

Variation of RBE with Dose and Dose Rate for a Miniature Electronic Brachytherapy Source

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ABSTRACT

A new miniature x-ray source with flexible high voltage cable allows significantly improved brachytherapy dose delivery. Changing source operating voltage varies the dose-depth characteristics of the radiation and changing beam current varies the dose rate. Because dose rate can equal or exceed that of a ¹⁹²Ir HDR source, questions have arisen about appropriate values of relative biological effectiveness (RBE) for radiation from the new source.

The problem is addressed using two simple modifications to the standard LQ model. First, the "1" in the formula for Relative Effectiveness, $1 + d/(\alpha/\beta)$, is replaced with the "maximum RBE at very low dose". Second, the relative duration of dose-per-fraction and repair rate-constant for radiation damage are incorporated by including the Lea-Catcheside dose-rate factor, G, in the α/β term. With these changes, the expression for RBE for a dose, d, is simply

$$RBE = (RBE_{max} + Gd/(\alpha/\beta)) / (1 + Gd/(\alpha/\beta)_{ref})$$

Assuming $\alpha/\beta = 3$ Gy (appropriate for late complications including breast fibrosis), $RBE_{max} = 2.0$, and that the tissue has a rapid repair component with $T_{1/2} = 0.4$ hours, then, for a 5 to 8 minute dose delivery time, G is 0.94 and the RBE for 3.4 Gy dose is 1.48. If a more realistic value of 1.5 is chosen for RBE_{max} , then the RBE for 3.4 Gy dose is 1.24. Given the rapid dose fall-off for low energy sources, alterations of 10-20% in RBE will be offset by radial distance variations of 1-2 mm from the target.

INTRODUCTION

- Xoft has developed an electronic high dose rate brachytherapy device. The Xoft microTube Flexible X-ray Probe delivers light, conformal doses of x-radiation to the inner surface of a body cavity such as an excised tumor bed. See Figures 1-2 (below).
- The Xoft Treatment System is designed to shorten radiation treatment time while significantly reducing complications to the skin and surrounding healthy tissue. The Xoft Treatment System does not require a heavily shielded environment, making treatment potentially available for patients without access to a facility with an HDR after loader. This technology eliminates handling and disposal of radionuclide sources.
- The initial application of the Xoft microTube Flexible X-ray Probe has been to the conservative treatment of breast cancer utilizing a balloon-based Partial Breast Irradiation System.

DEVICE DESCRIPTION

- The Xoft microTube Flexible X-ray Probe consists of a disposable, micro-miniature X-ray source integrated into a cooled, flexible, disposable probe.
- X-rays of 40-50 keV maximum energy are produced at the tip of the directable probe, which otherwise closely resembles current remote afterloading units.
- The X-ray source can be intensity modulated to mimic penetration and/or dose rate characteristics of many different isotopes, including HDR ¹⁹²Ir, ¹²⁵I and ¹⁰⁹Pd.
- Control variables are source operating voltage (penetration depth), beam current (dose rate), dwell time and dwell position.
- The Xoft microTube Flexible X-ray Probe can be inserted directly into tissue or into one or more lumens of an intracavitary or interstitial brachytherapy applicator, which is inserted during surgery (lumpectomy) or as an outpatient procedure up to five weeks later.
- This X-ray source is potentially appropriate for any accessible body cavity or excised tumor bed such as with breast cancer or gynecologic cancers.



Figure 1. X-Ray Source with Size Reference

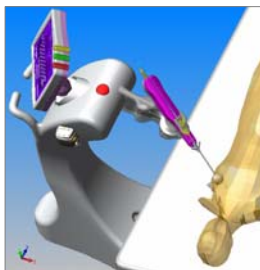


Figure 2. Xoft Treatment System with Flexible X-ray Probe

CALCULATIONS

It is known that low energy x-rays and gamma-emitting nuclides have a higher RBE than high energy and high dose rate x-rays. It is also known that RBEs which may be rather high (~2) at low doses and low dose rates, tend to have lower RBEs of about 1.2 at higher doses¹, but the relationship with dose rate has not been clearly defined quantitatively (until recently for low dose rate nuclides^{2,3}). The method involves remembering that RBE is the ratio of two equal doses of the different types of radiation that cause the same biological effect, in particular the same amount of log cell kill. RBE is then the ratio of the two Biologically Effective Doses (BEDs), which is the same (for identical physical doses) as the ratio of the two Relative Effectivenesses (REs).

This problem is basically simple using standard LQ modeling⁴ and R.G. Dale's method of replacing the "1" in the formula for Relative Effectiveness ($1 + d/(\alpha/\beta)$) with the "maximum RBE at very low dose."⁵ The results are consistent with previously published radiobiological experimental data (for example, reference 1) However, the present algorithm provides a clearer picture of the relationships than the often confusing biological results in the literature. The following examples show these relationships, first for dose-per-fraction only and then for dose rate changes.

A. Changes of Dose RBE Per Fraction for High and Low Energy Radiation

The first step is to calculate BEDs for high and low energy radiation where n fractions of the same dose per fraction are delivered. Equations 1 and 2 present the expressions for BED for high and low energy radiation, respectively. As noted above, Eq. 2 incorporates RBE_{max} . The effective RBE is the ratio of BED2 / BED1. Since BED equals Total Dose, nd, times RE, the same ratio will be found for the two REs, that is RE2 / RE1.

Assuming $\alpha/\beta = 3$ Gy, to be appropriate for late complications in most tissues including breast fibrosis, RE's are calculated for doses of 1 to 20 Gy (Table 1).

High energy & high dose rate x-rays

$$BED1 = nd (1 + d / (\alpha/\beta)) \dots \dots \dots (1)$$

Low energy & high dose rate x-rays

$$BED2 = nd (RBE_{max} + nd / (\alpha/\beta)) \dots \dots \dots (2)$$

Table 1. RBE for dose per fraction ranging from 1 to 20 Gy

	Standard High-Energy Radiation	Low-Energy Radiation	Effective Ratios RE2/RE1
d = 1 Gy	RE1 = 1 + 1/3 = 1.333	RE2 = 2 + 1/3 = 2.333	RBE = 2.333/1.333 = 1.78
d = 3 Gy	RE1 = 1 + 3/3 = 2.0	RE2 = 2 + 3/3 = 3.000	RBE = 3.000/2.000 = 1.50
d = 10 Gy	RE1 = 1 + 10/3 = 4.333	RE2 = 2 + 10/3 = 5.333	RBE = 5.333/4.333 = 1.23
d = 20 Gy	RE1 = 1 + 20/3 = 7.667	RE2 = 2 + 20/3 = 8.667	RBE = 8.667/7.667 = 1.13

This sequence and the figure below show clearly how the RBE of low-energy radiation falls with increasing dose-per-fraction (for the "late" effects, $\alpha/\beta = 3$ Gy) and easily reaches the region of RBE = 1 to 1.2. Note that the maximum RBE was assumed to be 2.0 in this example, but if a more realistic value of about 1.5 were used, the RBE for 3 Gy fraction size would become 1.25.

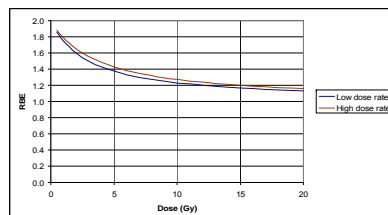


Figure 3. RBE as a function of dose per fraction and dose rate assuming RBE_{max} is 2.0.

CALCULATIONS

B: Changes of Dose Rate for High and Low Energy Radiation

These calculations show how RBE is also a function of dose rate, that is relative duration t of the dose-per-fraction and the repair rate-constant of radiation damage, $\mu = (\ln 2)/T_{1/2}$. This is dealt with by adding the well known Lea-Catcheside dose-rate factor G (Equation 3) into the α/β terms of equations 1 and 2 above.

$$G = (2/\mu t) [1 - (1/\mu t) (1 - e^{-\mu t})] \dots \dots \dots (3)$$

where $\mu = (\ln 2)/T_{1/2}$ and $T_{1/2}$ is the half-time for repair.

To give a practical example, let us assume that the dose rate is low enough so that each dose takes 20-30 minutes to deliver, and also that the tissue in question has a component of rapid repair so that the repairable damage (the β term) falls by 20%, which occurs for a $T_{1/2}$ of about 0.4 hours. Then $G = 0.8$ and the RBEs do not become quite so low, as shown by the ratios of RE5/RE4. This ratio is also plotted in the figure above as the "high dose rate" function. As can be seen, the impact of dose rate is secondary to the dose.

High energy & lower dose rate X-rays

$$BED4 = nd (1 + G.d / (\alpha/\beta)) \dots \dots \dots (4)$$

Low energy & lower dose rate X-rays

$$BED5 = nd (RBE_{max} + G.d / (\alpha/\beta)) \dots \dots \dots (5)$$

Table 2. RBE for dose per fraction ranging from 1 to 20 Gy and dose delivery time of 0.4 hours.

Standard High-Energy Radiation	Low-Energy Radiation	Effective Ratios RE5/RE4
d = 1 Gy RE4 = 1 + 0.8/3 = 1.266	RE5 = 2 + 0.8/3 = 2.266	RBE = 2.266/1.266 = 1.79
d = 3 Gy RE4 = 1 + 0.8x3/3 = 1.8	RE5 = 2 + 0.8x3/3 = 2.8	RBE = 2.800/1.800 = 1.55
d = 10 Gy RE4 = 1 + 8/3 = 3.667	RE5 = 2 + 10/3 = 4.667	RBE = 4.667/3.667 = 1.27
d = 20 Gy RE4 = 1 + 16/3 = 6.333	RE5 = 2 + 20/3 = 7.333	RBE = 7.333/6.333 = 1.16

Note again that these RBEs are slightly above those really expected because a maximum RBE of 2 was assumed.

DISCUSSION

Different dose rates and durations of exposure are dealt with by the G factor wherever appropriate⁶, separately if necessary for the different types of radiation, depending how they were each irradiated. Radiation conditions in this example were assumed to be equivalent, but if the standard radiation had been given at high dose rate, RE4 would be higher so the effective RBE would have been lower.

Brenner and colleagues are one of the very few groups to have addressed the question of relative biological effectiveness (RBE) of low energy X-rays from devices such as the Xoft X-ray Probe and they calculated that the RBE would be greater than that for ¹⁹²Ir and more comparable to ¹²⁵I.⁷ For the Photon Radiosurgery System of Photoelectron Corporation operating at 40 kV, Brenner *et al* calculated that the RBE would vary from approximately 1.2 to 2.1 with respect to ¹⁹²Ir depending on dose rate, total dose and depth. However, this RBE range was determined for "early responding endpoints" using an α/β ratio of 8 Gy.

CONCLUSION

For the miniature x-ray sources of interest, doses of 2 to 6 Gy are delivered to the tissue of interest in approximately 5 to 8 minutes so this simple model predicts an RBE of approximately 1.3. The steep fall-off of dose with distance for these low energy sources means that alterations of 10% or even 20% in RBE will be cancelled out by alterations of only 1 or 2 mm in radial distance from the target, which will be within practical variations of distances at which a dose prescription surface could be localized for treatment.

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