

# Reduction of the skin-effect dose of IMRT plan for patients with cancer in pelvic region

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**Abstract.** In the present study, it was aimed to investigate the optimized plan of radiotherapy with dose modulation in the pelvis to reduce the dose on the skin in patients having pelvic region radiotherapy. The series of images of 45 pelvic cancer patients were selected, intensity-modulated radiation therapy (IMRT) plan was made, the skin dose reduction was optimized, and evaluated verifying the plan verification. As a result, skin volume receiving dose  $\geq 10$ ,  $\geq 20$ ,  $\geq 30$ ,  $\geq 40$  and  $\geq 50$  Gy of the IMRT Skin plan were all less than those of the IMRT plan. Particularly, skin volumes receiving doses  $\geq 20$ ,  $\geq 30$ ,  $\geq 40$  and  $\geq 50$  Gy of the Skin IMRT plan were markedly lower than those of the IMRT plan, the reduction values were 8.76, 18.83, 46.84 and 100%, respectively. Furthermore, the Skin IMRT plan was no longer affected by the 50 Gy dose. In conclusion, the present study revealed that the skin's dose can be decreased with optimal plan processing; thus, this decrease

of the skin's dose ensures the continuation of radiotherapy and improved life quality of the patient.

## Introduction

According to the World Health Organization report in 2018, cancer is the leading cause of death worldwide; of the 9.6 million people who succumbed to cancer in 2018, the number of people who succumbed to colorectal cancer; colon occupied the second place with 862,000 cases; and the five common types of cancer were the following: lung with 2.09 million cases, breast with 2.09 million cases, colorectal with 1.8 million cases, the fourth position was prostate with 1.28 million cases and finally the non-melanoma skin cancer occupied the 5th position (1,042,056 new cases) (1). In 2020, these cancer's positions were 3rd and 4th (141259 and 1198073 new cases), respectively (2). Thus, it was found by the authors that the skin in the pelvis is more often irradiated than the skin in other areas. Based on the team's 10 years of experience working with radiation therapy using accelerators as well as reviewing a number of articles on skin care for radiation therapy patients such as that of Samantha Bostock, in the British Journal of Nursing issue 4, volume 25, 2016, it was realized that the most sensitive skin areas on patients' body were on the groin area, breast, and neck, respectively (3).

Even though there have been numerous studies on skin care for radiation patients, only a few studies aim to reduce the dose to the skin or evaluate the dose on the skin for radiation patients. In addition, the pelvic skin is an active area, difficult to keep clean, and prone to infection. The appearance of an acute reaction on this skin area reduces the body's beauty, affects the quality of life, and even leads to treatment interruption, reducing treatment quality and there may also be a risk of developing skin cancer (4,5).

Actually, during the treatment process, patients treated with radiation therapy are often affected by the side effects of radiation on their skin. The extent to which the skin reacts to radiation varies: From erythema, dry peeling, hyperpigmentation and purulent erosion. The degree of skin response to radiation depends on numerous factors including the area of the skin affected by radiation, type of irradiated energy, total radiation dose and radiation dose division. The present study aimed to identify the planning optimization of radiotherapy with dose modulation in the pelvis to reduce the dose on skin.

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**Abbreviations:** CT, computed tomography;  $D_{5\%}$ , dose corresponding to 5% of the volume of PTV on the DVH;  $D_{95\%}$ , dose corresponding to 95% of the volume of PTV on the DVH; DD, dose difference;  $D_{maxI}$ , max dose of the intestine;  $D_{meanI}$ , mean dose of the intestine;  $D_{maxB}$ , max dose of bladder;  $D_{meanB}$ , mean dose of bladder;  $D_{maxLF}$ , max dose of the left femoral head;  $D_{meanLF}$ , mean dose of the left femoral head;  $D_{maxRF}$ , max dose of the right femoral head;  $D_{meanRF}$ , mean dose of the right femoral head;  $D_{minPTV}$ , 3D min dose of PTV; IMRT, intensity-modulated radiation therapy; 3DCRT, three directions conformal radiotherapy; DTA, distance to agreement; DVH, dose volume histograms;  $D_{maxPTV}$ , 3D max dose of PTV;  $D_{meanPTV}$ , 3D mean dose of PTV; HI, homogeneity index; CI, conformity index; LINAC, linear accelerator; MU, machine unit; PTV, planning target volume; QA, quality assurance;  $V_{95\%}$ , volume of PTV corresponding to 95% of the prescribed dose on the DVH;  $V_{5\%}$ , volume of PTV corresponding to 5% of the prescribed dose on the DVH;  $V_{PTV}$ , volume of PTV; MLC, multileaf collimators

**Key words:** IMRT, HI, CI, gamma index, skin dose

## Materials and methods

**Materials.** The Unique LINAC has 80 MLC leaves, and only 6 MV photon energy. According to Varian guideline, Unique accelerator technology allows radiation therapists to perform a variety of radiotherapy techniques including: 2D, 3D, IMRT and RapidArc treatment.

Eclipse 13.5, which is the treatment planning system of accelerators, and brachytherapy machines, is developed by Varian Corporation. The eclipse TPS has Anisotropic Analytical Algorithm (AAA) for photons and Pencil Beam Convolution (PBC) Algorithm.

AAA algorithm is used to calculate the dose of these IMRT plans. The algorithm is dosimetry for photon beams based on dose superposition, which was released in 2005 by Varian Medical System and is used in the Eclipse TPS (6). Complex technique plans are used in modern radiotherapies including IMRT, RapidArc and Tomotherapy. A plan may have more than one hundred control points including MLC movement, gantry angle and collimator angle to induce dose variation in the patient. Radiotherapy plans are becoming increasingly complex and require great accuracy. It is extremely important to control the quality of a plan before starting it.

**Samples and sampling methods.** The sample size is calculated with the following formula:

$$n = \frac{Z_{1-\alpha/2}^2 \sigma^2}{d^2}$$

With confidence interval 99%  $Z_{1-\alpha/2}^2 = 2.56$ ; Standard deviation  $\sigma=2.5$ ; Error  $d=1$ . Hence the sample size is  $n=42$ . A total of 45 patients (42% male, 58% female) were selected to participate in the present study as presented in Table I (age range, 30-85 years; average age, 62 years) from May 2018 to May 2020 at Hanoi Oncology Hospital (Hanoi, Vietnam). The rate of disease stages T1, T2, T3, T4 are 9, 24, 36, and 31%, respectively. Since the sample size of 45 patients was small, Fisher's exact test was used in data analysis, and the data of this research were analyzed with Excel version 2013.

**Methods.** Step 1: A minimum of simulated CT images of 30 preoperative radiotherapy rectal cancer patients and a minimum of simulated CT images of 15 cervical cancer patients were selected. These image series, which were not scattered due to metal artifacts, were contoured all Organ At Risk (OAR) around planning target volume (PTV) according to the protocol (7). CT simulation image series were contoured: GTV, CTV, PTV: u + nodes with prescribed dose: 50,4 Gy; organs at risk: Volume of small intestine 15 Gy  $\leq$  120 ml or Dmax of small intestine <115%; Dmax of bladder: <115% or Dmax <50 Gy and <50% of volume having dose  $\geq$  40 Gy; Dmax of femoral <115% or Dmax <50 Gy and <10% of volume having dose  $\geq$  40 Gy; using 6 MV photon energy to make IMRT with Eclipse 13.5.

Step 2: IMRT plan was evaluated including D95% of PTV; Dmax of plan <107%; 2D dose distribution; analyze Dose Volume Histogram; homogeneity index (HI) and conformity index (CI); dose of PTV; dose of OAR (8).

Table I. The information of the selected patients.

Patient	Birth year	Sex	Type of cancer	Stages
1	1957	Male	Rectum	T1N0M0
2	1936	Male	Rectum	T4N0M0
3	1945	Female	Rectum	T3N2M0
4	1950	Male	Rectum	T4An0M0
5	1960	Male	Rectum	T4N2M1
6	1944	Female	Rectum	T3N0M0
7	1954	Male	Rectum	T2bNxM0
8	1972	Male	Rectum	T4bNxM1
9	1953	Male	Rectum	T4aN2M0
10	1941	Female	Rectum	T4aN1M1
11	1954	Female	Rectum	T4N1M1
12	1949	Female	Rectum	pT4aN2M0
13	1952	Male	Rectum	T3N0M0
14	1958	Female	Rectum	T3N1M0
15	1958	Male	Rectum	T3N1M0
16	1966	Male	Rectum	T2N0M0
17	1962	Male	Rectum	T3N1M0
18	1950	Male	Rectum	T3N0M0
19	1960	Male	Rectum	PTaN0M0
20	1954	Female	Rectum	T3N1M0
21	1967	Male	Rectum	T3NxM0
22	1954	Male	Rectum	cT4bNxM0
23	1957	Female	Rectum	T4bN1Mx
24	1951	Male	Rectum	T4NxM0
25	1944	Male	Rectum	T4N1M0
26	1935	Female	Rectum	T4N2M0
27	1961	Male	Rectum	cT3N0M0
28	1954	Female	Rectum	T2Bn1M0
29	1985	Female	Rectum	T3NxM0
30	1958	Female	Rectum	T2bN9M0
31	1958	Female	Cervix	T2bN0Mx
32	1974	Female	Cervix	T3N0M0
33	1948	Female	Cervix	T3bN0M0
34	1959	Female	Cervix	T2Bn0M0
35	1948	Female	Cervix	T2bN1M0
36	1967	Female	Cervix	T2bN0M0
37	1960	Female	Cervix	T2bN0M0
38	1944	Female	Cervix	T2bNxM0
39	1988	Female	Cervix	T2N0M0
40	1972	Female	Cervix	T3N0M0
41	1990	Female	Cervix	T4N3M0
42	1960	Female	Cervix	pT3N0M0
43	1969	Female	Cervix	T1Bn0M0
44	1967	Female	Cervix	T1bNxMx
45	1978	Female	Cervix	T3CN0M0

Step 3: The skin was released from the body contour with depth of 5 mm; IMRT plan was copied in step 2 called Skin IMRT. Skin IMRT were optimized with all optimization parameters of IMRT except skin with priority is 60.

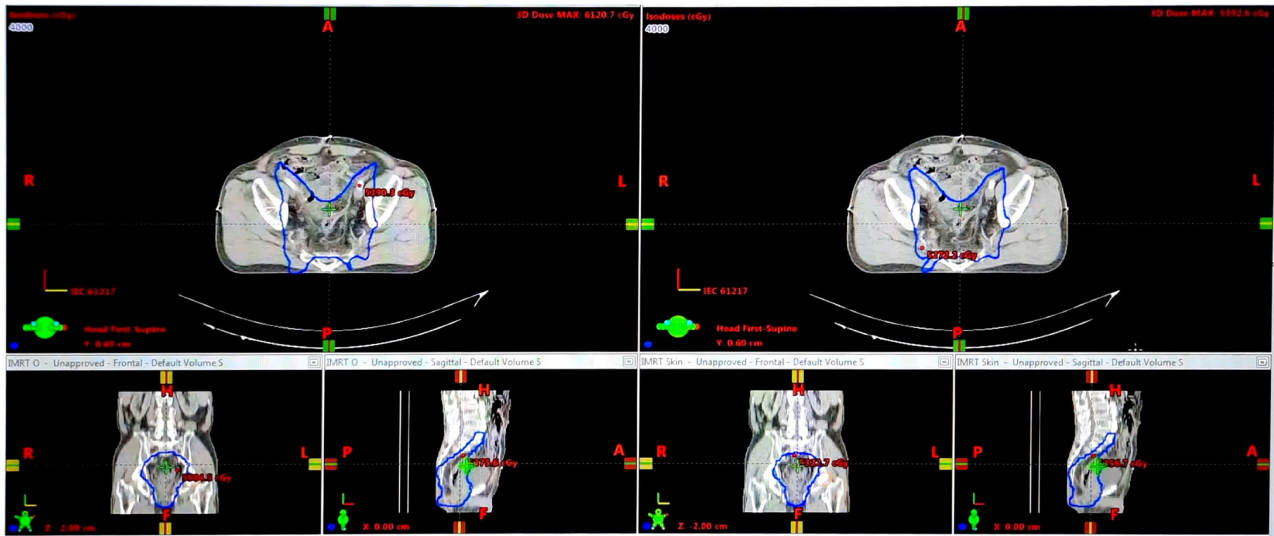


Figure 1. A total of 40 Gy isodose line on three images of IMRT plan (left side) and on three images of Skin IMRT plan (right side). IMRT, intensity-modulated radiation therapy.

Step 4: IMRT was compared with Skin IMRT plan of each patient in 2D distribution, dose of PTV, dose of OAR, dose volume histograms (DVH), HI, CI, dose of skin; quality assurance (QA) plan of IMRT plan and Skin IMRT plan was created with Delta4.

Step 5: QA plan was implemented with Delta4. The parameters of the software are distance to agreement (DTA) (3-mm), dose difference (DD) (3%), and gamma index >95%. DTA 3-mm: The acceptable interval between a point on the planned control result and a point with the same absolute dose value on the calculated result shall not be <3 mm (9). DD 3%: The calculated absolute dose value of a point with the measured absolute dose value should not be <3% (9). Gamma index is a combination of DTA and DD. The gamma index value is used to compare dose distribution between calculated and measured values. Gamma index is calculated with the following formula (9).

$$\gamma(r_m) = \min\{\Gamma(r_m, r_c)\} \forall (r_c) \leq 1 \quad (1)$$

Where  $r_m$  is the point in the actual measured dose distribution, and  $r_c$  is the point in the planned dose distribution;  $\Delta d_m = 3$  mm;  $\Delta D_M = 3\%$ ;  $D(r_c)$  is the absolute dose at  $r_c$ ;  $D(r_m)$  is the absolute dose at  $r_m$ .

$$\Gamma(r_m, r_c) = \sqrt{\frac{r^2(r_m, r_c)}{\Delta d_m^2} + \frac{\delta^2(r_m, r_c)}{\Delta D_M^2}}$$

$$r(r_m, r_c) = |r_m - r_c|$$

$$\delta(r_m, r_c) = D_c(r_c) - D_m(r_m)$$

Collected dose of PTV includes: 3D maximum dose of plan ( $D_{max}$ ), 3D maximum dose of PTV ( $D_{maxPTV}$ ), 3D minimum dose of PTV ( $D_{minPTV}$ ), 3D mean dose of PTV ( $D_{meanPTV}$ ), D5% (the dose value at 5% of the PTV volume point on DVH line), D95% (the dose value at 95% of PTV volume point on DVH line), V95% is the volume of PTV covered with 95% of the prescribed dose, and volume of PTV (VPTV). The dose of OAR includes: Volume of small intestine gets 15 Gy; maximum dose and mean dose of the small intestine, bladder, femur, and skin.

HI has been defined as the following formula (2): HI is used to evaluate the uniformity of dose distribution over the PTV volume, the ideal value of HI is zero. Therefore, the smaller the HI value is, the more uniform the dose distribution on the PTV is (10).

$$HI = 100\% \times \frac{D_{5\%} - D_{95\%}}{D_{pre}} \quad (2)$$

Where  $D_{pre}$ : Prescribed dose of PTV. CI has been defined as the following formula (3): This index relates to how well the 95% isodose conforms to the shape of the PTV. CI ideal value is one. The plan having CI to be near one has been proven improved than other plans (10).

$$CI = \frac{V_{95\%}}{V_{PTV}} \quad (3)$$

## Results

**Comparing 2D dose distribution.** When analyzing plans, the dose distribution on slice by slice between IMRT plan and Skin IMRT plan of each patient was compared. In Fig. 1, the 40 Gy isodose line is revealed on three images of IMRT plan (left side) and on three images of Skin IMRT plan (right side).

**Dose results of PTV.** The relative maximum dose of IMRT and Skin IMRT plan, the maximum and minimum absolute dose in both types of plan, the number following the  $\pm$  sign is a standard deviation are listed in Table II; P-values were calculated with Fisher's exact test, the sample size is 45. These values are compared with the prescribed values.

As demonstrated in Table III, V95% of the IMRT plan is a slightly higher than that of the Skin IMRT plan [ $865.75 \pm 379.81$  cm<sup>3</sup>; ( $P=0.00072$ ) vs.  $847.79 \pm 370.5$  cm<sup>3</sup> ( $P=0.00074$ )], and both values are suitable with the requested values. The number following the  $\pm$  sign is a standard deviation, P-values were calculated with Fisher's exact test, and the sample

Table II. Maximum dose of plan and dose results of PTV.

	IMRT		Skin IMRT		
	Collected value	Difference compared with requested value (%)	Collected value	Difference compared with requested value (%)	The requested values
$D_{\max}$ (%)	108.85±3.15; P=0.09	1.85	105.42±0.91; P=0.31	-1.58	<107%
$D_{\max\text{PTV}}$ (cGy)	5440.33±119.48; P=0.0023	0.88	5305.44±48.62; P=0.0057	-1.62	<5393 cGy
$D_{\min\text{PTV}}$ (cGy)	3924.24±328.67; P=0.0009	-18.04	3828.82±347.24; P=0.0009	-20.03	≥4788 cGy
$D_{\text{meanPTV}}$ (cGy)	5023.56±26.44; P=0.011	-0.33	4998.15±26.1; P=0.01	-0.83	5040 cGy

PTV, planning target volume; IMRT, intensity-modulated radiation therapy;  $D_{\max\text{PTV}}$ , 3D max dose of PTV;  $D_{\min\text{PTV}}$ , 3D min dose of PTV;  $D_{\text{meanPTV}}$ , 3D mean dose of PTV.

Table III. The volume of PTV has dose larger than 95% of the prescribed dose, and the volume has dose larger than 105% of the prescribed dose in IMRT and Skin IMRT.

	IMRT	Skin IMRT	The requested values
$V_{95\%}$ (cm <sup>3</sup> )	865.75±379.81; P=0.00072	847.79±370.5; P=0.00074	≥84258.35
$V_{105\%}$ (cm <sup>3</sup> )	4.16±8.21; P=0.041	0.24±0.689; P=0.5	0

PTV, planning target volume; IMRT, intensity-modulated radiation therapy;  $V_{95\%}$ , volume of PTV corresponding to 95% of the prescribed dose on the DVH; DVH, dose volume histograms.

Table IV. HI, CI value of IMRT and Skin IMRT.

	IMRT	Skin IMRT	Ideal value
HI	6.09±1.19; P=0.25	6.46±1.34; P=0.21	0
CI	0.976±0.017; P=0.54	0.957±0.026; P=0.529	1

HI, homogeneity index; CI, conformity index; IMRT, intensity-modulated radiation therapy.

size was 135 because on all the 45 DVHs of 45 plans three values were received per each DVH.  $V_{105\%}$  of the Skin IMRT plan was smaller and closer to the requested value than that of the IMRT plan. These results mean both plans are matched with the requested plan in terms of the dose of the PTV in plan, and the Skin IMRT had less hotpot points than the IMRT plan.

As shown in Table IV HI and CI values of the IMRT plan were closer to the ideal values than those of the Skin IMRT plan; the number following the  $\pm$  sign is a standard deviation, P-values were calculated using Fisher's exact test and the sample size was 45. These results revealed that the PTV of the IMRT plan covers improved and is more uniform with 95% isodose line than that of the Skin IMRT plan.

**Results dose value of OAR.** The affection dose on OAR around PTV of both IMRT and Skin IMRT plans were a little

different (Table V). In the aforementioned table, the number following the  $\pm$  sign is a standard deviation, P-values were calculated using Fisher's exact test, and the sample size was 135 because on all the 45 DVHs of 45 plans three values were received per each DVH. Specifically, the affection dose on the small intestine of the Skin IMRT plan was smaller than that of the IMRT plan [2097.82±607.16 cGy (P=0.00046) compared with 2188.68±718.64 cGy (P=0.0004)]. This result indicated that Skin IMRT significantly decreased the affection dose on the small intestine compared with the value of IMRT plan.

**Results of the QA plan and the machine unit (MU) number of plans.** As demonstrated in Table VI, DD, DTA, gamma index, and MU numbers of both IMRT and Skin IMRT plans were quite similar. In the aforementioned table, the number following the  $\pm$  sign is a standard deviation, P-values were calculated with Fisher's exact test, and the sample size was 45. The results pointed out that the optimal processing to reduce dose to skin doesn't affect the difference between the calculated dose and measured dose, and the MU number of the plans.

**The volume of skin gets 10, 20, 30, 40 and 50 Gy in IMRT and Skin IMRT plan.** The skin volumes receiving doses of  $\geq 10$ ,  $\geq 20$ ,  $\geq 30$ ,  $\geq 40$  and  $\geq 50$  Gy of the Skin IMRT plan were all smaller than those of the IMRT plan (Table VII). In the aforementioned table, the number following the  $\pm$  sign is a standard deviation, P-values were calculated using Fisher's exact test, and the sample size was 135 because on all the 45 DVHs

Table V. Maximum dose (Dmax) and mean dose (Dmean) of organ at risk in IMRT and Skin IMRT.

Types		IMRT	Skin IMRT	The difference (%)
Small intestine	D <sub>maxSI</sub> (cGy)	4791.29±505.7; P=0.0006	4749.19±481.82; P=0.0007	-0.88
	D <sub>meanSI</sub> (cGy)	2188.68±718.64; P=0.0004	2097.82±607.16; P=0.00046	-4.15
Bladder	D <sub>maxB</sub> (cGy)	4655.2±258.91; P=0.001	4609.456±256.65; P=0.0016	-0.98
	D <sub>meanB</sub> (cGy)	2975.22±532.9; P=0.0005	2953.95±497.11; P=0.0006	-0.71
Left femur	D <sub>maxLF</sub> (cGy)	4150.27±769.2; P=0.0003	4051.89±447.69; P=0.0004	-2.37
	D <sub>meanLF</sub> (cGy)	2171.87±395.3; P=0.0007	2169.41±373.9; P=0.0007	-0.11
Right femur	D <sub>maxRF</sub> (cGy)	4150.27±769.2; P=0.0004	4198.92±664.1; P=0.0004	1.17
	D <sub>meanRF</sub> (cGy)	2320.62±338.74; P=0.0008	2349.72±330.72; P=0.0009	1.25

IMRT, intensity-modulated radiation therapy; D<sub>maxSI</sub>, max dose of the small intestine; D<sub>meanSI</sub>, mean dose of the small intestine; D<sub>meanB</sub>, mean dose of bladder; D<sub>maxLF</sub>, max dose of the left femoral head; D<sub>meanLF</sub>, mean dose of the left femoral head; D<sub>maxRF</sub>, max dose of the right femoral head; D<sub>meanRF</sub>, mean dose of the right femoral head.

Table VI. The results of quality assurance plan, and the MU number of IMRT and Skin IMRT.

Type plan	IMRT	Skin IMRT
DD (%)	96.08±1.63; P=0.17	96.09±1.66; P=0.17
DTA (%)	98.77±1.15; P=0.25	98.87±0.89; P=0.31
Gamma index (%)	99.04±0.92; P=0.33	99.09±0.78; P=0.36
MU	1384.17±222.51; P=0.001	1380.17±220.54; P=0.001

IMRT, intensity-modulated radiation therapy; DD, dose difference; DTA, distance to agreement; MU, machine unit.

Table VII. The volume of skin gets 10 Gy (V10 Gy), 20 Gy (V20 Gy), 30 Gy (V30 Gy), 40 Gy (V40 Gy) and 50 Gy (V50 Gy) in IMRT and Skin IMRT plan.

	IMRT	SKIN IMRT	Reduction volume (%)
V <sub>10Gy</sub> (cm <sup>3</sup> )	294.02±105.93; P=0.0023	287.45±102.7; P=0.0027	-2.23
V <sub>20Gy</sub> (cm <sup>3</sup> )	52.64±30.3; P=0.009	48.03±28.85; P=0.0098	-8.76
V <sub>30Gy</sub> (cm <sup>3</sup> )	11.79±11.33; P=0.025	9.57±9.44; P=0.029	-18.83
V <sub>40Gy</sub> (cm <sup>3</sup> )	1.9±3.45; P=0.09	1.01±2.3; P=0.15	-46.84
V <sub>50Gy</sub> (cm <sup>3</sup> )	0.046±0.18; P=1.98	0	-100

of 45 plans three values per each DVH were received. The skin volume receiving a dose of ≥10 Gy in Skin IMRT was 2.23% smaller compared with this volume of the IMRT plan. Particularly, the skin volume receiving doses ≥20, ≥30, ≥40 and ≥50 Gy of the SKIN IMRT plan decreased significantly compared with that of the IMRT plan. The reduction values were 8.76, 18.83, 46.84 and 100%, respectively. Furthermore, the skin in SKIN IMRT plan was no longer affected by the 50 Gy dose.

## Discussion

Comparing dose distribution between the slice of IMRT plans with the slice of Skin IMRT, the results revealed that more isodose lines in IMRT plan cover on skin than those

of Skin IMRT, such as in Fig. 1; the 40 Gy isodose line of IMRT overlaid more skin area in compared with that of Skin IMRT plan.

The results of Tables II, III, IV and V pointed out that the IMRT was performed with more optimization to decrease the effective dose on the skin, small intestine, bladder and right femur. This optimization also decreased the hot spot of plan, the maximum dose on PTV; however, the mean dose of PTV also decreased. The decreasing in the mean dose of PTV could be acceptable (from -0.33 to -0.83%). The results of Table VI pointed to the number MU of the plan and the QA plan results of IMRT plan and Skin IMRT were the same. It means that the optimization for decreasing the effective dose of skin made decreasing the dose on other organs at risk, however, the optimization did not affect the quality of the plan.



Table VIII. Acute effects of radiation on the skin (5).

Tissue response	Onset/Duration	Clinical presentation
Erythema	Onset within 4-14 days of first treatment (dose 10-30 Gy), peaks at 4 -5 weeks. Resolves 2-6 weeks after last treatment	Faint to brisk redness that outlines treatment field. Intensifies as treatment continues. Increased skin temperature, slight edema.
Dry desquamation	As early as 3rd-4th week (40 Gy), but typically by 5th-6th; earlier with accelerated RT or chemotherapy. Resolves 3-4 weeks after completion of treatment	Dryness, flaking, and peeling often accompanied by itching, a layer of dry, dead, dark skin can accumulate over part or all of the treatment field and will eventually slough off. Mild pain
Hyperpigmentation	As early as 2-3 weeks of standard fractionated radiation therapy, depending on baseline skin pigmentation. Usually resolves 3 months-1 year following completion of treatment; occasionally chronic	Tanned appearance
Moist desquamation	Following 40-50 Gy or with trauma/excess friction, bolus material, or chemotherapy. Recovery usually 2-6 weeks after completion of treatment	Bright erythema, sloughing skin, exposed dermis, serous exudates and mucus oozing from skin surface moderate pain

There are numerous types of studies on the skin's dose in radiotherapy (1-5,11-23) including the previous study of Anscher (4), changes in the skin caused by radiation may appear from the first days of irradiation. Acute effects of radiation may occur within 6 weeks of radiation, while late effects appear after radiation therapy from a few months to a few years. The acute effects of radiation therapy are often considered transient because cells are usually capable of self-repairing. Late effects are usually long-lasting and are likely to become more severe over time. The severity of acute and late effects depends on radiation dose, duration of exposure, total irradiated dose, and location of the irradiated skin. From the presence and severity of acute effects on the skin, late effects can be predicted. Late skin effects including fibrosis or necrosis may occur with acute skin reactions. Side effects of radiotherapy on the skin, both acute and late, are local and limited to the irradiated site (5). Acute skin reactions to radiation include erythema, dry desquamation, hyperpigmentation and purulent exfoliation as shown in Table VIII (5). Not all patients develop an acute reaction. However, it is possible to have different reactions occurring simultaneously in the irradiation field.

Archambeau *et al* (5) described early and late skin changes as dose-dependent and as a reflection of changes in cellular components including the epidermis, dermis and blood vessels. In terms of classifying the acute effects of radiation therapy on cancer patients' skin, Cox *et al* (11) identified 5 levels: Grade 0, no response; Grade 1 (mild erythema, dry scaling, hair loss and decreased sweating); Grade 2 (moderate to strong erythema, patchy exudative dermatitis and moderate edema); Grade 3 (exudative dermatitis, in addition to skin folds and intense edema); and Grade 4 (ulcer, hemorrhage and necrosis) (11).

As pointed out in Table VII, the skin volume receiving a dose of  $\geq 10$  Gy in Skin IMRT decreased by only 2.23% compared with this volume of the IMRT plan. However, the skin volumes receiving higher doses (20, 30, 40 and 50 Gy)

sharply declined compared with these volumes of the IMRT plan. As aforementioned in the method section, Skin IMRT plans were optimized with all optimization parameters of IMRT except skin with a priority was 60. This priority is a little larger than the default priority value (50 is the default value), and very smaller than the priority of PTV, which was set 300. Thanks to these chosen priorities the quality of plans was not affected, but the skin volume receiving high dose was sharply decreased.

Comparing the results of Table VII with the results of Table VIII, it can be observed that if using the Skin IMRT plan in treatment, patients' skin is less affected by the high dose, and skin symptoms including dryness, flaking, scaly often with exudate, a layer of dry, dead, dark skin thickens during treatment and may peel off, moderate pain, tanning erythema, skin death, severe exudate, oozing from the skin surface, moderate pain, were significantly reduced. Radiation induced skin reactions were limited to moderate and mild erythema. The significant reduction of clinical symptoms will help enhance the quality of treatment and improve the patients' quality of life.

In conclusion, the present study identified the parameters to optimize the dose reduction effect on the skin in the pelvic IMRT plan. The dermal dose optimized plan has reduced the dose of dermal effects compared with the original plan. Particularly, the skin in the dermal dose optimization plan is no longer affected by the 50 Gy dose. Optimizing the dose reduction effect on the skin also contributes to reducing the average dose on the small intestine, and the planned hotpot but still maintaining the dose of PTV.

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## Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

## Authors' contributions

QBV purposed, designed the research, collected data and analyzed data, and reviewed and edited the final manuscripts. SDQ designed collecting data's protocol, collected and analyzed data, wrote the draft of the manuscript and prepared the documents for submission. THV, TV and TPT collected data and reviewed the manuscript. QBV and SDQ confirm the authenticity of all the raw data. All authors read and approved the final version of the manuscript.

## Ethics approval and consent to participate

The present study was approved (approval nos. 629/QĐ-BVUB and 2088/QĐ-BVUB) and sponsored by Hanoi Oncology Hospital (Hanoi, Vietnam).

## Patient consent for publication

All participants were explained and informed about the study, and oral informed consent was provided by all patients for participation in the study.

## Competing interests

The authors declare that they have no competing interests.

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