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Original Research Article

A Graphical Method to Estimate Dose per Fraction in High Dose Rate Brachytherapy by Adopting Linear Quadratic Model

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Abstract:

Purpose: The aim of present study is to evaluate graphically HDR (High dose rate) brachytherapy dose per fraction for gynecological cancers

Materials and Method: Biological Effective doses (BED) are widely used to provide a quantitative measure of the effectiveness of a treatment BED values, this study describes isoeffect lines with various doses per fraction to compare known and unknown dose per fraction in HDR brachytherapy.

Result: The region of BED 85Gy, the threshold dose per fraction is 4 fr of 6.5Gy, 5fr of 6Gy, 6fr of 5 Gy is harvested but 3 fr of 6 Gy BED 10 region is 55Gy only therefore this dosage level is not intercepts 85Gy, this is below consensus level for that reason 3 fr not considered in this study.

Conclusion: This graphical method confirms biological effective dose concept close agreement with clinical findings, this method proposed here can be used to identify same fraction numbers generates linear isoefffective lines with different dose level below 5 Gy and above 10Gy.

Keywords: BED – Biological Effective dose, HDR- High dose rate Brachytherapy, Gy- Gray, fr-fraction.

Introduction

The aim of radiotherapy is to delivery of sufficient dose to produce high probability of tumor control and minimal damage to the surrounding normal tissues, most of the radiotherapy centers are familiar with Low Dose Rate (LDR) Brachytherapy. Recently there has been a trend towards increased use of High Dose Rate (HDR) brachytherapy due to its advantages, namely that it eliminates radiation exposure to workers, it requires only short treatment times and that its dose distribution can be optimized by varying the dwell times[1]. HDR is given as fractionated treatments to decrease normal tissue toxicity, many radiotherapy centers are not familiar with fractionation schemes to be use in HDR brachytherapy. There is a marked difference between the biological effect in the tumor and those in late reacting normal tissues[2]. Fractionation in radiotherapy involves a number of competing radiobiological factors. The severity of tumor effects may be highly dependent on fraction size thus requiring the dose per fraction is relatively precise, in this article Linear Quadratic model (LQ) is used to estimate Biological Effective Dose (BED)[3]. A graph is drawn by assuming various values of fraction size and dose example 3, 4, 5, 6, fractions of 5 to 11Gy, this process based on the random selection of an HDR fraction number and dose per fraction is evaluated, from the graph different dose, number of fraction and dose per fraction is evaluated. The graphical value correlates with clinical findings, this article considers what fraction is the maximum for High Dose Rate Brach therapy.

Materials Methods

Biological Effective doses (BED) are widely used to provide a quantitative measure of the effectiveness of a treatment BED values which are function of both the radiobiological parameters of the irradiated tissues and the pattern of radiation delivery.

$$BED = nd\,[1 + d/\alpha/\beta] \quad (1)$$

Where n and dare number and size of the dose fractions and α/β are the respective linear and quadratic radio sensitivity co-efficient of the irradiated tissues BED is a measure of the biological dose delivered to a tumour or organ and it is the theoretical total dose that would be required to produce a particular isoeffect using an infinitely large number of small dose of fractions. Equation (1) shows no allowance for tissue repopulation effect is achieved through the use of a subtractive repopulation factor which takes account of the treatment time and the repopulation rate.

The BED expression further modified as

$$BED = nd\,[1 + d/\alpha/\beta] - K\,[T - T0] \quad (2)$$

Where T is overall treatment time, K (in unit Gy/ day) is the biological dose per day required to compensate for ongoing tumour cell repopulation, α/β are tissue specific parameters and actual values must be selected for each , when calculating tumour BED.

Fractionated HDR Brachytherapy

Consider a course of N, HDR brachytherapy applications given at constant time interval t and d be the prescribed dose per fraction the BED [4] is given by

$$BED = nd\,[1 + d/\alpha/\beta] - Kt \quad (3)$$

Where t is the overall treatment time and K is the daily dose required to combat cologne repopulation factor is defined as K =0.693 / (αTpot) Where α is the intrinsic sensitivity taken from α/β and Tpot cologenic potential doubling time [6] All calculation in this article involved the following published values

1. An α/β ratio of tumour 10 Gy
2. The K factor was 0.7 Gy/ day
3. α value 0.35Gy-1
4. T pot 3 days
5. Tolerance tumor tissue value of BED10 = 85 Gy

This article describes isoeffect lines with various doses per fraction to compare known and unknown dose per fraction in HDR brachytherapy.

Result

According to American Brachytherapy Society [7] the biological Effective Dose of 85 Gy is concise level for HDR treatments, for that reason this BED values was chosen as basis for our calculation. Let us consider this dose level become target figure, we wish to maintain same BED value with various dose per fraction by solving the equation (1) , this relation are solved by assuming various values of N (3, 4, 5, 6, …….) and D (5, 6, 7, 8,…).

Assuming that fractionated brachytherapy can be given from the range 3 to 6 Gy of dose and 5 to 11 fractions are calculated this process entirely based on integers selection of dose per fraction, this has been worked out in table.1 and similar type of calculation were executed with repopulation correction factor (K) from the table.2 A graph is drawn BED versus dose level is effect lines are plotted corresponding to the fraction size a normal line is drawn at 85 Gy region. Corresponding to the doses, these values are plugged out then it is compared with clinical findings.

In this calculation ≤ 10Gy of HDR regimen require to deliver total BED around 85Gy, it is obvious that the HDR treatment should not exceed 10Gy, the total dose required for given biological end points are generally lower than BED 85Gy, this calculation is repeated with repopulation correction factor to know how much dose is required to produce same effect, further eq (3) reworked by using assumed values

Table 1: Provides the increase in fraction number and dose per fraction beyond 10 fractions, it reveals BED 85 Gy of concise level. Example 3 fractions of 10 Gy, 4 fraction of 10Gy, 5 fraction of 9 Gy and 6 fraction of 7 Gy is equivalent dose to produce BED 85 Gy. A graph is plotted BED Versus dose with respect to fraction numbers thus the obtained graph is strictly isoeffective there is no intersection in between two difference fractionation lines.

Table 2: Provides that ≤ 10Gy dose equivalent value of 85Gy with repopulation correction factor K, it shows that both BED and BEDk becomes unity, example 10Gy/10Gy = 1, it is noted this calculation reveals BED concept and BEDk calculation both are good agreement in this example 10Gy is very important as it found that 10Gy is exactly same in both type of calculation, however the HDR fraction number lies below 10 fractions. Graphically both graphs are not isoeffective, the reason is repopulation correction factors are not constant values, it does not found in integer number all are fractional numbers, only table.1 considered because the contribution of isoeffect lines are additive in other hand both terminology gives same dose level for HDR regimen

Table 1: BED calculation without repopulation correction factor and with repopulation BED_k

Fraction Number	Dose per fraction d (Gy)	BED_{10}(Gy)	BED_K
4	5	30	29.37
	6	38.4	37.77
	7	47.6	46.97
	8	57.6	56.97
	9	60.8	60.17
	10	80	79.37
	11	92.4	91.77
5	5	37.5	36.87
	6	48	47.37
	7	59	58.37
	8	72	71.37
	9	85	84.37
	10	100	99.37
6	5	45	44.37
	6	58	57.37
	7	71	70.37
	8	86	85.37
	9	91	90.37

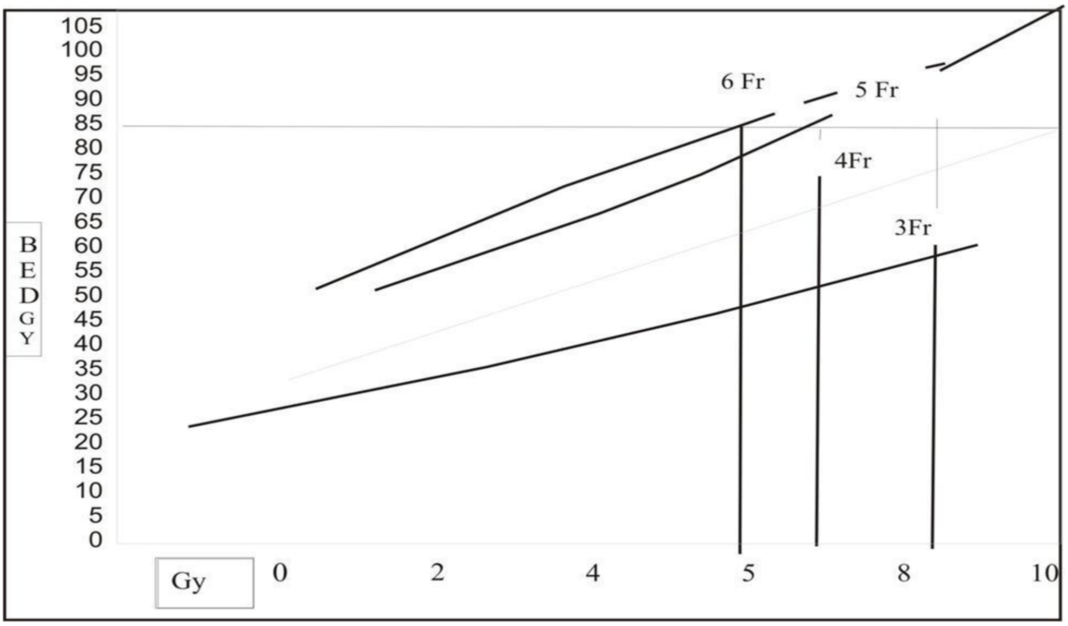

Figure 1: Isoeffective Graph is plotted from Table 1. Respective BED Values Versus Dose

BEDK with repopulation correction factor appears as fractional value not integer value, due to this reason isoeffect lines are not linear, above isoeffective lines plotted only without repopulation correction factor. Variation of isoeffective lines with variation of Dose per fraction is exactly expressed in above graph, the region of three fractions as not merges 85Gy and above 6fr isoeffective lines exceeds concise level, especially 3 to 6 fraction is ideal for HDR brachytherapy.

Table.2 Extracted value from graph

Number of Fractions (N)	Dose per fraction (D) Gy	BED Gy
4	10	85
5	5.7	44
6	5	44

Above tabular column 3 fractions not included, the reason is 3 fractions does not intercepts 85Gy normal line therefore this value not included in this study.

Table 3: Reference Values from Literature A Comparison between Clinical Findings and Graphical Method Values Are Given in the Table

Author (ref)	Number of fractions (N)	Dose per fraction (D) Gy	BED. Gy Gy
Nag	5	6	44
Rattka [9]	4	10	85
Joslin [10]	6	5	44

Discussion

The calculation presented here dose per fraction based on LQ – BED terminology, considering without repopulation correction factor the isoeffective lines are linear but with repopulation correction factor BED values are reduced by only 0.63Gy this value is fractional value due to this reason isoeffective lines are not linear, it is curvier and irregular geomentry, whereas in conventional BED formulation there is range of dose per fraction which would give maximum tumour cell kill while respecting a given level of normal tissue tolerance [8] therefore isoeffective lines without repopulation correction factor is consider for this study. The specific dose per fraction from graphical method is essential for a comparison of clinical outcome. Rattka [9] published clinical results of post-operative adjuvant cuff radiation therapy with HDR alone 4 fraction of 10Gy but graphical method findings 4 fraction of 10Gy is estimated. Joslin [10] compared the clinical results 6 fraction of 5 Gy is equivalent to HDR irradiation.

According to American Brachytherapy Society panel on HDR for endometrial cancer [11] suggested 5 fractions of 6 Gy. Lesser than 3 fractions the isoeffective curve is not additive and above six fraction isoeffective lines are not linear, thus we suggest that the isoeffective lines of HDR dose per fraction lies in between 3 to 6 fractions respectively. We need to determine the HDR dose per fraction required to deliver an equivalent tumour dose of about 85Gy of BED, this dose level is considered a critical dose to specify dose per fraction [7].

The reason for repopulation correction factor not included in this study because isoeffective lines are merge from one fraction size to other fraction size .The Significant role of this graphical method is good agreement with clinical data's provided by other authors. The region of BED 85Gy the threshold dose per fraction is 4 fr of 6.5Gy, 5fr of 6Gy, 6fr of 5 Gy is harvested but 3 fr of 6 Gy BED 10 region is 55Gy therefore this dosage level is not intercepts 85Gy below consensus level therefore 3 fr not considered in this study. It is obvious LQ model Graphical method prediction is exactly correlates with clinical findings.

Conclusion

This graphical method confirms biological effective dose concept close agreement with clinical findings this method proposed here can be used to identify same fraction numbers generates linear isoefffective lines with different dose level below 5 Gy and above 10Gy. 3 fraction and 7 fractions HDR treatment could not be executed, variations in dose are equivalent to variation of fraction size is increasing the isoeffective doses vice versa. These graphical method involved in brachythrapy are in all respects similar to those involved in clinical findings. Bio effect modeling studies have attempted to equate the biological effect of various brachytherapy techniques to quantify the potential gains to tumour control [11].

There is no particular or mysterious radiobiology specific to brachytherapy indeed is very useful to consider graphical method recently there is a wide spread interest in linear quadratic model has prompted by several authors to apply the associated concepts to guide protocol developments in HDR brachytherapy [12], however the aim to not produce mathematical formulations of the biological mechanism but rather an empirical formula, an adequate tool which can be easily used current clinical practice, the validity of this graphical method eventually limits to its validity will be more fully appreciated should clinical findings reflect a correlation in its predictions.

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