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GENERAL EQUATION FOR THE CALCULATION OF NOMINAL STANDARD DOSE

by

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In order to compare the biologic effect on normal tissue of various dose-time-fractionation regimes in radiation therapy, ELLIS (1968, 1969, 1971) has suggested the use of a nominal standard dose (NSD). The NSD is essentially a parameter which defines a particular iso-effect surface in a three dimensional space having axes: dose, time, number of fractions. If the same NSD is achieved by different dose-time-fractionation schedules, the damage to normal tissue is presumably the same. There is ideally, a single value for the NSD which represents connective tissue tolerance but which may vary from center to center — depending on dosimetry and judgement (as to what is clinically tolerable). In reality, 'tolerance' will depend on the location and the size of the volume treated, and hence one might have several NSD's — each one being appropriate for the treatment of a specific disease (or a class of diseases). According to ELLIS, one should compute the NSD for one or more treatment regimes which represent, in one's own judgement, connective tissue tolerance, and then adopt the average value as the tolerance NSD for one's own center. The NSD is then no longer a

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variable. Once the tolerance NSD is established, one no longer computes the NSD for a given treatment schedule, but rather a ret dose (ELLIS et coll. 1969) which is computed as a 'partial tolerance' (ELLIS 1969). If the ret dose is less than the NSD, the given schedule does not achieve full tolerance.

The calculation of NSD (or ret dose) for a single course of treatment is quite simple; however, for a split course where there is a gap (or gaps) in the treatment or where the dose per fraction is changed during a single course of treatment, the calculation is somewhat more complicated. In the examples of split-course calculations previously given in the literature (ELLIS 1968, 1969, WINSTON et coll. 1969), the NSD representing tolerance is presumed known, and the number of fractions or the dose per fraction are then adjusted until the treatment schedule attains the specified NSD. These are specific numerical examples, and no general equation has been derived for such calculations. Several of the examples available involve the use of a slide rule (WINSTON et coll. 1969) which tends to obscure the reasoning used in the calculations.

In this paper a general equation is derived which can be used to calculate the NSD (or ret dose) for any situation, and which is readily suitable for computer calculations of these quantities. A simple FORTRAN program for these calculations is described. We use this program routinely (as part of a larger program for calculation of depth dose and treatment time) in order to evaluate the proposed treatment schedule for each patient — the ret dose being printed out on the patient's treatment record. Our main program, which calculates and prints the entire treatment record for the patient, is interlocked so that an 'unreasonable' ret dose cannot be given.

Calculation of nominal standard dose. If the dose per fraction remains the same throughout the course of treatment, and the fractions are (more- or- less) evenly spaced in time, the NSD may be calculated from the formula

$$\mathrm{NSD} = \frac{D}{N^{0.24}\ T^{0.11}} \tag{1}$$

where N is the number of fractions, T is the time in days between the first and last fraction, and D is the total absorbed dose delivered. In actual practice a fixed number of fractions are given per week, and hence T and N are not independent variables. For a given number of fractions, the exact value of T will depend on the day of the week the first fraction is given; however, the average value of T (for an arbitrary starting day) may be approximated by (WINSTON et coll. 1969):

$$T = KN^{1.13} \tag{2}$$

Table

Fractionation scheme

No. of fractions/week	K
5 (Mon. – Fri.)	0.89
4 (M, T, Th, F)	1.13
3 (M, W, F)	1.51
2 (T, Th)	2.29
1	4.61

where K depends on the number of fractions per week and takes the values given in the Table. If we combine eqs (1) and (2), we obtain

$$NSD = N^{0.6357} K^{-0.11} d \qquad (3)$$

where $d = D/N$ is the dose per fraction.

The calculation of the NSD for a split-course of treatment is somewhat more complicated. If there are gaps in the treatment, eq. (1) no longer applies (nor does it apply if the dose per fraction or the number of fractions/week are changed during a course of treatment containing no gaps). The proper way to calculate the NSD for a split course is to use the concept of partial and residual tolerance (Ellis 1968, 1969). For example, if the NSD representing tolerance is 1 760 ret (corresponding to 6 000 rad given in 30 fractions, 5 times per week over 6 weeks), then an incomplete treatment of 3 000 rad given in 15 fractions results in a 'partial tolerance' of $(15/30) \times 1\,760 = 880$ ret (and not 1 133 ret as computed from eq. (3)). The 'residual tolerance' is then $1\,760 - 880 = 880$ ret. In the examples of split-course calculations previously given in the literature (Ellis 1968, 1969, Winston et coll. 1969), the NSD representing 'tolerance' is presumed known, and the number of fractions or the dose per fraction are then adjusted until the specified NSD is attained. It is therefore necessary to invert this reasoning in order to obtain the (unknown) NSD for a specified treatment schedule. This is precisely the problem that would face a (hypothetical) therapy center, which treated all patients with split-courses, in trying to establish their own tolerance NSD.

We will consider, for simplicity, a split course having a single gap as illustrated schematically below.

(N_1, d_1, f_1)		(N_2, d_2, f_2)
| ←— T_1 —→ |	←— T_G —→ |	←— T_2 —→ |
1st course	gap	2nd course

The total course consists of: N_1 fractions given in T_1 days using f_1 fractions/week and d_1 rad/fraction; followed by a gap of T_G days; followed by N_2 fractions given in T_2 days using f_2 fractions/week and d_2 rad/fraction. We assume that the NSD, which represents full tolerance, is specified (from our point of view we are starting with the desired answer). In order to reach full tolerance (in the absence of any gaps) at the dose/fraction and number of fractions/week specified in the first course, we would require N_1' fractions; where N_1' is found by solving eq. (3) for the number of fractions required to reach the specified NSD, i.e.,

$$N_1' = NSD^{1.573}\, K_1^{0.173}\, d_1^{-1.573} \tag{4}$$

where K_1 depends on f_1 according to the Table. The partial tolerance at the end of the first course is then (N_1/N_1') NSD. The partial tolerance at the end of the gap is somewhat smaller, due to recovery (or repair) during the resting period, and is given by

$$PT = \frac{N_1}{N'_1}\, NSD \left(\frac{T_1}{T_1 + T_G}\right)^{0.11} \tag{5}$$

The residual tolerance is then

$$RT = NSD - PT \tag{6}$$

The number of fractions that would be required to reach full tolerance (starting from the first day and with no gap) at the rate specified in the second course is

$$N'_2 = NSD^{1.573}\, K_2^{0.173}\, d_2^{-1.573} \tag{7}$$

The number of fractions required to deliver the residual tolerance in the second course, and thus bring the split course treatment up to full tolerance, is given by $(RT/NSD)N_2'$. If we require this number of fractions to be equal to the number of fractions specified for the second course, i.e.,

$$N_2 = \left(\frac{RT}{NSD}\right) N'_2 \tag{8}$$

then our calculation is self-consistent. That is, the second course — as specified — is exactly what is required to bring the treatment up to full tolerance. If we then combine eqs (4—8) and solve for the NSD explicitly, we obtain an equation which represents the NSD for a split course treatment, namely

$$NSD = \left[\left(\frac{N_1^{0.6357}\, d_1}{K_1^{0.11}}\right)^{1.573} \left(\frac{T_1}{T_1 + T_G}\right)^{0.11} + \left(\frac{N_2^{0.6357}\, d_2}{K_2^{0.11}}\right)^{1.573}\right]^{0.6357} \tag{9}$$

This equation is also valid if there is no gap ($T_G = 0$), but the course is split in the sense that the dose/fraction or the number of fractions/week is different for the two parts of the treatment. It is easy to show that eq. (9) reduces to eq. (3)

in the proper limit viz., $T_G = 0$, $K_1 = K_2 = K$ and $d_1 = d_2 = d$. Eq. (9) is therefore generally applicable.

For a course with two gaps, i.e., three courses, one can show by similar reasoning that the equation for the NSD is

$$\mathrm{NSD} = \left\{\left[\left(\frac{N_1^{0.6357}\, d_1}{K_1^{0.11}}\right)^{1.573}\left(\frac{T_1}{T_1+T_{G1}}\right)^{0.11} + \left(\frac{N_2^{0.6357}\, d_2}{K_2^{0.11}}\right)^{1.573}\right]\left(\frac{T_1+T_2+T_{G1}}{T_1+T_2+T_{G1}+T_{G2}}\right)^{0.11} + \left(\frac{N_3^{0.6357}\, d_3}{K_3^{0.11}}\right)^{1.573}\right\}^{0.6357} \quad (10)$$

The generalization required for any number of courses is then obvious.

It is necessary to point out that we have assumed the treatment to be a complete treatment, and the NSD thus calculated represents, in our judgement full 'tolerance' for that particular treatment. Tolerance, in this sense, will depend on the location of the irradiated volume as well as the size of the volume, e.g., when treating a large volume in the abdomen one usually must treat to a smaller NSD than would be used to treat a small volume in an extremity.

Calculation of ret dose. Once the NSD which represents connective tissue tolerance has been established, then all treatment schedules can be referred to this tolerance NSD for purposes of comparison. That is, one calculates a ret dose for a given treatment schedule — the ret dose being calculated as a partial tolerance. For an uninterrupted course of treatment the ret dose is computed as follows. If N′ is the number of fractions required to reach full tolerance and N fractions are given, the ret dose is

$$\text{ret dose} = \left(\frac{N}{N'}\right)\mathrm{NSD} = \mathrm{NSD}^{-0.573}\, N\, d^{1.573}\, K^{-0.173} \quad (11)$$

where eq. (3) has been used to compute N′. It is evident that two different centers will compute different ret doses for precisely the same treatment schedule if they have chosen different tolerance NSD's. In fact, the ratio of ret dose to NSD will be different, as is evident from eq. (11). (The two centers will, however, compute the same NSD for the same treatment schedule.)

For the split course treatment previously considered, the ret dose is given by

$$\text{ret dose} = \mathrm{NSD}\left[\frac{N_1}{N_1'}\left(\frac{T_1}{T_1+T_G}\right)^{0.11} + \frac{N_2}{N_2'}\right]$$

$$= \mathrm{NSD}^{-0.573}\left[\left(\frac{N_1^{0.6357}\, d_1}{K_1^{0.11}}\right)^{1.573}\left(\frac{T_1}{T_1+T_G}\right)^{0.11} + \left(\frac{N_2^{0.6357}\, d_2}{K_2^{0.11}}\right)^{1.573}\right] \quad (12)$$

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               PROGRAM NSD(INPUT,OUTPUT)
10003          DIMENSION TD(6),T(6),F(6),CN(6),TGAP(6),D(6),Q(6),TAU(6)
10003          READ 10, NC
10011       10 FORMAT(I1)
10011          CTT = 0.
10012          TOL = 0.
10013          DO 99 L=1,NC
10014          READ 20, TD(L), T(L), F(L), CN(L)
10027       20 FORMAT(4F10.0)
10027          IF(L .LT. NC) GO TO 88
10032          TGAP(L) = 0.
10033          GO TO 77
10033       88 READ 30, TGAP(L)
10041       30 FORMAT(F10.0)
10041       77 CTT = CTT + T(L) + TGAP(L)
10044          D(L) = TD(L)/CN(L)
10047          IFW = F(L)
10050          IF(IFW .EQ. 5) XK = .89
10054          IF (IFW .EQ. 4) XK = 1.13
10057          IF(IFW .EQ. 3) XK = 1.51
10062          IF(IFW .EQ. 2) XK = 2.29
10065          IF(IFW .EQ. 1) XK = 4.61
10070          C(L) = ( (CN(L)**.6357)*D(L)/(XK**.11) )**1.573
10105          TAU(L) = ( (CTT-TGAP(L))/CTT )**.11
10113          TOL = (TOL + C(L))*TAU(L)
10116       99 CONTINUE
10121          RNSD = TOL**.6357
10124          RETDOS = TOL * (1760.**-.573)
10131          PRINT 40,RNSD, RETDOS
10140       40 FORMAT(* NSD= *,F6.0,/,* RET DOSE= *,F6.0)
10140          STOP
10142          END
         COMMENT. NC= NUMBER OF COURSES
         COMMENT. OTT= OVERALL TREATMENT TIME(WEEKS)
         COMMENT. PARAMETERS FOR COURSE NO. L ARE- TD(L)= TOTAL DOSE(RADS),
         CONT. T(L)= TIME(WKS), F(L)= NO. FRACTIONS/WK, CN(L)= NO. FRACTIONS
         COMMENT. TGAP(L)= LENGTH OF GAP L (WKS)
         COMMENT. D(L)= DOSE PER FRACTION FOR COURSE NO. L
         COMMENT. TAU(L)= DECAY FACTOR FOR GAP L
         COMMENT. RNSD= NOMINAL STANDARD DOSE(RETS)
         COMMENT. RETDOS= RET DOSE (REFERRED TO AN NSD OF 1760 RETS)
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FORTRAN program for computing NSD and ret dose.

If the treatment reaches full tolerance, so that the ret dose is equal to the NSD, then the above equation reduces to eq. (9) as expected.

Computer calculation of NSD and ret dose. The previously derived equations can be easily incorporated into a computer program which will calculate the NSD or ret dose for any treatment schedule (no matter how complex). The program, listed in the Figure, calculates NSD and ret dose by an iterative process which generates the appropriate equation for the number of courses entered. The ret dose calculated is referred to an NSD of 1 760 ret.

A copy of the program suitable for use with a teletype terminal may be obtained, on request, from the author.

SUMMARY

A general equation is derived which can be used to calculate a nominal standard dose or ret dose for any treatment schedule, no matter how complex. A computer program for such calculations is described.

ZUSAMMENFASSUNG

Eine allgemeine Gleichung wird hergeleitet, die verwendet werden kann, um eine nominelle Standard-Dosis oder eine Ret-Dosis für jedes Behandlungs-Schema, wie komplex dieses auch sein mag, zu berechnen. Ein Komputerprogramm für solche Berechnungen wird beschrieben.

RÉSUMÉ

L'auteur présente une équation générale qui peut être utilisée pour calculer la dose standard nominale ou la dose ret pour tout plan de traitement, si compliqué soit-il. Il donne un programme d'ordinateur pour ces calculs.

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