

Exploration of Three-dimensional (3D) Dose-volume Parameters of Radiotherapy for Cervical Carcinoma

Gunma Cancer Center 1)Department of Radiology, 2) Department of Gynecology

Yoshizumi Kitamoto¹⁾, Katsuyuki Shirai¹⁾, Yumi Sato¹⁾, Keiko Higuchi¹⁾, Toshinobu Nishimura²⁾, Yoshio Tamaki¹⁾

Objectives

To retrospectively investigate treatment results and the incidence of late sequelae of cervical carcinoma patients treated with radiotherapy based on dose-volume parameters, which were recently recommended from Gynecological (GYN) GEC-ESTRO Working Group, calculated from CT-based 3D dose distribution.

Materials & Methods

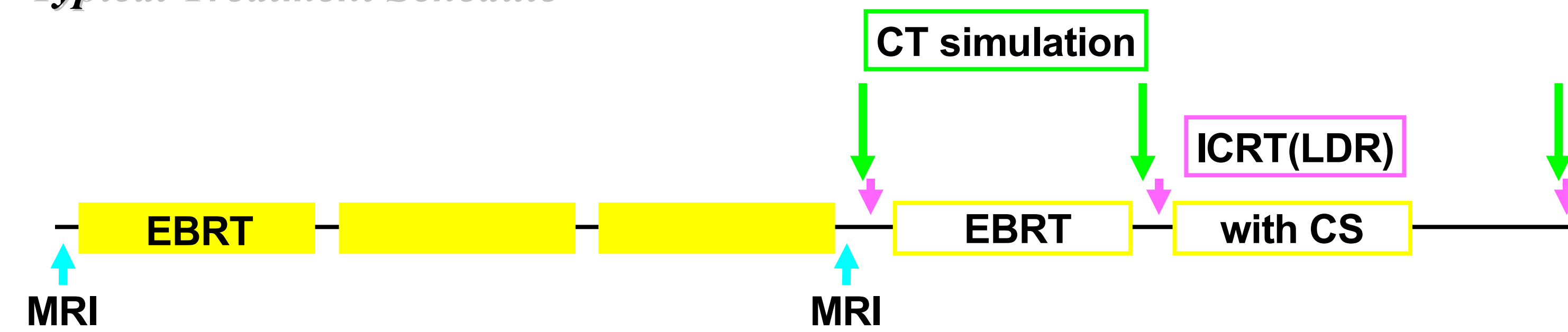
Patient Characteristics

Of cervical carcinoma patients treated with radiotherapy in our institute from Oct. 2003 to Feb. 2006, 22 patients without lymph node metastasis were selected in current study (Table 1).

No. of patients	22
Age	39-86 y. o. (mean: 64 y. o.)
PS	
0:	4
1:	16
2:	2
Pathology	
Sq:	19
Ad:	1
Others:	2
FIGO stage	
1B:	6
2A:	3
2B:	6
3A:	1
3B:	5
4A:	1

Table 1

Typical Treatment Schedule



External Beam Radiotherapy (EBRT)

- ✓ 10MV X-rays, AP/PA portals
- ✓ Whole pelvis before the first ICRT (Fig. 1a)
- ✓ Fields with center shields (CS) after the first ICRT (Fig. 1b)

Not available

Not available

Fig. 1a

Fig. 1b

Intracavitary Radiotherapy (ICRT)

- ✓ Low-dose rate (LDR) Cs-137 sources
- ✓ Intrauterine tandem and ovoid pairs (Fig. 2a, 2b)

Not available

Not available

Fig 2a

Fig 2b

- ✓ CT images (5 mm thick) after obtaining radiographs using the same couch
- ✓ Calculation of the dose distributions using radiotherapy planning system (XiO 4.3.1, CMS)

Contouring (Fig3)

Gross tumor volume (GTV) was contoured with reference to MRI images which were obtained before treatment and the first ICRT. High risk clinical target volume (HR CTV) included the GTV and the entire cervix. Intermediate risk clinical target volume (IR CTV) was the HR CTV with a margin of 1.0-1.5cm. The rectum was contoured from 3 cm below the ovoid sources up to the rectosigmoid junction. The rectal wall was defined 2 mm thick. The bladder was contoured with the Foley catheter and 80-100 cc of diluted contrast medium. The bladder wall was defined 3 mm thick.

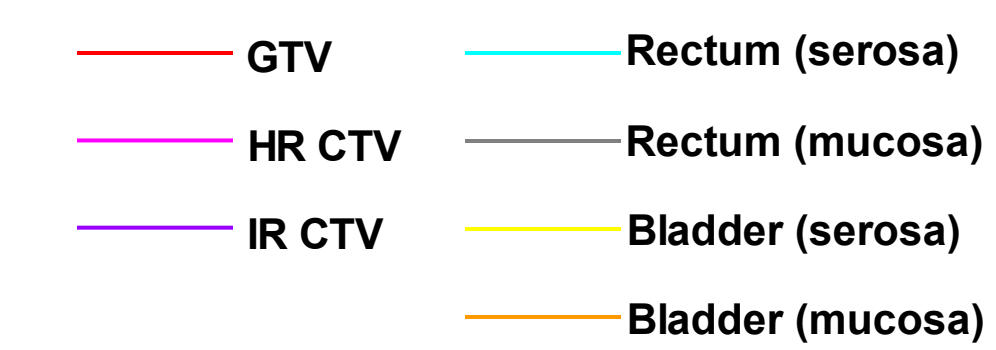


Fig 3

Not available

Coordinate data of the sources were projected to CT images using digitizer.

Parameters

Target
point A dose
D₁₀₀ and D₉₀ of the GTV and the HR CTV

Organs at risk (OAR) (rectum and bladder)
Maximum doses
Doses of ICRU reference points on CT images (Fig4)
D_{0.1cc}, D_{1cc} and D_{2cc} of the rectum and the bladder
D_{5cc} and D_{10cc} of the rectal wall and the bladder wall

Not available

Fig 4

We assumed that no radiation was delivered to primary tumor, rectum and bladder from EBRT after CS was employed.

Biological equivalent doses (BED) of EBRT and ICRT were added and converted to equivalent dose in 2 Gy fractions (EDQ₂) using the linear-quadratic radiobiological model.

BED & EDQ₂

EBRT: $BED_{EBRT} = nd[1 + 1/(\alpha/\beta)]$

ICRT: $BED_{ICRT} = D[1 + gD/(\alpha/\beta)]$
 $\mu = \ln 2/T_{1/2}$
 $g = 2[\mu(1 - \exp(-\mu t))]/(\mu t)^2$

EDQ₂: equivalent dose in 2 Gy fractions
 $EDQ_2 = BED(1 + 2/(\alpha/\beta))$
 $BED = BED_{EBRT} + BED_{ICRT}$
 $\alpha/\beta = 10 \text{ Gy for GTV and CTV}$
 $= 3 \text{ Gy for OARs}$

d=dose per fraction
D=total dose
n=number of fractions
T_{1/2}=repair half-time=1.5 h
t=exposure duration
μ= recovery constant

Evaluated points

- ✓ Relationship between local control and parameters
- ✓ Relationship between late rectal sequelae and parameters

Conclusions

The total dose of EBRT and ICRT for cervical carcinoma in our institute may be sufficient to control the primary lesion and less than the dose which causes severe late complications. In order to decide the optimal values of the parameters, more cases need to be analyzed. The lack of more detailed grading of complications and the difficulty in contouring of OARs (especially the rectum) may have posed limitations to the analysis. The ICRU rectal point dose showed tendency to predict the incidence of rectal bleeding in this study. (When more cases were added to the current study, our analysis showed that the ICRU rectal point dose was correlated to the incidence of rectal bleeding with statistical significance.)

Results

Treatment

EBRT:	50 Gy (40-60.4 Gy)
whole pelvis:	28.7 Gy (10-50 Gy)
pelvis with CS:	20.9 Gy (0-40 Gy)
boost for primary *:	1 case (10Gy)
ICRT(LDR):	3 times (median)
CCRT:	11 cases (50%)
weekly CDDP (40mg/m ²)	

* Because the patient refused the third ICRT

Table 2

Treatment Results

Median follow up time:	28.4 months (11.2-41.8 months)
Local control rate:	100%
Distant metastases:	1 case (pulmonary meta.)

Table 3

Late Sequelae

	Grade 0	1	2	3	4
Rectal bleeding	13	7	2	0	0
Bladder bleeding & Cystitis	16	5	1	0	0
Ileus	0	0	0	2	0
Anemia	0	0	0	1	1

Common Terminology Criteria for Adverse Events v3.0

Table 4

Parameters and Local effect

	Point A				GTV		HR CTV	
	Rt. A	Lt. A	mean A	Lower A	D ₁₀₀	D ₉₀	D ₁₀₀	D ₉₀
EQD ₂ (Gy)	67.1 ±7.9	68.2 ±8.3	67.6 ±8.0	66.8 ±8.2	88.4 ±21.2	114.2 ±29.2	56.1 ±6.3	74.7 ±8.2
Correlation with lower A:					NS	NS	p<0.01	p=0.05

Table 5

Parameters and Rectal bleeding

	Mean EQD ₂ (Gy)					
	ICRU D _{10cc}	Max	D _{0.1cc}	D _{1cc}	D _{2cc}	D _{5cc}
Bleeding(-) n=13	59.3	112.4	91.3	71.7	65.5	50.6
Bleeding(+) n=9	42.7 ±15.1 ±6.8	±27.8	±17.3	±9.9	±8.3	±6.7
p value	70.7 45.1 ±14.0 ±9.7	127.6 ±61.0	95.0 ±22.8	74.6 ±10.3	68.5 ±8.9	53.3 ±8.4

Table 6

p=0.08 p=0.53 **Discussion** p=0.42 p=0.40

✓ The parameters of 3D image-based radiotherapy for cervical carcinomas which were recommended by GYN GEC-ESTRO Working Group could be calculated retrospectively in actual clinical cases.

✓ All rectal parameters were not significant as for late rectal bleeding, but the dose of the ICRU rectal point tended to have a difference between patients with rectal bleeding and patients without rectal bleeding as compared with other rectal parameters in current study. More sensitive gradings for late sequelae (e.g. observations of endoscope) were needed. The problems were that peristalsis of the rectum during treatment cannot be ignored in cases of LDR ICRT, and that contouring of the superior portion of the rectum was more difficult in some cases.

✓ CT image-based radiotherapy for cervical carcinoma may be one method to predict or decrease the incidence of complications of OARs, but MRI images are needed for 3D image-based radiotherapy to utilize the information of the target. The evaluation for the parameters of the target was not possible in the current study because the local control rate 100%. While the lower value of the point A doses determines the duration of ICRT treatment, D₁₀₀ and D₉₀ of HR CTV may serve as substitutes for this purpose.