Comparison dose distribution between 3D-CRT, IMRT and VMAT techniques in stereotactic body radiation therapy for hepatocellular carcinoma

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Summary

Objective: To compare the difference of dose distribution and physical characteristics on treatment plans using three-dimensional conformal radiation therapy (3D-CRT), intensity modulated radiation therapy (IMRT) and volumetric modulated arc therapy (VMAT) coplanar (CP) and non-coplanar (NCP) techniques in the treatment of hepatocellular carcinoma (HCC) using stereotactic body radiation therapy (SBRT). *Subject and method*: Twenty HCC patients who previously underwent with SBRT using VMAT on TrueBeam STx linear accelerator were selected. Average CT obtained from 4 Dimension Computed Tomography Simulation (4D-CT) of patients were used to plan on Eclipse v13.6 by 3D-CRT, IMRT, and VMAT (CP and NCP) techniques. The prescription dose of 30 - 60Gy in 3 - 5 fractions was delivered for the planning target volume (PTV). Internal tumor volume (ITV) on average CT was determined by the sum of GTV contoured on ten phases of 4D-CT. The Organ at Risks (OARs) were contoured in average CT. All plans were optimized and evaluated based on the criteria in RTOG 1112. The dose distribution of OARs in DVH (dose volume histogram) and the targets at conformity index (CI), gradient index (GI), homogeneity index (HI), monitor unit (MU) were used to comparing between conformal and modulated techniques. *Result*: Using VMAT and IMRT, the volume conformity was better than 3D-CRT ($p<0.01$), reduced significant high dose at liver normal volume. However, 3D-CRT had much lower MU number than VMAT and IMRT techniques. There were no significant differences in OARs such as the heart, esophagus, spinal cord +5mm, chest wall, duodenum. *Conclusion*: VMAT improves the treatment volume coverage and significantly reduces the dose to the liver normal volume than 3D-CRT and IMRT techniques.

Keywords: SBRT, 3D-CRT, IMRT, VMAT, hepatocellular carcinoma, radiotherapy.

1. Background

According to statistic from the GLOBOCAN 2018, liver cancer is the sixth most commonly diagnosed cancer and the fourth leading cause of cancer death worldwide, with about 841,000 new cases and 782,000 deaths annually in the worldwide. Rates of both incidence and mortality are 2 to 3 times higher among men in most world regions, thus liver cancer ranks fifth in terms of global cases and second in terms of deaths for males. The most common type of primary liver cancer globally is hepatocellular carcinoma (HCC) [2]. Surgical resection is the standard therapy for liver malignancies including primary and metastatic liver cancer [3]. However, other factors such as comorbidities, advanced age, or unwillingness, the

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patient can't undergo surgery. So, other local therapies such as radiofrequency ablation, SBRT are used instead. However, radical treatment for HCC can be challenging due to poor liver function, tumor location and progression, and anatomical barriers. Furthermore, preservation of residual liver function is required [4].

SBRT is a new radiation treatment method to deliver, with high accuracy, a high dose of radiation to small and well-defined targets, utilizing either a single dose or a few fractions with a high degree of precision within the body [5]. Several studies using SBRT for HCC are reported high tumor response and local control rates [6], [7]. SBRT results improved local control rates: 94% and 82% at 1 and 2 years [8]. Nowadays, a SBRT plan can be made by 3D-CRT, IMRT, VMAT techniques. Using 3D-CRT, treatment duration can be over 30 minutes per fraction. Prolonged treatment times are not only uncomfortable for patients but also have the problem of intra-fraction motion during treatment. IMRT and VMAT allow faster in delivery of radiation treatment with variable gantry and dose rate.

In 2018, 108 Military Central Hospital have treated HCC with SBRT using VMAT on TrueBeam STx linear accelerator. The aim of this report was *to compare the differences between 3D-CRT, IMRT and VMAT technique about: The dose distribution in PTV, the dose to OARs, the dose to liver normal volume, CI, HI, GI, and MU number.*

2. Subject and method

2.1. Patient characteristics

From January 2018 until April 2019, twenty HCC patients were treated by SBRT using VMAT on TrueBeam STx linear accelerator. Tables 1 summarize the patient characteristics of this study.

All patients treated by SBRT in 3 - 5 fractions. The time between fractions was between 24 and 72 hours, with treatment delivered to all targets over 5 to 15 days (with 10 days being the preferred treatment time). Example three fractions per week on Monday, Wednesday, and Friday, respectively. As to the fraction size and total dose, these were determined on the basis of physicians' judgments about liver function [9].

Table 1. HCC patient characteristics

Early HCC stage, median stage after TACE, HCC has portal vein thrombosis or HCC patients waiting for a liver transplant.
Can ability to surgery or PEI, RFA.
ECOG: 0 - 2.
The number of tumor is 1 to 3, the size of each target ≤ 5cm, the total size target ≤ 10cm.
The volume of healthy liver > 700ml.

2.2. Imaging (4D-CT simulation)

All patients underwent fluoroscopy with immobilization devices including abdominal compression to evaluation the liver motion. Then they underwent computed tomography simulation in the treatment position with 4D-CT on GE 580RT 16 slices. The patient's breathing signal have recorded by Respiratory Gating for Scanners (RGSC). The slice thickness is 2.5mm. The patient lied on body fix blue bag immobilization in a supine position and arm up.

Figure 1. The patient lied on body fix blue bag immobilization and scan 4D-CT at 108 Military Central Hospital

2.3. Target volume and organ at risk delineation

The images data were reconstructed in ten respiratory phases, from 0% to 90%. An internal target volume (ITV) was delineated considering all tumor positions in the 4D-CT dataset. PTV was

determined by adding 0.5cm - 1.5cm to GTV. Liver motion was taken into account, and additional margins were added to account for motion.

The spinal cord +5mm, esophagus, stomach, duodenum, heart, small bowel, large bowel, skin, great vessels, skin, chest wall, and gallbladder were outlined as organs at risk (OARs).

2.4. Radiotherapy planning

All patients were previously planed on Eclipse version 13.6 software by VMAT and delivered on a Varian TrueBeam STx with HD120 MLC with 32 pairs MLC 2.5mm leaves in the central and 28 pairs MLC 5.0mm leaves peripherally. Prescription dose was 30 - 60Gy in 3 - 5 fractions base on the normal tissue constraints. The highest allowable prescription dose to the primary target while respecting normal tissue constraints should be used. The goal was 100% of the CTV was encompassed by the prescription dose. OARs were used for the treatment plan according to the guideline RTOG 1112 [1]. Dose calculations for all plans were calculated using the Eclipse Anisotropic Analytical Algorithm (AAA) with inhomogeneity corrections applied. Plans were normalized such that the prescribed dose covered minimum 95% volume of the PTV.

In this study, we re-planed all SBRT plans using 3D-CRT, IMRT and VMAT CP and NCP techniques on Eclipse version 13.6.

3D-CRT

The 3D-CRT plans consisted from 7 to 9 beams static coplanar with photon energy from 6 MV-10MV. Beam directions and weights were manually optimized according to the location of the tumor. All fields were designed by beams-eye-view and asymmetric [9]. Jaws and Multi-Leaf Collimator (MLC) were opened margin with the Planning target volume (PTV).

IMRT

The features of IMRT are the inverse treatment planning process and the use of large number of treatment fields or subfields that fall within the conformal beam's-eye view of the target [10]. So our IMRT plans generally consisted of 7 - 9 coplanar fields delivered using a sliding window technique and photon energy from 6MV - 10MV, not opposite field. All plans were given output and optimized with Eclipse version 13.6 according to the guideline RTOG 1112 [1]. Non-coplanar beams were not evaluated in these IMRT plans due to concerns over excessively prolonged.

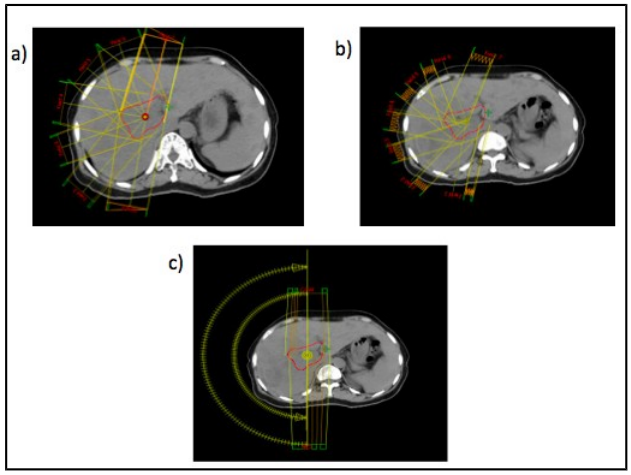

Figure 2. The arrangement of the field for 3 techniques a) 3D-CRT, b) IMRT, c) VMAT

VMAT-CP

The VMAT coplanar plans typically consisted from 2 to 3 half arcs, various collimator and gantry rotation with an isocenter to spare OARs. The couch was 0 degree for all arcs. Energy 6MV FFF and 10MV FFF be used depend on tumor location. Adjusted the weights, targets and dose limits of tumors and healthy organs to optimize the plan. In the process of optimizing VMAT, the dose of the treatment volume were usually placed 3 - 7% higher than the indicated dose, the OARs dose according to the guideline RTOG 1112 [1].

VMAT-NCP

VMAT-NCP plans were the same VMAT coplanar plans about the collimator, gantry rotation. VMAT-NCP plan consisted of from 2 to 3 half arcs. In there, one arc was CW at 5° couch angle and one arc was CCW at 355° couch angle [11].

2.5. Dosimetric analysis

The dose comparative analysis was performed using the 20 patient's plans. Dosimetric parameters were evaluated for target volumes and OARs. The maximum dose and mean dose on OARs ensured according to RTOG 1112 [1].

The dose distribution on the target volume: All plans are normalized to 100% prescription dose covers minimum 95% target volume. The Cumulative DVH of all plans were used to compare between 3D-CRT, IMRT, and VMAT CP and NCP according to the criteria of dose distribution on PTV.

OARs: The maximum dose (Dmax) in OARs (The spinal cord + 5mm, esophagus, stomach, duodenum, heart, small bowel, large bowel, skin, great vessels, skin, chest wall, and gallbladder) according to the guideline RTOG 1112 [1], given in Table 2.

Conformity Index (CI): The conformity index, in its various manifestations over the years, represents an attempt to measure objectively how well the distribution of radiation follows the shape of the I target. It was coverage dose of the target volume.

According to RTOG (1993) [12]: $CI_{RTOG} = \frac{PIV}{TV}$

PIV: Prescription isodose volume.

TV: Target volume.

The value of CI was in the range of 1.0 - 2.0 meaning the conformal dose level of target volume is good, if the CI value in the range of 0.9 - 1.0 or 2.0 - 3.5 is acceptable, CI value less than 0.9 or over 3.5 are not acceptable. The best of the CI value was 0.9 - 1.2 [1].

CI index was still in use at many Gamma Knife centers, but the new index proposed by Paddick [13] was used by an increasing number of centers because it does not produce false perfect scores. It's called CI Paddick index, Paddick et al published in the journal of Neurosurgery no 105 in 2006, the intersection of the TV_{PIV} and TV, allowed the assessment of the target's dose at the prescription dose. This is described as [13]:

$$CI_{Paddick} = \frac{(TV_{PIV})^2}{TV \times PIV} = \frac{TV_{PIV}}{TV} \times \frac{TV_{PIV}}{PIV}$$

where TV_{PIV} : Volume of the target covered by the prescription isodose.

Ideal value CI=1 when $\frac{TV_{PIV}}{TV} = \frac{TV_{PIV}}{PIV}$=1, mean that target volume has completely covered by the prescription dose.

Homogeneity Index (HI): Indicates the ratio between the maximum and minimum dose in the target volume and the lower value indicates a more homogenous dose distribution within this volume. In 1993, the Radiation Therapy Oncology Group (RTOG) proposed guidelines for routine evaluation of Stereotactic Radiation Therapy (SRT) plans based on several parameters and HI was described as:

$HI_{RTOG} = \frac{D_{max}}{DP}$ [12].

where D_{max}: The maximum dose.

DP: The prescription dose.

The lower (closer to one) the HI index, the better is the dose homogeneity.

Gradient Index (GI): Be defined as the ratio of the volume of half the prescription isodose to the volume of the prescription isodose. For a plan normalized to the 50% isodose line, it was the ratio of the 25% isodose volume to that of the 50% isodose volume. The GI will differentiate between plans of similar conformity, but with different dose gradients of the target volume.

Paddick (2006) [13] define as: $GI = \frac{PIV_{half}}{PIV}$

Where: PIV_{half}: The 50% isodose volume

PIV: The prescription isodose volume.

The value of GI was greater than unity. A value that was closer to unity represents a faster dose fall-off in normal tissue in the treatment plan, which may imply a lower dose to critical structures.

Monitor unit (MU)

At distances beyond a few cm from the field edge, the peripheral dose was dominated by accelerator head leakage, therefore proportional to total MU. Monitor units in each plan were compared as a risk index for potential radiation-induced secondary malignancies. The accelerators were calibrated to deliver 1cGy/MU to muscle at a depth

of maximum dose for a 10 × 10cm^2 field size and the source-to-surface distance is 100cm.

3. Result and discussion

The study patients were 19 male and 1 female with average 57 years old (range, 41 - 71 years old). The target volume of PTV for 20 patients were 126.87cm^3 (range 47 - 395.6cm^3). Study results are summarized in Table 2. All statistical tests were two-sided, with a threshold for statistical significance of p<0.05. Statistical analysis was undertaken using t-test.

All plans were shown good control in OARs according to RTOG 1112. However, there was a significant difference between the VMAT, IMRT and 3D-CRT plan in dose distribution and coverage dose at CI, CI Paddick, GI, and MU.

Table 2. Dosimetric comparison of 3D-CRT, IMRT, VMAT coplanar and VMAT non-coplanar

	3DCRT	IMRT	VMAT	VMAT/NON	p-value 3DCRT/ IMRT	p-value 3DCRT/VMAT
PTV						
CI	1.18 (1.07 - 1.34)	0.97 (0.86 - 1.12)	0.99 (0.87 - 1.11)	0.99 (0.88 - 1.15)	<0.01	<0.01
CI Paddick	0.74 (0.53 - 0.84)	0.90 (0.53 - 0.94)	0.90 (0.74 - 0.94)	0.90 (0.73 - 0.94)	<0.01	<0.05
GI	4.11 (2.7 - 5.25)	3.39 (2.39 - 5.06)	3.59 (2.34 - 5.33)	3.49 (2.44 - 5.24)	<0.01	<0.05
MU	1592.53 (945.6 - 3584.8)	3242.65 (1215 - 6389.7)	2755.89 (1150 - 6297)	2697.29 (1395 - 5421)	<0.01	<0.01
OAR						
Spinal cord + 5mm (cGy)	959.03 (292 - 1820.5)	1194.55 (489 - 1978)	1024.63 (445 - 1921.4)	1027.13 (488.2 - 1987.9)	0.08	0.59
Esophagus (cGy)	1382.69 (355 - 3759)	1491.91 (492.6 - 3060.8)	1430.16 (388.2 - 3275)	1436.32 (345.7 - 3281)	0.70	0.87
Stomach (cGy)	1952.68 (553 - 4160.4)	1664.56 (615.6 - 3305)	1579.5 (478 - 3123)	1601.17 (459.5 - 3139)	0.39	0.27
Duodenum (cGy)	2111.66 (41 - 4591)	1888.05 (45 - 3342)	1839.75 (45 - 3935)	1898.25 (45 - 3368)	0.65	0.59
Small Bower (cGy)	715.62 (6.5 - 2305)	704.08 (6.9 - 2786)	654.76 (8.4 - 2162)	648.12 (8.4 - 2178)	0.96	0.79
Large Bower (cGy)	1399.22 (10 - 5338)	1398.66 (10.7 - 3627)	1382.45 (12.4 - 4580)	1348.39 (12.5 - 3708)	0.99	0.97
Liver -GTV (cGy)	38.5 (18 - 58)	39.6 (22.3 - 66)	39 (22.8 - 57)	38.4 (22.6-56)	0.76	0.89
Heart (cGy)	1142.35 (31 - 4624.8)	1004.81 (33.5 - 3765.4)	938.94 (32.6 - 3798.5)	950.73 (33 - 3739)	0.75	0.64
Great Vessels (cGy)	1368.13 (426 - 3641)	1521.75 (631.8 - 3944)	1423.0 (426.5 - 3715)	1453.78 (452 - 3725)	0.52	0.82
Skin (cGy)	1872.05 (1075.8 - 3151)	1715.43 (925.6-3418)	1671.14 (822.8 - 3243)	1645.44 (885 - 3219)	0.52	0.40
Chest wall (cGy)	2988.53 (1420.8 - 5586)	2842.04 (1358.6 - 5606)	2719.41 (1298-5485)	2681.96 (1226.3 - 5272)	0.74	0.53
Gall bladder	2356.01	2255.99	2188.8	2211.0	0.85	0.85

(cGy)	(31.1 - 6335)	(31.6 - 4533)	(34.5 - 4615)	(34.9 - 4603)		

Figure 3 summarized CI. Both conformal and modulated techniques covered target volumes was good with CI value within the best range (0.9 - 1.2). IMRT and VMAT were similar about CI. However, VMAT CP and NCP were closer with ideal value than 3D-CRT. The 3D-CRT technique had CI value over, mean that liver normal volume had high dose was more. There was a statistically significant improvement in coverage target volume when using modulated techniques compared with 3D-CRT ($p<0.01$).

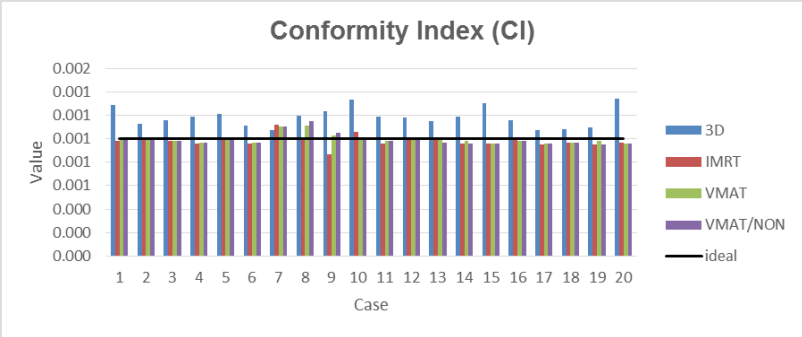

Figure 3. The comparison of the CI between three techniques

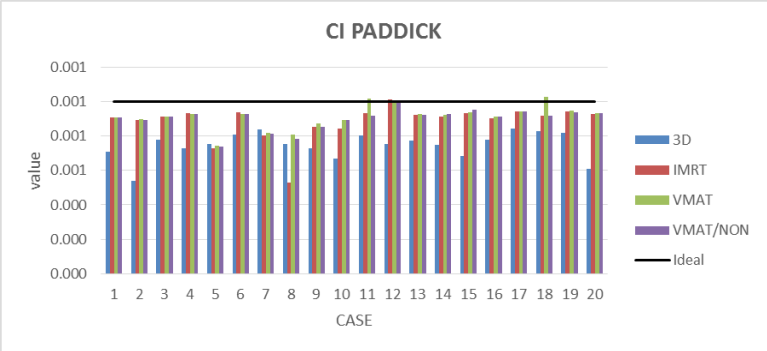

Figure 4. The comparison of the CI Paddick between three techniques

In our study, the CI Paddick of the plans made by VMAT techniques was the best, closest with ideal value = 1 (Figure 4). The CI Paddick of the plans made by 3D-CRT was less value. It demonstrated the 100% of the prescription dose was outside the target volume and the liver normal volume received high dose were significantly.

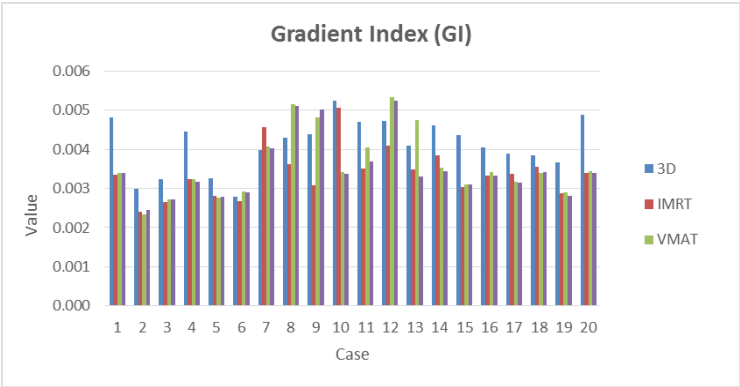

Figure 5. The comparison of the GI between three techniques: 3D-CRT, IMRT, VMAT CP and NCP

The GI also showed a significant difference between techniques. The IMRT and VMAT were similar in all plans and improved significantly compared with 3D-CRT ($p<0.05$). 3D-CRT reduced the dose to the OARs slower and the liver normal volume received a higher dose.

The average total MUs were 2755.89 (range, 1150 - 6297) for VMAT plans, 3242.65 (range 1215 - 6389.7) for the IMRT plans and 1592.5 (range 945.6 - 3584.8) for the 3D-CRT plans (Figure 6). The MUs for the 3D-CRT plans were significantly lower by an average of 2 times when compared against the modulated plans ($p<0.001$). In modulated plans, VMAT NCP had lower MU. With the more MU, the more time machine operates. In fact, the timing study demonstrated that the VMAT technique was also significantly faster than the 3D-CRT technique (9.2 minutes vs. 13 minutes).

We also compared the 50% of the prescription dose and significant difference in dose distribution (Figure 6).

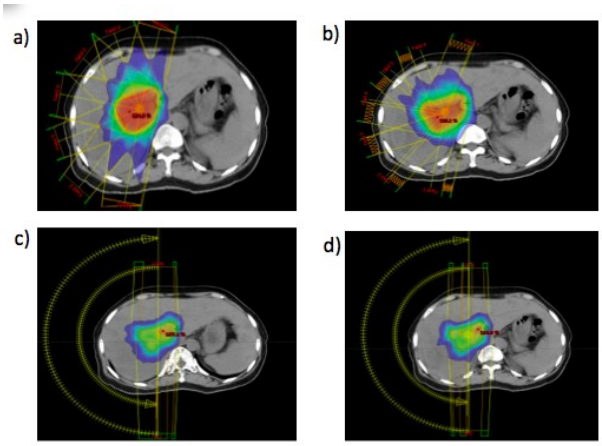

Figure 6. The dose distribution at 50% of the prescription dose between techniques for the example case. a) 3D-CRT b) IMRT c) VMAT CP d) VMAT NCP

4. Conclusion

VMAT and IMRT improved conformity compared to 3D-CRT. The VMAT NCP technique appeared to have the lowest dose to liver effective and other normal tissues. The main advantage of VMAT over 3D-CRT were significantly faster treatment delivery time. Shortened treatment times were anticipated to improve the tolerability of this treatment and reduce the chance of error due to intra-fraction motion. However, an additional problem with the VMAT NCP technique, with multiple arcs and couch rotations required time-consuming collision checks prior to commencement of treatment.

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