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**RADIOACTIVE ISOTOPES - METABOLIC, DIAGNOSTIC AND
THERAPEUTIC USES***

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Since the discovery of natural radioactive by Becquerel in 1896, and the isolation of radioactive radium by the Curies', the radioactive isotope has played an increasingly significant role in medicine (1). It has been utilized in medical research, diagnosis and therapeusis (2-6). Radioactive isotopes are unique among pharmacological agents since their specific biological effect arises from release of energy (7) in the form of alpha, beta, gamma and positron radiation. Each type of radiation characteristically penetrates its environment in such fashion that energy release per unit of distance traversed is proportionate to mass and bears a relation to energy. Alpha particles produce dense ionization over a short path (8-15 microns). Beta and positron particles, because of smaller mass, produce for a given path length much less dense ionization than alpha while the penetration is increased. Gamma radiation is an electro-magnetic wave similar to a high energy x-ray wave capable of penetrating far into dense matter but with least density of ionization along its track. Gamma radiation originating with the body can be easily detected with suitable instrumentation external to the body.

All of the radiations emitted by radioactive isotopes produce biological effects. These effects may be manifested by immediate or delayed injury or death to the cell, an alteration

in cellular function, temporary or permanent, and in a special category, injury associated with mitotic activity which may be inheritable. The different tissues vary markedly in their radio-sensitivity or response to this type of energy applied to the cell system or its constituents.

Information regarding the biological effects of radiation produced by radioactive isotopes has accumulated in time coming from many sources (8-10). Extrapolation of information derived in animal investigation to reactions and effects in man is subject to hazard. Increased accumulated human knowledge and experience can be achieved in the aged. Because effects of radiation require time to appear and because these delayed effects may be undesirable while the immediate effects may be desirable, radioactive isotopes provide a unique opportunity to develop better control of disease in the older individual (11).

In a consideration of the employment of radioactive isotopes, it is first necessary to clearly establish that as a drug class, radioactive isotopes are not a unified category of drugs but possess an additional unique property. This property may be constructed into any type of molecule. Radioactive isotopes are particularly useful for obtaining dynamic, distribution, metabolic and ultimate fate information of a molecule or drug.

453 003

With the use of radioisotopes, many studies can be accomplished better than by utilizing other procedures. Radioisotopes are particularly well suited for investigations concerned with effective action or modified by route of administration and the determination of metabolic pathways and the rates of traverse. Isotopically labeled drugs have added much information on drug absorption (12), localization (13), generalized distribution in organs and tissues (14) and the excretion routes. Unknown or intermediary metabolites have been discovered (14). Reactor technology has made production of almost any elemental radioactive isotope economically feasible in sufficient quantities for large scale and general application.

The differing kinds of energy emission make possible the selection of a nuclide that possesses the type of decay (energy, half-life and emission type) that is most efficient for the desired objectives. For example, alpha particles are most effective in tissue destruction, beta particles are less so but more readily adapted to localizing radioautography, while gamma emissions are most useful for external metering, monitoring and mapping of general body distribution and pathways which cannot be done with alpha emitters because of their short path. When radioactivity is incorporated into a molecule, it then generally becomes of

33 004

greater importance to determine the manner in which these compounds may be or are utilized, than in the basic nature of the compound itself. The total metabolic experience of the molecule must be considered as well as the response of the largest organ in the specific pathway of import. The application of radioactive nuclides to studies of metabolic utilization, to employment for diagnostic objectives and to utilization as therapeutic principle agents is in its infancy (15).

Radioactivity in itself is not entirely without risk (16-20). The degree of risk is arguable, some categorically say it is considerable (21) whereas others tend to equate clinical tests employing radioactivity in small tracer amounts to not significantly greater risks than are inherent in other clinical laboratory procedures (22). Whatever the long term risk may be, it is quite likely proportional to absorbed dose. In tracer quantities, there is no measurable short term risk. Therefore, constant efforts are being made to provide better tests by reduction of the required exposure without sacrificing sensitivity or precision. The rapid improvements being made in detecting and recording devices have kept the field in a state of high flux (23) and even as this is being written some of the procedures and techniques mentioned are, in all probability, already outmoded. Thus, it is desirable not to make extensive comment on procedures and techniques here but rather to discuss

the fundamental principles involved. Since time and degree of exposure determine the number and the extent of possible delayed manifestations of radiation exposure, it is clear that the application of clinical tests employing radioactivity require consideration of an age selection. In older individuals, with a less remaining life expectancy these tests utilizing radioactivity can be used more freely because of two factors: 1) an absolute time interval for delayed effect which may contribute a significant safety factor; and, 2) the relative amount of remaining physiological age span of the aged are not provoked in most instances by clearcut extraneous etiological factors (11). Relief is therefore attained by a complete or partial physiological correction or symptomatic alleviation. Degenerative diseases are among the types of disease prevalent in older persons in which the employment of radioactive nuclides may yield diagnostic information not otherwise attainable (24). Malignancy, which also has an increased frequency in older persons, is also susceptible to better evaluation (25) and in some instances palliation with radioactive elements (26-32).

Let us examine the utilization of radioactive nuclides in their capability of yielding information with respect to 1) the maintenance of circulatory integrity, 2) the maintenance of adequate excretory ability and capacity, 3) the capability of physical injury repair, 4) the normality as well as the abnormality of

gastrointestinal tract function, 5) better placement of materials in specific centers of the central nervous system with particular reference to ultimate therapeutic action, 6) neoplasia diagnosis and 7) neoplasia therapeusis.

With respect to maintenance of circulatory integrity a simple problem which frequently occurs is that of total blood flow to an extremity or a portion of an extremity (33-38). The addition of a known quantity of a gamma emitting isotope to the blood stream and measurement of its radioactivity over the specific region of interest when compared to an equivalent region taken as a norm can give this answer directly. Such vascular pathology as thrombosis and obstruction or simple spasm become apparent in a lessened number of counts. The interpretation of the reduced flow must be correlated with history, physical findings and symptomatology. Radioactive sodium, iodine, chloride and bromide are possible nuclides of many that can be used in such a test. The use of radioactive labeled red blood cells to determine total erythrocyte mass (39-46), blood volume (47-56), blood loss (57), cell production (53, 58-64), survival time (65-69) and haemoglobin labelling (70, 71), by addition of iron-59, chromium-51 and phosphorous-32 (72-75), is well established. Iodine-labeled human serum albumin (76-78) is employed in similar manner for blood volume determination. However in this application, the plasma

volume is determined directly by dilution. Similar labelling studies (survival measurements) have recently been done with white cells and platelets (74, 79-88). The more sophisticated and complex circulatory measurements for example are cardiac output, (89-99), coronary blood flow (100) and cerebral blood flow (101-103). For these a technical and complex interpretation of graphically recorded data are necessary to resolve an answer. In many clinics, these tests cannot be done because of the complex apparatus required and the sophisticated skills of the specialists are not available. Time certainly will cause these tests to become simplified and therefore find an ever increasing acceptance in physiological evaluation of circulatory competency and response to work loads. They should prove especially useful in establishing the cardiac reserve.

In any testing of the excretory systems, radioactive nuclides provide an exceptionally sensitive and easily applied test. The pattern of renal excretion of organic and inorganic compounds has been carefully and painstakingly studied. Consequently we know which compounds are excreted in such fashion that they give us information primarily regarding glomerular filtration or total renal blood flow. By incorporating a radioactive nuclide in these compounds, analytical procedures may be simplified and automation is made easier (104). When one is concerned with total renal blood

flow, by incorporating a suitable gamma emitter, such as radioactive iodine 131, into the molecule of diodrast (105, 106) or hippuran an external detector can be used which, when proper shielding and collimation is provided, will give information regarding the relative blood flow of one kidney to the other and, by appropriate scanning, the renal function can be estimated in terms of expected normal values (104-109). However the interpretation of excretory data of a single electrolyte is always very difficult since many factors operate to affect the ultimate quantities appearing in the urine. Specific excretion of specific compounds can readily be followed by collection of urine and measurement thereafter. For rapidly excreted gamma emitters, suitable scanning over the urinary bladder will be adequate. Large single crystal detectors usually found in whole body counters can be utilized which will count the entire specimen or human subject or areas thereof (115-131). With these types of tests, it should be possible to determine whether indeed there is an age related decrease in renal function or whether previous data suggesting this relation may be due to some other widespread change such as atherosclerosis. The use of radioactive iodine labeled rose bengal and other materials have given evidence of value in patients with hepatic and biliary disease (132-138). Skill and experience are necessary in interpretation of the results of these tests.

A problem constantly besetting older individuals is that of tissue repair following injury. The injury may be physical as a fracture, or a wound or biochemical such as a sensitivity resulting in agranulocytosis. Here the information to be gained with radioisotopes is general rather than specific. That is, procedures presently available have their major usefulness in gaining data on the behavior of older people as a class rather than the specific response of a specific individual to specific trauma. Development of a simple and effective method for incorporation of tritium into thymidine (139) has made possible studies on a wide scale of the role played by several cells in hematopoiesis. Thymidine is a precursor of deoxyribonucleic acid or DNA. Therefore incorporation of labeled thymidine into DNA by a cell demonstrates that cell is synthesizing DNA (140), and experience has shown this precedes cell division (141). Thus it is possible to follow a cell line through three or four cell generations. Moreover this can be done in an intact person as only a very small dose of label material need be given (142). The duration of label incorporation is very short - - perhaps under five minutes. In experimental and accidental fracture and trauma of animals, the cell responses and processes can be studied in full (143, 144). The applicability of studies on animals to man in this regard can be determined with a few patient studies. The frequency of severe fractures in the older person and the

difficulty of management eloquently attest to the need of more information on fracture management. A very pertinent series of observations have been made upon apparent functional capability of oste blasts in young and older mice (145, 146). In disorders affecting the synthesis of white blood cells particularly, a label introduced into the marrow can give specific information regarding the response of the patient either to the noxious or the restorative agent. A decrease or increase in the number of labeled cells gives a picture of the response of these cells to the agent of interest.

As a measure of normal gastrointestinal function there are a wide variety of applicable observations (147-160). Robertson, of Brookhaven National Laboratory, while observing the secretion of gastric hydrochloric acid found an equivalent production of hydriodic acid after I^{131} administration. Labeled amino acids can be given and, if labeled with carbon-14 the exhalation of carbon-14 dioxide can be followed (161). The appearance time of labeled carbon dioxide and its total quantity will give insight into the absorptive mechanism of the gut in relation to these compounds. Similar studies can be done with carbohydrates (162-167) and fats. These are readily accomplished since a continuous analysis of expired air can be carried out automatically (168-171). This analysis will record both the total carbon dioxide eliminated per unit of time

and volume, and the specific activity of the gas. If one has the device, the test is not difficult. These kinds of functional tests are really new to our armamentarium. They require no blood samples nor urine samples -- merely the donning of a mask so that expired air can be trapped and monitored. The use of cobalt labeled compounds for studies of sprue and pernicious anemia have become almost routine (172-200). Here only a very few centimeters of gut are tested for permeability so it is a highly specific test and not one of generalized absorption as are some of the other procedures previously mentioned.

Information giving more precise placement of specific centers of the central nervous with particular regard to ultimate therapeutic action is of the greatest interest. The example cited is from the Brookhaven work of Dr. Irving Schwartz on the appetite center (201). It is clear that in terms of disorders, this sort of information might lead to a better understanding of obesity which in itself seems to be associated with a decrease in longevity. The total quantity of food intake is a resultant of two stimuli - 1) a desire for food or appetite and 2) a feeling of satiety. It would seem that many cases of obesity might best be described as failure to achieve satiety rather than by a driving appetite. Investigations in the past have suggested that one of the critical functions of the hypothalamus is the integration of energy intake

112

and expenditure. This is believed to be accomplished by virtue of the interplay of a lateral neuronal integrating center or "intake drive center" and a medial "satiety center". Gold thioglucose given to mice may produce marked obesity -- a distinctly unusual condition for a mouse. When obesity results some of the gold compound has been locally deposited in the central nervous system. The quantity of gold thioglucose found localized in the brain tissue is less than one microgram per gram of tissue. Since the procedure requires two to six months to provoke obesity and thereby make certain the lesion has been produced, chemical analyses were not possible. Activation of gold to its beta emitting radioactive isotope and subsequent radioautography, however was readily carried out with this quantity of the metal. When this procedure was done, the radioautographic localization of activity in the central nervous system of obese animals, was found to be in agreement with the supposed location of the center. This combination of chemical specificity, activation and quantitative measurement of the element fixed as well as cytological localization by radioautography gives considerable promise of ultimately gaining a better understanding and knowledge of both known and suspected special centers in the central nervous system. Similar types of studies are being carried out with appropriate hormones which may give us better insight into their locus of action (202, 203).

Briefly, to touch upon neoplastic applications, first in diagnosis. The revelation of "cold" or "hot" nodules in the thyroid following radioactive iodine administration (204-217) is an example whereby this modality permits a suspected diagnosis to be developed which otherwise might well be missed. Employing radioisotopes and scanning techniques, the diagnostic problems associated with the employment of I^{131} have been discussed in a recent review (218). In other organs as the liver and spleen, similar types of cold or negative uptake regions may give eloquent testimony of metastases (219-222). In the realm of intracranial neoplasms, work has been carried out to develop a reliable diagnostic aid using radioactivity (223-229). In a number of clinics, there are now ten years experience with radioactive isotopes as the principle factor to compare with independent procedures for tumor localization. Diagnostically, the wider use has been recorded to gamma as opposed to beta-emitting isotopes. Iodine has most frequently and extensively been used both in the form as an inorganic salt and as an iodinated albumin (230-235). The best counting procedure is a matter of considerable discussion among the advocates of the several techniques. However it may be done, radioactive iodine has been found to be very useful by several clinics. A variant of this has been the adaptation of the positron emitter to this use. The positron emitter causes the annihilation reaction to occur which gives off directionally oriented

gamma rays. These appropriately detected are spatially oriented, so observation along two axes should suffice in principle to precisely locate the tumor. Arsenic-72, iodine-125 and other positron emitters have been and are under investigation (236-243). Simplicity of interpretation is its chief utility. The use of radioactive phosphorus in conjunction with a beta sensitive probe counter is an older procedure still found useful by a number of neurosurgeons (225). None of these procedures has been sufficiently superior to the others to achieve clear superiority nor to displace the older maneuvers of the neurologists, the radiologists and the neurosurgeons for tumor localization. Adaptations of positron scanner technique to other body regions give promise in localization of small metastases or primary sites otherwise not readily detectable such as in the pancreas (219).

The use of the radioactive isotope as a primary diagnostic agent for malignancy is yet to come. No metabolic abnormality unique to malignancy has yet been uncovered. Until this or some completely documented physiological difference has been accepted, the radioactive isotopes is only a secondary weapon in cancer diagnosis.

In the treatment of malignancy there is great promise in further exploitation of radioactive isotopes and possibly in the

use of fast electrons (244) and π -mesons (245). We shall not discuss the use of cobalt devices, for these gamma ray emitters are essentially identical to high voltage x-ray except in the energy spread of the beam. Internally administered beta emitters have been used to some advantage as palliative agents (246). The treatment of thyroid carcinoma with I^{131} is very valuable in that a small percentage of tumors will spontaneously take up significant amounts of iodine (247-251) or by proper drug manipulation can be induced to do so (252-258). Several excellent reviews have been written covering the problems and results of this kind of treatment (259-261). It is the only malignancy in which the physiological interaction of the tissue affected and the element administered result in a significant accumulation of radioactive isotope in the neoplastic tissue. The use of gallium (263-266) and phosphorus (267, 268) in the treatment of bone malignancy has been very disappointing. Radioactive phosphorus has been used to palliate leukemia (269, 270) but in this regard does not appear to be any more effective than radioactive sodium given in equivalent dose. In the treatment of polycythemia vera, radioactive phosphorus is possibly the treatment of choice (269). It is effective and can be given in fractionated doses without significantly increasing risk or decreasing effectiveness. Efforts to utilize other radioactive isotopes in an effective manner after systemic administration have in general been unsuccessful.

Local installation, injection or implantation of radioactive isotopes has been explored to alleviate pain, discomfort and disability (271-276). The injection of radioactive colloids (277) and particularly gold preparations into the body cavities for fluid suppression has been attended with a very modest degree of success, though the mechanism cannot be explained (278-283). Radiogold in doses ranging from 50 millicuries up instilled into body cavities results in a temporary but significant reduction of ascites in about 60 percent of the patients when the provoking disease is ovarian carcinoma (284). Although it has been suggested that gold be used as a prophylactic (285), in a small number of unpublished studies by Foster and Farr at Brookhaven no positive protection was demonstrated. The control of fluid accumulation is a property of the radiation effect and not of radiogold as some years ago, Foster and Farr demonstrated that short-lived radioactive chlorine given as sodium chloride had the same effectiveness in ascites associated with metastatic ovarian carcinoma (286). In pleural effusions, gold has similarly been used with similar effects (287-290). Again it is the radiation, since radioactive krypton was found to behave likewise (286). The advantage of the radioactive isotope over x-ray in these instances is the extreme degree of localization of the radiation, the ease of handling of the material and the flexibility these introduce into patient management.

Implantation of pellets or colloidal suspensions is being slowly developed (291-302). Results are in accordance with those predicted on the basis of calculated radiation doses to the tissues concerned. However, certainly better advantage can be derived from mixtures of radioisotopes to meet special geometric situations than has been done in the past. This type of approach to the inoperable lesion has been honored in the breach rather than in the observance. Systemic effects are nil the patient can frequently be kept ambulatory and much is to be gained by further exploration of this modality in local lesion control.

For ten years at Brookhaven efforts have been directed in utilizing a nuclear reactor to provoke a specific cytocidal reaction in neutron capture therapy (303-317). We have proceeded steadily at the development of this procedure whereby a boron-10 atom already in the tissue is at a special time disintegrated by capturing a thermal neutron. This reaction releases an alpha particle and an energetic lithium particle. The 2.4 MEV of energy is all absorbed within a volume about that of one cell. Under appropriate conditions the reaction can be utilized to destroy neoplasm leaving unscathed intermingled and juxtaposed normal cells. The mechanism is not understood but the results have increased in effectiveness by a very considerable degree. In one treatment lasting only one-tenth second, 100 percent of transplantable

neoplasma in mice have been caused to disappear permanently. In man in a single treatment of 100 seconds, effective treatment can be made to a depth of five centimeters with exquisite discrimination and with a sure kill. Technical advances now being consolidated should increase the depth and decrease further, the time of exposure (319-323). While thus far, these endeavors have been limited to tumors found in the intracranial region -- though some arose from other tissues -- there now exist evidence that consideration can now be given to other regions of the body. The theoretical promise of this procedure is slowly moving to a stage where the results may become clinically significant.

In summary, it is apparent that a discussion of radioactive isotopes considers all fields, is changing rapidly and involves all aspects of medicine both clinical and laboratory. Other extremely interesting applications of radioisotopes, which have not been considered in this review, to mention just a few examples, have been the incorporation of tritium into anticancer drugs for studies of distribution and concentration (324), metabolism of manganese (325), the use of xenon¹³³ in thoracography and lung ventilation (326, 327), and the incorporation of tritiated cytidine into various cancer investigations (328). The usefulness of these compounds in the clinic is not yet generally realized. In all aspects of geriatric medicine radioactive nuclides offer unusual advantages

and challenge in that much needed and useful knowledge might be obtained which would not be possible or feasible in other areas of medical research and practice.

BIBLIOGRAPHY

1. McCormick, J. A. Radioisotopes in Medicine and Human Physiology. TID-3514. U.S. Atomic Energy Commission. Washington, D.C.: Office of Technical Services, Department of Commerce. 1955.
2. Low-Beer, B. V. A., The Clinical Use of Radioactive Isotopes. Springfield: Charles C. Thomas. 1950.
3. Hahn, P. F. (Ed.), Therapeutic Uses of Artificial Radioisotopes. New York: John Wiley and Sons, Inc. 1956.
4. Claus, W. D., (Ed.), Radiation Biology and Medicine. Reading: Addison-Wesley Publishing Co., Inc. 1958.
5. Quimby, E. H. Feitelberg S. and Silver, S., Radioactive Isotopes in Clinical Practice. Philadelphia: Lea and Febiger. 1958.
6. Farr, L. E. Knipping, H. W. and Lewis, W. H., (Eds.), Clinical Aspects of Nuclear Medicine, Symposium with Special Reference to Cancer and Cardiovascular Diseases. Koln and Opladen: Westdeutscher Verlag. 1961.
7. Thomas, S. F., Radiation: A Chemical. J. Am. Med. Assoc., 175 783 (1961).
8. Radioisotopes in Agriculture: an Annotated Bibliography. TID 3078. U.S. Atomic Energy Commission. Oak Ridge, Tenn.: Technical Information Extension. 1957-58.
9. Comstock, M. Effect of Proton and Deuteron Irradiation on Biological Material. AECU-4358. Brookhaven National Laboratory, Upton, New York. 1958.
10. Radioisotopes and Radiation in the Life Sciences, 2nd Inter-American Symposium on the Peaceful Application of Nuclear Energy, Buenos Aires, 1960. Washington, D.C.: Pan American Union.
11. Farr, L. E., A Look at Atomic Medicine in Geriatrics, J. Gerontol. 13 27 (1958).
12. Hodge, H. C. and Sterner, J. K., Skin Absorption of Triorthocresyl Phosphate as Shown by Radioactive Phosphorous, J. Pharmacol. 79 225, (1943).

13. Way, E. L. and Adler T. K. The Pharmacologic Implications of the Fate of Morphine and Its Surrogates, *Pharmacol. Reviews* 12 383 (1960).
14. Boyd, E. S. The Metabolism of Lysergic Acid Diethylamide, *Arch. Inter. de Pharmacodynamie et de Therapie* 120 292 (1959).
15. Lushbaugh, C. C., Use of Radioisotopes and Radiation in the Diagnosis of Disease: Whole Body Counting, in 87th Congress Hearings Applications of Radioisotopes and Radiation in the Life Sciences. Washington, D.C.: Government Printing Office. 1961 (p. 45).
16. Maximum Permissible Amounts of Radioisotopes in the Human Body and Maximum Permissible Concentrations in Air and Water, National Bureau of Standards Handbook 52. Washington, D.C.: U.S. Department of Commerce. 1953.
17. Permissible Doses from External Sources of Ionizing Radiation, National Bureau of Standards Handbook 59. Washington, D.C.: U.S. Department of Commerce. 1954.
18. Radiological Hazards to Patients. Second Report of the Committee. Great Britain Ministry of Health. 1960.
19. Van Putten, L. M. Medical Aspects of the Utilization of Radioactive Isotopes, *Atomenergie*, 2 182 (1960).
20. Valentin, H. and Lehnert G. Strahlenschaden und Strahlenschutz in der Klinik. Farr, L. E., Knipping, H. W. and Lewis, W. H. (Eds.), *Clinical Aspects of Nuclear Medicine, Symposium with Special Reference to Cancer and Cardiovascular Diseases*. Köln and Oplanden: Westdeutscher Verlag. 1961 (p. 296).
21. Muller, H. J. Some Present Problems in the Genetic Effects of Radiation, *J. Cellular Comp. Physiol.* 35 Suppl. 1. 9 (1950).
22. Lushbaugh, C. C., Use of Radioisotopes and Radiation in the Diagnosis of Disease: Whole Body Counting, in 87th Congress Hearings Application of Radioisotope and Radiation in the Life Sciences. Washington, D.C.: Government Printing Office. 1961 (p. 27).
23. Kuper, J. B. H. Dosimetry and Instrumentation for Hazard Evaluation. Claus, W. D. (Ed.), *Radiation Biology and Medicine*. Reading: Addison-Wesley Publishing Co., Inc. 1958 (p. 429).

24. Lushbaugh, C. C., Use of Radioisotopes and Radiation in the Diagnosis of Disease; Whole Body Counting, in 87th Congress Hearings, Application of Radioisotope and Radiation in the Life Sciences. Washington, D.C.: Government Printing Office. 1961 (p. 40).
25. Brucer, M., Thyroid Radioiodine Uptake Measurements. ORINS-19. U.S. Atomic Energy Commission. 1958.
26. Moore, G. E. Use of Radioactive Diiodofluorescein in Diagnosis and Localization of Brain Tumors, *Sci.* 107 569 (1948).
27. Chou, S. N., Aust, J. B. Moore, G. E. and Peyton, W. T., Radioactive Iodinated Human Serum Albumin as a Tracer Agent for Diagnosing and Localizing Intracranial Lesions, *Proc. Soc. Exptl. Biol. Med.* 77 193 (1951).
28. Wrenn F. R., Jr. Good, M. L. and Handler P. Use of Positron-Emitting Radioisotopes for Localization of Brain Tumors, *Sci.*, 113 525 (1951).
29. Krohmer, J. S., Thomas, C. I. Storaasli, H. L. and Friedell H. L. Detection of Intracocular and Tumors with P-32, *Radiology*, 61 916 (1953).
30. Donn, A. and McTigue, J. Radioactive Phosphorous Uptake Test on Malignant Melanoma of the Eye, *Arch. Ophth.* 57 668 (1957).
31. Brucer M. Radioisotope Scanning. ORINS-20. U.S. Atomic Energy Commission. 1958.
32. Borkowski, C. J. Congressional Committee Hearing Statement on Instrumentation, in 87th Congress Hearings Application of Radioisotopes and Radiation in the Life Sciences. Washington, D.C.: Government Printing Office. 1961 (p. 329).
33. Kety, S. S., Measurement of Regional Circulation by the Local Clearance of Radioactive Sodium, *Am. Heart J.*, 38 321 (1949).
34. Shipley, R. H. and Clark, R. E. Measurement of Circulation Times with NaI-131 *Circ. Res.*, 4 456 (1956).
35. Blocker, T. G. Jr. Lewis, S. R. Perry, J. E. Tumbush, W. T. and Lynn, W. L. Rate of Disappearance of Interdermally Injected Radiosodium as an Index of Blood Flow in Normal and Chronically Ulcerated Legs, *Ann. Surg.*, 145 630 (1957).

36. Dobson, E. L. and Warner G. E. Measurement of Regional Sodium Turnover Rates and Their Application to the Estimation of Regional Blood Flow, *Am. J. Physiol.*, 189 269 (1957).
37. Gabelova, N. A. and Frank G. M. Study of the Rapid Transmigrations of Substances in an Organism Using γ -Emitting Isotopes, *Biophysics (USSR)*, 3 214 (1958).
38. Ellis, R. H. Jr. Tracer Method Examines Human Blood Circulation, *Nucleonics*, 17 56 (1959).
39. Hahn, P. F. Balfour, W. M., Ross J. F. Bale W. F. and Whipple G. H. Red Cell Volume Circulating and Total as Determined by Radioiron, *Sci.*, 93 87 (1941).
40. Hahn, P. F. Ross J. F. Bale, W. F. Balfour, W. M. and Whipple G. H. Red Cell and Plasma Volumes Circulating and Total as Determined by Radioiron and Dye, *J. Exp. Med.*, 75 221 (1942).
41. Gibson, J. G., Weiss, S. Evans, R. D., Peacock, W. C., Irvine, J. W., Jr., Good, W. M. and Kip, A. F., The Measurement of the Circulating Red Cell Volume by Means of Two Radioactive Isotopes of Iron, *J. Clin. Invest.* 25 616 (1946).
42. Hevesy, G. and Nylin G., Application of K-42 Labeled Red Corpuscles in Blood Volume Measurements *Acta Physiol. Scandinav.*, 24 285 (1951).
43. Hevesy, G. Thorium B-labeled Red Corpuscles, *Ark. Kemi*, 3 425 (1951).
44. Mollison, P. L. and Veall N. The Use of the Isotope Cr-51 as a Label for Red Cells *Brit. J. Haematol.*, 1 62 (1955).
45. Tudhope, G. R. and Wilson, G. M. A Comparison of Rb^{86} p³² and Cr^{51} as Labels for Red Blood Cells *J. Physiol.* 128 61 (1955).
46. Tudhope, G. R. and Wilson, G. M. The Use of Rubidium⁸⁶ as a Label for Red Cells *Brit. J. Haem.*, 2 75 (1956).
47. Meneely, G. R., Wells, E. B. and Hahn, P. F. Application of the Radioactive Red Cell Method for Determination of Blood Volume in Humans, *Am. J. Physiol.* 148 531 (1947).
48. Nickerson, J. L. Gregersen M. I. Root W. S. and Sharpe, L. M., Influence of Blood Incompatibilities on Measurement of Blood Volume by Cell Tagging Methods, *Proc. Soc. Exp. Biol. Med.* 75 61 (1950).

49. Berlin, N. I., Lawrence, J. H. and Garland, J., Blood Volume in Polycythemia as Determined with P-32 Labeled Red Cells, *Am. J. Med.* 3 747, (1950).
50. Yalow, R. S. and Berson, S. A., The Use of K⁴² Tagged Erythrocytes in Blood Volume Determinations, *Sci.*, 114 14 (1951).
51. Berlin, N. I., Hyde, G. M., Parson, R. J. and Lawrence, J. H., The Blood Volume in Various Medical and Surgical Conditions, *New Eng., J. Med.*, 247 675 (1952).
52. Hicks, D. A., Hope, A., Turnbull A. L. and Verel, D., The Estimation and Prediction of Normal Blood Volume, *Clin. Sci.*, 15 557 (1956).
53. Berlin, N. I., Lawrence, J. H. and Elmlinger, P. J., Recent Advances in the Knowledge of Total Red Cell Volume, Production and Destruction, *Blood* 12 147 (1957).
54. Albert, C. A., Eccleston, H. N., Jr., Rafii, A., Hunter, C. H., Henley, E. E. and Albert S. N., A Rapid Method for Preparing Washed Red Cells Tagged with Chromium⁵¹, *J. Lab. Clin. Med.*, 54 300 (1959).
55. Cohen, Y. and Ingrand, J., Study and Control of the Labelling of Erythrocytes with Chromium-51, *Rev. hematol.*, 15 217 (1960).
56. Czerniak, P. and Lauer, L., Hemovolumetry in Patients of True Polyglobulia Treated with P³², *Ann. radiol.* 3 R101 (1960).
57. Owen, C. A., Bollman, J. L. and Grindley, J. H., Radiochromium Labelled Erythrocytes for the Detection of Gastrointestinal Haemorrhage, *J. Lab. Clin. Med.*, 44 238 (1954).
58. Hemmeler, G., *Metabolisme du Fer*. Paris: Masson. 1951.
59. Granick, S., Iron Metabolism, *Bull. N. Y. Acad. Med.*, 31 81 (1954).
60. Bothwell, T. H., Callender, S., Mallett, B. and Witts L. J., The Study of Erythropoieses Using Tracer Quantities of Radioactive Iron, *Brit. J. Haematol.*, 2 1. (1956).
61. Giblett E. R., Coleman, D. H., Pirzio-Biroli, G., Donahue, D. M., Motulsky, A. G., and Finch, C. A., Erythokinetics: Quantitative Measurements of Red Cell Production and Destruction in Normal Subjects and Patients with Anemia, *Blood*, 11 291. (1956).

62. Keiderling, W., Schmidt H. A. E. and Lee, M., Untersuchungen über die Dynamik des Erythrozytenumsatzes mit Radioeisen (Fe-59) and Radiochrom (Cr-51). Fellingner, K. and Vetter, H., (Eds.), Radioaktive Isotopes in Klinik and Forschung. Munich: Urban and Schwarzenberg. 1957 (p. 24).
63. Pollycove, M., Iron Metabolism. Zollner, M., (Ed.) Thannhausers Lehrbuch des Stoffwechsels und der Stoffwechselkrankheiten, Stuttgart: George Thieme. 1957 (p. 835).
64. Stohlman, F. Jr., The Use of Fe⁵⁹ and Cr⁵¹ for Estimating Red Cell Production and Destruction: An Interpretive Review, *Blood*, 18 236 (1961).
65. Ebaugh, F. G., Jr., Emerson, C. P. and Ross, J. F., The Use of Radioactive Chromium-51 as an Erythrocyte Tagging Agent for the Determination of Red Cell Survival in Vivo, *J. Clin. Invest.*, 32 1260 (1953).
66. Necheles, T. F., Weinstein, I. M. and LeRoy, G. V., Radioactive Sodium Chromate for the Study of Survival of Red Blood Cells. I. The Effect of Radioactive Chromate on Red Blood Cells. *J. Lab. Clin. Med.*, 42 358 (1953).
67. Read, R. C., Wilson, G. W. and Gardner, F. H., Use of Radioactive Sodium Chromate to Evaluate Life Span of Red Blood Cells in Health and Certain Hematologic Distorders, *Am. J. Med. Sci.*, 228 40 (1954).
68. Pollycove, M., Elmlingen, P. J., Sarkes, L. A., Apt., L. and Ross, J. F., Radioiron Determination of Human Erythrocyte Life Span Distribution, *Clin. Res. Proc.*, 4 79 (1956).
69. Lajtha, L. G., The Use of Isotopes in Haematology. Springfield: Charles C. Thomas, Publishers, 1961 (p. 17).
70. Pearson, H. A. and Vertrers, K. M., Site of Binding of Chromium-51 to Haemoglobin, *Nature*, 189 1019 (1961).
71. Malamos, B., Belcher, E. H., Gyftaki, E. and Pinopoulos, D., Radioactive Tracer Studies of Haemoglobin Synthesis, Erythropoiesis and Red Cell Destruction in Congenital Haemolytic Anaemias. Farr, L. E., Knipping, H. W. and Lewis, W. H., (Eds.), Clinical Aspects of Nuclear Medicine, Symposium with Special Reference to Cancer and Cardiovascular Diseases. Koln and Opladen: Westdeutscher Verlag. 1961 (p. 107).

72. Cohen, J. A. and Warrings, M. G. P., The Fate of P^{32} Labeled Di-isopropylfluorophosphate in the Human Body and Its Use as a Labeling Agent in the Study of the Turnover of Blood Plasma and Red Cells, *J. Clin. Invest.*, 33 459 (1954).
73. Klaus, M. and Ley, A. B., The Measurement of Erythrocyte Survival with P^{32} Tagged Di-isopropylfluorophosphate (DFP²²), *Clin. Res. Proc.*, 4 80 (1956).
74. Pollycove, M., Dal Santo, G. and Lawrence, J. H., Simultaneous Measurements of Erythrocyte, Luekocyte and Platelet Survival in Normal Subjects with Di-isopropylfluorophosphate (DFP²²), *Clin. Res. Proc.*, 6 45 (1958).
75. Lajtha, L. G. The Use of Isotopes in Haematology. Springfield: Charles C. Thomas, Publishers. 1961 (p. 68).
76. Krieger, H., Storaasli, J. P. Friedell H. L. and Holden, W. D., A Comparative Study of Blood Volume in Dogs, *Proc. Soc. Exp. Biol. Med.*, 68 511 (1948).
77. Storaasli, J. P., Krieger, H., Friedell H. L. and Holden, W. D., Use of Radioactive Iodinated Plasma Protein in the Study of Blood Volume, *Surg. Gynec. Obst.*, 91 458 (1950).
78. Schultz, A. L., Hammarsten, J. F., Heller, B. I. and Ebert, R. V. A. A Critical Comparison of the T-1824 Dye and Iodinated Albumin Methods for Plasma Volume Measurements *J. Clin. Invest.*, 32 107 (1953).
79. Kline, D. L. and Clifton, E. E. The Life Span of Leucocytes in the Human, *Sci.*, 115 9 (1952).
80. Osgood, E. E., Tivey, H., Davison, K. B., Seaman, A. J. and Li, J. G., The Relative Rates of Formation of New Leucocytes in Patients with Acute and Chronic Leukaemias Measured by the Uptake of Radioactive Phosphorous in the Isolated Deoxyribosenucleic Acid, *Cancer*, 5 331 (1952).
- 81.. Lajtha, L. G., Ellis, F. and Oliver, R., Isotope Uptake of Individual Cells: Uptake of S^{35} Sulphate by Human Bone Marrow Cells *in vitro*, *Brit. J. Cancer*, 7 401 (1953).
82. Ottesen, J., On the Age of Human White Cells in Peripheral Blood, *Acta Physiol. Scand.*, 32 75 (1954).
83. McCall M. S., Sutherland, D. A., Eisentraut, A. M. and Lanz, H., The Tagging of Leukaemic Leukocytes with Radioactive Chromium and Measurements of the *In Vivo* Cell Survival, *J. Lab. Clin. Med.*, 45 717 (1955).

84. Leekema, C. H. W. and Cohen, J. A., Determination of the Life Span of Human Blood Platelets Using Labelled Diisopropylfluorophosphate, *J. Clin. Invest.*, 35 964 (1956).
85. Hamilton, L. D., Carbon¹⁴ Labeling of DNA in Studying Hematopoietic Cells. Stohlman, F., (Ed.), *Kinetics of Cellular Proliferation*. New York: Grune and Stratton. 1959 (p. 151).
86. Athens, J. W., Mayer, A. M., Ashenbrucker, H., Cartwright, G. E. and Wintrobe, M. M., Leukokinetic Studies I. Method for labelling Leucocytes with Diisopropylfluorophosphate (DFP³²), *Blood*, 14 303 (1959).
87. Maurer, A. M., Athens, J. W., Warner, H. R., Ashenbrucker, H., Cartwright, G. E. and Wintrobe, M. M., An Analysis of Leukocyte Radioactivity Curves Obtained with Radioactive Diisopropylfluorophosphate (DFP³²). Stohlman, F., (Ed.), *Kinetics of Cellular Proliferation*. New York: Grune and Stratton, 1959 (p.231).
88. Lajtha, L. G., *The Use of Isotopes in Haematology*. Springfield: Charles C. Thomas, Publishers. 1961 (p.68).
89. Pritchard, W. H., MacIntyre, W. J., Schmidt, W. C., Brofman, B. L. and Moore, D. J., The Determination of Cardiac Output by a Continuous Recording System Utilizing Iodinated (I-131) Human Serum Albumin, *Circulation*, 6 572 (1952).
90. Veall, N., Pearson, J. D., Hanley, T. and Lowes, A. E., A Method for the Determination of Cardiac Output: Preliminary Report, in *Proc. Second Radioisotope Conf.* (Oxford, July 19-23, 1954), Vol. 1. New York: Academic Press, Inc. 1954 (p. 183).
91. Huff, R. L., Feller, D. D., Judd, O. J. and Bogardus, G. M., Cardiac Output of Man and Dogs Measured by in vivo Analysis of Iodinated (I-131) Human Serum Albumin, *Circ. Res.*, 3 564 (1955).
92. Pritchard, W. H., MacIntyre, W. J. and Moir, J. W., The Determination of Cardiac Output by the Dilution Method Without Arterial Coupling, *J. Lab. Clin. Med.*, 46 939 (1955).
93. Hansen, A. T., Haxholdt, B. F., Husfeldt, E., Lassen, N. A., Munck, O., Sorensen, H. R. and Winkler, K., Measurement of Coronary Blood Flow and Cardiac Efficiency in Hypothermia by Use of Radioactive Krypton 85, *Scandinav. J. Clin. & Lab. Invest.*, 8 18b (1956).
94. Rejali, A. M., McIntyre, W. J. and Friedell, H. L., A Radioisotope Method Visualization of Blood Pools, *Am. J. Roentgenol. Rad. Ther., Nucl. Med.*, 79 129 (1958).

95. Carter, B. L., Johnsen, S. E., Loeffler, R. K. and Southard, M. E., A Critical Evaluation of External Body Surface Counting in the Determination of Cardiac Output with Radioactive Isotopes, *Am. J. Roentgenol., Rad. Ther., Nucl. Med.*, 82 618 (1959).
96. Kellershohn, C., de Vernejoul, P. and Delaloye, B.: The Dilution of a Tracer in a System of Cavities in Series Traversed by a Pulsing Fluid. Application to Cardiac Hemodynamics, *Compt. rend.*, 252 1394 (1961).
97. Ludes, H. and Lehnert, G., *Radioisotope in der Herzdiagnostik*. Jena: Gustav Fischer Verlag. (1958).
98. Yudilevich, D., Transport of K^{42+} , Na^{24+} and I^{131-} by the Pulmonary Circulation. Calculations of Cardiac Output and Volume from Dilution Curves Obtained in the Canine Heart-Lung Preparation, *Circ. Res.*, 9 925 (1961).
99. Ludes, H. *Radioisotope in der Kardiologie*. Farr, L. E., Knipping, H. W. and Lewis, W. H., (Eds.), *Clinical Aspects of Nuclear Medicine Symposium with Special Reference to Cancer and Cardiovascular Diseases*. Koln and Opladen: Westdeutscher Verlag. 1961 (p.430).
100. Mena, I., Kattus, A. A., Greenfield, M. A. and Bennett, L. R., Effect of Coronary Blood Flow on Radioisotope Dilution Curves Measured by Precardial Scintillation Detection, *Circ. Res.*, 9 911 (1961).
101. Nylin, G., Silfverskiold, B. P., Lofstedt, S., Regnstrom, O. and Hedlund, S., Studies on Cerebral Blood Flow in Man, Using Radioactive-labelled Erythrocytes, *Brain* 83 293 (1960).
102. Nylin, G., Hedlund, S. and Regnstrom, O., Studies of the Cerebral Circulation with Labelled Erythrocytes in Healthy Man, *Circ. Res.*, 9 664 (1961).
103. Nylin, G., Hedlund, S. and Regnstrom, O., Studies on Cerebral Blood Flow in Man Using Radioactive-Labelled Erythrocytes. Farr, L. E., Knipping, H. W. and Lewis, W. H., (Eds.), *Clinical Aspects of Nuclear Medicine Symposium with Special Reference to Cancer and Cardiovascular Diseases*. Koln and Opladen: Westdeutscher Verlag, 1961 (p.39).
104. Taplin, G. V., Meredith, O. M. Jr., Kade, H. and Winter, C. C., The Radioisotope Renogram: An External Test for Individual Kidney Function and Upper Urinary Tract Potency, *J. Lab. Clin. Med.*, 48 886 (1956).
105. Winter, C. C., A Clinical Study of a New Renal Function Test: The Radioactive Diodrast Renogram, *J. Urol.*, 76 182 (1956).

106. Winter, C. C., Unilateral Renal Disease and Hypertension: Use of the Radioactive Diodrast Renogram as a Screening Test, *J. Urol.*, 78 107 (1957).
107. Taplin, G. V., Meredith, O. M., Jr., Winter, C. C. and Johnson, S., Rose Bengal and Iodopyracet as Radiodiagnostic Agents in Liver and Kidney Diseases, *Ann. N. Y. Acad. Sci.*, 78 872 (1959).
108. Witcofski, R. L., Whitley, J. E., Meschan, I. and Painter, W. E., A Method and Parameters for the Analysis of Renal Function by External Scintillation Detector Technic, *Radiology*, 76 621 (1961).
109. Eysell, K., and Franzen, F., Radioisotope in der Nierenfunktionsdiagnostik. Farr, L. E., Knipping, H. W. and Lewis, W. H., (Eds.), *Clinical Aspects of Nuclear Medicine Symposium with Special Reference to Cancer and Cardiovascular Diseases*. Kohn and Opladen: Westdeutscher Verlag. 1961 (p.483).
110. Kaltreider, N. L., Meneely, G. R., Allen, J. R. and Bale, W. F., Determination of the Volume of the Extracellular Fluid of the Body with Radioactive Sodium, *J. Exp. Med.*, 74 569 (1941).
111. Corsa, L., Jr., Olney, J. M. Jr., Steenburg, R. W., Ball, M. R. and Moore, F. D., The Measurement of Exchangeable Potassium in Man by Isotope Dilution, *J. Clin. Invest.*, 29 1280 (1950).
112. Forbes, G. E. and Perley, A., Estimation of Total Body Sodium by Isotopic Dilution, *J. Clin. Invest.*, 30 558 (1951).
113. Edelman, I. S., James, A. H., Brooks, L. and Moore, F. D., Body Sodium and Potassium. IV. The Normal Total Exchangeable Sodium; its Measurement and Magnitude, *Metabolism*, 3 530 (1954).
114. Farr, L. E., The Use of Radioactive Isotopes in the Study of Extracellular Space. *Radioisotopes in Medicine*, 1953. U. S. A. E. C., Washington, D. C. 1955 (469).
115. Anger, H. O. and Rosenthal, D. J., Scintillation Camera and Positron Camera, in *Medical Radioisotope Scanning*, in Proceedings of a Seminar jointly organized by the International Atomic Energy and the World Health Organization. Vienna. February 25-27 1959 (p.59).
116. Bender, M. A. and Blau, M., Photoscanning, in *Medical Radioisotope Scanning*, Proceedings of a Seminar jointly organized by the International Atomic Energy Agency and the World Health Organization. Vienna. February 25-27 1959 (p.31).

117. Johns, H. E. and Cedarlund, J. F., Basic Principles of Scintillation Counting, in Medical Radioisotope Scanning, Proceedings of a Seminar jointly organized by the International Atomic Energy and the World Health Organization. Vienna. February 25-27 1959 (p.41).
118. Kakehi, H., Problems of Collimation, in Medical Radioisotope Scanning, Proceedings of a Seminar jointly organized by the International Atomic Energy Agency and the World Health Organization. Vienna. February 25-27 1959 (p.13).
119. Mehl, H. G., The Distribution of a Pure Beta-Emitter in the Human Body. Problems and Preliminary Results of Bremsstrahlung measurements in vivo, in Medical Radioisotope Scanning, Proceedings of a Seminar jointly organized by the International Atomic Energy Agency and the World Health Organization. Vienna. February 25-27 1959 (p. 125).
120. Pochin, E. E., Profile Counting, in Medical Radioisotope Scanning, Proceedings of a Seminar jointly organized by the International Atomic Energy Agency and the World Health Organization. Vienna. February 25-27 1959 (p.143).
121. Mallard, J. R. and Peachey, C. J., Recent Developments in Radioisotope Techniques: A Symposium. IV, A Quantitative Automatic Body Scanner for the Localization of Radioisotopes In Vivo, Brit. J. Radiol., 32 652 (1959).
122. Frost, D. and Werkes, H., A New Procedure for Representation of Weakly-Storing Tissues in Gamma Scintigraphy, Strahlentherapie, 113 461 (1960).
123. Hughes, D., Hodt, H. J., Newbery, S. P. and Sbresni, R. C., An Automatic Clinical Scintillation Scanner for Large Areas, Brit. J. Radiol. 33 462 (1960).
124. Mac Intyre, W. J., Crespo, G. C. and Christie, J. H., The Use of the Counting Rate Profile in Radioisotope Scanning Techniques. J. Nucl. Med., 1 262 (1960).
125. Scheer, K. E. and zum Winkel, K., Scintillography in Diagnostics and Therapy, J. Belge Radiol., 43, 294 (1960).
126. Bonte, F. J., Krohmer, J. S., Tseng, C. H. and Baldwin, M. C. L., Scintillation Scanning in Differential Diagnosis, J. Am. Med. Assoc., 175 221 (1961).
127. Cohn, S. H., Love, R. A. and Gusmano, E. A., Zinc-65 in Reactor Workers, Sci., 133 1362 (1961).

128. Entzian, W., Phantom Studies in Scanning Diagnostics, Atom-praxis, 7 7 (1961).

129. Meneely, G. R., (Ed.) A Symposium on Radioactivity in Man, Whole Body Counting and Effects of Internal Gamma Ray-Emitting Radioisotopes. Springfield: Charles C. Thomas. (1961).

130. Lippincott, S. W., Cohn, S. H., Hamel, H., Fine, S. and Korman, S., Determination of Radioactively Labeled Globulin Turnover by the Direct Whole-Body Counting Technique, J. Clin. Invest., 40 697 (1961).

131. Lippincott, S. W., Cohn, S. H., Robertson, J. S. and Farr, L. E., In Vivo Measurement by the Whole-Body Gamma Spectrometer of the Degradation Rate of I-131 Labeled Normal Albumin, Lab. Invest., 10 481 (1961).

132. Taplin, G. V., Meredith, O. M., Jr., and Kade, H., The Radioactive (I-131-tagged) Rose Bengal Uptake-Excretion Test for Liver Function Using External Gamma-Ray Scintillation Counting Techniques. J. Lab. Clin. Med., 45 665 (1955).

133. Brown, C. H. and Glasser, O., Radioactive (I-131-tagged) Rose Bengal Liver Function Test, J. Lab. Clin. Med., 48 454 (1956).

134. Bender, M. A. and Blau, M., Detection of Liver Tumors with I¹³¹ Rose Bengal, in Medical Radioisotope Scanning, Proceedings of a Seminar jointly organized by the International Atomic Energy Agency and the World Health Organization. Vienna. February 25-27 1959 (p.83).

135. Donato, L., Becchini, M. P. and Panichi, S., Liver Scanning with Colloidal Radiogold, in Medical Radioisotope Scanning, Proceedings of a Seminar jointly organized by the International Atomic Energy Agency and the World Health Organization. Vienna. February 25-27 1959 (p.87).

136. Bolt, W., Lehnert, G., Zerlett, G. and Ritzel, F., Radioisotopes in Liver Diagnosis, Atomkernenergie, 4 271 (1959).

137. Dienstbier, Z., Andrysek, O., and Brousil, J., Splenoportal Isotope Circulography, Atompraxis, 6 219 (1960).

138. Englert, E. Jr., Burrows, B. A. and Ingelfinger, F. J., Differential Analysis of the Stages of Hepatic Excretory Function with Gamma Emitting Isotopes. II. Attempts to Alter Rate Phenomena, J. Lab. Clin. Med., 56 193 (1960).

139. Taylor, H. J., Woods, P. S. and Hughes, W. L., The Organization and Duplication of Chromosomes as Revealed by Autoradiographic Studies Using Tritium-Labeled Thymidine, Proc. Natl. Acad. Sci. U. S., 43 122 (1957).
140. Cronkite, E. P., Bond, V. P., Fliedner, T. M. and Rubini, J. R., The Use of Tritiated Thymidine in the Study of DNA Synthesis and Cell Turnover in Hemopoietic Tissues, Lab. Invest., 8 263 (1959).
141. Feinendegen, L. E., Bond, V. P. and Painter, R. B., Studies on the Interrelationship of RNA Synthesis, DNA Synthesis and Precursor Pool in Human Tissue Culture Cells Studied With Tritiated Pyrimidine Nucleosides, Exptl. Cell Research, 22 381 (1961).
142. Rubini, J. R., Keller, S., Wood, L. and Cronkite, E. P., Incorporation of Tritiated Thymidine into DNA after Oral Administration, Proc. Soc. Exptl. Biol. Med., 106 49 (1961).
143. Gothman, L., Venous Transport of Na^{22} from Healing Fractures in the Rabbit Tibia, Acta Radiol., 54 469 (1960).
144. Greenberg, E., Pazianos, A., Corey, K. R., Kenny, P., Laughlin, J.S., and Pearson, O. H., Radioactive Calcium (Ca^{47}) Tracer Studies in Patients with Bone Lesions, Conference on Research on the Radiotherapy of Cancer, Proceedings American Cancer Society, Inc. New York. 1961 (p. 158).
145. Tonna, E. A., and Cronkite, E. P., Use of Tritiated Thymidine for the Study of the Origin of the Osteoblast, Nature, 190 459 (1961).
146. Tonna, E. A. and Cronkite, E. P., Cellular Response to Fracture Studied with Tritiated Thymidine, J. Bone & Joint Surg., 43A 352 (1961).
147. Morrow, P. E., Hodge, H. C., Neuman, W. F., Elliott, E. A., Blauchet, W. J. Jr., Fassett, D. W., Birk, R. E., and Mandrodt, S. J., The Gastrointestinal Non-Absorption of Sodium Cellulose Sulfate Labeled with S^{35} , J. Pharmacol., 105 273 (1952).
148. Stanley, M. M. and Thannhauser, S. J., The Absorption and Disposition of Orally Administered I-131 Labeled Neutral Fat in Man, J. Lab. Clin. Med., 34 1634 (1949).
149. Chinn, A. B., Lavik, P. S., Babb, L. I., Buckaloo, G. W., Stitt, R. M. and Abbott, W. E., Blood Isotope Levels Following a Test Meal of I-131 Labeled Protein, J. Lab. Clin. Med., 42 377 (1953).

150. Baylin, G. J., Sanders, A. P., Isley, J. K., Singleton, W., Hymans, J. C., Johnston, D. H. and Ruffin, J. M., I-131 Blood Levels Correlated with Gastric Emptying Determined Radiographically, 1 Fat Test Meal, Proc. Soc. Exper. Biol. and Med., 89 54 (1955).
151. Malm, J. R., Reemtsma, K. and Barker, H. G., Comparative Fat and Fatty Acid Intestinal Absorption Test Utilizing Radioiodine Labeling -- Results in Normal Subjects, Proc. Soc. Exp. Biol. and Med., 92 471 (1956).
152. Ruffin, J. W., Shingleton, W. W., Baylon, G. J., Hymans, J. C., Isley, J. K., Sanders, A. P. and Sohmer, M. F., Jr., I-131 Labeled Fat in the Study of Intestinal Absorption, New England J. Med., 255 594 (1956).
153. Sanders, A. P., Isley, J. K., Sharpe, K., Baylin, G. J., Shingleton, W. W., Hymans, J. C., Ruffin, J. M., and Reeves, R. J., Radioiodine Recovery in Feces Following an I-131 Labeled Fat Test Meal, Am. J. Roentgenol., 75 386 (1956).
154. Beres, P., Wenger, J. and Kirsner, J. B., The Use of Triolein in the Study of Absorptive Disorders in Man, Gastroenterology, 32 1 (1957).
155. Isley, J. K., Sanders, A. P., Baylin G. J., Sharpe, K. W., Hymans, J. C., Ruffin, J. M., Shingleton, W. W. and Wilson Jr., J. R., Use of I-131 Labeled Oleic Acid in Study of Gastrointestinal Function, Proc. Soc. Exp. Biol. and Med., 94 307 (1957).
156. McKenna, R. D., Bourne, R. H. and Matzko, A., The Use of I-131 Labeled Fat in the Study of Fat Digestion and Absorption in Normal Individuals and in Patients with Diseases of Fat Absorption, Gastroenterology, 32 17 (1957).
157. Duffy, B. J., Jr. and Turner, D. A., The Differential Diagnosis of Intestinal Malabsorption with I-131 Fat and Fatty Acid, Ann. Int. Med., 48 1, (1958).
158. Grossman, M. I., and Jordan, P. N., The Radio-iodinated Triolein Test for Steatorrhea, Gastroenterology, 34 892 (1958).
159. Kaplin, E., Edidin, G. D., Fruin, R. C. and Baker, L. A., Intestinal Absorption of Iodine (I-131) Labeled Triolein and Oleic Acid in Normal Subjects and in Steatorrhea, Gastroenterology, 34 901 (1958).

160. Schlüssel, H., Beitrag zur Frage der Bildung von Serumeiweiss durch die Darmmucosa und zur Transportfunktion des Serumalbumins für Schwefelamosauren. Farr, L. E., Knipping, H. W. and Lewis, W. H. (Eds.), *Clinical Aspects at Nuclear Medicine Symposium with Special Reference to Cancer and Cardiovascular Diseases* Köln und Opladen: Westdeutscher Verlag. 1961 (p. 443).
161. Tolbert, B. M., Lawrence, J. H., and Calvin, M., Respiratory Carbon-14 Patterns and Physiological State, in *International Conference on the Peaceful Uses of Atomic Energy Proceeding*. Genève. 1955. Vol. 12 New York: United Nations. 1956 (p.281).
162. Shreeve, W. W., Pathways of Carbohydrate Formation in Man. I. Isotope Dilution Distribution in Glucose from Non-Diabetic Subjects Given 1-C¹⁴ Acetate, *J. Clin. Invest.*, 37 999 (1958).
163. Shreeve, W. W. and Hennes, A. R., Pathways of Carbohydrate Formation in Man. II. The Effect of Diabetes and Glucocorticoid Administration on Isotope Distribution in Glucose from Subjects Given 1-C¹⁴-Acetate, *J. Clin. Invest.*, 37 1006 (1958).
164. Hennes, A. R. and Shreeve, W. W., Hormonal Effects of C¹⁴-Acetate Metabolism in the Human, *Proc. Soc. Exptl. Biol. Med.*, 100 246 (1959).
165. Shreeve, W. W., Labeling of Glucose, Ribose and Desoxyribose by 1- and 2-C¹⁴-Glycine in Regenerating Rat Liver, *J. Biol. Chem.* 234 246 (1959).
166. Shreeve, W. W., Hennes, A. R. and Schwartz, R., Production of C¹⁴O₂ from 1-and 2-C¹⁴-Acetate by Human Subjects in Various Metabolic States, *Metabolism*, 8 741 (1959).
167. Shreeve, W. W. and Tocci, P. M., Conversion of 1-C¹⁴-Acetate to Ketone Bodies in Diabetics, *Metabolism*, 10 522 (1961).
168. Tolbert, B. M., Kirk, M. and Baker, E. M., Continuous C¹⁴O₂ and CO₂ Excretion Studies in Experimental Animals, *Am. J. Physiol.*, 135 269 (1956).
169. LeRoy, G. V., Okita, G. T., Tocus, E. C. and Charleston, D., Continuous Measurements of Specific Activity of C¹⁴O₂ in Expired Air, *Internat. J. Appl. Radiation and Isotopes*, 7 273 (1960).
170. Hornicke, H., An Apparatus for Continuous Measurement of C¹⁴O₂ in the Exhaled Air of Medium-Sized and Large Domestic Animals, *Atompraxis* 7 295 (1961).

171. De Meutter, R. C. and Shreeve, W. W., Carbon-14 as a Tracer for Metabolic Studies in Man. Farr, L. E., Knipping, H. W. and Lewis, W. H., (Eds.), Clinical Aspects of Nuclear Medicine Symposium with Special Reference to Cancer and Cardiovascular Diseases. Koln und Opladen: Westdeutscher Verlag 1961 (p. 164).
172. Heinle, R. W., Welch, A. D., Scharf, V., Meacham, G. C. and Prusoff, W. H., Studies of Excretion (and Absorption) Co⁶⁰ Labeled Vitamin B₁₂ in Pernicious Anemia, Trans. Assoc. Amer. Physics, 65 214 (1952).
173. Meyer, L. M., Oral Administration of Co⁶⁰ Vitamin B₁₂ in pernicious Anemia, Proc. Soc. Exp. Biol. Med., 82 490 (1953).
174. Schilling, R. F., Intrinsic Factor Studies. II. The Effect of Gastric Juice on the Urinary Excretion of Radioactivity After the Oral Administration of Radioactive Vitamin B₁₂, J. Lab. Clin. Med., 42 860 (1953).
175. Swenseid, M. E., Halsted, J. A. and Libby, R. L., Excretion of Cobalt⁶⁰ Labeled Vitamin B₁₂ after Total Gastrectomy, Proc. Soc. Exp. Biol. Med. 83 226 (1953).
176. Best, W. R., White, W. F., Louis, J. and Limarzi, L. R., Experiences with the Schilling Test Using Co⁶⁰ Labeled Vitamin B₁₂ in Pernicious Anemia, Sprue and Other Conditions, J. Lab. Clin. Med., 44 767 (1954).
177. Bradley, J. E., Smith, E. L., Baker, S. J. and Mollin, D. L., The Use of the Radioactive Isotope of Cobalt (Co⁵⁸) for the Preparation of Labeled Vitamin B₁₂, Lancet ii 476 (1954).
178. Callender, S. T., Turnbull, A. and Wakisaka, G., Estimation of Intrinsic Factor of Castle by Use of Radioactive Vitamin B₁₂, Brit. Med. J., 1 10 (1954).
179. Glass, G. B. J., Boyd, L. J., Gellin, G. A. and Stephanson, L., Uptake of Radioactive Vitamin B₁₂ by the Liver in Humans: Test for Measurement of Intestinal Absorption of Vitamin B₁₂ and Intrinsic Factor Activity, Arch. Biochem. Biophys., 51 251 (1954).
180. Glass, G. B. J., Boyd, L. J. and Stephanson, L., Intestinal Absorption of Vitamin B₁₂ in Humans as Studies by Isotope Technique, Proc. Soc. Exp. Biol. Med., 86 522 (1954).
181. Baker, S. J. and Mollin, D. L., The Relationship Between Intrinsic Factor and the Intestinal Absorption of Vitamin B₁₂, Brit. J. Haemat. 1 46 (1955).

182. Baker, S. J. and Mollin, D. L., The Relationship Between Intrinsic Factor and Vitamin B₁₂ Absorption, *Rev. d'hematologie*, 10 180 (1955).
183. Callender, S. T. and Evans, J. R., The Urinary Excretion of Labelled Vitamin B₁₂, *Clin. Sci.*, 14 295 (1955).
184. Ellenbogen, L., Williams, W. L., Rabiner, S. F. and Lichtman, H.C., An Improved Urinary Excretion Test as an Assay for Intrinsic Factor, *Proc. Soc. Exp. Biol. Med.*, 89 357 (1955).
185. Glass, G. B. J., Boyd, L. J. and Gellin, G. A., Surface Scintillation Measurements in Humans at the Uptake of Parenterally Administered Radioactive Vitamin B₁₂, *Blood*, 10 95 (1955).
186. Mollin, D. L. and Baker, S. J., The Absorption and Excretion of Vitamin B₁₂ in Man, *Biochem. Soc. Symp.*, 13 52 (1955).
187. Booth, V. C. and Mollin, D. L., Plasma, Tissue and Urinary Radioactivity after Oral Administration of ⁵⁶Co Labelled Vitamin B₁₂, *Brit. J. Haemat.*, 2 223 (1956).
188. Doscherholmen, A. and Hagen, P. S., Radioactive Vitamin B₁₂ Absorption Studies: Results of Direct Measurements of Radioactivity in the Blood, *J. Clin. Invest.*, 35 699 (1956).
189. Mollin, D. L., Pitney, W. R., Baker, S. J. and Bradley, J. E., The Plasma Clearance and Urinary Excretion of Parenterally Administered ⁵⁸Co B₁₂, *Blood*, 11 31 (1956).
190. Rath, C. E., McCurdy, P. R., Duffy, B. J. Jr., and Howley, J. R., Value and Limitations of Cobalt-60 B₁₂ Test, *Am.J. Med.*, 20 954 (1956).
191. Goldberg, S. R., Trivedi, B. K. and Oliver, L., Radioactive Vitamin B₁₂ Studies: Experience With the Urinary Excretion Test and the Measurement of Absorbed Plasma Activity, *J. Lab. Clin. Med.*, 49 583 (1957).
192. Meyer, L. M., Bertcher, R. W. and Cronkite, E. P., Serum ⁶⁰Co Vitamin B₁₂ Binding Capacity in Some Hematologic Disorders, *Proc. Soc. Exp. Biol. Med.*, 96 360 (1957).
193. Miller, A., Corbus, H. R. F., and Sullivan, J. F., The Plasma Disappearance, Excretion, and Tissue Distribution of Cobalt-60 Labelled Vitamin B₁₂ in Normal Subjects and Patients with Chronic Myelogenous Leukemia, *J. Clin. Invest.* 36 12 (1957).

194. Mollin, D. L., Booth, C. E. and Baker, S. J., The Absorption of Vitamin B₁₂ in Control Subjects, in Addisonian Pernicious Anemia and in the Malabsorption Syndrome, *Brit. J. Haemat.*, 3 412 (1957).
195. Pollycove, M. and Apt, L., Absorption, Elimination, and Excretion of Orally Administered Vitamin B₁₂ in Normal Subjects and in Patients with Pernicious Anemia, *New England J. Med.*, 255 207 (1956).
196. Willigan, D. A., Cronkite, E. P., Meyer, L. M. and Noto, S. L., Biliary Excretion of Co⁶⁰-Labeled Vitamin B₁₂ in Dogs, *Proc. Soc. Exptl. Biol. Med.*, 99 81 (1958).
197. Cronkite, E. P., Henley, E., Driscoll, D. H., Meyer, L. M., Dohan, F. C., Jr., Rubini, J. R. and Wolins, W., Studies on the Kinetics of Intravenously Injected ⁶⁰Cobalt-Labeled Vitamin B₁₂ in Man, *Haematol. Latina*, 2 265 (1959).
198. Reizenstein, P. G., Cronkite, E. P., Meyer, L. M., and Usenik, E.A., Lymphatics in the Intestinal Absorption of Vitamin B₁₂ and Iron, *Proc. Soc. Exptl. Biol. Med.*, 105 233 (1960).
199. Rosenblum, C., Willigan, D. A., Meriwether, H. T. and Cronkite, E.P., Stability of Injected Vitamin B₁₂-Co⁶⁰ and Vitamin B₁₂ Content of Dog Liver, *Proc. Soc. Exptl. Biol. Med.*, 105 142 (1960).
200. Germamm, D. R., Cobalt⁶⁰ Tagged B₁₂ as a Diagnostic Tool in the General Isotope Laboratory, *Am. J. Roentgenol., Rad. Ther., Nucl. Med.*, 85 59 (1961).
201. Schwartz, I. L. - In preparation.
202. Fong, C. T. O., Silver, L., Christman, D. R. and Schwartz, I. L., On the Mechanism of Action of the Antidiuretic Hormone (vasopressin), *Proc. Natl. Acad. Sci. U. S.*, 46 1273 (1960).
203. Rasmussen, H., Schwartz, I. L., Schoessler, M. A. and Hochster, G., Studies on the Mechanism of Action of Vasopressin, *Proc. Natl. Acad. Sci. U. S.*, 46 1278 (1960).
204. Perlmutter, M., Slater, S. L., and Attie, J., Method for Pre-operative Differentiation Between Benign and the Possibly Malignant Solitary Non-Toxic Thyroid Nodule, *J. Clin. Endocrin. and Metabol.*, 14 672 (1954).
205. Johnson, P. C. and Beierwaltes, W. H., Reliability of Scintiscanning Nodular Goiters in Judging the Presence or Absence of Carcinoma, *J. Clin. Endocrinol. and Metabol.* 15 865 (1955).

206. Hummon, I. F. and Magalotti, M. F., Substernal Thyroid Identified by a Simple Radioiodine (I-131) Procedure, *Am. J. Roentgenol.*, 75 1144 (1956).
207. McConahey, W. M., Owen, C. A. Jr. and Keating, F. R. Jr., Clinical Appraisal of Radioiodine Tests of Thyroid Function, *J. Clin. Endocrinol. and Metab.*, 16 724 (1956).
208. Perlmutter, M. and Slater, S. L., Which Nodular Goiters Should "Be Removed?" A Physiologic Plan for the Diagnoses and Treatment of Nodular Goiter, *New Eng. J. Med.*, 255 65 (1956).
209. Sinclair, W. K., Abbatt, J. D., Farran, H. E., A., Harriss, E. B. and Lamerton, L. F., A Quantitative Autoradiographic Study of Radioiodine Distribution and Dosage in Human Thyroid Glands, *Brit. J. Radiol.*, 29 36 (1956).
210. Mitchell, M. L. Yamazaki, E. and Burrows, B. A., Impaired Iodine Metabolism in Functional Thyroid Carcinoma, *Proc. Ann. Meeting Endocrine Soc.* (1957).
211. Anger, H. O., Scintillation Camera, *Rev. Sci. Instruments*, 29 27 (1958).
212. Hofer, R. and Vetter, H., Scanning in Non-Cancerous Thyroid Disease, in *Medical Radioisotope Scanning. Proceedings of a Seminar Jointly Organized by the International Atomic Energy Agency and the World Health Organization, Vienna. February 25-27 1959 (p.213).*
213. Bauer, F. K., Scanning in Thyroid Cancer, in *Medical Radioisotope Scanning Proceedings of a Seminar Jointly Organized by the International Atomic Energy Agency and the World Health Organization. Vienna. February 25-27 1959 (p. 225).*
214. Merkulov, M. F., Modestov, V. K., Maslov, N. P. and Poberii, I. A., Distribution of Radioactive Iodine in Tumours of the Thyroid Gland, *Problems Oncol. (U. S. S. R.)*, 6 1275 (1960).
215. Pircher, F. J., Sitterson, B. W. and Andrews, G. A., The ORINS Linear Scanner in Diagnosis and Treatment of Thyroid Carcinoma with Iodine-131, *J. Nucl. Med.*, 1 251 (1960).
216. Seed, L., A Surgeon Views Radioactive Iodine and the Thyroid Problem, *Southern Med. J.*, 53 424 (1960).

217. Brucer, M., Anger, H. O., Bell, P. R., Francis, J. E., Harris, C.C., Morris, A. C., Aronow, S., Kyker, G. C., Ross, D. A., and Andrews, G. A., The Development of Radioisotopic Scanning, in 87th Congress Hearings, Applications of Radioisotopes and Radiation in the Life Sciences. Washington, D. C.: Government Printing Office 1961 (p.402).
218. Kutzin, H., Möglichkeiten und Grenzen der Schilddrüsendiagnostik mit Iod¹³¹. Farr, L. E., Knipping, H. W. and Lewis, W. H., (Eds), Clinical Aspects of Nuclear Medicine Symposium with Special Reference to Cancer and Cardiovascular Diseases. Köln und Opladen: Westdeutscher Verlag 1961 (p. 406).
219. Aronow, S., Thors, R. and Brownell, G. L., Positron Scanning of Liver and Spleen, in Medical Radioisotope Scanning Proceedings of a Seminar Jointly Organized by the International Atomic Energy Agency and the World Health Organization. Vienna. February 25-27 1959 (p. 105).
220. Winkelman, J. W., Wagner, H. N., McAfee, J. G. and Mozley, J. M., Visualization of the Spleen in Man by Radioisotope Scanning, Radiology, 75 465 (1960).
221. Johnson, P. M. and Herion, J. C., Technical Consideration in Scintillation Scanning of the Human Spleen, Radiology, 76 438 (1960).
222. Johnson, P. M., Wood, E. H. and Moring, S. L., Splenic Scintillation Scanning, Am. J. Roentgenol., Rad. Ther., Nucl. Med., 86 757 (1961).
223. Moore, G. E., Use of Radioactive Diidofluorescein in Diagnosis and Localization of Brain Tumors, Sci., 107 569 (1948).
224. Erickson, T. C., Larson, F. and Gordon, E. S., The Uptake of Radioactive Phosphorous by Malignant Brain Tumors, J. Lab. and Clin. Med., 34 537 (1949).
225. Selverstone, B., Solomon, A. K., and Sweet, W. H., Location of Brain Tumors by Means of Radioactive Phosphorous, J. A. M. A., 140 227 (1949).
226. Selverstone, B. and White, J. C., Evaluation of the Radioactive Mapping Technique in the Surgery of Brain Tumors, Ann. Surg., 134 387 (1951).
227. Selverstone, B., Sweet, W. H. and Ireton, R. J., Radioactive Potassium a New Isotope for Brain Tumor Localization, Surgical Forum, 36th Congress, 1950, 371 (1951).

228. Susen, A. F., Small, W. T., and Moore, F. D., Studies on the External Diagnostic Localization of Brain Lesions Using Radioactive Potassium, *Surgical Forum*, 36th Congress. 1950, 362 (1951).
229. Schneider, R. C., Pantek, H., Freeman, D. G. and Farris, R. G., Radioactive Phosphorous in the Localization of Brain Tumors, *J. Mich. State M. Soc.*, 54 434 (1955).
230. Chou, S. N., Aust, J. B., Moore, G. E. and Peyton, W. T., Radio - active Iodinated Human Serum Albumin as a Tracer Agent for Diagnosing and Localizing Intracranial Lesions, *Proc. Soc. Expt. Biol. Med.*, 77 193 (1951).
231. Chou, S. N., Moore, G. E. and Marvin, J. F., Localization of Brain Tumors with Radiiodide, *Sci.*, 115 119 (1952).
232. Dunbar, H. S., Localization of Brain Tumors with Radioactive Iodinated Serum Albumin, *Surg. Gynec. Obstet.*, 98 433 (1954).
233. Planiol, T., Diagnosis of Intracranial Lesions by Gamma - Encephalography, Using Human Serum Albumin Labelled With Iodine-131, in *Medical Radioisotope Scanning, Proceedings of a Seminar Jointly Organized by the International Atomic Energy Agency and the World Health Organization. Vienna. February 25-27 1959 (p.189).*
234. Bell, R. L., Concentration of Labelled Tri-Iodothyrenine and Radioactive Albumin in Human Cerebral Neoplasms, *J. Nucl. Med.*, 1 180 (1960).
235. McAfee, J. G. and Taxdal, D. R., Comparison of Radioisotope Scanning With Cerebral Angiography and Air Studies in Brain Tumor Localization, *Radiology*, 77 207 (1961).
236. Wrenn, F. R., Jr., Good, M. L. and Handler, P., Use of Positron-Emitting Radioisotopes for Localization of Brain Tumors, *Sci.* 113 525 (1951).
237. Wrenn, F. R., Jr. and Good, M. L., The Use of Radioisotopes for the Localization of Brain Tumors, *North Carolina Med. J.*, 13 231 (1952).
238. Brownell, G. L. and Sweet, W. H., Localization of Brain Tumors with Positron Emitters, *Nucleonics*, 11 40 (1953).
239. Benda, P., David, M. and Constants, J., Arsenic Radioactif 76 et Detection Preoperative des Tumeurs Cerebrales, *Rev. nuerol.*, 89 101 (1953).

240. Sweet, W. H. and Brownell, G. L., Localization of Intracranial Lesions by Scanning with Positron-Emitting Arsenic, *J. A. M. A.* 157 1183 (1955).
241. Brownell, G. L. and Sweet, S. H., Scanning of Positron-Emitting Isotopes in Diagnosis of Intracranial and Other Lesions, *Acta Radiol.*, 46 425 (1956).
242. Bagnall, H. J., Benda, P., Brownell, G. L. and Sweet, W. H., Positron-Scanning With Copper-64 in the Diagnosis of Intracranial Lesions. Partition of Copper-64 Versenate in, and Excretion from, the Body, *J. Neurosurg.*, 15 411 (1958).
243. Sweet, W. H., Mealey, J., Jr., Brownell, G. L. and Aronow, S., Coincidence Scanning With Positron-Emitting Arsenic or Copper in the Diagnosis of Focal Intracranial Disease, in *Medical Radioisotope Scanning, Proceedings of a Seminar Jointly Organized by the International Atomic Energy Agency and the World Health Organization. Vienna. February 25-27 1959 (p.163).*
244. Sokolova, N. V., The Biological Action and Use in Medicine of Fast Electrons, *Med. Radiol. (U. S. S. R.)*, 5 83 (1961).
245. Fowler, P. H. and Perkins, D. H., The Possibility of Therapeutic Applications of Beams of Negative - Mesons, *Nature*, 189 524 (1961).
246. Teplitz, R., Fox, B. W., Littman, M. S. and Littman, A., Intra-gastric Beta Irradiation with Ru-Rh¹⁰⁶ in Human Subjects: Results with Single Doses, *J. Nucl. Med.*, 2 187 (1961).
247. Keston, A. S., Ball, R. P., Frantz, V. K. and Palmer, W. W., Storage of Radioactive Iodine in Metastasis from Thyroid Carcinoma, *Sci.*, 95 362 (1942).
248. Seidlin, S. M., Marinelli, L. D. and Oshry, E., Radioactive Iodine Therapy: Effect on Functioning Metastases of Adrenocarcinoma of the Thyroid, *J. A. M. A.*, 132 838 (1946).
249. Fitzgerald, P. J. and Foote, F. W., Jr., Function of Various Types of Thyroid Carcinoma as Revealed by Radioautographic Demonstration of Radioactive Iodine (I-131), *J. Clin. Endocrinol.*, 9 1153 (1949).
250. Seidlin, S. M., Oshry, E. and Yalow, A. A., Spontaneous and Experimentally Induced Uptake of Radioactive Iodine in Metastases From Thyroid Carcinoma: Preliminary Report, *J. Clin. Endocrinol.*, 8 423 (1948).

453 243

251. Rawson, R. W., Marinelli, L. D., Skanse, B. N., Trunnell, J. and Fluharty, R. G., Effect of Total Thyroidectomy on the Function of Metastatic Thyroid Cancer, *J. Clin. Endocrinol.*, 8 826 (1948).
252. Rall, J. E., Miller, W. M., Foster, C. G., Peacock, W. and Rawson, R. W., The Use of Thiouracil in the Treatment of Metastatic Carcinoma of the Thyroid with Radioiodine, *J. Clin. Endocrinol.*, 11 1273 (1951).
253. Money, W. L., Fitzgerald, P. J., Godwin, J. T. and Rawson, R. W., The Effect of thiouracil on the Collection of Radioactive Iodine in Experimentally Induced Thyroid Tumors, *Cancer*, 6 111 (1953).
254. Sturgeon, C. T., Davis, F. E., Catz, B., Petit, D. and Starr, P., Treatment of Thyroid Cancer Metastases with TSH and I-131 During Thyroid Hormone Medication, *J. Clin. Endocrinol.*, 13 1391 (1953).
255. Collet, R., Tubiana, M. and Dutreix, J., Problems of Dosimetry Posed by the Utilization of Radioactive Iodine in Treatment of Cancer of the Thyroid, *J. Radiol. d'Electro*, 35 1 (1954).
256. Rawson, R. W., Radioiodine Therapy, The Thyroid. Werner, S. C., (Ed.), New York: Hoeber-Harper, 1955.
257. Maloof, F., Vickery, A. L. and Rapp, B., Evaluation of Various Factors Influencing Treatment of Metastatic Thyroid Carcinoma with I-131, *J. Clin. Endocrinol.*, 16 1 (1956).
258. Thomas, C. G., Jr., Hormonal Treatment of Thyroid Cancer, *J. Clin. Endocrinol.*, 17 232 (1957).
259. Rawson, R. W., Rall, J. E. and Robbins, J., Uses and Misuses of Radioactive Iodine in the Treatment of Cancer of the Thyroid, *Arch. Int. Med.* 92 299 (1953).
260. McDermott, M. V., Jr., Morgan, W. S., Hamlin, E., Jr. and Cope, O., Cancer of the Thyroid, *J. Clin. Endocrinol.*, 14 1336 (1954).
261. Hilton, G., The Role of Radioactive Iodine in the Treatment of Carcinoma of the Thyroid, *Brit. J. Radiol.*, 29 297 (1956).
262. Kutzin, H., Möglichkeiten und Grenzen der Schilddrüsendiagnostik mit Jod^{131} . Farr, L. E., Knipping, H. W. and Lewis, W. H., (Eds.), *Clinical Aspects of Nuclear Medicine Symposium With Special Reference to Cancer and Cardiovascular Diseases*. Köln und Opladen: Westdeutscher Verlag. 1961 (p.406).

263. Dudley, H. C., Imrie, G. W., Jr. and Istock, J. T., Deposition of Radiogallium (Ga-72) in Proliferating Tissues, *Radiology*, 55 571 (1950).
264. King, E. R., Mason, M. W., Messinger, H. B. and Dudley, H. C., A Preliminary Report on the Use of Gallium 72 in Clinical Tracer Studies, *Radiology*, 59 844 (1952).
265. Brucer, M., Andrews, G. A. and Bruner, H. D., A Study of Gallium 72. Summary and Conclusions, *Radiology*, 61 534 (1953).
266. Wolins, W. and Bond, V. P., Hematologic Findings in Human Beings Given Therapeutic Doses of Gallium-72, *Blood*, 13 865 (1958).
267. Tucker, F. R., The Use of Radioactive Phosphorous in the Diagnosis of Avascular Necrosis of the Femoral Head, *J. Bone and Joint Surgery*, 32B 100 (1950).
268. Arden, G. P. and Veall, N., The Use of Radioactive Phosphorous in Early Detection of Avascular Necrosis in the Fractured Neck in the Femur, *Proc. Royal Soc. Med.*, 46 344 (1953).
269. Tivey, H., The Prognosis for Survival in Chronic Granulocytosis and Lymphocytic Leukemia, *Am. J. Roentgenol.*, 72 68 (1954).
270. Firkin, B. G. and Williams, W. J., The Incorporation of Radioactive Phosphorous into the Phospholipids of Human Leukemic Leucocytes and Platelets, *J. Clin. Invest.*, 40 423 (1961).
271. Bloom, H. J. G., Treatment of Carcinoma of the Bladder, A Symposium. I. Treatment by Interstitial Irradiation Using Tantalum 182 Wire, *Brit. J. Radiol.*, 33 471 (1960).
272. Pavlova, L. I., Interstitial Radium Therapy of Malignant Tumours With the Aid of Nylon Tubes Containing Radiocobalt Granules, *Vestnik Rentgenol. i. Radiol.* 35 34 (1960).
273. Suit, H. D., Lloyd, R. S., Andrews, J. R. and Sneider, S. E., Technique for Intracavity Irradiation of the Nasopharynx, *Am. J. Roentgenol., Rad. Ther., Nucl. Med.*, 84 629 (1960).
274. Bloedorn, F. G., Cuccia, C. A. and Mercado, R., Jr., The Place of Interstitial Gamma-ray Emitters in Radiation Therapy, *Am. J. Roentgenol., Rad. Ther., Nucl. Med.*, 85, 407 (1961).
275. Bompiani, C., Alessandri, R., Fanucci, A., Loassess, A. and Marzano, E., Clinical Application of Hypophysectomy With Y^{90} , *Nuntius Radiol.*, 27 85 (1961).

276. Whitley, J. E., Blake, D. D., Witcofski, R. L., and Meschan, I., The Use of a Vaginal Applicator as an Adjunct to Treatment of Carcinoma of the Cervix, *Am. J. Roentgenol., Rad. Ther., Nucl. Med.*, 85 29 (1961).
277. Andrews, G. A., Knisely, R. M., Palmer, E. L. and Kretchmar, A.L., Therapeutic Usefulness of Radioactive Colloids, Comparative Value of Gold-198, Chromic Phosphate (P-32), Yttrium-90, and Lutecium-177 in Proceedings of the International Conference on the Peaceful Uses of Atomic Energy. Geneva. 1955. Vol. 10, New York: United Nations, 1956 (p.122).
278. Muller, J. H., Weitere, Entwicklung der Therapie von Peritonealcarcinosen bei ovarial carcinoma mit kunstlicher Radioaktivitat, *Gynaecologia*, 129 289 (1950).
279. Seaman, W. B., Sherman, A. I. and Bonebroke, M., Radioactive Gold in the Treatment of Malignant Effusions, *J. A. M. A.*, 153 630 (1953).
280. Simon, H., Radioactive Gold Treatment: Results in 35 Effusions Due to Cancer, *J. Mt. Sinai Hosp.*, 22 96 (1955).
281. Moses, C., Kent, E. and Boatman, J. B., Experimental and Clinical Studies with Radioactive Colloidal Gold in the Therapy of Serous Effusions Arising from Cancer, *Cancer* 3 417 (1955).
282. Muller, J. H., Experiences Since 1945 With Intraperitoneal and Intraplural Application of Artificially Radioactive Isotopes (Zn-63 and Au-198) in Carcinosis Originating in the Ovary, *Schweiz Med. Wchnschr.*, 84 509 (1954).
283. Neukon, S., Rivier, J. and Lerch, P., Effect of Radioactive Colloidal Gold in Plural and Peritoneal Effusions, *Schweiz Med. Wchnschr.*, 84 512 (1954).
284. Rosenthal, D. J. and Lawrence, J. H., Radioisotopes in Medicine. Claus, W. D., (Ed.), Radiation Biology and Medicine. Reading: Addison-Wesley Publishing Co., Inc. 1958 (p. 501).
285. Keetel, W. C. and Elkins, H. B., Experience With Radioactive Colloidal Gold in the Treatment of Ovarian Carcinoma, *Am. J. Obst.*, 71 553 (1956).
286. The Effects of Isotopic Radiation on Physiology and Histology of Body Systems, and the Exploration of the Use of Short-lived Radioactive Isotopes for Medical Purposes, Annual Report, July, BNL 246 (AS-7) 56 (1953).

287. Andrews, G. A., Root, S. W., Kerman, H. D. and Bigelow, R. R., Intracavitary Colloidal Radiogold in the Treatment of Effusions Caused by Malignant Neoplasms, *Ann. Surg.*, 137 375 (1953).
288. Andrews, G. A., Treatment of Pleural Effusion with Radioactive Colloids. Therapeutic Use of Artificial Radioisotopes. Hahn, P. F., (Ed.), New York: John Wiley and Sons, Inc. 1956 (p.295).
289. Colby, M. Y., Jr., Intracavitary Radioactive Colloidal Gold in the Treatment of Malignant Pleural Effusions, *Med. Clin. N. America*, 38 1133 (1954).
290. Kligerman, M. M. and Habif, D. V., The Use of Radioactive Gold in the Treatment of Effusion Due to Carcinomatosis of the Pleura and Peritoneum, *Am. J. Roentgenol.*, 74 651 (1955).
291. Hahn, P. F., Tumor Therapy by Direct Infiltration of Radioactive Colloidal Metallic Gold. A Manual of Artificial Radioisotope Therapy. New York: Academic Press, Inc. 1951 (p.186).
292. Walton, R. J. and Sinclair, W. K., Radioactive Solutions (Na-24 and Br-82) in the Treatment of Carcinoma of the Bladder, *Brit. Med. Bull.*, 8 158 (1952).
293. Hahn, P. F. and Carothers, E. L., Lymphatic Drainage Following Intrabronchial Instillation of Silver-coated Radioactive Gold Colloids in Therapeutic Quantities, *J. Thoracic. Surg.*, 25 265 (1953).
294. Crainz, F., Yttrium-90 for Intrauterine Pure Beta-ray Therapy of Climacteric Menorrhagia, in Second Radioisotopes Conf. Oxford. July 19-23, 1954. New York: Academic Press, Inc. 1954 (p. 11).
295. Allen, W. M., Sherman, A. I. and Arneson, A. N., Further Results Obtained in the Treatment of Cancer of the Cervix with Radiogold: A Progress Report, *Am. J. Obstet. Gynec.*, 70 786 (1955).
296. Vermotten, V. and Maxfield, J. G. S., The Use of Radioactive Cobalt in Nylon Sutures in the Treatment of Bladder Tumors: Technique and Case Reports, *J. Urol.*, 74 767 (1955).
297. Chevallier, A. and Burg, C., The Use of Colloidal Chromium Radiophosphate in the Treatment of Malignant Tumors, in Proceedings of the International Conference on the Peaceful Uses of Atomic Energy, Geneva. 1955. Vol. 10. New York: United Nations. 1956 (p. 115).
298. van Miert, P. J. and Fowler, J. F., The Use of Tantalum-182 in the Treatment of Early Bladder Carcinoma, *Brit. J. Radiol.*, 29 508 (1956).

299. Binnie, G. G. and Bates, N., Radio-cobalt Needles in Therapy, *Incl. J. Appl. Rad.*, 1 314 (1957).
300. Harper, P. V., Moseley, R. D. and Ironside, W. M., Experiences with Y-90 Hypophysectomy, *Intl. J. Appl. Rad.*, 3 83 (1958).
301. Mundinger, F., Ein Beitrag zur Dosimetrie und Applikationstechnik von Radio-Tantal (Ta-182) zur Langzeitbestrahlung von Hirngeschwulsten, *Intl. J. Appl. Rad.*, 3 93 (1958).
302. Flocks, R. H., Culp, D. A. and Elkins, H. B., The Present Status of Radioactive Gold in the Management of Prostatic Cancer, *J. Urol.*, 81 173 (1959).
303. Farr, L. E., Sweet, W. H., Locksley, H. B. and Robertson, J. S., Neutron Capture Therapy of Gliomas Using Boron-10, *Trans. Am. Neurol. Assoc.*, 79 110 (1954).
304. Farr, L. E., The Experimental Application of Neutron Capture Therapy to Glioblastoma Multiforme, *Acta Contra Cancrum*, 11 500 (1955).
305. Farr, L. E., Robertson, J. S. and Stickley, E., Use of the Nuclear Reactor for Neutron Capture Therapy of Cancer, *Intl. Conf. on Peaceful Uses of Atomic Energy*, Geneva. 1955.
306. Godwin, J. T., Farr, L. E., Sweet, W. H. and Robertson, J. S., Pathological Study of Eight Patients with Glioblastoma Multiforme Treated by Neutron Capture Therapy Using Boron-10, *Cancer*, 8 601 (1955).
307. Farr, L. E., The Medical Uses of Nuclear Reactors, *Bruxelles Medical*, 37 343 (1957).
308. Farr, L. E., Present Progress in Neutron Capture Therapy, *Acta Radiol. Interam.*, 7 65 (1957).
309. Stickley, E. E., Robertson, J. S. and Farr, L. E., The Nuclear Reactor as an Instrument of Medical Research and Therapy, *Advances in Nuclear Engineering*, 1 504 (1957).
310. Farr, L. E., The Development of the Nuclear Reactor as a Device for Medical Therapy and Diagnosis. Status in 1956. Claus, W. D., (Ed.), *Radiation Biology and Medicine*. Cambridge: Addison-Wesley. 1958 (p.522).
311. Farr, L. E., Lippincott, S. W., Haymaker, W. E., Yakovlev, P. I. and Kahle, W., Neuropathological and Topographic Anatomical Study of Whole Brains Following Neutron Capture Therapy for Glioblastoma Multiforme. *Acta Med., Belgica*, 227 (1958).

312. Farr, L. E., Neutron Capture Therapy: Its Experimental Trial in Glioblastoma Multiforme. Pack, G. and Ariel, I., (Eds.) Treatment of Cancer and Allied Diseases. New York: Paul B. Hoeber, Inc. 1959 (p.82).
313. Farr, L. E. Clinical and Experimental Testing of Principles of Neutron Capture Therapy. U. S. A. E. C. TID 7572. 1959 (p. 202).
314. Farr, L. E., Robertson, J. S., Stickley, E. E., Bagnall, H. J., Easterday, O. D. and Kahle, W., Recent Advances in Neutron Capture Therapy. Progress in Nuclear Energy, Ser. VII: Medical Sciences, Vol. 2 New York: Pergamon Press. 1959 (p.128).
315. Lippincott, S. W., Robertson, J. S., Bond, V. P., Cronkite, E. P., Easterday, O. D. and Farr, L. E., Pathologic Effects of Thermal Neutrons and the B^{10} (n, alpha) Li^7 Reaction on Skin, A. M. A. Arch. Pathol., 68 639 (1959).
316. Lippincott, S. W., Yamamoto, Y. L. and Farr, L. E., Radiation Effects of Neutron-capture Therapy on a Malignant Vascular Neoplasm of the Cerebellum, A. M. A. Arch. Pathol., 69 44 (1960).
317. Farr, L. E., Calvo, W. G., Haymaker, W., Lippincott, S. W., Yamamoto, Y. L. and Stickley, E. E., Effect of Thermal Neutrons on Central Nervous System, Arch. Neurol. xx 4 246 (1961).
318. Farr, L. E. and Konikowski, T., To be published.
319. Farr, L. E., A Physician's Consideration of Criteria of Nuclear Reactors for Medical Therapy and Research. Farr, L. E., Knipping, H. W. and Lewis, W. H. (Eds.), Clinical Aspects of Nuclear Medicine Symposium With Special Reference to Cancer and Cardiovascular Diseases. Koln und Opladen: Westdeutscher Verlag. 1961 (p. 179).
320. Stickley, E. E., The Medical Research Reactor at the Brookhaven Medical Research Center, Nature 183 1013 (1959).
321. Farr, L. E., The Brookhaven Medical Research Reactor, Sci., 130 1067 (1959).
322. Stickley, E. E. and Farr, L. E., Design and Performance of field-defining Apertures for Neutron Capture Therapy, Radiology, 75 602 (1960).
323. Glesser, W., Uber einen Therapeutischen Impulsreaktor fur Medizinische Zwecke. Farr, L. E., Knipping, H. W. and Lewis, W. H. (Eds.), Clinical Aspects of Nuclear Medicine Symposium With Special Reference to Cancer and Cardiovascular Disease. Koln und Opladen: Westdeutscher Verlag. 1961 (p.199).

324. Bolt, W., Ritzl, F., Toussaint, R. and Fahrman, H., Zytostatika und Radioisotope. Farr, L. E., Knipping, H. W. and Lewis, W. H., (Eds.), Clinical Aspects of Nuclear Medicine Symposium With Special Reference to Cancer and Cardiovascular Diseases. Köln und Opladen: Westdeutscher Verlag. 1961 (p. 239).

325. Cotzias, G. C., Borg, D. C., Bertinchamps, A. J., Hughes, E. R. and Papevasiliou, P. S., Nuclear Studies in Medicine: Manganese Metabolism. Farr, L. E., Knipping, H. W. and Lewis, W. H. (Eds.), Clinical Aspects of Nuclear Medicine Symposium With Special Reference to Cancer and Cardiovascular Diseases. Köln und Opladen: Westdeutscher Verlag 1961 (p. 49).

326. Venrath, H. and Rink, H., Die Regionale Ventilationsanalyse mit Hilfe des radioaktiven Edelgases Xenon 133 (Isotopentherakographie). Farr, L. E., Knipping, H. W. and Lewis, W. H., (Eds.), Clinical Aspects of Nuclear Medicine Symposium With Special Reference to Cancer and Cardiovascular Diseases. Köln und Opladen: Westdeutscher Verlag. 1961 (p. 320).

327. Endler, P., Das Radioaktive Isotop Xenon 133 und seine Anwendung bei der Isotopen-therakographie. Farr, L. E., Knipping, H. W. and Lewis, W. H., (Eds.), Clinical Aspects of Nuclear Medicine Symposium With Special Reference to Cancer and Cardiovascular Diseases. Köln und Opladen: Westdeutscher Verlag. 1961 (p. 454).

328. Feinendegen, L. E. and Bond, V. P., Observations on Nuclear RNA Labeled With Tritiated Cytidine in Human Cancer Cells in Culture (HeLa). Farr, L. E., Knipping, H. W. and Lewis, W. H., (Eds.), Clinical Aspects of Nuclear Medicine Symposium With Special Reference to Cancer and Cardiovascular Diseases. Köln und Opladen: Westdeutscher Verlag. 1961 (p. 465).

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