CyberKnife and EDGE in stereotactic body radiotherapy for pancreas cancer: a comparison of plan quality

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Abstract

Purpose: To perform a comprehensive comparison of the different stereotactic body radiotherapy (SBRT) plans between the Varian EDGE and CyberKnife (CK) systems for pancreas cancer.

Materials and methods: Fifteen patients with pancreas cancer were selected in this study. The median planning target volume (PTV) was 28.688cm 3 (5.736 to 49.246 cm 3). The SBRT plans for the EDGE and CK were generated in the Eclipse and Multiplan systems respectively with the same contouring and dose constrains for PTV and organ at risk (OAR). Dose distributions in PTV were evaluated in terms of coverage, conformity index (CI), new conformity index (nCI), homogeneity index (HI), and gradient index (GI). OARs, including spinal cord, bowel, stomach, duodenum and kidneys were statistically evaluated by different dose-volume metrics and equivalent uniform dose (EUD) . The volume covered by the different isodose lines (ISDL) ranging from 10% to 100% for normal tissue were also analyzed.

Results: All SBRT plans for EDGE and CK met the clinical requirement for PTV and OARs. . For the PTV, the dosimetric metrics in EDGE plans were lower than that in CK, except that D 99 and GI were slightly higher. The EDGE plans with lower CI , nCI and HI were superior to offer the better conformity and homogeneity for PTV. For the normal tissue, the CK plans were better at OARs sparing. The radiobiological indices EUD of spinal cord, duodenum, stomach, and kidneys were lower for CK plans, except that liver were higher. The volumes of normal tissue covered by medium ISDLs (with range of 20%~70%) were lower for CK plans while that covered by high and low ISDLs were lower for EDGE plans.

Conclusions: This study indicated that both EDGE and CK generated equivalent plan quality, and both systems can be considered as beneficial techniques for SBRT of pancreas cancer. EDGE plans offered the better conformity and homogeneity of dose distributions for PTV, while the CK plans could minimize the exposure of OARs.

1. Introduction

Pancreatic cancer is the fourth leading cause of cancer-related mortality worldwide with a 5-year survival rate approximately20% [1, 2]. For localized disase, surgery with complete resection represents the only potential treatment option associated with any substantive chance of cure [3, 4]. However, due to non-specific early symptoms and aggressive behavior of pancreatic cancer, most patients were diagnosed at relatively late stages[5]. Most studies have demonstrated that chemotherapy combined with radiation therapy is more effective than single-modality therapy, despite continuous controversies about the role of radiation therapy exist due to conflicting clinical outcomes[6, 7, 8, 9]. Surrounded by many important and radiosensitive gastrointestinal organs, such as duodenum and stomach, the convetional radiotherapy for pancreatic cancer seems not to effectively spare these organs while delivering high dose to target [7].

The advantage of fractionated radiation therapy[10, 11] is mainly that normal tissue has the ability to repair its DNA after radiation while malignant tissue not due to the inherent genomic instability.

Compared with three dimensional conformal radiotherapy (3DCRT), intensity modulated radiotherapy (IMRT) can reduce the dose of normal organs surrounding tumor, and also minimize the toxicity of gastrointestinal organs[12]. Goto Y and Colbert L E [13, 14] had performed IMRT and 3DCRT for local pancreatic cancer, and compared dosimetry and clinical outcomes. They verified that IMRT offered better dose constrains for target and organs at risk (OAR) compared to 3DCRT. Brown and Coworkers [15] also demonstrated that with the technology of IMRT, the prescription dose could be increased to 64.8 Gy, while maintained dose limits of OARs including spinal cord, liver, kidneys, and small bowel.

Although the IMRT provided a probability of better tumor control for locally pancreatic cancer, the organ motion and patient set-up errors during the treatment may affect the radiation dose of organs due to the complex site of OAR surrounding tumor[16]. As a new technique born of the synthesis of all of the above-mentioned advances, stereotactic body radiotherapy (SBRT) is becoming more widespread, and it is probably known as a promising method of radiotherapy for pancreatic cancer with greater normal tissue sparing [17, 18, 19, 20]. With ahigher dose per fraction, the dose gradient of SBRT plans is steeper than other conventional radiation, and have the better dose constrains of normal structures [21]. Lin et al. demonstrated the SBRT have the advantage of improving the local control for pancreatic cancer compared to the IMRT [22]. Kumar et al. [23] similarly made a dosimetric analysis of the SBRT plans with duodenal sparing using volumetric-modulated arc therapy (VMAT) and IMRT in locally advanced pancreatic cancer.

SBRT plans usually applied non-coplanar field arrangement, especially for the CyberKnife (Accuray, Inc, Sunnyvale) system [24].With 6D robotic arm and accurate tracking techniques, the CyberKnife, a 6MV linear accelerator, has high precision for dose delivery with a large degree of freedom, and the capability of real-time tumor positioning and correction. Qing et al performed the SBRT plans for locally advanced unresectable pancreatic cancer with CyberKnife, and showed lower normal tissue toxicity [25].

As a culmination in the field of radiosurgery, EDGE (Varian Medical Systems, Palo Alto, CA) has advantages of safety, noninvasive, comfortable radiosurgery in the treatment of new experience. The general application of EDGE is the intracranial SRS technique, which can eliminate small lesions of intracranial accurately; Another application is the SBRT technique of real-time tracking and dynamic irradiation technology, focusing on body dynamic target area constantly [26]. This machine is equipped with flattening filter (FF) and flattening filter free (FFF) beams, and the high resolution multileaf collimators (MLC) of 120 leaves with 2.5 mm widths at the isocenter [27, 28, 29]. Thus it could deliver higher dose rates more effectively and accurately while improving the conformity of dose distribution to the target simultaneously [28].

Currently, there is no study directly comparing dose distributions of SBRT plans between the CyberKnife(CK) and EDGE systems. In our study, two series of SBRT plans were generated using CK and EDGE platforms, respectively. We evaluated the different dosimetric metrics for target and noumal tissue, as well as analyzing the radiobiological indices to reflect the response of radiation therapy.

2. Materials And Methods

2.1. Patients data

This study performed a retrospective analysis of patients with pancreas cancer who had undergone SBRT. 15 patients with locally advanced unresectable pancreatic cancer were included in this study. CT simulation was performed on a Brilliance^{TM} Big Bore 16-slice CT scanner (Philips, Amsterdam, the Netherlands) with a slice thickness of 1.5 mm. Clinical target volume (CTV) and critical structures were contoured jointly by oncologist and radiologist based on the fusion of CT and magnetic resonance (MR) images on the MultiPlan® system (Accuray Inc., Sunnyvale CA; version 4.02). Planning target volume (PTV) were defined by expanding the GTV with 2 or 3 mm margin in all directions. The size of PTV ranged from 5.736 to 49.246 cm^3 (median 28.688). The critical normal tissue include spinal cord, bowel, stomach, duodenum, left kidney, right kidney and spleen were outlined according the Radiation Therapy Oncology Group (RTOG) for pancreatic cancer [30].

2.2. SBRT planning

According to the different prescribed dose, fifteen patients were divided into three groups, and each group consisted of five patients. The prescription dose for the three groups were of 37.5Gy/5F, 35.0Gy/5F, 32.5Gy/5F, respectively. After importing all image data of 15 patients into two systems, CyberKnife (CK) and EDGE, different SBRT treatment plans were designed by the same medical physicists The dose constrains of targets and normal tissue were set to meet the criteria of the RTOG 0848 and the report of AAPM Task Group No. 101 (AAPM TG-101)[31,32, 33], as shown in Table1.

The CK plans were designed in the Multiple TPS (version 4.0.2). The 6MV FFF photon beam was applied and dose rate was set to 800MU/min with one or two cones with size of 10～30mm. Beside the dosimetric constraints listed in Table 1, five “shells” expanded isotropically from PTV were used to make steep dose fall-off gradient. At the end of the optimization, beams and time reduction were used to make the plan clinically practical. All CK plans were optimized using the sequential process with the ray tracing algorithm.

The plans for EDGE system were generated with the Varian Eclipse® system (Varian Medical Systems, Palo Alto, CA; version 13.5),. A VAMT plan for each case was generated using two 360° arcs with the same isocentre at the geometric centre of PTV. The 10MV FFF photon beam was chosen with a high dose rate of 2400MU/min. All VMAT plans were optimized using the progressive resolution optimizer (PRO) and analytical anisotropic algorithm (AAA) with a grid size of 1.5 mm were applied in dose calculation. In order to make the plan comparisons valid, both CK and EDGE plans were nornalized to ensure ≥95% of PTV covered by prescription dose.

2.3. Evaluation metrics of PTV

As were listed in Table 1 and 2, the coverage and mean dose (D_{mean}) of PTV, as well as doses covered 99%, 95%, 5% and 1% of PTV (D_{99}, D_{95}, D_5, D_1) of PTV were categorized for plan evaluation. Meanwhile, the conformity index (*CI*), new conformity index (*nCI*), homogeneity index (HI), and gradient index (GI) were also used to quatify the plan quality. *CI* and *nCI* quatifying the target coverage and healthy tissue sparing were defined as follow [34]:

$$CI = \frac{V^{R_x}}{V_{PTV}^{R_x}} \quad (1)$$

$$nCI = \left(\frac{V^{R_x}}{V_{PTV}^{R_x}}\right) / \left(\frac{V_{PTV}^{R_x}}{V_{PTV}}\right) \quad (2)$$

where the V^{R_x} is the volume covered by prescription isodose line (PIDL), V_{PTV} is the target volume, and the $V_{PTV}^{R_x}$ is the volume of target covered by PIDL. Usually, *CI* and *nCI* values are greater than 1.0. Smaller *CI* and *nCI* imply a more conformal plan and the ideal values for both indices are 1.0.

The homogeneity index which mainly used to evaluate the degree of the dose uniformity inside the target volume [35] was defined as equation(3):

$$HI = \frac{D_2 - D_{98}}{D_P} \quad (3)$$

where the D_x is the dose that covers *x* percent volume of PTV, and the D_P is the prescription dose of target. Usually, *HI* >0, and *HI* = 0 means each voxel of target volume receives the same dose.

At the same time, in order to assess the degree of dose fall-off outsied the target volume , the gradient index has been applied, which is calculated according to the following equation[36]:

$$GI = \frac{V_{50\%}}{V_{100\%}} \quad (4)$$

where the $V_{x\%}$ is the absolute volumes covered by x% of PIDL. For SBRT plan, smaller value of *GI* means steeper dose fall-off and better normal tissue sparing.

2.4. Evaluation metrics of OARs

The maximum dose (D_{max}) and mean dose (D_{mean}) of all the contoured OARs were accessed. Moreover, organ specialized DVH metrics, for instance $D_{0.25cc}$ and $D_{1.2cc}$ of spinal cord, were also evaluated according to AAPM TG-101. The details of OAR evaluation metrics were listed in Table 2. At the saome time, equivalent uniform dose (EUD) was applied to convert the heterogeneous dose distributions into homogeneous dose. Based on the phenomenological model introduced by Niemierko, the EUD is defined as follows[37]:

$$EUD = \left(\sum_{i=1} v_i EQD_i^a \right)^{1/a} \quad (5)$$

where v_i is the percentage of voxels receiving dose D_i. The v_i and D_i values are acquired from the DVHs and the sum of v_i over all voxels equals 1. And parameter '*a*' denotes the seriality property for different organs, and is usually set to a positive value for OARs. The EQD is calculated as follows, which is defined as biologically equivalent dose of 2Gy per fraction:

$$EQD = D \times \frac{\left(\frac{\alpha}{\beta} + \frac{D}{n} \right)}{\left(\frac{\alpha}{\beta} + 2 \right)} \quad (6)$$

Where *n* denotes the number of fractions, The α/β is a parameter from the issue-specific Linear Quadratic (LQ) model of the certain organ, determining the fractionation sensitivity. The values of parameters *a* and α/β were listed in Table 4 according to reference[38].

2.5 Volumes covered by different ISDL

To analyze the details of dose distribution outside PTV, the absolute volumes of normal tissue that covered by *x* percent of prescription isodose lines (V_x) ranging from 100% to 10% with intervals of 10% were compared between CK and EDGE plans. Ratios between volumes of normal tissue (V_x) and PTV (V_{PTV}) were also calculated to minimize the effect resulted from different PTV volumes. Meanwhile, effective distance ΔR_{Eff} was applied to quatify the dose fall-off details of different ISDL, which is defined as follow:

$$\Delta R_{Eff} = R_{iso}^x - R_{PTV} \quad (7)$$

Where R_{iso}^x and R_{PTV} were the equivalent radius of spheres with volumes of V_x and V_{PTV}, which were calculated based on sphere volume formula $V=4\pi R^3/3$.

2.6. Statistical analysis

For those 15 patients with two different SBRT plans in EDGE and CK systems, a paired t-test statistical analysis were performed using the IBM SPSS statistical software version 21(SPSS Inc.,Armonk, NY) to determine the difference, and if P value <0.05, it was consider to have the statistical significance. All datas were listed in terms of mean value±standard deviation (SD).

3. Results

In total, a retrospective analysis of 15 patients with pancreas cancer was performed. The treatment plans of SBRT were designed in CK and EDGE systems, respectively. Plans generated in both platforms could

meet the clinical criteria of PTV coverage and OAR sparing. The median volume of tumor was 28.688cm^3(5.736 to 49.246 cm^3). All of CK and EDGE plans were normalized to ensure at least 95% of PTV covered by prescription dose.

3.1 Evaluation of PTV

The comparison of isodose lines from 30% to 100% of the prescription dose for a selected case was illustrated in Figure 1. It reveals that both plans have excellent conformity and adequate coverage for PTV. Besides, we can find that the 100% PIDL (with red color) of EDGE plan is closer to PTV boundary than that of CK plan.

The average DVHs of PTV for CK and EDGD plans are shown in Figure 2. From integral DVHs displayed in the upper row of Figure 2, we have found that PTV coverage of EDGE plans are a little higher than that of CK in all the three groups. Further, we have investigated the details of PTV DVHs in the way of differential as were displayed in the lower row of Figure 2, from which we may conclude that the voxel dose of EDGE plans are more closed to prescription dose than the one of CK. It is also indicated that both of the cold and hot point volumes of CK plans larger than those of EDGE plans. This means that EDGE plans are more conformal and homogeneous.

The dosimetric metrics of PTV including V_{100}, D_{mean}, D_{99}, D_{95}, D_5 and D_1 are displayed in Figure 3 and Table 2. To ensure cases with different prescription doses are comparible, all of the dose-volume metrics are expressed with percentage values. It is indicated that PTV coverage (V_{100}) is slightly higher for CK, which may results from different normalization methods. Dosimetric metrics including D_{mean}, D_{99}, D_{95}, D_5 and D_1 are smaller for EDGE except that D_{99} is a little higher compared with those of CK plans. This is consistent with Figure 2. Other evaluation indexes such as CI, nCI, HI and GI are displayed in Figure 4(a)~(d), and the statistical data is detailed in Table 2..The CI and nCI of PTV for EDGE plans are 0.986±0.019,1.037±0.020, respectively, which are smaller than those of CK plans with 1.184±0.076 and 1.222±0.072(as shown in Table 2). And HI of both plans are also compared, from which the values of 0.296±0.077 and 0.416±0.033 are obtained for EDGE and CK, respectively. It can be concluded that EDGE plans are superior in terms of conformity and homogeneity. However, GI for CK plans are more lower than EDGE, which implies the steeper dose fall-off gradient.

3.2 Evaluation of OARs

The average DVHs of organs at risk including spinal cord, bowel, stomach, duodenum, Liner, left kidney, right kidney and spleen are displayed in Figure 5(a)~(h). And Table 3 shows the results of dose-volume parameters of normal tissue. All criteria of the dose constrain for normal tissue were achieved in both systems. Compared with CK plans, the dosimetric metrics of spinal cord including D_{max}, $D_{0.25cc}$, $D_{1.2cc}$ were slightly higher for EDGE plans with significant statistical differences, which indicates the decreased sparing of spinal cord with EDGE. From Table 3, the D_{5cc} of bowel and the mean dose of bowel, stomach,

liver, and kidneys are slightly lower for EDGE plans with statistic difference ($p<0.001$), but other dose-volume metrics shows no difference.

In order to further compare the dosimetric parameters of organ at risk for EDGE and CK, we calculated the radiobiological parameter EUD by the equation(5)~(6) according the DVHs of spinal cord, bowel, stomach, duodenum, Liner, left kidney, right kidney and spleen, and the results are showed in Table 4. From the data of Table 4, the EUD values of spinal cord, duodenum, stomach, left and right kidneys are lower for CK plans, expect the liver having higher EUD value. And there are significantly statistic difference. But for bowel and spleen, both of two series plans have the similar value of dose-volume and no statistic difference.

3.3. Dosimetric comparison with different ISDL

The average volume of normal tissue covered by different prescription isodose lines are displayed in Figure 6. In the Figure 6(a) and (b), the EDGE plans have the less volumes of normal tissue for the lower and higher prescription isodose region than CK plans, which provide the superiority to control the hot spot of tumor. These results are also in consistent with the Figure 2 and 3. However, for the intermediate dose region with 20%~70% of prescription isodose, it is obvious that the volume of normal tissue received radiation dose for CK plans are less than EDGE plans, as accordance with the Figure 5 and Table 3. In the Figure 6(c), within the radius R of 0~1cm, the CK plans showed the steeper dose fall-off gradient, as same the shown in Figure 4. The average volumes, standard deviation(SD) and P values are listed in Table 5.

4. Discussion

In this study, we made a comprehensive plan quality comparison in terms of various dosimetric metrics for pancreatic cancer SBRT between Varian CyberKnife and EDGE systems. Both of the two techniques had the capability of producing clinically acceptable plans with adequate PTV coverage and OAR sparing. These results showed that EDGE plans offered the better conformity and homogeneity for PTV, while CK plans had slightly better dose coverage of PTV and the steeper dose fall-off gradient. For OARs, except D_{5cc} of bowel and the mean dose of bowel, stomach, liver, and kidneys are slightly lower for EDGE plans, the rest dose-volume metrics, as well as EUD were all lower for CK plans. When investigating the details of dose distribution outside PTV, it was obtained that the volumes covered by intermediate ISDL (ranging from 20–70%) were much lower for CK plans, while the EDGE plans indicated superior sparing for lower and higher dose region.

Our data indicated that the EDGD plans had the better conformity and homogeneity compared to the CK plans. This may be related to the field arrangement and delivery technuques for different platforms. On the one hand, hundreds of non-coplaner field were used for CK plans while only two coplaner 360° arcs were applied for EDGD plans. This results in that the entire dose being deposited within the plane of the arcs for EDGE plans, while the radiation dose was concentrated in the center of the target area with much

bigger degree of freedom for beam directions. At the same time, the hot spot in CK may be a litter larger than that of EDGE. On the other hand, the collimators of the two systems are also very different. CK plans only adopted 1 ~ 2 circular cones for beam shaping, but for EDGE system is equiped with high definition HD120 MLCs with spatial resolution of 2.5mm[26], which may made the better conformity and homogeneity of PTV for EDGE simultaneously, as shown in Fig. 1 ~ 3.

For the two series of plans, the CK plans used the 6MV FFF beams, while the EDGE chose the 10MV FFF beams. When removing the flattening filter, it can offer increasing dose rate and make the beam profile more forward at the central axis. At the same time, there are other advantages for FFF beams, such as reduction of the scattered radiation and treatment head leakage [28]. With the 10MV FFF modes, it could result in the relatively lower radiation dose exposure for OARs, as well as for the integrated body. However, in this study, the EDGD plans did not show any superiority for OAR sparing. Our previous study regarding to localized prostate cancer showed that EDGE plans not only provided better conformity and homogeneity for PTV, but also steeper dose fall-off gradient and superior OAR sparing. The inconsistent results may partly due to the different shapes of PTV that affect the dose distributions. The shape of pancreatic cancer had a relatively regular shape, approximately ellipsoidal, so that both of the two series of plans were made to meet the dose constrains of PTV easily. In the Multiplan system, five ‘shells’ were applied to limit the dose outside PTV, which may lead to better normal tissue sparing.

The delivery efficiency of beam is one of the most significant differences between the CK and EDGE systems. The average treatment time of per fraction was 2 ~ 3 minutes approximately for the EDGE, and 40 ~ 50 minutes approximately for the CK according to our clinical experience. On the one hand, the reduction of average delivery time can alleviate the discomfort of patients during radiotherapy. On the other hand, the effects of intra-fractional organs motion would be reduced by decreasing the treatment time for EDGE [39–41].

Our results did show that a dose escalation of SBRT for pancreas cancer in EDGE and CK systems both could reach the clinical criteria. But there are still some lmitations for this study. This study is a retrospective analysis and the SBRT plans for EDGE were not applicated in clinical practice. Further studies were warranted to assess the clinical utility and radiobiological responses. Another limitations is that there is no consistent results for PTV margins and the organs motion [42, 43]. Whether patient specialized PTV margins could be obtain for different platforms, and how much the margins would affect the dose distribution for surrounding normal tissue will be the next tissue for our further study.

5. Conclusion

A comparative quantitative assessment of the dosimetric and radiobiological indices of SBRT plans for 15 patients with pancreas cancer between CK and EDGE systems.We confirm that radiotherapy systems with different characteristics should be investigated and utilized to help radiation oncologists choose a proper SBRT method for each individual patient to get better therapeutic effects. Although the CK system

indicate better OAR sparing, the EDGE system can be regarded as an alternative option for SBRT of pancreas cancer, especially for patients who cannot remain lying in bed for a long time.

Declarations

Ethics approval and consent to participate

The study was approved by the institutional review board of our hospital.

Consent for publication

The consents for publication of data have been obtained from patients.

Availability of data and materials

Not applicable.

Competing interests

The authors state that they have no competing interests.

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Tables

Table1. Dose constrains of target and normal tissue for SBRT plans

Structure	Metrics	Objective
PTV	V_{100}(%)	≥95%
	PIDL	~70%
Spinal Cord	D_{max}(Gy)	<27Gy
	$D_{0.25cc}$(Gy)	<22.5Gy
	$D_{1.2cc}$(Gy)	13.5Gy
Duodenum	D_{max}(Gy)	32Gy
	D_{5cc}(Gy)	<18Gy
	D_{10cc}(Gy)	<12Gy
Bowel	D_{max}(Gy)	<35Gy
	D_{5cc}(Gy)	<19.5Gy
Stomach	D_{max}(Gy)	<32Gy
	D_{10cc}(Gy)	<18Gy
Liver	$V_{<17.5Gy(cc)}$	>700cc
Left kidney	D_{mean}(Gy)	<12Gy
	$V_{>23Gy}$(%)	<66.7%
Right kidney	D_{mean}(Gy)	<12Gy
	$V_{>23Gy}$(%)	<66.7%
Spleen	No constraint	

V_{xx}, the percentage of PTV or OAR volume recieving xx% prescription dose; PIDL, Prescribed isodose line; $V_{xx\ Gy}$, volume of PTV or OAR recieving at least *xx* Gy; $D_{xx\ cc}$, dose of PTV or OAR covers *xx* cc volume.

Table 2. The dosimetric indexes comparison of PTV between Cyberknife and EDGE plans.

Metrics	CK±SD	Edge±SD	p
V_{100}(%)	96.8±10.84	95.04±0.03	0.000
D_{mean}(%)	123.91±1.97	112.32±3.39	0.000
D_{99}(%)	93.28±2.53	97.13±0.64	0.000
D_{95}(%)	102.92±1.40	100.02±0.01	0.000
D_5(%)	137.83±2.30	125.40±7.13	0.000
D_1(%)	139.42±2.04	129.27±7.42	0.000
CI	1.184±0.076	0.986±0.019	0.000
nCI	1.222±0.072	1.037±0.020	0.000
HI	0.416±0.033	0.296±0.077	0.000
GI	3.070±0.222	4.145±0.312	0.000

Table 3. The dosimetric metrics comparison of OARs between Cyberknife and EDGE plans.

Structure	Metrics	CK±SD	Edge±SD	p
Spinal Cord	D_{max}	5.69±1.62	9.22±2.04	0.000
	D_{mean}	1.97±0.53	1.45±0.46	0.000
	$D_{0.25cc}$	5.12±1.49	8.39±1.79	0.000
	$D_{1.2cc}$	4.62±1.30	7.60±1.62	0.000
Duodenum	D_{max}	16.22±6.36	19.89±5.95	0.140
	D_{mean}	3.61±1.43	3.49±1.64	0.847
	D_{5cc}	8.34±3.71	11.15+5.59	0.143
	D_{10cc}	6.66±3.18	8.58±5.13	0.271
Bowel	D_{max}	19.98±5.25	20.56±2.80	0.516
	D_{mean}	2.81±0.75	1.63±0.59	0.000
	D_{5cc}	13.39±0.91	15.26±2.77	0.001
Stomach	D_{max}	20.68±4.87	21.57±6.52	0.422
	D_{mean}	4.49±1.73	2.82±1.62	0.000
	D_{10cc}	11.82±2.96	11.07±4.32	0.347
Liver	D_{mean}	2.67±1.23	1.23±0.20	0.000
	$V_{<17.5Gy}$(cc)	1299.07±251.72	1299.07±252.67	0.306
Left kidney	D_{mean}	2.21±0.76	0.39±0.20	0.000
	$V_{>23Gy}$(%)	2.80±0.89	2.75±1.09	0.798
Right kidney	D_{mean}	1.79±0.49	0.48±0.67	0.000
	$V_{>23Gy}$(%)	2.30±0.62	2.47±1.15	0.337
Spleen	D_{max}	7.56±2.20	8.23±3.60	0.450
	D_{mean}	2.16±0.77	1.70±1.19	0.027

Table 4. Comparison of the EUD for OARs between CK and EDGE plans.

Structure	α/β	*n*	EUD		
			CK±SD	Edge±SD	p
Spinal Cord	3	0.05	3.47±1.27	6.37±1.79	0.000
Duodenum	4	0.15	7.73±2.29	9.12±1.98	0.001
Bowel	4	0.15	10.34±3.30	10.54±3.75	0.722
Stomach	4	0.15	8.47±3.59	12.41±6.08	0.005
Liver	3	0.32	3.64±1.62	2.86±1.62	0.000
Left kidney	3	0.7	2.06±0.73	3.06±1.42	0.001
Right kidney	3	0.7	1.68±0.49	2.50±1.14	0.001
Spleen	3	0.5	1.67±0.58	2.17±1.72	0.159

EUD, equivalent uniform dose; SD, standard deviation.

Table 5. Volume comparison of normal tissue covered by different isodose lines.

Isodose	Volume(cc)			V_x/V_{PTV}			ΔR_{Eff}(cm)		
	CK±SD	Edge±SD	p	CK±SD	Edge±SD	p	CK±SD	Edge±SD	p
100%	5.81±3.06	0.83±0.45	0.000	0.23±0.06	0.04±0.02	0.000	0.13±0.04	0.02±0.01	0.000
90%	12.57±5.32	8.11±3.15	0.000	0.50±0.08	0.33±0.06	0.000	0.26±0.05	0.18±0.02	0.000
80%	21.09±8.33	17.83±6.62	0.006	0.84±0.10	0.72±0.11	0.004	0.40±0.06	0.35±0.04	0.004
70%	31.75±12.25	30.39±11.31	0.358	1.26±0.13	1.22±0.16	0.490	0.56±0.08	0.54±0.07	0.416
60%	46.06±17.62	49.55±18.49	0.112	1.82±0.17	1.98±0.24	0.057	0.74±0.11	0.78±0.10	0.067
50%	67.74±25.89	79.79±29.63	0.002	2.67±0.22	3.19±0.35	0.001	0.97±0.15	1.09±0.14	0.000
40%	106.21±40.78	135.81±51.41	0.000	4.16±0.30	5.40±0.53	0.000	1.31±0.20	1.53±0.21	0.000
30%	193.03±74.99	255.94±97.82	0.000	7.54±0.65	10.16±0.89	0.000	1.88±0.30	2.21±0.30	0.000
20%	553.84±264.31	590.73±212.06	0.237	21.21±4.91	23.58±2.03	0.098	3.26±0.67	3.42±0.44	0.098
10%	2158.22±921.62	1584.76±427.80	0.002	86.18±16.20	67.59±18.88	0.000	6.14±0.91	5.43±0.50	0.001

Figures

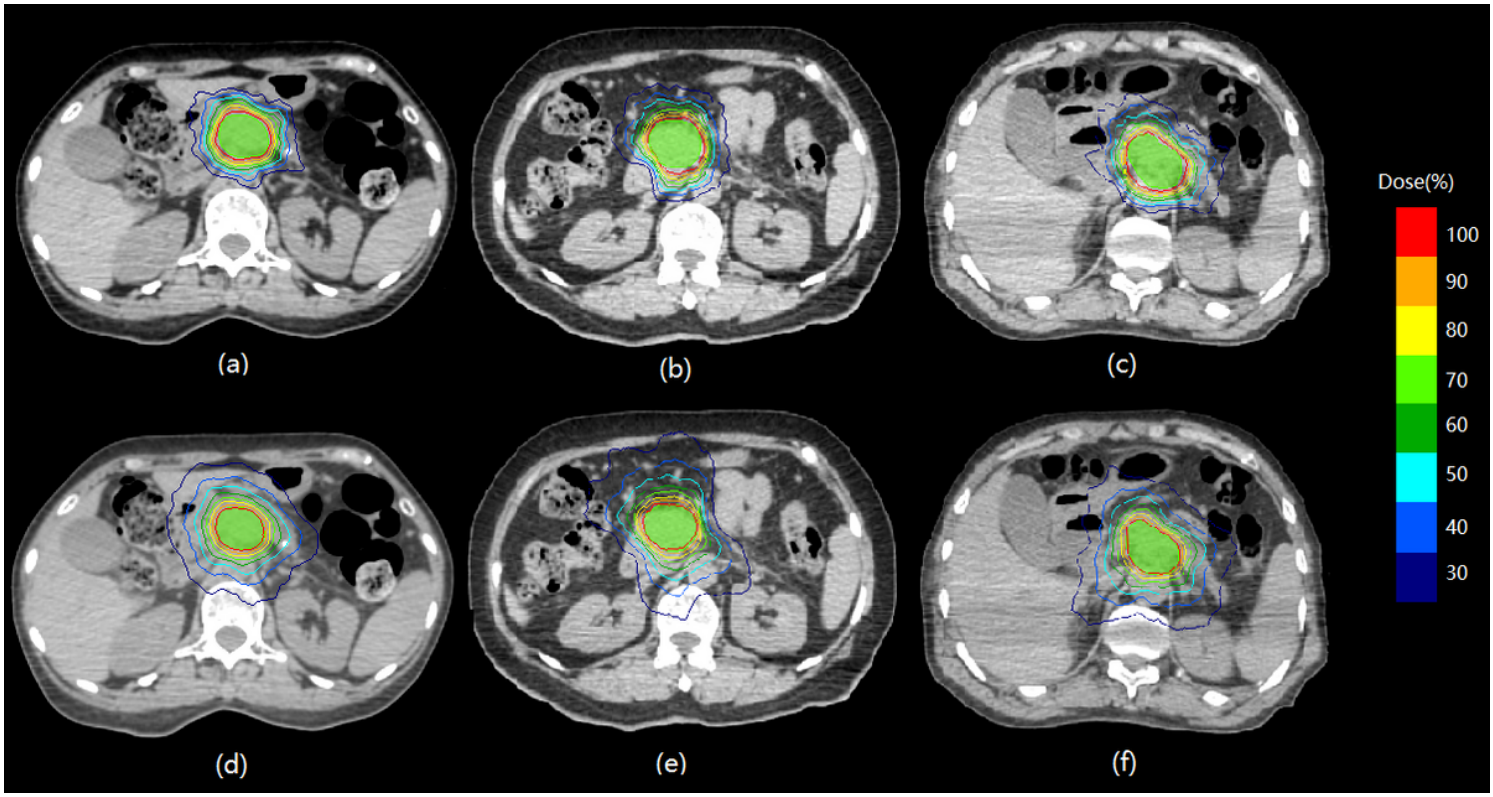

Figure 1

Comparison of planar dose distribution of one selected case. The upper row is for CK, and the lower row is for Edge.

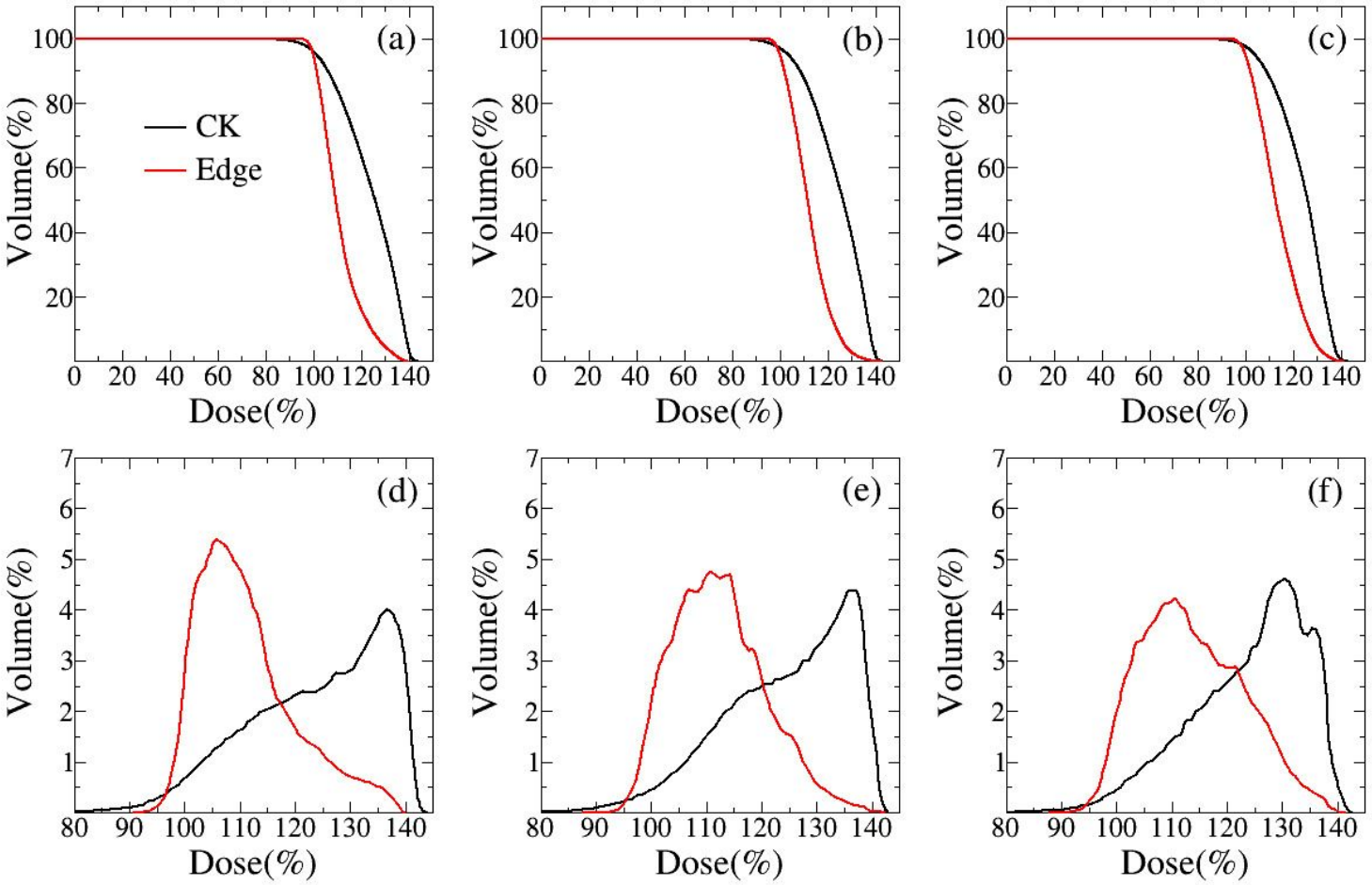

Figure 2

The average DVHs curves of PTV for plans with prescription dose of 37.5Gy/5F (left column), 35.0Gy/5F (middle column) and 32.5Gy/5F (right column). The upper and lower rows represent the integral and differential DVHs, respectively. The black line is for CK, and the red line is for EDGE.

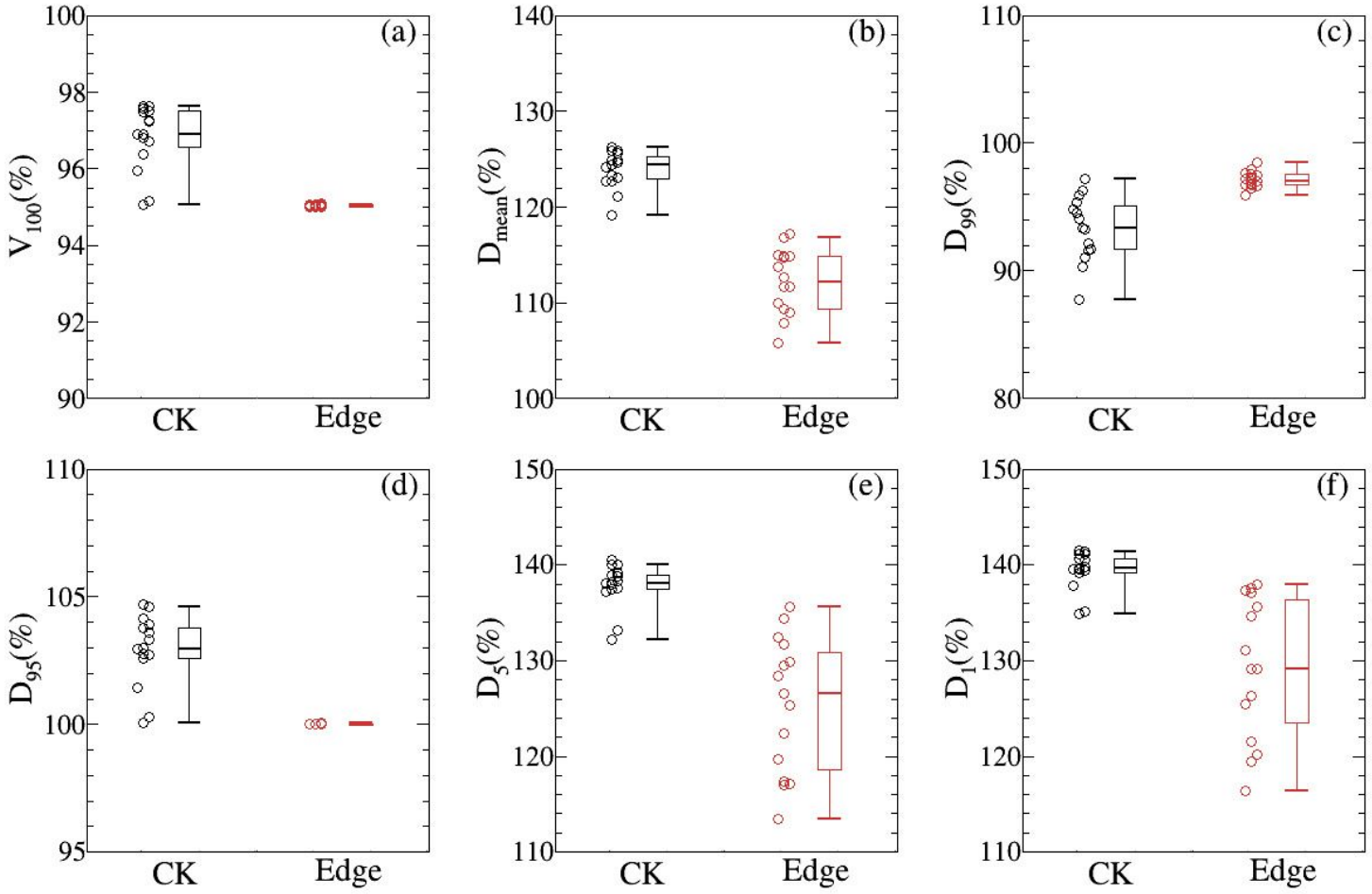

Figure 3

Comparison of different dosimetric metrics of PTV. (a) ~(f) is for V100, Dmean, D99, D95, D5 and D1, respectively. The black line is for CK, and the red line is for EDGE.

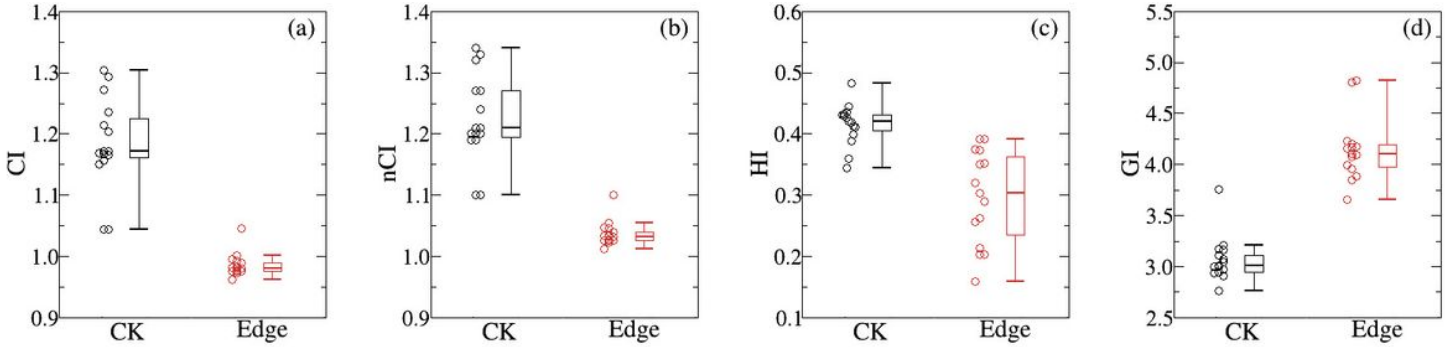

Figure 4

Comparison different evaluationindexes of PTV for EDGE and CK plans. (a) Conformal index (CI), (b) new conformal index (nCI), (c) homogeneity index (HI), (d) gradient index (GI). The black color is for CK, and the red color is for EDGE.

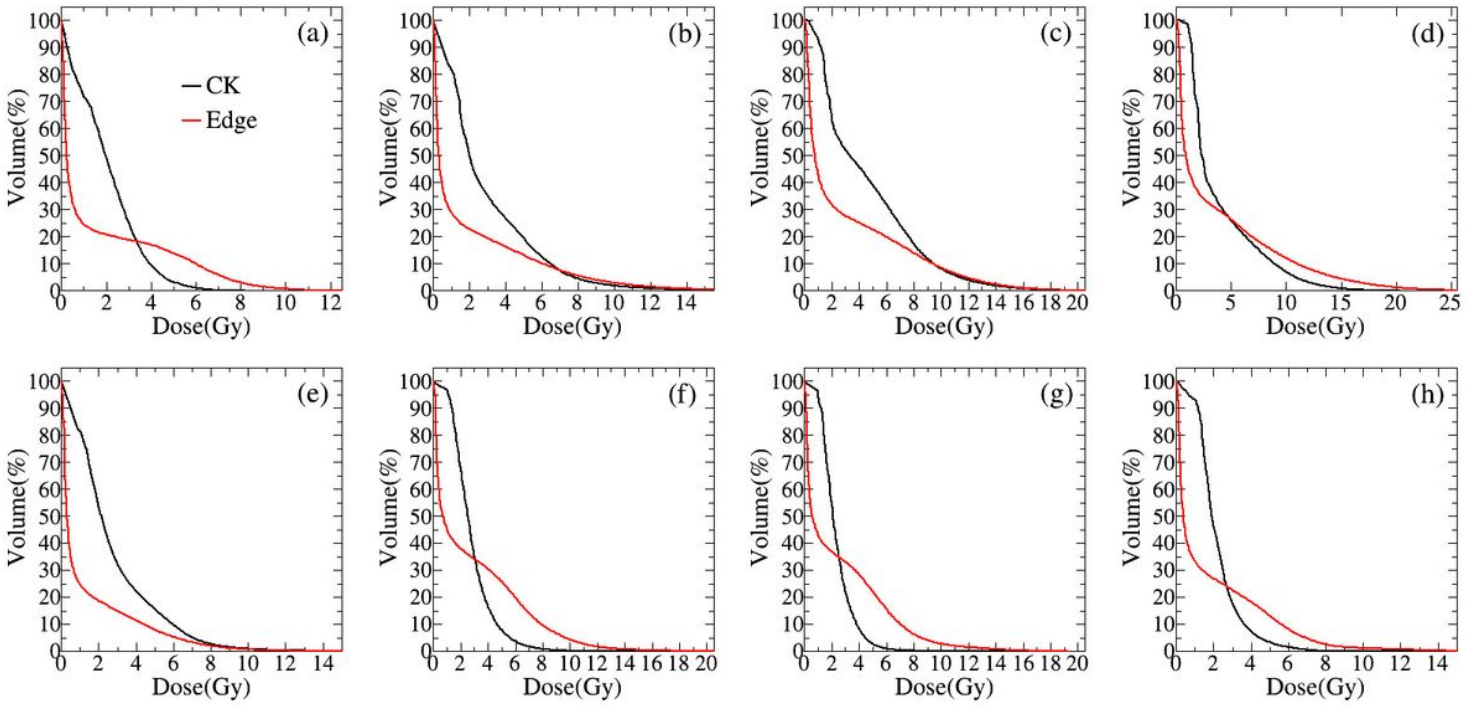

Figure 5

The average DVH curves of normal tissue adjacent to tumor: (a) spinal cord, (b) duodenum, (c) bowel, (d) stomach, (e) liver, (f) left kidney, (g) right kidney, and (h) spleen. The black line is for CK, and the red line is for EDGE.

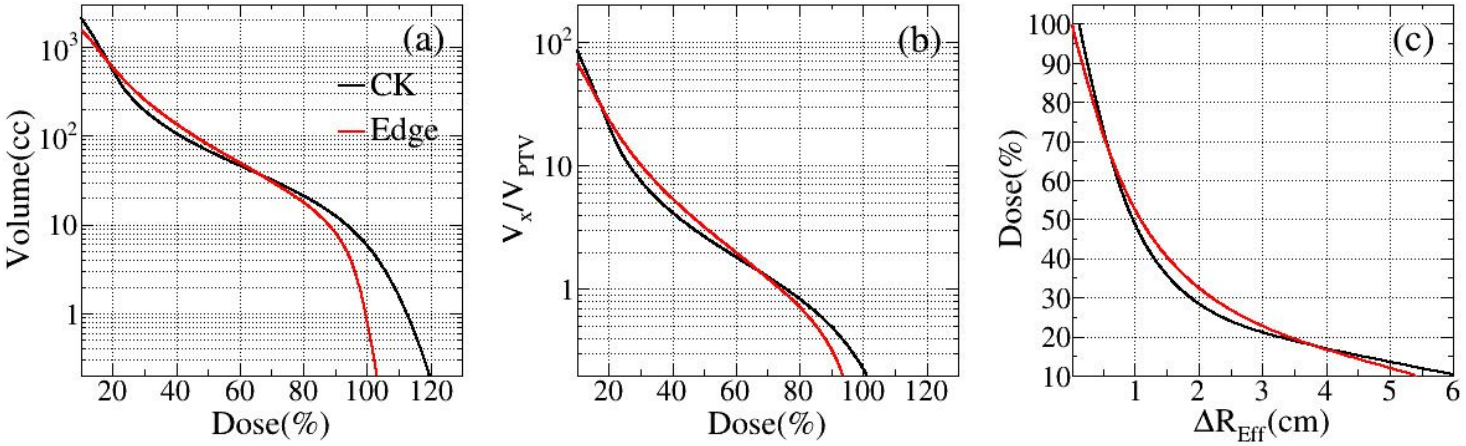

Figure 6

Comparison of normal tissue covered by different prescription isodose lines. (a) Absolute volumes (Vx), (b) the volume ratios (Vx/VPTV), (c) dose fall-off distancede (ΔREff) for different isodose lines. The black line is for CK, and the red line is for EDGE.