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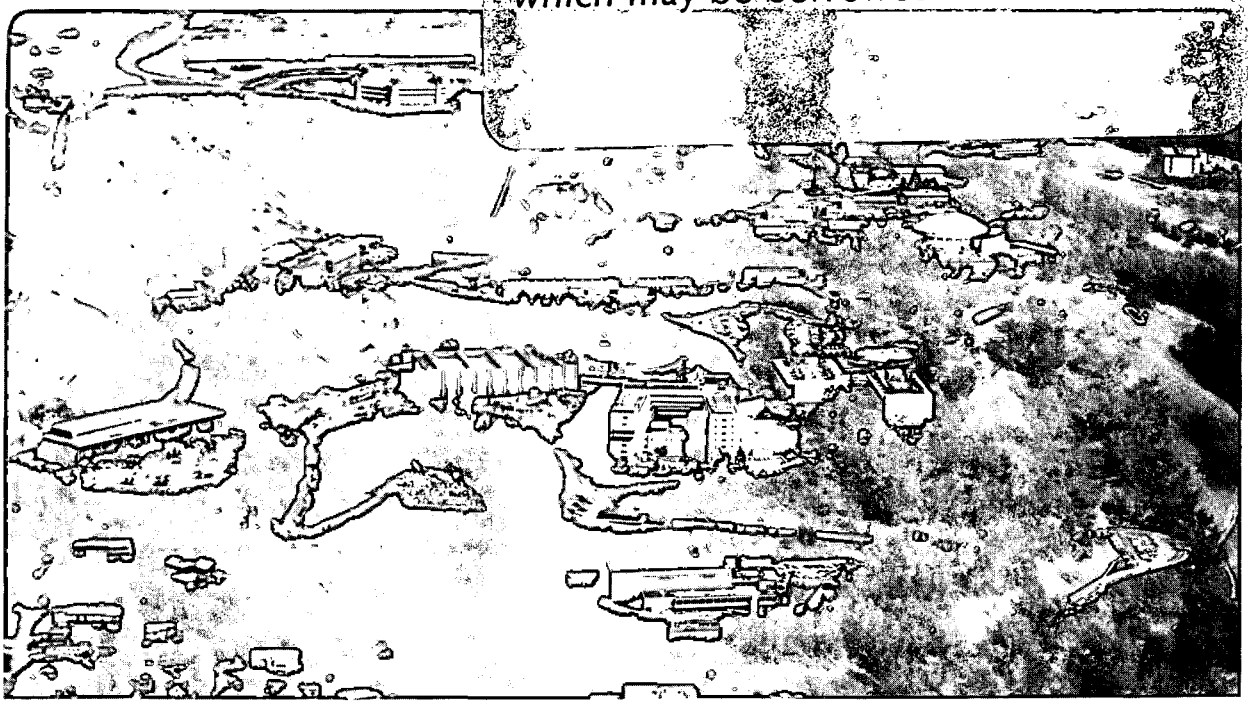

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A NEW COMPTON DENSITOMETER FOR MEASURING PULMONARY EDEMA

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Abstract

Pulmonary edema (P.E.) is the pathological increase of extravascular lung water found most often in patients with congestive heart failure and other critically ill patients who suffer from intravenous fluid overload. The chest x-ray, the standard method for validating the presence of P.E., is neither quantitative nor sensitive. A non-invasive lung density monitor that is accurate, easily portable, safe and inexpensive is needed for clinical use.

To deal with the problem of attenuation along the beam paths, previous gamma-ray techniques require simultaneous measurement of transmitted and scattered beams. Since multiple scattering is a strong function of the density of the scattering medium and the mass distribution within the detection geometry, there will be inherent uncertainties in the system calibration unless it is performed on a body structure closely matched to that of each individual patient. Other researchers who have employed Compton scattering techniques generally used systems of extended size and detectors with poor energy resolution. This has resulted in significant systematic biases from multiply-scattered photons and larger errors in counting statistics at a given radiation dose to the patient. We are proposing a patented approach in which only backscattered photons are measured with a high-resolution HPGe detector in a compact system geometry. By proper design and a unique data extraction scheme, effects of the variable chest wall on lung density measurements are minimized.

Preliminary test results indicate that with a radioactive source of under 30 GBq, it should be possible to make an accurate lung density measurement in one minute, with a risk of radiation exposure to the patient a thousand times smaller than that from a typical chest x-ray. The ability to make safe, frequent lung density measurements could be very helpful for monitoring the course of P.E. at the hospital bedside or outpatient clinics, and for evaluating the efficacy of therapy in clinical research.

Background

Medical Need

Pulmonary edema (P.E.) is a pathological state in which there is abnormal extravascular water storage in the lungs. Leakage of water from the blood vessels into the surrounding lung tissues increases the overall lung density upwards from its normal value of approximately 0.2 g/ml. P.E. results mainly from increased lung capillary pressure in congestive heart failure (a most common problem that can accompany all types of heart disease, acute and chronic). It is also a consequence of increased capillary permeability (due to lung injury resulting from many causes including drug overdose, pneumonia and head trauma)[1] and from intravenous fluid overload in critically ill patients. It impairs gas exchange in the lungs, leading to increased shortness of breath, and if unchecked, to profound disability and even death.

Many techniques have been explored to measure lung water[2] but in current medical practice, the chest x-ray is still the best laboratory technique for the detection of pulmonary edema. By examining the x-ray appearance of the lung, heart and great vessels, a skilled radiologist presently is best able to estimate the presence and severity of P.E. However, the chest x-ray is neither quantitative nor sensitive. P.E. can only be reliably detected by chest x-ray measurements when extravascular lung water content is increased by 30%[3]. Also, indicative changes in the roentgenogram often lag behind clinical improvement[4]. Frequent chest x-rays in critical patients are expensive and may entail excessive radiation exposure. Clinically, it is important to detect the onset of P.E. in order to effect early diagnosis and treatment.

Thus there is a clear need for a simple instrument that can routinely monitor the degree of P.E. as a guide to detection, proper treatment and prognosis. Methods that involve large radiation doses or require very expensive and massive equipment such as computerized axial tomography (CAT), positron emission tomography (PET), and nuclear magnetic resonance (NMR) scanners are not suitable for bedside or clinical use.

Analysis of Prior Art

No present technique, simple or complicated, exists for the accurate in vivo determination of lung water. A good indicator of lung water would be an accurate measurement of absolute lung density in a relatively homogenous region of the lung free of large blood vessels. In patients, such a region would be the right lower lobe near the chest wall.

Among various non-invasive techniques, Compton scattering seems to hold the most promise. In the 100 - 200 keV range, and in tissue, the interaction of gamma rays with matter is primarily via the Compton process. Compton scattering, being a direct measure of electron density of the medium, can be regarded as a true measure of mass density since electron densities are well known for various human tissues[5]. While the physics of Compton scattering is well understood, its application to lung density measurement has not been straightforward because the lung is surrounded by a chest wall of undetermined dimension and composition as shown in Fig. 1. This would invalidate any simple transmission or scattering measurement based on absolute count rates.

The usual approach of past investigators was to outfit the sources and detectors with collimators such that a "scattering volume" is defined by isoresponse curves within the homogenous portion of the lung volume. In order to deal with the problem of attenuation along the beam paths, a scheme has been devised such that by measuring two sets of transmitted and scattered count rates T1, T2 and S1, S2 respectively, there will be cancellations of attenuation effects if the paths along the transmitted and scattered beams are properly selected. There are a number of variations of this scheme. For example, Kaufman et al[6] have used a small-angle Compton scattering method with a single source and two detectors. Other systems using large

angle (usually 90°) Compton scattering use a second source whose energy is matched to that of the scattered beam. Even a three-source-three-detector system has been used to avoid the necessity of rotating either the system or the patient during the measurement[7]. In any case, the density ρ of the scattering volume is expressed as:

$$\rho = C\left(\frac{S1\ S2}{T1\ T2}\right)^{1/2} \qquad (1)$$

where C is a calibration constant depending on the scattering volume V and the geometric acceptances between sources and detectors to V.

While good precision can be achieved if strong enough sources (many Curies) are used in these systems, significant systematic biases exist when the size, density and indeed mass distribution of the subject differ from those of the calibration standards[8,9]. The basic problem is that the scattering volume V is defined in terms of singly-scattered photon geometry, so that when multiple scattering occurs differently between tne subject and calibration standard, the effective volumes are different. Multiple scattering is known to be a strong function of density and size of tne medium[10]. The need for transmission measurements dictates relatively large source-detector distances in order to accomodate the chest thickness and width of the patient. In addition, most investigators use detectors (NaI, CdTe or HgI) with poor energy resolution (several keV) and the wide energy windows set for these detectors have little discriminating capability against multiply-scattered photons.

A New Approach

Recognizing the problems of attenuation and multiple scattering in the chest wall which have bedeviled previous investigators who employed gamma-ray techniques, we are taking a patented new approach[11].

Consider an experimental set-up as depicted in Fig. 2. Here, a phantom consisting of a thin metal can 10 cm diameter by 10 cm tall is used to represent a uniform volume of the lung. The effect of the chest wall is simulated by a 6.5 mm plexiglas layer which intercepts the incident and exit beams. The density ρ of the "lung" within the can may be varied from 0.19 - 1.0 g/ml by mixing an appropriate amount of sawdust and water. A narrow beam of gamma-rays (from a Co^{57} source) is directed through the center of the can at a 35° angle with respect to the front of the detector housing which is intended to be parallel to the chest wall. The scattering volume along the narrow beam is viewed by a HPGe detector (about 1 cm cube) whose effective center is about 9 cm from that of the can. The scattering angles at various depths x along the beam are determined by the particular geometry and the corresponding energies of scattered photons E are calculated according to the Compton formula:

$$E = \frac{E_0}{1 + \alpha\,(1-\cos\theta)} \qquad (2)$$

where E_0 = 122 keV and α = 0.239.

The observed count rate from a scattering volume per unit distance along the beam can be expressed as:

$$\frac{\Delta N}{\Delta X} = \frac{\Delta N}{\Delta E}\ \frac{\Delta E}{\Delta\theta}\ \frac{\Delta\theta}{\Delta X} \qquad (3)$$

where $\Delta N/\Delta E$ is the observed energy spectrum and the other two terms are scale transformation factors as determined by the Compton equation and geometry. The net count rate (excluding background) may be considered to consist of six factors:

$$\frac{\Delta N}{\Delta E} \propto (F1)(F2)(F3)(F4)(F5)(F6) \qquad (4)$$

where:

- F1 is the transmission of the incident beam through the chest wall (with density ρ' and path length t) and will have the form $\exp(-\mu'\rho' t)$.
- F2 is transmission through depth X in the lung and will have the form $\exp(-\mu\rho x)$.
- F3 is the Klein-Nishina differential cross section which is proportional to ρ and has an angular dependency on θ the scattering angle in the source-detector plane:

$$\left[\frac{1}{1+\alpha(1-\cos\theta)}\right]^3 \left[\frac{1+\cos^2\theta}{2}\right] \left[1 + \frac{\alpha^2(1-\cos\theta)^2}{(1+\cos\theta)[1+\alpha(1-\cos\theta)]}\right] \qquad (5)$$

- F4 is the geometric acceptance between the scattering volume and the detector and would have a $1/d^2$ dependency where d is the mean distance between the scattering volume element and the detector.
- F5 is the transmission of the scattered beam through the lung with path length l and energy dependent attentuation coefficient μ' described by $\exp(-\mu'\rho l)$.
- F6 represents the transmission $\exp(-\mu'\rho' t)$ through the exit portion of the chest wall with density ρ' and path length t.

We should point out that $\Delta N/\Delta E$ is also modified by a finite resolution function which tends to smooth the spectrum.

With all these factors acting in concert, N can hardly be expected to have a simple functional dependence on X. However, we have discovered experimentally that with certain geometry and within limited ranges of variables, N is almost a pure exponential function! That is to say,

$$N = A\ \exp(-KX) \qquad (6)$$

or

$$\ln N = \ln A - KX \qquad (7)$$

where A and K are empirical constants. Furthermore, if K (the negative slope in the plot of ln N vs X) depends primarily on ρ and only weakly on other uncontrolled variables, a calibration of K with known densities could offer a unique way for density measurements.

There are several salient features in this new approach. First, it is an extremely simple one-source-one-detector system, thus it has an inherent advantage from the point of view of reliability. Second, since it is unnecessary to measure the transmitted beam, it is possible to design a very compact or close coupled system. In a well designed system, precision would only be limited by counting statistics. The tighter the geometry, the better will be the measurement precision at any given radiation dose. Third, compared with systems with large source-detector separations and poor energy resolution, the present approach should offer much more accurate performance by minimizing the effects of multiple scattering.

Basic to our approach is that variations in source strength and attenuation of the incident beam by the chest wall affect only counting statistics and has little effect on the slope K in Eq. 7. The chest wall could have a more significant effect on the scattered beams because there may be differential attenuations among them as they exit. This effect may be reduced by choosing a geometry that minimizes the size of the exit window thus assuring only small differences in path lengths and density variations in the exit window. The target volume is defined by the collimated incident beam and the measured energies of the Compton backscattered photons. Incorporation of a shield or

collimator at the exit window should further suppress multiply-scattered photons from reaching the detector.

Experimental Results

A system as shown in Fig. 2 has been assembled to conduct a preliminary check on the performance of this new approach.

A weak Co^{57} source (3 mCi) 3 mm in diameter is mounted in a lead housing. A 5 mm hole in the Ta collimator produces a beam with a half angle divergence of 50 mr. The diameter of the beam at the focal point of the detection system is then about 1.4 cm.

Figure 3 shows a typical spectrum accumulated over a long period (1430 min) to show the distribution of the counts from regions at various depths X along the beam. The corresponding scattering angles θ and energy E are also indicated. The counts from two asymptotic regions each 2 keV wide near the two ends of the spectrum are used to perform a simple background subtraction by linear interpolation. The net counts from each centimeter interval near the center of the scattering volume ($X = 2 \rightarrow 8$ cm) are then used in a linear regression analysis to determine K. The peak near $\theta = 75°$ is due to scattering from the entrance plastic "chest wall" of 6.5 mm thick. Being outside the primary beam, the exit chest wall does not show in the spectrum. Its presence is manifested only in the reduced count rates of the scattered beams.

The distributions of count rate per cm interval as a function of depth X are plotted in Fig. 4. The two cases illustrated here are for lung densities 0.25 and 0.50 g/ml. While the 6.5 mm plastic "chest wall" has reduced the countrate by about 25%, the values of K are only reduced by 2-3% with no correction applied.

By placing the phantom inside the rib cage of an actual human skeleton, we found that the presence and the orientation of a rib in the exit beam had little effect on the determination of K, although the sensitivity for the geometry used in this test was poorer than the one in Fig. 2.

Using similar procedures for determining K, a calibration curve (without the chest wall) has been obtained for K against the gravimetric density ρ as shown in Fig. 5. We note that K varies linearly with ρ in the range of $\rho = 0.19 \rightarrow 1.0$ g/ml for this geometry according to the regression equation:

$$K = 0.132 + 0.176\,\rho \qquad (8)$$

We found that most of the departures of the data points from the regression line were due to non-uniform packing of the sawdust in the phantom. The reproducibility of K is typically better than 0.5% for long counting times. Since

$$\frac{\Delta\rho}{\rho} = \frac{K}{0.176\rho}\,\frac{\Delta K}{K} \qquad (9)$$

the corresponding reproducibility in ρ is then from 2.4% to 1.1% in the density range of $0.2 \rightarrow 0.6$ g/ml.

To estimate the precision obtainable in a clinical situation where statistical errors are important, six measurements were made for 60 min each at a density of 0.3 g/ml. The result showed a standard deviation in K of 1.9%, equivalent to a density error of 0.02 g/ml. If the source strength were to be increased to 0.18 Ci, then the same measurement precision can be expected from a one minute measurement on a patient. The maximum radiation dose in soft tissue from this measurement is estimated to be 1.9 mr.[12] Thus, even if a 1-Curie (37 GBq) source is used to cope with the attenuation by the chest walls, the maximum dose will still be approximately 10 mr over a small area of about 1 cm^2. Therefore, the radiation risk is less than a thousandth of that from a typical hospital x-ray which delivers up to 100 mr over the entire chest.

We have made further measurements using the same experimental arrangement as that in Fig. 2 except that the target-detector distance has been increased slightly to accommodate thicker absorbers and a 1.3 mm thick Ta shield in front of the detector window. The Ta shield has an opening 3 cm wide by 1 cm tall so that multiply-scattered events originating away from the primary beam path would be largely rejected from the fit region of the energy spectrum. We found that with plexiglas absorbers of 26 mm thick in the primary beam or 22 mm thick in the exit beam, the variations in K have been less than 1% at a target density of 0.5 g/ml.

Conclusion

Our unique data extraction scheme has allowed us to make direct "lung" density measurements using only Compton backscattered photons in spite of the presence of a "chest wall". The possibility of employing a very simple and compact one-source, one-detector system geometry minimizes the effect of multiple scattering and reduces the amount of radiation required. The use of a high-resolution HPGe detector not only allows us to define target volumes from photon energies but also helps to reject multiply-scattered photons. The suppression of extraneous counts can be further improved by some detector collimation. These factors acting in concert allow us to project the development of a clinical lung density monitor that is inherently more accurate and can fulfill all the other requirements of portability, cost and safety.

Our continuing research and developmental effort is intended to include the following:

- In-depth study of the validity of the measurement principles.
- Detailed investigation of all physical and geometrical parameters, including radiation sources, which would improve measurement sensitivity and accuracy.
- Design and construct preliminary detector and data acquisition system with particular emphasis on improving spacial resolution and reducing detector background.
- Engineer and construct automated data acquisition system including complete software development, for rapid density determination.
- Together with medical consultants, define and evaluate optional geometries to accommodate patient variations and other clinical requirements.
- Design and construct prototype field instrument.
- Conduct field experiments on animal and human subjects.
- Validate results with other techniques such as NMR tomography and histology.
- Institute iterative designs and technology transfer.

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References

1. Crandall, Edward D., moderator, "Recent Developments in Pulmonary Edema", Annals of Internal Medicine, Vol. 99, pp. 808-822 (1983).

2. Staub, Norman C. and James C. Hogg, "Conference Report of a Workshop on the Measurement of Lung Water", Critical Care Medicine, Vol. 8, No. 12, pp. 752-759 (1980).

3. Staub, Norman C. "The Measurement of Lung Water Content", Journal of Microwave Power, Vol. 18, No. 3. pp. 259-263 (1983).

4. Garnett, E.S., C.E. Webber, G. Coates, W.P. Cockshott, C. Nahmias and N. Lassen, "Lung Density: Clinical Method for Quantitation of Pulmonary Congestion and Edema", J. Canadian Med. Assoc., Vol. 116, pp. 133-134 (1977).

5. Shrimpton, P.C., "Electron Density Values of Various Human Tissues: in vitro Compton Scatter Measurements and Calculated Ranges", Phys. Med. Biol., Vol. 26, No. 5, pp. 907-911 (1981).

6. Kaufman, L, G. Gamsu, C. Savoca, S. Swann, L. Murphey, B. Hruska, D. Palmer and J. Ullman, "Measurement of Absolute Lung Density by Compton Scatter Densitometry", IEEE Trans. on Nucl. Sci., NS-23, No. 1, pp. 399-605 (1976).

7. Webber, C.E. and G. Coates, "A Clinical System for the in vivo Measurement of Lung Density", Medical Physics, Vol. 9, No. 4, pp. 473-477 (1982).

8. Huddleston, A.L., D. Bhaduri and J. Weaver, "Geometrical Considerations for Compton Scatter Densitometry", Medical Physics, Vol. 6, No. 6, pp. 529-522 (1979).

9. Coates, G. and C.E. Webber, "The Influence of Certain Physical and Physiological Factors on the in vivo Measurement of Lung Density", Medical Physics, Vol. 9, No. 4, pp. 478-483 (1982).

10. Burgess, A.E., "Voltage, Energy and Material Dependence of Secondary Radiation", Medical Physics, Vol. 8, No. 1, pp. 33-38 (1981).

11. Loo, Billy W. and Fred S. Goulding, "Method and Apparatus for Measuring Lung Density by Compton Backscattering", U.S. Patent filed on Oct. 17, 1985.

12. Greenhouse, Anthony, health physicist, Lawrence Berkeley Laboratory, private communication.

13. Eycleshymer and Schoemaker, A Cross Section Anatomy, New York City: Appleton Century Croft, 1970 [c. 1911].

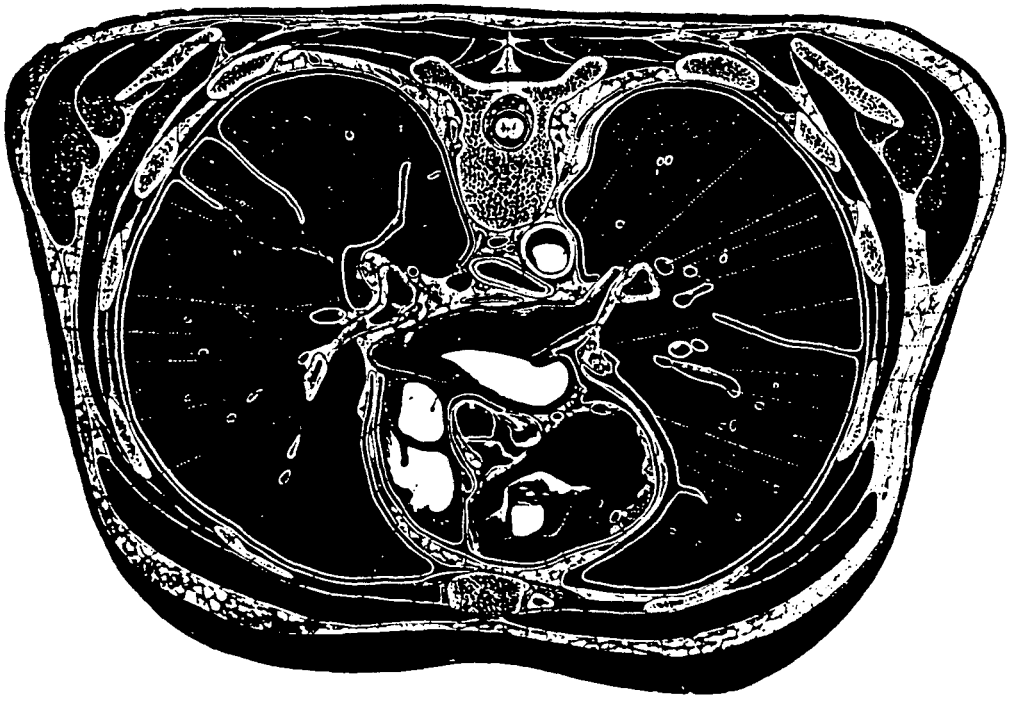

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Fig. 1. A transverse section of the chest at the level of the mid-portion of the third rib anteriorly. (From Ref. 13.)

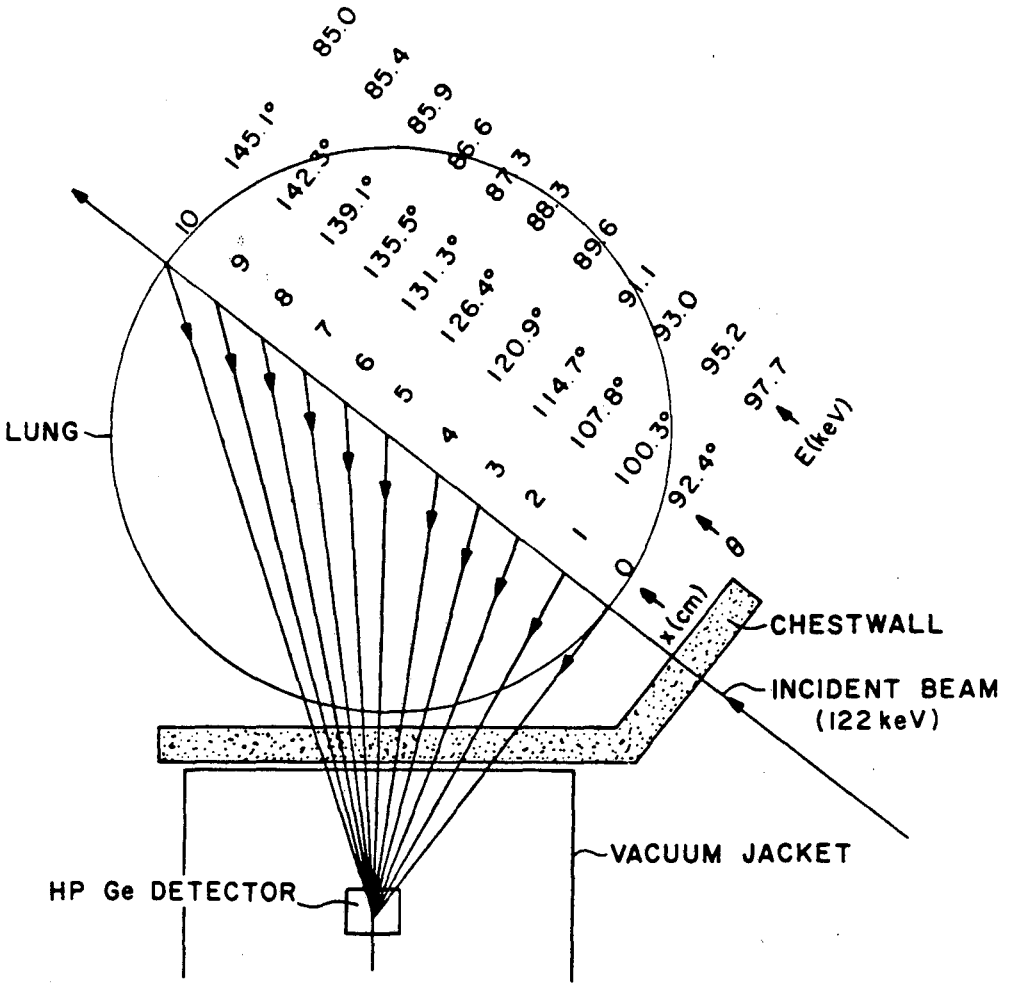

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Fig. 2. An experimental set-up of the new Compton densitometer.

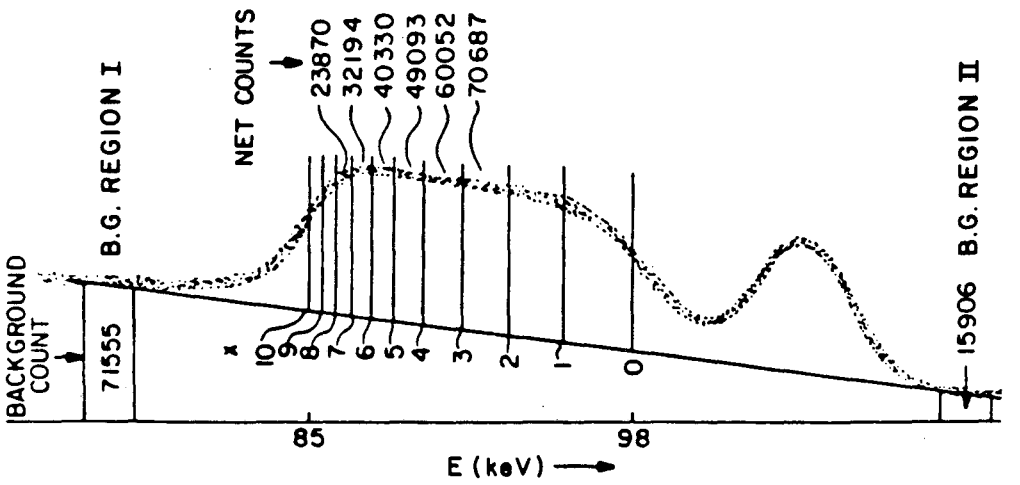

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Fig. 3. A sample energy spectrum obtained with the system illustrated in Fig. 2.

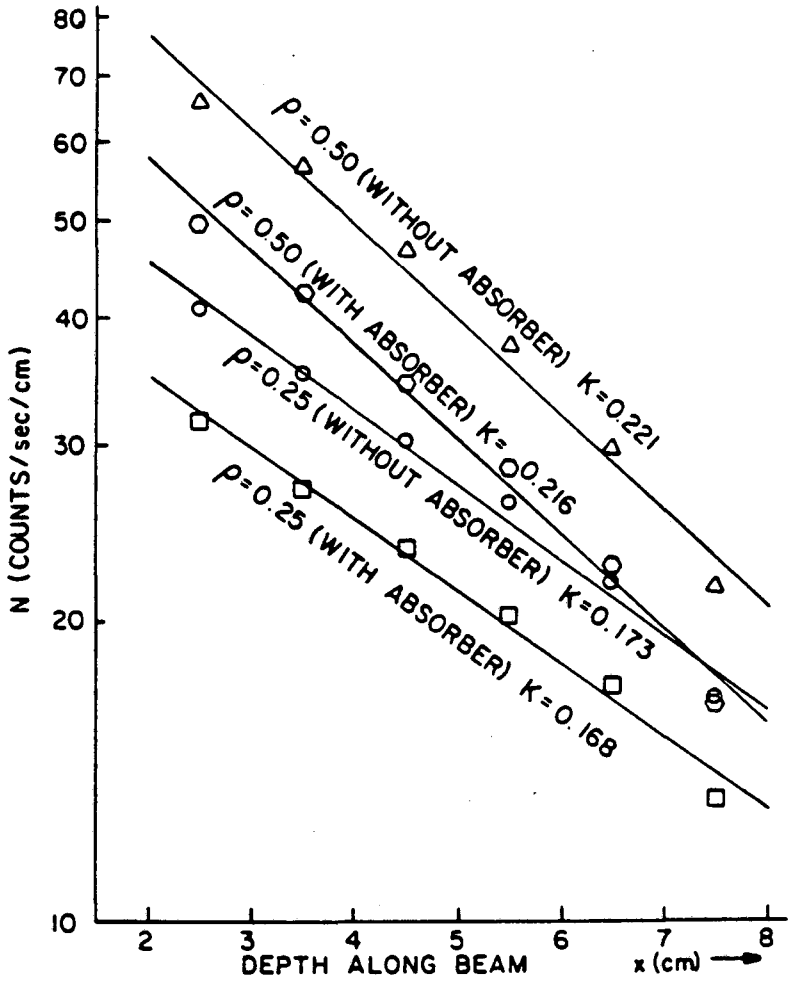

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Fig. 4. The exponential dependence of countrate N on depth X.

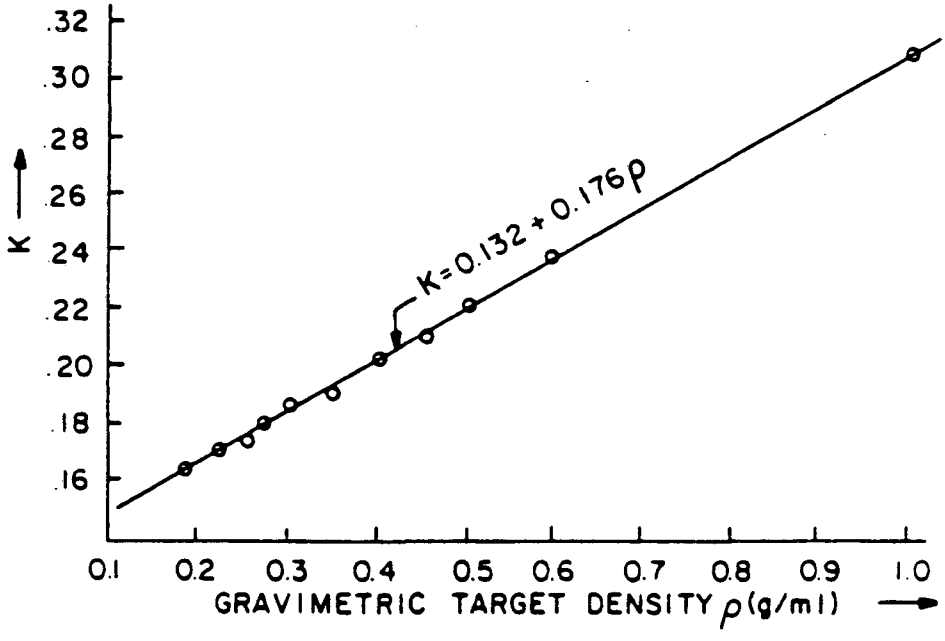

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Fig. 5. Results of a system calibration showing the linear relationship between the empirical attenuation factor K and target density ρ.

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