Lawrence Berkeley National Laboratory
Recent Work

Title

SOMATIC EFFECTS - CANCER ESTIMATES OF RADIATION DOSES IN TISSUES AND ORGANS IN THE SINGLE-COURSE RADIOTHERAPY PATIENTS TREATED FOR ANKYLOSING SPONDYLITIS IN ENGLAND AND WALES

Permalink

https://escholarship.org/uc/item/0860s6s1

Author

Fabrikant, J.I.

Publication Date

1979

eScholarship.org Powered by the California Digital Library
University of California

To be published as a Chapter in THE EFFECTS ON POPULATIONS OF EXPOSURE TO LOW LEVELS OF IONIZING RADIATION, 1979 REPORT OF THE ADVISORY COMMITTEE ON THE BIOLOGICAL EFFECTS OF IONIZING RADIATIONS, Washington, D. C.: Division of Medical Sciences, National Academy of Sciences - National Research Council

LBL-8709 c.2
Preprint

SOMATIC EFFECTS - CANCER
ESTIMATES OF RADIATION DOSES IN TISSUES AND ORGANS IN THE SINGLE-COURSE RADIOTHERAPY PATIENTS TREATED FOR ANKYLOSING SPONDYLITIS IN ENGLAND AND WALES

Jacob I. Fabrikant and John T. Lyman

RECEIVED
LAWRENCE
BERKELEY LABORATORY

FEB 26 1979

LIBRARY AND
DOCUMENTS SECTION

January 1979

Prepared for the U. S. Department of Energy
under Contract W-7405-ENG-48

TWO-WEEK LOAN COPY

This is a Library Circulating Copy which may be borrowed for two weeks. For a personal retention copy, call Tech. Info. Division, Ext. 6782

LAWRENCE BERKELEY LABORATORY
UNIVERSITY OF CALIFORNIA

LBL-8709 c.2

DISCLAIMER

This document was prepared as an account of work sponsored by the United States Government. While this document is believed to contain correct information, neither the United States Government nor any agency thereof, nor the Regents of the University of California, nor any of their employees, makes any warranty, express or implied, or assumes any legal responsibility for the accuracy, completeness, or usefulness of any information, apparatus, product, or process disclosed, or represents that its use would not infringe privately owned rights. Reference herein to any specific commercial product, process, or service by its trade name, trademark, manufacturer, or otherwise, does not necessarily constitute or imply its endorsement, recommendation, or favoring by the United States Government or any agency thereof, or the Regents of the University of California. The views and opinions of authors expressed herein do not necessarily state or reflect those of the United States Government or any agency thereof or the Regents of the University of California.

To appear in:

The Effects on Populations of Exposure to Low Levels of Ionizing Radiation, 1979
Report of the Advisory Committee on the Biological Effects of Ionizing Radiations

Division of Medical Sciences, National Academy of Sciences - National Research Council
Washington, D.C. 20006, 1979

Chapter V

Somatic Effects - Cancer

Estimates of Radiation Doses in Tissues and Organs in the Single-Course Radiotherapy Patients Treated for Ankylosing Spondylitis in England and Wales

Jacob I. Fabrikant, M.D., Ph.D.[1]
Biology & Medicine Division
Lawrence Berkeley Laboratory
University of California, Berkeley[2]

and

Department of Radiology
University of California School of Medicine
San Francisco

and

John T. Lyman
Biology & Medicine Division
Lawrence Berkeley Laboratory

[1]Professor of Radiology, University of California School of Medicine, San Francisco

[2]Mailing Address: Donner Laboratory, University of California, Berkeley, California 94720

This work was supported by the Office of Health & Environmental Research of the U.S. Department of Energy under contract No. W-7405-ENG-48 and the Environmental Protection Agency.

E. Estimates of Radiation Doses in Tissues and Organs in the Single-Course Radiotherapy Patients Treated for Ankylosing Spondylitis in England and Wales

The available data on patients with ankylosing spondylitis who received a single treatment course with x rays in the Doll and Smith study[4,5] were reviewed, to estimated some radiation doses in tissues and organs giving rise to excess leukemias and cancers of heavily irradiated sites. It was not possible to review the radiotherapy charts of each patient, and it was therefore necessary to make assumptions on, for example, the selection of patients, the extent and severity of disease, the method of therapy, the radiotherapy dosimetry, and exposures, the tissues irradiated, and the doses absorbed. The number of assumptions was kept to a minimum; it was recognized that the selection of patients and the clinical courses of treatment chosen by the radiotherapist in individual cases were, understandably, extremely variable. In spite of these limitations, however, it has been possible to make reasonable assumptions, to develop a model of what probably occurred in the radiotherapy planning and treatment of these patients, on the basis of conventional orthovoltage radiotherapy of the 1930s-1950s. The estimates of radiation doses absorbed thus derived, however, are imprecise and must be further corrected as new information becomes available, not only with respect to the assumptions made above, but also with respect to subtle information still lacking--for example, on the location of the organ during treatment and on the fraction of the organ or tissue that was irradiated.

Patients Studied

Of the original 14,558 patients in the ankylosing-spondylitis study group, 4,421 (30.4%) patients who had received only one course of treatment

were studied by Doll and Smith.[4,5] The average period of followup for patients who had only one course of treatment was 16.2 yr. In addition, 52 patient histories and clinical courses of disease were carefully detailed in the M.R.C. 295 Report;[3] these patients had all developed leukemia after either single or multiple courses of x ray therapy.

Radiotherapy Dosimetry and Treatment Planning

The radiotherapy dosimetry of patients was carefully reviewed and reconstructed in the M.R.C. 295 Report.[3] The most likely treatment ports, x ray qualities, dose fractions, etc., were used, and depth-dose data for conventional orthovoltage x ray therapy was used.[2] The patients were classified in two groups, on the assumption that about one-third in the series were treated in the late 1930s and early 1940s, and two-thirds were treated in the late 1940s and early 1950s. For the earlier patients in the series, it was assumed that the equipment used was a 100-kVp radiotherapy x ray machine with an HVL of 2 mm aluminum at a 30-cm focus-skin distance (FSD). For the later patients in the series, it was assumed, that the equipment used was a 200-kVp radiotherapy x ray machine with an HVL of 1 mm Copper at a 50-cm FSD.

It was assumed that the entire spine (cervical, thoracic, lumbar, and sacral) and sacroiliac joints were treated in the single course of radiotherapy. Therefore, on the basis of the range of rectangular skin-field dimensions for spinal and sacroiliac fields desribed in the M.R.C. 295 Report[3] (see Appendix B) and the fact that multiple fields were used, it was assumed that in this analysis depth-dose data for a 200-cm^2 field[2] would be appropriate to estimate organ-dose characteristics. The positions of the cervical, thoracic, lumbar, and sacral spine were determined from the data

of Brinkley and Masters,[1] on the assumption that all ankylosing-spondylitis patients were treated in the prone position. The positions of the various organs and tissues of the thorax, abdomen, and pelvis were determined from contours and relationships from computed-tomography images, cadaver correlative anatomy published by Gambarelli et al.,[6] and descriptions in Gray's Anatomy;[7] it was recognized that computed-tomography patients and cadaver transverse sections are examined in the supine position.

Patient Selection, Treatment, and Clinical Course

To obtain some understanding of the rationale of patient selection and course of radiotherapy, the histories of the 52 ankylosing-spondylitis patients who developed leukemia outlined in the M.R.C. 295 Report[3] were carefully reviewed. No selection process could be ascertained with regard to severity of disease at the time of the first course of radiotherapy, nor for the failure of palliation that warranted a second or additional courses of radiotherapy. Thus, it was assumed that these leukemia patients were no different from all other ankylosing-spondylitis patients when they began radiotherapy. For the purposes of the following analysis, therefore, it was assumed that these patients were not selected on the basis of severity of their disease or of any other predisposing factors and were therefore representative of all 14,558 patients in the study at the start of their radiotherapy for ankylosing spondylitis.

It was further assumed that the large group of patients who required retreatment (7,453, or 51.2%)[4,5] did not enter into their initial course of radiotherapy with a plan for retreatment. In other words, all patients were treated in the hope of palliating their disease in the first course of

radiotherapy. There was no way for the radiotherapist to predict that a given patient in the series would require more than a single course of therapy for palliation, and thus each patient who received multiple courses of radiotherapy was initially judged to be a single-course patient and treated accordingly. This would obtain for all 14,558 patients, and therefore for the 52 patients who ultimately developed leukemia. It is of interest that 34 (65.4%) of the initial 52 patients who developed leukemia did receive additional courses of x ray treatment.

Estimation of Mean Exposure of the Spinal Bone Marrow

On the basis of the clinical and radiotherapeutic histories of the 52 ankylosing-spondylitis patients, it was assumed that the general clinical trend was to begin with a single course of treatment. This resulted in a mean spinal bone-marrow exposure for the initial course of therapy for all 52 patients of 542 $\pm$ 355 R (Figure 1). Thereafter, if a patient returned for additional radiotherapy because of recurring disease, each additional course of therapy up through the fourth course resulted in an increment of 346 $\pm$ 319 R in mean spinal bone-marrow exposure. Both in the initial treatment course and in later courses, the standard deviations were extremely large. It was assumed, therefore, that the average spinal marrow exposure for all 4,421 patients who received a single course of therapy was 542 $\pm$ 355 R. The average exposure of the spinal bone marrow represented a very wide spectrum of exposures selected by the radiotherapist. This suggested extreme variability in treatment techniques and in the clinical response of patients.

The average exposure of the spinal bone marrow in the 18 single-course patients who developed leukemia[3] was 668 $\pm$ 325 R. This value is not

significantly different from the mean spinal marrow exposure of all 52 patients after the first course of radiotherapy.

Estimation of Radiation Doses Absorbed in Tissues and Organs in Heavily Irradiated Sites

On the basis of the assumptions outlined above, the average radiation doses to the spinal bone marrow and to the organs and tissues in heavily irradiated sites have been calculated (Table 1). It was assumed that all leukemias and cancers arose in irradiated tissues and organs.

The estimated absorbed dose for leukemia was based on the assumption that spinal bone marrow constitutes 42.3% of the active bone marrow and the assumption that leukemia arose in irradiated bone marrow in the spine.

The estimated absorbed dose for lymphoma (excluding Hodgkin's disease) was based only on the position of the most prominent lymph nodes in the mediastinum of the thorax. These included the lymph nodes lying in and around the trachea and the bifurcation of the main bronchi. If lymphomas arose in the lymph nodes of the posterior mediastinum, the dose would have been much higher, and the risk would be reduced; if the lymph nodes of the anterior mediastinum were involved, the risk would be increased.

The position of the esophagus varies considerably in the thorax; and kyphosis in ankylosing-spondylitis patients would affect its position. If neoplasms arose in the upper esophagus, the radiation dose could have been higher, and the risk lower. Because many patients received lumbar spine irradiation, it is possible that the distal esophagus, although more anterior (and thus receiving a smaller dose), could have been in the irradiated fields more frequently. The cervical portion of the esophagus was not included in this analysis.

TABLE 1

Estimated Radiation Doses in Tissues and Organs in Heavily Irradiated Sites in Patients with Ankylosing Spondylitis After a Single Treatment Course with X Rays

Site of Cancer	Dose, rads[a]
Spinal bone marrow (leukemia	214
Lymphoma, mediastinal, lymph nodes excluding Hodgkin's disease	306
Esophagus	306
Stomach	67[b]
	89[c]
Colon	57
Pancreas	90
Bronchus	197[d]
Bone	1,950[e]
	505[f]
Spinal cord and nerves	698
Kidney	46[g]
Bladder	31[h]

[a] Based on average spinal bone-marrow dose of 505 rads.

[b] Assumes 50% of stomach irradiated; hypersthenic configuration.

[c] Assumes 67% of stomach irradiated; asthenic configuration.

[d] Assumes 80% of bronchial epithelium irradiated.

[e] Dose to apatite (calcium-protein matrix).

[f] Dose to spinal bone-marrow cells and endosteal lining cells of bone-marrow cavities.

[g] Lightly irradiated site; assumes 10% of organ (both kidneys) in irradiated field.

[h] Lightly irradiated site; assumes 33% of organ in irradiated field.

The lower value for the absorbed dose in stomach assumed that half of it was irradiated: this may have occurred in hypersthenic patients. The higher value assumed that two-thirds of the stomach was irradiated; this may have occurred in asthenic patients.

The absorbed dose in the colon was based on the assumption that one-third to one-half the colon was in the irradiated field, primarily the transverse colon, the sigmoid, and the rectum. The dose in the pancreas assumed irradiation of the head and the portion of the body of the pancreas anterior to the lumbar spine; this accounts for two-thirds of the organ.

The dose estimated in the bronchus assumed that bronchial cancers arose in the primary and secondary branches. Further branching--say, to the tertiary portions--would increase the amount of bronchial epithelium, but decrease the probability of the epithelium's being situated in the irradiated field. It was assumed that 80% of the bronchial epithelium was irradiated.

The absorbed dose in bone was low, with a large range. Corrections were made for x ray absorption in bone relative to soft tissue, i.e., for osteocyte lacunae and bone-marrow cell spaces. The lower dose estimate refers to the bone marrow of the vertebral bodies, transverse and spinous processes, pedicles, etc. The higher estimate refers to the apatite (calcium-protein matrix). It was assumed that only the spine and the sacroiliac joints were irradiated, and no corrections were made for irradiation of other bony structures, such as ribs.

The absorbed dose estimated in the spinal cord and spinal nerves (nerve root and dorsal and ventral branches) originating from the cord assumed that these structures were in the field of irradiation. The dose could have been higher, because the cord and the origins of the spinal nerves are closely related to the surrounding bone of the spinal column.

Conclusions

The estimates of absorbed doses of x rays in bone marrow and heavily irradiated sites in the radiotherapy patients with ankylosing spondylitis in England and Wales after a single treatment course of x rays are extremely crude and are based on very limited data and on a number of assumptions. Some of these assumptions may later prove to be incorrect, but the general principles are valid and are probably reasonably appropriate. It is therefore important to place these estimates of absorbed dose into perspective, recognizing that they may be somewhat inaccurate, but not grossly so. It is probable that they are correct to within a factor of 2. This is particularly important for cancers of heavily irradiated sites with long latent periods. The mean followup period for the single-treatment-course anklosing-spondylitis patients was 16.2 yr, and an increase in cancers of heavily irradiated sites may appear in these patients in the 1970s in tissues and organs with long latent periods for the induction of cancer.

The accuracy of these estimates is severely limited by the inadequacy of information on doses absorbed by the tissues at risk in the irradiated patients. The information on absorbed dose is essential for an accurate assessment of dose-cancer incidence analysis, which could provide valuable insights into the mechanisms of cancer induction in man. Furthermore, in this unusually valuable human series of irradiated patients, the information on radiation dosimetry entered on the clinical radiotherapy charts is central to any reliable determination of somatic risks of radiation with regard to carcinogenesis in man. The work necessary to obtain these data is under way in England: only when they are available can more precise estimates of risk of cancer induction by radiation in man obtained.

REFERENCES

1. Brinkley, D. and Master, H.E., "The Depth of the Spinal Cord Below the Skin." Brit. J. Radiol. 40: 66-67, 1967.

2. Brit. J. Radiol. N.S., Supplement No. 5, 1953. Scientific Subcommittee of the Hospital Physicists' Association (1953). Central Axis Dept Dose Data for X-Radiation of Half Value Layers from 0.01 mm Al to 15.0 mm Cu, Cobalt-60 Radiation, H.V.L. 11 mm Pb, and Beta Radiation, 22, MeV.

3. Court-Brown, W.M. and Doll, R., "Leukemia and Aplastic Anemia in Patients Irradiated for Ankylosing Spondylitis." M.R.C. Report 295, London, Her Majesty's Stationery Office, 1957.

4. Doll, R. and Smith, P.G. Mortality from Cancer and Other Causes After Radiotherapy for Ankylosing Spondylitis: Further Observations. Cited in Sources and Effects of Ionizing Radiation. United Nations, Nerw York, 1977.

5. Smith, P.G. and Doll, R. Age and Time Dependent Changes in the Rates of Radiation Induced Cancers in Patients with Ankylosing Spondylitis Following a Single Course of X-Ray Treatment. Proc. Intern. Atomic Energy Agency Symposium on Late Biological Effects of Ionizing Radiation. Paper IAEA-SM-224/711, Vienna, 1978.

6. Gambarelli, J., Guerinel, G., Chevrot, L., and Mattei, M. Computerized Axial Tomography. Springer-Verlag, New York, 1977.

7. Gray, Henry, Anatomy of the Human Body, 29th Edition, Charles M. Gross, ed., Lea & Febiger, Philadelphia, 1973.

This report was done with support from the Department of Energy. Any conclusions or opinions expressed in this report represent solely those of the author(s) and not necessarily those of The Regents of the University of California, the Lawrence Berkeley Laboratory or the Department of Energy.

TECHNICAL INFORMATION DEPARTMENT
LAWRENCE BERKELEY LABORATORY
UNIVERSITY OF CALIFORNIA
BERKELEY, CALIFORNIA 94720