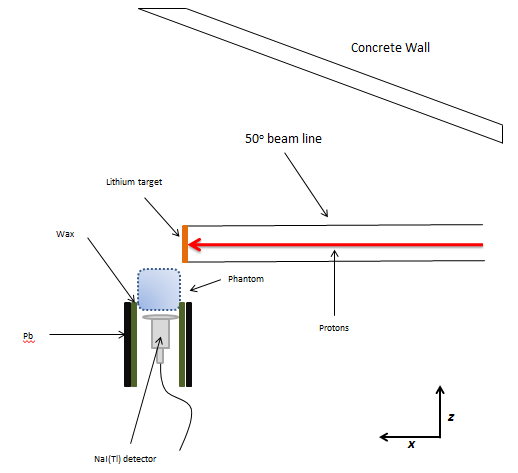
It is important to be able to measure nitrogen via the 14N(n,γ)15N reaction *in vivo* for a number of reasons. Firstly, it is a convenient, accurate and non-invasive method to determine protein content in the human body, which can be used as a benchmark to assess changes in content over time in patients who have suffered from trauma, disease or malnutrition. Secondly, it is useful as a tool to help in determining the other body composition compartments by eliminating that portion of total body composition, not by estimation, as in some studies, but by accurate measurement, thus narrowing the margin for error when other body compartments cannot be assessed directly. For example, as explained in detail in Chapter 1, the three-compartment model uses the technique of bioelectrical impedance analysis to measure total body water, which is then used as a fixed proportion to estimate fat-free mass, thus assuming a protein estimate. However, if the subject is ‘non-normal’ and does not fit into the standardized assumptions, then protein content can be under- or over-estimated. The four-compartment model, with the addition of bone density measurements, is more accurate than the three-compartment model. However, protein is again measured indirectly by making estimates. As bone density measurements are based on experimental data from ashed bone with the addition of hydration factors and attenuation coefficients, the latter of which are very similar in value for estimating fat mass and fat-free mass when using DXA for bone density measurements, any inaccuracy will again result in an over- or under-estimation of protein. By measuring protein via nitrogen using neutron activation analysis, and physically measuring the other body compartments, an accurate assessment of the individual subject can be made and any necessary treatment would, therefore, be more effective than using only estimates or, in some extreme cases, guesswork. Thirdly, it can be used as a more straightforward and non-invasive alternative to the Kjeldahl and Dumas methods to determine the protein content in food.

During early investigations of measuring nitrogen at McMaster University, it was discovered that, as nitrogen content increased, hydrogen counts decreased, beyond the level of physical content of hydrogen in the phantom. Extensive investigations concluded that, if hydrogen were to be used as an internal standard for the measurement of nitrogen, then the results should be adjusted positively by 7.01± 0.1% for typical human body content nitrogen. Flux suppression has been investigated elsewhere[68], however that work concentrated on flux suppression (neutron absorbing elements and neutron self-shielding) in nuclear reactors and the equations derived from the work are unsuitable for application to proton accelerators, as the neutron spectrum is different for a reactor.

Using the 14N(n,γ)15N reaction to measure the prompt γ-rays that decay from the capture state of 15N directly to the ground state 15% of the time, a region of interest can be determined, which should contain only those decays from nitrogen, as there are no other elements that are activated by neutron capture and emit γ-rays in this same region of interest. However, interference arises from γ-rays in the 17 MeV energy region, arising from the 7Li(p,γ)7Be reaction of the accelerator target, used to liberate the neutrons for the nitrogen measurements. The Compton portion from these γ-rays overlaps the region of interest for nitrogen and so a method was devised to eliminate them. During these measurements, it was determined that the best beam energy and current for the maximum penetration of neutrons and detection of the resulting γ-rays through a body-sized phantom was 2.5 MeV proton energy and 0.3 μA current. By implementing the use of a proton chopper, the unwanted high energy γ-rays can be filtered out after identification of the best pulsing length and counting time. This, combined with a pileup rejector, can result in further reduction of unwanted counts in the nitrogen region of interest, improving the overall precision of the system. Although the KN accelerator could be used for these feasibility studies, the length of time lost due to long periods of ‘down time’ as a result of the age of the machine (built in 1955) making it susceptible to frequently breaking down and the fact that replacement parts are hard to acquire, makes these breakdowns a major issue. The skill required to replicate specific beam conditions is not trivial and again adds to the whole issue of reliability in creating a steady neutron field as, and when, required by the experimenter. If this project is to move beyond the feasibility stage to an actual patient facility, then serious consideration should be given to acquiring a dedicated neutron-producing accelerator, such as the relatively inexpensive compact D-D accelerators, which could bring the whole system into the ‘portable’ arena. Using a D-D accelerator would also eliminate the issue of unwanted high energy γ-rays, as they are not produced in the D-D reaction, however, pulsing would still be useful to separate γ-rays produced by fast neutron events from those produced by thermal neutron events.

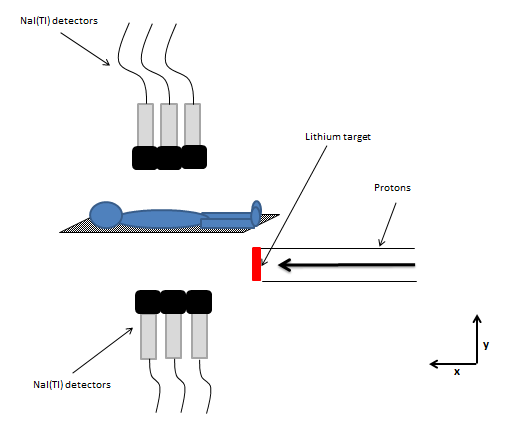
***7.2 Future Work***

The ultimate goal of the nitrogen detection system is to measure *in vivo* nitrogen in the human body. The practicalities of achieving this would mean that the patient would be most comfortable in a supine position, considering that the minimum length of time required to perform the measurements would most likely be 30 minutes. In order to make this possible, a feasibility study is required to detect γ-rays from nitrogen at an angle of 90o to the beam line, horizontally rather than vertically at this stage, as shown in Figure 7.1, as the orientation for a feasibility study would have no bearing on the results, even though the final measurements would be done vertically, with the patient supported horizontally, as shown in Figure 7.2. Monte Carlo simulations would be necessary to determine the level of shielding required, including any improvements that may arise from the use of collimation and reflector materials.



*Figure 7.1 90o Positioning of phantom and detector for feasibility study*

A platform to support the bed on which the subject lies would have to be engineered, as well as supports for the proposed positioning of the NaI(Tl) detectors, above and below the subject. It may even be sufficient to position all six of the detectors above the subject, thus eliminating the need for extra neutron shielding around the detectors that would be positioned below, as they would be more vulnerable from activation than those above, where the subject provides a level of natural shielding.



*Figure 7.2 Proposed positioning of patient and NaI (Tl) detectors*

Improvement in the detection of nitrogen should be possible with the implementation of a digital pulse-processing system, currently in its early stages of testing at McMaster University. The system is supplied by CAEN and is capable of providing time markers in order to be able to recover cascade nitrogen counts. The principal idea is to use coincidence summing in order to isolate nitrogen cascade events from the background, thus recovering much more than the 15% presently detectable. The six NaI(Tl) detectors provided at the same time as the CAEN system should also improve detection by capturing more of the γ-rays from the 14N(p,γ)15N reaction than is currently achievable.

An alternative to the proton chopper would be a raster system consisting of a rotating disk, with slots cut into the edges of the disk pointing towards the centre. The speed of the disk would dictate the frequency of the beam pulsing and has the advantage of being a lot more stable to beam focusing fluctuations. The main disadvantage is that it is more difficult to control the cycle length, ie the ‘beam off’ time, or when counting would take place. However, a raster system would be useful for analyzing nitrogen, and hence protein, content in food, which is an important field of study, as discussed briefly in Chapter 2. It would certainly rival current popular methods such as the Dumas and Kjeldahl methods in time spent analyzing the samples and the fact that it is a non-destructive method.

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##### **Appendix**

c Created on: Thursday, October 17, 2013 at 10:19

c graphite

5 236 -2.16 -180 181

6 236 -2.16 -183 181

c cooperite

7 257 -2.29 201 -200

c target holder

500 8 -8.6 -520 550 -555 $brass cap

510 4 -2.702 (510 -520 555 -560 ):(-520 560 -565 ): $ aluminum

(500 -520 -575 565 ):(575 -570 500 -530 ):(570 -580 525 -530 ):

(525 -530 -550 585 )

520 280 -1 -510 555 -560 $water coolant

c Phantom

9 282 -1 302 -303 304 -305 306 -407 #206

c neutron counter inside phantom position 0 cm

206 281 1.074e-006 207 -208 -206

c experimental space

901 204 -0.001225 -900 (-306 :303 :307 :-302 :-304 :305 )#5 #7 $ our space

#500 #510 #520

902 0 900 $ outside world

c Graphite beam guide

180 rpp -20 20 -20 20 30 60

181 cz 6.5

183 rpp -10 10 -10 10 0 30

c Cooperite

200 rpp -25 25 -25 25 -30 30

201 rpp -10 10 -10 10 -30 30

c target holder

500 500 cz 2.1

510 500 cz 2.3

520 500 cz 2.5

525 500 cz 3

530 500 cz 4.8

550 500 pz 0

555 500 pz 0.26

560 500 pz 0.88

565 500 pz 1.22

570 500 pz 1.72

575 500 pz 1.52

580 500 pz 2.22

585 500 pz -1.1

c our space

900 rpp -50 50 -50 50 -40 100

c Phantom

302 px -11.5

303 px 11.5

304 py -13

305 py 13

306 pz 68

307 pz 95

c neutron counter 0 cm size and position

206 c/y 0 84.5 1

207 py -12

208 py 12

mode n

c TARGET HOLDER (Brass Cap & Aluminum)

m4 13027. 1 $MAT4

m8 29000. -67 $MAT8

30000. -33

c GRAPHITE

m236 6000.60c -1 $MAT236

c COOPERITE

m257 5010.70c 4 $MAT257

11023.70c 2 8016.70c 22 6000.70c 23

1001.70c 49 17000.66c 1

c WATER COOLANT

m280 1001. -0.111915 $MAT280

8016. -0.888085

c BF3 COUNTER

m281 5010. -0.031569 $MAT281

5011. -0.127809 9019. -0.84056

c 6% N PHANTOM

m282 1001. -0.105397 $MAT282

8016. -0.808889 6012. -0.025714 7014. -0.06

tr500 0 0 -3.22

imp:n 1 7r 0 $ 5, 902

c imp:n 1 2r 102 20 96 9 $ 5,

c 14 32 87 254 713 $ 10,

c 1761 3279 7517 1r 1 0 $ 15,

c imp:p 1 8r 0 $ 5, 902 mt236 grph.60t

mt280 lwtr.60t

c --------------------- SOURCE CARD ---------------------

c

c Proton energy 2.440MeV, 0-180 deg, Generated 20120620

sdef: pos=0 0 35 vec=0 0 -1 dir=d501 erg=fdir d502

sc501 angular probability pdf - differential values

NOTE: The rest of the source card is not included, for brevity.