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THYROID RADIONUCLIDE UPTAKE MEASUREMENTS

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FOREWORD

Tests of thyroid function based on measurements of the uptake of radioiodine by the gland (thyroid uptake tests) constituted one of the first diagnostic applications of radioactive tracers and have been widely used in the diagnosis and investigation of thyroid diseases. In 1960 the International Atomic Energy Agency invited a group of consultants to draw up a standardized procedure for such uptake measurements. The recommendations of this group related primarily to measurements of the uptake of ^{131}I 24 hours after its oral administration - the basis of the thyroid uptake test most commonly performed in 1960 - and were published in a number of scientific journals.

During the ensuing decade thyroid uptake tests underwent considerable development. New radionuclides were utilized, new instruments and techniques for the measurement of uptake were devised, and an increasing emphasis was placed on uptake measurements made relatively soon after administration of the radioactive tracer. Parallel development took place in tests involving the use of radionuclides but based on measurements of parameters other than uptake. In view of these advances the Agency decided in 1970 to convene a second panel of experts to review the status of thyroid uptake tests and to up-date, and where necessary amend, the 1960 recommendations.

This panel met at the Agency's Headquarters from 17 to 21 May 1971 and its report has been submitted for publication to scientific journals in the English, French, Russian and Spanish languages. The various working papers presented during the meeting, which contain information supplementary to that given in the report, have been gathered together in this document, in order that they may be available to all interested persons.

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CLINICAL REQUIREMENTS FOR THYROID RADIOISOTOPE UPTAKE MEASUREMENTS

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ABSTRACT

This paper discusses the clinical requirements for thyroid uptake tests in relation to other tests of thyroid function, with particular reference to the assessment of the response of the thyrotoxic patient to therapy. The 20-minute thyroid uptake test is especially useful for the latter purpose since it indicates the underlying functional state of the thyroid as distinct from its rate of hormone production, can be used for repeated assessments and is itself unaffected by antithyroid drugs.

Introduction

Thyroid function tests have been of great value in the diagnosis of thyroid disease, but until recently they have been of little use in management. If in the thyrotoxic patient one wants to confirm the clinical diagnosis, then thyroid function tests are useful. If, on the other hand, one wants to know whether drugs or destructive treatment will ultimately give the best results, then thyroid function tests are usually of no help whatever. Help is needed because each form of treatment of thyrotoxicosis has a major disadvantage. As far as radioiodine therapy is concerned the chief trouble has been the high incidence of late hypothyroidism. After subtotal thyroidectomy the incidence of relapse and hypothyroidism taken together has generally been considerable. The chief problem with antithyroid drug therapy is that half the patients relapse after completing a normal course of treatment. If one could predict at the beginning, or during the first few months, of treatment which patients would relapse and which would remain euthyroid after longterm antithyroid drug therapy, then treatment could be rationalized by using radioiodine or surgery for those patients unsuitable for drug therapy.

Diagnostic Use

Chemical measurements (PBI, thyroxine iodine, free thyroxine index) are used more frequently than thyroid radioiodine uptake measurements. But considerable use of thyroid uptake measurements continues. In one clinic the monthly figures were -

Thyroxine iodine estimations	500
Thyroid radioiodine uptake	50

Initial assessement of Graves' disease

We have reexamined the question whether any of the features of thyrotoxicosis observed at the initial assessment correlate with a good prognosis after antithyroid drug therapy. Factors which show a significant difference in the group of patients who remained euthyroid after completion of treatment include goiter size, 2-minute thyroid radioiodine uptake, 20-minute thyroid radioiodine uptake, and protein-bound iodine.

Assessment of response during antithyroid drug treatment

When assessing the response to treatment during antithyroid drug therapy one requires information of four different kings.

1. Is the patient hyper- eu- or hypothyroid, i.e., what is the level of thyroid hormone production?
2. What is the underlying functional state of the thyroid as distinct from the level of thyroid hormone production?
3. What is the prognosis, i.e., is the patient drug-responsive and suitable for longterm antithyroid drug therapy, or is she relapse-prone and better treated by operation or radioiodine?
4. If longterm antithyroid drug therapy is being given, when can treatment be discontinued?

The 20-minute thyroid uptake during antithyroid drug therapy. The 20-minute thyroid radioiodine uptake measures a different parameter of iodine metabolism compared with conventional uptake measurements which has special clinical value in patients receiving antithyroid drug therapy. This is because it reflects principally the iodide trapping function of the thyroid, i.e., the accumulation of iodide ion by the thyroid gland. Radioiodine tests of this type allow assessment of thyroid function during treatment with antithyroid drugs, and are unique in that they indicate the underlying functional state of the thyroid as distinct from the level of thyroid hormone production (Figs. 1 and 2). The tracer dose has to be given intravenously since otherwise the rate of absorption from the gut would interfere with the result of the test.

Perhaps it is fair to draw an analogy between the 20-minute uptake and the ESR during treatment of tuberculosis or rheumatic fever. The ESR reflects the activity of the tuberculous disease and when it returns to normal it is of good prognostic significance. However, there is no guarantee that the ESR will not rise again, the result of reactivation of the disease, and it seems that exactly the same is true of the 20-minute thyroid uptake in thyrotoxicosis (Figs. 3 and 4).

<u>Assessment of Response After Antithyroid Treatment</u>

After antithyroid drug therapy is discontinued, it is usually unnecessary to make measurements of both thyroid uptake and circulating hormone. The latter alone is sufficient since the values are concordant. However, in three patients unexpected results were observed.

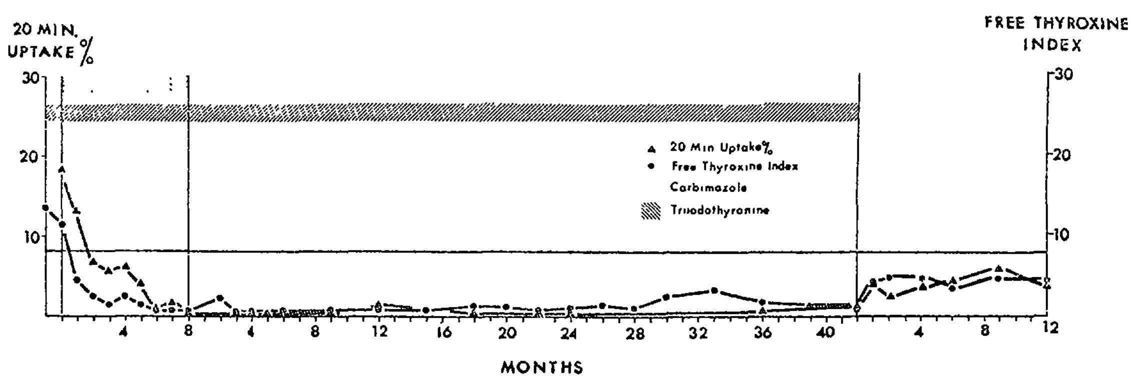

Fig. 1

Drug-responsive patient. After 8 months treatment with carbimazole the 20-minute uptake fell below 1 %. Suppression of thyroid function continued for the next 42 months until triiodothyronine was discontinued. Then normal values were observed.

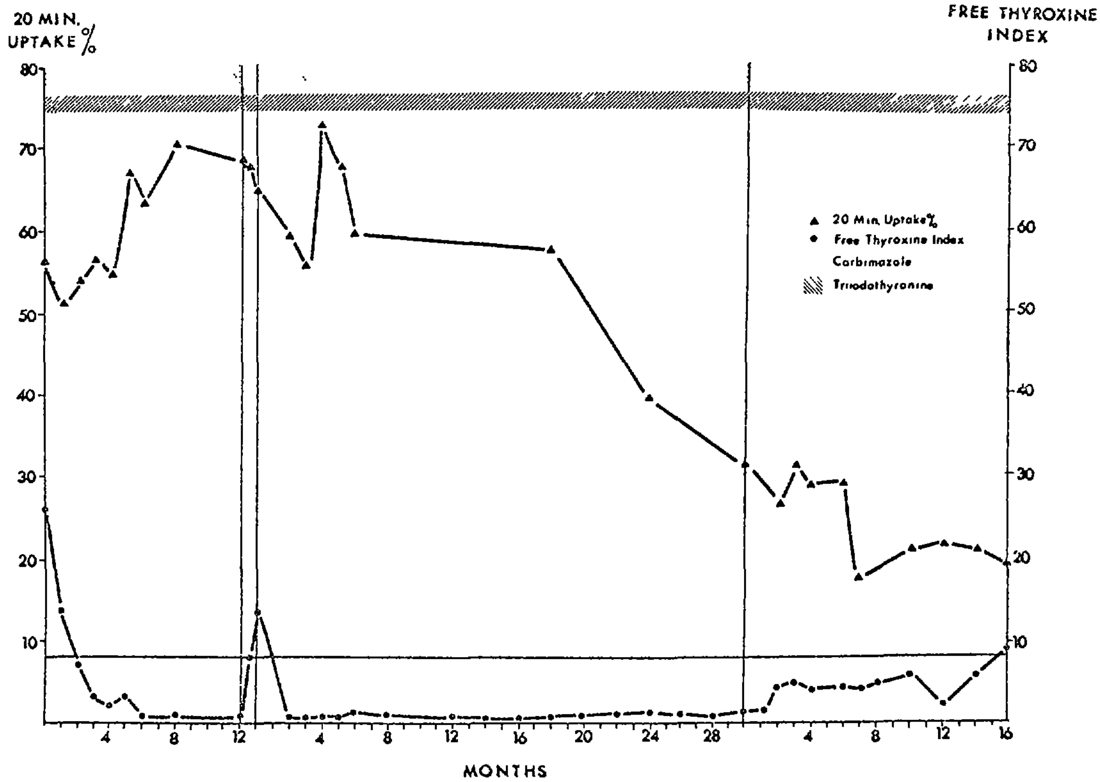

Fig. 2

Relapse-prone patient. After 12 months treatment the thyroid uptake had not fallen. When carbimazole was discontinued there was an abrupt recurrence of severe thyrotoxicosis. A second course of carbimazole lasting 30 months was given.

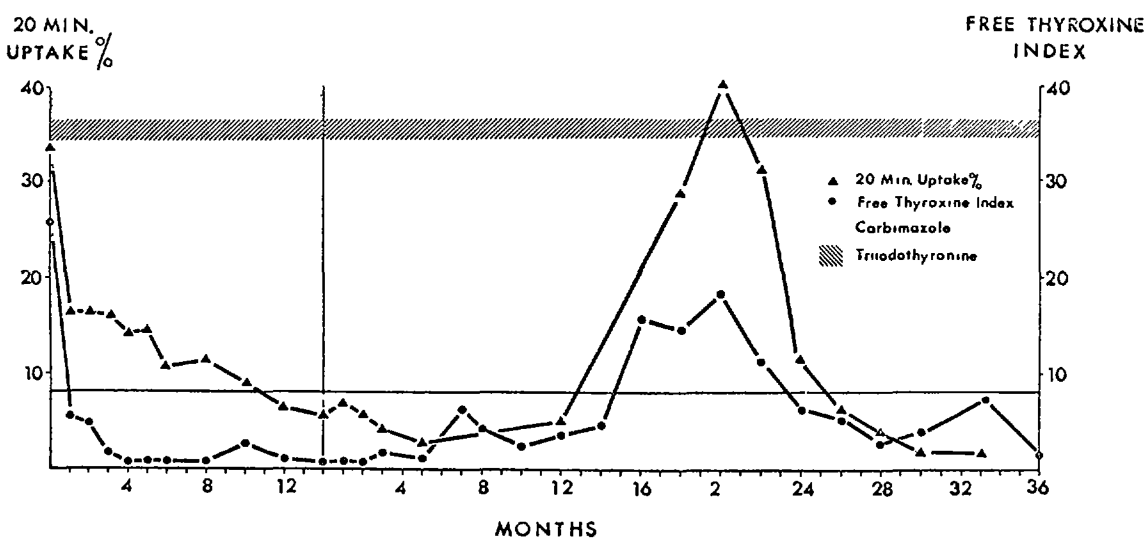

Fig. 3

Self-limiting recurrence of thyrotoxicosis, after remaining in remission for one year following completion of antithyroid drug therapy.

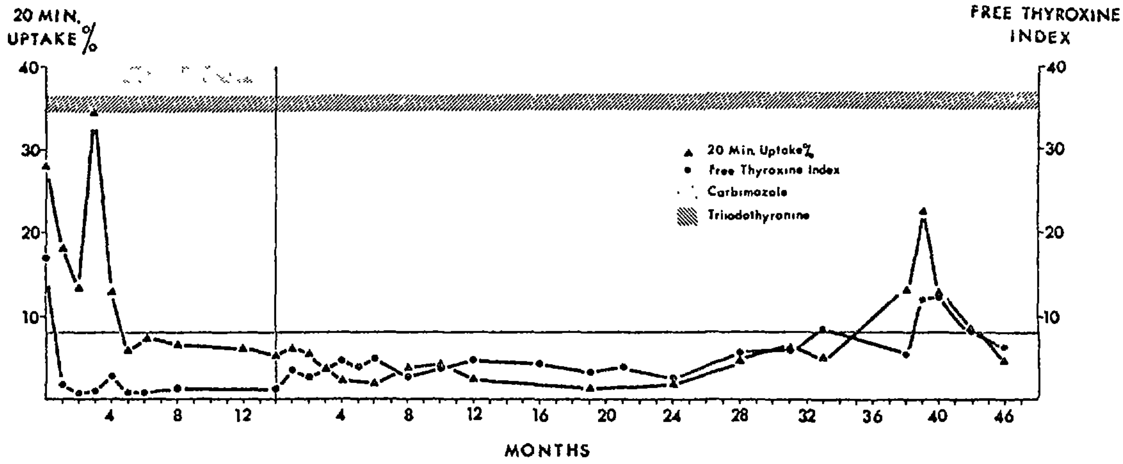

Fig. 4

This patient remained euthyroid for approximately 3 years after completing antithyroid drug therapy, and then she developed transient and incomplete features of thyrotoxicosis associated with elevated 20-minute thyroid uptake and free thyroxine index.

OBSERVATIONS ON THE RATIONALE FOR THYROID UPTAKE MEASUREMENTS: A POLEMIC

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ABSTRACT

This paper discusses the rationale for thyroid uptake tests and the requirements that such tests should satisfy. It is concluded that extremely precise measurements of uptake are not required and that relatively simple equipment and procedures can be used. A number of requirements that should be satisfied are listed.

There have been many proposals directed at improvement of the thyroid radionuclide uptake measurement. These proposals chiefly have been concerned with improvement of the physical accuracy of the measurement dealing with such factors as anatomical variations in gland size and depth, extra-thyroidal neck activity, body background, etc. Some proposals, however, have been more concerned with reducing the amount of radioactivity involved and/or reducing the absorbed radiation dose to the patient. Both of these objectives, singly and in combination, are certainly worthy goals.

Some of these proposals involved methods or equipment significantly beyond the minimum necessary complication or sophistication. Indeed, some schema require multiple measurements with multiple detectors, clearly well beyond the minimum requirement for estimation of "gland activity" by comparative counting.

It would seem appropriate in discussions leading to possible recommendations concerning standardized thyroid uptake measurement equipment and methodology to examine the clinical rationale of the measurement itself.

Why are thyroid uptake measurements requested? What is their clinical value, from a pragmatic point of view? Perhaps a useful point of view may be established by listing some of the reasons for thyroid uptake measurements and commenting on them.

Thyroid uptakes are useful for the following:

1. to provide evaluation of response to stimulation (thyroid stimulating hormone, TSH) and suppression (triiodothyroinine, T-3 and thyroxine T-4) of thyroid function. Comment: Two measurements are required, one to establish a baseline before stimulation or suppression and a second to indicate the change from baseline uptake.
2. to provide a factor for calculation of therapeutic dosages of radioiodine. Comment: It is to be remembered that response to radioiodine therapy is not necessarily proportional to uptake hence there are needed,
3. sequential measurements in support of evaluation of thyroid function after therapeutic doses are administered. Comment: The patient's symptoms may perhaps be better for evaluation, hence the old saying, "Don't treat the uptake, treat the patient's symptoms." However, trends of uptake measurements might indicate response to therapy more quickly than would be possible without them, though T-3 or T-4 studies might be as effective.
4. to provide a means of study of organification in the presence of enzyme defects in familial goitrous cretinism.
5. as a <u>part</u> of a total endocrine evaluation.

There may be other purposes claimed, but these constitute a majority of clinical applications.

In all of these situations, comparison counting of the patient against a reasonably chosen"standard," carried out with good technique, is probably quite sufficient for adequate clinical results. To a certain extent, the patient serves as his own "control" in the baseline study, thus providing some relief from the need for physical assay of gland activity of extreme or absolute accuracy. The only "accuracy" required is that needed for establishment of ranges of normal and abnormal response.

In further assessment of the value of the thyroid uptake, it is to be noted that it is of limited value when used alone. Rather, the thyroid uptake measurement is generally used as a part of a thyroid screening profile (1).

A single thyroid uptake measurement, unaccompanied by other function studies, does not indicate:

1. distribution of activity within the gland
2. functioning extra-thyroidal tissue
3. position of the thyroid in the pituitary-thyroid axis (degree of autonomy). A hyperfunctioning autonomous nodule may account for an ostensibly euthyroid uptake and, indeed, may be suppressing the remainder of the gland.
4. iodine-starved gland. This is important in iodine-poor regions of the world where a hypothyroid person may present a "hyper-trapping" thyroid gland.
5. chronically high levels of exogenous iodine, present in the diet and medications in affluent countries.

Therefore, a single, isolated, thyroid uptake measurement, for which there should be some claim of need for extreme physical accuracy, is of limited clinical value and may even be misleading.

In view of these clinical considerations, it is our position that the thyroid uptake measurement does not merit the use of highly complicated methods nor intricate devices in an effort to obtain an extremely precise assay of thyroid radioactivity. We believe that in the clinical rationale of the thyroid uptake measurement there is nothing to indicate the need for anything other than careful technique using properly operating simple equipment.

Our concept of "simple" equipment includes a scintillation counting system consisting of:

1. an NaI (Tl) scintillation crystal 2.5 cms. x 2.5 cms. or larger,
2. some sort of means (collimator) for confining the field of view of that detector to about 15-20 cms. in diameter at 20 cms. crystal-to-skin distance.
3. at least threshold discrimination as a means of energy-selective counting ("window" or spectrometric counting is cerainly desirable, though by no means essential).

In addition we believe that this simple equipment should include:

4. a spectrally competent neck phantom for holding the "standard" source.
5. an attenuator to eclipse, but not completely obliterate, activity in the thyroid gland. (We do not agree with the statement on page 8 of Measurement of Radioactivity In Body Organs, Report of an IAEA Panel, which states "It is important that the shield be thick enough to ensure that no radiation originating in the thyroid itself is recorded during the background measurement.") A certain penetration by radiation of the Oak Ridge B filter (2) was a part of the rationale of the "ORINS methods".

6. means of positioning the principals in the measurement with respect to each other such that reproducibility is easily obtained.

7. a procedure that is simple, requiring the absolute minimum number of measurements without movement of the detector. A"B-filter" extra-thyroidal background may or may not be spectrally or physically superior to a "thigh background." However, it requires no movement of the detector with respect to the patient, and may thus reduce technical error.

We submit that the use of the simplest equipment and methodology possible in thyroid uptake measurements is consistent both with the clinical rationale of the measurement and the means easily available throughout the world.

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RADIOIODINE DOSIMETRY AND THE USE OF RADIOIODINES OTHER THAN ^{131}I IN THYROID DIAGNOSIS

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ABSTRACT

Of the 24 radioisotopes of iodine, only four, ^{123}I, ^{125}I, ^{131}I and ^{132}I have been utilized clinically to any significant extent. Optimal use of radioiodine involves the consideration of a particular isotope's physical properties in relation to the economics and logistics of shipment, the quality of generated clinical studies, and radiation dosimetry.

In this paper, ^{123}I, ^{125}I and ^{132}I are critically evaluated with reference to each of these considerations. In terms of absorbed dose to the thyroid, ^{123}I and ^{132}I are the isotopes of choice, giving doses about 1/70 and 1/100 of the dose from ^{125}I and ^{131}I respectively. Because of its abundant high energy photons, ^{132}I is impractical for thyroid imaging procedures. Its very short half-life and availability in a generator system, however, give advantages of low radiation dose and applicability in serial thyroid function studies. The relatively long half-life (60 days) and ready availability of ^{125}I are economical advantages. Equivocal clinical results and an only slightly lower radiation dose than ^{131}I, however, are significant disadvantages. The isotope ^{123}I, in addition to giving a low radiation dose, theoretically provides the best combination of physical properties for clinical utilization. Until now, however, the economics of ^{123}I production and contamination with the higher energy isotope, ^{124}I, have limited its utilization. Despite the ^{124}I contamination, high resolution images have been obtained, particularly with a gamma camera and pinhole collimator, and newer methods of production hold promise of large amounts of high purity ^{123}I.

Clinical use of radioiodine isotopes

Though there are 24 possible radioisotopes of iodine, only eight have potential use in medicine, namely those with mass numbers of 121, 123, 125, 126, 128, 130, 131 and 132. Cyclotron produced ^{128}I with only a 25-minute half-life was the first radioiodine used in man almost simultaneously by

Hertz, Roberts and Evans (1) on the East Coast and Hamilton (2) on the West Coast. After this initial attention, little other use of ^{128}I has been reported, and it has never received active clinical use.

The four radioisotopes of iodine that have reveived the most clinical attention, ^{123}I, ^{125}I, ^{131}I and ^{132}I, with their principle properties, are noted in Table I. A number of factors are important in the choice of a radioisotope with optimal characteristics. These factors must be considered in light of the particular circumstances extant in a particular clinical laboratory. Many of the important properties involved in optimizing the use of radioiodine are detailed in Table I. These factors narrow down to three general considerations, namely, the economics and logistics of shipment, quality of the clinical studies and the radiation dosimetry.

Those radioisotopes with shorter half-lives and accelerator production are the most expensive and difficult to obtain. The quality of the clinical procedures is very dependent on the characteristic gamma radiations and their abundance. Photons of either very low or very high energy can interfere with optimization of studies. Low energies result in considerable tissue absorption whereas high energies result in appreciable collimator penetration. Dosimetry, to be covered in detail in the later portion of this paper, is dependent on the mode of decay and the physical half-life.

For diagnostic purposes, it is preferable that a radionuclide have only penetrating radiation. In practice, the half-life need be no longer than the biological event being measured. Wagner and Emmons proposed the average life as a practical measure of the optimization of the physical half-life (3). That is, the closer the average life approximates the time of a biological event, the more ideal is its dosimetry. However, particular clinical circumstances must dictate the optimization of a radioisotope of iodine. In one circumstance, economics may dictate the use of a radioisotope that results in both a higher radiation dose and less than an optimal quality clinical study. Ideally, a radioisotope of iodine for clinical use should be readily available and economical, should have an optimal abundance of pure gamma photons for high resolution collimation and minimal tissue absorption, and should have an average life approaching the time of the biological event, with the least radiation dose possible. Each clinician will thus have to make his own optimization between these extremes.

Limited use of one other radioiodine isotope, ^{130}I, has been reported and is briefly mentioned. Its favourable 12.5 hour half-life is somewhat outweighed by the high energy 1150 and 740 keV gamma photons for routine clinical use. Pfannenstiel _et al_. (4) have reported on its use in the study of total body retention of radioiodine after thyroid stimulating hormone (TSH) in post-surgical thyroid carcinoma patients.

Iodine-132

This radioiodine isotope has received most clinical use in Europe, particularly in England. It is the shortest lived radioiodine in clinical use, consequently with a short average life. It is available from the decay of 3.2-day fission-produced ^{132}Te in a generator, offsetting its short half-life of 2.3 hours (Table I). Azeuedo and Trancoso (5) have reported generators to be useful for up to 3 weeks in remote laboratories. As will be seen in dosimetry calculations, the β^- particles emitted during the decay are offset by the short half-life, resulting in a low radiation dose per unit activity. Consequently, some investigators in Europe have used ^{132}I only in children (6). Of primary concern, however, are the very high energy (Table I) gamma photons which make collimation difficult, if not impossible.

Because of the short physical half-life, thyroid measurements must be made soon after ^{132}I injection, usually at 4 hours, when body background is still very high from the residual high concentration in the inorganic iodide space. The high-energy gammas would appear to make body background correction subject to considerable measurement errors. Levy and Ashburn (7) have reported on a technique that apparently has relative clinical value. However, they indicate that the prime use of ^{132}I is for study of variations in the same individual with time and pharmacological manipulation, and they do not recommend the test in the general patient population due to the low differential uptake range between extremes of thyroid function (8). Twenty-four hour radioiodine uptake seem to have a wider acceptance and the 3.3-hour average life does not approximate the timing of this procedure.

As Levy and Ashburn have reported, a prime asset of ^{132}I is the study of thyroid function with special uses such as pharmacologic manipulation with tri-iodothyronine (T_3) and TSH,because tests can be repeated in close temporal relationship (9, 10, 11). With longer-lived radioiodines, contributions from previously administered activity introduce significant errors in subsequent measurements.

Practical thyroid imaging with ^{132}I has been said to be impossible by Myers who excludes ^{132}I from his list of clinically useful radioisotopes of iodine (12). Collimators for use with ^{132}I could be designed, but would affect the radiation dose advantages for ^{132}I, plus imaging would have to be done with unacceptably high body backgrounds. Nonetheless, Guntermann has reported successful scintigraphy with ^{132}I (13). It is doubtful if the procedures described would be widely adopted. Thus ^{132}I does have advantage in low radiation dose, serial thyroid function studies, but probably does not have place in the general nuclear medicine laboratory because of its poor imaging properties.

Iodine-125

Iodine-125 has one of the longest physical half-lives, 60 days, yet the lowest-energy photons of any of the clinically used radioiodines (Table I). These characteristics make possible certain unique capabilities in diagnostic studies with this radioisotope, as Myers has outlined (12). This radioisotope is as readily available as ^{131}I in most areas, and indeed its long physical half-life gives it some additional economic advantages. Estimates of its radiation dose vary widely and are probably dependent upon the misconception of ^{124}I photons as penetrating radiation, as will be discussed under the dosimetry section. In terms of 24-hour thyroid uptake determination, ^{125}I has an exceptionally long average life. The quality of clinical procedures with ^{125}I is very dependent upon a number of technical factors, which, if not recognized, can certainly deteriorate or even nullify results.

Great care must be taken to assure that one uses properly designed instrumentation with ^{125}I. With a half value of only 0.17 cm in aluminium, one must be certain to use NaI(Tl) crystals "canned" with the thinnest aluminium foil. Also, satisfactory electronics must be utilized. Presently gamma cameras cannot be satisfactorily employed with such low-energy photons. Of critical importance to the use of this radioisotope is the significant tissue absorption, i.e. 1.7 to 1.8 cm half-value-layer (Table I). Iodine-125 used for thyroid function studies must employ appropriate measures for thyroid depth correction. Studies in our laboratory for correction of thyroid depth have indicated an average thyroid depth of 2.6 cm with a range of 0.6 to 4.5 cm (Fig.1). Riccabona (14) has alluded to this problem: however, the only accurate approach to thyroid depth appears to be that advocated by Rollo (15). This technique employs the inverse square principle with thyroid counting distances of 18 and 25 cm. However, with the tissue absorption factors offsetting the high photon abundance, the standard measuring distances plus the more recent higher radiation dose estimates from ^{125}I (see dosimetry) would not seem to give the radioisotope as much clinical advantage as proposed by Rollo (15). Photopeak to Compton-scatter correction as published by our laboratories (16) is not feasible with ^{125}I because of the extremely low photon energy.

Tissue absorption factors are also significant in thyroid imaging with ^{125}I. More superficial aspects of the thyroid are going to be imaged with greater efficiency. Substernal thyroid extension may be a particularly difficult problem with ^{125}I. Clinical studies with ^{125}I by Riccabona et al. (14) to intermediate by Charkes et al. (17) to no advantage by Artagaveytia et al. (18). Moll et al. have reported that ^{125}I scintigraphy at tissue depths greater than 2 cm are inferior to ^{131}I or $^{99}Tc^m$. (19).

There has been some agreement that ^{125}I can be useful in delineating superficial thyroid nodules (20), which may be its principal imaging advantage.

In contrast to ^{132}I, use of ^{125}I for pharmacologic manipulations such as with T_3 and TSH would appear to have the same drawbacks as ^{131}I, namely continued retention by the thyroid gland. On the other hand, for evaluation of long-term biological events such as radioiodine kinetics, the long physical half-life of ^{125}I can be used to advantage, especially in children, as we have previously reported (21). Although not in the scope of this paper, it must be emphasized that ^{125}I has distinct advantages in various in vitro studies of thyroid function (12).

Iodine-123

Myers has stated that "^{123}I fulfills the criteria for an ideal gamma isotope more than any other radioisotope of iodine" (12) and, theoretically, this appears to be true. He has reported initial early work with low resolution scintigraphy (22). The 13.3-hour half-life is certainly long enough to accomplish satisfactory clinical studies, indeed the average life of 19.2 hours approaches the 24-hour thyroid uptake time more closely than any of the other radioiodine isotopes (Table I). The 159 keV gamma makes collimation nearly ideal and has a very satisfactory tissue half value layer of 4.7 cm. Pure electron capture decay plus the relatively short half-life result in the lowest radiation absorbed dose, save ^{132}I, as discussed later.

For all purposes, ^{123}I appears ideal: however, of more concern than with any of the other radioisotopes of iodine, are the modes of production and the concomitant economics. This radioisotope can be produced only in an accelerator, but by a number of reactions. It continues to be commercially available from the Oak Ridge National Laboratories, produced by the ^{123}Te (p,N) ^{123}I reaction, and is very expensive compared with ^{131}I or ^{125}I.

Our initial enthusiasm for ^{123}I was aimed at the exploration of alternate, less expensive, production techniques for this radioisotope. Sodd et al. (23) have recently reported our results to date with most of the possible production reactions. As a consequence of the extensive studies, we have advocated the indirect production technique of $^{122}Te(^{4}H,^{3}n)$ $^{123}Xe \xrightarrow{2.1\ hr} {}^{123}I$ for reasons explained below. The ultimate economics for commercial use of this reaction are the subject of continuing investigation.

Our early, initial clinical studies in 30 thyroid patients were designed to compare ^{123}I with ^{131}I assuming the theoretical advantages of the more ideal radioisotope (24). A high-resolution, low-energy 1045-hole collimator (Fig.2) was used for ^{123}I and a 31-hole, medium energy collimator for ^{131}I. In addition, ^{123}I imaging was done with the gamma camera and pinhole collimator. Both 28 and 159 keV images at 6 and 24 hours were performed with ^{123}I at approximately equal information densities. The resultant studies were read by a blinded technique by a panel of four physicians. To our disappointment, ^{131}I images were still preferred, with gamma camera images being preferred with ^{123}I. Twenty-eight keV studies were judged inferior.

Further analysis of cyclotron products including our own as well as those of ORNL revealed higher than anticipated amounts of ^{124}I, as reported by Sodd et al. (25). Goolden et al. (26) have also reported on the problem of ^{124}I contamination in clinical ^{123}I studies.

Additional studies were performed to evaluate the effect of ^{124}I contamination on a thyroid scanning system (Fig.3). Thirty-one, 73 and 1045 hole collimators were evaluated. As can be seen, the high-energy (511, 602, 722 and 1690 keV of ^{124}I) scatter contribution to the 159 keV photopeaks of ^{123}I is approximately equal (2, 3%) with the 31-hole collimator with pure or contaminated ^{123}I. However, high energy scatter with contaminated ^{123}I represents 28 % of the total photopeak counts with the 1045-hole collimator. The 73-hole collimator is imtermediate in its response. Cerium-139 was used as a "mock" ^{123}I source as well as to evaluate the contribution of the 1 % abundant 500 keV gamma photon of ^{123}I.

Further studies in 35 additional patients were then performed. In Fig. 2, it is noted that at the photopeak energy of ^{123}I, the 31-hole collimator has very high resolution. In the second patient study, use of the 31-hole collimator with ^{123}I was added to the protocol. The same panel of four physicians again judged the results. In this series, no significant difference was found between ^{131}I and ^{123}I with the 31-hole collimator, however, 300 μCi amounts of ^{123}I activities were administered vs. 100 μCi of ^{131}I. The panel of physicians again concluded that the 28 keV images were inferior. Six-and 24-hour studies were judged to be of about equal quality. Of import, the gamma camera scintiphotos were considered, overall, to be superior to the rectilinear scans. The dose reduction resulting from the use of ^{123}I should be stressed, especially as regards studies in children and pregnant women.

More recently, a limited number of patients have been studied with commercially available ^{123}I. Studies with ^{123}I containing ^{124}I at a level of about 10 % show degradation of resolution when the 73-hole collimator was utilized. Very good views were obtained with the 31-hole collimator and the gamma camera. Similar studies at a level of ^{124}I contamination of 29 % produced images of inferior quality with the 73-and 31-hole collimators. However, excellent images were obtained with the gamma camera. It must be emphasized that despite ^{124}I contamination, in all our studies, gamma camera images were of as high a quality or superior to rectilinear scans. We have postulated that these superior results have a two-fold explanation. First of all, the tungsten insert and single pinhole combination with the gamma camera eliminate the scattering of the high energy photons (511, 602, 722 and 1690 keV) of ^{124}I from the septa in the focusing collimator used with rectilinear scanners. Secondly, the 0.5"NaI(Tl) crystal is not efficient for such high energies and will thus, in part,"disregard" the ^{124}I photons. The inferior quality of the 28-keV scans probably results from the excessive amount of scattered radiation from higher energy photons.

Thyroid uptakes with ^{123}I in our laboratories have been found to correlate well with ^{131}I (24). Whereas the degree of tissue absorption with ^{123}I is not nearly as great as with ^{125}I, correction for thyroid depth should be made. If one employs maximum sensitivity by placement of the detector crystal in contact with the neck, it becomes mandatory to correct for thyroid depth. High-sensitivity thyroid uptakes can be performed utilizing our previously reported technique for photopeak to Compton-scatter correction of thyroid depth. Thyroid depth correction curves for a family of thyroid phantoms are seen in Fig. 4 utilizing "mock ^{123}I". Uptakes can be performed easily with as little as 0.01 μCi of ^{123}I which represents a total absorbed radiation dose reduction of 10,000 to 100,000 over the usual techniques with ^{131}I. These are most important considerations in pregnant women and the pediatric population.

Another advantage of ^{123}I is the ability to perform 24-hour thyroid uptakes and images on patients after standard courses of T_3 suppression and TSH stimulation without significant interference from previously administered ^{123}I.

In summary, clinical utilization of the theoretical ideal characteristics of ^{123}I has been somewhat hampered by the presence of the high-energy contaminant, ^{124}I. For the interim, use of the pinhole collimator and the gamma scintillation camera seem to obviate the resolution problems in imaging with contaminated ^{123}I, resulting in high quality images. Further development of indirect methods of production of high purity ^{123}I, especially if made more economical, will greatly increase the potential use of ^{123}I. Lastly, promise of production of multicurie amounts of ^{123}I has been suggested through the use of high energy photon accelerators and spallation reactions (Fig.5). It is anticipated that contamination will be as great, or a greater problem, with direct ^{123}I production by these techniques. We anticipate that the indirect reaction through ^{123}Xe will be found to be the ultimate answer to the economical spallation production of large amounts of ^{123}I of high purity.

Radioiodine dosimetry

The average absorbed doses to the total body and to specific organs from ^{123}I, ^{125}I, ^{131}I and ^{132}I are presented in Table II. These values were calculated according to the schema of Loevinger and Berman (27).

$$\bar{D} = \frac{\tilde{A}}{m} \sum_i \Delta_i \quad \phi_i$$

Where $\bar{D}$ is the average dose in rads, $\tilde{A}$ is the cumulative activity in μCi-h, m is the mass of the target in grams, Δ is the equilibrium dose constant in g-rad/μCi-h, and ϕ is the absorbed fraction.

The nuclear parameters (Δ_i) for the four radioiodines were taken from the work of Dillman (28, 29). For purposes of dose computation, these equilibrium dose constants were divided into penetrating and non-penetrating as shown in Table II. The absorbed fractions (ϕ_i) as a function of photon energy are available in MIRD Pamphlet No. 5 (30). However, for the absorbed doses present in this paper, an effective absorbed fraction ($\bar{\phi}$) for all the penetrating radiations from each radioisotope was utilized. The same Monte Carlo approach described in MIRD Pamphlet No. 5 was employed, but absorbed fractions were obtained for the complete photon spectrum rather than for individual photon energies. When multiplied by the total penetrating equilibrium dose constant ($\bar{\phi} \sum_i \Delta_i$), the value obtained is equivalent to the computation of $\sum_i \Delta_i \quad \phi_i$ using the individual ϕ_i values in MIRD Pamphlet No. 5. A summary of these effective absorbed fractions for the radioisotopes of iodine is presented elsewhere (31).

The cumulative activities, $\tilde{A}$, were determined as $\int_0^\infty A(t)dt$. The biological distribution functions used were approximations of computer solutions derived from the Berman et al. iodine model (32) and represent the average normally functioning adult thyroid. The maximum thyroid uptake of radioiodine was assumed to be 27 %, and the final thyroid biological half-life was taken as 68 days. Both of these assumptions are based on human data reviewed in a recent publication by Wellman et al. (21).

It is readily apparent from the dosimetry data given in Table II that, as expected, the absorbed dose to the thyroid is in all cases the limiting factor. With the exception of ^{125}I, these absorbed doses are slightly lower than the previously published estimates summarized by Hine and Johnston (33). This is presumably attributable in part to more precise biological and physical parameters and the utilization of the absorbed fraction method of dosimetry. It should be noted that specific absorbed fraction $(\frac{\phi}{m})$ were used for the thyroid dose calculations. Based on extensive autopsy data, Wellman et al. (21) found an average adult thyroid weight of 16 grams, but the currently accepted standard for thyroid weight is approximately 20 grams (34), and the available absorbed fraction data (30, 31) have been calculated using this latter figure.

Previously published estimates of the absorbed dose to the thyroid from ^{125}I range from 0.4 to 1.4 rads/µCi (33). The estimate given in Table II suggests that the higher values are more realistic. The lower estimates may possibly be attributable to an overestimation of the penetrating characteristics of the radiations from ^{125}I. The penetrating radiations from ^{125}I account for 33 % of the absorbed dose while representing 66 % of the available energy. On the other hand, the penetrating radiations from ^{123}I account for only 27 % of the absorbed dose while representing 86 % of the available energy (see Table III).

This same reasoning can be used to indicate the significance of the β^- radiations emitted in the decay of ^{131}I and ^{132}I. The penetrating radiations account for only 8 % and 13 % of the absorbed doses from ^{131}I and ^{132}I respectively, while representing 61 % and 82 % respectively of the available energy (see Table III).

Based strictly on dosimetric considerations, either ^{123}I or ^{132}I would be the radioiodine isotope of choice for clinical procedures, since the thyroid absorbed doses from these two isotopes are about 1/70 of the dose from ^{125}I and about 1/100 of the dose from ^{131}I. This is of particular importance with respect to radioiodine studies in pregnant women and in children (21).

Inherent in the thyroid absorbed dose computations presented in this paper is the assumption that the radioiodine is uniformly distributed within the thyroid gland. Ultimately, thyroid dosimetry must consider the actual distribution of the radioiodine at the cellular level, since radioiodine concentrates in the thyroid follicles (35). Such a non-homogeneous distribution of activity represents more of a hazard than homogeneous distribution due to the potential existence of very high absorbed doses in a small amount of tissue. Anspaugh (35) has considered the non-homogeneous distribution of ^{131}I in the thyroid and concludes that the absorbed dose remains essentially homogeneously distributed. Similar assumptions may or may not be valid for the other radioiodine isotopes with their different spectral compositions, particularly ^{125}I and its low energy radiations, as suggested by Myers (12).

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TABLE I

CLINICALLY USED RADIOIODINE ISOTOPES

Mass #	T 1/2	Average Life	Decay Modes	Principal γ Photons keV (% abundance)	Tissue (H_2O) Half Thickness cm.*	Source
123	13.3 H	19.2 H	EC	28(92), 159(84)	1.7, 4.7	ACCELERATOR
125	60 D	86.4 D	EC	28(137), 35(7)	1.7, 1.8	FISSION
131	8.1 D	11.7 D	β^-	640(9), 364(80)	8.0, 6.3	FISSION
132	2.3 H	3.3 H	β^-	670(100), 760(93) 520(30), 1.41(13)	8.1, 8.6 7.2, 11.6	FISSION VIA GENERATOR

*For respective γ photons

TABLE II

Average Absorbed Doses*

Organ	Mass (grams)	Radioiodine Mass Number	Absorbed Dose (rads/μCi administered)
Thyroid	16	123	.015
		125	1.04
		131	1.5
		132	.015
Liver	1833	123	.00003
		125	.0005
		131	.0005
		132	.0001
Stomach**	160	123	.0009
		125	.001
		131	.008
		132	.006
Salivary glands	80	123	.0007
		125	.004
		131	.007
		132	.006
Ovaries	8.8	123	.00001
		125	.00001
		131	.00005
		132	.00001
Testes	38	123	.00002
		125	.00001
		131	.00004
		132	.00004
Red marrow	1500	123	.00002
		125	.0002
		131	.0002
		132	.00004
Total body	70000	123	.00003
		125	.0006
		131	.0008
		132	.0001

*The uncertainties in these values may be as high as 50%.

**For purposes of dosimetry, the upper GI contents have been added to the stomach contents due to their close proximity.

TABLE III

Total Equilibrium Dose Constants ($\Sigma\Delta_I$)

(g-rad/μCi-h)

Radioiodine Mass Number	Penetrating	Nonpenetrating
123	.3674	.0591
125	.0878	.0446
131	.8042	.4134
132	4.9035	.9982

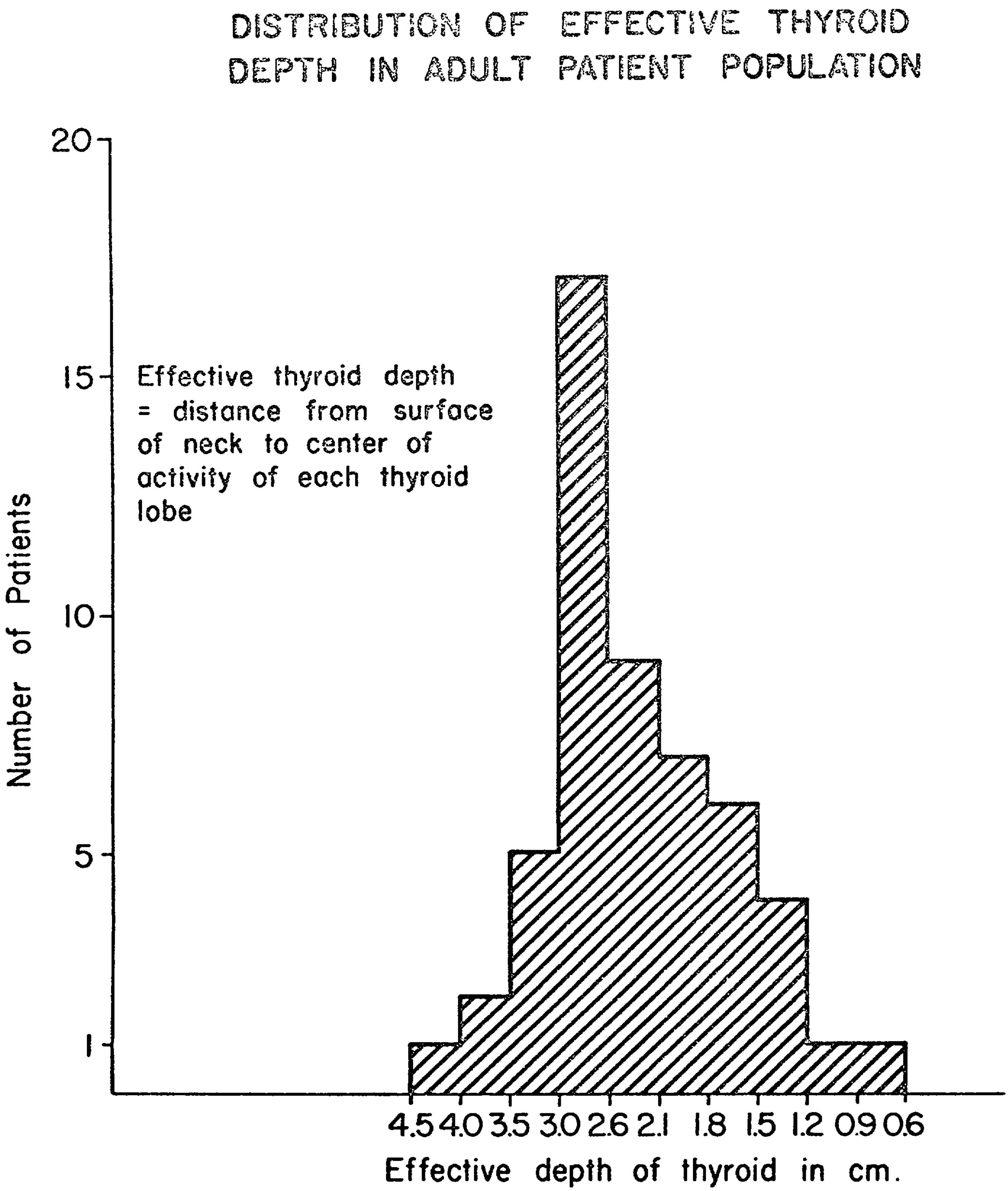

Fig. 1. Effective thyroid depth distribution in a group of patients studies with the photopeak : Compton ratio method of uptake.

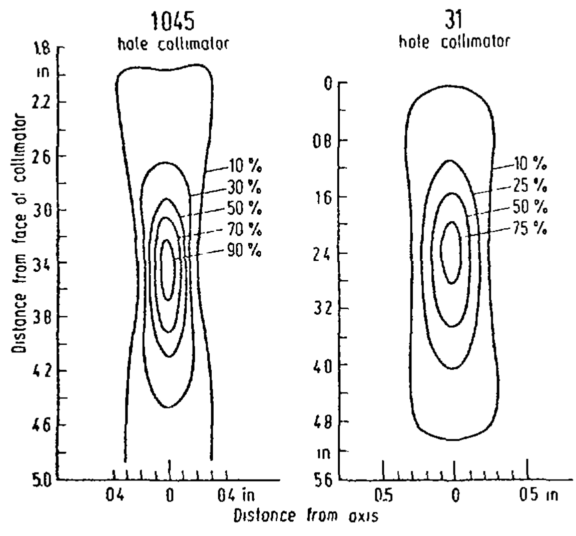

Fig. 2. Isoresponse characteristics of a 1045 hole high resolution low energy and a 31 hole medium resolution high energy collimator with 140 keV ^{99m}Tc photons.

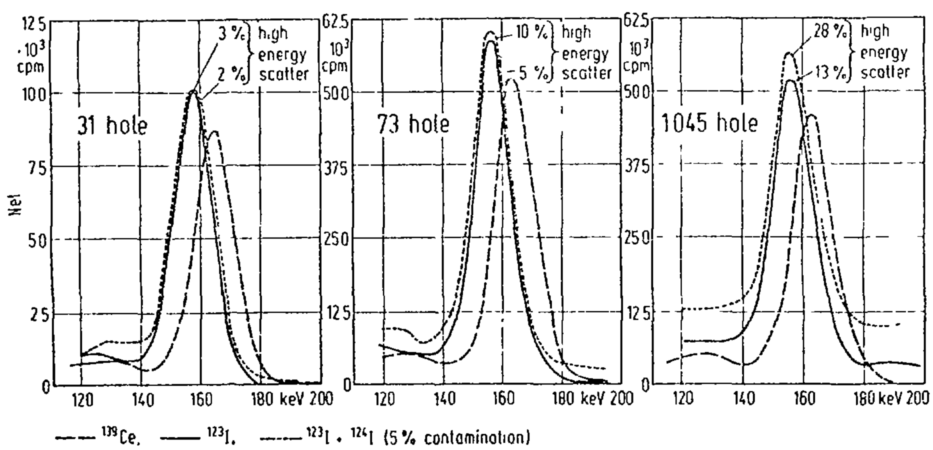

Fig. 3. Effect of high energy photon scattering on 1045, 73 and 31 hole collimator systems on the 159 keV photopeak of ^{123}I.

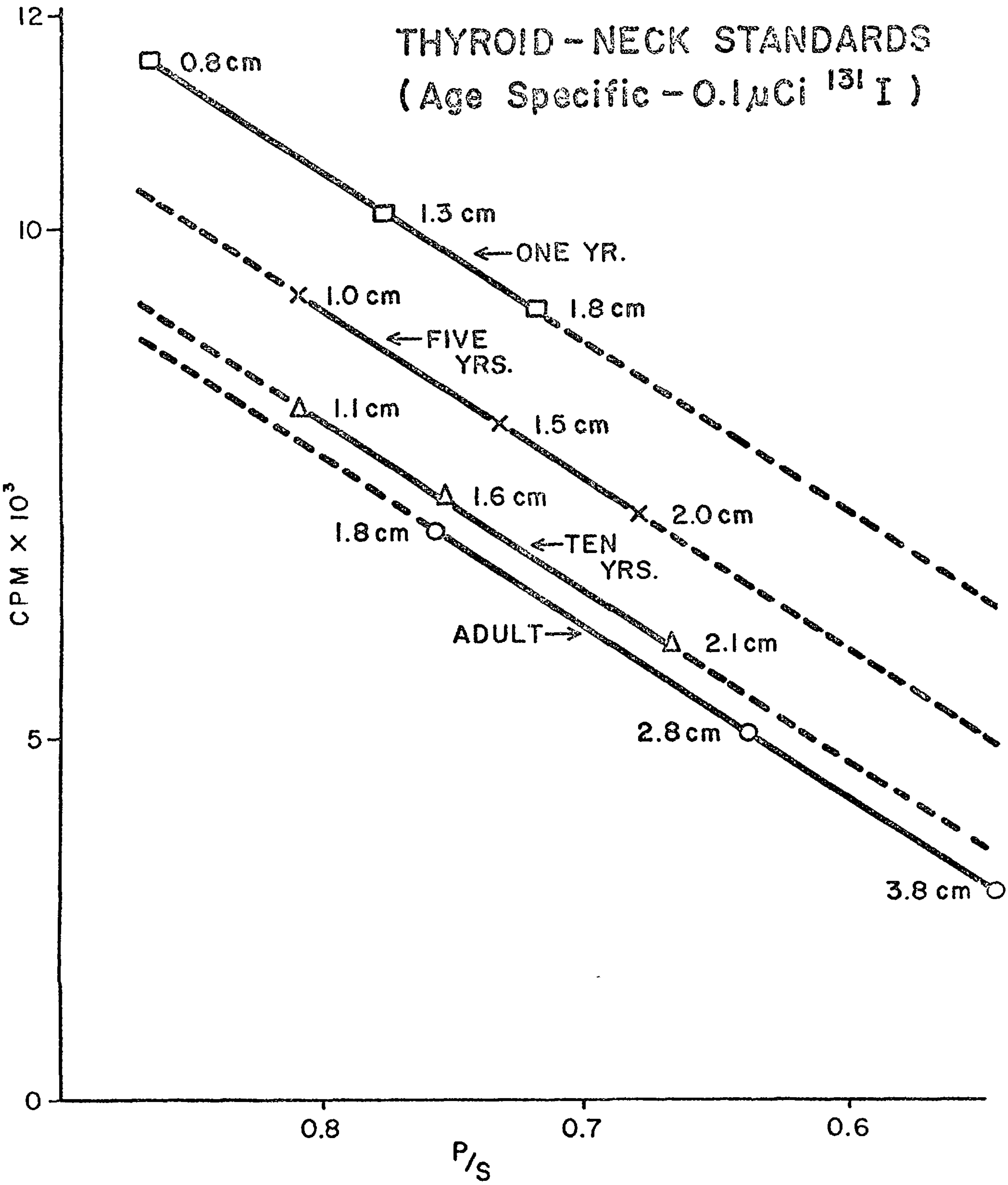

Fig. 4. Photopeak to scatter standard corrections curves for a family of thyroid phantoms with "mock ^{123}I" - ^{139}Ce.

SPALLATION PRODUCTION* OF ^{123}I

$$^{127}I\ (p,5n)\ ^{123}Xe \xrightarrow{\beta^+} {}^{123}I$$

$$^{126}Te\ (p,4n)\ ^{123}I$$

*IN SYNCHROCYCLOTRON OR LINEAR ACCELERATOR
200 MEV PROTONS

Fig. 5. Spallation reactions for direct and indirect production of ^{123}I.

THYROID I-131 UPTAKE MEASUREMENT AND THE DETERMINATION OF EFFECTIVE HALF-LIFE OF I-131 IN PATIENTS WITH THERAPEUTIC DOSES

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ABSTRACT

This paper describes comparative studies of uptake and effective half-life of ^{131}I in the thyroid in patients receiving diagnostic and therapeutic doses of the radioisotope. Uptake of diagnostic doses was measured conventionally. Uptake of therapeutic doses was measured using the same scintillation detector at a working distance of 150 cm and a pulse-height analyzer with a narrow window aligned on the 0.364 MeV peak in the gamma-ray spectrum. The results showed considerable individual variation. The mean values for 24-hour uptake of diagnostic and therapeutic doses were 71.5 % and 65.6 % respectively, the mean difference being 5.9 % and its standard deviation 15 %. The effective half-life was often shorter for therapeutic than for diagnostic doses and was further shortened by repeated therapy, the mean values after one, two and three therapeutic doses being 5.3 days, 4.5 days and 3.3 days respectively. It was concluded that accurate assessment of the radiation dose to the thyroid in the individual case requires direct measurement of the uptake and effective half-life.

I. Introduction

When the treatment with I-131 for hyperthyroidism is made, it is an important problem to know how much irradiation dose would be given to the thyroid tissues. This dose is considered to be a function of administered dose of I-131, weight of the thyroid gland, thyroid uptake of I-131 and effective half-life of I-131 in the thyroid gland.

Of these factors, the thyroid uptake and the effective half-life will be discussed in this paper. In general, the thyroid uptake and the effective half-life required for determining the I-131 administration dose are obtained from the results of the test dose given to the patients before the administration of the therapeutic dose. However, the thyroid uptake and the effective half-life would not be always the same in diagnostic and therapeutic doses.

So it is recommeded to measure the thyroid uptake of I-131 and the effective half-life at each time when the I-131 therapy dose is administered.

We carried out following work.

(1) The method of measuring the correct thyroid uptake in the case having a therapeutic dose was studied by using the body phantoms.

(2) The I-131 thyroid uptake and the effective half-life were measured on the patients who had been given the therapeutic doses.

(3) The difference between the thyroid uptakes of patients with therapeutic doses and those with diagnostic doses given prior to the I-131 treatment was discussed.

II. Methods and Results

1. Method of measuring the thyroid uptake of I-131 in therapeutic dose.

This method was established by one of our colleagues, Dr. Y.TATENO, and published in Acta Radiologica Japonica, Vol. 23, No. 8, P. 983-986 (1963). The summary of this paper is as follows.

The therapeutic dose of I-131 to be administerd to a patient with hyperthyroidism is usually 3 - 10mCi. This dose gives theoretically more than one million counts per minute, if the thyroid uptake is calibrated by the routine diagnostic methods. On the other hand, the resolving time of scalers used in most clinical laboratories is 10 microseconds at the shortest. When the count on these scalers reaches one million counts per minute, the counting loss becomes 15 - 25% of the total. Therefore, it is difficult to measure correct thyroid uptake by the routine method when a therapeutic dose is applied. To obtain the correct thyroid uptake in regard to a therapeutic dose, the counting rate should be reduced.

A. Methods

(1) Measuring instrument

The instrument being used in our Department for routine thyroid uptake measurement was employed.

a. Medical spectorometer with scaler: Toshiba ML-412

b. Crystal size: NaI(Tl) 2.5 x 2.5 cmø

c. Phantom: ORINS neck phantom

(2) Methods of decreasing counting rate

To restrict the maximum counting loss to 1%, the counting rate should be under 50,000 counts per minute with the routine counter. On the other hand, if 5mCi of I-131 would be taken up by the thyroid gland from a therapy dose, the counting rate will reach about 900,000 c/m by the standard method of measuring thyroid uptake in regard to a diagnostic dose. Namely, the counting rate should be reduced to about 1/30. For this purpose the following five methods were put in trial.

a. Measuring at a distance of 150cm
b. Using a thicker A-filter (1.25cm Pb)
c. Inserting a suitable additional cone into the collimator to make the opening area of the crystal smaller
d. Measuring the 637 keV peak (637 ± 5 keV)
e. Making the window of the photopeak narrower (364 ± 5 keV)

(3) Body phantom

Three kinds of body phantom with high, medium, and low body background levels were used for the experiment. Three mCi of I-131 was put into the thyroid gland of 25ml. Assuming that the administered dose is 5mCi, the thyroid uptake would be 60%. Three different background levels of the phantom were prepared by 2mCi, 250μCi, and 0μCi I-131 dose.

(4) Standard source

A small test tube containing 5mCi of I-131 in the chemical form of NaI solution of 5ml was used as a standard source in the ORINS neck phantom.

After the measurement the standard source and the body phantom were left for 35 days. When the radioactivity of I-131 had decayed to the level of the diagnostic dose, they were measured again by the routine method. The uptake was 59.7 ± 0.4%. This value was considered as the thyroid uptake rate of the body phantom, and the results obtained by various methods of measuring the therapeutic dose were compared with one another, and discussed.

B. Results

Tab. 1 shows the experimental results.

a) Of the methods measuring at the distance of 150cm, the integral method gives a good result when the body background is low. However, if the body background is high, the uptake decreases. The correct results were obtained with differential method independent of the body background levels.

b) The method using a thicker A-filter (1.25cm Pb) brings lower values both in integral and differential methods.

c) The method inserting an additional cone into the collimator gives a lower value by differential method. In integral measurement, a correct result is obtained, when the body background is low. However, the uptake becomes lower, if the body background level is high.

d) The method measuring the cesium peak alone gives a lower value than the A-filter method.

e) The method using a narrower window causes a higher uptake value.

As the conclusion the differential method measuring at the distance of 150cm obtained the most correct value among the therapeutic dose measurements by using the body phantoms.

To check whether the body phantoms would be considered similar to patients in measurements, the results of the various measuring methods on the 26 patients treated with I-131 were compared with one another and are shown in Tab. 2.

Since the correct uptake value of a patient is unknown, the differtial method at the distance of 150cm was taken for its correct answer based upon the phantom experiments. The deviations of uptakes with various measuring methods are shown in the table. The results obtained from the clinical cases are quite similar to those of phantom experiments, especially those with 40% body background.

2. Determination of effective half-life of I-131 in patient with a therapeutic dose

By the method of thyroid I-131 uptake measurement which was mentioned in item 1 the thyroid uptake for the patients treated with I-131 were measured chronologically. From the data obtained the effective half life was determined and the results were compared with that of diagnostic dose measured before the I-131 therapy. Then the difference in the effective half lives between the diagnostic and therapeutic doses was discussed.

A. Methods

(1) Measuring instrument

The same as item 1

(2) Method of measurements

i) Crystal-skin distance

In the case of diagnostic dose 40cm

In the case of therapeutic dose 150cm (sometimes 200 - 300cm)

ii) Counting method

Differential counting method 364 ± 30 keV

iii) Neck phantom

ORINS type

(3) Calculation of thyroid uptake (T.U.)

$$T.U. = \frac{P - Pb}{S - Sb} \times 100$$

where P : Patient's counting rate

Pb: Patient's background counts

S : Counting rate of the standard source

Sb: Background counts in the standard source measurement

(4) Determination of the effective half-life

The thyroid I-131 uptake dose measured chronologically was plotted along the ordinate on a semi-logarithmic graph paper against time (days) along the abscissa. After confirming that the relationship appears to be linear, the effective half-life was determined from the days through which the dose became one half of the initial value.

(5) Calculation of the irradiated dose

The Quimby's method was employed. The weight of thyroid gland was calculated from the Allen-Goodwin's formula, and the area of thyroid gland was obtained from the scan image.

(6) Patients

All the cases are hyperthyroidism treated with I-131. The number of patients are 150 in 1969 - 1971. The dose of I-131 for treatment is 3 - 10mCi at one time in each case.

B. Results

(1) Difference between the patients' thyroid uptakes after the administration of diagnostic and therapeutic doses.

To all the patients treated with I-131 a diagnostic dose was administered before the treatment and the thyroid uptake was measured. After a therapeutic dose was given thyroid uptake was measured again on the same patient, and both data were compared. The thyroid uptakes (24hrs) of diagnostic and therapeutic doses in 150 patients were plotted along the ordinate and the abscissa respectively as shown in Fig. 1 to investigate the correlation between them. The dots on the graph scattered about the 45° line through the origin, but generally speaking, the thyroid uptake of a therapeutic dose is lower compared with that of a diagnostic dose. The mean value of the 24 hour uptakes in 150 patients with therapeutic doses is 65.6%, while that of diagnostic doses measured before the therapy is 71.5%.

Tab. 3 shows the distribution of the differences between uptakes of a diagnostic dose and a therapeutic dose in all cases. The mean value of the differences in uptakes of 150 cases is 5.9%. From this result it is clear that the uptakes of therapeutic doses are lower in general. Plotting these data, a distribution curve shown in Fig. 2 is obtained. The standard deviation is ± 14.5%. This large value means that the differences in uptakes are dispersed. In other words, the uptakes of diagnostic and therapeutic doses are not always the same and there is considerable variety in the differences.

(2) Comparison between the effective half lives of I-131 given by diagnostic and therapeutic doses.

The comparison of the effective half lives of I-131 given by diagnostic and therapeutic doses on 11 cases is shown in Tab. 4.[2] As seen from the table the effective half-life obtained with a therapeutic dose are clearly shorter than that with a diagnostic dose. The mean value of the former is 4.6 days and the latter 3.9 days.

(3) The effective half life of a therapeutic dose and the frequency of therapy.

The effective half lives of patients with therapeutic doses were measured by three groups; those in the first, second, or third group were measured in connection with the first, second or third therapy respectively. The mean value of the first therapy group was 5.3 days, the second 4.5 days and the third 3.3 days. There is a tendency that the I-131 therapy dose shortenes the effective half life as the number of the therapy increases. Sometimes, the variation of the effective half life reaches several days for the same person depending on the time of different I-131 administration. However, its mean value becomes shorter as the number of therapy becomes large.

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Methods	Body Background	0%	5%	40%
150cm	int.	59.7%*	58.5%	56.2%
	dif.	59.4%	60.1%	60.2%
A-filter	int.	58.9%	57.9%	57.2%
	dif.	55.9%	56.3%	57.5%
Inserted cone	int.	60.0%	60.0%	58.1%
	dif.	57.8%	58.3%	58.8%
637 ± 30 keV		56.4%	55.9%	55.7%
365 ± 5 keV		61.3%	61.0%	61.2%

Tab.1 Results of the phantom experiment

* Mean Value of 10 measurments
True answer is 59.7 ± 0.4%

Methods		Deviations of Uptake * +
150cm	int.	0%
	dif.	- 4.2%
A-filter	int.	- 1.7%
	dif.	- 1.9%
Inserted cone	int.	- 0.8%
	dif.	- 1.0%
637 ± 30 keV		- 1.7%
365 ± 5 keV		+ 0.1%

Tab.2 Results of the clinical experiment

* Uptake ratios calculated by 150cm 364 ± 30 keV method are taken for standards.

\+ Mean value of 26 patients with hyperthyroidism treated with I-131

T.U.diag. - T.U.thera.(%)	1969 - 1971 24hr.
- 20% ~	4 cases (2.7%)
- 10% ~ - 19%	15 " (10.0%)
- 0.1% ~ - 9%	32 " (21.3%)
0% ~ 9%	44 " (29.3%)
10% ~ 19%	34 " (22.7%)
20% ~ 29%	12 " (8.0%)
30% ~ 39%	5 " (3.3%)
40% ~ 49%	3 " (2.0%)
50% ~	1 " (0.7%)
Total cases (mean value of the differences)	150 cases (+5.9%)

Tab.3 Differences between the thyroid I-131 uptakes of patients with diagnostic and therapeutic doses.

Case	E.H.L. of Diag. Dose	E.H.L. of Therap. Dose
1	5.8 days	2.4 days
2	6.5 "	4.0 "
3	4.4 "	2.0 "
4	5.7 "	4.3 "
5	5.6	4.6 "
6	3.4 "	2.5 "
7	3.2 "	2.8 "
8	5.5 "	5.2 "
9	3.5 "	3.9 "
10	4.4 "	5.5 "
11	2.6 "	5.0 "
Mean	4.6 days	3.9 days

Tab.4 Effective half lives of diagnostic and therapeutic doses.

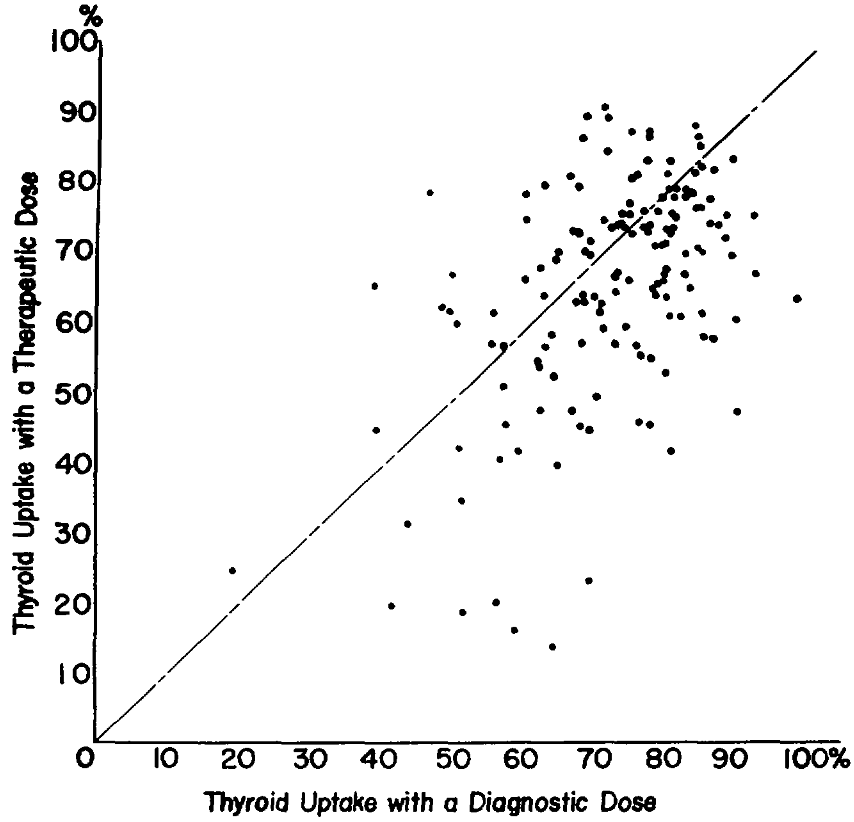

Fig. 1 Correlation of the 24hr. thyroid I-131 uptakes with diagnostic and therapeutic doses.

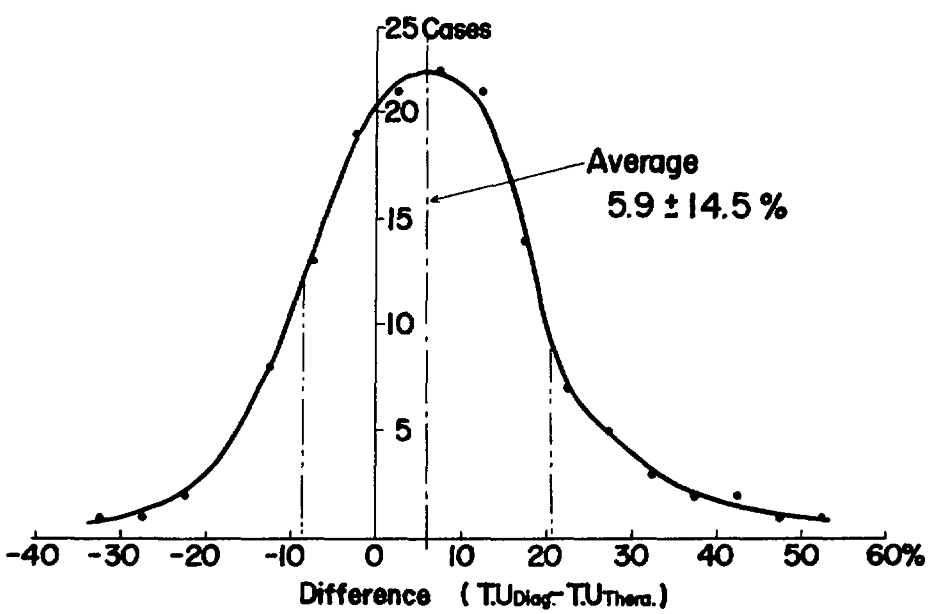

Fig. 2 Distribution curve of the differences between the thyroid I-131 uptakes of patients with diagnostic and therapeutic doses.

THE MEASUREMENT OF THYROID UPTAKE USING $^{99}Tc^m$

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ABSTRACT

This paper surveys the clinical value of early thyroid uptake tests with $^{99}Tc^m$, describes methods of carrying out such tests and presents preliminary clinical results obtained using these methods. Since $^{99}Tc^m$ in the form of pertechnetate is trapped by the thyroid in the same manner as iodide, but does not become organically bound, the early uptake of $^{99}Tc^m$ is an index of the iodide-trapping function of the thyroid independent of its iodine-binding function. The 20-minute $^{99}Tc^m$ uptake test is a simple and reliable test of thyroid function, and since it can be carried out repeatedly it is particularly valuable in following the progress of patients undergoing therapy with antithyroid drugs. One method of carrying out the test using a dual-detector scanner for the measurement of uptake and another using a single-detector scanner are described and their relative merits discussed. Preliminary clinical results obtained by these methods, including the results of suppression tests carried out with $^{99}Tc^m$ and the results of long-term follow-up studies on patients treated with antithyroid drugs, are presented.

1. INTRODUCTION

Recent work has suggested that it is possible to predict which patients are likely to obtain a remission with antithyroid drug therapy by carrying out tests of thyroid function during treatment. About 50% of patients given carbimazole and L-triiodothyronine (T3) showed suppression of thyroid uptake within three to six months of starting treatment (1,2). Suppression in these patients was tested by measuring thyroid uptake 20 minutes after an intravenous dose of ^{132}I. The likelihood of remission was found to be high in patients whose thyroid uptake was suppressed under these circumstances.

There are difficulties in interpreting radioiodine uptake measurements in patients who are being treated with drugs which depend for their theraputic effect on interference with with the organic binding of iodine. It has been claimed that early thyroid uptake measurements are unaffected by such drugs and that they can be used to measure the thyroid iodide concentrating mechanism or trap (3,4). Whether or not this is so will depend on the rate at which trapped iodide becomes bound, on the time at which the measurement is made and on the extent to which organic binding of iodine is impaired by the antithyroid drug.

Berson and Yalow (5) examined in some detail the kinetics of trapping and binding. They concluded from their studies that binding took place with great rapidity and that iodide once trapped became bound almost instantaneously. In support of their findings it can be readily demonstrated that perchlorate prevents any further accumulation of radioiodine by the thyroid but produces no demonstrable loss of radioactivity from the gland even when given intravenously. These observations suggest that in the unblocked thyroid gland early uptake measurements are essentially measurements of iodide already bound although the earlier the measurement is made the more it will approximate to a measurement of the thyroid trap.

Radioiodine can be used to measure the thyroid trap provided organic binding is completely inhibited. In patients undergoing treatment however, organic binding is not completely inhibited. Hence a measurement at 20 minutes represents partly organically bound iodine and partly trapped iodide. It is not certain, therefore, what is being measured if radioiodine is used in these circumstances particularly if measurements before treatment are compared with measurements carried out during treatment.

The studies of Ibbertson and his colleagues (6) are relevant to this problem. These workers measured thyroid clearance at varying intervals during the first 20 minutes after an intravenous dose of radioiodine. The same measurements were repeated after two weeks' treatment with carbimazole. The earliest clearance, which was made between 0 and 5 minutes, showed no significant fall but clearances at later times did fall after treatment; the later the time of measurement, the greater the fall. This differential effect on thyroid clearance in relation to the time of the measurement is consistent with the known action of carbimazole on organic binding, that is to say the later the measurement is made the more it will be influenced by organic binding. This means that a fall in the 20 minute uptake during treatment with carbimazole is due partly to impairment of organic binding and this effect must be taken into account if conclusions on thyroid suppression are based on this measurement.

When serial tests of thyroid function are required during treatment it is advantageous to use a test which measures the ability of the thyroid to trap iodide because this function is not directly affected by drugs such as carbimazole which act at a later stage in thyroid hormone biosynthesis. $^{99}Tc^{m}$ in the form of pertechnetate is concentrated in the thyroid in the same way as iodide but it does not become organically bound. The uptake of this radionuclide reflects the magnitude of the thyroid trap and this measurement can be used as an index of thyroid activity (7). We started using $^{99}Tc^{m}$ primarily for the purpose of following the progress of patients undergoing treatment with an antithyroid drug. Experience however has shown that it is a simple and reliable test of thyroid function and we now use it routinely in place of an early radioiodine uptake measurement.

2. METHODS

2.1. Procedure

Several workers have used radioisotope scanners for measuring the uptake of $^{99}Tc^{m}$ by the thyroid (7,8,9,10). An essential part of all these methods is the correction for extrathyroidal radioactivity. Two techniques are described below, one using a dual, the other a single detector scanner.

The dual detector method is a modification of that described by de Garreta et al. (10) and by Williams et al. (11).

A fixed volume of $^{99}Tc^{m}$-pertechnetate (0.5 to 1mCi) in a syringe was counted in a mechanical jig between the two scanner detectors. Twenty minutes after an intravenous injection the thyroid scan was started. The scanner speed (approximately 90cm min^{-1}) was measured at the end of the scan. The line spacing on the scan was 0.4 cm. The maximum antero-posterior thickness of the patient's neck in the region of the thyroid was determined with a pair of calipers. The scan was divided into three rectangular areas. One contained the thyroid image. The other two areas, one above and one below the thyroid were used to correct for extrathyroidal activity. They were chosen so as to exclude the submandibular salivary glands and any region of high uptake below the thyroid gland. The number of dots in each region was counted using a standard cell counter.

For the single detector method the same procedure as above was followed but with this method the depth of the thyroid has to be determined. This was done by scanning both sides of the neck several times with the patient facing parallel to the direction of movement of the detector and seated on a chair provided with a head rest. The configuration of the neck requires that the detector be tilted at approximately 45^{o} so that the collimator axis passes through the thyroid. The position of the front of the neck was identified on the scan with the aid of a light pointer in the collimator. The outline of the neck was obtained using a strip of lead and this, together with the scan, was used to estimate the position of each lobe of the thyroid relative to the front of the neck.

2.2. Equipment

A Picker Magnascanner with two 7.6 cm diameter NaI detectors and type 2102A collimators was used for both methods. With the single detector method only the upper detector was used. With the dual detector method an aluminium plate 1mm thick was fixed in front of the upper collimator and pulses from the two detectors were fed to the dot-tapper. For calibration of the injected dose the collimators were removed and both detectors were fitted with brass plates 2.8 cm thick in order to reduce the count rate which was measured on an additional scaler. The scanner speed was measured by feeding a known pulse rate (e.g. mains frequency) to the dot tapper via the 'dot factor' scaling unit and measuring the dot spacing.

2.3. Correction procedures

2.3.1. Dual detector method - Corrections are necessary to take account of variation in neck thickness and size of the scan area and changes in the scanner speed, because all these factors affect the scanner response. Correction for these factors eliminates the necessity for scanning a phantom each time a test is carried out.

The scanner was calibrated by measuring the count rate from a test dose of $^{99}Tc^m$ contained in a plastic syringe which was positioned midway between the two detectors of the scanner by means of a jig. For this procedure the collimators were removed and brass discs were fixed in front of each detector. $^{99}Tc^m$ in a glass model gland (volume 30 ml) was positioned with its upper surface 0.5cm below the surface of a 20 x 20 cm perspex tank filled with water to a depth of 10 cm. The phantom was then scanned and the dots on the scan within the area enclosing the image of the model thyroid were counted. This procedure was repeated for various depths of water in the tank. The number of dots divided by the syringe count rate and multiplied by the dot factor was plotted on semilogarithmic paper against the depth of water in the tank. The calibration factor thus obtained (T) relates the counts in a scan to the counts obtained from a dose of $^{99}Tc^m$ in a syringe (Fig.1). The effective neck thickness is taken to be 1 cm less than the antero-posterior neck diameter (de Garreta et al. 1968). The correction for scanner speed is carried out by comparing the distance between a given number of dots on the scan and a corresponding measurement performed during the phantom calibration procedure.

When a radioactive source is scanned, the dots on the scan are distributed over an area considerably larger than the source. In order to relate the number of dots on the scan to the amount of radioactivity in the source, all these dots must be counted. Since $^{99}Tc^{m}$ is also concentrated in regions in the vicinity of the thyroid, it is rarely possible to select an area of sufficient size to include all the dots due to activity within the thyroid while excluding these other regions where $^{99}Tc^{m}$ is concentrated. It is possible, however, to use a smaller region for dot counting, and to make a correction for the uncounted dots outside it. This correction factor (F) is the ratio of the total number of dots (i.e. those within a large area) on a phantom scan due to the activity in the source, to the number within a smaller area enclosing the source (Fig.2). The factor has a separate value for each such smaller area.

2.3.2. Single detector method - With a single detector the dependence of sensitivity on thyroid depth was determined by scanning the model thyroid at several depths below the surface of the water. These measurements were used to derive a calibration factor (A) which was used to estimate the count rate which would have been obtained from a thyroid at zero depth (Fig.3).

2.4. Calculation of the results

2.4.1. Dual detector method - The uptake as a percentage of the dose is obtained from the following expression:

$$\% \text{ Uptake} = \frac{100\,(N - RB)}{C} \cdot \frac{D}{FT} \cdot \frac{L}{P} \cdot e^{\lambda t}$$

where

N = number of dots in thyroid area of scan
B = number of dots in extrathyroidal areas of scan
R = ratio of thyroid to extrathyroidal areas
D = scanner dot factor
C = count rate from dose syringe

F = area correction factor

T = calibration factor = $Ke^{\mu(11-d)}$, where $\mu = 0.037\text{cm}^{-1}$
d = neck thickness (cm) and K = ratio of number of dots multiplied by dot factor in phantom calibration scan to count rate obtained from the dose in the syringe.

$e^{\lambda t}$ = correction for decay for time (t) between dose measurement and the beginning of the scan

L = distance between a number of dots obtained from standard pulse rate during scan

P = distance between the same number of dots obtained from standard pulse rate during calibration of phantom scan

2.4.2. Single detector method

$$\% \text{ Uptake} = 100 \frac{(N - RB)}{C} \frac{D}{FKA} \frac{L}{P} e^{\lambda t}$$

The symbols have the same meaning as before, except that C and K refer to count rates measured with one detector only, and A is the correction for thyroid depth. If the two lobes of the thyroid are found to be at significantly different depths then each lobe is considered separately for the depth correction.

2.5. Patients

The uptake of $^{99}Tc^m$ by the thyroid has been measured in 18 normal volunteers and in 100 patients with thyrotoxicosis. For the past year this measurement has been used in all patients suspected of being thyrotoxic. $^{99}Tc^m$ uptake has also been measured in 30 patients who were eventually shown to be euthyroid. Most of these patients had a non-toxic goitre.

Suppression tests have been carried out in 30 patients. Twenty of the patients were thyrotoxic and some were being maintained on carbimazole while the test was carried out. The remaining ten patients either had a non-toxic goitre or were in remission after treatment with an antithyroid drug. The test consisted of an initial $^{99}Tc^m$ uptake measurement which was repeated after the administration of 120μg of T3 daily for a week.

Serial measurements of $^{99}Tc^{m}$ uptake have been carried out in a group of patients undergoing medical treatment for thyrotoxicosis. The patients were given carbimazole in an appropriate dose with the addition of T3 80μg daily after the first month. Measurements were carried out immediately before and at intervals during treatment. Treatment was stopped if the $^{99}Tc^{m}$ uptake fell to within the normal range but was otherwise continued for a period of 18 months. Further measurements were carried out at intervals after the antithyroid drug had been stopped.

3. RESULTS

3.1. Reproducibility of the method

Measurement of the uptake of $^{99}Tc^{m}$ was repeated using the dual detector method in 20 patients at an interval of one day wherever possible, although in one case the interval was one week, and in two cases it was one month (see Table 1). The measurements were made at approximately the same time after injection of the dose. The uptakes ranged from 0.8% to 22% and the difference between the two measurements for each subject was used to estimate the standard error of the measurement, which was 0.73% of the dose. The difference between each pair of measurements was unrelated to the magnitude of the thyroid uptake. The error due to counting statistics (1 s.d.) was 0.11%. Counting statistics are not therefore a major source of error.

3.2. Single v. dual detector

Thyroid uptakes measured using the dual detector and single detector methods were compared in 14 patients (Table 2). The single detector measurements were normally started within five minutes of finishing the dual detector measurement. When individual corrections for variations in thyroid depth are made the average difference between the uptake measured by the two methods is not significant. If a mean depth of 2.3 cm is assumed for the thyroid, once again there is no significant difference between this value and that obtained using the two detector method. A preliminary conclusion from this small series is that a single detector scanner can be used for measuring $^{99}Tc^m$ uptake and that the estimation of thyroid depth for each individual is unnecessary.

3.3. Uptake measurements

Values for $^{99}Tc^m$ uptake in the normal subjects and in the patients with thyroid disorders are shown in Fig. 4. The mean value in normal subjects was 1.6% ± 0.7(1 s.d.). Six of the thyrotoxic patients had normal values and 7 of the patients with non-toxic goitre had values above the upper limit of the normal range.

3.4. Suppression tests

The results of the suppression tests are shown in Table 3. None of the thyrotoxic patients showed a fall in uptake in excess of 15% of the initial uptake. In several patients the second value was higher than the first and in some cases this difference is significant. Thyroid uptake was suppressed in the patients with non-toxic goitre and in the 4 thyrotoxic patients who were in remission at the time the test was carried out. According to our data a fall in thyroid uptake of at least 50% of the initial value can be expected in non-toxic patients and using this as an index of suppression the thyrotoxic patients can be readily distinguished from the euthyroid group.

3.5. Serial measurements in patients undergoing treatment

The sequential changes in $^{99}Tc^m$ uptake in patients being treated with carbimazole are of interest but they have proved less powerful in predicting the outcome of treatment than was anticipated. If thyroid uptake shows a progressive and consistent fall to within the normal range the likelihood of remission is high. This type of response is illustrated in Fig. 5. In this patient treatment with carbimazole and T3 was discontinued after 8 months. Within a month $^{99}Tc^m$ uptake had reverted to its pretreatment levels. Further tests carried out two, three and four months after stopping treatment showed a return towards normal. At the end of this time a T3 suppression test caused the uptake to fall to within the normal range. Nine months later the uptake was still just above the upper limit of the normal range but normal suppression was again demonstrable. Two years after stopping treatment this patient was euthyroid, in vitro tests were normal and the response to T3 suppression was also normal.

A normal suppression test does seem to indicate a state of remission but it may only be temporary and a relapse may occur within the space of a year or so. This sequence of events is shown in Fig. 6. Treatment with carbimazole was discontinued in this patient after 11 months. The rebound in uptake and subsequent suppression with T3 were consistent with a remission. Thyroid status and PBI remained normal for a year but after a further six months the uptake failed to suppress with T3. Six months later the patient was clinically thyrotoxic and all thyroid function tests were indicative of hyperthyroidism.

Patients who fail to achieve a normal value are likely to relapse fairly soon but here again there are exceptions. Some patients showing this type of response have remained euthyroid for a year or more after discontinuation of treatment.

4. DISCUSSION

The measurement of thyroid uptake using radioactive iodine has been accepted as a simple and useful test of thyroid function. An early measurement is more likely to reflect the rate at which the gland accumulates iodine. Since $^{99}Tc^{m}$ is concentrated in the thyroid in the same way as iodide it is relevant to consider whether it is likely to have any advantages over the various radioactive isotopes of iodine which are currently available.

The main problem associated with the measurement of early thyroid uptake is that of finding a relatively simple and convenient method of correction for extrathyroidal radioactivity. Methods for determining uptake by scanning depend on the net difference in dot density between the thyroid and extrathyroidal regions at the time of measurement and are not based on assumptions about changes in extrathyroidal radioactivity relative to time. In a situation where the concentration of radioactivity in the gland may not be greatly in excess of that in the surrounding tissues and where the proximity of the salivary glands is a complicating factor, the determination of thyroid uptake by a scanning method is probably more accurate than any other.

The accuracy of the method as carried out at present appears adequate when used in association with a suppression test. The small series which has been studies by both the dual and single detector methods indicates that if the upper limit of the normal range is raised from 3.0 to 3.6% then this will allow for a thyroid depth of up to 5cm, which is more than twice the average depth found in our series. This would eliminate the necessity of performing an additional 'depth' scan and permit the measurement of $^{99}Tc^{m}$ uptake using single detector scanners which are widely available.

Other radioisotopes which give a radiation dose comparable to that from $^{99}Tc^{m}$ and which are suitable for an early uptake measurement are ^{132}I and ^{123}I (12). ^{132}I, however, emits high energy gamma rays which preclude the use of a scanner and this introduces problems associated with correction for extrathyroidal activity. We have no experience of the comparative value of ^{132}I and $^{99}Tc^{m}$ in clinical practice. ^{123}I would be satisfactory from a scanning and radiation dose viewpoint but this radioisotope is not yet widely available. There is one other difficulty that might arise if the ^{123}I uptake were to be measured by a scanning method. With this radioisotope the rate of uptake will be increased and maintained for a long period because organic binding of iodine is taking place. The effect of this will be to introduce errors associated with the precise timing of the measurement. These errors are much less important when $^{99}Tc^{m}$ is being used because the uptake has usually reached a maximum value within 15 to 20 minutes.

In our experience $^{99}Tc^m$ uptake measurements have proved very satisfactory in clinical practice. In the absence of a direct comparison it cannot be said that they are any more efficient than early radioiodine uptake tests in differentiating between euthyroid and hyperthyroid individuals but we think it unlikely that such a comparison would reveal any great differences. Previous experience with radioiodine tests invariably has shown that some thyrotoxic patients have a normal uptake and that a high uptake is found in a proportion of patients with non-toxic goitre. This problem of the overlap between the two groups can usually be resolved by carrying out a suppression test.

Attempts to predict the outcome of antithyroid drug treatment on the basis of thyroid suppressibility have met with limited success (13,14). Suppression is not necessarily indicative of long term remission and patients who fail to suppress do not always relapse when treatment is discontinued. Despite these limitations the examination of thyroid function during treatment may sometimes be helpful and for this purpose a $^{99}Tc^m$ uptake would seem to be the most appropriate method.

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Table 1 REPRODUCIBILITY OF UPTAKE METHOD

NO.	UPTAKE % 1ST MEASUREMENT	UPTAKE % 2ND MEASUREMENT	MEAN UPTAKE %	ABSOLUTE DIFFERENCE BETWEEN UPTAKES %	DIFFERENCE AS % OF MEAN UPTAKE
1	12.7	13.0	12.9	0.32	2.5
2	1.8	1.5	1.7	0.25	15
3	3.6	3.6	3.6	0.03	0.8
4	6.9	6.5	6.7	0.34	5.1
5	8.9	8.8	8.9	0.06	0.7
6	8.0	7.0	7.5	1.04	14
7*	6.7	5.4	6.2	1.29	21
8	10.9	12.0	11.4	1.17	10
9*	4.5	4.8	4.7	0.3	6.5
10	22.3	21.2	21.8	1.1	5.1
11*	4.5	4.8	4.7	0.24	5.2
12*	7.9	6.7	7.3	1.22	17
13	2.1	1.4	1.7	0.74	43
14	3.9	2.8	3.3	1.18	35
15	1.1	0.8	0.9	0.30	33
16	5.0	5.8	5.4	0.78	15
17	9.7	9.6	9.6	0.05	0.5
18	1.6	1.3	1.4	0.37	26
19	8.4	9.4	8.9	0.99	11
20	5.9	4.0	4.4	0.85	19

* The interval between these measurements was more than one day : No 7 23 days, No 9 6 days, No 11 36 days, No 12 29 days

Table 2 COMPARISON OF UPTAKES USING DUAL AND SINGLE DETECTOR SCANNER METHODS

NO.	DUAL DETECTOR METHOD %	SINGLE DETECTOR METHOD WITH INDIVIDUAL DEPTH CORRECTION %	DIFFERENCE FROM DUAL DETECTOR RESULT %	SINGLE DETECTOR METHOD USING MEAN DEPTH OF 2.0 cm %	DIFFERENCE FROM DUAL DETECTOR RESULT %
1	7.6	7.2	- 0.35	7.0	- 0.59
2	2.0	2.0	+ 0.04	2.0	- 0.04
3	1.9	2.4	+ 0.56	2.3	+ 0.40
4*	18.7	24.3	+ 5.7	20.6	+ 1.95
5	1.3	1.2	- 0.07	1.2	- 0.05
6	9.6	8.7	- 0.88	9.4	- 0.25
7	2.6	2.1	- 0.54	2.1	- 0.47
8	4.8	5.7	+ 0.92	5.5	+ 0.74
9	5.3	5.4	+ 0.04	5.7	+ 0.32
10	1.8	1.5	- 0.31	1.5	- 0.32
11	1.0	1.2	+ 0.27	1.3	+ 0.30
12	5.5	4.9	- 0.63	4.8	- 0.75
13	2.5	2.7	+ 0.15	2.7	+ 0.20
14	21.4	20.6	- 0.82	20.9	- 0.5
		MEAN (absolute)	0.79		0.38

* In this case the measurements were done at 27 and 38 minutes after injection. It is most probable that the uptake was still increasing during this time. This result has been excluded in calculating the means.

TABLE 3. T3 SUPPRESSION TESTS USING $^{99}Tc^m$ UPTAKE MEASUREMENTS

PATIENT	EUTHYROID PATIENTS $^{99}Tc^m$ UPTAKE (%) BEFORE T3	AFTER T3	PATIENT	THYROTOXIC PATIENTS $^{99}Tc^m$ UPTAKE (%) BEFORE T3	AFTER T3
1. B.K.	0.9	0.1	9. A.C.	1.7	1.9
2. H.W.	1.0	0.0	10. A.H.	1.8	2.1
3. L.P.	1.4	0.2	11. M.N.	2.0	2.2
4. A.S.	2.1	0.7	12. C.M.	2.1	3.1
5. B.P.	3.0	0.4	13. S.L.	2.2	1.9
6. Z.B. (i)	3.3	0.3	14. A.T.	2.3	2.3
Z.B. (ii)	4.1	0.4	15. R.K.	2.3	1.9
Z.B. (iii)	5.0	1.6	16. P.H.	3.1	4.5
7. D.C.	8.4	1.7	17. A.G.	3.5	3.0
8. C.H.	8.6	2.0	18. A.H.	3.8	3.5
			19. J.K.	5.0	4.2
			20. S.O.	7.5	7.0
			21. S.N.	7.5	7.2
			22. M.H.	8.3	9.4
			23. A.L.	8.4	7.4
			24. A.B.	9.0	8.9
			25. B.T.	12.0	15.3
			26. M.A.	17.0	23.0
			27. B.H.	18.9	21.4
			28. V.H.	22.2	20.8

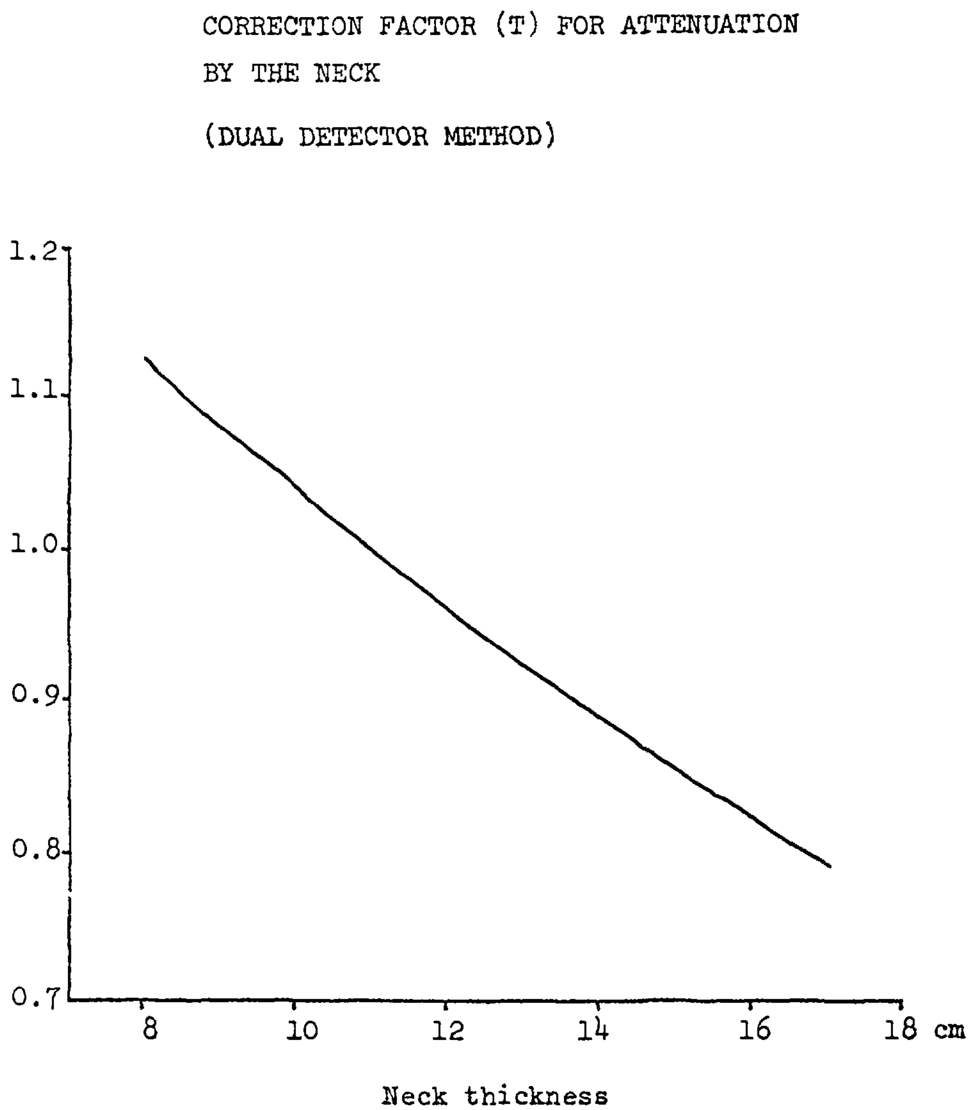

FIGURE 1 Correction factor (T) for attenuation by the total neck thickness (dual detector method).

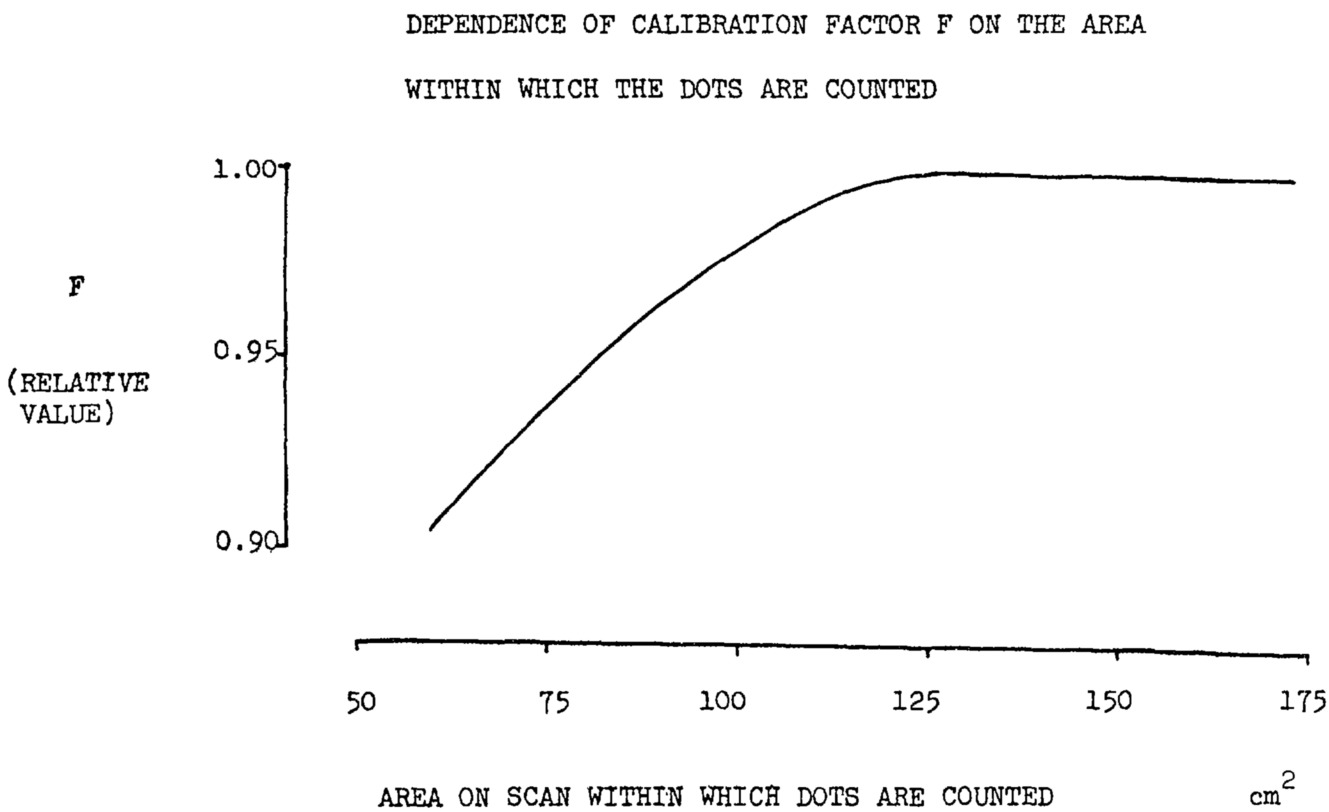

FIGURE 2 Dependence of the calibration factor (F) on the area on the scan within which dots are counted.

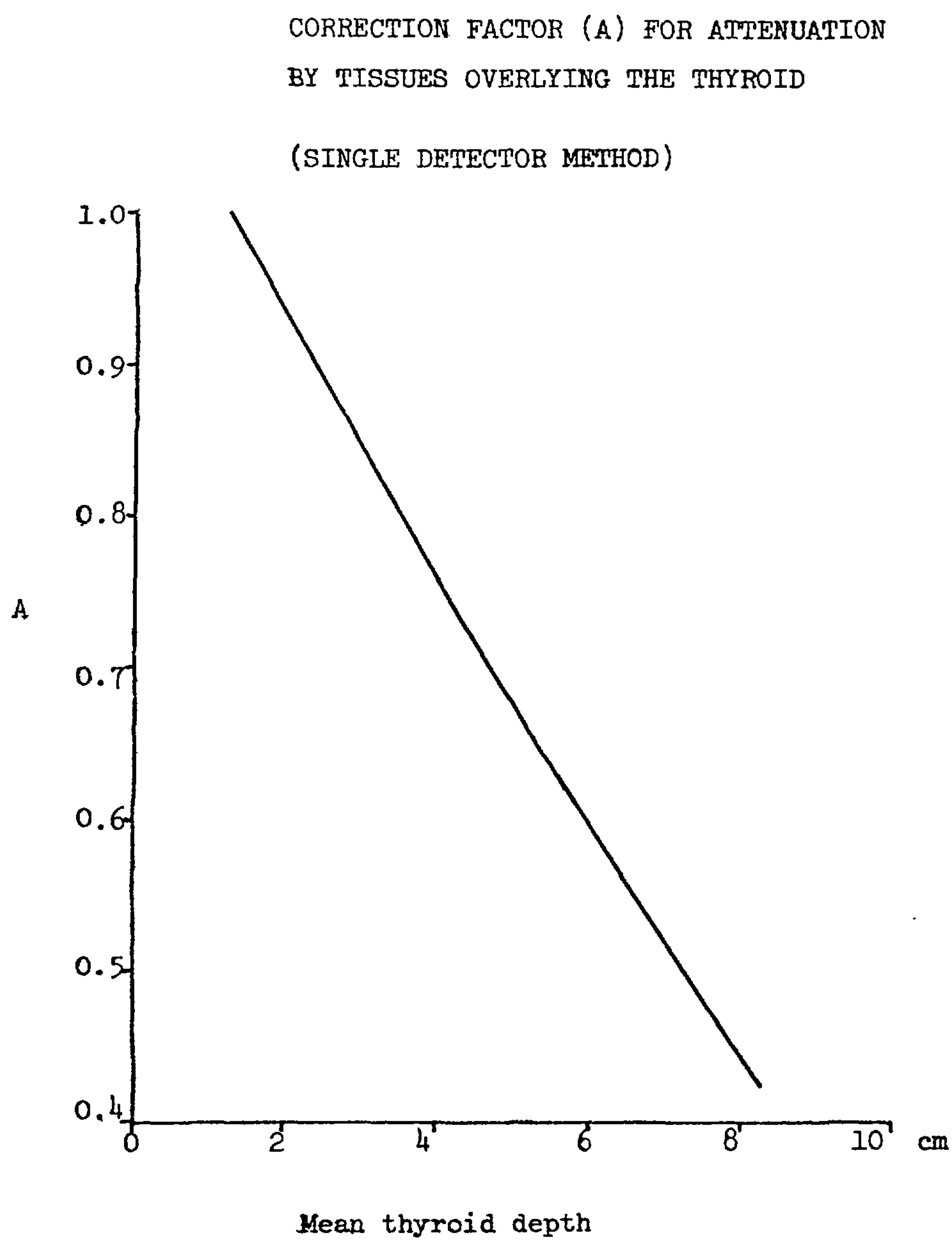

FIGURE 3 Correction factor (A) for attenuation by tissues overlying the thyroid (single detector method).

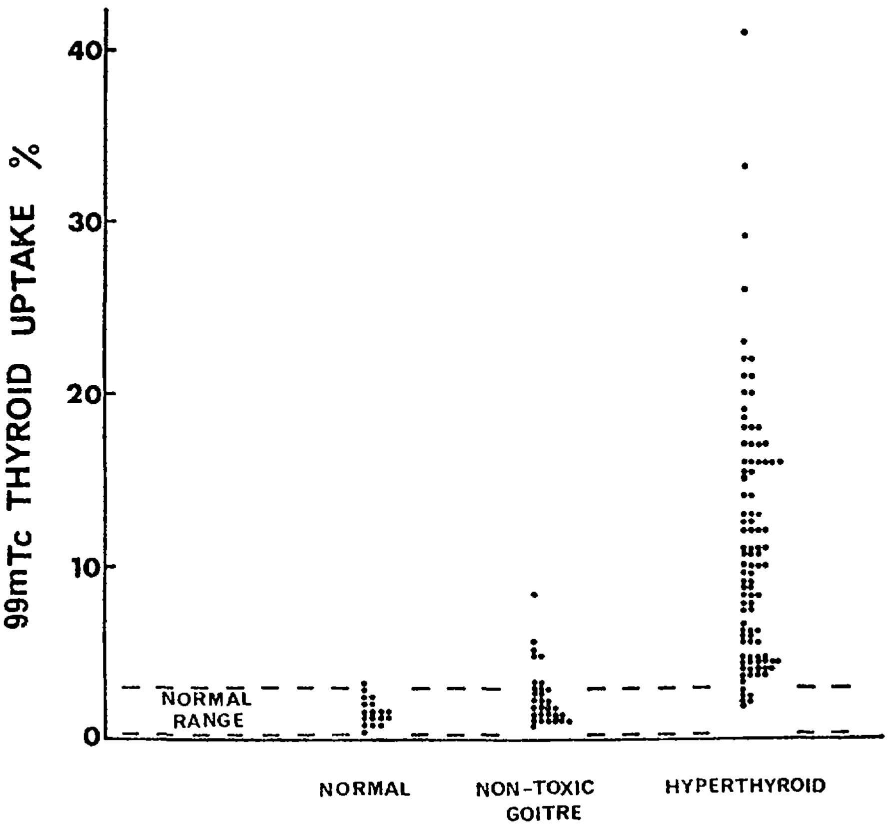

FIGURE 4 Values for $^{99}Tc^{m}$ uptake in normal subjects (18).
Patients with non-toxic goitres (30).
Patients with thyrotoxicosis (100).

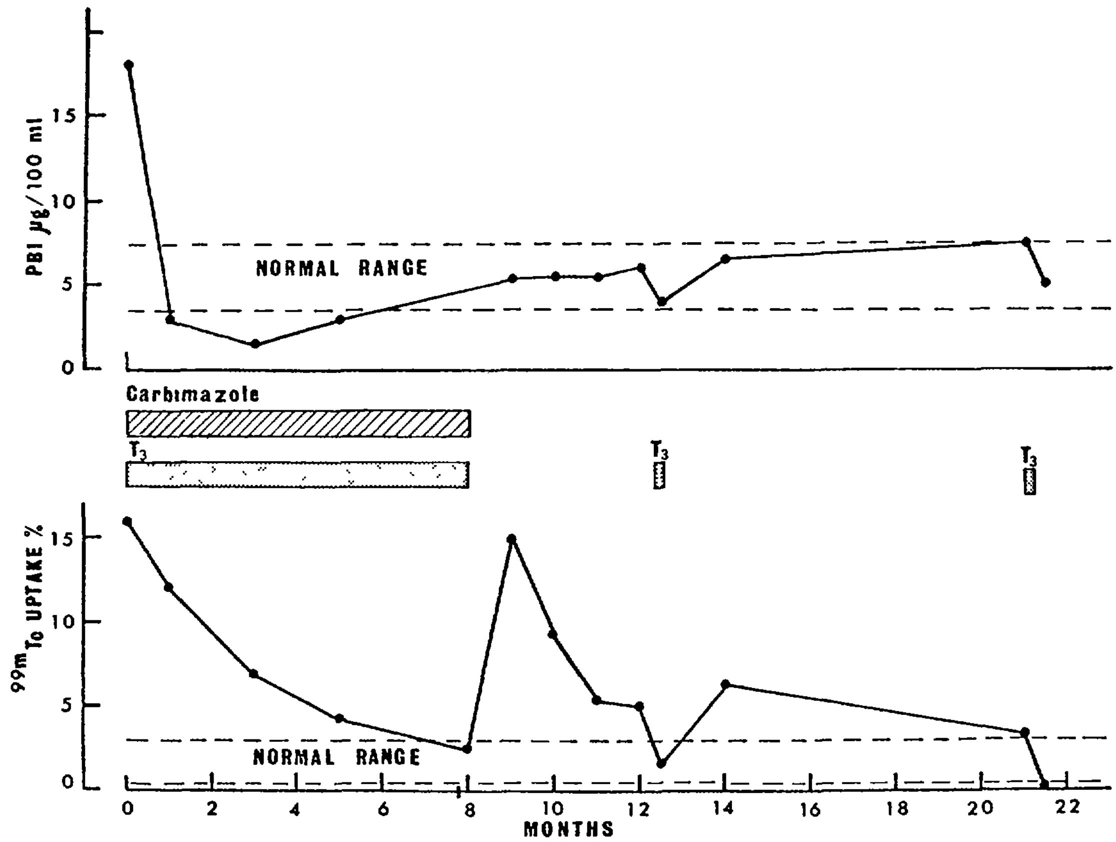

FIGURE 5 Serial $^{99}Tc^{m}$ uptake measurements in a patient during and after treatment with carbimazole and T3. This patient was in remission two years after stopping treatment.

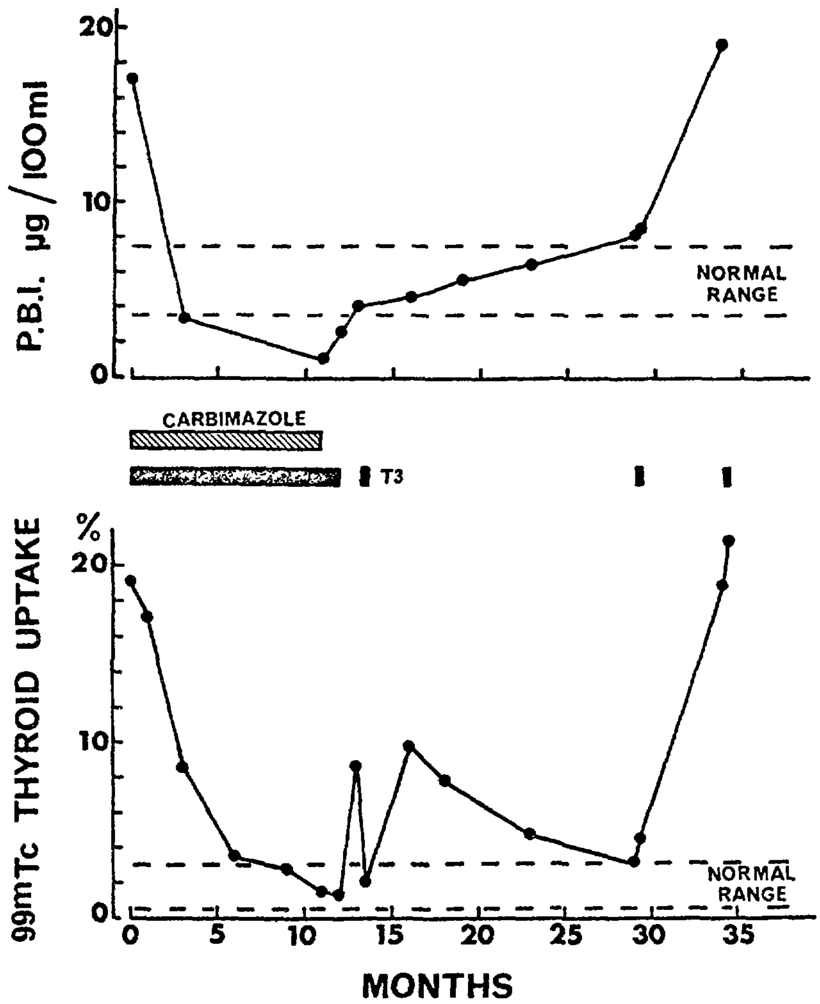

FIGURE 6 Serial $^{99}Tc^{m}$ uptake measurements in a patient during and after treatment with carbimazole and T3. Suppression was demonstrable in this patient at the time she stopped taking carbimazole but she relapsed about 18 months later.

THE MEASUREMENT OF THE THYROID UPTAKE OF ^{99m}Tc, ^{131}I and ^{132}I at EARLY TIMES AFTER ISOTOPE ADMINISTRATION

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ABSTRACT

This paper describes a method using a single-detector scanner for measuring the early uptake of $^{99}Tc^{m}$, ^{131}I or ^{132}I by the thyroid. The method was tested by comparing the uptake values obtained in 16 subjects on five occasions during the 45 minutes following administration of the tracer with those obtained on two interpolated occasions by means of a fixed collimated scintillation detector fitted with a standard thyroid collimator. In only one case was there a significant difference between the two sets of measurements. It was shown that the ^{131}I activity detected with the fixed detector was equal to that in a 15.8 cm diameter circle on the scan. The method described also permits the measurement of extrathyroidal activity. From the results of such measurements mean values for the extrathyroidal $^{99}Tc^{m}$ and ^{131}I activity detected by the fixed detector at different times after administration of the tracer were calculated. These values were used to formulate equations from which the early uptake of these radionuclides can be calculated from measurements with the fixed detector, if shortage of time or other considerations preclude the use of the more accurate scanning method.

When studying the concentrating mechanism of iodide or pertechnetate (the iodide trap), it is important to measure thyroid uptake at early times after tracer administration. At these early times it is possible to separate the concentrating and the chemical organification (binding) mechanisms of the gland[1-4].

The activity of tracer in the neck when viewed by a standard uptake counter is distributed in thyroidal and extra-thyroidal regions. In investigations of thyroid gland uptake soon after radioiodide administration correction for the extra-thyroidal activity is of particular importance. At these early times the extra-thyroidal activity is at a maximum and the thyroidal activity is at a minimum. This correction for extra-thyroidal activity is easily made using an isotope imaging system. Then the tracer in the gland is easily identified. Therefore in this paper we describe a method of measuring the thyroid uptake of ^{99m}Tc and ^{131}I using a conventional scintiscanner. The resulting measurements of extrathyroidal activity in the field of view of the standard collimator[(5)] have been used as a basis of a method of measuring tracer uptake using an uptake counter. This latter method is used in circumstances where a large number of patients are to be studied, or where a scintiscanner is not available.

The Use of a Scintiscanner to Measure Thyroid Uptake

Method

A tracer dose of 25-50 μCi of ^{131}I or 1 mCi of ^{99m}Tc is intravenously administered. Either a Picker V magnascanner (50 μCi ^{131}I) or a Selo DS 4/4 scintiscanner (25 μCi ^{131}I) are used to scan the subject. Scanning is started at any time after 30 sec after tracer administration. A line spacing of 8 mm is used and a speed of 100 cm/min (Picker V) or 72 cm/min (Selo DS 4/4). The area scanned starts just above the thyroid gland and extends to below the sternal notch. The scan is completed in 2 - 4 min. The pulse height analyser of the scanner is set to detect pulses equivalent to the energy range 310 - 410 keV for ^{131}I and 120 - 160 keV for ^{99m}Tc. In each case a broad focus collimator is used with a focal length of 12.5 cm. In every case the dot factor is adjusted so that all the dots are clearly resolved.

A 'box' is drawn round the thyroid on the scan. This box if of such dimensions that it just covers all the thyroid uptake. A second box is drawn just beneath this box, with the same width and enclosing two scan lines. The number of counts in each box are summed. The extrathyroidal activity in the thyroid box is taken as the counts in the second box times half the scan lines in the first box. This background is subtracted from the counts in the thyroid box to give the thyroid counts. After scanning the subject, a thyroid phantom, similar to the I.A.E.A. phantom[6] but filled with water, is scanned containing an aliquot of the injection solution. The dots due to the activity in the phantom thyroid are then counted and all the uptake counts are expressed as a percentage of the 'phantom' counts.

Justification of Background Area

Two subjects with no thyroid uptake were studied to determine how satisfactory the chosen background area was. For these two patients with no thyroid uptake the mean difference between the true background in the thyroid box and the estimated background using the second box was nearly zero[7].

Relationship of Scanning Method To Uptake Counter - ^{131}I

In order to relate the scintiscan uptakes to those measured using a standard I.A.E.A. collimated uptake counter, 16 subjects were scanned after being given ^{131}I. In this study we did not draw boxes in the scans, but constructed circles. The first circle was 15.8 cm in diameter and represented the average sensitive volume viewed by the collimated counter[5]. 15.8 cm is approximately the cross sectional diameter at mid neckdepth. The end of the collimator is 8.5 cm from the surface of the neck. The neck diameter is assumed to be 13.0 cm[7]. The background counts were found by counting the dots in a semi circle area underneath the circle of diameter 15.8 cm. Scans were made at five intervals during the first 45 min after tracer administration and uptake counts were made at 7 and 14 min using a NaI(Tl) crystal with a standard thyroid collimator[5].

Result of Comparison

Fig. 1 shows the measurements of neck activity of ^{131}I for each patient as recorded by the scanner (Us) and the collimated scintillation counter (Uc) at 7 min after the ^{131}I injection. The values of Us are derived from the best fit curves drawn through all the data for each patient. The results show that there was a significant difference between Us and Uc (that is a difference greater than three standard deviations) for only one patient. Similar results were found at 14 min after ^{131}I administration[7].

Measurement of Neck Extrathyroidal Activity

We have shown that it is possible from the scintiscan to measure the extrathyroidal activity plus the thyroidal activity. We have already outlined a method to measure the thyroid uptake and hence it is possible by subtraction to measure the extrathyroidal activity detected using the collimated thyroid uptake detector[5]. This has been done for both ^{131}I and ^{99m}Tc at times up to 36 min after intravenous administration of the tracer[7,8]. The results are shown in figs. 2 - 5. The extrathyroidal activity is expressed either as a percentage of the dose given or as a percentage of the dose not in the thyroid.

Discussion

It can be seen in figs 2 - 5 that there is considerable variation in the neck extrathyroidal activity. Even when this activity is expressed as a percentage of the dose given which is not in the thyroid, a variation of 4 to 11% of ^{131}I dose is found at 3 min after isotope administration and a variation of 3.5 to 9% of ^{99m}Tc at 3 min after the intravenous administration of ^{99m}Tc. These percentage activities are considerably larger than the normal thyroid uptakes of ^{131}I and ^{99m}Tc at 3 min after administration and it is clear that if the thyroid uptake of iodide tracers are to be measured accurately at these early time intervals, an isotope imaging system must be used. Often, however, this is not feasible due to the large number of patients, the amount of data processing required with imaging systems and the availability of a suitable imaging system. Therefore we have used the average values found for the neck extrathyroidal activity seen by a standard thyroid uptake counter(5) to formulate equations to measure thyroid uptake using an uptake counter. These equations are based largely on the rate of fall of extra thyroidal activity. Fig. 6 shows this rate of fall compared with the rate of fall of plasma activity in one subject. It can be seen that the rate of fall of extrathyroidal neck activity (expressed as a percentage of the activity given) falls at a much slower rate than plasma activity. The average rate of fall of the extrathyroidal activity of ^{131}I (expressed as a percentage of the dose not in the thyroid) was found to be 14% between 2 and 20 min. The average value of extra-thyroidal activity (% dose not in thyroid) was 7% at 2 min after administration. Hence

If the neck uptake at 2 min is greater than 7%: Neck uptake 2 min = Thyroid uptake 2 min + 7/100 (100 - Thyroid uptake 2 min), i.e., Thyroid uptake 2 min = 1/0.93 (Neck uptake 2 min - 7), Neck uptake 20 min = Thyroid uptake 20 min + 6/100 (100 - thyroid uptake 20 min), i.e., Thyroid uptake 20 min = 1/0.94 (Neck uptake 20 min - 6.0).

If the neck uptake at 2 min is less than 7%: Neck uptake 2 min = Extrathyroidal activity 2 min, Neck activity 20 min = Thyroid Uptake 20 min + 86/100 x ETA 2 min/100 x (100 - Thyroid uptake 20 min), i.e., Thyroid uptake 20 min

$$= \frac{\text{Neck uptake 20 min} - 0.86 \text{ Neck uptake 2 min}}{1 - 0.0086 \text{ Neck uptake 2 min}} \% \text{ dose.}$$

The equivalent equations using ^{99m}Tc are found as follows:-

The mean ^{99m}Tc extrathyroidal activity is 6.65% of activity not in the thyroid at 3 min and 5.46% at 20 min. Then the thyroid uptake of ^{99m}Tc is calculated as

Neck uptake of ^{99m}Tc at 3 min(U3) = Thyroid uptake of ^{99m}Tc at 3 min (T3) $+ \frac{6.65(100 - T3)}{100}$

i.e. Thyroid uptake at 3 min $= \frac{U3 - 6.65}{0.934}$ % dose

At 20 min:

Neck uptake of ^{99m}Tc at 20 min (U20) = Thyroid uptake of ^{99m}Tc at 20 min (T20) $+ \frac{5.46}{100} \times (100 - T20)$

i.e. Thyroid uptake of ^{99m}Tc at 20 min $= \frac{(U20 - 5.46)}{0.945}$ % dose.

If the neck uptake at 3 min is less than 6.65%, we must consider that this is all extrathyroidal activity and the thyroid uptake is negligible. Then

$U20 = T20 + U3 \times 0.82 \times (100 - T20)/100$ % dose.

i.e. Thyroid uptake at 20 min =

$$\frac{(U20 - 0.82 \times U3)}{(1 - 0.82\ U3/100)} \text{ \% dose}$$

These equations have been used to study a large group of patients where sequential measurements of thyroid uptake of ^{99m}Tc and ^{132}I are made at 2 and 20 min after administration[9]. This study involved two approximations of the equations

(1) The use of ^{132}I rather than ^{131}I

and (2) The use of 2 min ^{99m}Tc uptake rather than 3 min ^{99m}Tc uptake.

However, when sequential measurements are made, it is likely that errors arising due to innaccuracies in measuring thyroid uptake, are eliminated in the comparison of uptakes.

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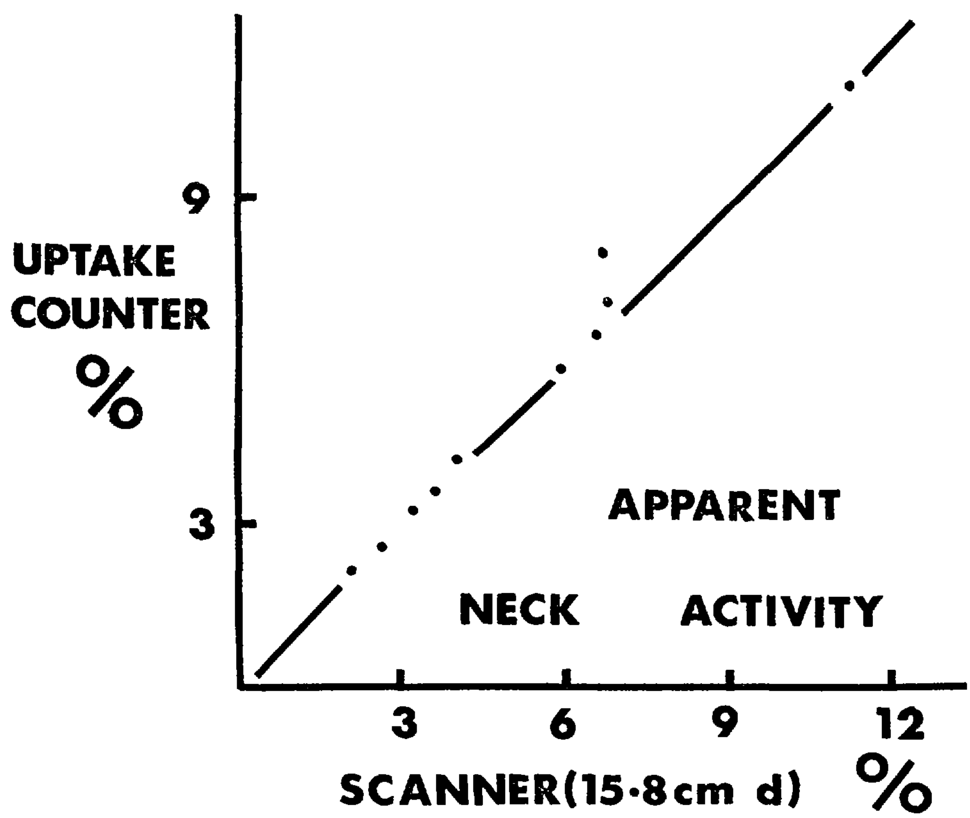

Fig. 1 A comparison of total neck activity as measured by the scintiscanner (15.8 cm circle) and the standard uptake counter[5].

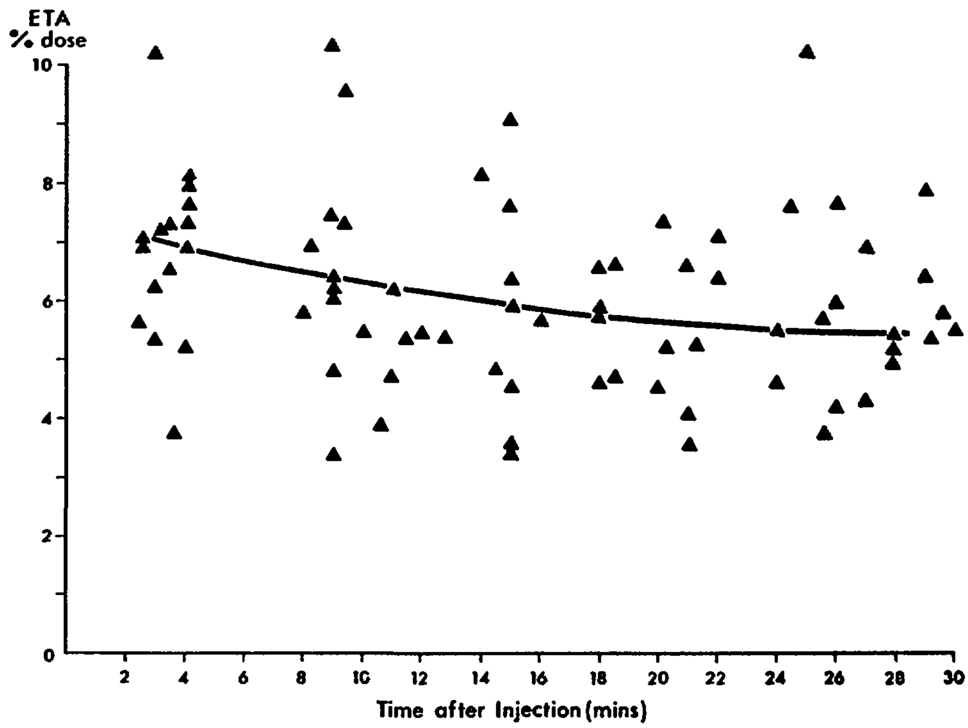

Fig. 2 Relation between the contribution from extrathyroidal neck activity and time after administration of the radioisotope in 16 patients. (^{131}I)

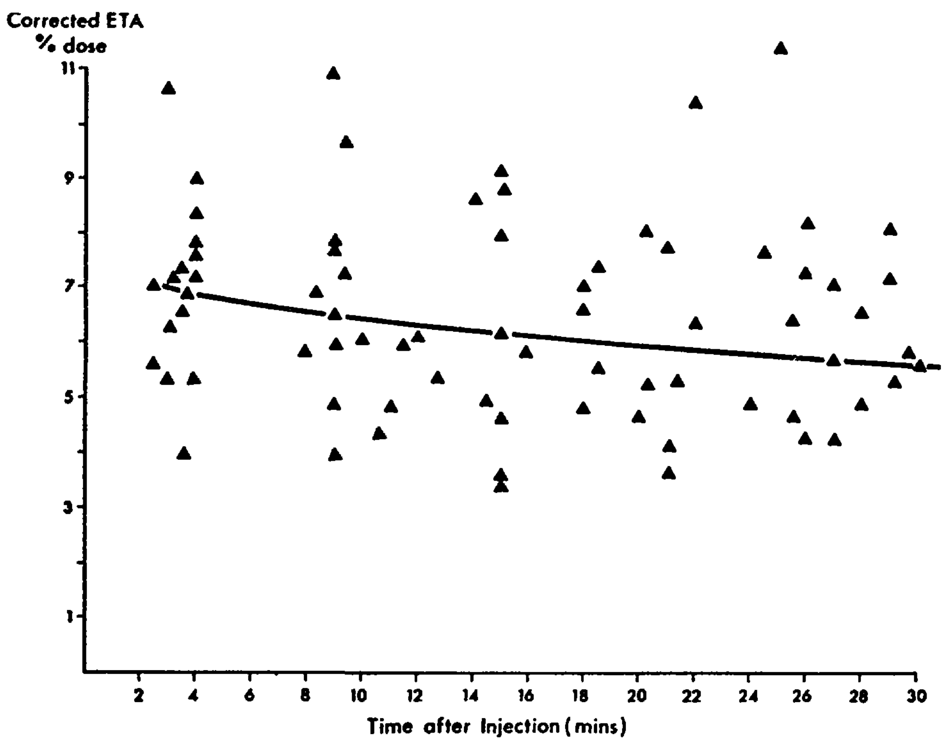

Fig. 3 Relation between the contribution from extrathyroidal neck activity (as % dose not in thyroid) and time after administration of the radioisotope in 16 patients. (^{131}I)

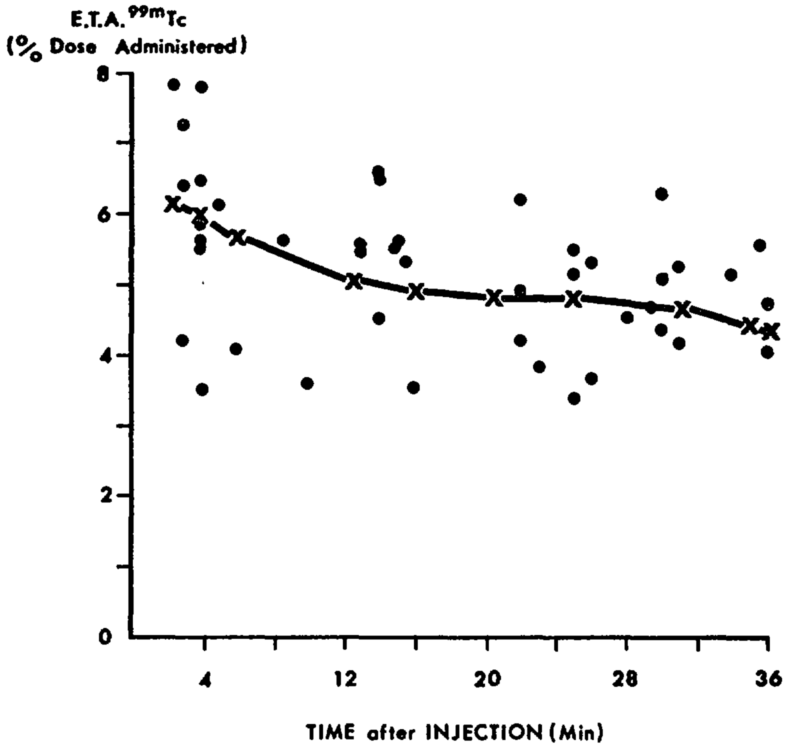

Fig. 4 Best-fit line to component of extrathyroidal activity of ^{99m}Tc seen by thyroid collimator. Extrathyroidal activity = $6.77 - 0.25t + 0.108t^2 - 0.00016t^3$ % dose (t in min).

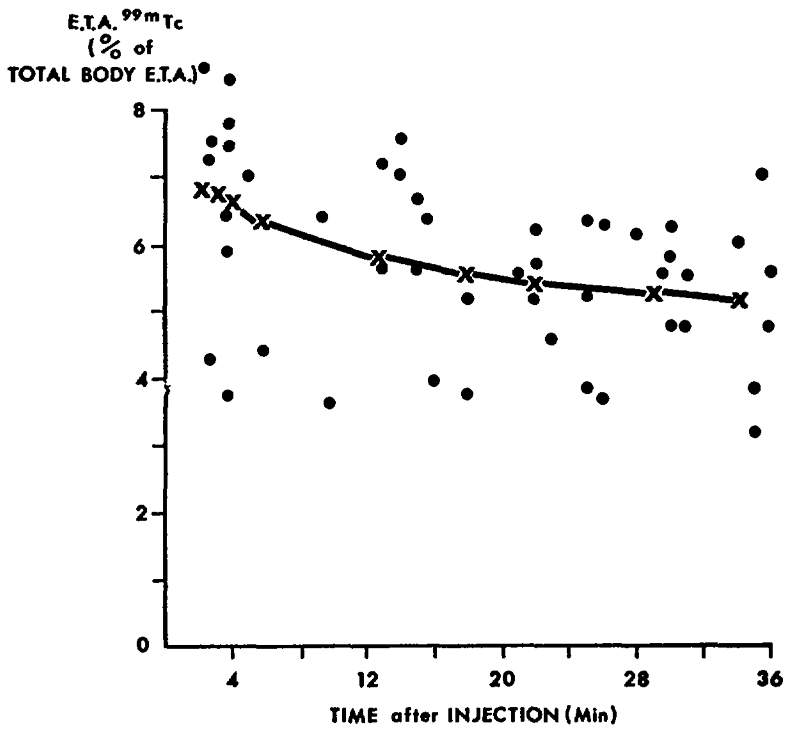

Fig. 5 Best-fit line to extrathyroidal activity of ^{99m}Tc expressed as percentage of total-body extrathyroidal activity. Extrathyroidal activity = $7.09 - 0.16t + 0.005t^2 - 0.00006t^3$ % body extrathyroidal activity (t in min).

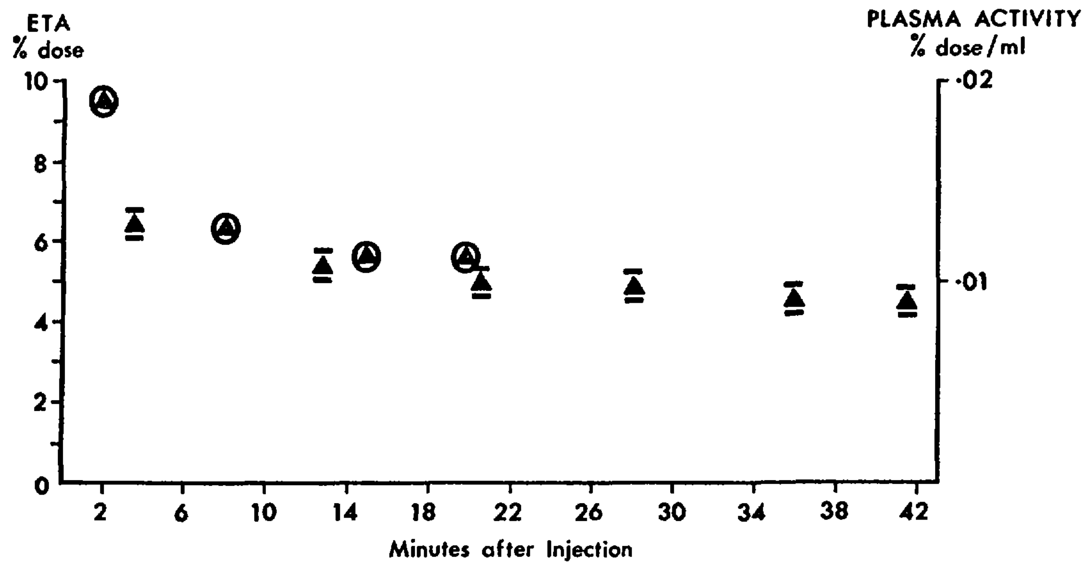

Fig. 6 Relation for one patient between ETA (% dose) and plasma activity (% dose/ml) and time after administration of 500 µCi ^{131}I.

ETA: triangles between parallel lines.

Plasma Activity: triangles in circles.

THE MEASUREMENT OF THE KINETIC CONSTANTS DESCRIBING THE THYROIDAL CONCENTRATION AND ORGANIC BINDING OF IODIDE AND PERTECHNETATE

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ABSTRACT

This paper describes studies of the kinetics of iodide-trapping and iodine-binding by the thyroid in normal and hyperthyroid subjects based on computer analysis of the data resulting from serial $^{99}Tc^{m}$ and ^{131}I uptake measurements made with a single-detector scanner during the 45 minutes following the administration of the mixed tracers. Studies were carried out on 10 normal and 4 hyperthyroid subjects to whom carbimazole had been given to block iodine-binding by the thyroid. Analysis of these data yielded values for the unidirectional iodide clearance into the thyroid and the fractional iodine-binding rate. Further studies were carried out on 15 normal and 7 hyperthyroid subjects to whom no carbimazole had been given. Analysis of these data yielded values for the unidirectional iodide clearance into the thyroid, the fractional iodide loss rate from the thyroid and the fractional iodine-binding rate. The results indicate a very significantly higher unidirectional iodide clearance and a significantly higher fractional iodine-binding rate in hyperthyroid as compared with normal subjects. No significant differences in fractional iodide loss rates was observed between the groups studied. The significance of the findings is discussed.

Introduction

Inorganic iodide is concentrated from blood by the thyroid gland. In the normal thyroid this iodide is organified and cannot then be discharged by perchlorate[1,2]. The observed thyroid uptake and the observed plasma clearance of radioiodine by the thyroid gland depend both on the concentration and the organification mechanism. Certain anti-thyroid drugs (e.g. carbimazole) given in the correct amounts do however eliminate the organification of iodide in the thyroid. The uptake and loss of radioiodide can then be simply attributed to the concentrating mechanism[1,2] and is similar to the uptake and loss of the pertechnetate ion which is also concentrated by the thyroid gland[3]. The measurement of the unidirectional clearance of pertechnetate into the thyroid and its loss from the thyroid has been made by graphical analysis of the thyroid uptake plot of pertechnetate[4]. In the same way it is possible to measure the unidirectional clearance of iodide due to the iodide concentrating mechanism and the intrathyroidal loss rate of iodide provided carbimazole is given to prevent thyroidal organification of iodide.

In addition to the measurement of the accumulation and the loss rate of iodide, with organification blocked, we have made an analysis of the thyroidal iodide uptake curve and have found the best fit kinetic constants. This analysis was made using a digital computer and evaluates the unidirectional clearance, the loss rate and the binding rate of iodide.

A <u>Materials and Method (Carbimazole Studies)</u>

Fourteen subjects were included in this study. Clinical details of these subjects are shown in table 1. Ten were euthyroid and four were thyrotoxic.

All the subjects were given 120 mg of carbimazole divided into four doses over 24 hours, the last dose being given one hour before the test started. Each subject was given 50 µCi of ^{131}I and 1 mCi of ^{99m}Tc pertechnetate by intravenous injection without any iodide or pertechnetate carrier. The thyroid uptakes of ^{131}I and ^{99m}Tc pertechnetate were then found at several times after isotope administration. These thyroid uptakes were measured using a Picker V magnascanner, by making successive scans of the thyroid region[5]. Each scan took approximately three minutes and it was found possible to complete at least nine scans in the first 45 minutes after isotope administration. Two sets of scans were made. The first scan was done under ^{99m}Tc counting conditions (detecting pulses equivalent to 125 to 155 keV). The second scan was done under ^{131}I counting conditions (detecting pulses equivalent to 300 to 420 keV). Each ^{99m}Tc and ^{131}I scan measured the thyroid uptake at the mid time of the scan. Alternate scans were made to measure the pertechnetate and iodide uptakes. The dots on the scintiscans were converted to percentage uptakes of the administered dose by counting the dots in selected parts of the scan relating these dots to the dots produced by scanning an aliquot of the administered dose in a standard thyroid phantom(6). Also the dots in the ^{99m}Tc scan due to ^{131}I were estimated by counting an ^{131}I standard in the same thyroid phantom under both ^{131}I and ^{99m}Tc scanning conditions. Blood samples were taken at 2, 8, 15, 30 and 45 minutes after isotope administration. These blood samples were separated and 2 ml of serum from each sample were counted in an automatic well NaI scintillation counter (*Nuclear Chicago Model No. 4227). This instrument has two spectrometer channels. One channel was set to detect pulses from ^{99m}Tc and ^{131}I in the energy range equivalent to 100 to 180 keV. The second channel was set to detect pulses from ^{131}I in the equivalent energy range of 300 to 420 keV. These serum activities were converted to fractions of the dose administered by counting a diluted 2 ml aliquot of the injected solution. Also a 2 ml aliquot of ^{131}I counts in the ^{99m}Tc counting channel.

Calculation (Carbimazole Studies)

The analysis of the uptake and plasma data to measure unidirectional clearance and intrathyroidal loss rate has been fully described in a previous communication(4).

Essentially it depends upon the following differential equations describing the rate of change of thyroid uptake of ^{131}I or ^{99m}Tc.

$$\frac{dq_t}{dt} = -k_{TB} \cdot q_t + C.q_s \qquad \text{equ.1.}$$

q_t = Thyroid uptake (% dose)

q_s = Serum activity (% dose/ml)

k_{TB} = Fractional loss rate from the thyroid (min^{-1})

C. = Unidirectional clearance into the thyroid (ml/min)

Hence $$\frac{1}{q_s}\frac{dq_t}{dt} = -k_{TB}\frac{q_t}{q_s} + C. \qquad \text{equ. 2.}$$

Therefore if $\frac{1}{q_s}\frac{dq_t}{dt}$ is plotted against $\frac{q_t}{q_s}$ a straight line will be found with slope k_{TB} and ordinate intercept C. $\frac{dqt}{dt}$ and q_t were found from the thyroid uptake plot and q_s found from the serum activity curve for both ^{131}I and ^{99m}Tc.

In comparing the accumulation of iodide and pertechnetate into the thyroid we shall use the unidirectional clearance. This serum clearance is the rate of iodide and pertechnetate uptake into the thyroid.

Results (Carbimazole Studies)

The thyroid uptakes and plasma activities were plotted as shown in figs. 1(a) and (b). Tangents were then drawn to the uptake plots and C. and k_{TB} found for each subject using the calculation described. These values are shown in table 1. The thyrotoxic subjects show large clearances and hence no mean value is given for the unidirectional clearance. In every subject except JO the iodide unidirectional clearance is greater than the pertechnetate unidirectional clearance. The relation between these two clearances are shown in fig. 2. The best fit line to these data is:

$$C._I = 0.845\ C._{TcO_4} + 50.7 \qquad \text{equ. 3.}$$

The best fit line through the origin is given by:

$$C._I = 1.586\ C._{TcO_4} \qquad \text{equ. 4.}$$

Both these lines are severely affected by the values of subject JO. (^{99m}Tc Unidirectional Clearance = 329 ml/min).

The mean ratio of the two unidirectional clearances shown in table 1 is 2.20 (SEM 0.29). No significant difference was found between the k_{TB} of pertechnetate and iodide in either the normal or thyrotoxic subjects.

B <u>Materials and Methods (Binding Studies)</u>

Twenty-two subjects were studied. Fifteen were hyperthyroid and seven were euthyroid. A dose of 25 µCi of ^{131}I as iodide was given by intravenous injection. Venous blood samples were taken at 2, 8, 18, 35, 105 and 150 minutes after injection. Serum aliquots were counted in an automatic well scintillation counter with the pulse height analyser set to cover the range 320-390 keV. A standard containing an aliquot of the dose was counted together with the samples, and the sample activity was expressed as a percentage of the ^{131}I administered.

The thyroid uptake was measured using a Selo DS 4/4 scintiscanner. The technique used was similar to that previously employed to measure the thyroid uptake of iodide and pertechnetate[5].

<u>Calculation (Binding Studies)</u>

The open three compartment model is shown in Fig. 3. The fundamental equations describing the material balance in this model are

$$\frac{dI_T}{dt} = C.I_B - k_{TB}.I_T - k_b.I_T \qquad \text{equ. 5.}$$

$$\frac{dI_b}{dt} = k_b I_T \qquad \text{equ. 6.}$$

These equations may be solved for I (TOTAL), the total thyroidal ^{131}I activity[7]. Values of C, k_B, and k_{TB} are then inserted until the best fit is found between the measured uptake values and the solution of the equations. These values of C, k_B and k_{TB} are then the best estimate of these kinetic constants. The thyroid radioiodine uptake has been analysed in the 15 thyrotoxic and 7 euthyroid subjects. The analysis was performed using an 8K PDP8-I computer (Digital Equipment Corporation) with a programme written in FOCAL.

Results (Binding Studies)

The results are presented in Table 2 and a typical result is shown in Fig. 4. All the hyperthyroid subjects had greater unidirectional clearance values than any of the euthyroid subjects. The mean hyperthyroid unidirectional clearance was 196.0 ml min^{-1} compared to 36.8 ml min^{-1} for euthyroid subjects. The difference is significant ($p < 0.001$). The mean binding rate k_b in the thyrotoxic subjects (0.110) is significantly greater than in the euthyroid subjects (0.066) ($p < 0.025$). There is no significant difference between the mean exit rate k_{TB} in the two groups ($p > 0.05$).

Conclusions

The importance of these data lie in scarcity of other measurement of these kinetic constants. Berson and Yalow[2] have however measured the unidirectional clearance and the k_{TB} of iodide in a group of thyrotoxic subjects. They found a mean value of 337 ml/min for the unidirectional clearance of iodide and 0.38 min^{-1} for the k_{TB} of this group of thyrotoxic subjects. One normal subject had an unidirectional clearance of 40 ml/min and a k_{TB} of 0.047 min^{-1}. Shimmins et al.[4] have measured the unidirectional clearance and k_{TB} of pertechnetate in a group of hyperthyroid and euthyroid subjects. Mean values of 287 ml/min for the clearance and 0.088 min^{-1} for k_{TB} were found in the hyperthyroid group. The euthyroid subjects had a mean value of 36.8 ml/min for the clearance and 0.083 min^{-1} for the k_{TB}. The value of the mean unidirectional clearance of pertechnetate found in the present study of 32.1 ml/min for the euthyroid subjects is therefore near our previous findings.

The mean value of 64.7 ml/min for the euthyroid unidirectional clearance of iodide (Carbimazole studies) is higher than the unidirectional clearance found in the binding studies (36.8 ml/min). Both are much higher than the net iodide thyroidal clearance[8] in euthyroid subjects (22.6 ml/min). This difference may be due to the type of analysis, the use of carbimazole or the different partients studied. When the same analysis, as was applied to the binding studies was applied to the carbimazole studies, similar values were found[9]. Hence the values obtained are independent of the analysis method. The ten patients given carbimazole were repeated without carbimazole and the pertechnetate kinetic parameters found. Although the values were reduced, the difference was not significant. The difference in the mean values of the iodide unidirectional clearance may then be due partly to the use of carbimazole to block binding and also partly due to the different selection of patients studied.

The exit rate constant k_{TB} for iodide was also found to be higher in the carbimazole studies (0.059 min^{-1} compared to 0.030 min^{-1}). This difference was however, not statistically significant.

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Subject	Sex	Diagnosis	Thyroid Status	PERTECHNETATE Thyroid Unidirectional Clearance (ml/min)	PERTECHNETATE k_{TB} (min^{-1})	IODIDE Thyroid Unidirectional Clearance (ml/min)	IODIDE k_{TB} (min^{-1})
AL	F	Depression	Euthyroid	38	0.117	50	0.071
CR	F	Cerebrovascular Accident	Euthyroid	25.5	0.152	44	0.048
KN	M	Hypertension	Euthyroid	41	0.041	119	0.079
LO	F	Respiratory Infection	Euthyroid	64	0.096	100	0.123
RUN	F	Chronic Bronchitis	Euthyroid	10.6	0.071	24.5	0.037
SM	F	Diarrhoea	Euthyroid	15.3	0.031	51.0	0.049
GL	F	Mintral Stenosis	Euthyroid	27.0	0.043	56	0.066
PH	F	Asthma	Euthyroid	22.8	0.035	82	0.050
FE	F	Epilepsy	Euthyroid	8.6	0.024	28.8	0.028
RUT	F	Asthma	Euthyroid	68.5	0.055	92.0	0.038
Mean				32.1	0.067	64.7	0.059
SEM.				6.6	0.013	10.0	0.008
JO	M	Thyrotoxicosis	Thyrotoxic	329	0.042	296	0.031
MU	F	Thyrotosicosis	Thyrotoxic	70.5	0.165	164	0.115
MCA	F	Thyrotoxicosis	Thyrotoxic	66.0	0.067	190	0.069
NE	F	Thyrotoxicosis	Thyrotoxic	171.0	0.031	221	0.035
Mean				159	0.076	217.8	0.063
SEM.				61.6	0.030	28.6	0.019

Table 1

The results of the studies where carbimazole was given to block the organification of iodide.

Subject	Sex	Thyroid Status	Unidirectional Clearance, C ml min^{-1}	Exit Rate k_{TB} min^{-1}	Binding Rate, k_b min^{-1}
W.C.	M	Thyrotoxic	676.7	0.016	0.184
E.H.	F	Thyrotoxic	69.2	0.014	0.049
M.H.	F	Thyrotoxic	382.6	0.015	0.118
E.L.	F	Thyrotoxic	200.1	0.010	0.170
M.L.	F	Thyrotoxic	100.8	0.017	0.071
I.McA.	F	Thyrotoxic	171.2	0.031	0.080
J.McA.	F	Thyrotoxic	205.7	0.024	0.067
A.McK.	F	Thyrotoxic	319.8	0.027	0.170
M.McL.	F	Thyrotoxic	109.4	0.010	0.072
D.McM.	F	Thyrotoxic	95.1	0.038	0.135
V.McN.	F	Thyrotoxic	83.8	0.016	0.134
S.McP.	F	Thyrotoxic	112.5	0.045	0.120
S.P.	F	Thyrotoxic	107.4	0.016	0.090
M.R.	F	Thyrotoxic	196.7	0.023	0.074
S.S.	F	Thyrotoxic	109.7	0.030	0.110
Mean		Thyrotoxic	196.0	0.022	0.110
(S.E.M.)			(41.4)	(0.003)	(0.011)
A.B.	F	Euthyroid	41.4	0.009	0.042
C.H.	M	Euthyroid	45.2	0.046	0.050
W.K.	M	Euthyroid	27.9	0.016	0.092
E.McF.	F	Euthyroid	30.1	0.048	0.104
E.McI.	F	Euthyroid	30.9	0.038	0.053
E.McP.	F	Euthyroid	30.1	0.017	0.007
A.W.	M	Euthyroid	52.3	0.038	0.115
Mean		Euthyroid	36.8	0.030	0.066
(S.E.M.)			(3.6)	(0.006)	(0.015)

TABLE 2 ANALYSIS OF TRAPPING AND BINDING FUNCTIONS IN 15 THYROTOXIC AND 7 EUTHYROID SUBJECTS (Results of Binding Studies)

Subject S.M.

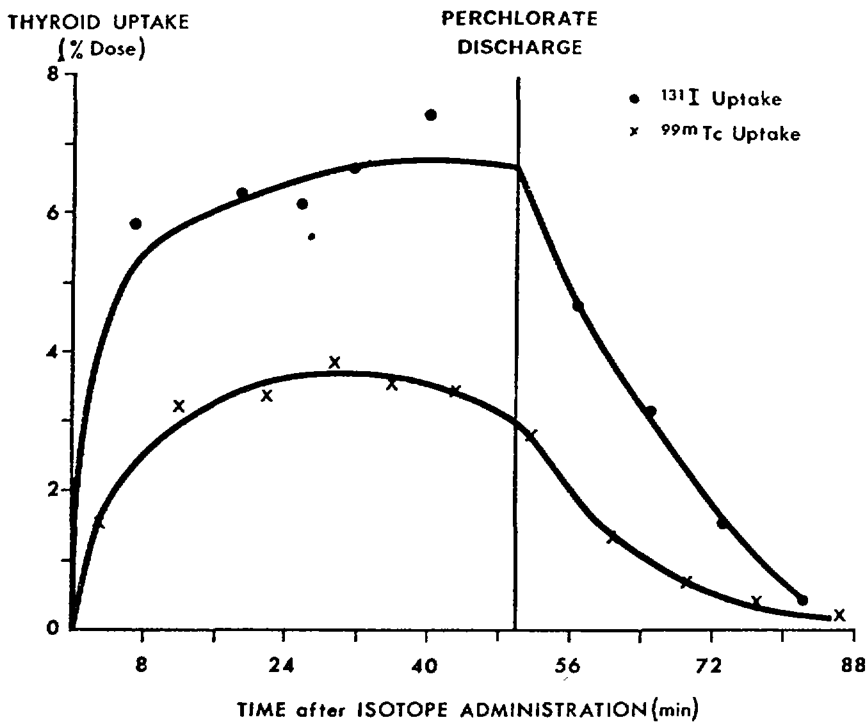

Fig. 1 (a) Thyroidal ^{131}I and ^{99m}Tc for subject SM is seen to be discharged by perchlorate 50 minutes after isotope administration. The action of the perchlorate is seen to take place almost immediately after administration.

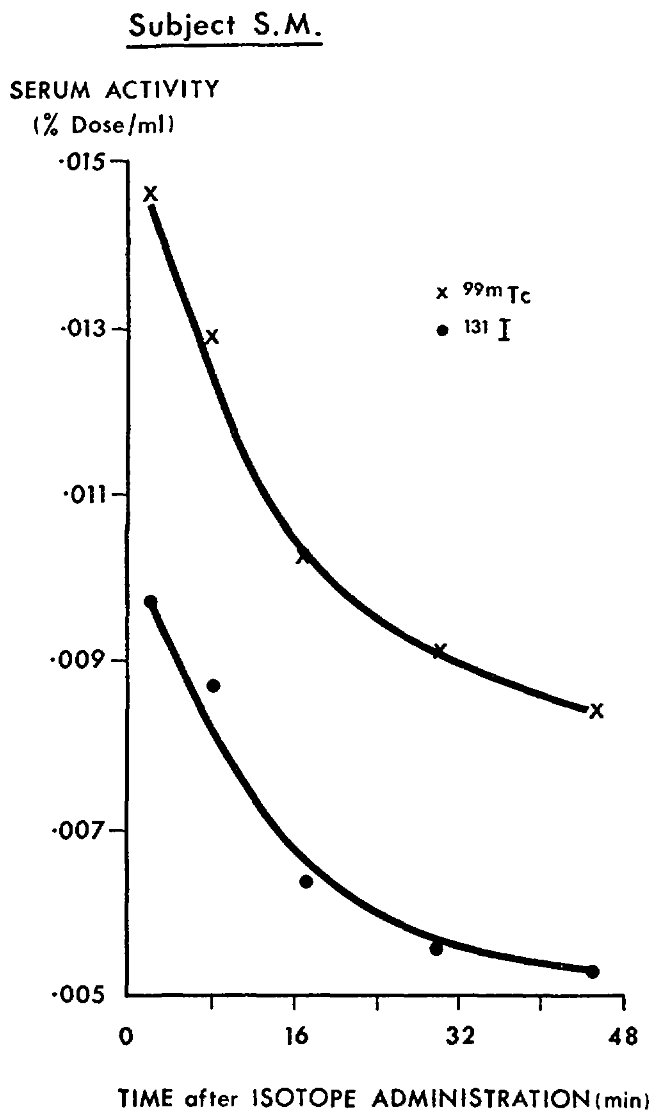

Fig. 1 (b) The serum activities of ^{131}I and ^{99m}Tc are seen prior to perchlorate discharge. In every case, the ^{99m}Tc serum activity is higher than the corresponding ^{131}I activity.

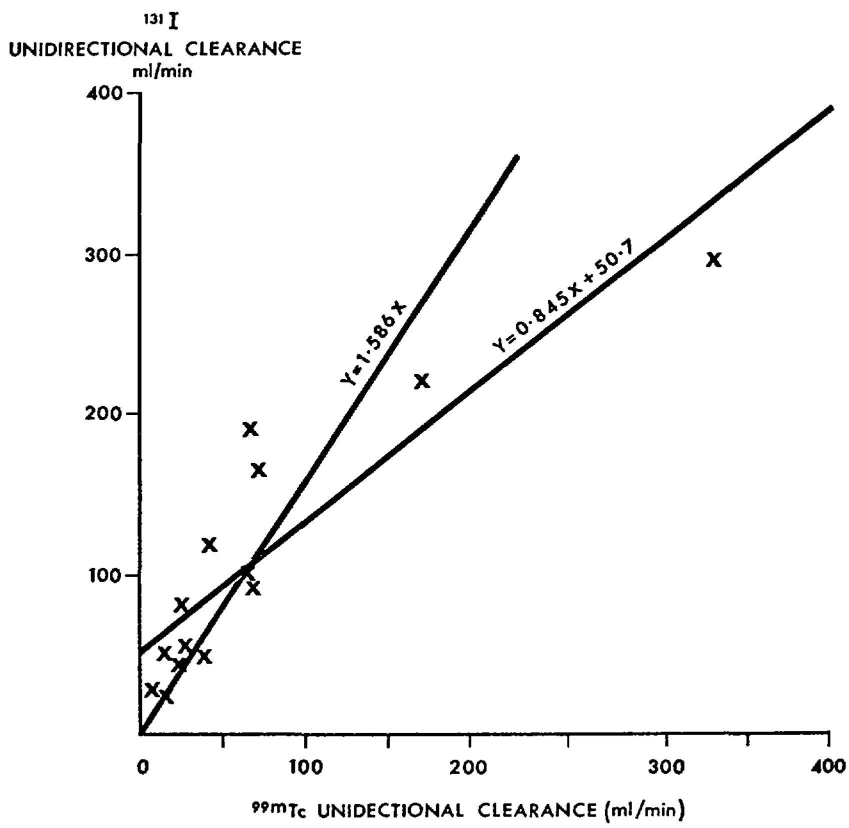

Fig. 2 The best fit lines correlating unidirectional clearance of ^{131}I and unidirectional clearance of ^{99m}Tc are shown. The unidirectional clearance of ^{131}I is, except in one subject, always greater than the unidirectional clearance of ^{99m}Tc.

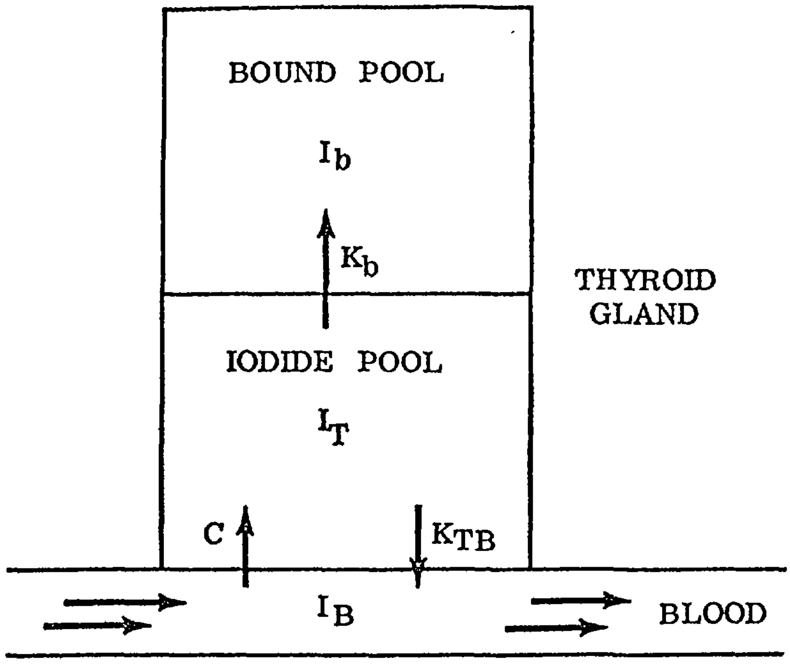

Fig. 3 The open three compartment model of iodide trapping and binding.

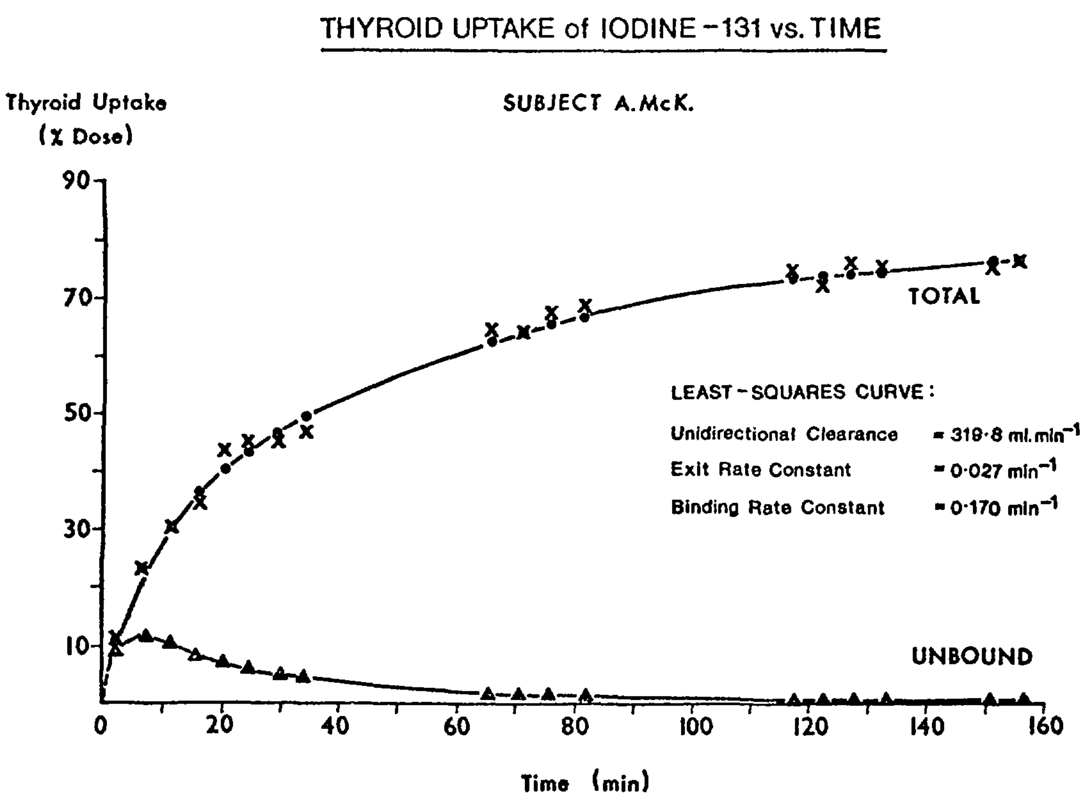

Fig. 4 The results of the kinetic analysis (binding study) for subject A.McK. (hyperthyroid).

Summary

An open three compartment model of the human thyroid has been used. This model contains three kinetic constants; the unidirectional clearance; k_{TB} the fractional loss rate of iodide from the gland; and k_B the fractional organic binding rate of iodide in the gland. The unidirectional clearance (c) and k_{TB} have been evaluated for iodide and pertechnetate when the organic binding of thyroidal iodide was blocked by carbimazole (i.e. $k_B = 0$). The unidirectional clearance (c), k_{TB} and k_B have also been evaluated for iodide for subjects not given carbimazole. A comparison of the results of these two studies suggest that carbimazole may affect the rate of thyroidal iodide trapping.

QUANTITATIVE SCINTIGRAPHY IN THE STUDY OF EARLY THYROID UPTAKE

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ABSTRACT

This paper first reviews the general problems inherent in early thyroid radionuclide uptake measurements, with particular reference to clinical requirements, choice of radionuclide, choice of measuring device and processing of the data obtained. It then describes the author's personal experiences in carrying out measurements of $^{99}Tc^{m}$ uptake by means of a technique involving off-line computer analysis of digital data from a single-detector scanner recorded on magnetic tape. The computer program used allows correction of the data for radioactive decay, subtraction of background, smoothing, computation of the total number of counts recorded within a given contour of constant percentage counting rate and computation of the area enclose within such a contour. The results of detailed physical studies aimed at establishing the technique used on a firm basis are given in detail, particular attention being given to the problems arising from variations in the depth of the thyroid and in the level of extrathyroidal radioactivity. Illustrative results obtained in a single hyperthyroid patient are also presented and the clinical value of the technique discussed.

INTRODUCTION

Thyroid uptake measurement using ^{131}I is a suitable and accurate enough technique for usual clinical purposes.

However, the interest of early uptake measurements is now emphasized. In this case, the correction methods for the neck extrathyroidal activity (ETA) are not yet satisfactory (1), (2), (3), (4) and (5).

Furthermore, for these early uptake measurements, the use of ^{132}I instead of ^{131}I provides a lower radiation dose to the subject, but needs heavy and expensive devices. Moreover, it does not permit scintigraphy, and needs double-tracer methods (6).

Then the use of $^{99}Tc^{m}$ for both scintigraphic and dynamic studies seems to be of great interest (7), (8), provided that only the uptake and not the hormonosynthesis is considered.

An ETA correction formula was proposed for iodide (9) and pertechnetate (10), but scattering is important; it gives only mean values.

A "wash out" method by thiocyanate injection was also described (7), or different thigh activity correction formulas.

But these correction methods are unsatisfactory. Furthermore the low energy of the $^{99}Tc^{m}$ gamma rays (140 keV) increases the rôle of thyroid depth and thickness.

For these reasons, the usual methods with a non-imaging fixed detector are inadequate, and scintigraphic methods have been described by several authors.

First, we shall discuss general problems and give our personal results in a second part.

GENERAL PROBLEMS

1 - AIM AND PHYSIOLOGICAL PROBLEMS

The general aim of these methods is the measurement of thyroïd uptake at a given time which should provide clinical informations.

A - Time and duration

Iodide uptake occurs early and a 20 minutes measurement is mostly used (7) (8) (10) (11).

Variations of cervical activity are quick in the first minutes (8). The measurement duration must then be short enough so that the required value remains a constant.

For moving systems, the scanner speed varies between 30 - 50 cm/min (8) and 1 m/min with a 0,85 cm line spacing (9).

B - Signification

These measurements are made under different circumstances :

1 - The purpose can be to perform comparative measurements on the same patient (stimulation or suppression tests) (12) (13) (14). The result by itself is not of great interest ; it needs to be compared with the others.

Reproductibility is then the most important requirement and relatively great methodologic errors can be accepted. For instance, when the uptake is overestimated because one has omitted the depth correction, the result of a suppressibility test will remain correct.

2 - On the contrary, the purpose can be to confere a diagnostic value to one measurement. Under these conditions, the methodological care and exactness will play a prominent part.

It is the same when these results are used to establish clearances or other functional parameters.

II - RADIOISOTOPES

131 Iodine was first used (10) (18). Its medium energy (364 keV) gamma Rays provide the advantage of a low depth attenuation (18) (19).

99 m Technetium is now more widely used. In spite of its lower energy, it provides a considerable radiobiological advantage since the average dose delivered to the thyroïd is only 0,1 rad for 1 m Ci injected (20).

III - DETECTOR DEVICE

A - Sensitivity

With the commonly used activities (1 mC.), there is always enough sensitivity to avoid statistical inaccurracies unless the uptake is very low.

B - Spectrometry

Its importance was shown by JOHNSTON and BRILL (21) who dwelt on the varaibility of the COMPTON/photopeak ratio with depth. Most workers use a narrow pulse-height window, centered on the photopeak (120-160 keV (10)) or do not specify their measurement conditions.

It is however an important point : the measurements should be made always under the same conditions and a "drift" should be avoided.

But a wider-pulse-height window might be better, since the purpose is not to obtain a fine resolution scan image but a method for counting the sum of the dots.

One can think that the depth attenuation can be partially reduced this way, modifying the COMPTON/peak ratio. However, the threshold must remain high enough to avoid the lead X rays.

As far as we know, only general considerations have been made on this problem (21) but were not yet applied to the specific problem of thyroïd uptake.

C - Collimator. Sensitivity variations versus depth

"The response to a large thin plane source, having constant activity per unit area, does not depend on the distance from the source if attenuation is neglected and certain approximations are made (19) (22). "

Furthermore, HARRIS says (23) that "the quantative value of counts from a scanner, moving or stationary, is reinforced by the fact that, as long as the scan completely covers the target, the total counts recorded are independant of source distance ".

However, that is only true when the "summed" area (i.e the aera inside of which the dots are counted) is wide and more especially when the depth increases. That would lead to consider a too wide area for counting the whole of the thyroïd activity and so, to increase the part of the E.T.A. (cf infra).

Furthermore, the attenuation in water of the Technetium gamma rays should not be neglected, although it depends upon the size of the source and the detection conditions (21).

Several ways were then chosed :

1- ANDROS et al.(7) use a correction table versus thickness and depth of the thyroïd gland as they are estimated on clinical and scintigraphic data.

2 - ATKINS et al. (8) consider tath the errors in the determination of these correction factors are so important that they have no actual interest. In the same way, HILDITCH et al (9) discuss this problem in the use of 131 I without giving any answer but in later papers they do not discuss this point when applying the same method to Technetium uptake (10) (14).

3 - However, this fact is important as pointed out by ARIMIZU et al. (19) and WILLIAMS and De GARRETA (11) (24), who emphasize the need of a depth-independance response of the detector.

This is obtained by ARIMIZU (19) by perfoming two scans in prone and supine position, and directly by WILLIAMS with a dual detector scanner. It is then necessary to take into account the neck thickness (11) and to add up the dots by a convenient way. Arithmetic and geometric means are discussed.

4 - However, we think that this problem is less important in quantitative scanning of the thyroïd becauseit is a thin and superficial organ and there are two reasons of this :

a - the part of the lower detector (which "sees" the nape of the neck) is minor : its contribution is also less important than a phantom study could make believe. Under these conditions indeed, the effect of bone attenuation is neglected ; now the bone thickness and distance from the thyroïd gland are quite variable according to the patient.

b - Furthermore, the thyroïd is usually thin and superficial except for big goiters and the depth variations in efficiency remains within acceptable limits. But this point must be experimentally tested by every laboratory to avoid a great inaccuracy in the uptake determination.

IV - DATA OUTPUT AND HANDLING

A - Data output

The simplest way is to count directly the dots on the scan image. For this purpose, it is easier to use a high dot factor and a wide space lining.

In fact, it is better to use a computer for data processing (18).

B - Choice of the area limits

The methods using directly the dot scintiscan with direct manual counting allow only very simple calculations derived from gross estimated areas of simple geometric shape. These methods are inaccurate, the more so as the pertechnetate E.T.A. is heterogenous.

The use of a computerized method should provide a better answer to this problem. However, TAUXE (18) chosed "the lowest counting level which most closely corresponded to the outline of the thyroïd gland (above background threshold) " but without defining the exact signification of "most closely".

Indeed, "the presence of a high level of radioactivity in neighbouring organs may, however, seriously interfere with the measurement of radioactivity in body organs by quantative scintigraphy." (25)

We have observed that the apparent limits of the gland can be widely modified by the level of E.T.A., and this can be the source of erroneous results when it is not corrected.

C - Calibration-

Calibration problems for a great part depends upon the variations of efficiency with depth.

If efficiency is depth independant (or little dependant) the shape of the phantom is not critical (11) (18) (but it is not always so).

Two procedures can then be used for calibration :

1/ with each measurement, an aliquot of the injected solution is introduced in a more or less "anatomic-like" phantom and the measures are made in the same way on a "phantom-neck" and on the patient. (9) (18).

2/ using a thyroïd "anatomic-like" phantom, a calibration factor is carefully determined between this phantom and a syringe. This calibration factor is then used to calculate the thyroïd counts/syringe ration for each patient (11). We prefer this second way.

-:-:-:-:-:-

PERSONAL RESULTS

MATERIALS AND METHODS

1 - Scanner and data out put

We used a conventionnal moving one head scanner (MECASERTO M.O.4 L) with a 3 inches diameter crystal and a 61 honeycone holes lead collimator. The scanning speed was 2,5 cm/sec, with a 2,5 mm line spacing.

The pulse height analyser window was set between 105 and 175 keV. Summation of pulses was perfomed each 1,25 mm and recorded on a Kennedy incremental magnetic tape together with timer signals.

2 - Phantoms and calibration

We used an "antomic-like" moulded thyroïd plexiglass phantom filled with water, the inner volume of which was 51 ml and the surface projection 2,540 mm^2 . The mean thickness is then 2 cm.

This thyroïd phantom was placed in a plastic box, 30 x 11 x 9, cm ; filled with 3 liters of water ; and depth could be adjusted.

For calibration, a 2 ml syringe was used, filled with a pertechnetate solution, ready to be injected. This syringe was placed in a hole situated 3 cm deep in a plexiglass cubic block of 12 x 12 x 12 cm. Two scans were performed, before and after the injection.

3 - Computer Processing and date output.

Magnetic tapes are fed into a high speed digital computer (UNIVAC 1107) to reconstitute the data matrix, each line being 2,5 mm and each column 1,25 mm.

The program allows background and decay corrections (for a scan or from one scan to another), smoothing following a chosen method, cells summing when necessary.

Moreover, what is essential for our purpose, it can give the total number of courts and for each needed level (in percentage) the surface inside of this level and the corresponding number of counts. We have chosen each 5 % level from 0 to 50 %.

It is also possible to use an automatic-plotter to obtain a colour scanimage, each colour corresponding to a zone between two isopercentage limits.

RESULTS

1 - Choice of the collimator-skin distance (h cm)
(Study on a line source)

A line 99 m Technetium source was placed 3 cm 'eep in plexiglass (mean depth of the thyroïd gland) and spread functions were reformed for several "collimator-skin" distances.

Results are given in fig. 1 a, b, c.

The most important are:

1 - Under these conditions, focusing of the collimator is obtained for h = 8 cm, i.c. collimator focus is at h + d = 11 cm.

2 - At h = 8 cm, both sensitivity and resolution are optimal, but from h = 6 cm until h = 9,5 cm, sensitivity remains over 90 % of this maximum.

We have then made the following measurements (role of depth) both for h = 8 cm and for h = 6 cm. The decrease with depth was less important for h := 6 cm than for h = 8 cm (an explanation of this is that the focusing effect provides some compensation for the depth effect). (fig. 2 b). All results will now be given for a collimator-skin distance : h = 6 cm.

2 - Variations with depth (d cm).

a) line source

Spread functions were obtained for different depths in plexiglass.

Results are given in fig. 2 a, b, c.

The important result is that efficiency remains over 90 % from 0,5 until 4.0 cm depth. It decreases very quickly after 4.0 cm, to 70 % at 5 cm and 58 % at 6 cm.

This means that efficiency does not change too much and provides a good technique for uptake evaluation, with an inaccuracy due to variations in depth nor exceeding 10 to 15 % on the result, unless the measurement is made on a large goiter.

b) Thyroïd-phantom source

Quantitative scans were performed at different thyroïd depths in water. Results are summarized in table 1 and II (three percentages only are showed here).

Main results are :

1° - The shape and size of the chosen isopercentage surfaces (S_{12} , i.e. surface inside of which the counting rate is over 12 % of the maximum count-rate over the thyroïd gland S 31.63 and S 45.33) are undependant on depth. This can be shown on table I and directly on the scans which are not represented here because they are coloured documents.

2° - The isopercentage which best fits the actual thyroïd surface is near 30 %. This point will be developed later.

3° - The decrease of counts with depth is not critical between 0,5 and 2.0 cm, since the total number of counts remains over 87 % (table II). It falls at 75 % at 3.0 cm depth. We find again the result of the study with a line source : this factor remains acceptable, except for the large goiters (our phantom is bigger than a normal thyroïd gland, it is like a moderate goiter).

4° - Whatever isopercentage taken, this decrease is nearly the same. We have shown in fig. 3 that obtained for the S 31 surface.

C - Consequences for calibration

TABLE I - Values of the surfaces S_i (corresponding to the inner side of an isopercentage line i %) for different depths of the thyroïd phantom.

depth(cm)	mm2 S 12 %	S 31,6 %	S 45,3 %
0	3,694	2,675	1,962
0,5	3,656	2,600	1,850
1	3,650	2,675	2,112
1,5	3,625	2,662	2,031
2	3,637	2,581	1,925
2,5	3,650	2,706	2,037
3	3,525	2,594	1,894

TABLE II - Number of counts tatalized in the different S_i surfaces at different depths (the second number in a division below the first is normalized at 100 % for 0,5 cm depth)

depth	inside of S 12 %	S 31.6 %	S 45.3 %
0	16,774 (108)	14,862 (109)	12,379 (111)
0,5	15, 485 (100)	13,571 (100)	11,076 (100)
1.0	15,013 (97)	13,423 (99)	11,710 (105)
1,5	14,069 (91)	12,528 (92)	10,628 (96)
2.0	13,535 (87.4)	11,855 (87.5)	9,904 (89.5)
2,5	12,389 (80.0)	11,101 (81.8)	9,398 (84)
3.0	11,860 (76.6)	10,541 (78)	8;702 (78.5)

Depth plays a part in the determination of a calibration factor. This one must be estimated at a fixed depth, for instance 1 cm below the water surface and will be applied to any patient with an error which cannot be precisely estimated, but which will stay lower to 10 % , in most cases.

The choice of isopercentage can be made arbitrarily since the S_i surfaces widths do not change with depth.

For the syringe, we retained a large surface ($S_1$0) to take into account all the informations coming from the source.

For the thyroïd phantom however, we have taken the isopercentage which fits best the actual thyroïd surface. This point has no importance when no extra thyroïdal activity is present, but becomes useful in the opposite case. We found a calibration factor (or syringe factor S.F.) 0.96

3 - Variations with extrathyroïdal activity (E.T.A.)

The thyroïd phantom was filled with 100 microcuries 99 Tc and placed 1 cm deep in a tank filled up with water, in which increasing amounts of pertechnetate were added.

Its thickness was 9,2 cm. Their respective positions are shown in fig. 4.

Scans were performed for several E.T.A. and results are given in tables III and IV.

Several points are of interest :

a) in each column (i.e. for each isopercentage of the maximum activity) both activity (A_i) and surface (S_i) (corresponding to the inner side of the isopercentage line i %) increase with E.T.A.This was evident for A_i since total activity increases, but not for S though it is not surprising.

b. It appears on table III that the isopercentage line that best fits the actual phantom surface projection (i.e. 2,540 mm^2) increases with E.T.A. between 25 and 30 % for the first line (E.T.A. = 0) ; 45 % for E.T.A. = 23.10^{-5} (fraction of thyroïd activity / mm^2). This point is not taken into account by most authors but seems for us of great importance.

c) For each line on table III and IV (i.e. for each E.T.A. level) it is possible to determine the best fitting percentage (F.P.) and the corresponding number of counts (F.A) inside of this "fit-percentage". This interpolation can be made by simple calculation (arithmetic interpolation or graphically (as shown in fig 5.) or computer-calculated.

Then, we can establish a table of F.P. and F.A. versus E.T.A. (table V) and plot the graph of F.P. versus E.T.A. (fig 6)

Thus, it is easy to correct for extra thyroïdal activity using a simple calculation method:

F.A. is equal to the sum of counts due to both intra thyroïdal (I.T.A.) and extra thyroïdal activities in the actual thyroïd phantom surface (2,540 mm^2)

$$\text{Thus : I.T.A. (counts)} = \frac{\text{F.A.}}{1 + 2{,}540 \times \frac{7.2}{9.2}\ \text{E.T.A.}}$$

The corrective term $\frac{7.2}{9.2}$ is due to the 2 cm mean thyroïd thickness in a deep 9.2 cm deep.

	I (isopercentages %)										
E.T.A.	5	10	15	20	25	30	35	40	45	50	
0	4,531	3,618	3,253	2,937	2,672	2,409	2,137	1,847	1,628	1,340	
0,68	6,097	3,853	3,416	3,044	2,794	2,503	2,234	1,994	1,731	1,503	
1,87	8,581	4,144	3,525	3,162	2,872	2,562	2,306	2,028	1,809	1,584	
2,44	14,325	4,994	3,684	3,240	2,931	2,650	2,362	2,103	1,869	1,616	
5,38	12,916	6,428	3,966	3,294	2,956	2,712	2,412	2,119	1,750	1,494	
7,35	14,103	8,872	4,871	3,575	3,109	2,775	2,494	2,256	2,034	1,737	
11,3	15,075	12,272	7,641	4,531	3,381	2,921	2,659	2,309	2,000	1,741	
23,0	15,700	14,606	13,616	11,356	7,919	5,175	3,587	2,866	2,531	2,203	

TABLE III - Values of S obtained for several isopercentages and several extra thyroïdal activities.
(E.T.A. : fraction of the intrathyroïdal activity / $mm^2 \times 10^{-5}$).
S_i means the surface corresponding to the inner part of an isopercentage line i % , expressed in mm^2.

		I (isopourcentages %)									
E.T.A	T (scan surface)	5	10	15	20	25	30	35	40	45	50
0	8688	7663	7358	7146	6887	6607	6264	5844	5331	4824	4255
0,68	10,409	8,609	7,908	7,660	7,359	7,099	6,732	6,331	5,919	5,400	4,895
1,87	11,504	9,808	8,398	8,043	7,743	7,434	7,029	6,629	6,134	5,691	5,181
2,44	12,842	11,363	9,162	8,437	8,061	7,719	7,339	6,881	6,402	5,915	5,328
5,38	14,282	12,919	10,475	8,983	8,395	8,007	7,665	7,157	6,593	5,786	5,161
7,35	15,680	14,610	12,589	10,151	9,042	8,527	8,072	7,612	7,164	6,690	5,980
11,3	18,753	17,736	16,591	13,500	10,656	9,323	8,660	8,210	7,517	6,819	6,163
23,0	28,319	27,457	26,990	26,254	23,887	19,340	14,965	11,982	10,410	9,577	8,673

TABLE IV – Number of counts (A) obtained for several isopercentages and several extrathyroïdal activities. A_i means the number of impulsions counted in the inner part of an isopercentage i %.

Results of this calculation are shown on table V.

Then thyroïd uptake is immediately given using the calibration factor S^F as shown in part 2 c.

4 - Determination of E.T.A.

a - Assumptions.

So far all calculations were performed with known values for thyroïd size and extra thyroïdal activities. They were then only verifications upon the validity of the used process.

Since we did not repeat these experiments with other size thyroïd phantom, we must then make some assumptions to answer the actual question, i.e. determine E.T.A. , thyroïd size and then I.T.A. and uptake.

The most important is that the relationship between the fit percentage F.P. and E.T.A. remains the same as given in fig. 6.

Once this point is assumed, it becomes necessary to find a way to calculate E.T.A. from the processed data of a scan (i.e. S and A).

b- E.T.A. Determination

Table III can provide a relationship between E.T.A. values and data extracted from the $S_{E.T.A.,I}$ matrix. We are now trying such computer calculations, and two ways are possible :

1° - We can use a line regression method to determine a formula, the form of which being :

$$E.T.A. = \Sigma\, a_i\, S_i$$

Two problems remain unclear :

- Are the low values of i (5 and perhaps 10) useful as the corresponding surface becomes too large for high values of E.T.A. (extra thyroïdal activity is not indeed an infinite extended source, according to the actual size of the neck) ?

Is a normalization factor necessary, and if so which one is the best ? There is no answer without further experiments with other-sized thyroïd phantoms .

II° - The shape of the curves S versus isopercentage I (one of these is shown fig. 5) is not the same for the different E.T.A. values. This point needs further computer studies, but a gross graphic study can already be performed.

An eye study of the S/isopercentage curves family (as this shown fig. 5) shows two points :

- an inflexion point is noted for the low percentages, but only for the high E.T.A. curves ; that could be due to the limited size of the E.T.A. containing tank.
- a slope breaking can be seen on all the curves and this breaking off point is translated to higher percentages when E.T.A. increases. Gross determination of the breaking off point absciss (B) is shown on fig. 5. Such determination for the whole curves family allows to plot a curve ofB versus E.T.A. (fig 7).

III - Whatever is the relationship established between the S matrix and E.T.A., it must be assumed that it remains true for any actual patient's thyroïd gland.

5 - CLINICAL APPLICATION (Exemple)

Results obtained by a patient (who was hyperthyroïd) are shown on table VI, and the S_i and A_i curves are plotted (fig. 8).

B is readed out on this curver (9) and this value is reported on fig. 7., that gives E.T.A. value (2.5×10^{-5}). Then F.P. is extracted from fig. 6 (30.8) and reported on fig 8. So are deperminated F.S. (Fit surface ; i.e. actual surface) (2,220 mm^2) and F.A. (9,200 counts).

After that, I.T.A. is calculated according to the formula given before (3 C) :

$$I.T.A. = \frac{F.A.}{1 + F.S. \times E.T.A.}$$

REMARK

The correcting factor $\frac{7.2}{9.2}$ is not used here because there is in the thyroïd a vascular part without any significance of uptake, because the thyroïd thickness is unknown, and because it lies on the thickest part of the neck.

Finally, uptake is given by :

$$\text{Uptake \%} = \frac{\text{I.T.A.}}{\text{syringe counts}} \times \text{calibration factor} \times 100$$

$$\text{There the result is} = \frac{8,780}{38,600} \times 96 = 22 \text{ \%}$$

E.T.A.	F.P.	F.A	I.T.A.
0	28.75	6,390	6,390
0,68	29.2	6,800	6,700
I.87	30.5	6,980	6,720
2.44	31. 5	7,150	6,800
5.38	33	7,400	6,680
7,35	34.7	7,600	6,630
11. 3	36.5	8,150	6,660
23	45	9,577	6,600

TABLE V - For several values of E.T.A., the results of F.P. and F.A are given as obtained by plotting the curves as shown in fig. 5. (Phantom studies)

F.P. means the fit percentage
F.A. the total number of counts in the inner side of this fit percentage
I.T.A. means the actual number of counts due to intra thyroïdal activities.

When an other and more accurate point will be reliable in the determination of F.T.A., the following will remain unchanged (but shall be computerized too).

DISCUSSION

1 - Phantom

The plexiglass wall of the phantom, 1.5 mm thick, modifies the spatial distribution of the isopercentage surfaces. This seems not to be of great importance.

2 - Depth

We have seen the important part played by this factor : with our one head collimator, the accuracy limit cannot fall lower than 10 % (on the result).

3 - Limits

The most important fact we noticed is that the apparent size of the gland (as determined for instance by the 40 % isopercentage) increases together with extra thyroïdal activity.

Our method permits to determine not only the uptake, but also the actual size of the thyroïd gland. This point could be of great interest, for instance in the determination of the therapeutic activity to be given for a radioiodine treatment.

4 - E.T.A. determination

This is the most criticable point as shown previously. However, it seems to be preferable to any method using geometric area below the thyroïd gland for correction factor, which neglects both E.T.A. and I.T.A. heterogeneities.

5 - Clinical interest

This computer-assisted method is sophisticated and expensive, and that is perhaps the major criticism which can be made.

It is then justified only when it provides irreplaceable results in the evaluation of the thyroïd function. This point needs further studies, but it is probably true certain circumstances only.

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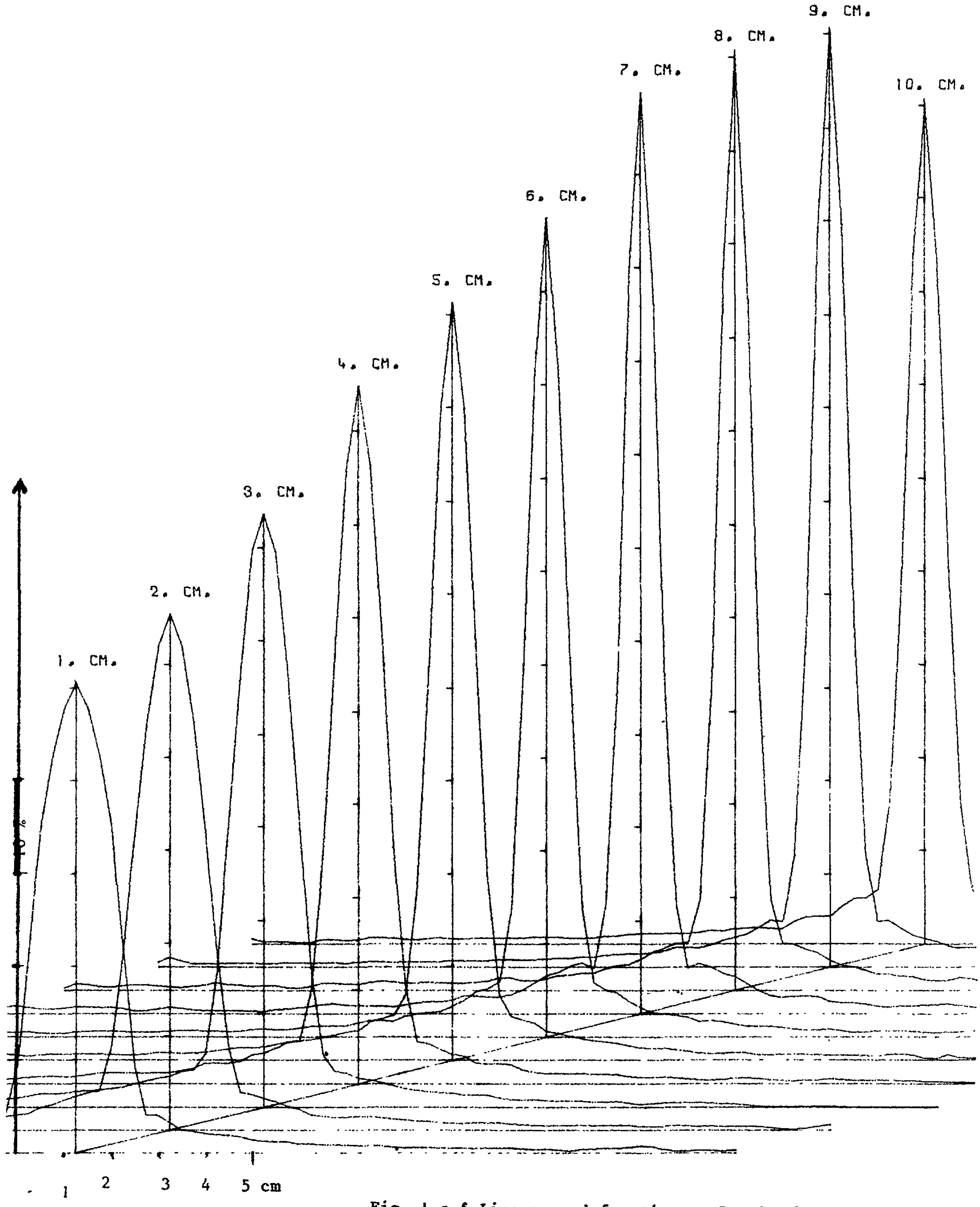
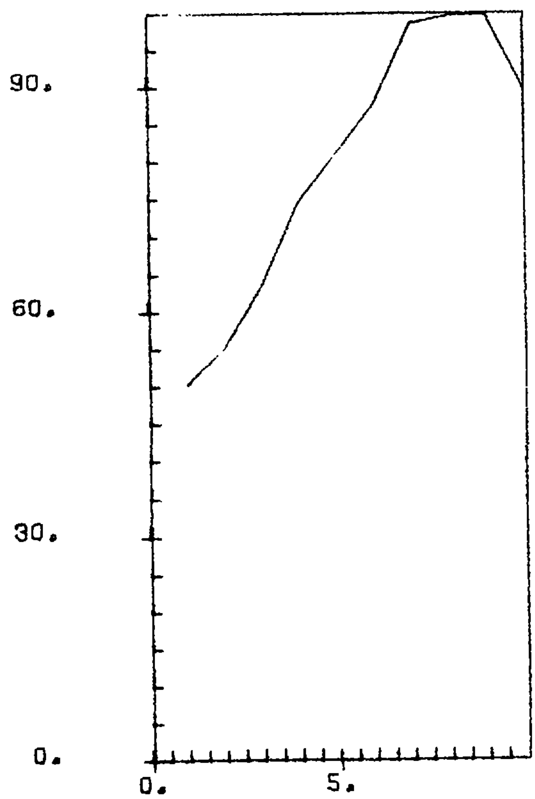


Fig. 1 a § Line spread function . Depth of source d=3 cm
Collimator - skin distance h varying at 1 cm increments -

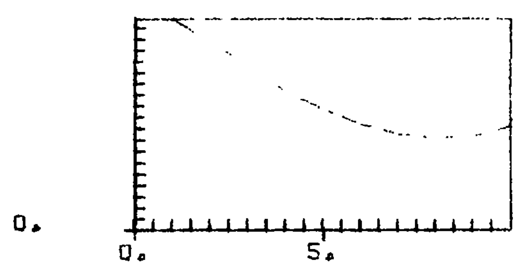
max. efficiency



depth (cm)

Fig. 1 b - Efficiency versus collimator - skin distance h (cm) (depth = 3 cm) (line source)

Index resolution (mm)



depth (cm)

Fig. 1 c - Resolution index (width of the curve at half its maximum amplitude) versus h

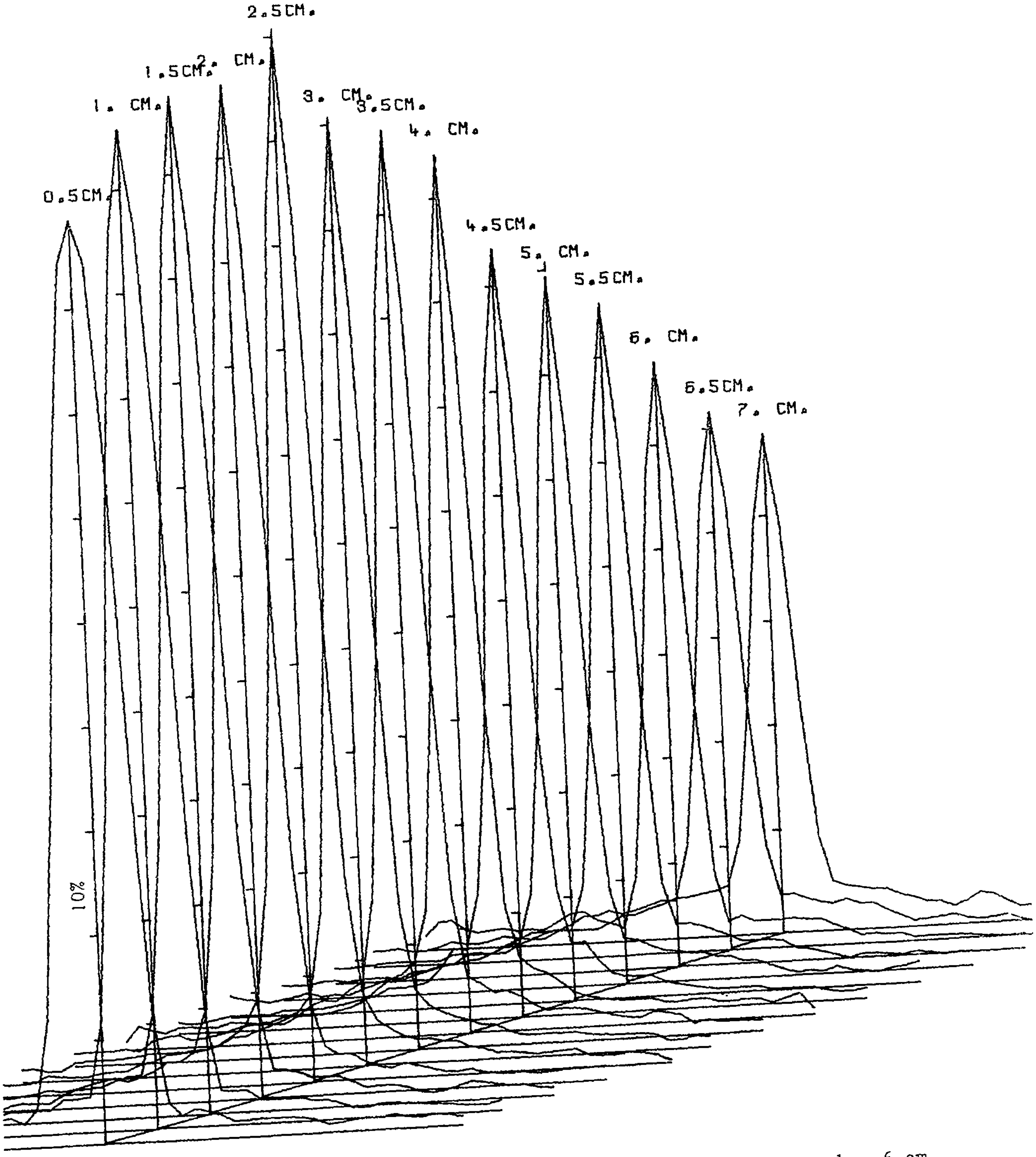


Fig. 2 a - Line spread function - Collimator-skin distance h = 6 cm
Depth d varying at 0,5 cm increments from 0.5 to 7 cm in plexiglas

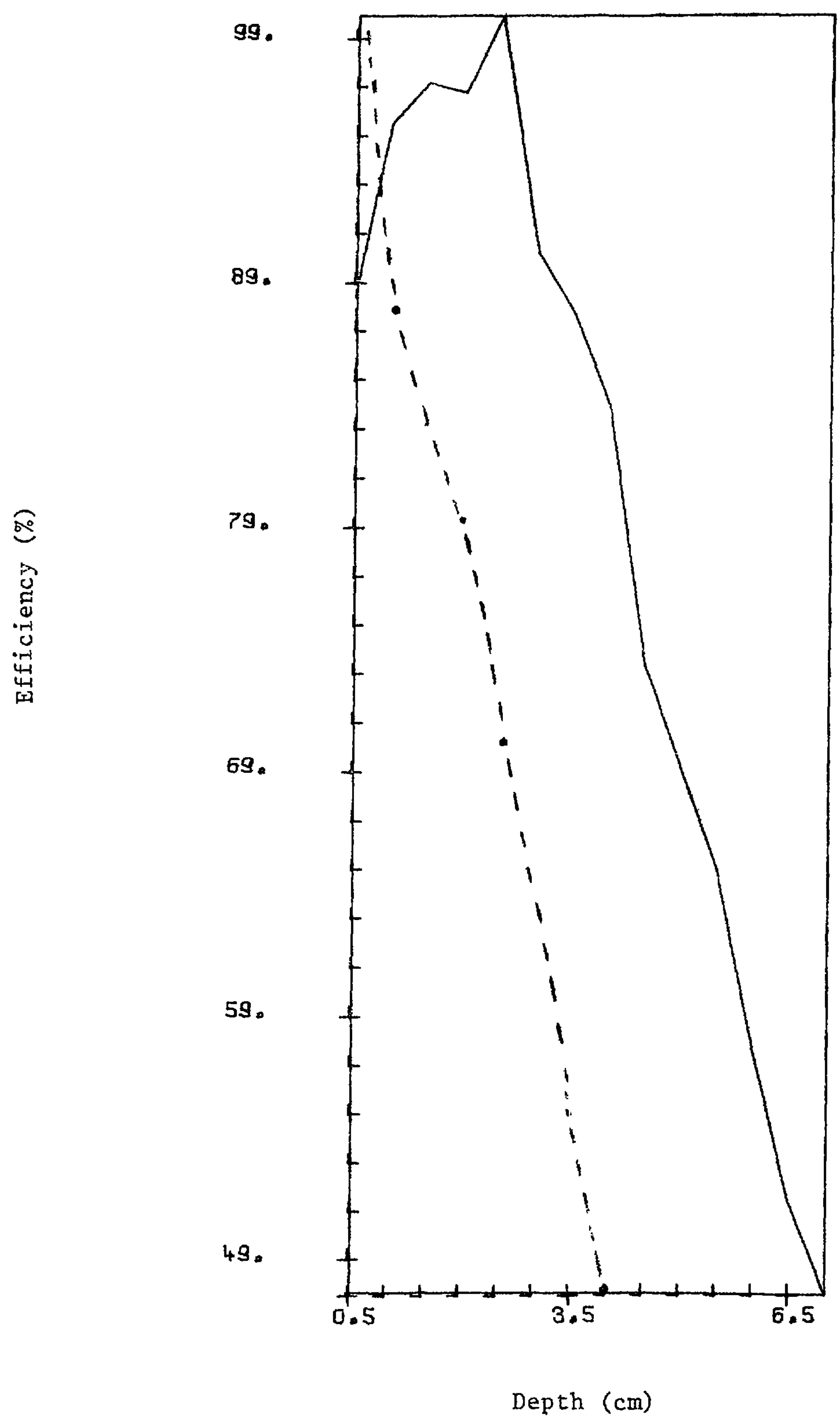


Fig. 2 b - Efficiency versus dep-h d (0,5 cm increments) -
The solid line is from h = 6 cm and the dotted line from h = 8 cm

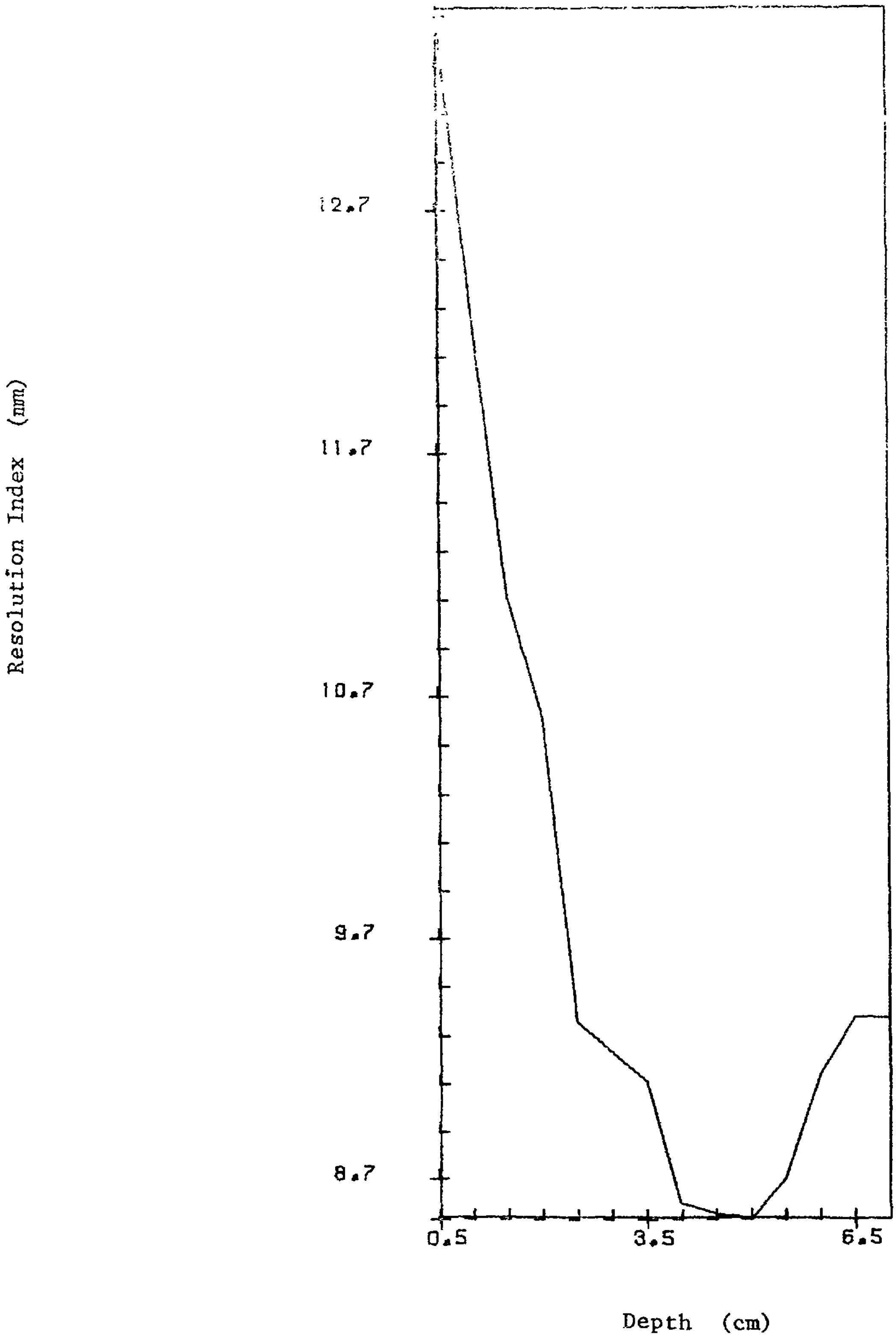


Fig. 2 c - Resolution index versus d (h = 6 cm)

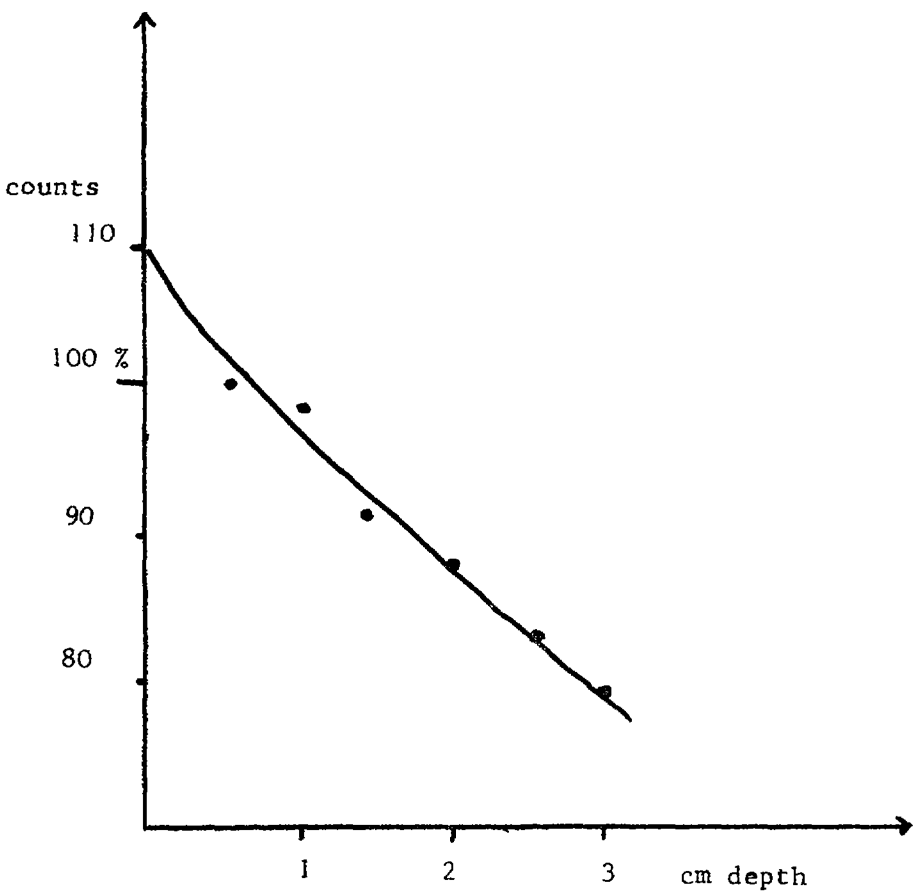


Fig 3 : Variation of number of dots inside of S_1 versus thyroïd phan depth

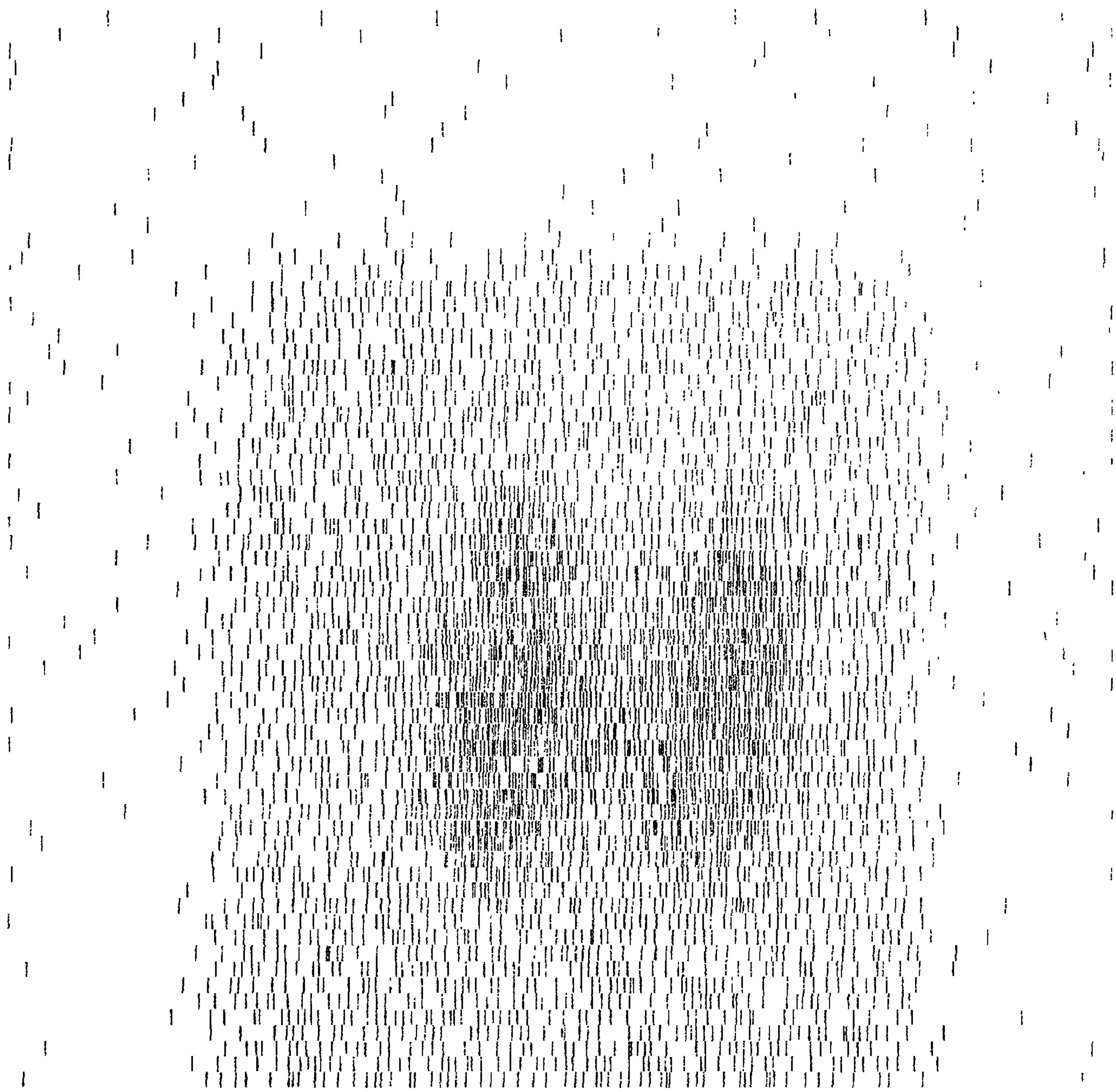


Fig 4 : Untreated scan (showing the limits of the thyroid phantom and of the surrounding water-filled box).

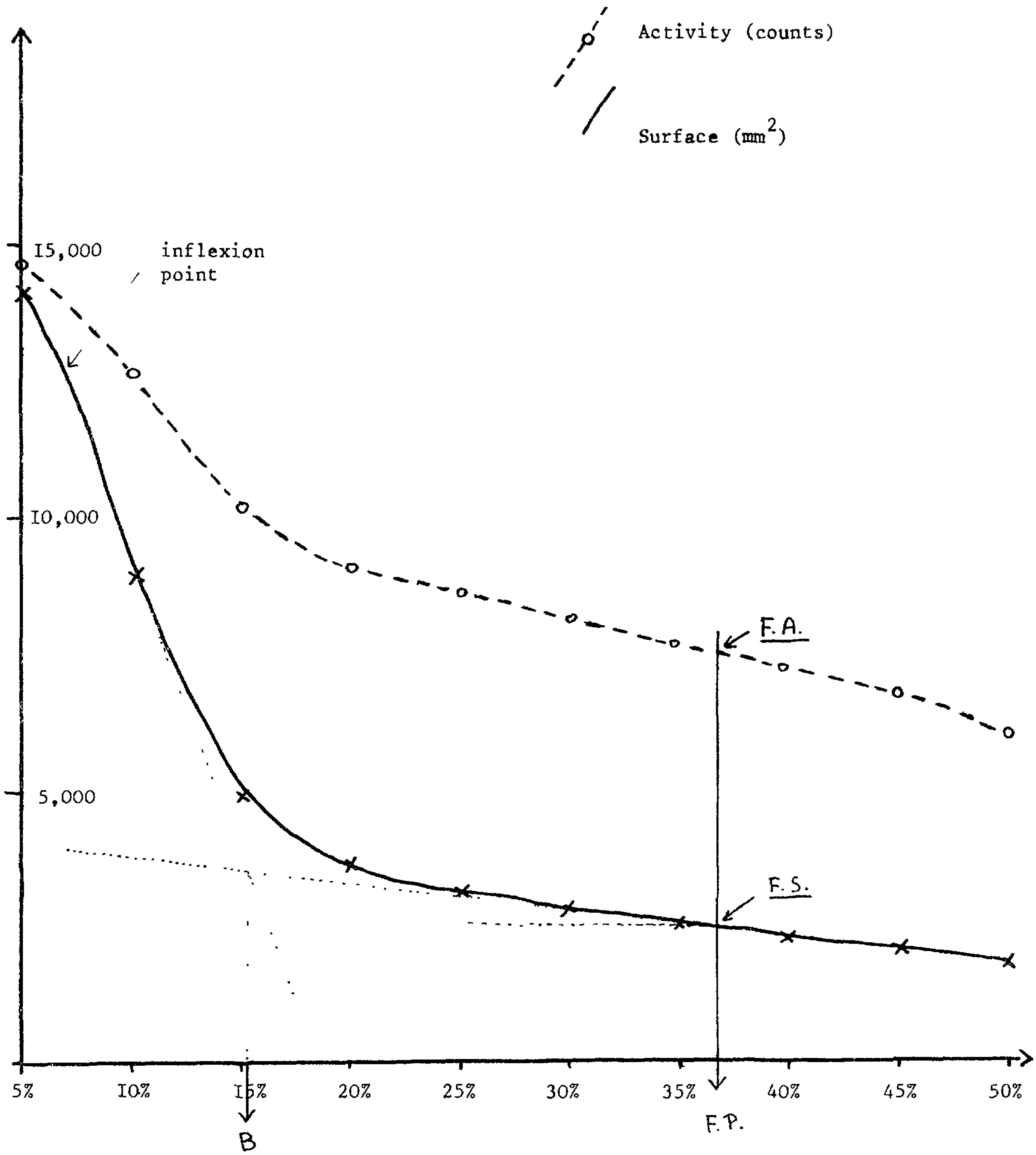


fig.5 Variations of S_i (mm^2) and A_i (counts) versus I (E.T.A.= 7.35 X 10^{-5})

Determination of F.P. and corresponding values of F.S.(=actual surface)and F.A.

Determination of B

(see text)

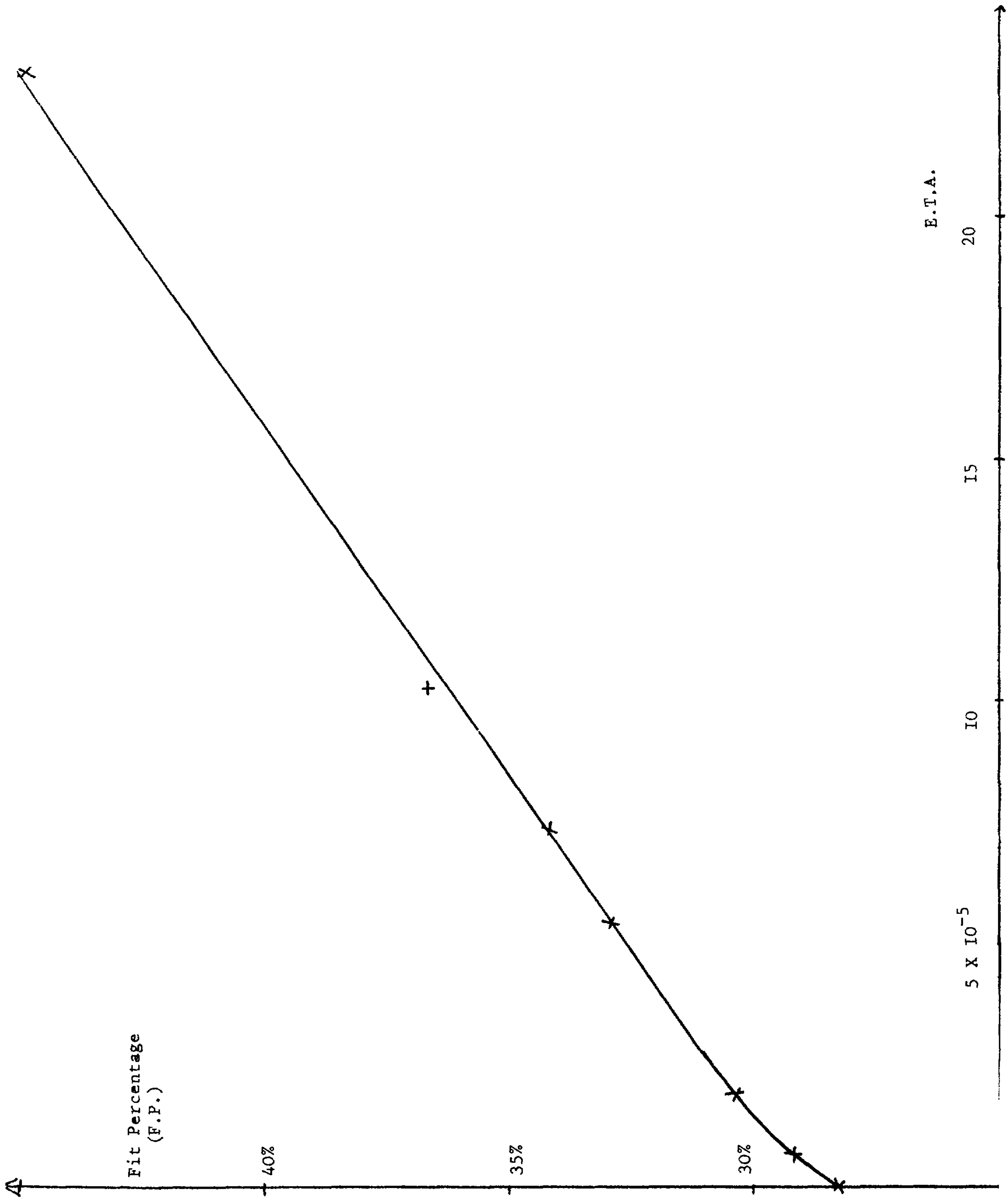


fig.6 Variation of the fit percentage (F.P.) versus extrathyroïdal activity(E.T.A.)

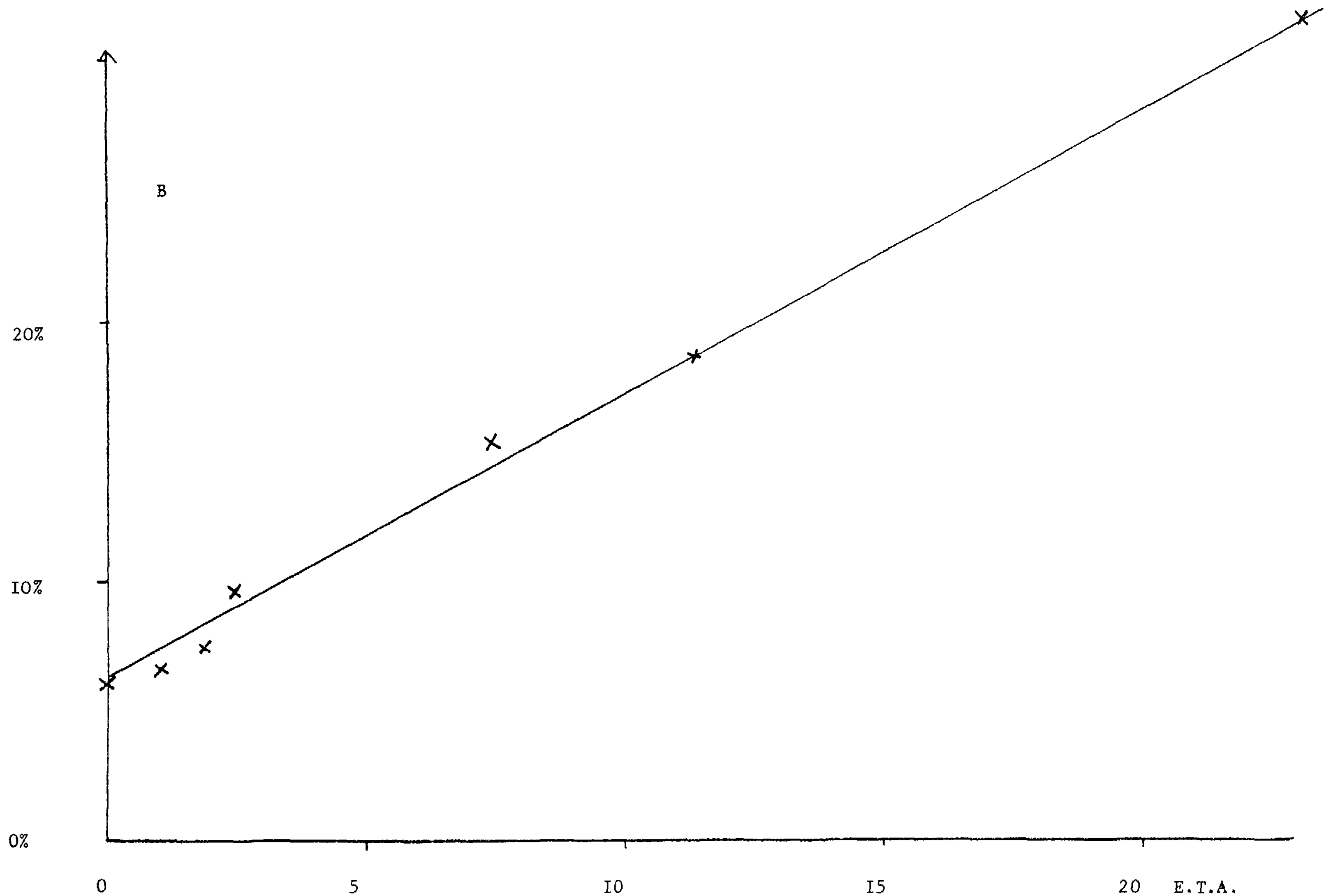


fig.7 Variation of B (absciss of the slope breaking off point) versus E.T.A.

Each point is obtained as shown on fig.5

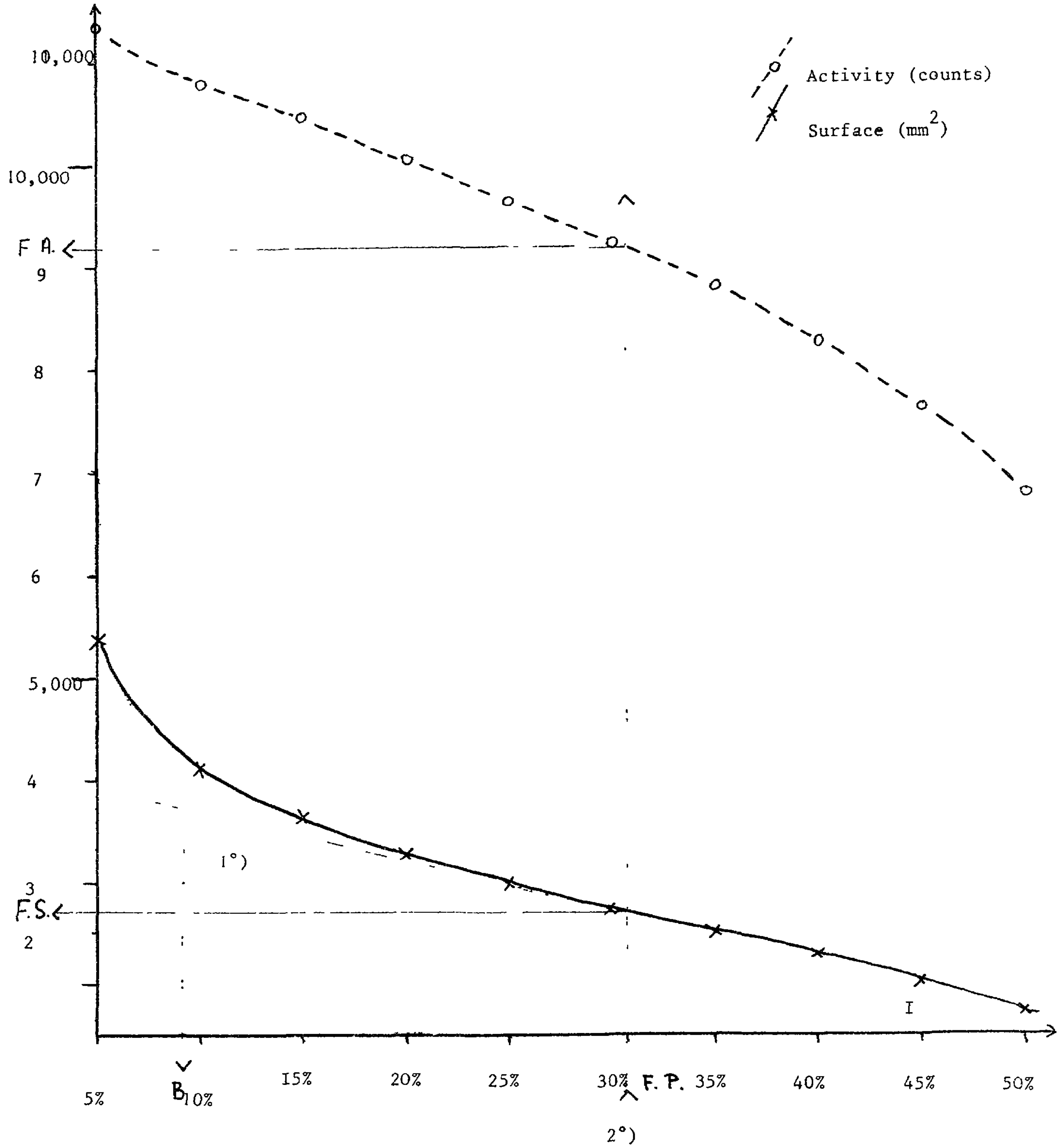


FIG. 8 Variation of S_i(mm^2) and A_i(counts) versus I (%) § Mrs G...)

1°) Graxphical determination of B

2°) Using the calculated value of F.P. , graphical determination of F.S. and F.A.

see text

THE PERFORMANCE OF THE IAEA STANDARD COLLIMATOR FOR THYROID RADIOIODINE UPTAKE MEASUREMENTS WITH RADIONUCLIDES OTHER THAN ^{131}I

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ABSTRACT

The paper describes studies of the performance of a standard collimator developed by the International Atomic Energy Agency for thyroid ^{131}I uptake tests with other radionuclides used for thyroid uptake tests, in particular ^{125}I, $^{99}Tc^{m}$, ^{123}I and ^{132}I. With the first three of these radionuclides, both the sharpness of the cut-off and the effectiveness of the side shielding were better than with ^{131}I, in accordance with predictions based on the energy of their photon radiation. With ^{132}I, however, which emits γ rays of up to 1.39 MeV in energy, performance was found to be grossly inadequate both as regards cut-off and side shielding, and a considerable increase in the thickness of the lead alloy would be necessary to achieve a satisfactory performance.

INTRODUCTION

In November 1960, the International Atomic Energy Agency (IAEA) sought the advice of a group of experts on a project of assistance to its Member States in the calibration and standardization of thyroid radioiodine uptake measurement techniques. This group developed a set of recommendations which have since been published in a number of journals and in several languages (1), these recommendations applying primarily to 24-hour ^{131}I uptake measurements. Three of them, relating to shielding and collimation of the radiation detector, were as follows:

3.2.1. The visual field at the working distance should be preferably 12 and certainly not greater than 15 cm in diameter in adults and proportionally smaller in children. This field is defined as the region within which the counting rate from a point source of ^{131}I does not fall below 90 per cent of the value recorded at the centre of the field if the point source is moved at the working distance.

3.2.2. If the source is moved at the working distance beyond the edge of the visual field, the counting rate should fall to 50 per cent or less as the distance increases by 20 per cent, and to 5 per cent or less as this distance increases by a further 20 per cent.

3.2.3. With a further movement of the point source away from the axis at the working distance, the counting rate should fall rapidly and remain below 1 per cent of the maximum value except in the region behind the crystal which is defined by a solid angle not exceeding 25 per cent (one π). Within this region, the counting rate should not exceed 15 per cent of the maximum value.

Since none of the collimators then available commercially met these specifications, a standard collimator having the recommended characteristics was developed. This collimator, which is shown in Fig . 1, was likewise intended primarily for 24-hour ^{131}I uptake measurements and was designed to have a field of view 13.5 cm in diameter when used at a working distance of 25 cm. A detailed description of it, and its performance with ^{131}I, has been published.

Since that time, radionuclides other than ^{131}I, notably ^{99m}Tc, ^{123}I, ^{125}I and ^{132}I, have been increasingly employed in investigations of thyroid function. It could be predicted that the performance of the standard collimator would be perfectly satisfactory with ^{125}I, ^{99m}Tc and ^{123}I, which emit photons with energies lower than those of the γ rays of ^{131}I, but that its performance would be inadequate with ^{132}I which emits γ rays with energies considerably higher than those of ^{131}I. This paper describes studies undertaken with the object of confirming these predictions.

METHODS

The experimental arrangements were similar to those previously described (2). The scintillation probe used in conjunction with the collimator incorporated a sodium iodide crystal 1 inch in diameter and was coupled to a scaler through a single-channel pulse-height analyzer set to operate as a simple discriminator. Measurements were carried out in air with point sources prepared by evaporation from solutions of the various radionuclides in light Perspex holders. Since ^{123}I (γ-ray energy 0.159 MeV) was not readily available, ^{47}Sc (γ-ray energy 0.160 MeV) was used in place of this radionuclide. For each radionuclide, the discriminator was set near the lower limit of the main photo-peak in the pulse-height spectrum, thus excluding the greater part of the Compton-scattered radiation from the measurements; the settings used are shown in Table I.

TABLE I

Discriminator Settings Used

Radionuclide	Energy of predominant X or γ ray (MeV)	Discriminator setting (MeV)
^{125}I	0.027	0.020
^{99m}Tc	0.14	0.10
^{47}Sc	0.16	0.10
^{132}I	0.78	0.60

RESULTS

Visual field

Figs. 2, 3, 4 and 5 show the results of studies of the visual field of the collimator with ^{125}I, ^{99m}Tc, ^{47}Sc (for ^{123}I) and ^{132}I at a working distance of 25 cm. In these studies the sources were moved along the arc of a circle 25 cm in radius centred at the mid-point of the front surface of the crystal housing. In each case the data are compared with those for ^{131}I previously reported.

Side shielding

Figs. 6, 7, 8 and 9 show the results of similar studies of the adequacy of side shielding with the same radionuclides, the sources being moved around the probe-collimator system at a distance of 40 cm from the mid-point of the front surface of the crystal housing. Again, in each case the data are compared with those for ^{131}I previously reported.

DISCUSSION

The results confirm the predicted satisfactory performance of the standard collimator with ^{125}I, ^{99m}Tc and ^{123}I, with all of which the sharpness of the cut-off as the source is moved beyond the edge of the visual field and the effectiveness of the side shielding are better than with ^{131}I. Indeed, it should be possible with all of these radionuclides, above all with ^{125}I, to reduce considerably the thickness of the lead alloy in all parts of the collimator and still satisfy the recommendations of the expert group.

With ^{132}I on the other hand, the performance of the collimator is grossly inadequate. The lowest counting rate recorded as the source is moved beyond the edge of the visual field amounts to 1.5 per cent of the value recorded in the centre of the field, whilst counting rates of more than 10 per cent of the latter value are recorded when the source is moved to the side of the probe-collimator system. Since ^{132}I emits γ rays with energies up to 1.39 MeV, and even higher, (the predominant γ rays having an energy of 0.78 MeV), a considerable increase in thickness of the lead alloy would be necessary to achieve a satisfactory performance with this radionuclide. This is all the more true since its short physical half-life limits its use to early uptake tests in which measurements must be undertaken under conditions of relatively low uptake and relatively high extrathyroidal radioactivity.

ACKNOWLEDGEMENT

The advice and guidance of Dr. E. H. Belcher in this project are gratefully acknowledged.

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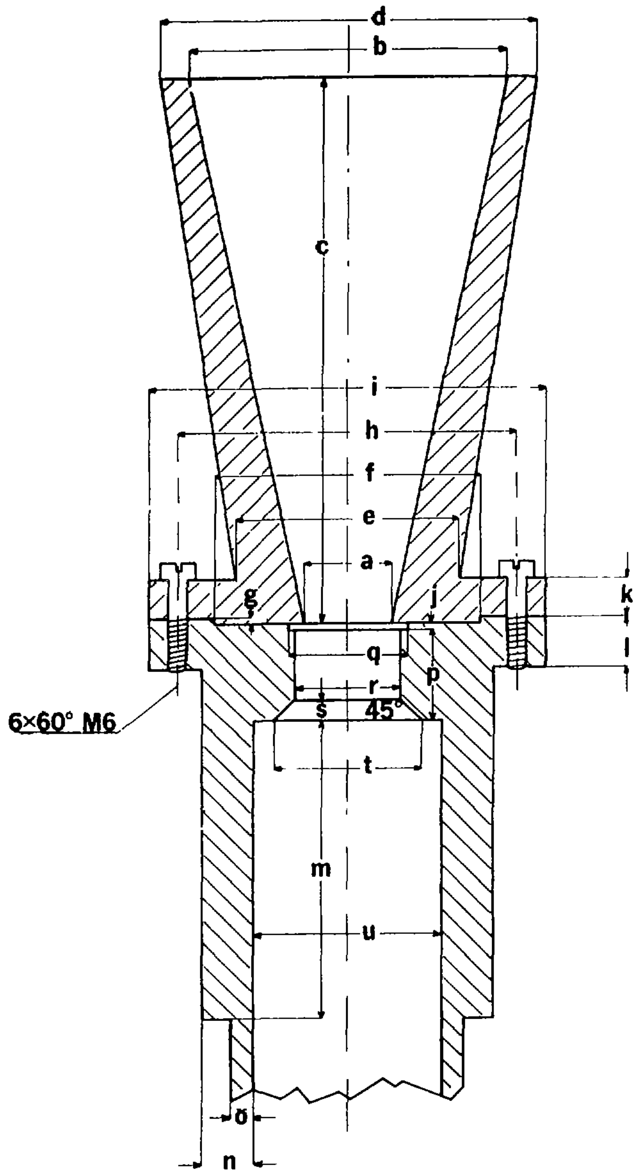
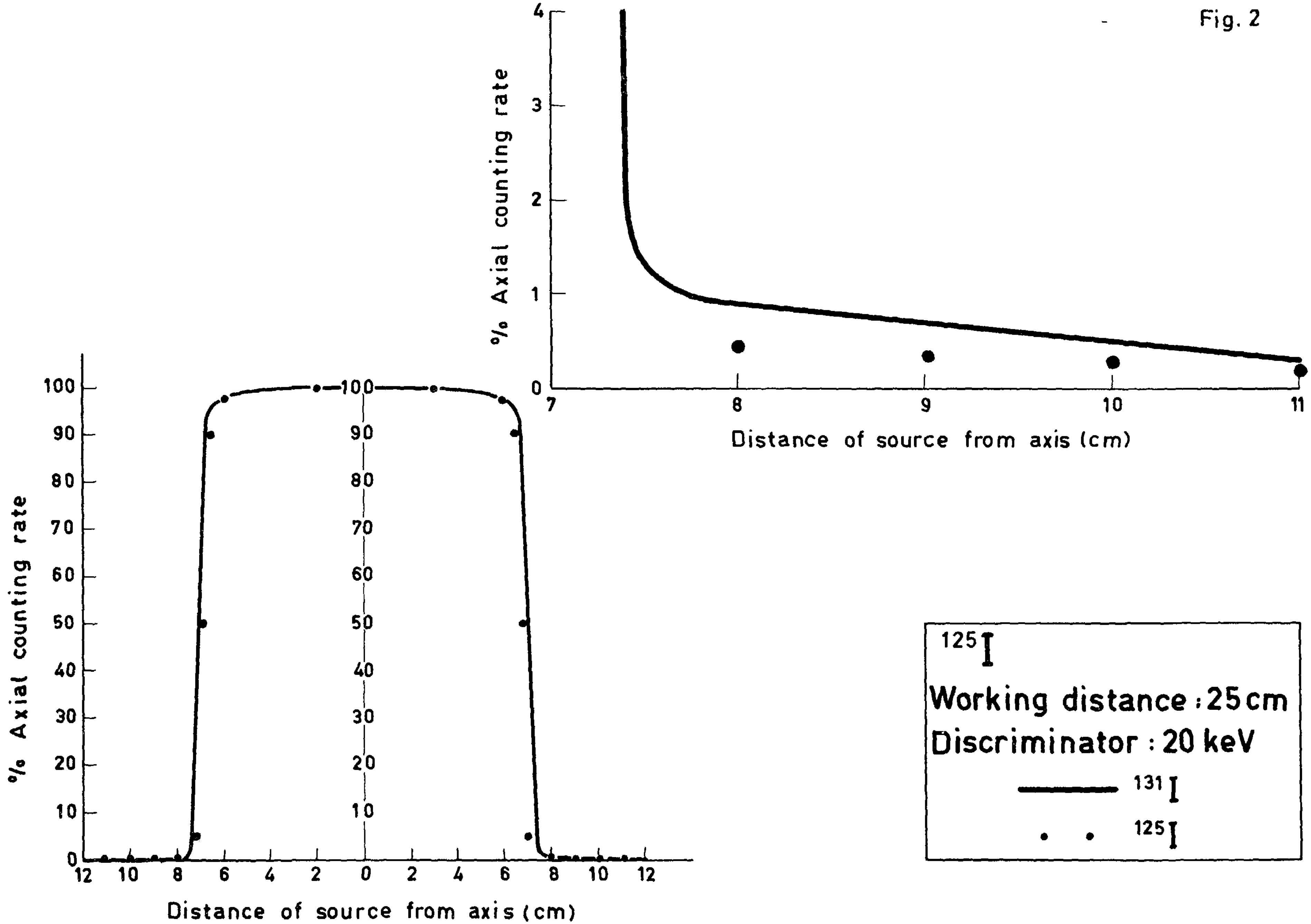
Fig. 1



a	3.1	h	11.5	o	0.75
b	10.8	i	13.5	p	3.3
c	18.6	j	0.2	q	4.05
d	12.8	k	1.3	r	3.6
e	7.7	l	1.7	s	0.7
f	9.0	m	10.2	t	5.0
g	0.2	n	1.75	u	6.4

Fig. 2


% Axial counting rate
Distance of source from axis (cm)
% Axial counting rate
Distance of source from axis (cm)
125 I
Working distance : 25 cm
Discriminator : 20 keV
131 I
125 I

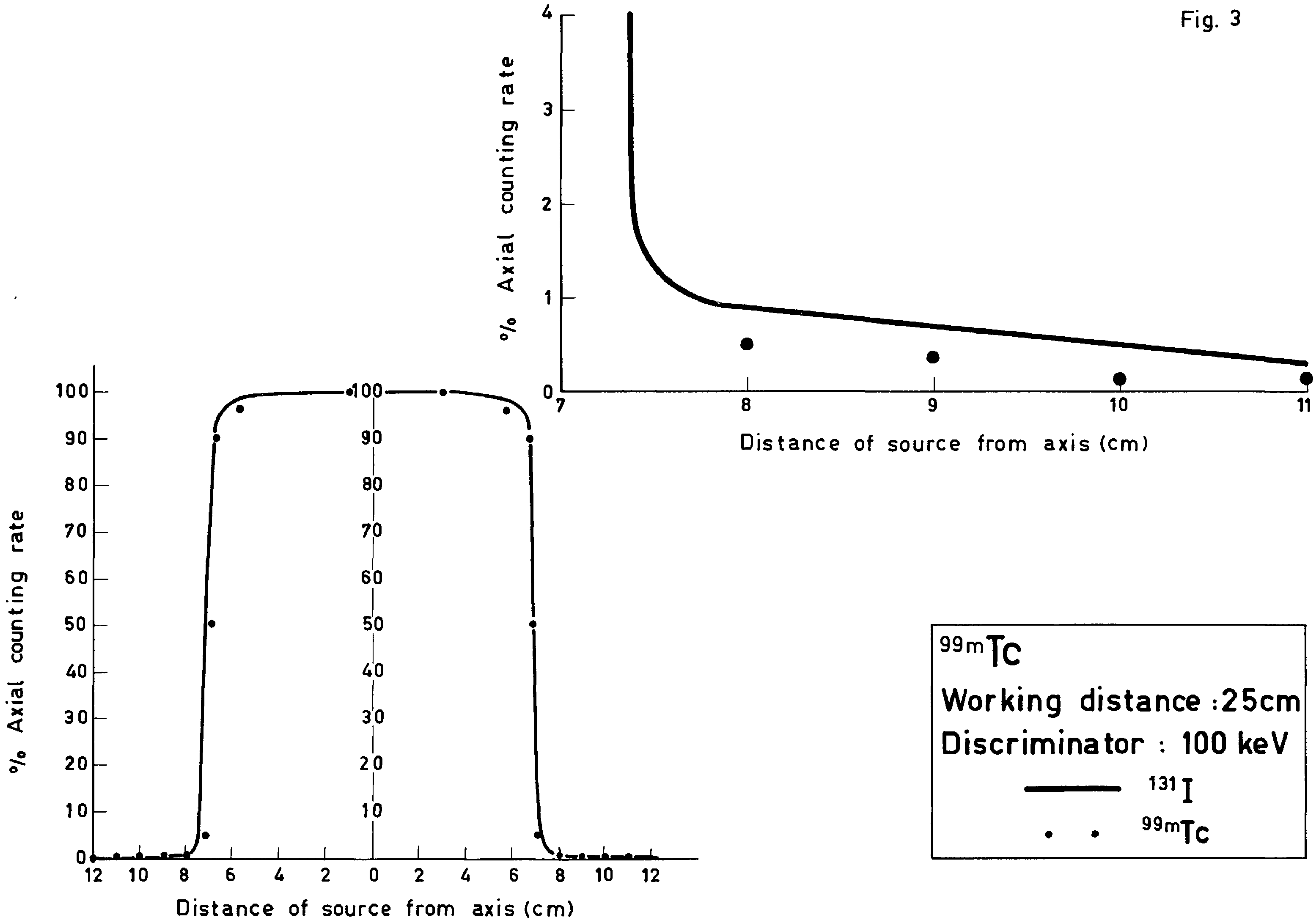
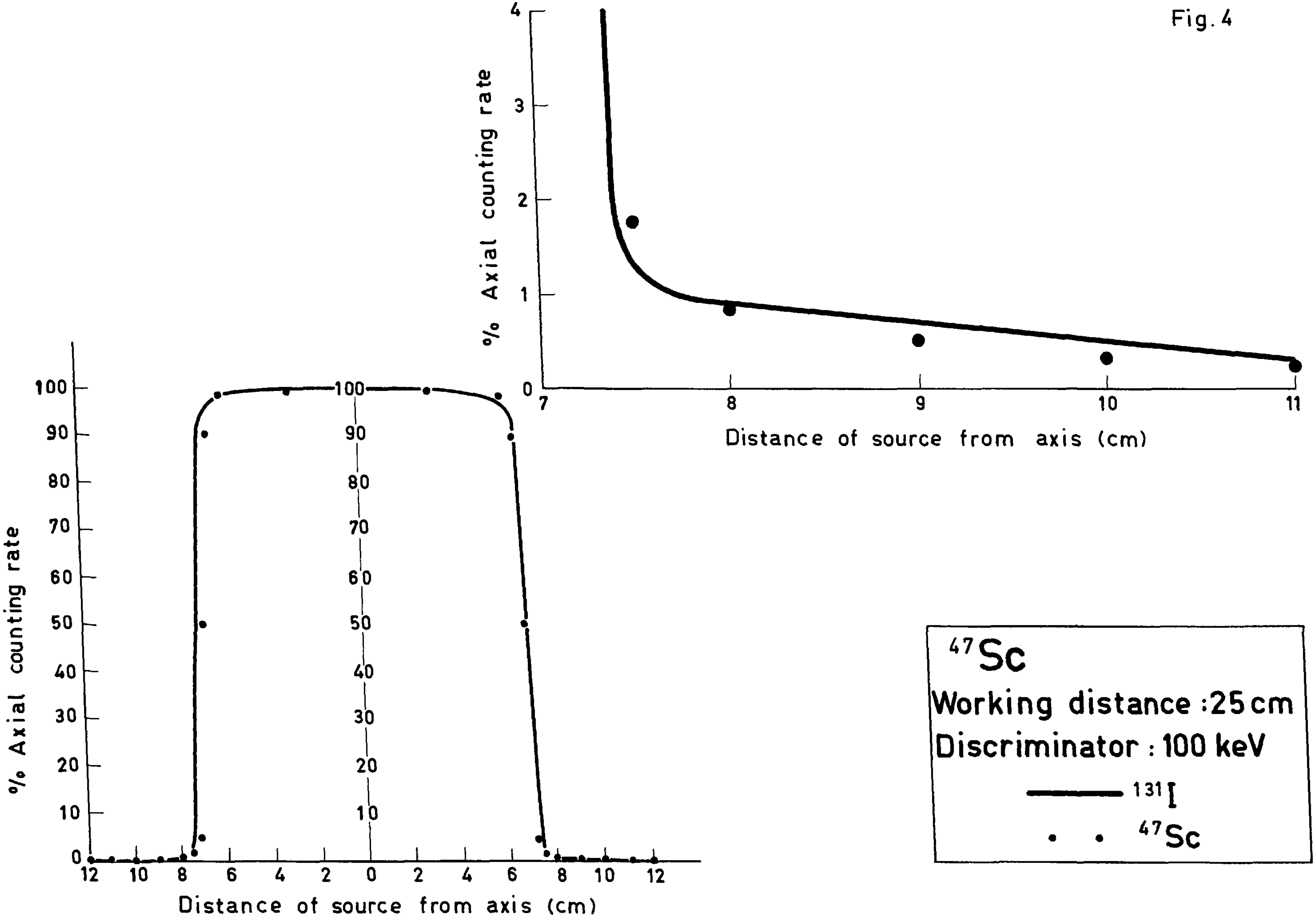
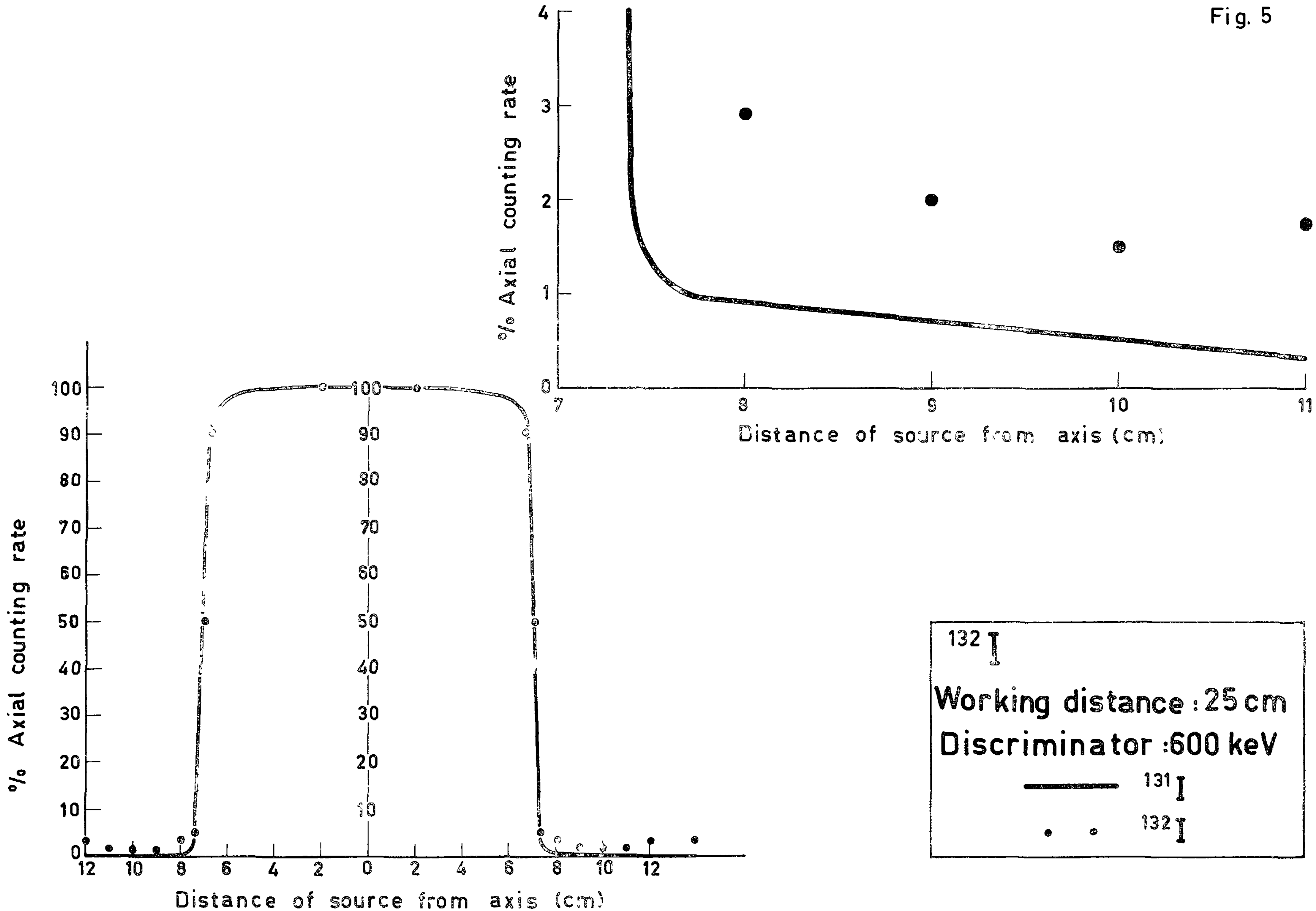

% Axial counting rate
Distance of source from axis (cm)
% Axial counting rate
Distance of source from axis (cm)
99mTc
Working distance :25cm
Discriminator : 100 keV
131I
99mTc

Fig. 3



% Axial counting rate
Distance of source from axis (cm)
% Axial counting rate
Distance of source from axis (cm)
47Sc
Working distance :25 cm
Discriminator : 100 keV
131I
47Sc

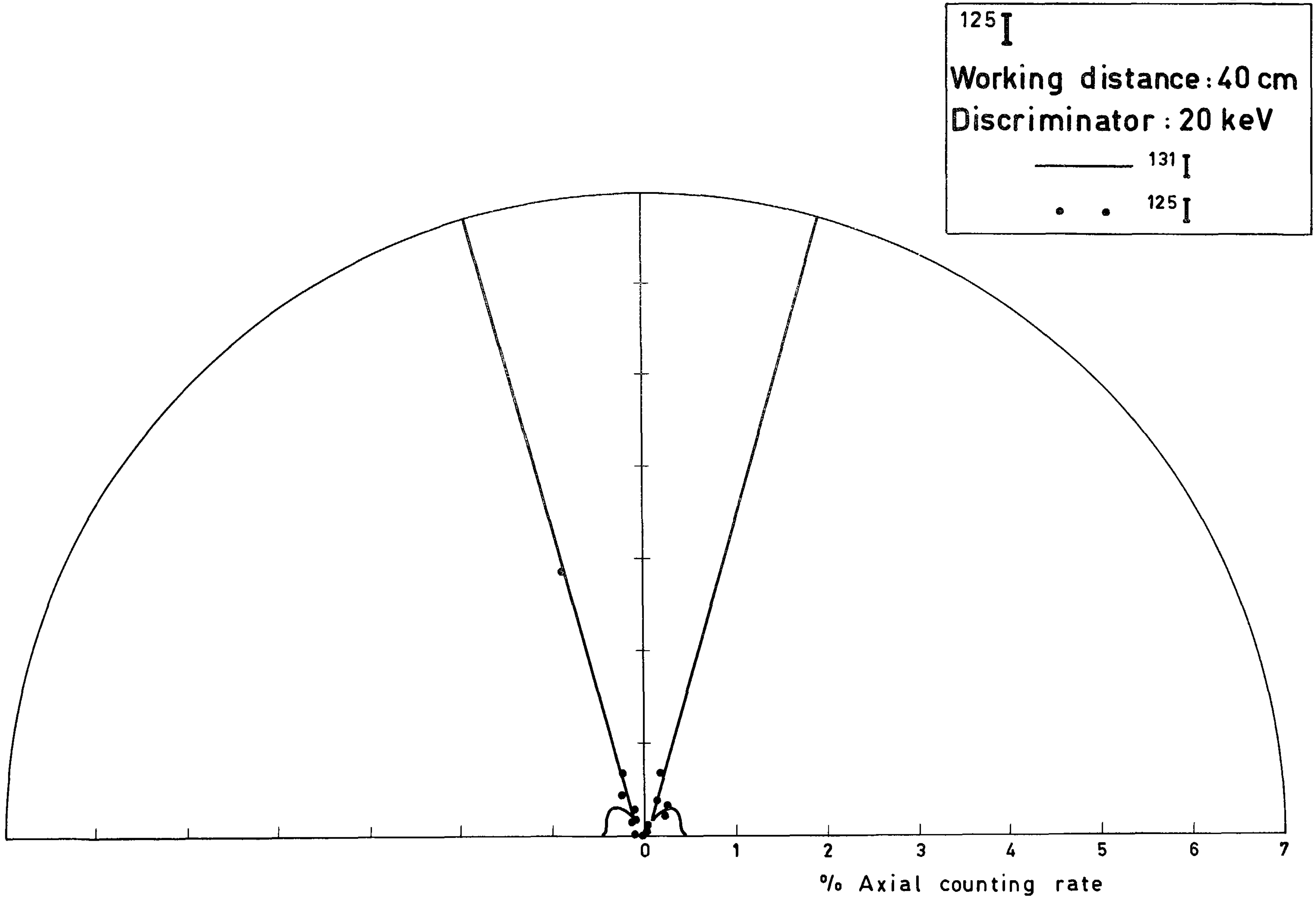
Fig. 4



% Axial counting rate
Distance of source from axis (cm)
% Axial counting rate
Distance of source from axis (cm)
132 I
Working distance : 25 cm
Discriminator : 600 keV
131 I
132 I

Fig. 5

Fig. 6



125 I
Working distance: 40 cm
Discriminator: 20 keV
131 I
125 I
0
1
2
3
4
5
6
7
% Axial counting rate

Fig. 7

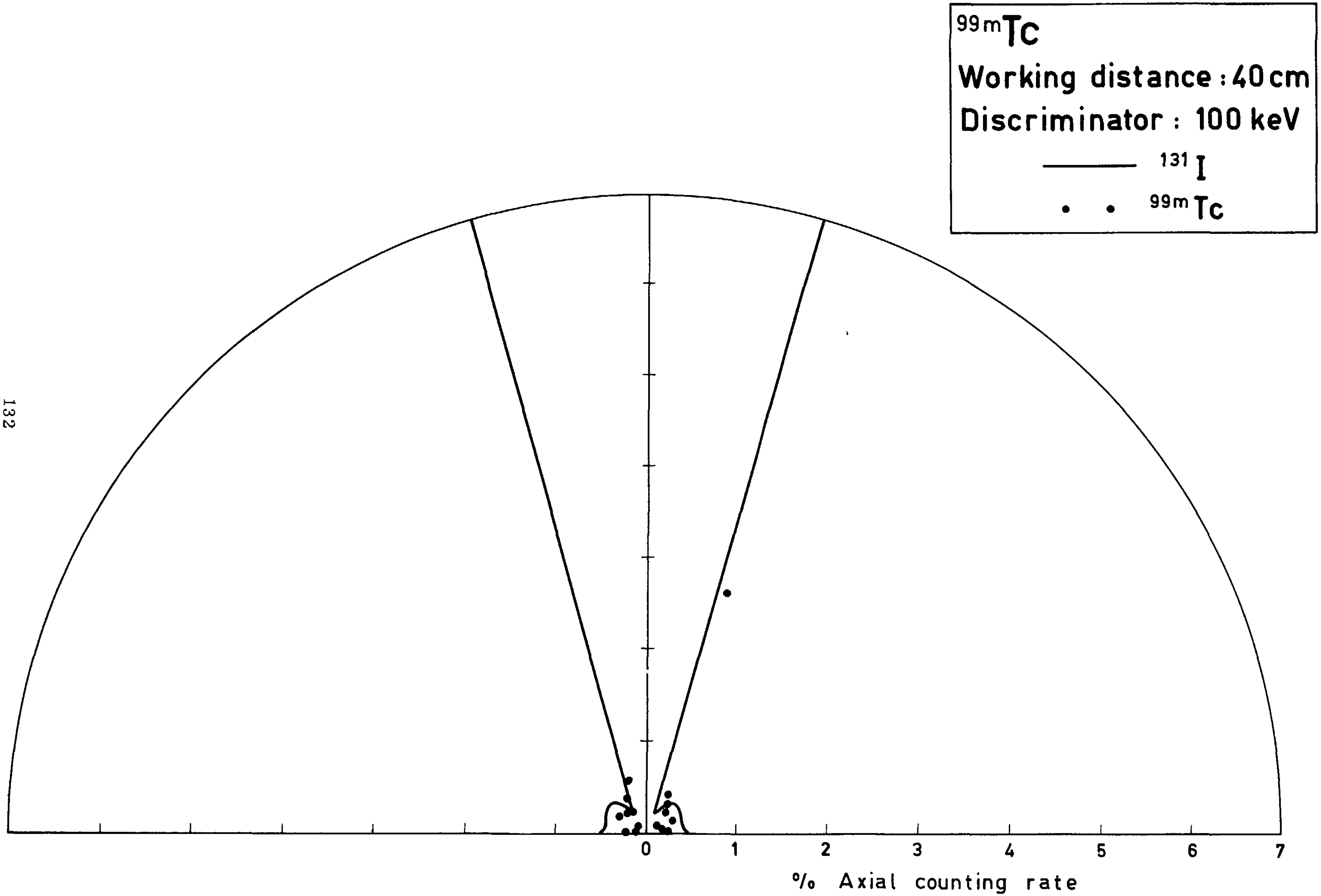

^{99m}Tc
Working distance : 40 cm
Discriminator : 100 keV
^{131}I
^{99m}Tc
0
1
2
3
4
5
6
7
% Axial counting rate

Fig. 8

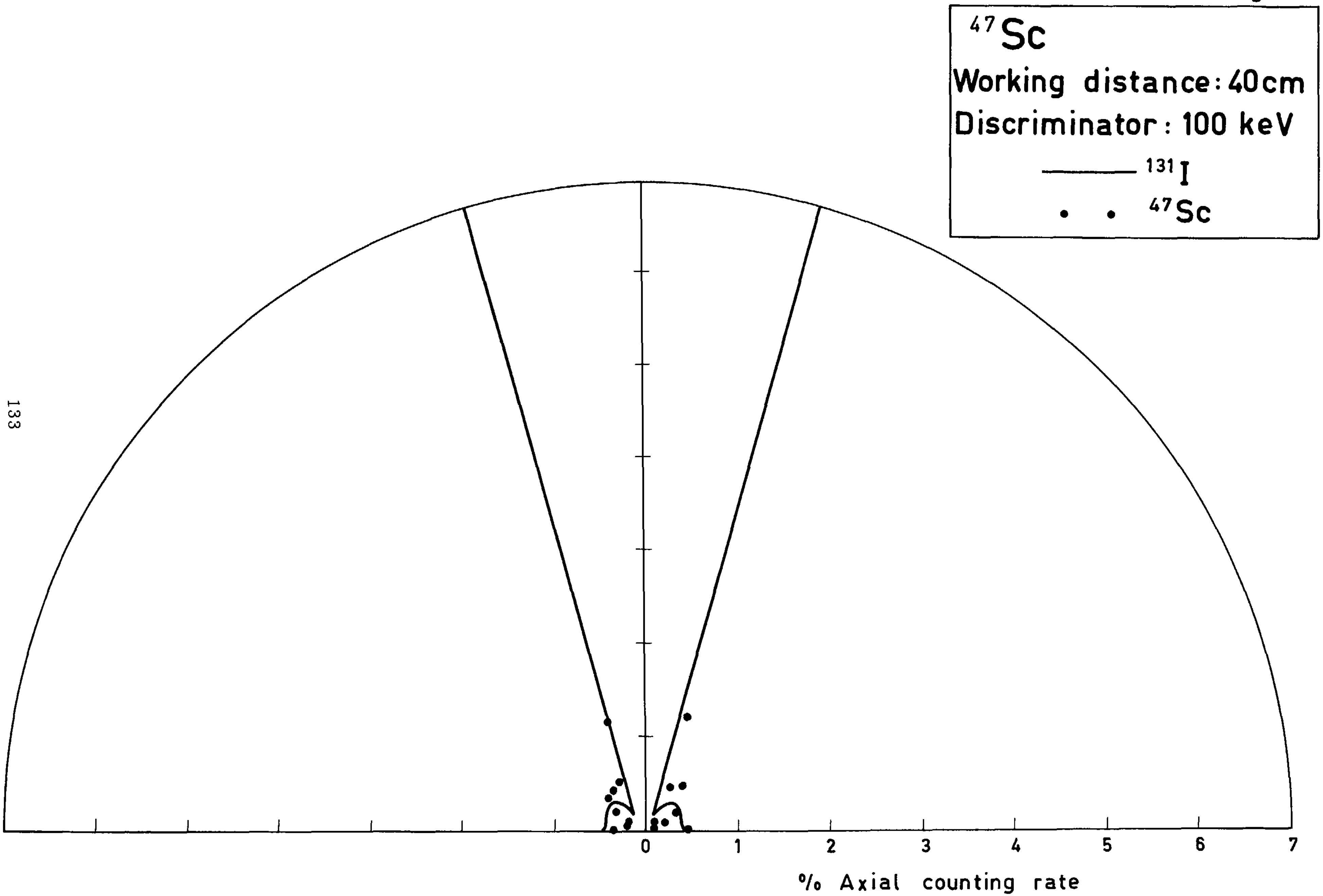
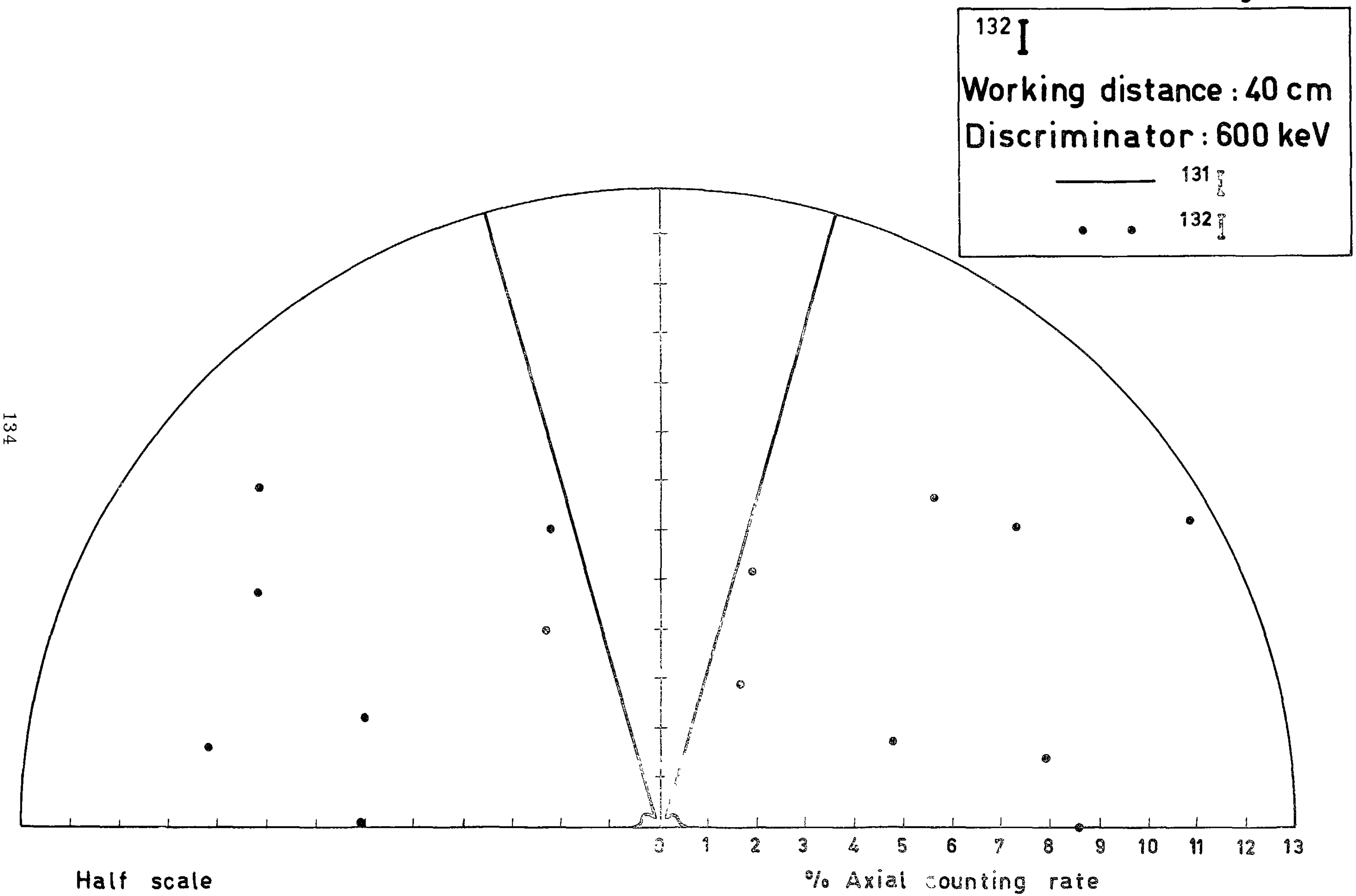

^{47}Sc
Working distance: 40cm
Discriminator: 100 keV
^{131}I
^{47}Sc
0
1
2
3
4
5
6
7
% Axial counting rate

Fig. 9


132 I
Working distance : 40 cm
Discriminator : 600 keV
131 I
132 I
0 1 2 3 4 5 6 7 8 9 10 11 12 13
Half scale
% Axial counting rate

SPECTRAL REGION ASSESSMENT OF THE INFLUENCE OF THYROID DEPTH ON THYROID RADIOIODINE UPTAKE

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ABSTRACT

This paper describes a sensitive technique for thyroid radionuclide uptake measurements based on the use of detectors with large field of view placed in contact with the neck of the subject. The technique depends on correction of the measurements for variation in detector-to-thyroid distance, which is estimated in terms of the photo-peak to scatter ratio of the pulse-height spectrum of the scintillation detector pulses, the observed ratios being compared with those found in measurements on phantoms with "thyroids" at different depths. Two variants of the technique, one using a single-detector and the other using a dual-detector system are described. The results of comparative experimental studies of these techniques and the ORINS standard technique in ^{131}I and ^{123}I uptake measurements are presented. These indicate that the single-detector technique offers an increase in sensitivity of about 20 times and the dual-detector technique an increase of 300 - 500 times as compared with the ORINS technique with a concomitant increase in accuracy resulting from the inclusion of a correction for variation in the depth of the thyroid. The dual-detector technique is shown to offer particular promise for ^{123}I uptake measurements. A protocol for comparative studies of thyroid radionuclide uptake measurement techniques based on measurements on terminal patients is described and results obtained on a single patient presented.

Thyroid uptakes remain the most frequently used radioisotope function test in nuclear medicine, accounting for 58 % of all procedures and, likewise, for a considerable proportion of the total radiation dose administered medically (1). Approximately a decade ago, the pioneering work of Brucer et al. led to the formulation of a standard technique for thyroid uptake which could be employed in almost any laboratory with a variety of equipment (2). The well known ORINS technique established a detector-to-neck distance of about 25 cm as optimum to reduce inverse square counting effects and positioning errors and still maintain satisfactory counting statistics to obtain patient studies in a reasonable amount of time. This technique has been widely adopted; a report by Crespo et al. reviews results of an international survey of thyroid uptakes, finding wide use of the ORINS technique (3). In the latter studies, utilizing very controlled variables, 80 % of the laboratories were found to be within 10 % of one another in thyroid uptake estimation.

Significant advances in instrumentation, plus a wider availability at reasonable costs over the last few years, would warrant a re-evaluation of presently used thyroidal uptake techniques. The ORINS method was postulated on the basis of the inverse square law such that at a 25 cm detector-to-neck (DTN) distance the thyroid appeared satisfactorily as a point source. Thyroid depth was considered a negligible variable with a minimal effect in terms of the total counting distance. However, variations in photopeak attenuation and associated Compton scatter also results from variable amounts of tissue underlying the thyroid. The ORINS technique does not inherebtly correct for these variations.

A revised uptake method which will inherently correct both for the detector-to-thyroid distance (DTD), and hence the inverse square law, as well as the variable photopeak attenuation due to variable depths of the thyroid has previously been proposed by our laboratory (4). In brief, the technique utilised detectors with a large field of view and an efficient geometry which are in contact with the surface of the neck. DTD is measured by an intercomparison of photopeak to scatter ratios in a study subject with those found in standard, variable thyroid depth phantoms. In present study reports the results evaluating the effect of variable thyroid depths in phantoms simulating adult and children's necks.

Methods

A 400 channel Packard multichannel analyzer was used in conjunction with (1) a 1" x 1" NaI(Tl) uncollimated crystal having 1" lead shielding and (2) dual 3" x 1-1/2" NaI(Tl) uncollimated crystal havine 1/4" lead shielding with their central axes at right angles as previously described (4). Spectra of a 10 μCi ^{131}I standard were analyzed for the 0.364 MeV photopeak, the scatter region of the spectrum below the Compton valley of the 0.364 MeV photopeak, and the combined integral count of the photopeak and scatter regions. Thyroid neck phantoms with variable depth thyroid inserts simulating an adult (20 g), 10 year old (10 g), 5 year old (5 g), and newborn to one year (1 g) were fabricated from poly-methylmethacrylate. Thyroid depths were graduated in steps of 0.5 cm. The principle studies were carried out in the adult phantom which is to the exact dimensions of the ORINS phantom with the modification of variable depth thyroid inserts. (The 2.8 cm depth insert duplicates the ORINS phantom) (2). A 100 ml flask containing the 10 μCi ^{131}I standard solution placed on 1" of fiberboard as a scatter medium was also used for intercomparison since such phantoms are used in many radioisotope laboratories. Comparative studies of the effect of thyroid depth in the phantoms as well as comparison with the 100 ml flask were carried out with both detector systems placed on the surface of the "neck" and at a 25 cm detector-surface distance.

Iodine-123 produced in a cyclotron by the $^{121}Sb(\alpha,2n)$ ^{123}I reaction was evaluated in the adult phantom to determine the feasibility of correcting for thyroid depth compared to previous experience with ^{131}I. A dual 3" x 1/4" NaI(Tl) crystal system with counterbalanced detector head was specially designed for use with ^{123}I. Iodine-123, with a monoenergetic gamma-ray of 159 keV and a 27 keV X-ray can be used very effectively with this 1/4" crystal with significantly less background counts than with thicker crystals.

Results

The mean effective thyroid depth, i.e. apparent centre of activity of the thyroid from the neck surface, in 53 adults was found to be 2.6 cm with a median value of 2.8 cm (Fig.1.). The distribution is somewhat skewed to more superficially placed glands. From these data, an average effective depth in the adult phantom of 2.8 cm was used throughout the comparative experiments.

In Table I, the results with the 1" x 1" NaI(Tl) detector are contrasted. At the standard distance of 25 cm with integral counting, there is a positive error of 13 % and a negative error of 9 % (% as used indicates percentage error of uptake), with a ± cm deviation from the mean depth of 2.8 cm. Photopeak counting has a +21 % and -15 % error. These two procedures are the most commonly used variants of the ORINS technique. Interestingly, integral counting has the least inherent error in thyroid depth is not taken into account. Surface counting, as would be anticipated, results in much exaggerated errors when compared to the 25 cm distance. However, counting rates can be increased approximately 20 times by surface counting. Use of the 100 ml flask does closely approximate the mean thyroid depth conditions for both photopeak and integral counting, being +5 % and -6 % respectively. This latter finding also explains a consistent mean difference of about 7 %, previously found between the results with the dual crystal system and the standard uptake system.

Similar results were obtained with the dual crystal system seen in Table I. Errors due to thyroid depth, if not corrected, are of about the same magnitude for 25 cm standard distance counting, but somewhat greater with the 1" x 1" crystal for surface counting with the exception of integral counting in the 100 ml flask. However, the count rate is increased by a factor of 300 - 500 times with the dual crystal surface counting when compared to the 25 cm position with the 1" x 1" crystal.

Phantom studies utilizing ^{123}I in Fig.2 reveal a satisfactory linear response of the P/S ratio with thyroid depth. A similar linear response was also produced by the specially developed 1/4" x 3" dual crystal system (Fig.3.). It is noted that some change with time in the slope of the depth response line is due to an increasing influence of the contamination from ^{124}I. Thyroid depth response has also been found to be linear, using the phantom with a Ge(Li) detector system (Fig.4.).

In age-specific thyroid neck phantoms (Fig.5.), linear P/S ratio depth responses are also found. It is evident that the adult phantom cannot be used satisfactorily with children.

Discussion

The analysis would suggest that an appreciable error of approximately 10 % can result in thyroid uptakes utilizing the standard uptake technique with integral counting. Paradoxically, photopeak or window counting leads to an even larger error, +21 % to -15 %. If one utilized the "A" filter system of the ORINS technique, the results should simulate photopeak counting and thus have this magnitude of error (2). This additional variation due to thyroid depth may be to some extent responsible for confusing overlap between hypo-, eu- and hyper-thyroid uptake findings.

The considerable increase in sensitivity achieved in surface counting is evident and desirable. When combined with a system for thyroid depth correction, the technique appears to offer the possibility of elimination of a presently uncorrected error in thyroid uptake systems, making them more precise.

The recent newcomer to the family of iodine radionuclides, namely ^{123}I, has very ideal characteristics with no β-emission and a 159 keV gamma (5). Furthermore, its physical half-life appears to be optimum for the biological characteristics of thyroidal iodine uptake (6).

It is intriguing to consider the possibility of the dose reduction that could result with use of ^{123}I, i.e. about a factor of 100 with the increased sensitivity of the dual crystal uptake system (500 X) totalling to about a 5×10^4 reduction in dose.

An automatic system which will greatly simplify the mechanics of using this more complicated technique is presently being developed. However, a small dual-channel analyzer and predetermined standard depth-response graphs for each phantom could be used very readily. Also the technique is readily adaptable to a simple computer program (DULXTLUP) seen in Table II. The slope of the standard curve has been found to be highly reproducible and can be incorporated into the computer program as well as into the electronics of the automatic uptake system. Furthermore, the constant slope only makes it necessary to make one thyroid neck phantom measurement at the mean depth, i.e. no more than with other standard procedures. From Fig.5 it is evident that a constant relationship exists between the age-specific phantoms such that constants can be used in the computer program to convert measurements in the adult phantom to age specific results.

Addendum

Protocol for cadaver studies

The "standard" uptake system generally consists of a 1" x 1" crystal (collimated or uncollimated) and a 25 cm detector-neck counting distance. The standard iodine solution is in a 100 ml flask and extrathyroidal iodine activity is corrected for by using a "B" filter (4" x 4" x 1/2" piece of lead) placed over the thyroid. Variants to this technique use a high count (at 25 cm or on the surface) instead of the "B" filter to correct for the extrathyroidal activity. As discussed in this paper, variations in thyroidal depth have some effect even on uptake measurements made using the 25 cm DND, and a relatively large effect on uptake measurements made using this "standard" system with the crystal in contact with the neck. However, there is a very large increase in sensitivity when surface counting is used, and a counting system utilizing surface counting and a P/S ratio to correct for thyroid depth variations has been described.

Comparison studies among the various systems are informative, but the ultimate test of each system would be its ability to determine the absolute activity in a thyroid gland at any given time. The following protocol utilizing terminal patients with thyroid counting before and after autopsy when the patient expires has been set up for this purpose.

1. Prepare a calibrated ^{131}I solution. (1 μCi/ml is a convenient concentration).

2. Calibrate the counting systems which are to be used to count the thyroid gland following autopsy. (A falcon container with the known activity in 10, 20, 30 and 40 ml solutions was used for the data which will be given later).

3. Run a calibration curve for the dual crystal system using 1 μCi at depths of 1.8, 2.8 and 3.8 cm in the neck phantom. This curve represents CPM/μCi vs. P/S ratio.

4. Determine the CPM/μCi for the 1" x 1" crystal using 1 μCi in a 100 ml flask and a 25 cm counting distance.

5. Administer approximately 10 μCi of ^{131}I to terminal patient. (It does not need to be from precisely calibrated stock solution).

6. When the patient expires, make the following measurement prior to autopsy:

6a Determine P/S ratio for dual crystal uptake system:

(a) Photopeak CPM over thyroid

(b) Scatter CPM over thyroid

(c) Photopeak CPM over thigh

(d) Scatter CPM over thigh

$$P/S = \frac{a - c}{b - d}$$

6b Determine thyroid CPM using the 1" x 1" crystal and the "B" filter with a 25 cm counting distance:

(a) CPM over neck without "B" filter

(b) CPM over neck with "B" filter

Thyroid CPM = a - b

6c Determine thyroid CPM using the 1" x 1" crystal with a thigh count at both the 25 cm distance and on the surface of the thigh:

(a) CPM over neck

(b) CPM 25 cm from thigh

(c) CPM on contact with thigh

Thyroid CPM = a - b and/or a - c

7. Following autopsy, count the thyroid gland in the precalibrated detection system in the appropriate geometry.

8. From the above data the following calculations can be made:

8a Absolute thyroid activity CPM from No. 7 divided by the CPM/μCi determined in No. 2 for the appropriate geometry.

8b Absolute activity by dual crystal system photopeak CPM over thyroid from No. 6a divided by the CPM/μCi found by entering the calibration curve determined in No. 3 with the P/S ratio found in No. 6a.

8c Absolute activity using the 1" x 1" crystal and the "B" filter thyroid CPM from No. 6b divided by the CPM/μCi found in No. 4.

8d Absolute activity using 1" x 1" crystal and the thigh count. Thryoid CPM from No. 6c divided by the CPM/μCi found in No. 4.

Results

Following are the results from one patient given 10 μCi of ^{131}I approximately 10 hours prior to expiration. The only deviation from the protocol was in the use of a 4" x 4" collimated crystal instead of a 1" x 1" crystal.

1. Absolute thyroid activity determined by counting the gland following autopsy was .08 μCi.
2. Absolute activity determined by the dual crystal uptake system was .06 μCi.
3. With the 4" x 4" and the "B" filter, the absolute activity was .03 μCi.
4. With the 4" x 4" and the thigh count at 25 cm, the absolute activity was .11 μCi.
5. With the 4" x 4" and the thigh count on contact with the thigh, the absolute activity was .08 μCi.

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TABLE 1

Thyroid Uptake Errors (%)
1" Crystal
DND 25 cm

Spectral Region	100 ml flask	Phantom - depths from mean (2.8 cm)	
		1 cm	+1 cm
Photopeak	+5	+21	-15
Integral	-6	+13	-9
DND 0 cm			
Photopeak	+52	+49	-29
Integral	+34	+38	-24

Dual 1" x 3" Crystals
DND 25 cm

Spectral Region	100 ml flask	Phantom - depths from mean (2.8 cm)	
		-1 cm	+1 cm
Photopeak	+25	+17	-17
Integral	+7	+10	-11
DND 0 cm			
Photopeak	+34	+41	-24
Integral	+9	+23	-78

DULXTLUP

DUAL CRYSTAL ^{131}I THYROID UPTAKE

INPUT

PHOTOPEAK COUNTS FOR PATIENT'S NECK AND THIGH
PHOTOPEAK COUNTING TIMES FOR NECK AND THIGH
SCATTER COUNTS FOR PATIENT'S NECK AND THIGH
SCATTER COUNTING TIMES FOR NECK AND THIGH
PHOTOPEAK CPM FOR STANDARD
SCATTER CPM FOR STANDARD

OUTPUT

4 AND/OR 24 HOUR ^{131}I THYROID UPTAKE(S)

TABLE 2

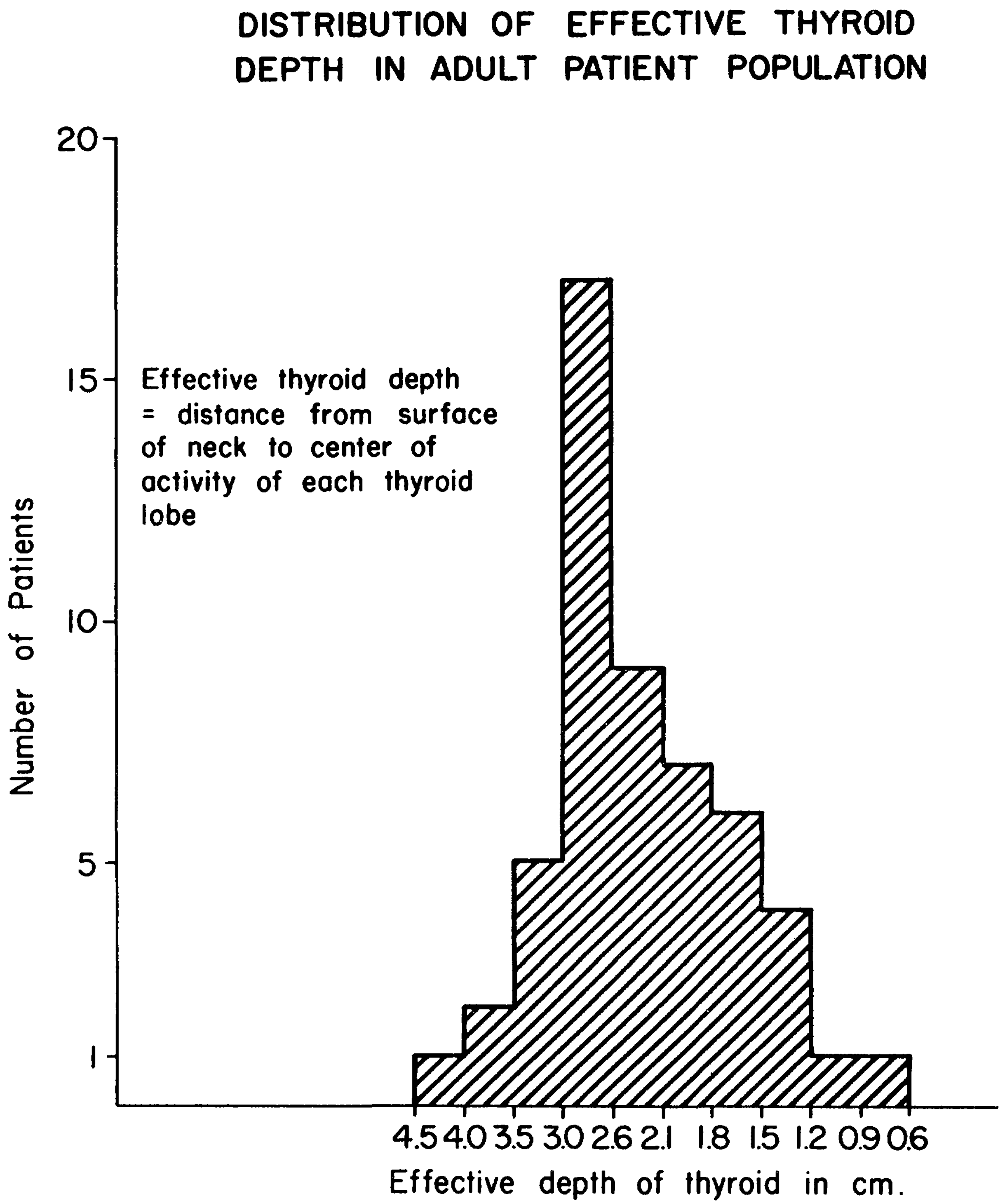

DISTRIBUTION OF EFFECTIVE THYROID DEPTH IN ADULT PATIENT POPULATION
Number of Patients
20
15
10
5
1
Effective thyroid depth = distance from surface of neck to center of activity of each thyroid lobe
4.5 4.0 3.5 3.0 2.6 2.1 1.8 1.5 1.2 0.9 0.6
Effective depth of thyroid in cm.

Fig.1.

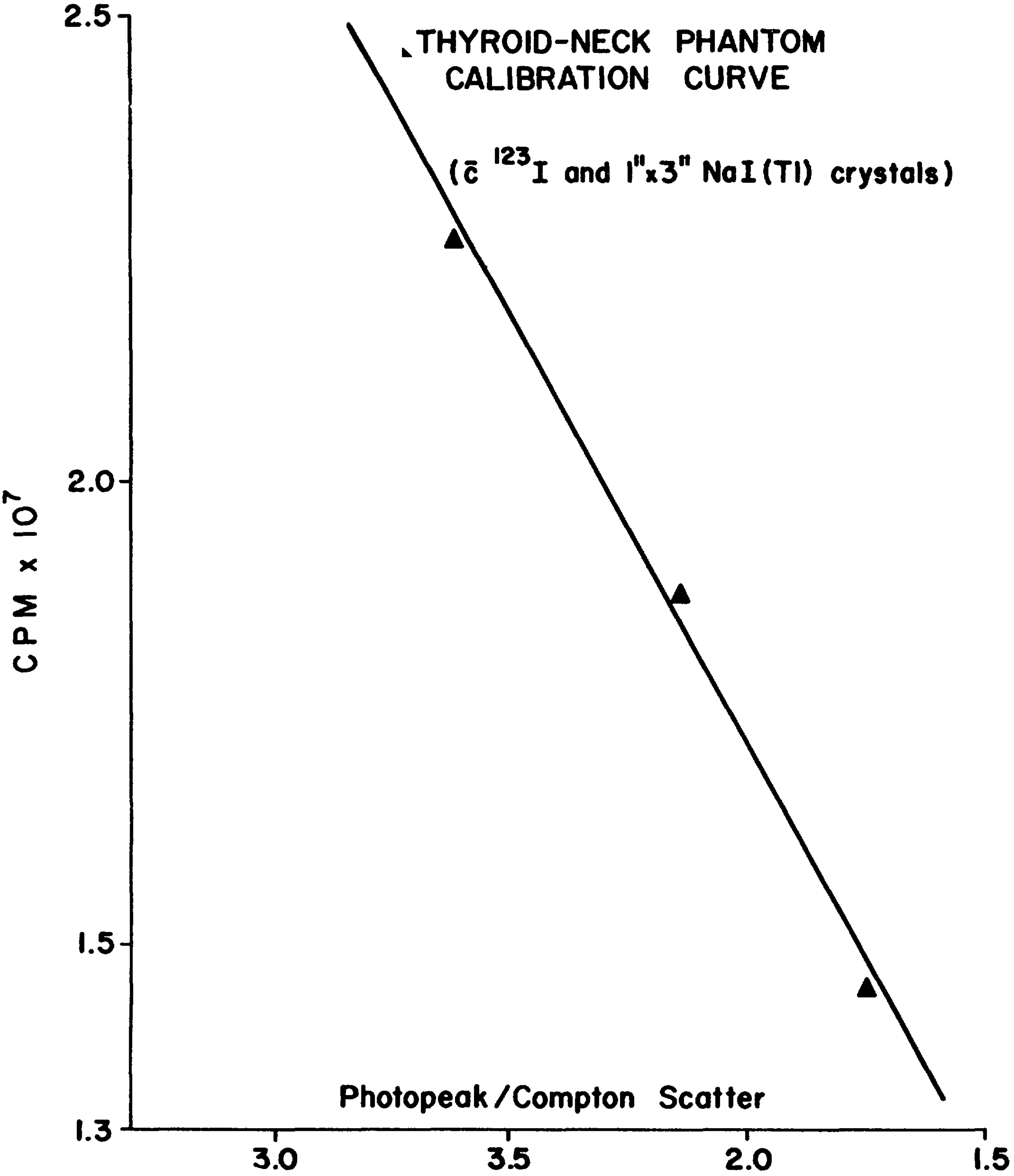

THYROID-NECK PHANTOM
CALIBRATION CURVE
(c̄ 123I and 1"x3" NaI(Tl) crystals)
2.5
2.0
1.5
1.3
CPM x 10^7
Photopeak/Compton Scatter
3.0
3.5
2.0
1.5

Fig.2.

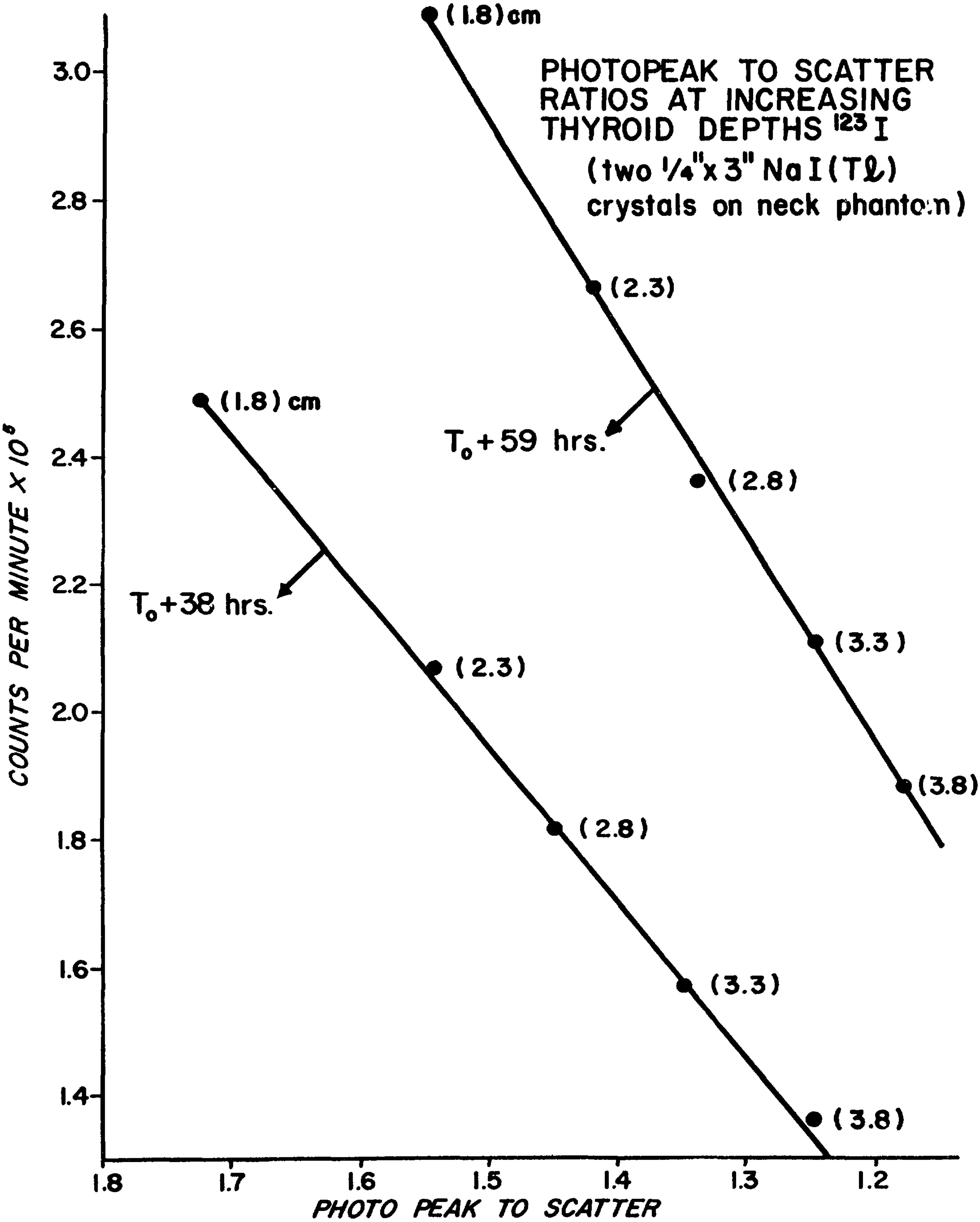
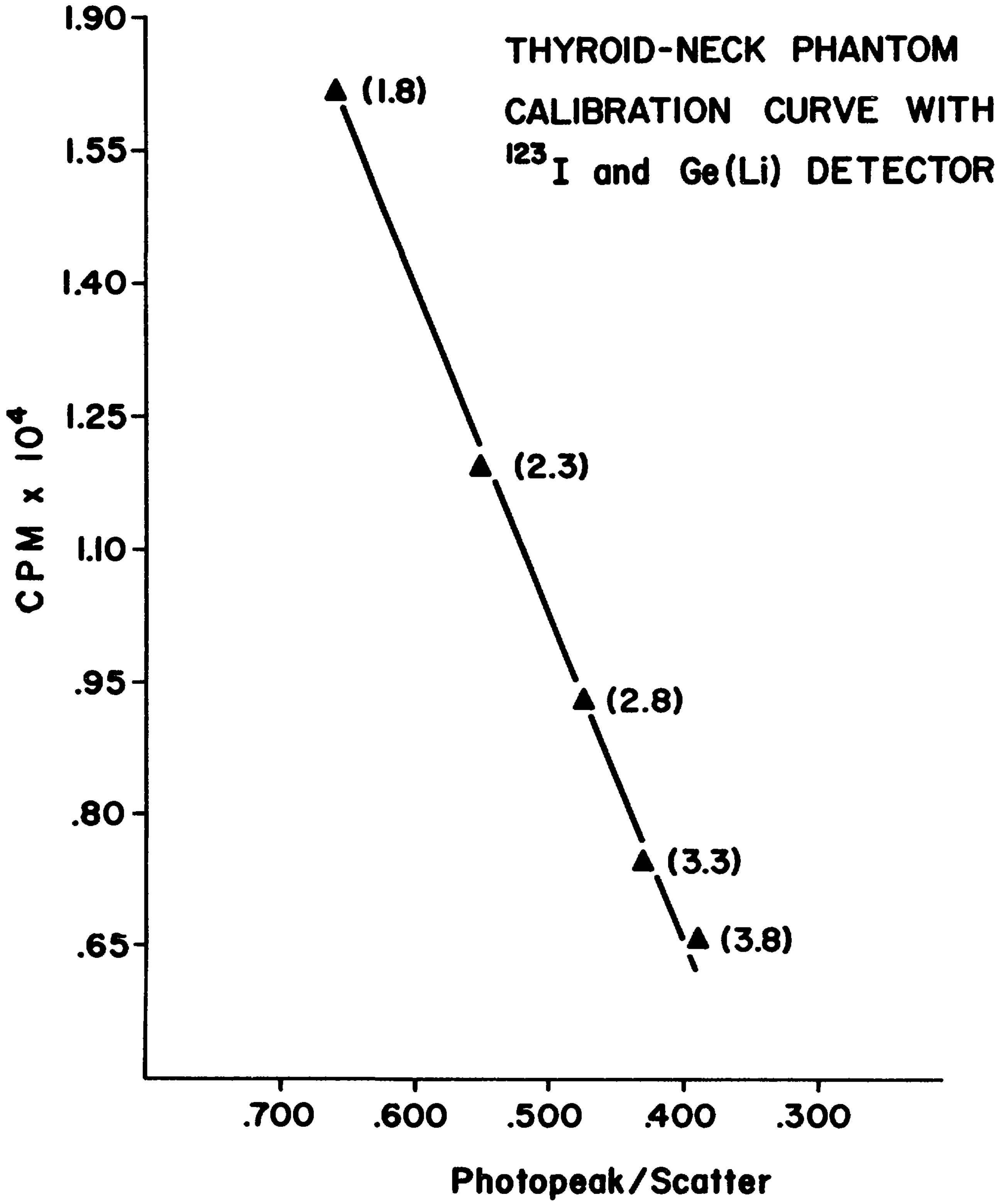

PHOTOPEAK TO SCATTER RATIOS AT INCREASING THYROID DEPTHS 123 I
(two 1/4" x 3" NaI(Tl) crystals on neck phantom)
(1.8) cm
(2.3)
(2.8)
(3.3)
(3.8)
T0 + 59 hrs.
T0 + 38 hrs.
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
COUNTS PER MINUTE × 10⁵
1.8
1.7
1.6
1.5
1.4
1.3
1.2
PHOTO PEAK TO SCATTER

Fig. 3.



THYROID-NECK PHANTOM
CALIBRATION CURVE WITH
123I and Ge(Li) DETECTOR
CPM x 10⁴
1.90
1.55
1.40
1.25
1.10
.95
.80
.65
(1.8)
(2.3)
(2.8)
(3.3)
(3.8)
.700
.600
.500
.400
.300
Photopeak/Scatter

Fig. 4.

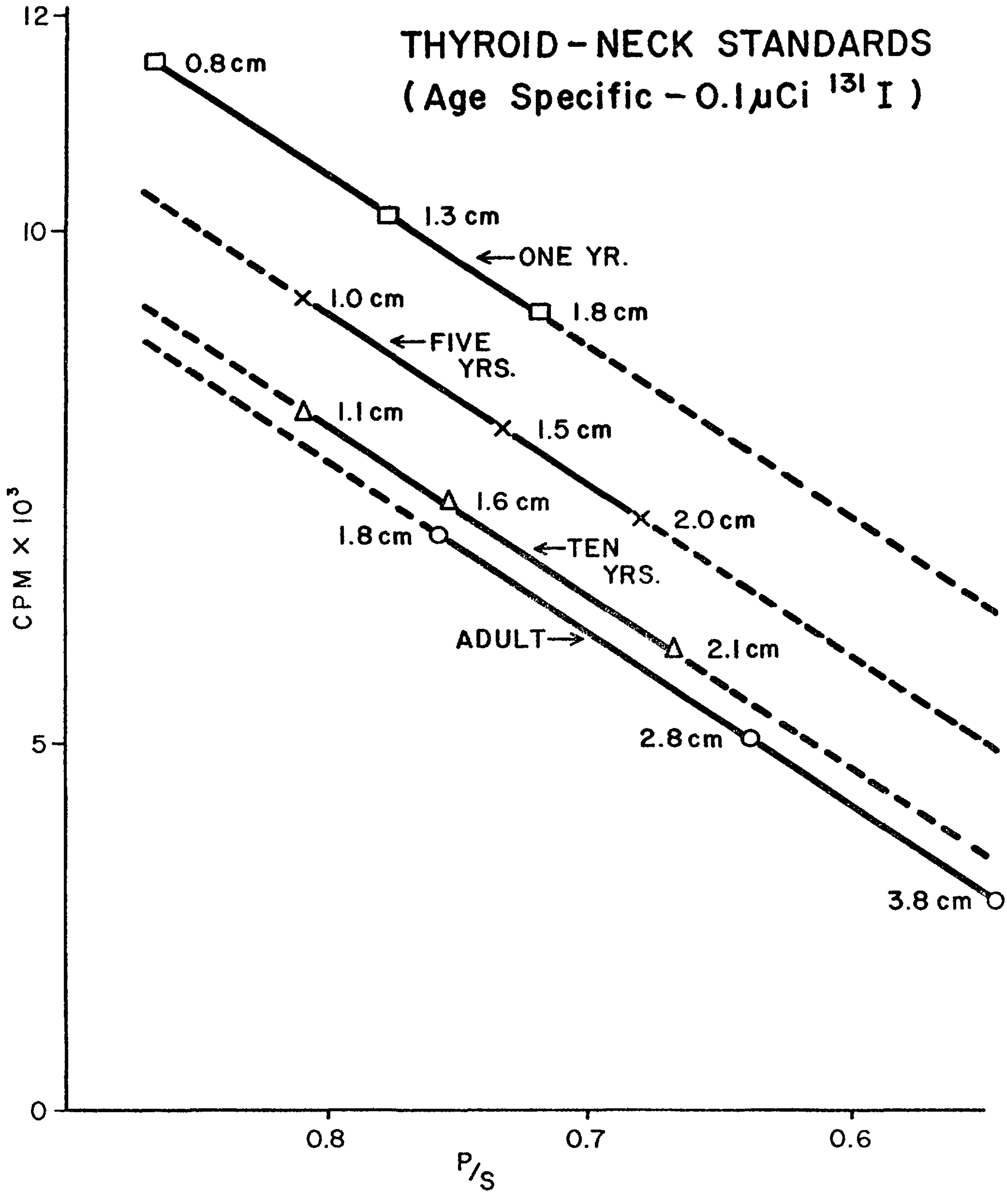

THYROID-NECK STANDARDS
(Age Specific - 0.1μCi 131 I)
12
10
5
0
CPM × 10³
0.8
0.7
0.6
P/S
0.8 cm
1.3 cm
1.8 cm
←ONE YR.
1.0 cm
1.5 cm
2.0 cm
←FIVE YRS.
1.1 cm
1.6 cm
2.1 cm
←TEN YRS.
1.8 cm
2.8 cm
3.8 cm
ADULT→

Fig. 5

METHOD OF MEASURING THYROID I-131 UPTAKE BY A DIGITIZED SCINTIGRAM OF THYROID GLAND

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ABSTRACT

This paper describes a method using a dual-detector scanner and on-line computer for measuring the late uptake of ^{131}I by the thyroid. The method can be applied during routine scans of the thyroid and was found to give results in general agreement with those obtained by the ORINS standard method.

1. Introduction

In an effort to obtain the thyroid I-131 uptake by processing the data on the digital scintigram of thyroid gland, an experiment has been carried out.

Using an on-line computer system, by which the total counts of a certain area can be calculated briefly, the thyroid I-131 uptake measurement was made from routine scan data of thyroid gland.

2. Method

The scanner used for thyroid scanning consists of two detectors facing each other above and below with the 5"ø x 2" NaI Crystal. It is a kind of the whole body scanner, from which two systems of the positioning signal of the detector (X, Y) and the output signal (Z) can be taken out. These data are memorized in the 4K words computer (HITAC 10). The sampling of output signals can be done with the interval of 1mm for the scanning direction (X direction) and of 2, 4, 6----mm for the spacing direction (Y direction). In the thyroid scanning a scan matrix is made by sampling the counts in the area of each 4 x 4mm. The scan area of the thyroid gland ranges between around 10 x 10cm and 15 x 15cm and the number of whole data points is 600 to 1300. The scan matrix is displayed by CRT and the whole counts in the area containing the thyroid gland are calculated by the program, which is used to obtain the total counts in a certain rectangle, and typed out.

The thyroid scan was made on patients 24 hours after the administration of 40 - 80μCi of I-131, and at the same time the data were put into the computer memory. The scan conditions are as follows:

Scan speed:	50cm/min.
Spacing:	2mm
Collimator:	
Focusing distance:	7.5cm
Number of holes:	163 holes
Type:	Honey cone type
Measurement:	
Photo peak of I-131:	364 keV
Window width:	100 keV
Standard source:	I-131 capsule containing the same dose as administered to patients.
Neck phantom:	ORINS type

The phantom scan was made with the same conditions as the patient and the background data were obtained at the same time.

3. Results obtained

(A) Basic experiment

Two acrylic neck phantoms (ORINS type) were used; a thyroid gland phantom (6 x 6cm²) made by filter paper with 50μCi of I-131 was put into one of them and 50μCi of I-131 capsule was placed in the other. The computer scan was done on each of them. Then the effect of the size of the scan area and the clearance under the pinhole collimator on the total counts was investigated. Also the dependence of the thyroid uptake on the depth of thyroid gland was examined.

(1) Relationship between scan area and its summing counts.

In the routine thyroid scanning the scan areas generally range from 10 x 10cm² to 14 x 14cm² . The scan matrices were determined as follows: The maximum area is 14 x 14cm² , and on the areas of 12.4 x 12.4, 10.8 x 10.8, 9.2 x 9.2 and 7.6 x 7.6cm² , respective summing counts were calculated. The area of 7.6 x 7.6cm² would be the smallest size, in which thyroid image can just be fit. Fig. 1 shows the relationship between the scan area of the neck phantom with thyroid source and its summing counts with 6cm clearance as well as the relationship between the scan area of the neck phantom with standard source and its summing counts with the same clearance. The summing counts of both sources decrease in number in the same inclination as the area decreases. If the counts of the area 14 x 14cm² is taken to be 100%, the counts in 7.6 x 7.6cm² decrease by 12%.

From the result obtained it is certain that the scan area should be as large as possible. However, since the total counts of the thyroid and standard sources decrease in the same inclination, one can expect the correct result even in the small area, if only the thyroid gland is contained and the total counts of the thyroid and standard sources are compared in the same area.

(2) Change in the summing counts due to the difference in the clearances.

The clearance of 6cm was selected as a standard and the distance was increased and decreased by 4cm from the standard point. From the digitized scans of the neck phantoms with thyroid and standard sources the summing counts were calculated. The data obtained in the area of 14 x 14cm^2 are shown in Fig. 2. The summing counts decrease slightly as the clearance increases. In the smaller areas the tendency is almost the same.

(3) Change in the summing counts due to the difference in the depth of thyroid gland.

The thyroid gland is thin compared with other organs of the body and located near the skin surface. The absorption and scattering of gamma-rays by tissues are relatively small. The relation between the depths of thyroid glands and the uptake values was investigated, by the ORINS standard method and the digitized scan technique using neck phantoms.

The depths of the 6 x 6cm^2 thyroid gland source were changed in the neck phantom and the thyroid uptake values were calculated (Tab. 1). In the range of the depths of 1 to 2.5cm from the surface the thyroid uptakes decrease essentially in a straight line, and its decreasing rate is about 5% per 4mm. In this experiment the thyroid uptakes obtained by the digitized scan technique were in agreement with those by the ORINS standard method.

(B) Clinical cases

On 30 patients who underwent the thyroid scanning the digitized scan was carried out (Fig. 3). From these data the thyroid uptakes were calculated and compared with those obtained by the ORINS standard method. The results were shown in Fig. 4. Of 30 cases, 5 cases which are plotted by the symbol^ were determined by adding the signals of the upper and lower detectors. In other 25 cases (symbol: •) the thyroid uptakes were calculated with the upper detector alone. The data obtained are scatterd about the 45 degree straight line through the origin.

Among 25 cases of the difference between the thyroid uptakes determined by the digitized scan technique and the ORINS standard method, the greatest difference is 8.1%, but 76% of the whole cases give the difference within ± 5%.

4. Discussion

By the digitized computer processing of the scintiscan matrix, many clinical data such as the scintigrams, the image processing, the summing counts of a certain area etc. are obtained in a single test. Accordingly the burden to patients is reduced. In this experiment, the method in which the thyroid I-131 uptake measurement can be done simultaneously with a scintigram is studied.

There was some disagreement between the thyroid uptake values obtained by the two method in clinical cases. This disagreement must have come from the fact that the routine scan data were put into the computer memory. Accordingly scan areas were not always the same. In some cases the image of the thyroid gland was not located at the center, but located in a corner of the matrix. For this reason errors would have been made even if the area of the scan matrix was the same.

On the other hand, since the accuracy of mechanism of a scanner might be one of the factors of the error in this technique, the stability of the scan speed and the width of spacing should be checked closely in advance of performing tests.

5. Summary

The method of measuring thyroid I-131 uptake by the digitized scan matrix is one of the simple and good methods. It can be carried out utilizing the routine scan data. The uptake values obtained by this method agreed well with those by the ORINS standard method.

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Depth of the Thyroid Gland	ORINS Standard Method	Digitized Scan Technique	Ratio
1.0 cm	57.1%	56.7%	0.993
1.5	55.4	54.8	0.989
1.8	53.5	53.0	0.991
2.1	51.2	50.9	0.994
2.5	49.4	50.2	1.016

Tab. 1 Comparison between the Thyroid Uptake Values obtained by the ORINS Standard Method and Digitized Scan Technique

True value of uptake	53.3%
Counting area	14 x $14 cm^2$
Clearance	6cm

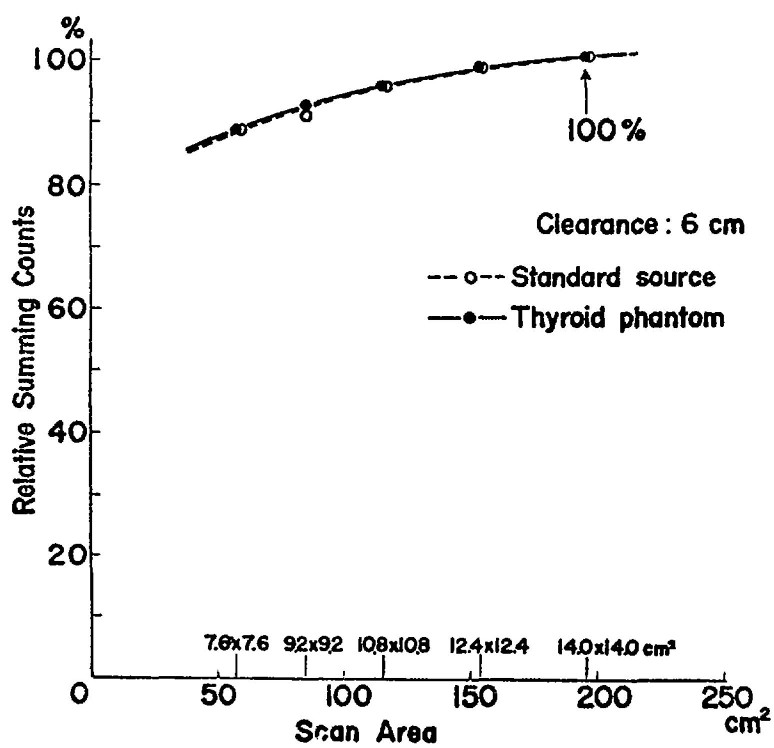

Fig. 1 Relationship between the scan area of the neck phantom with I-131 source and its summing counts.

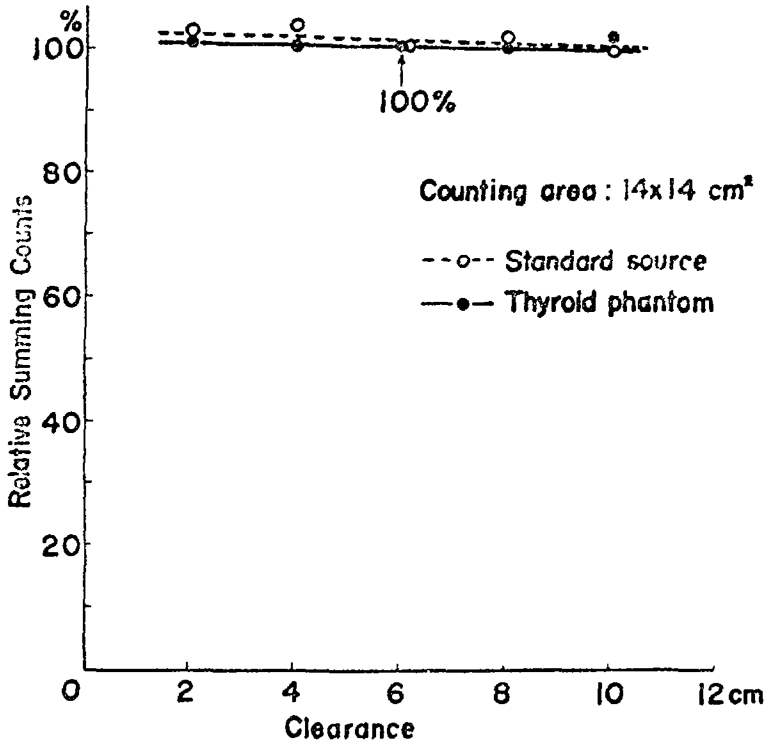

Fig. 2 Relationship between the clearance and the summing counts in the scan area.

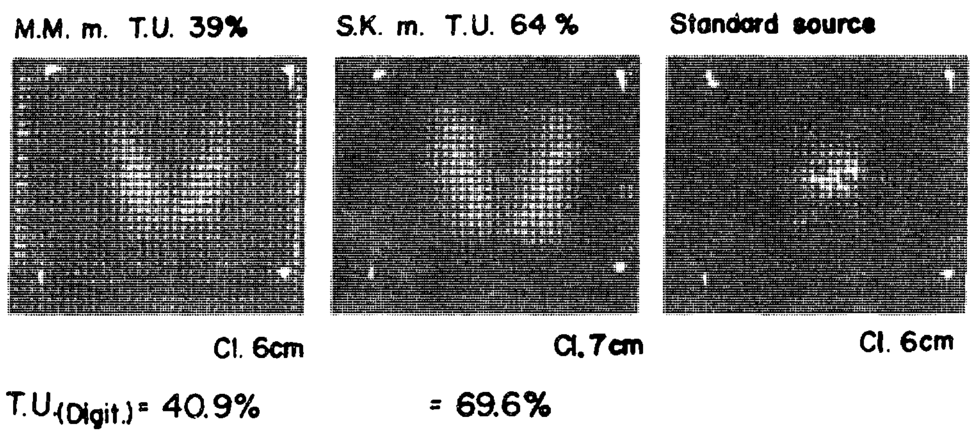

Fig. 3 Images of thyroid gland and standard source in digitized scan matrices.

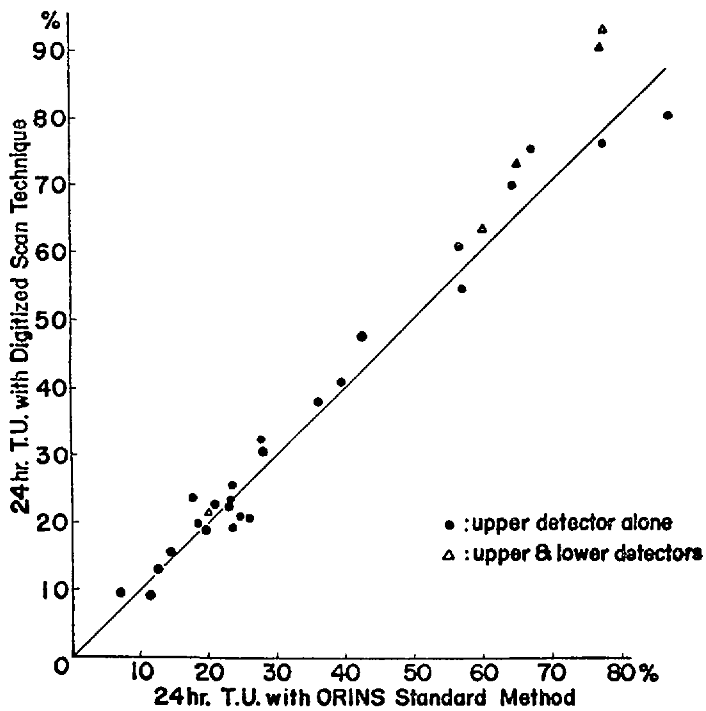

Fig. 4 Correlation between the 24hr I-131 thyroid uptake with ORINS standard method and the thyroid uptake with digitized scan technique.

THYROID I-131 UPTAKE MEASUREMENT WITH A SCINTILLATION CAMERA

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ABSTRACT

This paper describes experimental and clinical studies aimed at the development of a method using a gamma-camera with a pin-hole collimator for measuring the late uptake of ^{131}I by the thyroid. Attempts to measure uptake under the condition used for thyroid scintigraphy, namely with the surface of the collimator at a working distance of 2 - 5 cm from the surface of the neck gave values significantly lower than those obtained by the ORINS standard method, the difference between the two values reaching 38 %. At a working distance of 20 - 25 cm scintigraphy was no lonter practicable and the statistical errors in the measured uptakes were larger because of the reduced counting rates, but the values obtained were in general agreement with those obtained by the ORINS standard method.

1. Introduction

To obtain a scintigram of the thyroid gland with a scinticamera, a pinhole collimator is usually used to enlarge the image of thyroid gland which is small compared with other body organs. If the thyroid I-131 uptake measurement is made simultaneously with the scintigram of the thyroid gland, it would be very convenient for us. This method has already been tried by some persons. However, the problem is whether or not we can achieve correct results with this method. Some experiment has been carried out by using a scinticamera with a pinhole collimator to study the thyroid I-131 uptake measurement.

2. Method of Experiment

The instrument used is a Nuclear Chicago's scintillation camera Pho/Gamma III with a pinhole collimator of 4.8mm diameter. The conditions of the thyroid uptake measurement with a scinticamera are the same as taking scintiphotos, namely the I-131 main peak of the gamma energy of 364 $\pm$ 45 keV is used for both cases. The results obtained were compared with the routine thyroid uptakes.

As a basic experiment 4 kinds of the disk sources of filter paper with 50μCi of I-131 were employed. The diameters of them are 2, 4, 7 and 10cm. The relation between the clearance under the bottom of the collimator and the counting rates was examined (Fig. 1). Three kinds of I-131 filter paper in the shape of thyroid gland were made and placed in the ORINS type neck phantom. The relationships between the clearances and the counting rates as stated before were investigated to see their effect on the uptakes.

As a clinical experiment the uptake measurements were carried out at two different clearances, the one is at the distance of 2-5cm, and the other is at 20-25cm. In the short distance method, as the thyroid gland is shaped large enough in the visual field of the detector, the room background counts, instead of the body background counts, were subtracted from the counts of the patient or the neck phantom with a standard source. on the other hand, in the 25cm distance method, a part of the body is taken into the visual field of the detector. The B filter method is used and the body background counts are subtracted instead of the room background counts.

3. Results obtained

A. Basic experiment

(1) The effect of change in the clearance upon the thyroid uptakes.

A I-131 disk source of 2cm diameter was placed right under the pinhole of the collimator, and the counting rate was measured changing the clearance. The counts decrease in number by the distance inverse square law. They rapidly decrease in number up to around 6cm distance and then relatively slowly. In the practical thyroid gland scintigraphy the clearance is usually 2 to 5cm, and so the change in the counting rates is high in the neighborhood of this point. For example, if there is a measuring error of ± 1mm in the 3cm clearance, the change in the counting rates will reach ± 7%. In the case of the 25cm clearance, if the same change in the counting rates is allowed, the measuring error will be ± 8mm. As a consequence the correct measurement of the clearance is required in the short distance method.

Next, the change in the clearances and the counting rates is investigated when the I-131 source sizes are changed. In Fig. 3 the change in the ratio of the counting rates of each disk source to those of a point source is shown. For the clearance above 20cm the change in the counting rates is small enough to be neglected. However, when the clearance is 3 to 5cm the difference in the counting rates is large and can not be neglected. As the diameter of the source becomes larger, the counting rates are reduced and this factor causes errors. If the source is large, the sensitivity of the detector in the center and the periphery will differ from each other, and the counting rates will decrease as a whole.

(2) Size of the image on the crystal surface and the counting rate.

The advantage of the short distance method for scintigraphy consists in the improvement of resolution due to the image enlargement and the increase in the counting rate. However, the counting rate is also effected by the sizes of the source and the image on the crystal surface. As the source becomes larger, and the clearance smaller, the image size on the crystal will be enlarged and the counting rate reduced.

Figure 4 shows the above-mentioned relationship. Namely, the image size indicated by the length of one side in cm is plotted along the abscissa against the ratio of the counting rates along the ordinate for three kinds of the I-131 filter paper phantoms of the thyroid gland with the clearances of 6, 10, 16 and 21cm. The large, medium and small sizes of the thyroid phantoms are 8 x 8cm, 6 x 6cm and 4 x 4cm respectively and the I-131 capsule is used as a standard source.

The ratios of the counting rates at various clearances to the standard source were measured. In the case of the large sized image the ratio of the counting rate is low. For example, the ratio is 65% when the image is 22 x 22cm on the crystal surface (Fig. 5a). As the image size becomes smaller (Fig. 5b), the ratio approaches 100%. Accordingly, when the thyroid uptake measurement is made by using a scinticamera, the clearance should be large enough to attain a correct value. If a standard source having almost the same size as the patient's thyroid gland is used, the correct answer will be obtained. However, there is a problem that a standard source of the suitable size should be made at each measurement.

B. Clinical experiment

On 23 patients to whom 40-80μCi of I-131 in capsules was administered per os, 24 hour thyroid uptakes were determined by the routine thyroid uptake measurement. Within 30 minutes after this measurement, the thyroid uptakes were taken again by the short distance method and the 25cm distance method using a pinhole scinticamera. The results are shown in Fig. 6, and 7. In the short distance method the thyroid uptakes are low compared with the routine method, and the maximum difference reached 38%. On the other hand, in the 25cm distance method the counting rates become smaller and the statistical errors larger. However, the data obtained agree well with those of the routine method admitting the statistical counting errors.

4. Discussion

If the short distance method, in which the clearance is 2 to 5cm, is used, we can obtain the thyroid scintigraphy at the same time. But it is difficult to determine the correct uptake owing to the error made in measuring the distance, and the difference between the counting rates at the center and the periphery on the crystal surface caused by the image enlargement. The condition of the neck skin surface varies in each case and the error of a few millimeter can be easily made in the measurement of clearance. The sensitivity as the function of the source position is expressed as follows:

$$S \propto \frac{Zd^2}{16(1^2 + Z^2)^{3/2}}$$

where

S: Sensitivity
d: Diameter of the pinhole
1: Distance between the point source and the center
d: Distance between the pinhole and the point source

By this formula the sensitivity at the point 3cm apart from the center, which is located 5cm below the pinhole, was calculated and obtained the value of 63%. As the clearance becomes smaller, the sensitivity of the periphery of crystal lowers. When a point source like a capsule is used as a standard the uptakes will be smaller than those obtained by the routine method. If a standard source, which has the same size as the patient's thyroid gland, is used, the correct uptake will be expected.

In the 25cm distance method the measurement of the distance and the enlargement of the image meet no problem. However, the counting rate is usually reduced and the accuracy of measurement becomes lower. To cover the disadvantage, it is necessary to take a longer time for the measurement.

5. Summary

(1) Basic and clinical experiments on the thyroid I-131 uptake measurement were carried out using a pinhole scintillation camera.

(2) In the short distance method, in which the thyroid uptake measurement can be made at the same time with the thyroid scintigraphy, the values obtained are in general low compared with the routine method. It cannot be expected that a correct thyroid uptake is determined by this method.

(3) It is recommended that the thyroid uptake measurement is made separately from the thyroid scintigraphy by the 25cm distance method.

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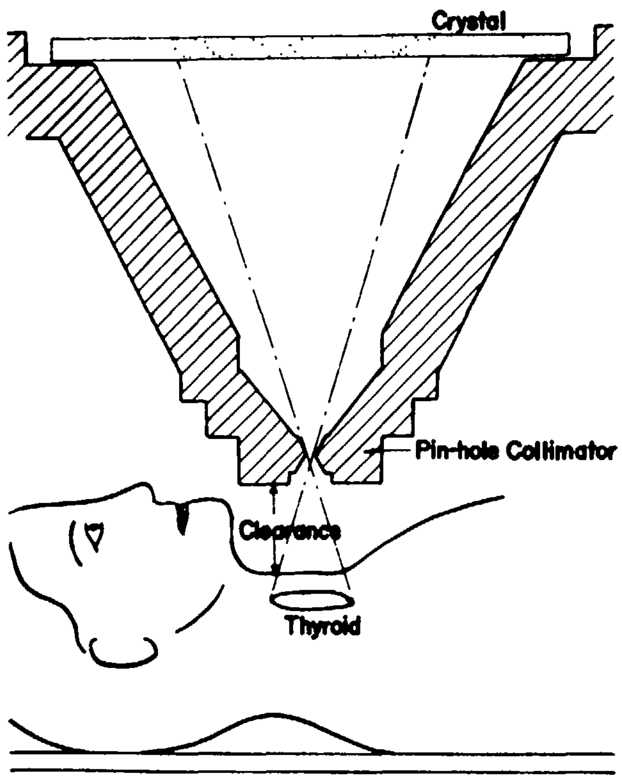


Fig. 1 Schematic diagram of the thyroid uptake measurement using a scintillation camera with a pinhole collimator.

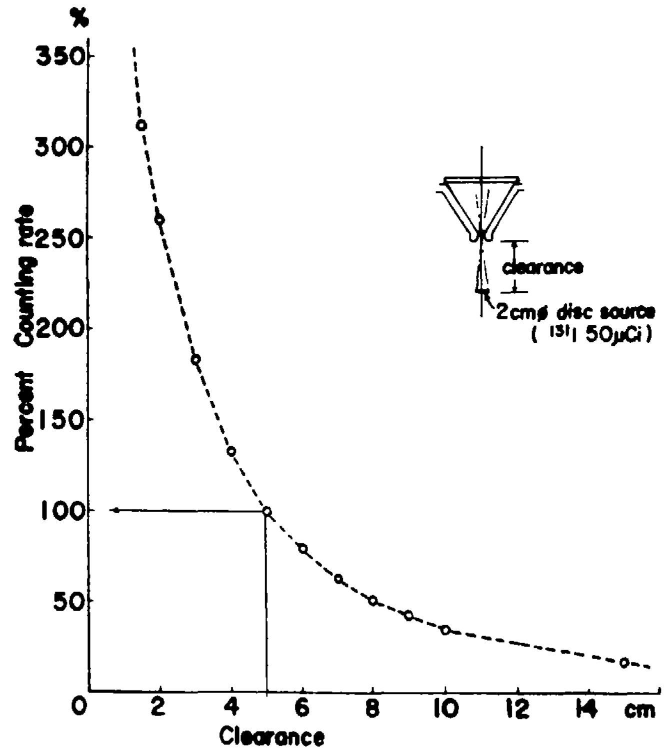


Fig. 2 Percent counting rate of a 2cmφ disk source of I-131 (50μCi) in air against clearance below a pinhole collimator.

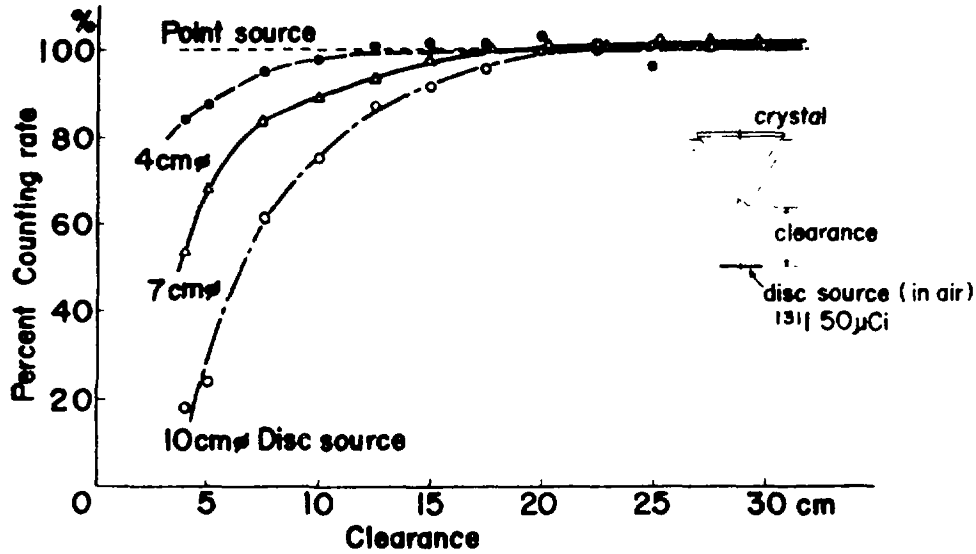


Fig. 3 Percent counting rate of I-131 disk source to a point source against clearance below the pinhole collimator for three disk sources.

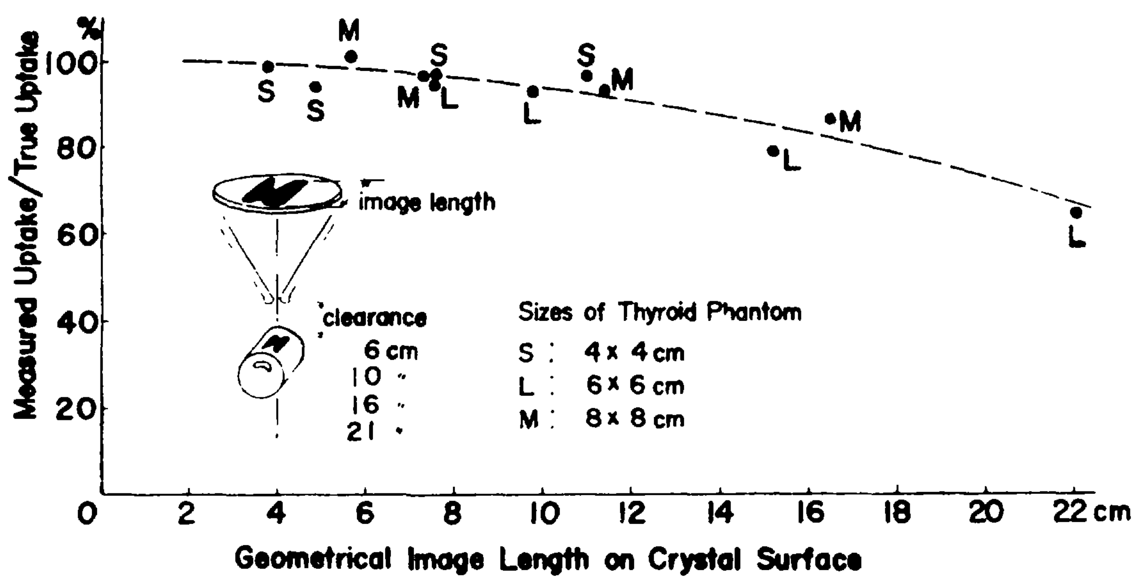
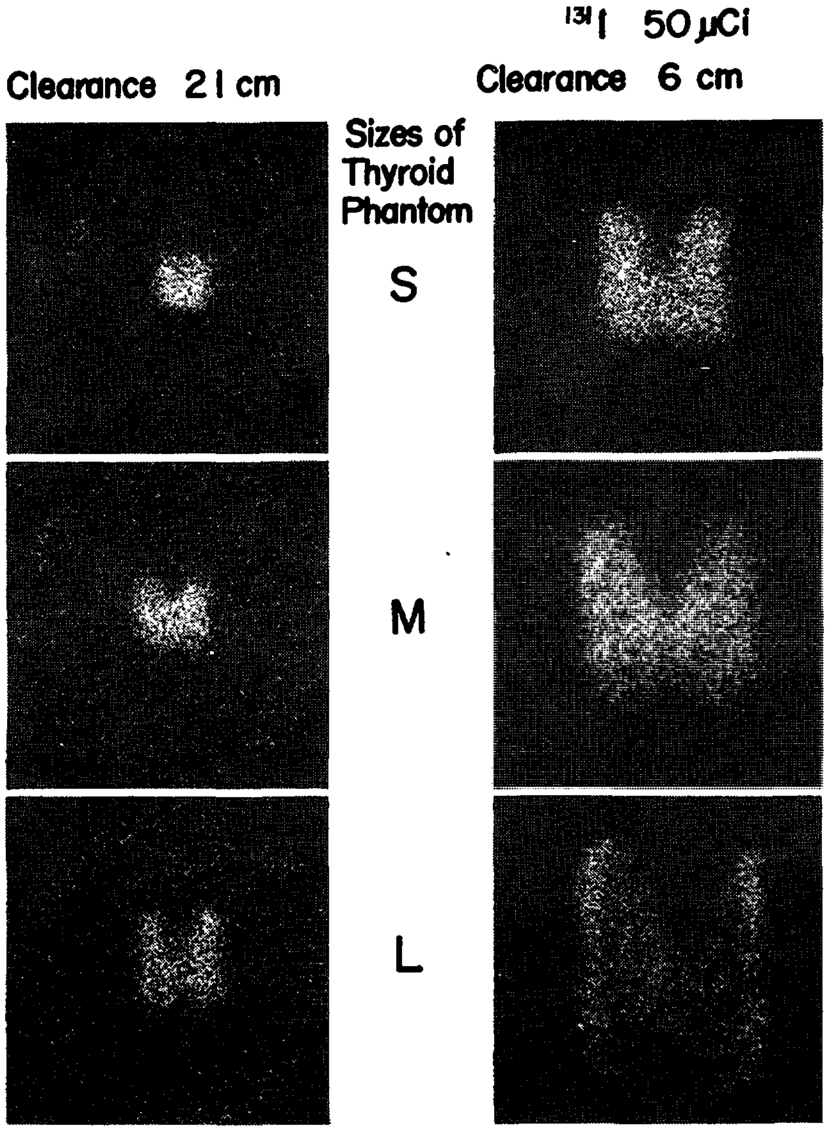


Fig. 4 Percent ratio of measured uptake to true uptake against geometrical image length on the crystal surface.



b. a.

Fig. 5 Scintiphotos of thyroid phantoms containing 50μCi of I-131 taken by a pinhole scintillation camera.

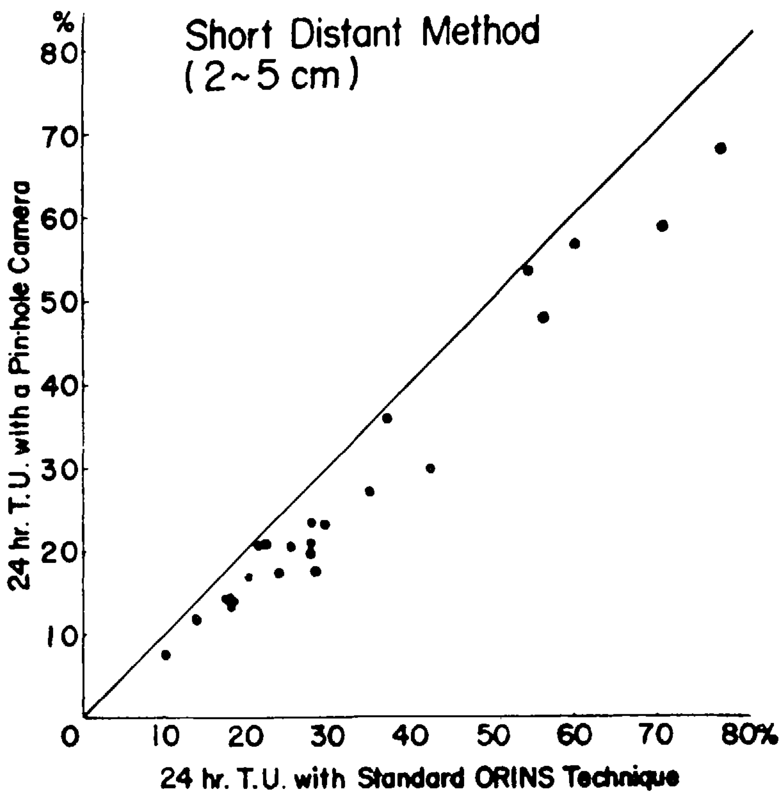


Fig. 6 Correlation between the 24hr I-131 thyroid uptake with a pinhole camera and the uptake with the standard ORINS technique.

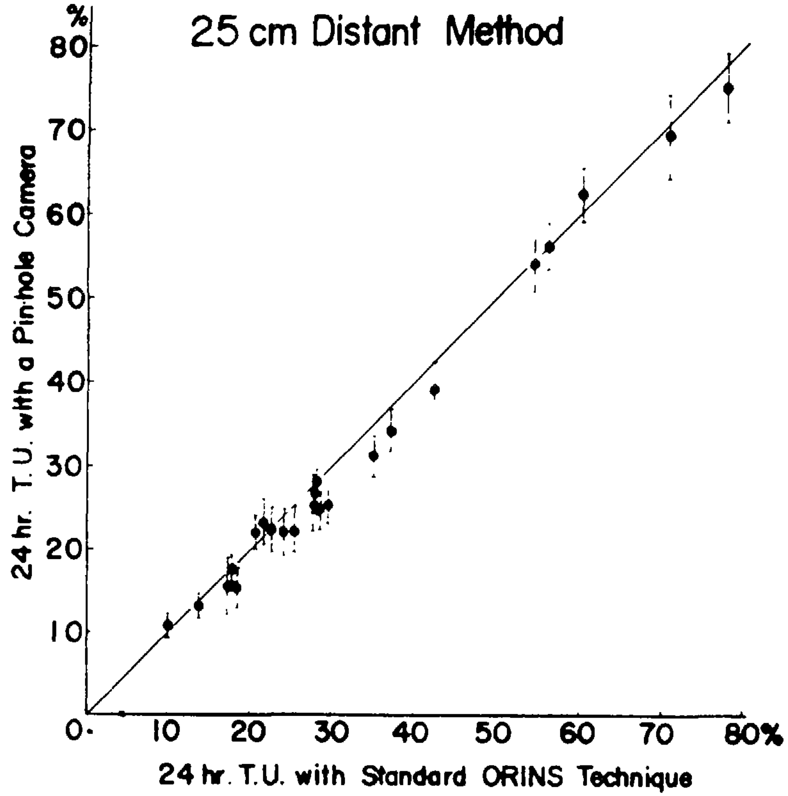


Fig. 7 Correlation between the 24hr I-131 thyroid uptake with a pinhole camera and the uptake with the standard ORINS technique.

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