High and Low Dose-rate Brachytherapy for Cervical Carcinoma

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For the brachytherapy component of the radiation treatment of cervical carcinoma, high dose rate (HDR) is slowly replacing conventional low dose rate (LDR) due primarily to radiation safety and other physical benefits attributed to the HDR modality. Many radiation oncologists are reluctant to make this change because of perceived radiobiological disadvantages of HDR. However, in clinical practice HDR appears to be as effective as LDR but with a lower risk of late complications, as demonstrated by one randomized clinical trial and two comprehensive literature and practice surveys. The reason for this appears to be that the radiobiological disadvantages of HDR are outweighed by the physical advantages.

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Radioactive isotopes were first used for the treatment of cervical carcinoma at the beginning of the 20th century, soon after the discovery of radioactivity in 1896 (1, 2). For the next 60 years such treatments were delivered exclusively at low dose rate (LDR), not because LDR was considered superior to high dose rate (HDR), but simply because high-activity sources suitable for HDR therapy were not available. It was not until the dawning of the age of nuclear energy and the development of nuclear reactors in the 1940s and 50s that high-activity source production became feasible. HDR sources began to be applied to brachytherapy in the early 1960s. By then, radiation oncologists had accumulated 60 years of experience in LDR treatment of carcinoma of the cervix, with good results, so it was not too surprising that only a few were willing to change from LDR to HDR at that time. What *is* surprising, however, is that today, after 30 years of experience with HDR and tens of thousands of patients treated with reportedly excellent results, HDR brachytherapy still seems to be unacceptable to most radiation oncologists as a viable replacement for LDR for the treatment of cervix cancer. For example, a recent survey in the United States, a country where new technology usually is adopted readily, showed that in 1996 only about 16% of Ca cervix patients receiving brachytherapy were being treated with HDR (3). A similar predominance of LDR probably exists in most other countries, although Japan is an exception: Japan was one of the first countries to show wide acceptance of HDR and presently almost all brachytherapy for cervix Ca is delivered with HDR (4). The main reason for this is the great concern of the Japanese people and government about radiation exposure, presumably a legacy from the Hiroshima and Nagasaki atomic bomb experience. With LDR many people are exposed to radiation in addition to the patient, whereas with HDR only the patient is exposed.

In this review, clinical results achieved with HDR will be presented and compared with those with LDR. Potential radiobiological explanation of these results will be given. First, however, it is instructional to discuss the major rationale for the original introduction of HDR, namely radiation protection, as well as other potential physical advantages of the HDR technique, such as stability of applicators, improved dose distributions, utility, convenience, and economic considerations.

PHYSICAL ASPECTS OF HDR

Radiation safety

For the first 50 years or so of Ca cervix brachytherapy, applicators were first loaded with radium (or later cesium) sources and then inserted 'live' into the patient. The 'active' patient then lay in a hospital bed for up to a week, irradiating nurses, visitors and adjacent patients. Physicians inserting the applicators and physicists loading them were also exposed. This constituted the highest source of radiation exposure to medical personnel. The first signifi-

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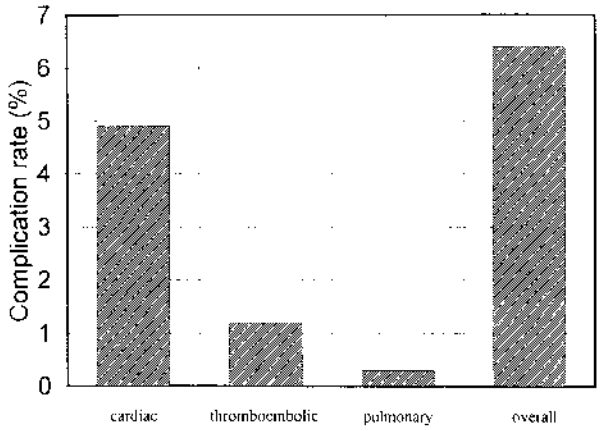

Fig. 1. Life-threatening perioperative complications with conventional LDR brachytherapy for gynecological cancers (16).

cant breakthrough in reducing these exposures in Ca cervix brachytherapy came in the early 1960s with the advent of 'afterloading', whereby applicators were inserted into the patient 'cold' and then loaded with the radioactive sources at a later time (5–8). The principal beneficiary of this new technique was the physician, because inserting the sources into the patient could be performed much more rapidly. However, exposure of physicists, nursing staff and visitors was reduced only a little, if at all. It was not until the introduction of remote afterloading (RAL) that these latter exposures were reduced. This occurred in the mid-1960s for both HDR and LDR. The first RAL unit for HDR was the Brachytron, introduced in 1964 by Henschke (9), followed shortly after by the development of the Cathetron in England (10), the Ralstron in Japan (11), the Buchler unit in West Germany (12), and the Decatron in East Germany (13). More recent additions to the HDR armamentarium have come from Nucletron (The Netherlands), GammaMed (Germany), CIS-US (France), AGAT (FSU), Omnitron (USA) and Varian (USA) (14).

Shortly after the appearance of the first HDR remote afterloader, along came the first LDR units, the Cervitron and the Curietron, both developed following the pioneering work of Swedish medical physicist, Rune Walstam (15). Since the mid-1980s, Nucletron LDR units have become the most common of these machines. These LDR units do not, however, completely solve the radiation safety problem because the patients are still treated in hospital beds in rooms not heavily enough shielded to eliminate all exposure of staff and adjacent patients. Furthermore, these LDR units are left under the supervision of nursing staff with little radiation safety training. Dislodged sources and applicators are obvious potential safety hazards. With HDR such problems present an even more significant hazard for both staff and patient because of the very high source activity. However, since HDR procedures are usually performed within radiotherapy departments, qualified personnel are readily available to handle such emergencies.

Reduced hospitalization

A second major reason for conversion from LDR to HDR is reduced hospitalization. For each LDR patient about one week of hospitalization is required, whereas, with HDR, this can be reduced to a maximum of one day. In many countries, hospitalization of patients is very expensive and methods to reduce this cost are encouraged (see economic considerations later). In others, the availability of hospital beds is a problem, especially beds in rooms suitably placed or shielded for LDR brachytherapy. There is also the problem of morbidity due to the long periods of bed-rest associated with LDR treatments. For example, Dusenbery et al. (16) observed over 6% life-threatening perioperative complications associated with LDR brachytherapy. Their results are illustrated in Fig. 1. Finally, there is the problem of applicator stability during the long periods of hospitalization required for LDR treatments.

Stability of applicators

One concern with LDR intracavitary brachytherapy is the stability of positioning of the applicators during the long periods of treatment. Dose calculations are performed soon after the applicators are inserted and before they are loaded. The patient is then moved to a hospital bed where the applicator is loaded. This is followed by several days of relatively free movement in bed during the time of treatment. Movement of the applicators is inevitable, yet it is common practice to assume that the dose distributions calculated before the start of treatment remain the same throughout. On the few occasions that a second dosimetric

Table 1

Effect of applicator motion during LDR cervix cancer brachytherapy† (17)

Mean I.C. treatment time (h)	Mean % increase in dose rate			
	Point A	Bladder	Rectum	Rectum/bladder combined
44.3 ± 1.5*	$+2.4 \pm 0.9$*	$+6.9 \pm 5.5$*	$+19.0 \pm 8.2$*	$+12.6 \pm 4.8$*

† Data from Ljunggren et al. (18), King (19), Corn et al. (20), Joelsson & Bäckström (21), King (pers. comm., 1995), and Coetzee (pers. comm., 1996).
* Standard errors of the means.

Table 2

Patient distribution and clinical results achieved for the Chandigarh randomized clinical trial of HDR vs. LDR for cervical cancer brachytherapy (27)

Stage	HDR patients	LDR patients	HDR		LDR	
			LC (%)	5-yr. survival (%)	LC (%)	5-yr. survival (%)
I	35	39	91	78	92	74
II	90	93	76	65	79	62
III	111	114	71	43	76	50
Overall	236	246	76	58	80	58

study has been performed on completion of treatment, this assumption has been shown to be erroneous. For example, a recent study of data from five institutions where dose distributions have been determined both at the beginning and at the end of an intracavitary application with LDR has demonstrated that 'hot-spot' dose rates to bladder and rectum increase during treatment at an average rate of 7% and 19% respectively, with negligible change in the dose rate to Point A (17). This data can be found in Table 1. With the HDR modality, such instability is not a problem because of the short treatment time, the potential for fixation of applicators during the period from dose planning through to the end of irradiation and, in many practices, the availability of radiographic systems in the treatment room so that the patient does not need to be moved at all after insertion of the applicators.

Another potential advantage of HDR is the better packing/retraction possible because of the short treatment times: with just local analgesics, patients are able to withstand more 'aggressive' forms of packing or retraction than would be tolerated during the long applications of LDR therapy. Finally, because most HDR units employ a single stepping-source technology, an infinite variety of source arrangements is possible and this makes optimization of dose distributions a potential benefit. Such optimization has become possible at low dose rate also with the advent of pulsed brachytherapy (PB). Indeed, this has been the major impetus for the development of PB, which uses multiple fractions (pulses) of treatment with a stepping source of about one-tenth the activity of an HDR source, with pulse length and time between pulses arranged so as to deliver a similar total dose in a similar overall time as with conventional LDR (22). Of course, PB does not have the advantages of better fixation, retraction, and packing as does HDR. Nor does it have all the radiation safety benefits as HDR. Finally, in some respects both conventional LDR and PB are not as convenient to apply as is HDR.

Convenience

LDR brachytherapy, whether delivered by conventional means, remote afterloading, or PB, is inconvenient to both patients and staff. It is inconvenient to the patient because it necessitates long periods of confinement to a hospital bed, often with limited nursing care and visitor privileges. Furthermore, it is inconvenient to staff because the application procedure has to be performed outside of the radiotherapy department. The radiation oncologist has to leave the department to insert and remove the applicators and to visit the patient during therapy, and the physicist has to survey the patient's room. With HDR all these procedures occur in the radiotherapy facility. However, with HDR such advantages are somewhat counterbalanced by the need to have the physicist and/or physician available during each HDR application in case of emergencies, such as obstructed sources, broken source cables, etc. The inconvenience to the physicist of having to develop a treatment plan and to set and check the machine parameters, all in a short period of time before each fraction of treatment, also needs to be considered. In general, HDR treatment of a patient is considerably more physics-intensive than LDR, and thus requires more physics support. Such physics staffing requirements will have a negative effect on the economic aspects of HDR treatment, although this tends to be offset by certain savings.

Economic considerations

Several studies have shown that the expense of HDR brachytherapy is probably comparable to that of LDR or perhaps in some circumstances even less (23–26). However, it is clear that such comparisons are highly practice-specific due to the high initial costs required to establish a new HDR program. These include the cost of the HDR unit and ancillary equipment and the shielded treatment room, although the latter might not be necessary if a shielded room is already available (e.g. an old Co-60 teletherapy room). With such high initial expenditure, only a 'busy' HDR practice is likely to prove a cost-effective replacement for an existing LDR practice. How 'busy' a practice needs to be depends on such factors as costs associated with hospitalization of LDR patients, operating room (OR) costs (most LDR applications require more OR sessions than are needed for HDR), and costs associated with the alternative LDR treatments. With LDR remote afterloading, only one patient can be treated at a

Table 3

Rates of late morbidity observed in the Chandigarh randomized clinical trial (27)

Severity	Bladder		Rectosigmoid		p-value
	HDR (%)	LDR (%)	HDR (%)	LDR (%)	
Grades 1+2	3.8	3.7	5.9	17.5	<0.001
Grades 3+4			0.4	2.4	>0.05
Overall	3.8	3.7	6.4	19.9	<0.001

time, whereas with HDR, as many as 10 patients can be treated daily, i.e., a total of about 2500 treatments can be delivered annually. Then, if each Ca cervix patient needs, say, five fractions, each HDR RAL unit can treat 500 or more new patients annually, whereas one LDR unit can treat only about one-tenth as many.

Clearly, HDR brachytherapy for the treatment of carcinoma of the cervix has physical attributes that make it an attractive alternative to LDR. Furthermore, conversion from LDR to HDR can be economically beneficial. However, conversion from a modality for which there has been almost a century of clinical experience, with good results, is not appropriate unless there is convincing evidence that HDR is at least as safe and effective.

CLINICAL EXPERIENCE WITH HDR

For most radiation oncologists the only truly convincing evidence of the efficacy of a new modality of treatment is a prospective randomized clinical trial comparing the new technique with the conventional one. For HDR cervix cancer brachytherapy, only one such trial has been completed. This trial was conducted at the Postgraduate Institute of Medical Education and Research, Chandigarh, India, from 1986 to 1989 (27). This involved treatment of 482 previously untreated patients with invasive squamous cell carcinoma of the cervix. Patients were randomized to receive either LDR brachytherapy at 0.55–0.65 Gy/h or HDR at 9–9.5 Gy/fraction to Point A. Pelvic teletherapy used for the LDR and HDR patients was identical. A total of 246 patients were randomized to receive LDR treatment and 236 HDR. Distribution by FIGO Stage is shown in Table 2. For early-stage patients with small tumors, the predominant treatment was by intracavitary therapy. Total Point A doses were 75 Gy in two fractions for LDR, or 38 Gy in four fractions for HDR. Patients with more extensive disease received 35 Gy in one fraction with LDR, or 18 Gy in two fractions with HDR, the major modality of treatment for these patients being external beam.

Local control and five-year disease-free survival results (life-table) are also shown in Table 2. There were no statistically significant differences between the LDR and HDR results for either local control or survival. Morbidity, however, was a different matter. The authors defined moderate-to-severe morbidity as Radiation Therapy Oncology Group RTOG Grades 3–5. No Grade 5 complications (fatal) were observed. Although there was no difference between LDR and HDR in the rates of bladder complications (overall, 3.7% and 3.8% respectively), late rectosigmoid morbidity was higher for the LDR patients (Table 3). The overall rectosigmoid complication rates were 19.9% for LDR and 6.4% for HDR. This difference was statistically significant ($p < 0.001$). The moderate-to-severe rectosigmoid morbidity rates were 2.4% (LDR) and 0.4% (HDR), but there were too few such complications to demonstrate a statistically significant difference ($p > 0.05$).

This randomized clinical trial clearly demonstrates that HDR brachytherapy for the treatment of carcinoma of the cervix with Point A doses as high as 9–9.5 Gy/fraction is as effective as LDR and that such results can be achieved with less morbidity. However, this is just a single randomized clinical trial at a single institution. Before accepting this one trial as providing the ultimate evidence for the efficacy of HDR, it is important to review all available clinical data to determine whether they support the Chandigarh conclusions.

There have been numerous non-randomized studies of HDR vs. LDR for Ca cervix brachytherapy. One such study actually started out as a prospective randomized clinical trial of LDR vs. HDR. This was initiated in 1975 at the Osaka University Hospital, Japan (28). From 1975 to 1979 patients were randomized in order of their registration. However, from 1979 to 1983 strict randomization was abandoned, partly because '...many older patients were referred to HDR because of the advantages of HDR, which had became apparent by that time' (28). Unfortunately, this caused the patient population to be biased such that older patients and patients with advanced disease were more likely to receive HDR compared with LDR. Such known bias makes it impossible to use the results for a comparison of LDR with HDR. Fortunately, many retrospective, non-randomized studies do not exhibit such biases. Space prohibits review of all these studies, but suffice it to report that most of them concluded that both survival and morbidity were comparable, HDR vs. LDR. Many of these reports indicated that there were fewer complications observed with HDR, but usually the numbers were insufficient to make the trend statistically significant. In order to improve the statistics, a review of the data from several institutions was undertaken in two studies.

Table 4

Patient distribution and 5-year (crude) survival data determined in the meta-analysis of the Ca cervix brachytherapy results from 56 institutions by Orton, et al. (30)

Stage	HDR patients	LDR patients	5-year survival		p-value
			HDR (%)	LDR (%)	
I	1 327	630	82.7	82.4	>0.05
II	2 891	1 271	66.6	66.8	>0.05
III	2 721	1 464	47.2	42.6	0.005
IV	221	56	20.4	14.3	>0.05
Overall	7 468	4 738	60.8	59.0	0.045

The first of these multi-institutional studies was that of Fu & Phillips (29), in which they reviewed results from ten published comparisons of HDR with retrospective, or sometimes concurrent, LDR data. A total of 1764 patients treated with HDR was compared with 2370 LDR patients. However, no attempt was made to perform a meta-analysis by combining the data, although the qualitative conclusion was reached that '...most of the non-randomized studies suggest similar survival, local-control, and complication rates using fractionated remote afterloading HDR intracavitary brachytherapy combined with external beam irradiation for carcinoma of the cervix compared to historical or concurrent LDR controls' (29). It should be noted that most of the facilities in this study used Point A doses of 7–8 Gy/fraction for 3–6 weekly fractions.

A more extensive multi-institutional study including 17068 patients treated with HDR and 5666 with LDR at 56 institutions was published by Orton et al. (30). This involved a combination of both published data and information, collected via a questionnaire. A meta-analysis was performed on the combined data sets. The overall 5-year survival rates were similar (Table 4), being 60.8% for HDR and 59.0% for LDR although, because of the large number of patients, the difference bordered on statistical significance ($p = 0.045$). However, since no randomization was involved, use of p-values to demonstrate statistical significance in this context is questionable, especially with such comparable survival rates. For Stage III patients, however, the difference in five-year survival rates was somewhat more significant, being 47.2% for HDR compared with 42.6% for LDR ($p = 0.005$). The average Point A dose/fraction for these patients was 7.5 Gy for HDR and the average dose rate for LDR was 0.85 Gy/h. It is noteworthy that, in the Fu & Phillips study (29), only two of the 10 institutions (31, 32) reported any significant differences in survival between LDR and HDR, and this was improved survival with HDR, primarily for Stage III patients.

Differences in morbidity rates were even more significant (Table 5). Complication rates were lower for HDR vs. LDR for both severe (2.2% vs. 5.3%, $p < 0.001$) and moderate plus severe (9.1% vs. 20.7%, $p < 0.001$) injuries. Interestingly, these moderate plus severe morbidity rates are similar to the combined rates for the studies reviewed by Fu & Phillips (Table 6) (29), which were 12.5% for HDR vs. 18% for LDR, although these authors did not perform such a meta-analysis in their report. Also of interest, as far as complications are concerned, is the effect of dose/fraction. Orton et al (30) showed that lower doses/fraction produced fewer complications. This is illustrated in Fig. 2. Similar observations at several individual institutions have led to reduction in dose/fraction and concomitant increases in fractionation (33–35).

In summary, one randomized prospective clinical trial, one survey of published studies of non-randomized comparisons of LDR and HDR treatments, and one meta-analysis, have all demonstrated that local control and survival results are similar for LDR and HDR, but HDR can be delivered with less morbidity. Such clinical results are somewhat surprising because it has long been believed that LDR must be the ultimate form of brachytherapy and that it has to be radiobiologically superior to HDR.

RADIOBIOLOGICAL CONSIDERATIONS

The 'belief' that LDR brachytherapy has to be the best is based on the premise that late-reacting normal tissue cells repair sublethal damage more effectively than do cancer

Table 5

Late complication rates observed for the Ca cervix meta-analysis of Orton et al. (30)

Severity	Patients at risk		Complication rate		p-value
	HDR	LDR	HDR (%)	LDR (%)	
Grade 4	10 331	5 274	2.2	5.3	<0.001
Grades 3+4	10 887	4 709	9.1	20.7	<0.001

Table 6

Meta-analysis of the late morbidity rates derived from the data reported for six institutions by Fu & Phillips (29). Such an analysis was not presented in the original article

Site	Patients at risk		Complication rate		p-value
	HDR	LDR	HDR (%)	LDR (%)	
Rectum	681	1 923	8.8	13.0	<0.01
Bladder	681	1 923	3.7	5.0	>0.05
Overall	681	1 923	12.5	18.0	<0.001

cells. Sublethal damage represents the occurrence of single-strand breaks in DNA molecules. A single-strand break can be repaired if sufficient time for repair transpires before a second single-strand break transforms the first break into a (lethal) double-strand break (36). Repair of sublethal damage is thus a low dose or low dose-rate phenomenon, and apparently normal tissue cells are better able to accomplish this repair than are tumor cells. It is this repair advantage that normal cells exhibit over tumor cells that is the rationale for conventional LDR brachytherapy and fractionation in teletherapy. This phenomenon is demonstrated by the different shapes of the cell-survival curves illustrated in Fig. 3: survival curves for late-reacting normal tissue cells tend to be curvier and to have a shallower initial slope compared to cancer cells (36). At doses lower than those at the crossover point of the two curves, survival of normal cells exceeds that of tumor cells. However such low doses are not sufficient to kill all the cancer cells in a typical tumor, so multiple low-dose fractions have to be delivered, with enough time between fractions to allow for complete repair. Such fractionated radiotherapy survival curves are shown in Fig. 4. For each successive fraction the two curves gradually diverge. For the same reason, the curves diverge in a similar way for treatments at low dose rate, as illustrated in Fig. 5. Since LDR is essentially equivalent to an infinite number of low-dose fractions which ought to produce maximum divergence between these two cell-survival curves, it would appear that LDR has to be the ultimate form of brachytherapy.

Note that Figs. 3–5 have been constructed using the linear-quadratic (LQ) cell-survival model (36, 37). This is the most widely accepted model for representing the effect of repair on radiobiological damage and it has been used extensively in the literature on LDR and HDR brachytherapy. It will be used here to demonstrate repair characteristics of normal and cancer cells, and how damage to these cells is effected by changes in dose rate and fractionation.

One of the major problems with the LQ model is that the parameters α, β and $t_{1/2}$ are not known very accurately for any specific normal tissue or cancer cells, where α and β are parameters that define the initial slope and the 'curviness' of the survival curve, respectively, and $t_{1/2}$ is the half-time for repair of sublethal damage (36). The ratio α/β tends to be low for late-responding normal tissues ('curvy' survival curve) and high for tumors, whereas differences in $t_{1/2}$ between these tissues is less well established. Recent studies, however, have shown a trend toward slower rates of repair for late-reacting normal tissue compared with tumor cells, with values of $t_{1/2}$ for these normal tissue cells averaging about 1.5 h compared with

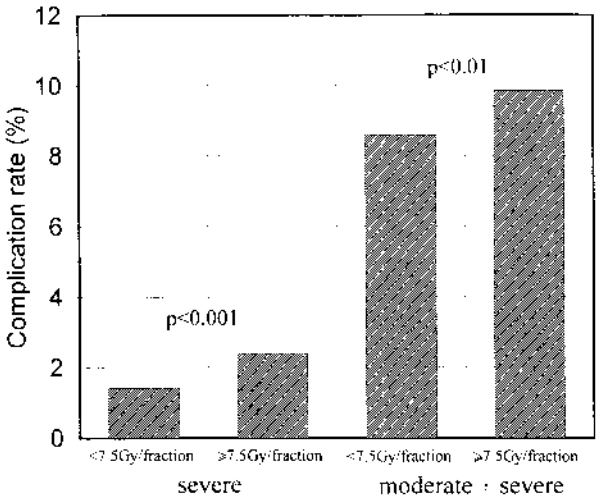

Fig. 2. The effect of dose/fraction to Point A on severe (grade 4) and moderate plus severe (grades 3 and 4) late rectal and bladder complications, as reported by Orton et al. for HDR brachytherapy for cervical carcinoma (32).

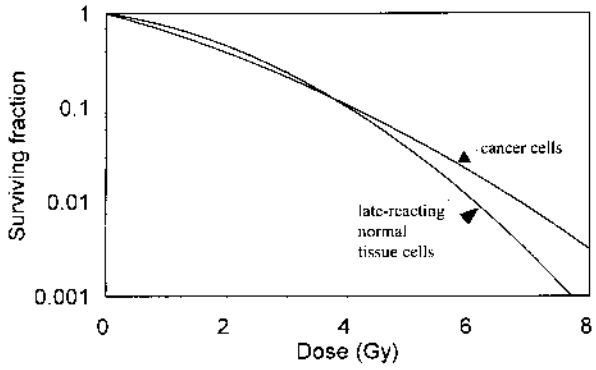

Fig. 3. Typical log cell surviving fraction curves for late-reacting normal tissue and tumor cells irradiated acutely. The linear quadratic model has been used to construct these curves with α/β values 2.5 Gy and 10 Gy for normal and tumor cells, respectively (36).

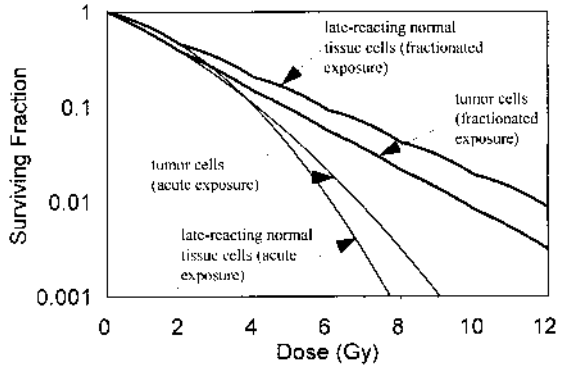

Fig. 4. Illustration of how fractionation, with dose/fraction below the crossover point of the acutely exposed cells (Fig. 3) results in higher cell survival for late-reacting normal tissue compared to tumor cells (17, 36). The same LQ-model parameters as those for Fig. 3 have been used to construct these curves.

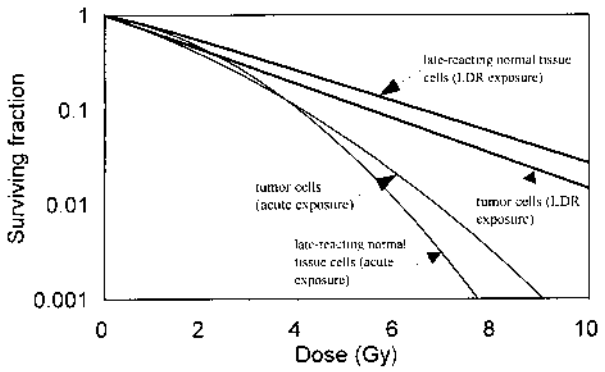

Fig. 5. Illustration of low LDR treatment results in higher cell survival for late-reacting normal tissue compared to tumor cells. The same LQ-model parameters as those for Fig. 3 have been used with half-time for repair of 0.5 and 1.5 h for tumor and normal-tissue cells, respectively, and dose rate 0.4 Gy/h for the LDR exposures (17).

about 0.5 h for tumor cells (36, 38). This slower rate of repair of late-reacting normal tissue cells will be more detrimental for LDR than for HDR. This is because, with LDR, tumor cells will benefit most during the time of irradiation due to their more rapid rate of repair, whereas with HDR the treatments are too short for any significant repair to occur, even for tumor cells, and the time between fractions is long enough to allow for complete repair, even for slow repairing normal cells.

The α, β and $t_{1/2}$ values used to construct Figs. 3–5 and subsequent figures in this article have been carefully selected to best demonstrate the radiobiological differences between LDR and HDR and, in particular, to show how HDR could be radiobiologically superior to LDR. However, Figs. 3–5 are not entirely realistic because it has been assumed that the dose to normal tissues is effectively the same as that to tumors, whereas a major benefit of brachytherapy is that the radioactive sources are placed in and around the tumor. Hence, normal tissues are 'spared' from the high doses delivered to the tumor. Such sparing of normal tissues has been represented by Dale (39) by the so-called 'geometrical sparing factor', where:

$$\textit{geometrical sparing factor } f = \frac{\textit{effective normal tissue dose}}{\textit{effective tumor dose}}$$

For brachytherapy, f will generally be equal to or less than 1.

These concepts have been used frequently in publications that show that a course of fractionated HDR brachytherapy can be designed to be equivalent to an LDR regimen such that the effects on both normal tissues and tumor are equivalent (17, 36, 39–41). For example, Fig. 6 illustrates that, as LDR dose rate is decreased in order best to take advantage of the repair differences between normal tissues and tumor, the HDR dose/fraction needs to be reduced in order to maintain equivalence. As shown in Fig. 6, for LDR treatment at dose rates about 0.8 Gy/h, only modest geometrical sparing ($f = 0.7$–0.8) is required in order for HDR regimens at 7–9 Gy/fraction to be radiobiologically equivalent. However, this simple modeling does not demonstrate why HDR treatments with this fractionation have proven *less toxic* than LDR for the treatment of cervical carcinoma, especially if LDR treatments at dose rates lower than 0.8 Gy/h are used for comparison. For example, Fig. 6 shows that equivalence to LDR at 0.4 Gy/h could be achieved by 7–9 Gy/fraction HDR regimens only with very extensive geometrical sparing ($f < 0.5$), which is probably not realistic. The likely reason for this apparent disparity between theory and practice is the increase in dose rate to rectum and bladder that occurs during a protracted LDR treatment that was demonstrated earlier (see Table 1). It has been shown that if this increase occurs gradually as the treatment progresses, the effect on the equivalent HDR regimen can be dramatic (17). This is demonstrated in Fig. 7, which shows that an LDR application at 0.4 Gy/h can be replaced by HDR at 7.5–9.5 Gy/fraction with just a modest ($f = 0.7$)

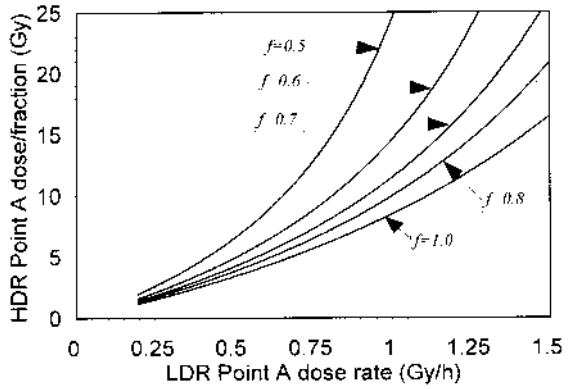

Fig. 6. Equivalent HDR Point A dose/fraction required to replace an LDR regimen at various dose rates (17). These curves have been constructed using the same LQ model parameters as those used for the previous figures.

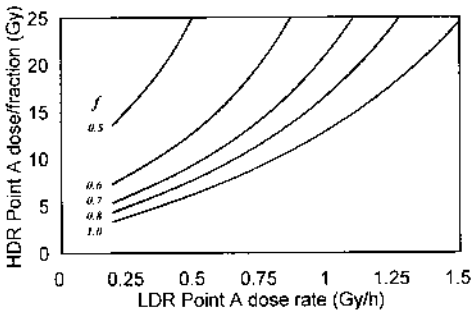

Fig. 7. Same as Fig. 6, but with correction for applicator motion during LDR treatment.

geometrical sparing of normal tissues. Furthermore, LDR at 0.8 Gy/h with $f = 0.7$ can be replaced by HDR regimens with a dose/fraction considerably higher than 10 Gy. This demonstrates a potential reason for the lower complication rates observed clinically with HDR delivered at about 7.5 Gy/fraction when compared with LDR at 0.8 Gy/h.

SUMMARY AND CONCLUSIONS

For the treatment of carcinoma of the cervix, HDR brachytherapy has some physical advantages over LDR, the most obvious being reduction in radiation hazards, reduced hospitalization, and improved stability of the applicators. The last of these advantages, coupled with geometrical sparing of normal tissues inherent with brachytherapy and possibly slower rates of repair of sublethal damage for late-responding normal tissue cells than for tumor cells, can lead to a radiobiological advantage for HDR compared with LDR. This radiobiological advantage has been demonstrated by reduced late normal tissue complication rates for the same 5-year survival rates in one randomized prospective clinical trial and two literature and practice surveys, especially if the dose/fraction to Point A is 7.5 Gy or lower. It can be concluded, therefore, that HDR brachytherapy for the treatment of carcinoma of the cervix is a viable alternative to conventional LDR.

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