Radiotherapy Results of Uterine Cervix Cancer Stape B
Overall Survival, Prognostic Facters, Patterns of
Failure and Late Complications

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<u>Purpose</u>: Treatment of choice for uterine cervix cancer stage IIB is radiotherapy. We analyzed survivals, prognostic factors, patterns of failure and complications.

<u>Materials and Methods</u>: This is a retrospective analysis of 167 patients with stage IIB carcinoma of uterine cervix treated with curative external pelvic and high dose rate intracavitary radiotherapy at the Department of Therapeutic Radiology, Soonchunhyang University Hospital from August 1985 to August 1994. All the patients followed up from 3 to 141 months(mean 60 months) and age of patients ranged from 31 to 78 years at presentation(mean : 55 years).

Results: Overall complete response rate was 84%. The response rate for squamous cell carcimoma and adenocarcinoma were 86% and 60%, respectively. Overall 5-years survival rate and disease free survival rate was 62 and 59%, respectively. Mass size and treatment response were significant prognostic factors for survival. Pathologic type and parametrial involvement were marginally significants prognostic factors. Local failure was 43 cases, distant metastasis was 14 cases and local failure plus distant metastasis was 3 cases, and most of local failures occurred within 24 months, distant metastasis within 12 months after treatment. Twenty eight(16.8%) patients developed late rectal and urinary complications. There were tendency to increasing severity and frequency according to increased fractional dose and total(rectal and bladder) dose.

<u>Conclusions</u>: Survival rate was significantly related to tumor size and radiotherapy response. Tumor size should be considered in the clinical staging. To increased survival and local control, clinical trials such as decreasing duration of radiotherapy or addition of chemotherapy is needed. To detect early recurrence, regular follow up after RT is important. Because total rectal and bladder doseaffected late complications, meticulous vaginal packing is needed to optimize dose of normal tissues and to decrease late complications.

Key Words: Cervix cancer, Radiotherapy, Prognostic factor, HDR ICR, Complication

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			, ,	ł 167	
1 program	. Pap smear	가 screening	. (IVP: intravenous	X-ray pyelogram),	,
.1, 2)	2	가 가		·	
	7¦ , 5 60- 53% . <sup>3-8)</sup>	가 65% 78%	5040 cGy) 180-200cGy 4	4000	-5400cGy( 5 4cm
			В	540-600cGy	가 .
20	, 가 가	9, 10)	가 1-2 Tandem	(HDR RALSTI Ovoid	RON) 1
	. FIGO 가	가	2 500cGy 6	8 18 400cGy 7- <sup>7</sup> 5cGy 8	A 10 51 A
,	, 11, 12) , 13, 14) 15)		8000-8200cG		
	1985 8 1994	4 8	Foley catheter X-	7cc	가 가
,	2 167			•	3
	·				,
1985 8	3 1994 8	FIGO			4-6
(Federation	of Gynecology and Obste ) 2				7 0
0- 00				3 가	6
Co-60	1	98			,

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500cGy
                                                                                    12 (86 %)
RTOG/EORTC
                                                 SOMA
Scale<sup>17)</sup>
                        가
                                                                              151
                                                                                        129 (85%)
                                grade 1
                                                                                       5
                                                                                              3 (60%)
                                                                        (Table1).
              grade 2
                            2
                                                                2.
                                           , grade 3
                                                                             2
                                                                                       5
                   가
                                                                           59%
                                                                                     (Fig. 1, 2). 5
                                                                   62%
grade 4
                                                                                                               152
                                                                                                      167
                                                                 40
                                                                                 90%
                                                                                                         50
          31
                     78 (
                                        55 )
                                                              119
                                                                                                53% 63%
                                                                   40
                                      162 (
                                                                                                    (p > 0.1),
         , 97%)
                                   (3%)
                                                                                     12g/dL
                        3
                                    141
                                                   60
                                                             56%
                                                                      66%
                               30
  )
                                                                          (p > 0.1).
                                                                   25%
                                                                           63%
                                                                                                      (p > 0.1).
Kaplan-Meier
                                                                                                    375cGy
                                                                                                                 400
                                                                                                  49%, 61%
rank test
                                         Cox-regression
                                                             cGy, 500cGy
                                                                                          70%
SPSS(Statistical Package for the Social Sciences)
                                                                                                             160
                                                                        63%
                                                                                                가 6
                                                                                                 43
                                                                                                 0%
                                                                                        (p=0.0966).
  1.
                                                                                               88
                        167
10
                         157
                                                               Table. 1. Response by Initial Parameter
                                       84%
                            132
                                          14
                                                   13
                                                                                         No. of patients
                                                                                                     CR*
                                                                                                            p-value
                                               143
(93 %)
                                   40
119 (83%)
                                                     가
                                                               Age(years)
                                                                               40
                                                                                                   13(93)
119(83)
79(89)
                                                                                            14
143
81
66
45
75
152
5
131
26
95
                                                                                                            0.3483
12g/ dL
                                  (78%)
                                                                               40
                               35
                                                               Size
                                                                               4cm
             12gdL
                                   66
                                                                                                    54(82)
35(78)
66(88)
                                                                                                            0.2246
                                                                               4cm
                                                               Hemoglobin
                                                     가
                                                                               12g/dL
    (88\%)
                                                                                                            0.1392
                                                                             12g/dL
squamous
adenoca.
                                                               Pathology
                                                                                                   129(85)
3(60)
4cm
                  81
                          72 (89%)
                                                                                                            0.0145
                               54 (82%)
          4cm
                       66
                                                                                                   108(82
                                                               Parametrial
                                                                             unilateral
                                                                                                    24(92)
78(80)
                                                               Involvement
                                                                             bilateral
375cGy
400cGy
                                                                                                            0.2107
                                                               ICR Fx
         131
                   108 (82%)
                                                                                                    42(88
                     26
                              24 (92%)
                                                                             500cGy
                                                                                                            0.7548
                                                               *CR: complete response
                               375cGy
```

42 (88%)

78 (80%), 400 cGy

48

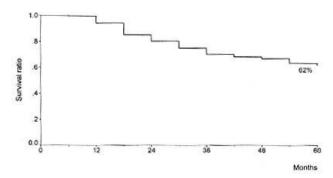


Fig. 1. Actuarial survival rate for paients with stage IIB uterine cervix cencer.

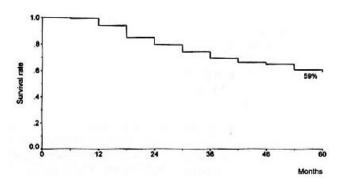
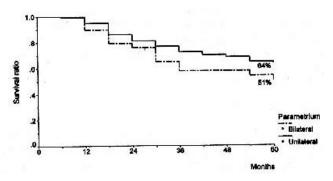
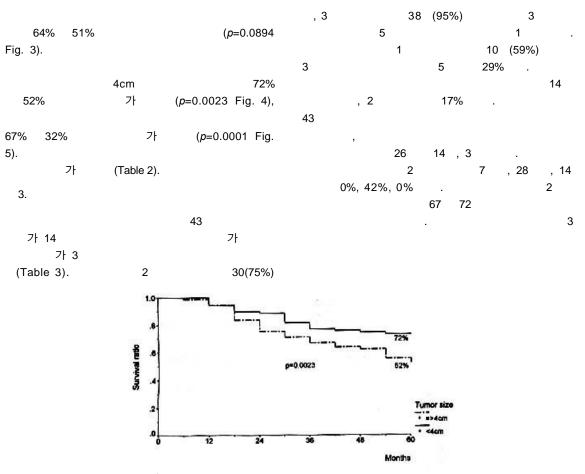


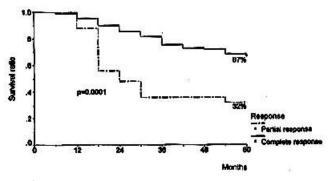
Fig. 2. Actuarial survival rate for patients with stage IIB uterine cervix cancer.



**Fig. 3.** Survival rate by parametrium involovement for patients with stage IIB uterine cervix cancer.



**Fig. 4.** Survival rate by tumor size for patient with stage IIB uterine carvix cancer.



**Fig. 5.** Survival rate by radiotherapy response for patient with stage IIB uterine cervix cancer.

Table 2. Actuarial Survival by Initial Parameters

Factors	No. of patients(%)	5YSR*(%)	p-value	
-actors		513K (%)	Univariate	Multivariate
Age(years)			0.7694	> 0.05
< 40	45(0)	50		
40	15( 9)	53		
Size	152(91)	63	0.0023	0.0022
< 4cm	85(54)	72		
4cm	72(46)	52		. 0.05
Hemoglobin	. =( )	<b>0</b> -	0.1873	> 0.05
< 12g/dL	47(37)	56		
12g/dL Fotal dose(A-point)	80(63)	66	0.0570	. 0.05
< 7500cGy			0.8578	> 0.05
7500cGy	18(11)	53		
Hypertension	149(89)	63	0.3723	> 0.05
yes	6(4)	25	0.3723	> 0.05
no	160(96)	63		
Pathology	100(00)	00	0.0966	> 0.05
squamous	159(96)	63	0.0000	× 0.03
adenoca Parametrial involvement	6(`4)'	0		
unilateral			0.0894	> 0.05
bilateral	138(83)	64		- 0.00
Response	29(17)	51 67		
CŘ.†	132(84) 25(16)	67 32	0.0001	0.0002
PR <sup>‡</sup>	23(10)	J <u>Z</u>		<del></del>

 $^*$ 5YSR : 5 year survival rate,  $^\dagger$ CR: complete response,  $^\dagger$ PR : partial response

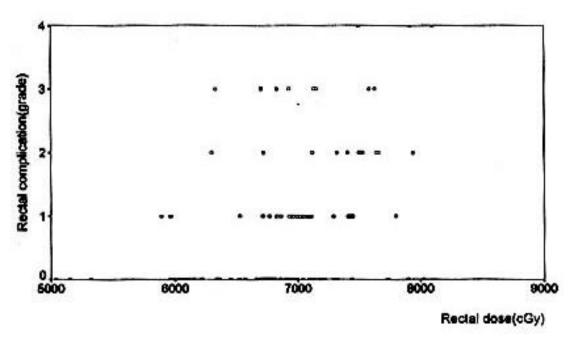


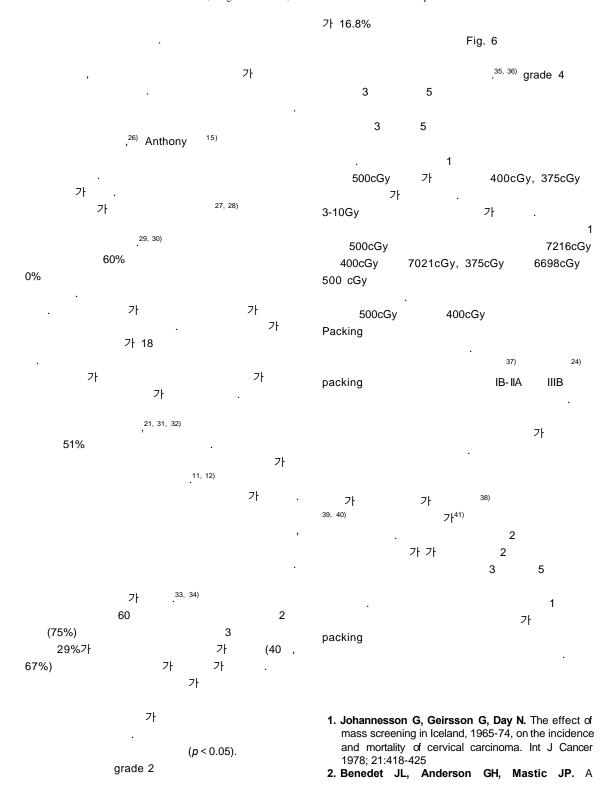
Fig. 6. Scatterplot of rectal complications by rectal dose.

1800cGy 2000cGy			가
7 18	3)	5	60-65%
14	18-20)	18-3 5	
	• ′	5 12-2	53-78% 5%
	4-8)	12 2	J 70
4.			
RTOG/EORTC SOMA Scales grade 2 28(16.8%) 38	,12, 21)		가 가
1 500cGy			
18 6 (33%) 가			
가 grade 3			
400cGy 375cGy 가			가
(Table 3). Fig. 6 grade 1-4			•
(Scatterplot)			
	IIB 5	62%	,
•	26% (Fig 1, Table 3).		
	(Fig 1, Table 6). 가 .		
			12 14)
가	가		. 13, 14)
			22-24)
Table 3. Patterns of Failure	40		
No. of patients LR*(%) LR+DM(%) DM*(%)	53% 40	가	
Size < 4cm 85 16(19) 8(14)	. Jenkin Stryker	25)	
4cm 72 24(33) 3(4) 6(8) Response CR 132 24(18) 3(2) 13(10)	가 25%		, 가
PR 25 17(68) Total 167 43(24) 3(2) 14(8)	25 /0	가 6	<b>71</b>
*LR: local recurrence, †DM: distant metastasis			

Table 4. Patterns of Complication

가 .

		No of patients	Complication No.			
			Grade2	Grade3	Grade4	Total(%)
Site	Bowel Genitourinary	167 167	9 11	8 5	3 2	20(12) 18(11)
ICR Fx	500cGy 400cGy 375cGy	18 51 98	2 4 14	1 9 3	3 2	6(33) 15(29) 17(17)



- comprehensive program for cervical cancer detection and management. Am J Obstet Gynecol 1992; 166:1254-1259
- Eifel PJ, Berec JS, Thigpen JT. Cancer of the cervix, vagina and vulva In: DeVita VT, Hellman S, Rosenberg SA. Cancer: Principle and Practice of Oncology, Fourth ed. Philadellphia, PA: Lippincott. Co 1992: 1433-1478
- Kim JH, Youn SM, Kim OB. Hydroxyurea with radiation therapy of the carcinoma of the cervix IIA, IIB. J Korean Soc Ther Radiol 1995; 13:369-375
- Shin KH, Ha SW, Yoo KY. Analysis of pretreatment prognostic factors in stage IIB carcinoma of the uterine cervix. J Korean Soc Ther Radiol 1992; 10:227-236
- Ma SY, Cho HL, Shon SC. Survival and complication rate of radiation therapy in stage I and II carcinoma of uterine cervix. J Korean Soc Ther Radiol 1995; 13:349-357
- Lee KJ. Results of radiation therapy for carcinoma of the uterine cervix. J Korean Soc Ther Radiol 1995; 13:359-368
- Kang KM, Ryu MR, Chang GY et al. The results of curative radiotherapy for carcinoma of uterine cervix.
   J Korean Soc Ther Radiol 1993; 11:149-158
- Fu KK, Phillips TL. High-dose rate vs. low-dose rate intracavitary brachytherapy for carcinoma of the cervix. Int J Radiat Oncol Biol Phys 1990; 19:791-796
- 10. Orton CG, Seyedsadr M, Somnay A. Comparison of high and low dose rate remote afterloading for cervix cancer and the importance of fractionation. Int J Radiat Onclo Biol Phys 1991; 21:1425-1434
- 11. Toita T, Nakano M, Higashi M et al. Prognostic value of cervical size and pelvic lymph node status assessed by computed tomography for patients with uterine cervical cancer treated by radical radiation therapy. Int J Radiat Oncol Biol Phys 1995; 33:843-849
- **12.** Lowrey GC, Mendelhall WM, Millon RR. Stage IB or IIA-B carcinoma of the intact uterine cervix treated with irradiation: A multivariate analysis. Int j Radiat Oncol Biol Phys 1992; 24:205-210
- 13. Lanciano RM, Won M, Coia LR et al. Pretreatment and treatment factors associated with improved outcome in squamous cell cancer of the uterine cervix: a final report of the 1973 and 1978 Patterns of Care studies. Int J Radiat Oncol Biol Phys 1991; 20:667-676
- 14. Rutledge FN, Mitchell MF, Munsell M et al. Youth as a prognostic factor in carcinoma of the cervix: a matched analysis. Gynecol Oncol 1992; 44:123-130
- 15. Fyles AW, Pintilie M, Manchul CA et al. Prognostic factors in patients with cervix cancer treated by radiation therapy: results of a multiple regression analysis. Radiation and Oncology 1995; 35:107-117
- **16. Huh SJ, Kang WS.** Treatment planning software for high dose rate remote afterloading brachytherapy of

- uterine cervix cancer. J Korean Soc Ther Radiol 1986: 4:183-186
- 17. Philip R, Louis SC, Louis FT, et al. Late effects of normal tissue (LENT) scoring system. Int J Radiat Oncol Biol Phys 1995. 31:1049-1091
- **18. Fletcher GH.** Cancer of uterine cervix. Janeway Lecture. Am J Roentgenol Radium Ther Nucl Med 1971; 111:225-243
- Marcial VA, Amato DA, Marks RD, et al. Split course versus continuous pelvis irradiation in carcinoma of the uterine cervix: A prospective randomized clinical trial of the Radiation Therapy Oncology Group. Int J Radiat Oncol Biol Phys 1983; 9:431-436
- 20. Perez CA, Breaux S, Madoc-Jones H, et al. Radiation therapy alone in the treatment of carcinoma of uterine cervix. Analysis of tumor recurrence. Cancer 1983; 51:1393-1402
- Kovalec JJ, Perez CA, Lockett MA. The effect of volume of disease in patients with carcinoma of the uterine cervix. Int J Radiat Oncol Biol Phys 1991; 21:905-910
- 22. Meanwell CA, Kelly KA, Wilson S, et al. Young age as a prognostic factor in cervical cancer: analysis of population based data from 10,022 cases. Br Med J 1988; 296:386-391
- 23. Sigurdsson K, Hrafnkelsson J, Geirsson G, et al. Screening as a prognostic factor in cervical cancer: analysis of survival and prognostic factors based on Icelandic population data, 1964-1988. Gynecol Oncol 1991; 43:64-70
- **24. Choi DH, Huh SJ.** Radiotherapy results of early uterine cervix cancer. J Korean Soc Ther Oncol 1996; 14:33-39
- 25. Jenkin RD, Stryker JA. The influence of blood pressure in survival in cancer of the cervix. Br J Radiol 1968 ;41:913-920
- Bush RS. The significance of anemia in clinical radiotherapy. Int J Radiat Oncol Biol Phys 1986; 12:2047-2054
- 27. Grigsby PW, Perez CA, Kuske RR, et al. Adenocarcinoma of the uterine cervix: lack of evidence for a poor prognosis. Radiother Oncol 1988; 12:289-294
- 28. Miller B, Flax S, Arheart K and Photopulos G. The presentation of adenocarcinoma of the uterine cervix. Cancer 1993; 72:1281-1287
- 29. Eifel PJ, Morris M, Oswald MJ et al.

  Adenocarcinoma of the Uterine cervix: prognosis and patterns of failure of 367 cases treated of the M. D. Anderson Cancer Center between 1965 and 1985. Cancer 1990; 65:2507-2513
- **30. Hopkins MP, Morley GW.** A comparison of adenocarcinoma and squamous cell carcinoma of the cervix. Obstet Gynecol 1991; 77:912-917
- **31. Horiot JC, Pigneux J, Pourquier H, et al.** Radiotherapy alone in carcinoma of the intact uterine cervix according to G. H. Fletcher guidelines: a French cooperative study of 1383 case. Int J Radiat

- Oncol Biol Phys 1988; 14:605-610
- **32.** Lanciano RM, Won M, Hanks GE. A reappraisal of the International Federation of Gynecology and Obstetrics staging system for cervical cancer. Cancer 1992; 69:482-488
- Kim SH, Choi BI, Lee HP, et al. Uterine cervical carcinoma: Comparison of CT and MRI findings. Radiology 1990; 175:45-51
- 34. Lanciano RM, Martz K, Coia LR, et al. Tumor and treatment factors improving outcome in stage II IB cervical cancer. Int J Radiat Oncol Biol Phys 1991; 20:95-100
- 35. Striker JA. Bartholomew M, Velkley DE, et al. Bladder and rectal complications following radiotherapy for cervix cancer. Gynecol Oncol 1988; 29:1-11
- 36. Clark BG, Souhami L, Roman TN, et al. Rectal complications in patients with carcinoma of the cervix treated with concomitant cisplatin and rectosigmoid complications a result of radiotherapeutic treatment. Int J Radiat Oncol Biol Phys 1994; 28: 1887-1895
- Huh SJ. Result of radiation therapy of the cervix cancer stage IIIB. J. Korean Soc Ther Radiol 1993; 11:143-148
- 38. William M, Michael D, Debra E, et al. Stage lb and IIA-B carcinoma of the intact uterine cervix: Impact of Tumor Volume and the Role of Adjuvant Hysterectomy. Semin Radiat Oncol 1994; 4:16-22
- 39. Perez CA, Grigsby PW, Castro-Vita H, er al. Carcinoma of the uterine cervix. I. Impact of prolongation of overall treatment time and timing of brachytherapy on outcome of radiation therapy. Int J

- Radiat Oncol Biol Phys 1995; 32:1275-1288
- 40. Hsu WL, Wu CJ and Jen YM et al. Twice-per-day fractionated high versus continuous low dose rate intracavitary therapy in the radical treatment of cervical cancer: A nonrandermized comparison of treatment results. Int J Radiat Oncol Biol Phys 1995; 32:1425-1431
- **41. Brunet J, Alonoso C, Llanos M, et al.** Chemotherapy and radiotherapy in locally advanced cervical cancer. Acta Oncol 1995; 34:941-944

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                                                                 60- 65%
                        1994 8
          : 1985
                 8
                 2
                      198
                                                     167
                           3
                                               60
                                                                          30
                                    141
               31
                       78 (
                                     55 )
    Kaplan-Meier
                                           log-rank test
Cox-regression
                                                                  가
                                                     chi-square
      linear trend
                               84%
       86%
                                         60%
         . 5
                                        62%
                     5
                                              59%
                                                                     . 57
          가
                                     가
                                                             3
                                                                      29%
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                 28 (16.8%) 38
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가
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packing