The treatment outcome of the combination therapy of high-dose rate intra-cavity brachytherapy (HD-ICBT) and Intensity-modulated radiation therapy (IMRT; TomoTherapy) with central-shielding (CS) for cervical cancer

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Introduction

Reduction of the rectal dose is a critical issue for high-dose-rate intra-cavity brachytherapy (HDR-ICBT) of cervical cancer. Because Asian patients have smaller physique compared with Caucasians, it is difficult to keep enough space between HDR-ICBT source and rectal wall. Therefore in Japan, the standard external-beam radiation therapy (EBRT) is a combination of the whole pelvic radiation therapy (WPRT) and a sequential WPRT with central-shielding (WPRT-CS) to reduce the rectal dose prior to HDR-ICBT using three-dimensional conformal radiation therapy (3D-CRT). In 3D-CRT, the CS was a simple rectangular block placed at the midline to reduce rectal dose before HDR-ICBT. The aim of this study was to evaluate quality of treatment planning, the treatment outcome and tolerance of the combination of HDR-ICBT and EBRT which is consisted of WPRT and WPRT-CS using IMRT/TomoTherapy.

Patients and Methods

Thirty consecutive cervical cancer patients treated from 8/2011 to 10/2016 were included in this retrospective analysis. IMRT was performed using TomoTherapy, started with the WPRT followed by WPRT-CS. The total dose of WPRT and WPRT-CS was 50-50.4 Gy/25-28 Fr. The fractions ratio of WPRT and WPRT-CS was determined depending on tumor volume reduction during WPRT. The schedule of the IMRT and HDR-ICBT showed in *Fig. 1*.
In WPRT-CS, the dose to the rectum and uterus regions that received the intensive dose of HDR-ICBT was reduced using the IMRT technique.
The dose to the lymph-node regions including pre-sacral region was maintained. The dose to rectum was defined as that of the International Commission on Radiation Units and Measurements (ICRU) reference point. Toxicities associated with treatments were evaluated using the Common Terminology Criteria for Adverse Events v4.0.

Results

The median follow-up time was 32.5 (range, 4-78) months. *Table 1* shows patients characteristics. The median duration of all treatment including WPRT, WPRT-CS and HDR-ICBT was 53 days (range, 39–64 days). Two-year LC, DFS, and OS rates for the entire cohort was 89.9%, 83.3%, and 86.3% (*Fig.2*).Chemotherapy concomitant with radiation therapy consisted of weekly cisplatin applications (40 mg/m2 of the body surface area) and was given to 22 of the 30 patients (73.3%). It was delivered from 2 to 6 courses; the median was 5 courses**.** *Fig.3* shows dose distribution of WPRT-CS in 3DCRT and IMRT. *Table 2* shows pattern of failure. Three patients experienced a local recurrence in the pelvis.
At the last-follow-up, 5 patients died from the disease and 4 of them died of distant metastases. Remaining one died of regrowth of the primary tumor. Only one patient died of regrowth of the primary tumor. No acute or late ≥ grade 3 genitourinary or gastrointestinal toxicities were observed. Twenty-one patients (70 %) developed ≥ Grade 3 acute HT including at least one of white blood cell decreased, platelet count decreased and/or anemia. There were no other severe late toxicities (≥ Grade 3) associated with treatments.

Tab. 1

Parameters	N
Total no. of patients	30
Age (years), median (Range)	64(38-91)
Primary tumor size/diameter (mm)	46 (10-70)
Performance status	
0	22
1	7
2	1
Histopathology	
SCC	25 (83.3%)
adenocarcinoma	1 (3.3%)
mucinous adenocarcinoma	2 (6.7%)
papillary adenocarcinoma	1 (3.3%)
Carcinoma	1 (3.3%)
FIGO	
IB	6
IIA	2
IIB	13
IIIA	1
IIIB	7
IVA	1

Fig.1

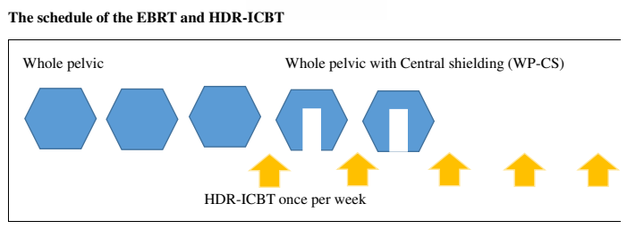
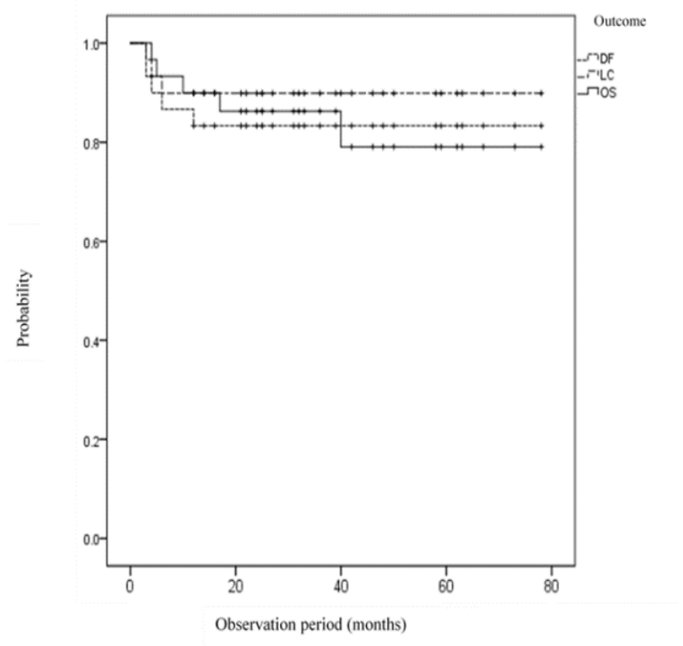


Fig.2



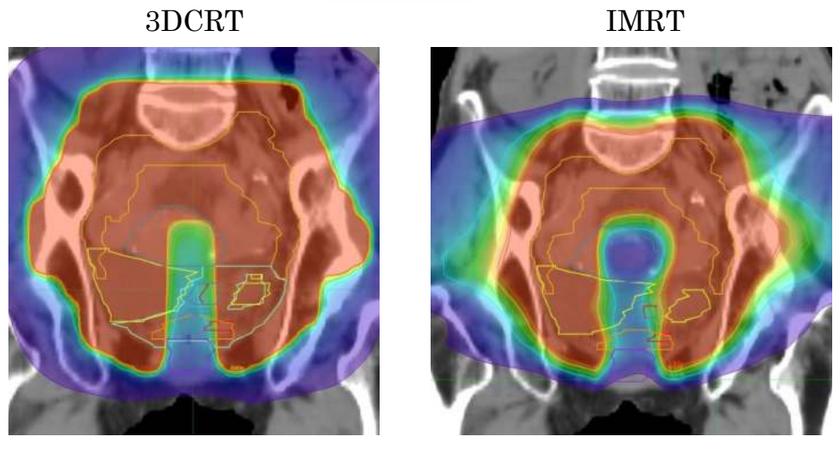
Tab. 2

Pattern of failure

Failure site	N		Histopathology	Last follow
Local + Distant Metastasis	2	primary recurrence and lung and liver metastasis	SCC	DOD
		primary recurrence and multiple lung metastasis	mucinous adenocarcinoma	DOD
Only Local	1	primary recurrence within radiation fields	SCC	DOD
Distant metastasis	1	primary tumor got controlled	Carcinoma	DOD
PAN	1		SCC	alive with d free
PAN + SCN	1		mucinous adenocarcinoma	DOD

PAN: para-aortic lymph node metastasis, SCN: supraclavicular lymph node metastasis, DOD: Died of disease

Fig. 3



Conclusion

In the present study, Tomotherapy with CS resulted in excellent local control and intermediate-term good tolerance rates. Further studies are required to determine the indications, long-term efficacy, and possible late toxicities.