Yonsei Medical Journal
Vol. 43, No. 6, pp. 737 - 748, 2002

Fractionated High-Dose-Rate Brachytherapy in the Management of Uterine Cervical Cancer

Hee-Chul Park, Chang Ok Suh, and Gwi Eon Kim

Department of Radiation Oncology, Yonsei Cancer Center, Brain Korea 21 Project for Medical Science, Yonsei University College of Medicine, Seoul, Korea.

It is well known that intracavitary radiotherapy (ICR), either alone or in combination with external-beam radiotherapy (EBRT) is an essential component of the radiation treatment of uterine cervical cancer. Although low-dose-rate (LDR) brachytherapy has been successfully applied to the management of such patients, several radiation oncologists have experience of using high-dose-rate (HDR) brachytherapy with promising clinical results over the past 4 decades. However, there has been a considerable reluctance by radiation oncologists and gynecologists in North America to employ the HDR remote afterloading technique instead of the more firmly established LDR treatment modality. In contrast, the HDR-ICR system is rapidly gaining acceptance in Korea since the introduction of the Ralstron, remotely controlled afterloading system using HDR Co-60 sources, at the Yonsei Cancer Center in 1979. According to brachytherapy statistics reported by the Korean Society of Therapeutic Radiology and Oncology, in 1997, brachytherapy was performed upon 1,758 Korean patients with uterine cervical cancer, of whom approximately 83% received HDR brachytherapy. In this review, we present our experiences of HDR-ICR for the treatment of uterine cervical cancer. In addition, we discuss the controversial points, which are raised by those considering the use of HDR-ICR for uterine cervical cancer; these issues include physical and radiobiological considerations, and the prospect of future technical improvements.

Key Words: Cervical cancer, radiotherapy, high-dose-rate, brachytherapy

INTRODUCTION

External-beam radiotherapy (EBRT), either alone or in combination with intracavitary radiation (ICR) has long been accepted as the standard treatment for uterine cervical cancer patients. Even though a clinically relevant set of reference points and treatment volumes remains controversial, the brachytherapy technique of ICR is believed to be an essential part of radiotherapy. After the first use of radioactive isotopes at the beginning of the 20th century, low-dose-rate (LDR) ICR has been almost exclusively employed in the treatment of uterine cervical cancer. This was not because LDR was considered biologically superior to high-dose-rate (HDR), but simply because high-activity sources suitable for HDR treatment were unavailable.[1]

Historically, HDR sources were first applied to brachytherapy by Henscke[2,3] and O'Connell[4] in the early 1960s. Interest in HDR-ICR has steadily grown in European countries and East Asia during the past four decades, partly because of the elimination of radiation exposure hazard for medical staff and the need for hospitalization, and because prolonged immobilization and long treatment times are largely avoided. Although several radiation oncologists have accumulated HDR experiences with promising clinical results, there remains considerable reluctance on the part of radiation oncologists and gynecologists in North America to employ the HDR remote afterloading technique instead of the firmly established LDR treatment modality. For example, a recent survey initiated by the American Brachytherapy Society, in a country where new technology is usually readily adopted, showed that only about 16% of patients with uterine cervical cancer were being treated with HDR in

Received September 4, 2002

Reprint address: requests to Dr. Gwi Eon Kim, Department of Radiation Oncology, Yonsei Cancer Center, Yonsei University College of Medicine, C.P.O. Box 8044, Seoul 120-752, Korea. Tel: 82-2-361-7631, Fax: 82-2-312-9033, E-mail: gekim@yumc.yonsei.ac.kr

1996.[5] In contrast, the HDR-ICR system has gained rapidly nationwide acceptance in Korea, since the introduction of the Ralstron, a remotely controlled afterloading system that uses HDR Co-60 sources, at the Yonsei Cancer Center in 1979.[6,7] Moreover, the total number of patients treated by HDR brachytherapy has steadily increased.[8] According to brachytherapy statistics reported by the Korean Society of Therapeutic Radiology and Oncology, in 1997, brachytherapy was performed upon 1,758 Korean patients with uterine cervical cancer, of whom approximately 82% received HDR-ICR (Table 1).

In practice, several advantages are claimed for the remotely afterloading HDR-ICR system versus the LDR-ICR system. These include: 1) the short treatment time, 2) reduced radiation exposure of medical personnel, 3) no major anatomy changes during treatment, 4) no overnight nursing and resultant daycare-based treatment, 5) minimal risk of ischemia of the vaginal vault epithelium due to prolonged pressure from colpostats and packing, 6) improved physical dose distributions are attainable using the HDR stepping source technology and better geometrical sparing of normal tissues, 7) more exact treatment planning and the possibility of optimizing treatment plans. Despite the practical advantages of HDR, its cost effectiveness is controversial. The HDR system is more costly, and in the case of Ir-192, requires extensive source changes at 3-month intervals. From the physical point of view, there are considerable differences between HDR and LDR for the treatment of uterine cervical cancers. The most important differences are associated with radiation protection, fixation and the positioning of sources and applicators, the mechanical aspects, and overall convenience.[9] The characteristics of HDR and LDR-ICR systems are compared in Table 2.

Apart from the differences in the physical characteristics of the two modalities, it is often said that the radiobiological drawbacks of HDR involve the heavily fractionated regimen, which compromises the inherent advantages of HDR treatment, especially in terms of patient and physician convenience and cost. However, many clinical studies of HDR brachytherapy in uterine cervical cancer have shown similar levels of local control and equal, if not less, late complications with as few as 5-6 fractions.[7,8,10,11] This can be partly explained by potential radiobiological advantages of HDR over LDR. At sites closer to the applicator, the HDR delivers a higher biologically

Table 1. Annual Brachytherapy Statistics in Korea, Reported by the Korean Society of Therapeutic Radiology and Oncology (1991-1997)

Statistics	Year	Modality	
		High-dose-rate	Low-dose-rate
No. of hospital	1991	16	13
	1992	18	10
	1993	20	9
	1994	23	10
	1995	27	10
	1997	29	7
No. of patients	1991	859 (44%)	1,079 (56%)
	1992	1,106 (55%)	906 (45%)
	1993	1,185 (62%)	730 (38%)
	1994	1,063 (64%)	592 (36%)
	1995	1,258 (73%)	469 (27%)
	1997	1,450 (82%)	308 (18%)

(Modified from the article reported by Huh et al.,[8] 1999).

Table 2. Comparison of the Characteristics between High-Dose-Rate and Low-Dose-Rate Intracavitary Radiotherapy Systems

	Direct insertion of low-dose-rate sources	Afterloading with low-dose-rate sources	Remote afterloading with high-dose-rate sources
Sources	Ra, Cs, Co	Ra, Cs, Co	Cs, Co, Ir
Exposure of medical staff	(+++)	(+)	(-)
Treatment time	24 - 48 hours	24 - 48 hours	10 - 20 minutes
Physical/mental burden for patient	(+++)	(+++)	(+)
Danger of urinary infection	(++)	(++)	(-)
Applicator movement during therapy	(++) - (+++)	(++) - (+++)	(-)
Need to shield ward	(+)	(+)	(-)
Biological disadvantage	(-)	(-)	(+)
Cost of device	(-)	(-)	(+++)

Ra, Radium; Cs, Cesium; Co, Cobalt; Ir, Iridium.

effective dose (BED) than LDR; at sites on the distal side of the prescription point, the BED from the HDR is lower than from the LDR.[12] Another potential benefit of HDR relates to differences in rates of repair between tumor and normal tissues. Tumor cells, on average, tend to repair sublethal damage faster than normal tissue cells do.[13,14] During protracted LDR treatments, tumor cells will be better able to repair sublethal damage compared to during HDR treatments. For normal tissues, there would be reduced repair during the course of LDR brachytherapy than for tumors.[14] Furthermore, no repair occurs during, and all repairs occurs between HDR fractions, as long as the interfraction interval is 24 hours or more. Despite arguments that outcomes of HDR have relied upon selected retrospective experiences, and that there exist no high quality prospective studies, recent efforts adds a radiobiological basis to the use of HDR brachytherapy for the treatment of uterine cervical cancer.

In this review, we present our experiences of HDR-ICR for the treatment of uterine cervical cancer. We also discuss several points of controversy, which are important considerations when commencing HDR-ICR for uterine cervical cancer. These included physical and radiobiological considerations, and future prospects for technical improvements.

HDR EXPERIENCES AT THE YONSEI CANCER CENTER

Although the early history of brachytherapy at the Yonsei Cancer Center goes way back to May 1959, when radium-226 sources were employed, we abandoned the LDR-ICR system upon the introduction of the Ralstron 303 utilizing Co-60 sources in 1979. Later another HDR system, the Gammamed 12i with iridium-192 sources, was installed at our institution in 1989. All patients with gynecologic cancers are now being treated by HDR and not LDR treatment. Between January 1971 and December 2000, a total of 5,651 patients with uterine cervical cancer were treated by brachytherapy at the Yonsei Cancer Center, 4,818 were treated by HDR and the remainder were treated by LDR before 1980 (Table 3).

Moreover, our group has previously published an interim analysis, which compared HDR and LDR results, and which indicated that HDR-ICR is a radiotherapy technique that is safe enough to be used as an alternative to conventional LDR-ICR brachytherapy.[6] Suh et al. finally reported the long-term follow-up results, which found that HDR-ICR and conventional LDR-ICR produced similar survival rates.[7] The 5 - year actuarial survival rates for the HDR group were 78% in stage IB, 68% in stage II, and 51% in stage III, whereas 5 - year actuarial survival rates for the

LDR group were 88% in stage IB, 66% in stage II, and 55% in stage III. Complete response rates were not significantly different for all stages of disease, 77% in the HDR group and 80% in the LDR group, respectively. There were no increased late complications, and even much less bowel and bladder complications (Table 4). Recently, Kim et al. observed, on comparing HDR- and LDR-ICR, that there was no evidence of greater radiation resistance to HDR brachytherapy for adenocarcinoma of the uterine cervix.[11] The 5-year survival rates of adenocarcinoma obtained with HDR were slightly better (61%) than those obtained with LDR (58%), even though late complication rates for the HDR group were slightly higher than those for the LDR group, most of the complications were classified as grade 1. It was explained that the higher late complication rates for the HDR group may be due to higher rectal or bladder doses.[11] However, this aspect could not be compared due to the lack of point dose information in the LDR group. Given these results, it is apparent that HDR-ICR brachytherapy is considered a safe and feasible radiotherapy technique as compared with conventional LDR-ICR brachytherapy, and provides an equivalency of local control, survival, and complication rates regardless of the histologic type of uterine cervical cancer.

However, unfortunately, only a few large-scale clinical trials with sufficient patients to adequately document clinical results of HDR-ICR have been undertaken. We retrospectively analyzed the treatment results for 1,686 patients who had been treated by radiotherapy schemes, which included HDR-ICR, between 1986 and 1996. The patient characteristics are listed in Table 5. Most patients received radiotherapy alone, but approximately 25% of patients received various schedules and combinations of chemotherapeutic agents, either with neoadjuvant therapy or concomitantly with radiotherapy. Five-year actuarial survival and

Table 3. Number of Uterine Cervical Cancer Patients, Treated with Brachytherapy between 1971 and 2000 at the Yonsei Cancer Center

Year	Low-dose-rate	High-dose-rate		Total
		Ralstron 303 (Co^{60})	Gamma Med (Ir^{192})	
71 - 75	432	0	0	432
76 - 80	401	230	0	631
81 - 85	0	956	0	956
86 - 90	0	1147	112	1259
91 - 95	0	703	621	1324
96 - 2000	0	0	1049	1049
Total	833	3036	1782	5651

Table 4. Comparison of the Incidence of Late Complications

Complications	Low-dose-rate (%)	High-dose-rate (%)
Bowel complication	14/165 (8.4)	13/354 (3.7)
Mild	8 (4.8)	10 (2.8)
Moderate	6 (3.6)	3 (0.9)
Severe	0 (0.0)	0 (0.0)
Bladder complication	4/165 (2.4)	5/354 (1.4)

(From the article reported by Suh et al.,[7] 1990).

disease-free survival for these patients were 80% and 77%, respectively. The survival rates according to the Federation International Gynecology and Obstetrics (FIGO) stages and treatment modalities are presented in Table 6. These results are comparable with the results of a collective review by Petereit, et al.,[15] as well as those of other institutions in Korea (Table 7).[8,16-21] Interestingly, the treatment results were outstandingly better than those of other institutions, particularly for those with FIGO stage IB and IIIB disease. In fact, the survival rate of 94% for FIGO stage IB patients from a recent analysis of patients treated between 1986 and 1996 shows a large improvement of 32%, compared to 78% survival of previous result reported by Suh et al.[7] During the years 1979-1983 of the early implementation of HDR-ICR, treatment was given 3 times a week to a total dose of a median 39 Gy at point A, using a dose of 3 Gy/fraction. Central shielding for EBRT was done from the beginning or after the delivery of 20 Gy of EBRT in patients with stage I disease, in an attempt to reduce radiation-induced complications. This early central shielding may be partly influenced by anxiety about the physical and radiobiological uncertainties of HDR brachytherapy. Additionally, our results indicate that the role and benefit of systemic chemotherapy remain to be further investigated, although a few randomized clinical trials of concurrent chemoradiotherapy have recently shown meaningful benefits for patients with high-risk factors.[22,23]

Table 5. Patient Characteristics Treated with Radiotherapy Including High-Dose-Rate Intracavitary Radiotherapy

Characteristics		No. of patients
FIGO Stage	IB	269
	II	1096
	III	304
	IV	17
Treatment modality	RT alone	1268
	Neoadjuvant chemotherapy plus RT	224
	Concurrent chemotherapy and RT	194
Total		1686

(From the unpublished analysis of treatment outcome for uterine cervical cancer patients, treated with radiotherapy including high-dose-rate intracavitary radiotherapy between 1986 and 1996 at the Yonsei Cancer Center).
FIGO, The Federation International Gynecology and Obstetrics (FIGO); RT, Radiotherap.

Table 6. Five-Year Survival Rates According to Treatment Modality

FIGO Stage	RT alone		Neoadjuvant chemotherapy plus RT		Concurrent chemotherapy and RT	
	No. of patients	5-year Survival (%)	No. of patients	5-year Survival (%)	No. of patients	5-year Survival (%)
IB	241	93.7	13	91.7	15	100
II	781	83.1	149	78.2	166	84.6
III	233	56.6	59	67.1	12	60.6
IV	13	35	3	0	6	100

(From the unpublished analysis of treatment outcome for uterine cervical cancer patients, treated with radiotherapy including high-dose-rate intracavitary radiotherapy between 1986 and 1996 at the Yonsei Cancer Center).
FIGO, The Federation International Gynecology and Obstetrics (FIGO); RT, Radiotherapy.

Table 7. Comparison of the Results of High-Dose-Rate Brachytherapy at Different Institutions

Institutions	Year	No. of cases	5-year survival rates according to FIGO stage (%)					
			IB	IIA	IIB	IIIA	IIIB	IV
In Korea								
Yonsei Cancer Center	2002	1686	94		82.7		58.7	31.1
Moon CW, et al.[11]	1990	331			81			
Kim OB, et al.[12]	1993	226	86	84.5	75.8		55.7	37.5
Kim JC, et al.[13]	1995	135	88.9	85.7	73.8		37.5	
Kim JH, et al.[14]	1995	64		78.8	72.8			
Choi DH, et al.[15]	1996	80	85.6	53.2				
Kim ES, et al.[16]	1998	167			62			
In the other countries								
Review by Petereit et al.[10]	1999	5619	85		68		47	

FIGO, The Federation International Gynecology and Obstetrics.

THE ISSUES, WHICH DESERVE TO BE DISCUSSED

Combination of EBRT and ICR

The goal of treatment for uterine cervical cancer patients is to improve the therapeutic ratio by optimizing the EBRT and ICR components. EBRT is used to 1) shrink bulky endocervical tumors to enable them to be brought within a higher-dose portion of the ICR dose distribution, 2) improve tumor geometry by shrinking exocervical tumor that may distort the anatomy and prevent optimal brachytherapy, and 3) sterilize disease in the parametrium and lymph nodal areas that may receive an inadequate dose by ICR. Generally, the complication rates of the rectum and bladder significantly increase on increasing dose to the whole pelvis, irrespective of brachytherapy techniques, but more often, clinically significant injuries may develop from relatively small regions of hot spot within the rectum by the brachytherapy technique. Therefore, proper combinations of EBRT and ICR to balance the ratio of tumor control and radiation complications are necessary for the successful treatment of uterine cervical cancer.

A recent report from the Washington University group suggested that early use of a midline block may increase the risk of paracentral recurrences, particularly for patients with uterosacral involvement.[24] They proposed an option to increase the whole pelvis dose and rely less on brachytherapy. However, although EBRT plays a critical role in sterilizing pelvic wall disease and in improving tumor geometry, too much reliance on EBRT might compromise the chance of central disease control and increase the risk of complications. In contrast to a combination of EBRT and LDR-ICR, the best dose optimization for a combination of EBRT and HDR has not been established. Our group rarely increases the central dose of EBRT beyond 45 Gy, even in patients who have had bulky lesions or a poor response to EBRT, because higher EBRT doses not only unacceptably reduce the deliverable dose of ICR, but also increases the risk of radiation-induced complications. Lee et al. recommended that the treatment plan should be designed so that the sum of EBRT and HDR-ICR BED10 to the bladder and rectum do not exceed 90 Gy, in order to reduce the incidence of late complications, in their analysis of treatment results for FIGO IB uterine cervical cancer (Table 8).[25] Chung et al. also reported that the rectal point doses and whole pelvis dose appeared to be useful prognosticators of late rectal complications (Table 9).[26] On the basis of these observations, we believe that proper optimization of EBRT and HDR-ICR deserves special emphasis for the suc-

Table 8. Five-Year Survival Rate and the Incidence of Late Rectal and Bladder Complications Related to the Biologically Effective Dose

Midline BED10* (Gy)	No. of patients	5-year survival (%)†	No. of complications (%)‡
≤ 80	21	83.3	2 (9.5)
81 - 90	47	93.3	6 (10.6)
91 - 100	10	100	5 (30.0)
101 - 110	75	86.5	23 (24.0)
>110	9	100	2 (22.2)

(From the article reported by Lee et al.[25], 2002).
*Midline BED_{10}=EBRT midline BED_{10} + ICR point A BED_{10}.
†p=0.40.
‡p=0.02.
BED, Biologically effective dose; EBRT, External beam radiotherapy; ICR, Intracavitary radiotherapy.

Table 9. Incidence of Grade 2, 3 Rectal Complications by Dose Statistics

Dose statistics	No. of grade 2, 3 complication	p-value
Whole pelvis dose without midline shielding (Gy)		
36	5/50 (10%)	< .05
36 < and < 40	3/14 (21%)	
≥ 40	7/24 (29%)	
Total rectal dose by contrast; R (Gy)		
< 65	4/38 (11%)	< .05
65 - < 75	5/29 (17%)	
≥ 75	6/21 (29%)	
Total rectal dose by ICR reference point; DR (Gy)		
< 65	2/21 (10%)	< .05
65 - < 75	5/41 (12%)	
≥ 75	8/26 (31%)	

(Modified from the article reported by Chung et al.,[26] 1996).
R, Total mucosal dose checked in barium contrast simulation image; ICR, Intracavitary radiotherapy; DR, Total rectal dose checked by ICRU 38 reference point.

cessful radiotherapy of uterine cervical cancer.

Fractionation issues

Over the decades, HDR-ICR systems have been increasingly used for the treatment of uterine cervical cancer in the absence of a consensus on fractionation guidelines. Even though recent achievements on the repair kinetics of tumor and normal tissues continue to provide some valuable points, it is still unclear as to what schedules are optimum. Therefore, there exist a wide range of fractionation schedules varying from 3.0 to 16.76 Gy (median 7.45) in a collective review by Orton.[14,27] Since the linear-quadratic (LQ) model demonstrates that the dose/fraction must be so low (less than 3 Gy/fraction) for HDR to be equivalent to LDR, reducing the fraction size would seem to be ideal in light of the radiobiological consequences for normal tissue. The fraction size

of 3 Gy used during early implementation period of our group is one of the smallest mentioned in a collective review by Orton.[14,27] However, this prolongs the overall treatment duration, which may directly affect the tumor control rate. Generally, the equivalence to LDR at 0.5 Gy/hour is achievable with a HDR exceeding 5 Gy/fractions, as long as the time between fractions is considerably longer than normal tissue repair half-time.[14] In addition, clinical trials that adopted a median of 7 Gy/fraction achieved a measure of success.[15] For these reasons, we are now using a higher fraction size (5 Gy, weekly twice $\times$ 6 treatment sessions) in an attempt to reduce patient discomfort, and to enhance the physician's convenience without compromising the cure rate. However, several investigators have emphasized that the individual fraction size should be kept to less than 7.5 Gy because of the increasing risk of toxicity with larger fraction sizes.[27,28]

In addition to the effects of HDR-ICR fraction size, it is likely that the incidence and severity of radiation-induced complications and the rates of tumor controls are greatly influenced by the EBRT component. In fact, the determination of the most efficient HDR-ICR fractionation scheme cannot be determined, if EBRT components are not considered. Hence, there exists a real need to determine the effects of EBRT and ICR in combination. Doses from different treatment modalities cannot be added linearly to determine the combined effect. There is a marked difference between the biological effects in the tumor and those in late-responding normal tissues. Recently, attempts to utilize the concept of BED have been made for this purpose. BED using α/β ratio of tumor and normal tissue was plotted against a tumor control and the complication rate, to determine the existence of a dose-response relationship for local control, and the potential dose threshold in terms of complications. In the analysis of Petereit et al., noticeable information was not detected due to the lack of fractionation details.[15] However, some series have been reported with adequate fractionation details and a careful analyses of rectal complications.[29] Our group also demonstrated that the rectal complication rate increased when the sum of the EBRT midline BED3 and point A BED3 by ICR exceeded 130 Gy3.[25]

Directions in the planning process

The conditions for successful treatment do not merely involve the selection of fractionation schemes, but a qualitative planning process. Despite a relatively higher cure rate, occasionally, the adjacent normal organs are at risk of receiving a higher radiation dose that exceeds normal tissue tolerance limits, because of anatomical proximity of the rectum and bladder or because of suboptimal radiotherapy techniques. The anterior rectal wall surrounding the posterior fornix is often the site of the maximum radiation dose and is the most common site to suffer localized radiation damage. Fletcher described the following conditions that should be met for successful ICR: 1) The geometry of the source positions (applicator) must prevent underdosed regions on and around the uterine cervix; 2) An adequate dose must be delivered to the paracervical areas; 3) Mucosal tolerance must be respected. These comments also apply to HDR-ICR, and the skills necessary to achieve these goals in different anatomical situations can only be learned with experience. Attention to the following may help to achieve an optimal placement. To deliver a adequate dose to paracervical tissues, the tandem should be sufficiently long if anatomy permits (up to 7 - 8 cm). The tandem should be placed so as to obtain parity between the bladder and the rectum (ideally about 1/3 of the way from S1-2 to the tip of the pubis). In order to optimize the ratio between the dose at depth and the vaginal mucosal dose, the largest colpostats compatible with patients' comfort should be used. Too much separation of the colpostats tends to leave a cold spot in the region of the uterine cervix. The axis of the tandem should be central between the colpostats on the AP view and usually should bisect them on the lateral view. Care should be taken to have adequate packing to displace the vaginal mucosa. Patients who have favorable anatomy tend to receive higher tumor doses and have a broader therapeutic window, than patients with a narrow vagina and a short uterine length.[30,31]

Despite the optimal ICR technique, the multitude of dosimetric descriptions, particularly for ICR, make comparisons very difficult, partly due to the variety of dose prescriptions and dosimetry

systems employed. The most reliable attempt to specify a clinically relevant set of reference points and treatment volumes comes from the International Commission on Radiation Units and Measurements (ICRU) Report[38,32] even though a few authors have advocated that the ICRU definition of the reference volume is inappropriate for HDR-ICR for cervical carcinoma. However, the evaluation and comparison of clinical results will be more meaningful if a standard system of reference points is used regardless of the different planning approach used by institutions. The American Brachytherapy Society recommends prescribing to a new point called "point H" (Fig. 1). Keeping the dose to the rectal and bladder points to below 80% of the prescribing dose (dose to point A or H). When prescribing the dose, clinicians rigidly depend on the doses to reference points. There is a tendency to underdose patients who have favorable anatomy that permit delivery of a higher dose without undue morbidity, and it is also possible to cause an unacceptable risk of complications.

Three-dimensional brachytherapy planning

Some researchers recognized the poor reliability of reference points in their computed tomography (CT)-based analyses.[33,34] As a result of advanced computer technology, attempts have been made to prescribe the dose based on 3-dimensional (3-D) dosimetry (Fig. 2). This might provide a valuable

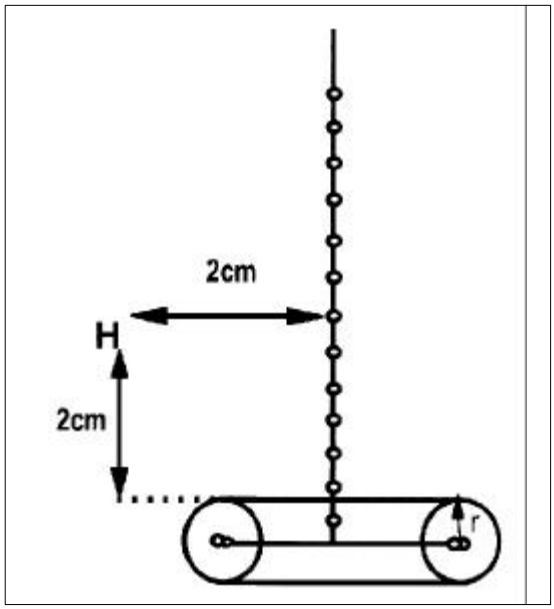

Fig. 1. An Illustration of the Geometry Relevant for Intracavitary Prescription, Dosimetry, and Reporting, as Recommended by The American Brachytherapy Society. (Finding Point H begins with drawing a line connecting the mid-dwell positions of the ovoid. From the intersection of this line with the tandem, move superiorly along the tandem for 2 cm plus the diameter of the ovoid (including the cap), and then 2 cm perpendicular to the tandem in the lateral direction.)

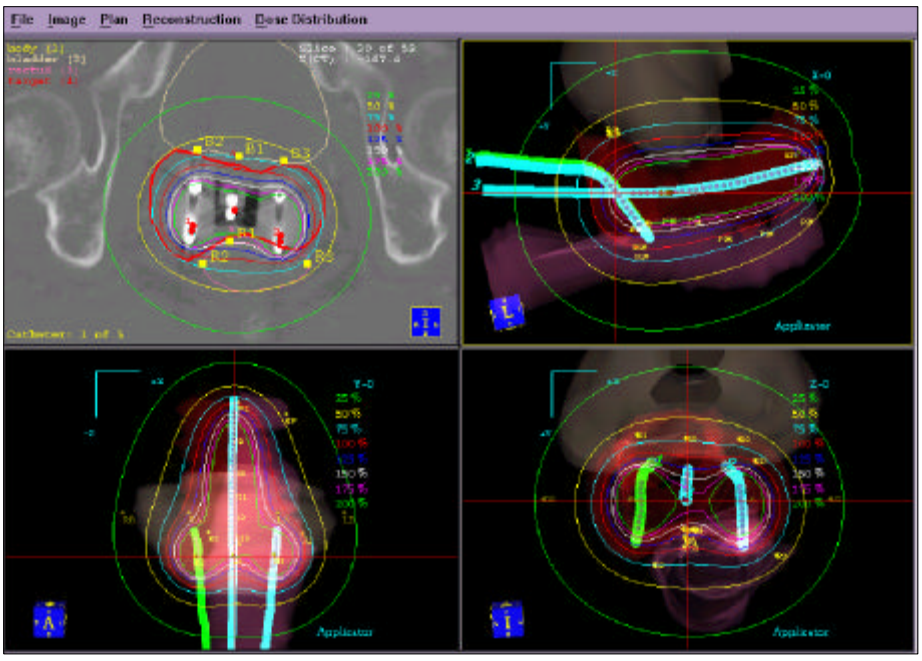

Fig. 2. Example of Treatment Planning Based on Computer Tomography-Assisted 3-Dimensional (3-D) Dosimetry. (3-D brachytherapy planning process enhances the ability, to limit the dose to critical organs while delivering the appropriate dose to the target volume.)

leap for the conformal treatment planning of ICR for uterine cervical cancer, and is awaited by the majority of radiation oncologists. However, we do not know what are the critical clinical target volumes (CTV), nor do we know what dose must be delivered. Such issues may necessitate new knowledge about tumor control probability (TCP) and normal tissue complication probability (NTCP) data, which is high-quality data that correlates recurrence and outcome with variations in the 3-D distributions achieved with traditional empirically derived prescriptions.

CONCLUSIONS

HDR-ICR allows integration (or interdigitation) of EBRT and ICR, which can lead to a shorter overall duration of treatment and potentially to better tumor control. The fact that the HDR-ICR scheme gains gradual acceptance in practice; especially in Korea is a clinical reality. However, there remains a paucity of high quality prospective studies, which demonstrate that the loss of a dose-rate effect does not compromise the therapeutic ratio. Furthermore, consensus has not been achieved regarding the best technique of arriving at an ideal fractionation scheme, and for regarding the way to of integrating EBRT and HDR-ICR. For these reasons, the optimal HDR-ICR scheme for the treatment of uterine cervical cancer presently must be based only on a single institution with significant experience.

The guidelines of HDR-ICR treatment at the Yonsei Cancer Center are presented in Fig. 3. The EBRT doses have something to do with the ICR fractionation strategies. The relative doses given by EBRT when used in combination with ICR

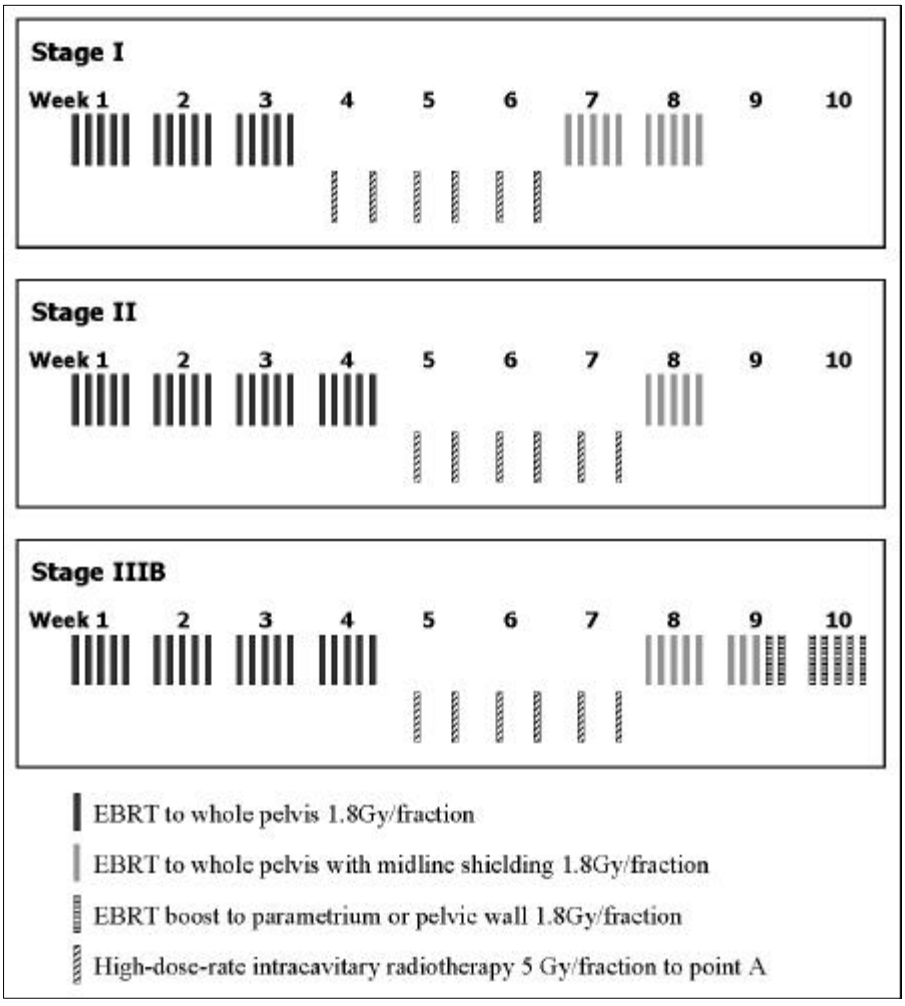

Fig. 3. Yonsei cancer center schemes for the treatment of uterine cervical cancer.

depend upon the initial volume of the disease, the ability to displace the bladder and rectum, the degree of tumor regression during pelvic irradiation, and institutional preferences. As we have achieved favorable treatment results with our guidelines and have optimized these over a period of more than 30 years, our guideline can be recommended as a valuable reference for the commencement of HDR-ICR for the treatment of variably situated uterine cervical cancer.

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