

https://dspace.org/

Physical and biological parameters affecting the reaction of human tissues and tumours to ionizing radiation: a statistical and experimental study of the development of methods for determining therapeutic ratios, optimal dosage factors, and a theoretical prognosis in clinical radiation therapy

2015-02-09
http://hdl.handle.net/10539/16953

Downloaded from a DSpace repository. https://dspace.org/

GENERAL SUMMARY

The physical mechanisms underlying the absorption of ionising radiation in tissues are reviewed. In particular, the principles of radiation dosimetry, insofar as they affect reactions in the tissues and tumours of the various subjects studied, are examined in detail. The nature of radiation reactions in man is studied from the quantitative aspect, and the dosage data for specific end-results in a variety of tissues and tumours is tabulated. Tissue tolerances and tumour lethal doses are defined in terms of Median effective doses and the associated coefficients of variation. Six technical variables (quality, time, volume, radiosensitivity, recovery, and diffusion constants) are shown to influence the reaction, and an 'iso-effect' formula incorporating these factors is proposed. This function has the general form $D = E.T^{n}.L^{-q}/\eta$, where 'D' is the physical dose in rads, 'E' the standard radiosensitivity factors 'T' the over all time in days, 'L' the field-diameter in decimeters, 'n' and 'q' the recovery and diffusion exponents respectively, and η the relative biological efficiency for the particular quality of radiation used.

The quality factor, as assessed by the half-value layer, kilovoltage, average wavelength, or rate of linear energy transfer (LET) is considered in relation to the relative biological efficiency (RBE) for animal and human tissues of various types of radiation. By simple graphical interpolation, the RBE-factors required for incorporation into the iso-effect formula are derived, and shown to be valid at least in the range of clinical interest. Taking $\eta = 1.00$ for radium γ-rays and megavoltage radiations, its value is shown to be 1.403 (± .024) for orthovoltage rontgen rays, and approaches a factor of 3 in the superficial therapy range.

The influence of the time factor upon the median effective doses is considered. Published data on the effects of variation in dose-rate, interruption of exposure, manner of fractionation, and over-all time are analysed and suitable parameters for various tissues and tumours are derived, the

recovery functions of skin and epidermoid cancer being n = 0.33 and 0.22 respectively. The critical time interval appropriate to a continually decaying isotope source is shown to be around 2.75 times the corresponding half-life. The effect of varying the size and shape of the irradiated volume upon the intensity of the reaction is analysed, and appropriate parameters for a variety of anatomical and geometrical configurations are estimated. The factor 'q' is 0.33 for skin and probably zero for tumours. This datum completes the information required to formulate a composite iso-effect function, incorporating all relevant tissue and tumour variates and parameters simultaneously.

The validity of the iso-effect formula is reconsidered as a physical or mathematical model system, and it is shown that the hypothesis of a single exponentially decaying 'substance' is untenable. A heterogeneous mixture of such substances could give a satisfactory, though much more complex, function, but this is found to fit observed data little better than the simple empirical iso-effect formula given. A least-squares regression of skin reactions upon dosage, and a probit analysis of tumour dosage data derived from 310 patients (150 skin reactions, 100 cases of epidermoid cancer, and 60 mammary carcinomas) treated in the Hospital, gave estimates for the empirical parameters virtually identical with those obtained by analysis of published data.

The analysis introduces the <u>therapeutic ratio</u> as a strict biometrical concept associated with any given combination of technical factors, and the <u>statistical prognosis</u> (probability of uncomplicated cure) is shown to be a function of this ratio. Using the mathematical model, one could compute the <u>optimal dose</u>, the effect of time and area factors upon the prognosis, the comparative value of precalculated and individualised dosage schemes, and also devise clinical dosage nomograms whereby optimal treatment factors may be applied directly in practical radiotherapy. It is concluded that statistical analysis of enough relevant clinical data would permit the development of optimal dosage schemes for most human tumours, with a corresponding improvement in cancer cure rates.

GENERAL SUMMARY

The physical mechanisms underlying the absorption of ionizing radiation in tissues are reviewed. In particular, the principles of radiation dosimetry, insofar as they affect reactions in the tissues and tumours of the various subjects studied, are considered in detail. The nature of radiation reactions in man is studied from the quantitative aspect, and the dosage data for specific end-results in a variety of tissues and tumours is tabulated. Tissue tolerances and tumour lethal doses are defined in terms of median effective doses and the associated coefficients of variation. Six technical variables (quality, time, volume, radiosensitivity, recovery, and diffusion constants) are shown to influence the reaction, and an 'iso-effect' formula incorporating these factors is proposed. This function has the general form $D = E.T^{n}.L^{-q}/\eta$, where 'D' is the physical dose in rads, 'E' the standard radiosensitivity factor, 'T' the over-all time in days, 'L' the field-diameter in decimeters, 'n' and 'q' the recovery and diffusion exponents respectively, and η the relative biological efficiency for the particular quality of radiation used.

The quality factor, as assessed by the half-value layer, kilovoltage, average wavelength, or rate of linear energy transfer (LET) is considered in relation to the relative biological efficiency (RBE) for animal and human tissues of various types of radiation. By simple graphical interpolation, the RBE-factors required for incorporation into the iso-effect formula are derived, and shown to be valid at least in the range of clinical interest. Taking $\eta = 1.00$ for radium γ-rays and megavoltage radiations, its value is shown to be 1.403 (± .024) for orthovoltage rontgen rays, and approaches a factor of 3 in the superficial therapy range.

The influence of the time factor upon the median effective doses is considered. Published data on the effects of variation in dose-rate, interruption of exposure, manner of fractionation, and over-all time are analysed and suitable parameters for various tissues and tumours are derived, the

recovery functions of skin and epidermoid cancer being $n = 0.33$ and 0.22 respectively. The critical time interval appropriate to a continually decaying isotope source is shown to be around 2.75 times the corresponding half-life. The effect of varying the size and shape of the irradiated volume upon the intensity of the reaction is analysed, and appropriate parameters for a variety of anatomical and geometrical configurations are estimated. The factor 'q' is 0.33 for skin and probably zero for tumours. This datum completes the information required to formulate a composite iso-effect function, incorporating all relevant tissue and tumour variates and parameters simultaneously.

The validity of the iso-effect formula is reconsidered as a physical or mathematical model system, and it is shown that the hypothesis of a single exponentially decaying 'substance' is untenable. A heterogeneous mixture of such substances could give a satisfactory, though much more complex, function, but this is found to fit observed data little better than the simple empirical iso-effect formula given. A least-squares regression of skin reactions upon dosage, and a probit analysis of tumour dosage data derived from 310 patients (150 skin reactions, 100 cases of epidermoid cancer, and 60 mammary carcinomas) treated in the Hospital, gave estimates for the empirical parameters virtually identical with those obtained by analysis of published data.

The analysis introduces the <u>therapeutic ratio</u> as a strict biometrical concept associated with any given combination of technical factors, and the <u>statistical prognosis</u> (probability of uncomplicated cure) is shown to be a function of this ratio. Using the mathematical model, one could compute the <u>optimal dose</u>, the effect of time and area factors upon the prognosis, the comparative value of precalculated and individualised dosage schemes, and also devise clinical dosage nomograms whereby optimal treatment factors may be applied directly in practical radiotherapy. It is concluded that statistical analysis of enough relevant clinical data would permit the development of optimal dosage schemes for most human tumours, with a corresponding improvement in cancer cure rates.

Author Cohen L
Name of thesis Radiation Parameters 1960

PUBLISHER:
University of the Witwatersrand, Johannesburg
©2013

LEGAL NOTICES:

Copyright Notice: All materials on the University of the Witwatersrand, Johannesburg Library website are protected by South African copyright law and may not be distributed, transmitted, displayed, or otherwise published in any format, without the prior written permission of the copyright owner.

Disclaimer and Terms of Use: Provided that you maintain all copyright and other notices contained therein, you may download material (one machine readable copy and one print copy per page) for your personal and/or educational non-commercial use only.

The University of the Witwatersrand, Johannesburg, is not responsible for any errors or omissions and excludes any and all liability for any errors in or omissions from the information on the Library website.