

COMPARISON OF LDR TO HDR IN TREATMENT OF CERVICAL CANCER.

SAIPIN TANGKARATT, M.D.¹

Objective; To compare the treatment results between LDR and HDR in FIGO stage IIB cervical cancer, in terms of disease survival and late normal tissues complications.

Materials and methods; From Jan 1997 to Dec 1998, Prospective non-randomized study was conducted. About 161 patients with pathological diagnosis of FIGO stage IIB cervical cancer were included in the study. All patients were treated with combination of external beam radiation and brachytherapy. The patients were divided into 2 groups for difference brachytherapy protocols. The first group of patients was treated with 1-2 fractions of LDR, and the other group of patients was treated with 4-5 fractions of HDR. Total tumor dose to point A was 80-85 Gy.

Results; All of 161 patients had complete radiation treatment as planned. Ninety patients entered in LDR protocol, and 71 patients entered in HDR protocol.

The age of patients with LDR and HDR ranged from 29-82, and 29-80 years, respectively. The mean age was 45 years in both groups. The common subtype of both groups was squamous cell carcinoma, for LDR and HDR, accounted about 86% and 77%, respectively. The evaluable patients for LDR and HDR were 82 and 66, respectively. Three year survival of patients treated with LDR and HDR were 63.4% and 68% respectively. Fourteen of 52 responders patients (26.9%) with LDR had grade I proctitis, and 4 of 52 patients (7.7%) had grade I cystitis. About 6 of 45 responders patients with HDL had grade I proctitis, 1 of 45 patients had grade II proctitis, and 1 of 45 patients (2.2%) had cystitis.

Conclusion; The study has shown the comparable results with a slightly better survival of HDR than LDR (68.2% VS 63.4%) without significant difference ($p = 0.544$). About late normal tissue complications, the LDR showed more than HDR for proctitis and cystitis (26.9% VS 15.6% and 7.7% VS 2.2%), respectively. ($P = 0.062$)

Keywords; LDR (Low dose rate), HDR (High dose rate), Brachytherapy.

INTRODUCTION

Carcinoma of uterine cervix was the most common cancer in Thai women 1. Combination of external beam and brachytherapy was the standand treatment of cervical cancer 2. In the beginning of brachytherapy in 1903, radium-226 was the first radionuclide used in the treatment with satisfactory results. Because of the radiation

hazard to medical personnels by decay radon gas and its long half life (1600 years), other radionuclides with short half life, such as cesium137, cobalt60, iridium192 etc were used instead of radium. In 1950, Dr.Henscke in Memorial Hospital developed manual after loading technique in brachytherapy. After 1970,

¹ Division of Radiation therapy, National Cancer Institute Bangkok, Thailand.

many technologies in radiation treatment were developed, such as advances in computer technology, modern imaging system (CT scans, MRI) and advances in physics dosimetry. Such development lead to rapid improvement in brachytherapy in terms of computerized remote after loading system and resulted in an improvement of accuracy with safty of brachytherapy.

Because of more HDR machine available with combination of computerized planning system many institutes shifted the installation from LDR to HDR. In our institute, the HDR machine (Nucletron Ir-192) was installed in Jan 1997, and was used to treat cervical cancer in parallel to the former LDR machine. Hence, we have conducted this study, with the aim to compare the results of both machines in treatment of FIGO stage IIB cervical cancer in terms of survival and late normal tissue complications.

METERIALS AND METHODS.

From Jan 1997-Dec 1998, patients with pathological proven FIGO stage IIB cervical cancer were included in the study. All patients were treated with combination of external beam and intracavitary brachytherapy.

External beam radiation. Co-60 machine or Linac 6 MV was used to the whole pelvis, anterior/posterior opposing fields. The superior border extended from upper border of lumbar 5 to 1 cm beyond the bottom of obturator foramina, the lateral fields were 2 cm from lateral pelvic walls, tumor dose was 4000 cGy, daily dose was

200 cGy. The lateral pelvic walls were boosted in additional 1000 cGy.

Intracavitary brachytherapy. The patients were divided into 2 groups for either LDR or HDR.

For LDR, one-two weeks after complete external beam, the patients were treated with 1-2 fractions of LDR, with Fletcher applicators, tumor dose to point A was 2800 cGy or 2 x 1500 cGy.

For HDR, the patients were treated with 4-5 fractions of HDR weekly during course of external beam radiation (external beam was omitted on the day of HDR). Tumor dose to point A was 5-6 Gy per fraction. Total tumor dose to point A, combination of external beam and brachytherapy (both LDR and HDR) was 80-85 Gy.

RESULTS

About 161 patients with pathological proven FIGO stage IIB cervical cancer were included in this study. All patients had complete the treatment as planned. Ninety patients entered in LDR protocol, and 71 patients entered in HDR protocol. The age of patients in LDR and HDR group ranged from 29-82 and 29-80 years, respectively. The mean age was 45 years in both groups. Squamous cell carcinoma was the most common subtype in both groups, accounted of 90 (86%), and 71 patients (77%), respectively. AS shown in table 1.

Table 1 Pathological classification Number of patients. (%)

	LDR	HDR
Squamous carcinoma	77 (85.5%)	55 (77.5%)
Adenocarcinoma	7 (7.8%)	14 (14.7%)
Adenosquamous carcinoma	5 (5.6%)	1 (1.4%)
Anaplastic carcinoma	1 (1.1%)	-
Malig neuroendocrine tumor	-	1 (1.4%)
Total	90 (100%)	71 (100%)

Duration of treatment for LDR and HDR ranged from 6-8 weeks, mean 6.8 weeks, and 5-6 weeks, mean 5.4 weeks, respectively.

Seven of 90 patients in LDR group lost to follow-up, and one patient died 14 months after complete radiation from congestive heart failure. Thirty of 82 evaluable patients (36.6%) had

treatment failure (19 patients with locoregional recurrence, and 11 patients with distant metastasis). Five patients in HDR group lost to follow-up. Twenty-one of 66 evaluable patients (31.8%) had treatment failure (13 patients had locoregional recurrence, and 8 patients developed distant metastasis). As shown in table 2.

Table 2 Results of treatment. Number of evaluable patients (%)

	LDR	HDR
Locoregional recurrence	19 (23.2%)	13 (19.7%)
Distant metastasis	11 (13.4%)	8 (12.1%)
Complete response	52 (63.4%)	45 (68.2%)
Total	82 (100%)	66 (100%)

With minimal follow-up of 36 months, there were 14 and 4 patients of the 52 responders in LDR group (26.9, 7.7%) developed grade I proctitis and grade I cystitis, respectively. Six and 1 patient of the 45 responders in HDR group

(13.3%, 2.2%) developed grade I proctitis and grade I cystitis, respectively. Only one patient in HDR group had grade II proctitis. As shown in table 3.

Table 3 Late normal tissues complications Number of patients (%)

	LDR	HDR
Grade 0	34 (65.4%)	37 (82.2%)
Grade I proctitis	14 (26.9%)	6 (13.3%)
Grade II proctitis	0	1 (2.2%)
Grade I cystitis	4 (7.7%)	1 (2.2%)
Total	52 (100%)	45 (100%)

DISCUSSION

Radiation therapy with combination of external beam and brachytherapy has been the standard treatment of cervical cancer.^{1,2} With LDR brachytherapy (radium-226 or cesium-137 source)

and after manual loading technique, good treatment results were achieved with more safety to medial personnels.^{3,4} After introduction of HDR with more advanced computerized planning

system and remote after loading system, many institutes have shifted the treatment from LDR to HDR.^{5,6,7} There were several rationals for this change, the first was due to out-patient treatment basis that might reduce the hospital cost. The second was its reproducible planning, which might ensure more accurate dosimetry.⁸ The third was the short treatment time, that caused more convenience and comfortable of the patients than overnight hospitalization etc.

Several published data suggested that dose-fractionation of HDR was the important factor in tumor control and late normal tissue complications^{9,10,11} C.G.Orton & Armny had reported "An International Review on Patterns of Care in Cancer of the Cervix", including 56 facilities with 17,000 patients treated with HDR.¹² the mean of number of fraction and dose per fraction were 4.82 and 7.45 Gy, respectively. The crude 5 year-survival of this review was slightly better for HDR than LDR. In the survey data of Orton, the complications of HDR is fewer than LDR. Studies from Japan,^{5,7} the result in survival between HDR and LDR were comparable, with more severe and more frequent in late normal tissues complications. The difference results from reviewing study might due to variable of complications description, variable of treatment techniques, and variable of dose-fractionation.¹³

In our study, there was a slightly better 3 year-survival of HDR than LDR in terms of more locoregional control and less distant metastasis ($p = 0.544$). Rational for the better survival of HDR might due to its shorter overall treatment time than LDR. This result could be comparable to previous reported of the correlation between longer overall treatment time and worse prognosis.^{14,15,16} In this study, fewer complications of HDR was noted, in both proctitis and cystitis without statistical significance ($p = 0.062$).

CONCLUSION

The HDR brachytherapy is comparable to former LDR treatment with minimal better survival and less normal tissue complications. More prospective randomized studies are needed to establish the optimal dose-fractionation schedule treatment in HDR to ensure the better results in treatment of cervical cancer.

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