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GAMMA-N ACTIVATION OF CANCER PATIENTS

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Abstract

High energy gamma radiation (8 to 30 MeV) is gaining acceptance for radiation therapy of patients with deep cancers. This radiation is of sufficient energy to induce photonuclear activation of the elements in the human body. Our results of measurements of nitrogen and phosphorus in an anthropomorphic phantom, a cadaver, and a cancer patient with bremsstrahlung radiation from 15 MeV electrons demonstrate the feasibility of a method to monitor these two elements in the human body in vivo by measuring the radioactivity induced in these targets by photonuclear reactions.

INTRODUCTION

High energy gamma radiation is a well established treatment modality for some cancer patients /1/. Irradiation of the human body with high energy photons (> 8 MeV) results in photoactivation of tissue elements. Photoactivation analysis of biological and environmental samples has been reviewed in refs. /2-4/. Photoactivations of animals to measure tumor and capillary blood flow and total body oxygen, nitrogen and carbon have been reported in refs. /5-7/. There is evidence that higher than normal levels of some trace elements are present in cancerous tissue /8-11/. Cancer patient treatment requires fractionation of the total radiation dose, which may be as high as 60 Gy, into doses of up to 3 Gy per treatment. Could this radiation be sufficient for in vivo elemental analysis of human tissues?

The present work demonstrates that the activity induced following a single treatment is sufficiently large to monitor nitrogen and phosphorous from the irradiated volume. The results of nitrogen and phosphorous measurements in an Alderson phantom, cadaver, and cancer patient following irradiation with high energy photons, under similar irradiation conditions as those of the cancer patient, are presented.

METHOD AND MATERIALS

The endoergic nature of the photonuclear reaction requires that the gamma radiation be above the threshold value for the reaction to occur. For low Z elements this threshold energy is above 10 MeV with the exception of deuterium (2.2 MeV) and beryllium (1.67 MeV). For intermediate and high Z elements the threshold energy is above 8 MeV. The cross section for photonuclear reaction is few millibarns above the threshold energy and it peaks about 6 MeV above it (giant resonant region). The cross section increases with Z up to few hundreds of milibarns for heavy elements.

During photonuclear reaction gamma ray is absorbed in the nucleus with subsequent ejection of a particle. In the case when a neutron is emitted the resultant daughter (A-1 nuclei) is unstable. It will usually decay by positron emission followed by emission of two annihilation (511 KeV) gamma rays. Some of the photonuclear characteristics of the major elements present in the human body are summarized in Table 1.

The high energy gamma radiation used for patient treatment was produced by clinical electron accelerator (Varian, Clinac 20) with thick target

TABLE 1

Photonuclear characteristics of the major isotopes
in the human body

ISOTOPE	% of Total* Body Weight	Isotope Abundance	Threshold energy (MeV)	Half-Life $T_{1/2}$ (min)	Emission lines (MeV)
^{16}N	61.00	99.76	15.7	2.030	0.511
^{12}C	23.00	98.89	18.7	20.400	0.511
^{1}H	10.00	99.98	-	-	-
^{14}N	2.60	99.64	10.6	9.970	0.511
^{40}Ca	1.40	96.94	15.6	0.015	0.511
^{31}P	1.10	100.00	12.3	2.500	0.511
					2.16 (0.5%)
^{32}S	0.20	95.00	15.1	0.044	0.511
					1.27 (1.1%)
^{39}K	0.20	93.30	13.1	7.63	0.511
					2.17 (99%)
				0.016	0.511
^{23}Na	0.14	100.00	12.4	2.6 y	0.511
					1.27 (90%)
^{35}Cl	0.12	75.77	12.5	32.200	0.511
					1.17 (9%)
					2.14 (25%)
					3.32 (9%)

* Total weight of a standard man is 70 Kg ref. /12/.
** % of lines per disintegration.

(converter) and thick flattening filter. The maximum end point of the bremsstrahlung radiation was 15 MeV with a dose rate of 3 Gy/min. Consequently, only some of the elements mentioned in Table 1 were activated. It has been estimated that only a few percent of the total gamma flux from the Clinac-20 was useful (above 10 MeV) for photoactivation /2,9/.

The induced activity was monitored by counting the annihilation gamma rays with a 30% high purity Ge and 2"x6" long NaI detectors. Consecutive spectra in the energy range from 0 to 2.6 MeV were collected for 30 seconds each in a multichannel analyzer during an overall period of 30 minutes. Spectrum from each counting period was stored on a magnetic tape for a later analysis. The time interval between consecutive counting periods was a few milliseconds. Phantom samples were counted 1 min post-irradiation, while the cadaver and the patient were counted 2 min post-irradiation.

The measured spectra were obtained from single elements and mixtures. A 1800 ml liver Alderson phantom, placed in a human shaped trunk, was filled with a solution containing nitrogen, phosphorous, and potassium at 57 g, 5.2 g, and 5.0 g respectively. This composition is similar to that of a standard man /12/. The trunk was filled with regular water. Spectra were also taken from a cadaver and from a liver cancer patient. The irradiation conditions for these cases were identical to those of the cancer patient.

The net number of counts in the 511 KeV photopeak was calculated from each of the stored spectra. These net counts were used subsequently in a non-linear least-squares analysis to resolve the complex decay curve into its components. The function fitted was of the general form

$$A(t) = \sum_i A_{1i} \exp(-A_{2i} t). \quad (1)$$

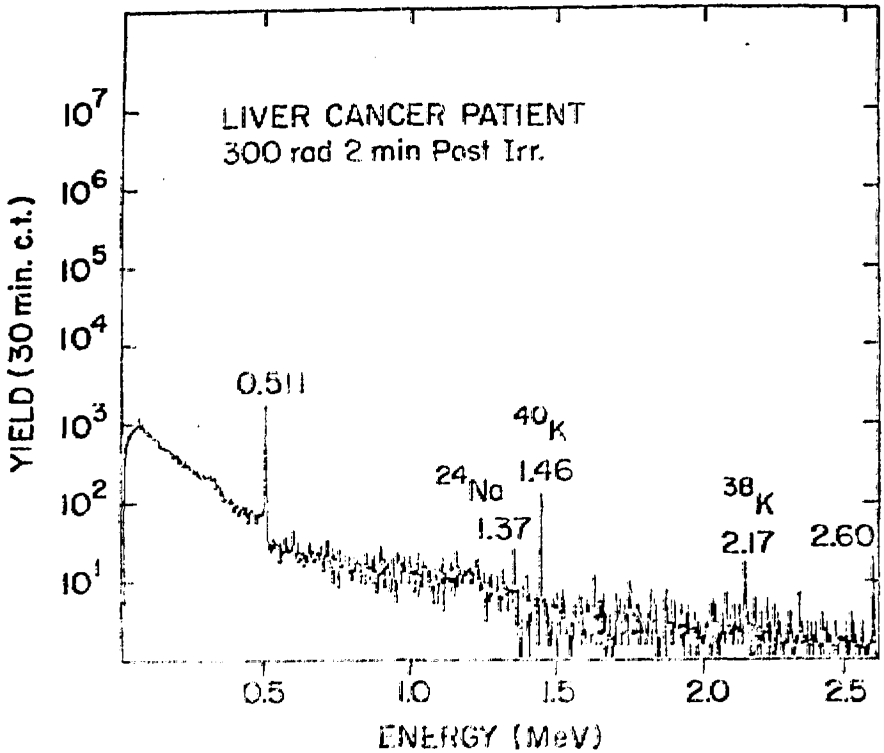

Fig. 1 Gamma-ray spectrum measured from a patient

After many trials the number of free parameters was limited to two, A_{11} and A_{12}. The parameters in the exponent were replaced with the decay time constants of nitrogen and phosphorus. The least-squares programs were taken from ref. /10/.

RESULTS

The 511 KeV positron annihilation photopeak is the dominant peak in the spectrum. There are two background peaks at 1.46 MeV from ^{40}K and 2.60 MeV, which remained constant and independent of the sample analyzed, except for the potassium chloride samples. In addition, there are two small peaks at 2.17 MeV from ^{38}K following photoactivation, and at 1.37 MeV from ^{24}Na following neutron activation. It should be noted that all high energy (> 8 MeV) medical accelerators produce neutrons. The mean neutron energy from the present machine is about 1 MeV. There were no additional photopeaks noted which were useful for elemental identification. Fig. 1 shows a post-irradiated liver cancer patient counted for 30 min as described. All the peaks are identified in the graph.

The complex decay curves, obtained from the net counts in the annihilation peak, were resolved into one, two, and three components as indicated by eq. 1. It was determined that a two component system, of nitrogen and phosphorus, provided the most reliable results. The contribution of potassium to the annihilation peak was negligible. This was consistent with the low intensity of the 2.17 MeV photopeak. At this point there were only two free parameters in the fitted function A_{11} and

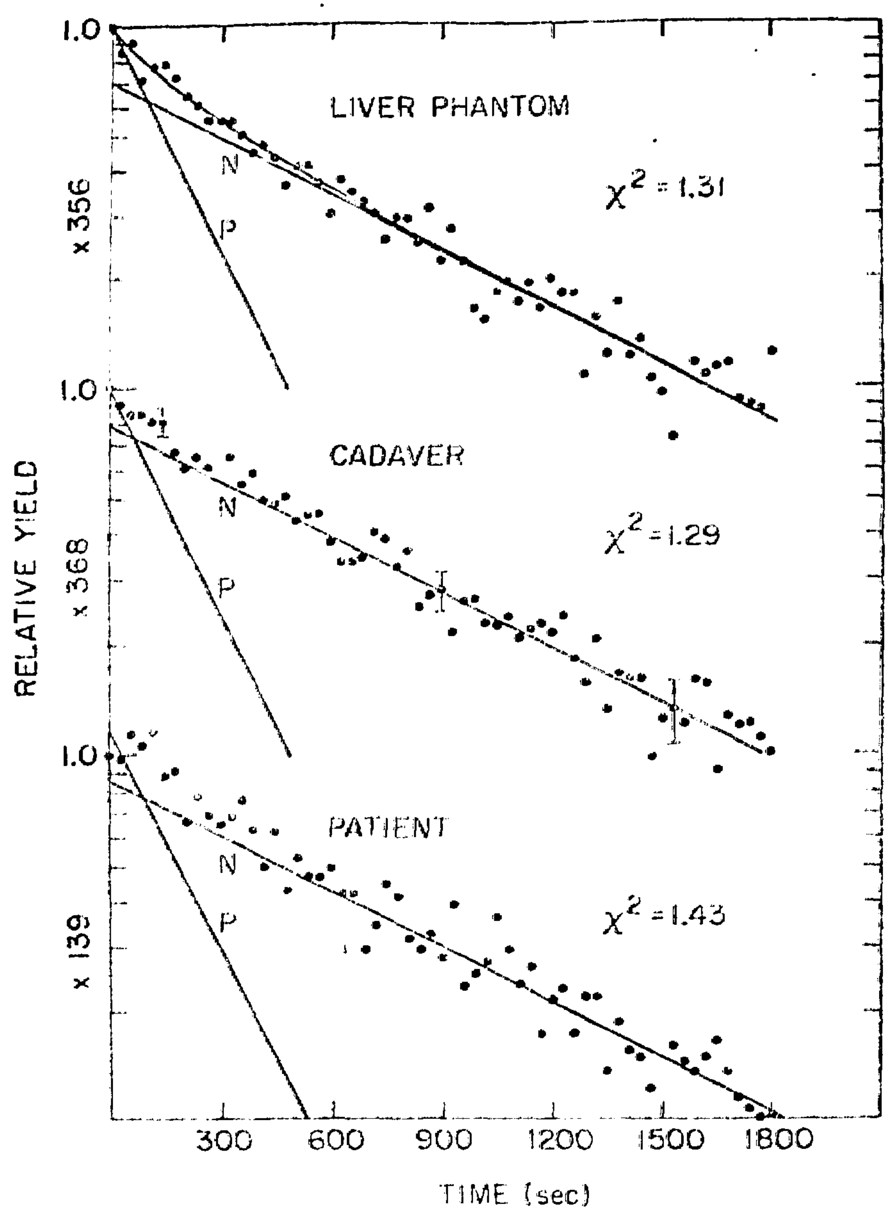

Fig. 2 *Deconvolution of the decay curves. The error bars are ± 1 SD.*

A_{12}. The least-squares fits of nitrogen and phosphorus components to the decay curves derived from the liver phantom, cadaver, and a liver cancer patient are shown in Fig. 2. The reduced Chi-square values for each fit are included in the figure. The accuracy of the least-squares analysis was also tested by comparing the sum of the time integrals (I) of nitrogen and phosphorus decay curves with the measured total number of counts. These results for liver phantom, cadaver and patient are given in Table 2. A_N and A_P are the coefficients obtained from the least-squares analysis, they correspond to A_{11} and A_{12} respectively. These coefficients were used

TABLE 2

Results of the least-squares analysis and the 511 KeV photopeak intensity

	A_N	I_N	A_P	I_P	I_{NP}	Measured	%diff.
LP. NPK[1]	237±1.6[2]	5971	109±10	786	6757	6689±1.3	1.0
LP. 0.9 NPK[3]	221±1.8	5568	62±16	447	6015	5959±1.3	0.9
Cadaver	287±1.6	7231	70±16	505	7736	8188±1.2	-5.8
Patient	119±2.5	2998	44±17	317	3315	3523±1.9	-6.3
LP. NPK-NaI[4]	1460±0.8	36783	505±05	3642	40425	39628±0.7	2.0

(1) liver phantom with nitrogen, phosphorus and potassium
(2) ± one standard deviation expressed in percent
(3) nitrogen is reduced by 10%.
(4) 2" x 6" long NaI detector was used for this measurement.

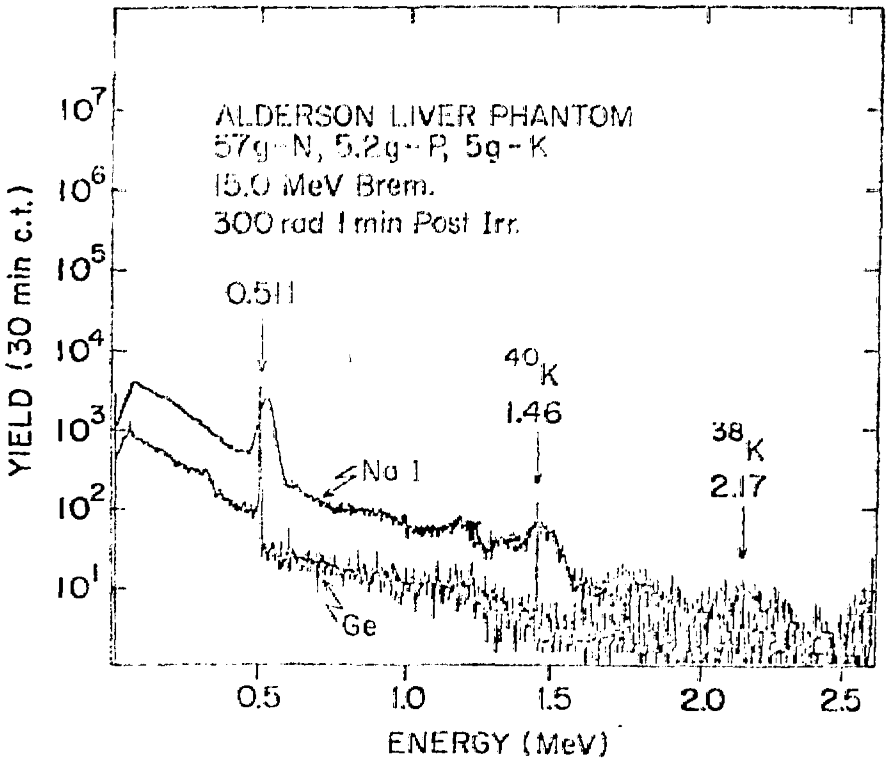

Fig. 3 Comparison of the spectra taken with HP-Ge and NaI detectors under identical conditions.

to integrate eq. 1 to obtain I_N and I_P. The % diff. is the percent difference between the calculated number of counts I_{NP} and the total measured intensity of the annihilation peak. In the final set of measurements the HP-Ge detector was replaced by a NaI detector. The worse energy resolution of the NaI detector was compensated by its higher counting efficiency. These two spectra are compared in Fig. 3 and the results are summarized in Table 2.

CONCLUSIONS

The 15 MeV bremsstrahlung radiation produced by a Clinac-20 is sufficient to excite elements with low threshold energy and high concentrations in the body. The two elements monitored in this work are nitrogen and phosphorus. Although potassium is photoactivated to ^{38}K when 1/2 lb of KCl was used, its higher threshold level prevented production of sufficient activity to be monitored in a patient. Also, the peak at 2.16 MeV was too weak to provide any additional information on the presence of ^{38}K. No other elements were identified in the spectrum except to ^{24}Na (small peak) due to neutron activation. All the other photopeaks belonged to the background.

The measured spectra with HP-Ge detector provided precision for the nitrogen of about [illegible]%, and for phosphorus 15%. Using NaI detector the precision for nitrogen and phosphorus improved to 1% and 5% respectively. The least-squared fittings were satisfactory. The quality of the fits weretested by the low value of the reduced Chi-square, comparison of the time integrals with the total number of counts, and inspection of the residual spectra. However, the signal can be improved further by using more detectors and by improving the shielding of the detectors (NaI detector was unshielded). Better future arrangements around the patient will improve considerably the counting geometry of the patient.

Ten percent change in the liver phantom nitrogen content resulted in 6.7% change in the nitrogen activity (A_N, Table 2). It is within the quoted errors since one standard deviation change in each activity yields a 10% difference in the nitrogen signal, as expected. The large difference in the phosphorus intensity is not clear at present, sample preparation is suspected since other readings were rather consistent.

Present work demonstrates the feasibility to monitor nitrogen and phosphorus in post-irradiated cancer patients. The measurements were limited to the liver only, but it need not be so. Every irradiated organ or part of the body is activated. However, the counting geometry becomes more complicated. At present, the usefulness of the method is being tested to find whether the nitrogen signal, which is related to the protein and the cell membrane mass, provides information on the efficacy or progress of the radiation treatment. It is speculated that the nitrogen signal should decrease with progress of the treatment since the cancerous cells are being killed and removed from the cancer region.

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