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THE USE OF NUCLEAR RESONANT SCATTERING OF GAMMA RAYS
FOR IN VIVO MEASUREMENT OF IRON

MASTER

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1. INTRODUCTION

The study of elemental composition of human body in vivo is of considerable value in medical research and clinical practice¹). A knowledge of the quantity of the element in specific organs may aid in diagnosis and repeated measurements over a period of time may be used to monitor the effect of treatment. Of the nuclear methods only those that allow sufficient penetration into the bulk medium of the human body could be used. This limits the techniques to those employing either neutrons, energetic charged particles or photons. Neutrons have been used extensively for the in vivo measurement of Ca, Na, Cl, P, N, H, and Cd^{2,3,4}). These methods are now established as useful diagnostic tools. Energetic protons have been used for the determination of Ca in the spine⁵) and elemental analysis using mesonic x-rays have also been proposed^{6,7}). McNeil⁸) considered the possibility of gamma ray activation analysis for the in vivo elemental determination, using high energy bremsstrahlung. X-ray fluorescence has been used recently for the in vivo determination of cadmium, lead and iron^{9,10,11,12}).

A method of analysis using the nuclear resonant scattering (NRS) of gamma rays is described. This method has been used previously in analysis of some mineral ores, principally copper and nickel^{13,14}). Although this method has been limited to investigation of only few elements^{15,16}), it has a large potential for the determination of elements in vivo as it is very specific to the element under investigation and the possibilities are still largely unexplored. In this paper the method and some results obtained in in vivo measurement of iron in patients are presented.

2. PRINCIPLE OF THE METHOD

In nuclear resonant scattering of gamma rays, the nucleus of the target under interest is raised to its excited state by gamma rays and then decays back to the ground state by emission of a gamma ray. For the measurement of iron, the nucleus of ^{56}Fe is raised to its first excited state, 847 keV. The lifetime of this level is 7 ps. The cross section for the excitation of this level exhibits resonance behavior: the reaction may occur only when the energy of the incident gamma rays falls within the energy width of the 847 keV level, which is approximately 1 eV at room temperature. Because of the sharp resonant behavior, the main experimental problem is to obtain a gamma-ray source with sufficient intensity in the energy region of the first level of ^{56}Fe .

The obvious choice for a source of gamma radiation is an isotope that decays through the state of the nucleus under investigation. A suitable isotope for the excitation of ^{56}Fe is ^{56}Mn which decays by β^- emission to the first excited state of ^{56}Fe , and thus supplies the necessary 847 keV gamma rays. However, due to recoil of the nucleus in the emission and absorption processes, the energy of the excited photon is not sufficient to develop resonance condition. The recoil energy deficit is computed from

$$\Delta E = E_0^2/Mc^2 \quad (1)$$

where E_0 represents the gamma-ray energy and M the mass of the recoiling nucleus. For ^{56}Fe , the recoil deficit is approximately 14 eV. This recoil loss can be restored with the aid of radioactive decay-induced Doppler broadening. If the photon is emitted from a moving nucleus, the change in the energy dE of the photon is

$$dE = E_0 \frac{v}{c} \cos \theta \quad (2)$$

where v represents the velocity of the nucleus and θ is the angle between the direction of the motion and the emission of the photon. In the radioactive decay-induced Doppler energy shift, the nucleus is set into motion through recoil resulting from the emission of a particle prior to the emission of the exciting gamma ray. The energy of the emitted gamma ray resulting from Doppler broadening can be expressed as

$$E(v, \theta) = E_0 \left[1 + \frac{v}{c} \cos \theta - \frac{E_0^2}{2Mc^2} \right] \quad (3)$$

If the energy spectrum of the particle preceding the gamma ray is known, it is possible to calculate the microspectrum of the exciting gamma-rays. In the $^{56}\text{Mn} \rightarrow ^{56}\text{Fe}$ decay, the 847 keV gamma-ray is preceded by four cascades which lead to the 847 keV level. In 47% of the decays there is a direct population of this level by a β -particle transition, with an endpoint energy of 2.84 MeV. This transition alone can add as much as 54eV to the energy of the emitted gamma-ray.

The velocity of the recoiling nucleus will shift the gamma-ray energy only when the nucleus has a collision time which is large compared to the 7 ps lifetime of the 847 keV level. This is because the gamma-ray must be emitted by the moving nucleus before it loses its velocity as a result of collisions with neighboring atoms. This condition can best be fulfilled when the radioactive source is in a gaseous phase, since it then has sufficiently large intermolecular distances. Fig. 1 shows a diagrammatic representation of the emission line in both the solid and the gaseous phase. It has been calculated¹⁶⁾ that in the gaseous phase, about 0.75% of the gamma rays have the energy

required to develop resonance. For this fraction of resonant gamma rays, the effective cross section for the measurement of ^{56}Fe is about 14 mb.

3. FACILITY FOR THE IN VIVO DETERMINATION OF ELEMENTS

3.1 Source Preparation

For the measurement of ^{56}Fe , the source consists of 1.3 mg of MnCl_2 placed in an evacuated quartz capsule of 15 cm^3 in volume. The source is irradiated for 4 h in a neutron flux of $5.5 \cdot 10^{14}\text{ n s}^{-1}\text{ cm}^{-2}$ and then stored for about 1 h to reduce the activity from ^{37}Cl . The ^{56}Mn activity at the start of the measurement is 650 mCi.

3.2 Irradiation-detection Facility

The irradiation detection facility consists of a rectangular lead cask with stainless steel lining which includes the compartment for the tube furnace. The furnace is used to bring the source to a gaseous phase by heating to about 1000°C . It consists of 2.5 cm diameter nickel tubing wound with nichrome wire. The temperature of the source was measured with a chromel-alumel thermocouple in contact with the tube. Fig. 2 shows a cross-sectional view of the facility and Fig. 3 shows the lead cask and the furnace. Since the heated source emits strong thermal radiation, it is necessary to protect the patient from the heat with a heat shield made of aluminum sheet. This aluminum sheet is used also to eliminate the dose due to β -particles emitted from the source. The detection system consists of two HPGe detectors having total relative efficiency of 50% and resolution of 1.9 keV. The detectors are heavily shielded on the side with 5 cm layer of Bi, and their face is covered with 0.64 cm lead disc to reduce the count rate of the low energy radiation scattered by the body at about 90° to the incident photon beam. Fig. 4 shows a typical spectrum obtained in the measurement of Fe.

4. PHANTOM AND PATIENT STUDIES

In order to obtain accurate results, it is important to investigate such factors as patient geometry, organ depth and spatial sensitivity. Since the attenuation of the 847 keV gamma ray in tissue is not negligible ($\mu = 0.08 \text{ cm}^{-1}$), it is necessary to locate the organ under investigation (liver or heart) in the patient by the means of ultrasound. The amount of the overlying tissue is determined, and a correction made by using experimentally determined correction factors. The correction curves Fig. 5 were determined by moving a liver-like container filled with Fe solution within a tank of water and recording the resonant yield for each position. The determination of iron in the patient is made by comparison with a result obtained from measurement of an Alderson antropomorphic phantom containing known amounts of Fe in liver or heart.

An additional important factor that requires investigation is the effect of the molecular form of the target. This effect may arise from a different broadening of the absorption line for various compounds. In addition to the thermal component, the energy of the atom contains another component arising mainly from the zero-point energy of vibration. Any effects due to the molecular form of the target may be of importance since the iron used in the phantom is in ionic form ($\text{Fe}(\text{NO}_3)_3$ in water) where as a different molecular form may be present in the organ of the patient. The effect of absorption line width of the effective NRS cross-section was investigated by changing the temperature of an iron scatterer. In solids the Doppler width has to be calculated by taking into account the crystalline binding which is characterized by the Debye temperature. In such case the actual temperature is replaced by an effective temperature which is somewhat larger than the actual temperature of the scatterer¹⁷). Table 1 shows the results obtained in this experiment. It can be observed that the

broadening of the absorption line by a factor of 2.64 did not affect the NRS effective cross-section. It can be inferred from this that the microspectrum of the incident gamma ray does not vary rapidly in the region of the absorption line, and the use of a gaseous $^{56}\text{MnCl}_2$ source minimizes the effects due to possible difference in the absorption line width.

The effect of different molecular forms of iron was investigated using the compounds shown in Table 2. Using solution of $\text{Fe}(\text{NO}_3)_3$ as a reference the resonant yield from other iron forms is shown in Table 2. It can be observed that the yield from the solid compounds is not significantly different from the iron in solution. Although the yield obtained from Fe_2O_3 is slightly higher, this could be due to in part the errors introduced by the correction for the self absorption effects.

The clinical facility previously described is used to measure iron in the liver and heart of patients suffering from iron overload diseases. In these patients the liver content iron may vary from 0.2 to 14.3 g and 0.04 - 0.62 g in the heart. In order to assess the effectiveness of chelating agents in removing iron from the body it is necessary to have information on the iron stores status. For the measurement of the iron in the liver the patient lies prone such that the liver is positioned above the collimated source. The gamma rays resonantly scattered from the iron in the organ are measured at 90° . Fig. 6 shows a spectrum obtained from a liver of a patient suffering from thalassaemia major. By comparison with the phantom, the concentration of iron in the liver for this patient was estimated to be 6.3 ± 1.9 mg/g. The dose to the liver was 1.7 rem.

5. DISCUSSION

A method for a measurement of iron in an organ of a living human has been described. The specificity of the technique is an important consideration.

Since the absorption line is only about 1 eV wide the problems of interference from other elements is negligible. The method is not limited to the detection of iron. Elements of interest which may be detected at physiological concentrations by NRS include Mg (using ^{24}Na vapour source) ^{28}Si (using ^{28}Mg vapour source) and ^{65}Cu (using $^{65}\text{ZnI}_2$ vapour source).

It is observed that the yield of NRS for iron is independent of the chemical form of the scattering element. This is important, since it does not require a phantom with the same iron form as that found in the organ.

FIGURE CAPTION

1. Diagramatic representation of the line shapes and positions of the 847 keV ^{56}Mn gamma rays emitted and absorbed by ^{56}Fe . The emission line shape in the gaseous phase is shown for illustration only.
2. The cross section of the facility for NRS of body elements.
3. Lead case and the tube furnace which houses the source.
4. A typical spectrum obtained in NRS from a phantom containing Fe in the liver.
5. Correction curves for correcting for different liver geometries, normalized to a geometry of an antropomorphic Alderson phantom.
6. Spectrum obtained from a liver of a patient suffering from iron overload disease. Iron concentration 6.3 ± 1.9 mg/g.

REFERENCES

- 1) S. H. Cohn, K. J. Ellis, I. Zanzi, D. Vartsky and J. F. Aloia, Atomic Energy Rev. Vol. 18 (1980) 599.
- 2) IAEA, In-vivo Neutron Activation Analysis, STI/PUB/322 (1973).
- 3) D. Vartsky, K. J. Ellis and S. H. Cohn, J. Nucl. Med. 20 (1973) 1158.
- 4) J. S. McLellan, B. J. Thomas, J. H. Fremlin and T. C. Harvey, Phys. Med. Biol. 20 (1975) 88.
- 5) R. F. ~~Silbert~~ ³, A. M. Koehler, J. M. Sisterson and R. Wilson, Phys. Med. Biol. 22 (1977) 817.
- 6) R. L. Hutson, Trans. Am. Nucl. Soc. 18 (1974) 98.
- 7) M. C. Taylor, L. Coulson and G. C. Phillips, Rad. Res. 54 (1973) 335.
- 8) K. G. McNeill, Physics Today 27, No. 4 (1974) 75.
- 9) L. Ahlgren and S. Mattsson, Phys. Med. Biol. 24 (1979) 136.
- 10) L. Ahlgren and S. Mattsson, Phys. Med. Biol. 26 (1981) 19.
- 11) L. Wielopolski, D. N. Slatkin, D. Vartsky, K. J. Ellis and S. H. Cohn, IEEE Trans on Nucl. Sci. 1 (1981) 114.
- 12) R. Zeimer, M. Belkin, E. Leitersdorff and E. A. Rachinilewitz, J. Lab. Clin. Med. 91 (1978) 24.
- 13) B. D. Sowerby, Nucl. Instr. Meth. 94 (1971) 45.
- 14) B. D. Sowerby, Nucl. Instr. Meth. 108 (1973) 317.
- 15) D. Vartsky, B. J. Thomas, D. J. Hawkes and J. H. Fremlin, Phys. Med. Biol. 21 (1976) 970.
- 16) D. Vartsky, K. J. Ellis, D. M. Hull and S. H. Cohn, Phys. Med. Biol. 24 (1979) 689.
- 17) W. E. Lamb, Phys. Rev. 55 (1939) 190.

TABLE 1

NRS YIELD R VERSUS TARGET TEMPERATURE

T ACTUAL °K	T EFF °K	DOPPLER WIDTH eV	R(T)/R(293°K)
77	182	0.66	1.03 ± 0.04
293	331	0.89	1.00 ± 0.04
693	710	1.30	0.95 ± 0.04
973	982	1.53	1.01 ± 0.04
1273	1273	1.74	1.02 ± 0.04

TABLE 2

<u>COMPOUND</u>	<u>RESONANT YIELD</u>
$\text{Fe}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$ IN H_2O	1.00 ± 0.08
$\text{Fe}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$	1.12 ± 0.08
Fe_2O_3	1.14 ± 0.04
FeSO_4	0.98 ± 0.06
FE METAL	0.96 ± 0.03

Fig. 1

Fig. 2

Fig. 3

21-APR-81 16:25:00 SE=2/ 3 DU=1/ 2 AC=:2 DE=LOG DE= 52.174 +
 GE FULL SPECTRUM_

	ACQGRP	3
	GROUPS	4
PHA	MEANS	1024
SETUP	DIGOFF	1
	CPS	0

	PRESET	0	ELAPSED	0
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TIME	00:00:00		00:02:12	
REAL				

Fig. 5

08-AUG-80 12:49:56 $\overline{QA}=2/$ 2 $\overline{QU}=2/$ 1 $\overline{AC}=12$ $\overline{QE}=$ 348 $\overline{QE}=$ 755.576 -
IRON LIVER 43MIN21SEC-

Fig. 6