



RADIOBIOLOGICAL QUALITATIVE EVALUATION OF HIGH DOSE RATE INTRACAVITARY BRACHYTHERAPY FOR GYNECOLOGICAL CANCERS.

Radiology

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ABSTRACT

The purpose of this study is to evaluate quality of high dose rate (HDR) intracavitary brachytherapy by adopting figure of merit (FOM) concept. The data of twenty patient's dose to the critical organ was evaluated; an ideal intracavitary application must have FOM value close to ten. FOM value higher or lower than ten correspond to treatments, which overall are likely to greater or lesser than reference. a graph has been plotted to extract abnormal values. FOM values are evaluated for all patients, we found all scored below tolerance value, but two patients scored more than tolerance value for rectum, in case of bladder one patient scored greater value.

KEYWORDS:

Linear quadratic Model, Biological Effective Dose, figure of merit

INTRODUCTION

Radiotherapy normally involves the use of various combinations of external beam irradiation and brachytherapy, the latter component of which may be fractionated and delivered at low, medium or high dose rate^[1]. A wide variety of treatment techniques have evolved in recent years, there has been move towards the use of remote controlled after loading systems which deliver to the brachytherapy component. Gynecological radiotherapy is therefore a subject of major radiobiological significance, but analytically it is complicated by the fact that irradiated volumes can vary considerably and by the presence of unavoidable dose gradients associated with all types of brachytherapy^[2]. Early attempts at quantification of biological effects used empirical power-law models which is used to express biological effect in terms of the total physical dose, dose rate, number of fractions, overall time etc. A number of drawbacks have been identified with such models, it is well established that, for a given total dose, changes in fractionation, dose rate, lead to changes in biological effect, the magnitude of which will depend on the nature of the tissue irradiated^[3]. Since clinical radiation doses are ultimately limited by the biological tolerance of the critical normal tissues. However Dale and Sinclair^[4] have proposed the figure of merit (FOM) concept with which to rank different treatment options. FOM takes into account the BED values for tumours and critical organs. Those alternative treatments which are most likely a given reference treatment will have FOM values close to 10. FOM values higher or lower than 10 respectively correspond to treatments which over all are likely to be better or worse than the reference. The aim of present study was to calculate FOM value of an intracavitary application, which should be considered as safe to bladder and rectum. Twenty patient's dose distributions are collected and we evaluated FOM value.3

MATERIALS AND METHODS

Twenty patients are diagnosed carcinoma of cervix who had received curative radiotherapy in the form of a combination of external beam radiotherapy followed by HDR intracavitary brachytherapy were prospectively included in this study. External beam radiotherapy was delivered 50 Gy in 25 fractions over five weeks on a Elekta linear accelerator teletherapy machine, after two weeks, intracavitary radiotherapy was delivered by HDR machine using Gamma med applicator. Computerized tomography based image reconstruction was executed, computation of dose distribution was carried out on an Eclipse treatment planning system, point-A is the prescription point, mrking points in bladder rectum are receiving maximum dose were considered for evaluation, the total dose delivered in HDR intracavitary brachytherapy is 2 fractions of 5 to 9 Gy / fractions over 14 days.

BED values for the prescribed points of the rectum and bladder were evaluated for a low dose rate (LDR) reference treatment with the help of an LDR brachytherapy equation proposed by Dale^[5] and the Parameters given in Table.1.The LDR reference treatment was taken as 25 Gy^[6,7] BED to the rectum and bladder was evaluated from the mean rectal dose and mean bladder dose. The Biologically effective

dose (BED)^[8] delivered by a treatment consisting of 'N' fractions each of magnitude d (Gy) to the dose limiting, or critical, late reacting normal tissue (BED) late and (BED) tumour are given by^[9]

$$BED_{late} = nd [1 + d / (\alpha/\beta)_{late}] \quad [1]$$

$$BED_{tum} = nd [1 + d / (\alpha/\beta)_{tum}] - KT \quad [2]$$

where n, number of fractions and d, dose per fraction (α/β)_{late} and (α/β)_{tum} are the fractionation factors for the late-responding normal tissue and tumor respectively. For the tumor alone, the product KT is the factor that accounts for cellular repopulation during treatment^[10,11].

FOM was evaluated with the following methodology^[4,12]
 $FOM = [10 (BED_{new} / BED_{ref}) tum^x]^x$ ^[3]

Where,

$$Z = 2.5 \text{ when } (BED_{new} / BED_{ref})_{tum} \geq 1.0 \quad [4]$$

$$Z = 8.0 \text{ when } (BED_{new} / BED_{ref})_{tum} < 1.0 \quad [5]$$

$$X = (BED_{ref} / BED_{new})_{crit} \quad [6]$$

$$Y = 2 \text{ when } (BED_{new} / BED_{ref})_{crit} \geq 1.05 \quad [7]$$

$$Y = 1 \text{ when } (BED_{new} / BED_{ref})_{crit} < 1.05 \quad [8]$$

X, Y and Z score the new regime in terms of its effects on both the tumor and late-reacting normal tissues relative to those of the reference regime. Z produces a tumor score favoring the maintenance or increases in the tumor BED and X, Y then modify this tumor score according to the effects of the new regime on the late-reacting normal tissue BED^[13].

Table .1.LQ model parameters to evaluate BED values^[11].

Criteria	* / (Gy)	* μ (hr-1)	*K (Gy/day)
Rectum	3.87	0.46	0.0
Bladder	4.00	0.46	0.0
Prescription point (Tumour)	10.0	0.693	0.5

* / - tissue specific parameter. * μ - repair constant * K - repopulation factor.

The relative importance attributed to each of the effects described above will determine the values chose for X, Y and Z and the final FOM value. Using the values given in eq^[3], ideal treatments that are generally better than the reference treatment is associated with FOM > 10; FOM values < 10 indicate an impaired therapeutic ratio^[4]. In this article, we first calculated BED values for rectum and bladder and to estimate FOM value for the same, the FOM concept was used to rank various options for an ideal intracavitary application.

Results

BED values for the prescribed points of rectum and bladder were

evaluated for low dose rate LDR reference treatment was taken as 25Gy^[2,6,7]. The BED to rectum and bladder was evaluated from the mean rectum, bladder dose from treatment planning system, reference bladder and rectum dose taken as 40% from prescribed dose. External beam was delivered using Elekta Linear accelerator teletherapy machine, treatment modality is four field box technique bladder rectums are localized by means of computerized tomography scan. Isodose distribution of sixty to seventy percentage lines crossing on the critical organ. Reference dose is obtained from Table.2 BED values are calculated with repopulation correction factor, Volume correction and overall treatment time, FOM values are evaluated for all patients we found all are scored below 10, teletherapy is not included in this study.

Table.2. Percentage of Point –A dose delivered to normal tissue at risk for late effects during intracavitary brachytherapy of the uterine cervix. Taken from Brennar and Hall^[1,14]

Site	Percentage of Point-A dose	Reference
Rectum (anterior)	45 ± 12 52	Bidmead and Staffurth Joslin
Rectum (midpoint)	43 ± 15 35 ± 8	Krishnan et al. Martel
Rectum (posterior)	63 ± 24	Hunter et al.
Bladder (midpoint)	57 ± 20 49 ± 15	Krishnan et al. Martel
Bladder (anterior)	35 ± 11	Krishnan et al.
Sigmoid	28 ± 7	Bidmead and Staffurth

Reference bladder, rectum, and sigmoid dose, described by various authors

Table.3. Clinical data of high dose rate intracavitary brachytherapy

*BED new Point *Gy	Bladder Dose *Gy	Rectum Dose *Gy	*FOM Rectum	*FOM Bladder
26.25	4.35	6.3	10.5	7.4
23.8	5.6	5.6	6.2	6.7
28.8	3.2	4	8.3	4.9
19.2	3.6	4.8	1.2	1.2
28.8	4.32	6.4	10.9	8.3
23.8	2.52	7	4.1	8.9
26.2	9	7.5	6.1	4.1
21.4	7.8	7.8	1.8	8.6
23.8	6	4.2	7.8	7.2
23.8	7	2.8	14	4.2
28.8	1.76	2.8	1.6	2.2
26.2	10.2	5.1	14	3.2
28.8	5.28	5.28	7.3	10.9
23.8	7	7	4.3	4.2
23.8	3.36	3.5	4.1	6.9
19.2	4.0	4.32	1.2	1.2
23.8	6.7	7.8	3.1	5.4
23.8	7.4	8.9	8.9	7.4
26.2	4.2	3.9	5.4	6.9
28.8	8	6.4	6.4	8

*BED – Biological effective dose. *FOM – Figure of merit. *Gy – Gray.

The bladder rectum dose derived from Table.3 it is derived based on sound radiobiological principles; whether it has any relevance to the treatment of the cervix by intracavitary brachytherapy is a more debatable point^[14]. The normal tissues most at risk for developing late effects as sequel to treatment of the cervix are the rectum bladder and sigmoid. Sakata et al^[15] examined the incidence of radiation induced late rectal complications by analyzing measured rectal dose data in patients with cancer of the uterine cervix, treated with high dose rate intracavitary brachytherapy. Doses were measured in 105 patients with cancer cervix during high dose rate intracavitary brachytherapy, using a semiconductor dosimeter that can measure five points in the rectum simultaneously. On basis of these measurements, equivalent doses, to which the biologically equivalent doses were converted as if given as fractionated irradiation at a rate of 2 Gy per fraction, were calculated as components of the cumulative dose at five rectal points in the intracavitary brachytherapy combined with the external whole pelvic

dose. The calculated values of equivalent doses for the late effects at the rectum ranged from 15 to 100 Gy (median 60 Gy for patients who did not develop complications and 76 Gy for patients who subsequently developed grade II and III complications). The data showed a very definite dose-response relationship, with a threshold for complications at approximately 50 Gy and the curve starting to rise more steeply at approximately 60 Gy. The steepest part of the curve had a slope equivalent to approximately 4% incidence for every 1 Gy increase in equivalent doses. The radiation tolerance doses, 5% and 50% complication probability, were about 64 and 78 Gy, respectively. The data almost agree with the prescribed dose for rectal radiation tolerance on the basis of recorded human and animal data. The probability of rectal complications increased drastically after reaching maximal rectal doses of greater than 60 Gy.

Fig.1. Shows total BED reduced to log scale and FOM value for bladder dose lies in between 1.76 to 10.2 Gy one patient scored FOM value greater than 10, three patient scored FOM value lesser than 3, majority of the patient scored FOM value in between 3 to 9. Table.2. Shows the BED values for prescription point varied from 19.2 Gy to 28.8 Gy for new treatments, the standard deviation 2.4

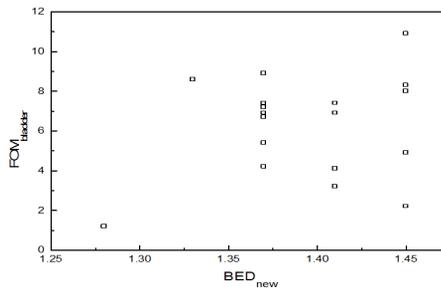


Figure -1. FOM bladder versus BED new

Fig.2. Shows total dose reduced to log scale versus FOM value for rectum is produced from Table.2 Three Patients had rectal FOM values greater than 10, two patient were both rectum and bladder FOM shows same values 1.6 and 6 respectively, standard deviation is 3.4. Two patient shows FOM value 14 therefore total dose, from prescribed point should be reduced. For tumor FOM value greater than unity. For critical it is lesser than unity.

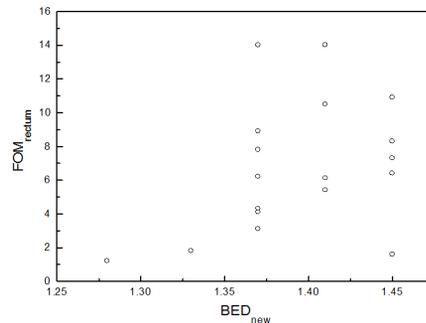


Figure -2 .FOM rectum versus BED new.

Fig.3 relation between bladder dose and bladder FOM given in figure. As the dose per fraction increased the FOM value slightly increases. Fig.3 shows one patient scored bladder dose FOM 10.9

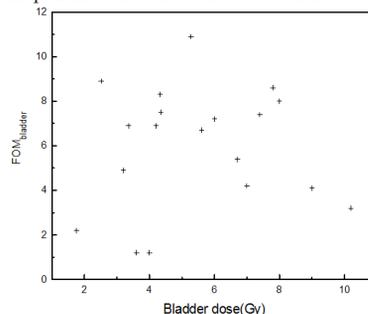


Figure-3. FOM bladder versus bladder dose

Fig.4 depicts the rectum dose versus FOM value. Two patients scored more than 10 [16]. the scatter gram Fig .1 and Fig .2 shows regular pattern of FOM value it seems to be align in straight line as BED increases FOM value also increases.

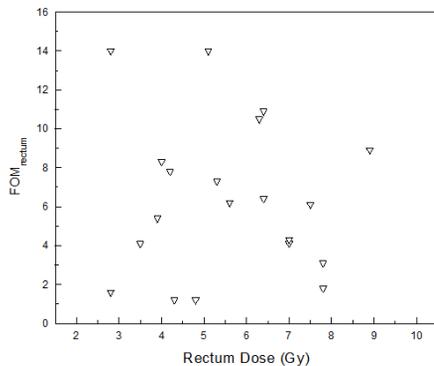


Fig.4. rectum versus rectum dose

Discussion

In this research we found that perfect intracavitary application like bladder rectum dose are within accepted limit say 40% dose from prescribed dose point, is not possible to evaluate, because FOM value depends on reference value. It is very difficult to incorporate an ideal intracavitary application; those who are having higher value of bladder and rectum more than 40% from prescribed dose were included in this study. Two patients scored FOM value more than 10 for rectum , in case of bladder one patient scored FOM greater than 10 (10.9). Fig 1, 2, and 3 are in fact fairly robust with regard to changes in patient anatomy. Although few clinical trials have examined the consequence of high dose rate brachytherapy can provide excellent therapeutic results. [17]. there are two factors; one physical and the other radiobiological can explain the efficacy of high dose rate brachytherapy [14]. Tumour over kill occurs very close to the radiation sources while surrounding and physical structures are preserved from physical dose effect and prescribed dose should be reduced, if FOM value more than 10.

Conclusion

The mathematical exercise FOM helps to quantify the quality of an ideal intracavitary application [2] that can be applied once a treatment has been considered to be over dose these FOM concepts is applicable.

It also provides a computational frame work within which salvage options may be identified [18]. There is a remedy if FOM value maximized with decrease dose to the critical organ, therefore dose to the prescribed point should be reduced, Further important factor that will contribute to making HDR techniques acceptable is that applicators to retract normal tissues away from the intracavitary radioactive source can be achieved by proper packing around the applicators [19,20]. Good physical optimization can lead to good radiobiological optimization; radiobiology cannot be improved by poor intracavitary application. Although the significance of this prospective analysis can be judged only in the light of clinical situation, therefore FOM concept may be included in treatment planning system itself to perform radiobiological evaluation of an ideal treatment.

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