Adrenal Stereotactic Body Radiation Therapy: The Effects of a Full and Empty Stomach on Radiation Dose to Organs at Risk

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Abstract

Introduction

Adrenal recurrence after radical resection of the primary lesion is common. However, the adrenal glands are surrounded by radiosensitive organs such as the pancreas, kidneys, small intestine, and stomach. Treatment planning therefore requires many regulations due to the dose limit to the organ at risk. Radiotherapy can be adjusted for gastric capacity. We therefore performed an OAR analysis for SBRT to the left adrenal gland based on gastric state (empty or full stomach) at the time of irradiation. We examined whether it was possible to reduce the dose to OAR.

Materials and Methods

A sample of 20 randomly selected stomachs was arranged in descending order from largest to the smallest size and divided into two groups of 10. The “empty group” is defined as the smaller stomach group (n = 10), while the “full group” is the larger stomach group (n = 10). Planning target volume (PTV) adds a 3 mm margin to the GTV. The prescribed PTV dose was 54 Gy / 6 fx and D 95 coverage of PTV(CTV) (the dose to 95% of the PTV volume). We compared the difference in OAR radiation dose between the two stomach volume groups.

Results

Gastric OAR dose in the empty group was significantly lower than in the full group (D5 and D10). However, the OAR dose to the left kidney in the empty group was statistically significantly higher than in the full group (V12, V15, and V21).

Conclusion

When SBRT was performed on the left adrenal gland, it was found that the smaller the stomach size, the lower the radiation dose to the stomach. The stomach is an abdominal organ that can be artificially resized. It is therefore better to perform SBRT on patients who have an empty stomach.

Introduction

Evidence of the effectiveness of Stereotactic Body Radiation Therapy (SBRT) has recently been published [1–11]. It has also been reported that curative treatment for oligometastasis from primary tumor in the setting of local tumor control improves disease-free recurrence time and overall survival. The adrenal glands are often the site of a solitary metastasis, especially from lung cancer [3–11].

There is also a form of adrenal recurrence after radical resection of the primary lesion. There are reports that there is an advantage to use SBRT when there is an adrenal metastasis at the time of lung or breast cancer diagnosis, or when an adrenal metastasis appears after the completion of primary tumor treatment [3–11].

However, the adrenal glands are surrounded by radiation-sensitive organs, such as the pancreas, kidneys, small intestine, biliary system, and stomach. Treatment planning therefore requires many regulations due to the dose limit to the organ at risk (OAR). Radiation therapy can be adjusted for gastric capacity and cholecystic capacity (both include dietary restrictions). We therefore performed an OAR (Intestine, Pancreas, Liver, Right kidney and spinal cord) analysis for SBRT to the left adrenal gland based on gastric state (empty or full stomach) at the time of irradiation. We examined whether it was possible to reduce the dose to OAR.

Materials & Methods

A sample of 20 randomly selected stomachs were arranged in descending order from the largest to the smallest size and divided into two groups of 10. The random sample was drawn from patients who have been imaged from the diaphragm to the pelvis by with a diagnostic imaging CT scan (regardless of disease). Patients with gastric cancer, pancreatic cancer, a history of abdominal surgery, metastases to locations other than the adrenal glands, ascites, cirrhosis, and renal atrophy were excluded. The “empty group” was defined as the smaller stomach group (n = 10), while the “full group” was the larger stomach group (n = 10). All radiation plans were created with a 3D treatment planning system (Elekta’s XiO® treatment planning system and focal contouring system, Hamburg, Germany). An Elekta Synergy linear accelerator with 6 MV photon energy was used.

Adrenal ground and OAR were outlined by a 19 year experienced abdominal radiation oncologist. Eleven and sixteen year experienced medical physicists created the beam plans and the same radiation oncologist evaluated them. The radiation therapist performing the contouring and the medical physicist performing the treatment plan were blinded to patient information. Gross tumor volume (GTV) is the volume of the entire tumor, and clinical target volume (CTV) adds a 3 mm margin to the GTV. Since the adrenal glands are retroperitoneal organs and move less, Planning target volume (PTV) is in the same range as CTV. We set this because a large PTV causes the PTV to overlap with the pancreas and intestinal tract. The prescribed PTV dose was 54 Gy / 6 fx and D 95 coverage of PTV (the dose to 95% of the PTV volume). OAR dose limits are shown in Table 1. The capacity of the stomach was measured for its effects on OAR. Treatment regimens were analyzed with a dose volume histogram, and a one-way analysis of variance was performed. All data are presented as mean ± standard deviation. We defined $P < 0.05$ as statistically significant. All statistical analyses were performed using the Excel statistical software package (Excel-statistics 2015; Social Survey Research Information Co., Ltd., Tokyo, Japan). This study is a retrospective cohort comparison study. Informed consent was waived, and an opt out was available on the hospital homepage.

Results

The stomach size of the empty group was 226 ± 98 cm^3, and the size of the full group was 480 ± 91 cm^3. A sample image of SBRT is shown in Fig. 1. The relationship between stomach size and OAR dose was measured. The gastric OAR dose in the empty group was significantly lower than in the full group (D5 and

D10) (Table.2). However, the OAR dose to the left kidney in the empty group was statistically significantly higher than in the full group (V12, V15, and V21). All other organs (Intestine, Pancreas, Liver, Right kidney, and spinal cord) had equivocal OAR doses between the two groups.

Discussion

It is believed that a smaller stomach is better separated from the left adrenal gland, which is why it received a smaller radiation dose. The pancreas is between the left adrenal gland and the stomach. Both the pancreas and the adrenal glands are retroperitoneal organs, but the stomach is not. In addition, although the image was taken in the supine position this time, it is possible that the distance between the stomach and the left adrenal gland can be further increased by positioning the patient in the left lateral decubitus or prone position.

In contrast to the stomach, the kidney is in contact with the adrenal gland as a retroperitoneal organ, and it is difficult to control its movement. However, it was observed that the larger the stomach, the lower the dose to the left kidney. The reason for this could be that the stomach squeezes the pancreas and the kidneys dorsally, causing the kidneys to move caudally and have a reduced radiation exposure.

It was comprehended that it would be difficult to reliably measure the small intestine because it is in a different position every day. In fact, even with a cone beam CT the position of the small intestine changes every time. It is true that drinking water when treating the stomach may change the dilation of the duodenum, but this degree of dilation varies from day to day, so it is difficult to control the small intestine.

The dose to the pancreas was not affected by stomach morphology. This is considered to be due to the close proximity of the left adrenal gland and the pancreas. However, the size of the pancreas also varies greatly for each patient, and visceral fat may easily adhere to the area around the pancreas, which may also be reduced by gaining weight.

Clinical practice

An empty and full stomach had an opposite effect on OAR to the stomach and left kidney during adrenal irradiation. It is therefore necessary to choose whether to prepare for this by reducing the dose to the stomach or reducing the dose to the left kidney. Findings here also suggest that it is useful to obtain treatment planning CTs with an empty and full stomach, permitting the creation of two SBRT plans.

In terms of choosing between SBRT with an empty or full, it is appropriate to decide this based on renal function and gastrointestinal condition (gastritis, etc.). Adrenal tumors are more likely to be metastatic deposits than primary tumors. Chemotherapy is often used for metastases, so it would be desirable to reduce the radiation dose to the kidneys in such cases.

It is also necessary to consider the positional relationship of organs, especially given differences in visceral fat between patients. The distance between the organ and the adrenal gland was not taken into

consideration in this work, but it is expected that the more visceral fat, the greater the distance between the adrenal gland and the irradiated organ. If increasing the amount of visceral fat reduces the dose to OAR, temporarily gaining weight may be a solution to this issue.

Limitations

The following three issues can be considered for improvements in future works: 1) SBRT to the right adrenal gland. Unlike the left adrenal gland, the right adrenal gland has less OAR but might involve an increased radiation dose to the inferior vena cava and biliary/bile duct pancreatic duct. Verification of this is required; 2) Decrease the radiation dose to the target due to increased OAR restrictions as the dose increases. In general, the higher the dose, the higher the cure rate (SBRT to the lungs and liver in particular). It is therefore important to find a dose that can be traded off [6, 7]. 3) It is desirable to place a gold marker in order to improve accuracy, but there is a risk of inserting it percutaneously. Since it the adrenal gland is an organ that cannot be seen on X-ray, reproducibility is usually attempted by aligning it with the position of the vertebral body. However, it is also necessary to consider a method for narrowing the PTV margin by placing a gold marker.

Future Outlook

It is expected that the number of indications for SBRT will continue to increase in the future. It is necessary to establish a plan to protect OAR by administering the minimum prescribed dose. Techniques for artificially moving the position of the OAR (sometimes PTV) to remove the heart from the irradiation field, such as respiratory synchronization that is used in breast conserving therapy in the management of left breast cancer will continue to be required. It is true that the shape of the body surface and the appearance of MR-Linac have made it possible to understand information on the body's surface and well within the abdomen. However, there are not many devices on the market yet. Therefore, if the organ position can be controlled by some kind of pretreatment, it is worth attempting.

Conclusion

When SBRT was performed on the left adrenal gland, it was found that the smaller the stomach size, the lower the dose to the stomach. The stomach is an abdominal organ that can be artificially resized. Therefore, it is better to perform SBRT on patients with an empty stomach. Furthermore, since it is easy for the empty stomach to have the same stomach shape every time due to fasting, it is better to plan SBRT on an empty stomach than to plan with the full stomach.

Declarations

Ethical Approval and Consent to participate

National Clinical Trial number UMIN000043471

Consent for publication

All authors approved

Availability of supporting data

Available

Competing interests

None

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None

Authors' contributions

Conception and design of the study: Tanaka, Taniguchi, Ono

Analysis and interpretation of data: Nakaya

Collection and assembly of data: Nakaya

Drafting of the article: Tanaka, Kiryu, Makita

Critical revision of the article for important intellectual content: Tanaka

Final approval of the article: Matsuo

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Conflict of interest

There are no conflicts of interest to report.

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References

1. Helis CA, Hughes RT, Nieto K, Ufondu A, Daugherty EC, Farris MK. Adrenal SBRT: a multi-institutional review of treatment outcomes and toxicity. *Clin Exp Metastasis.* 2020;37(5):585-592. doi: 10.1007/s10585-020-10052-0
2. Chen WC, Baal JD, Baal U, et al. Stereotactic body radiation therapy of adrenal metastases: a pooled meta-analysis and systematic review of 39 studies with 1006 patients. *Int J Radiat Oncol Biol Phys*. 2020;107(1):48-61. doi: 10.1016/j.ijrobp.2020.01.017.
3. Rudra S, Malik R, Ranck MC, et al. Stereotactic body radiation therapy for curative treatment of adrenal metastases. *Technol Cancer Res Treat.* 2013;12(3):217-24. doi: 10.7785/tcrt.2012.500320.
4. Malone J, Pantarotto JR, Tiberi D, Malone S. Adrenal oligometastasis cured with stereotactic ablative radiotherapy. *Radiol Case Rep*. 2020;15(11):2266-2270. doi: 10.1016/j.radcr.2020.08.056.
5. König L, Häfner MF, Katayama S, et al. Stereotactic body radiotherapy (SBRT) for adrenal metastases of oligometastatic or oligoprogressive tumor patients. *Radiat Oncol*. 2020; 15(1):30. doi: 10.1186/s13014-020-1480-0.
6. Plichta K, Camden N, Furqan M, et al. SBRT to adrenal metastases provides high local control with minimal toxicity. *Adv Radiat Oncol.* 2017; 2(4):581-587. doi: 10.1016/j.adro.2017.07.011.
7. Figura NB, Oliver DE, Mohammadi H, et al. Novel dose escalation approaches for stereotactic body radiotherapy to adrenal oligometastases: a single-institution experience. *Am J Clin Oncol*. 2020; 43(2):107-114.
8. Voglhuber T, Kessel KA, Oechsner M, Vogel MME, Gschwend JE, Combs SE. Single-institutional outcome-analysis of low-dose stereotactic body radiation therapy (SBRT) of adrenal gland metastases. *BMC Cancer*. 2020;20(1):536. doi: 10.1186/s12885-020-07030-w.
9. Buergy D, Rabe L, Siebenlist K, et al. Treatment of adrenal metastases with conventional or hypofractionated image-guided radiation therapy - patterns and outcomes. *J. Anticancer Res.* 2018;38(8):4789-4796. doi: 10.21873/anticanres.12788.
10. Sonier M, Chu W, Lalani N, Erler D, Cheung P, Korol R. Implementation of a volumetric modulated arc therapy treatment planning solution for kidney and adrenal stereotactic body radiation therapy. *Med Dosim*. 2016;41(4):323-328. doi: 10.1016/j.meddos.2016.09.001.
11. Arcidiacono F, Aristei C, Marchionni A, et al. Stereotactic body radiotherapy for adrenal oligometastasis in lung cancer patients. Br J Radiol. 2020;93(1115):20200645. doi: 10.1259/bjr.20200645.

Tables

Table 1. Organ at risk (OAR) dose constraints applied for three fraction SBRT (54Gy / 6fx for CTV) CTV is equal to PTV

(Biological effective dose [BED10]) 102Gy Equivalent dose 2Gy (EQD) 85Gy

Radiation dose limited to OAR.

	D0.1 cc	D5.0 cc	D10.0 cc	V12 Gy	V15 Gy	V21 Gy
Stomach	≤ 22Gy		≤ 16Gy			
Intestine	≤ 22Gy	≤ 17 Gy	≤ 11Gy			
Pancreas	≤ 22Gy		≤ 12Gy	≤ 50%		≤ 30%
Liver					≤ 50%	≤ 30%
Kidneys (Left)				≤ 25%		
Kidneys (Right)				≤ 25%		
Kidneys (together)					≤ 35%	
Spinal cord	≤ 22Gy					

DX (the dose to X% of the OARs volume) at X values of 0.1, 5.0, 10.0 cc.

VX (the percentage of the OARs volume that received more than X Gy)

CTV; Clinical target volume, PTV; Planning target volume

Table 2a. Two medical physicists planned treatment within the dose limits.

Planned by Medical physicist 1

		Empty	Full	p-value
PTV	**D 0.1 cc**	65.80	66.00	0.31
	D 5 cc	56.10	55.90	0.52
	D10 cc	42.40	43.10	0.47
	V12 Gy	99.90	99.90	0.50
	V15 Gy	99.60	99.80	0.22
	V21 Gy	96.80	99.80	0.38
Stomach	**D 0.1 cc**	19.90	20.10	0.45
	D 5 cc	13.70	15.90	**0.03**
	D10 cc	12.10	14.60	**0.01**
	V12 Gy	9.20	7.80	0.69
	V15 Gy	2.30	2.50	0.42
	V21 Gy	0.00	0.00	-
Intestine	**D 0.1 cc**	17.80	15.30	0.20
	D 5 cc	13.40	11.00	0.17
	D10 cc	12.20	9.60	0.15
	V12 Gy	4.20	5.10	0.60
	V15 Gy	1.30	2.10	0.66
	V21 Gy	0.00	0.00	-
Pancreas	**D 0.1 cc**	45.60	38.90	0.23
	D 5 cc	26.30	19.20	0.13
	D10 cc	20.50	13.60	0.09
	V12 Gy	73.40	48.40	0.06
	V15 Gy	60.90	39.50	0.08
	V21 Gy	37.90	22.20	0.08
Liver	**D 0.1 cc**	15.40	13.60	0.24
	D 5 cc	11.50	10.40	0.30
	D10 cc	10.40	9.30	0.29
	V12 Gy	2.00	0.80	0.12

	V15 Gy	0.50	0.10	0.14
	V21 Gy	0.00	0.00	-
Left kidney	**D 0.1 cc**	50.30	50.70	0.53
	D 5 cc	33.80	29.40	0.15
	D10 cc	25.20	20.80	0.12
	V12 Gy	23.80	15.60	**0.01**
	V15 Gy	19.10	12.90	**0.01**
	V21 Gy	12.60	8.40	**0.03**
Right Kidney	**D 0.1 cc**	9.80	8.40	0.13
	D 5 cc	6.90	5.90	0.21
	D10 cc	5.50	5.10	0.38
	V12 Gy	0.40	0.00	0.17
	V15 Gy	0.00	0.00	-
	V21 Gy	0.00	0.00	-
Spinal cord	**D 0.1 cc**	14.00	14.00	0.50
	D 5 cc	7.80	7.40	0.42
	D10 cc	2.20	1.20	0.22
	V12 Gy	5.90	10.40	0.92
	V15 Gy	2.20	4.60	0.84
	V21 Gy	0.00	0.00	-

DX (the dose to X% of the Organ at Risks [OARs] volume) at X values of 0.1, 5.0, 10.0 cc.

VX (the percentage of the OARs volume that received more than X Gy)

Table 2b. Two medical physicists planned treatment within the dose limits.

Planned by Medical physicist 2

		Empty	Full	p value
PTV	**D 0.1 cc**	66.00	66.00	0.50
	D 5 cc	56.00	53.40	0.29
	D10 cc	44.00	40.30	0.32
	V12 Gy	99.90	99.90	0.50
	V15 Gy	99.30	99.40	0.57
	V21 Gy	97.30	97.70	0.58
Stomach	**D 0.1 cc**	19.80	20.30	0.32
	D 5 cc	13.80	15.60	**0.03**
	D10 cc	12.30	14.30	**0.02**
	V12 Gy	7.70	6.90	0.36
	V15 Gy	2.50	2.20	0.37
	V21 Gy	0.00	0.00	-
Intestine	**D 0.1 cc**	17.40	15.60	0.28
	D 5 cc	13.10	11.10	0.23
	D10 cc	11.50	9.90	0.26
	V12 Gy	3.40	6.20	0.20
	V15 Gy	1.40	2.40	0.27
	V21 Gy	0.00	0.00	-
Pancreas	**D 0.1 cc**	45.40	37.30	0.19
	D 5 cc	25.80	19.10	0.16
	D10 cc	20.00	13.50	0.12
	V12 Gy	70.70	44.10	0.06
	V15 Gy	61.10	36.80	0.06
	V21 Gy	38.30	22.00	0.08
Liver	**D 0.1 cc**	16.10	15.40	0.39
	D 5 cc	12.60	11.90	0.38
	D10 cc	11.50	10.60	0.34
	V12 Gy	2.60	0.70	0.06

	V15 Gy	0.40	0.20	0.26
	V21 Gy	0.00	0.00	-
Left kidney	**D 0.1 cc**	49.20	50.20	0.58
	D 5 cc	32.10	29.60	0.30
	D10 cc	23.70	22.00	0.34
	V12 Gy	22.20	15.50	**0.01**
	V15 Gy	17.70	12.90	**0.03**
	V21 Gy	10.70	9.00	0.22
Right Kidney	**D 0.1 cc**	10.70	11.30	0.61
	D 5 cc	8.10	9.00	0.34
	D10 cc	6.90	8.00	0.30
	V12 Gy	2.60	2.30	0.55
	V15 Gy	0.50	1.50	0.26
	V21 Gy	0.00	0.00	-
Spinal cord	**D 0.1 cc**	14.60	16.20	0.15
	D 5 cc	7.80	6.90	0.30
	D10 cc	2.50	1.30	0.15
	V12 Gy	6.40	8.90	0.80
	V15 Gy	1.90	3.00	0.72
	V21 Gy	0.00	0.00	-

DX (the dose to X% of the Organ at Risks [OARs] volume) at X values of 0.1, 5.0, 10.0 cc.

VX (the percentage of the OARs volume that received more than X Gy)

Figures

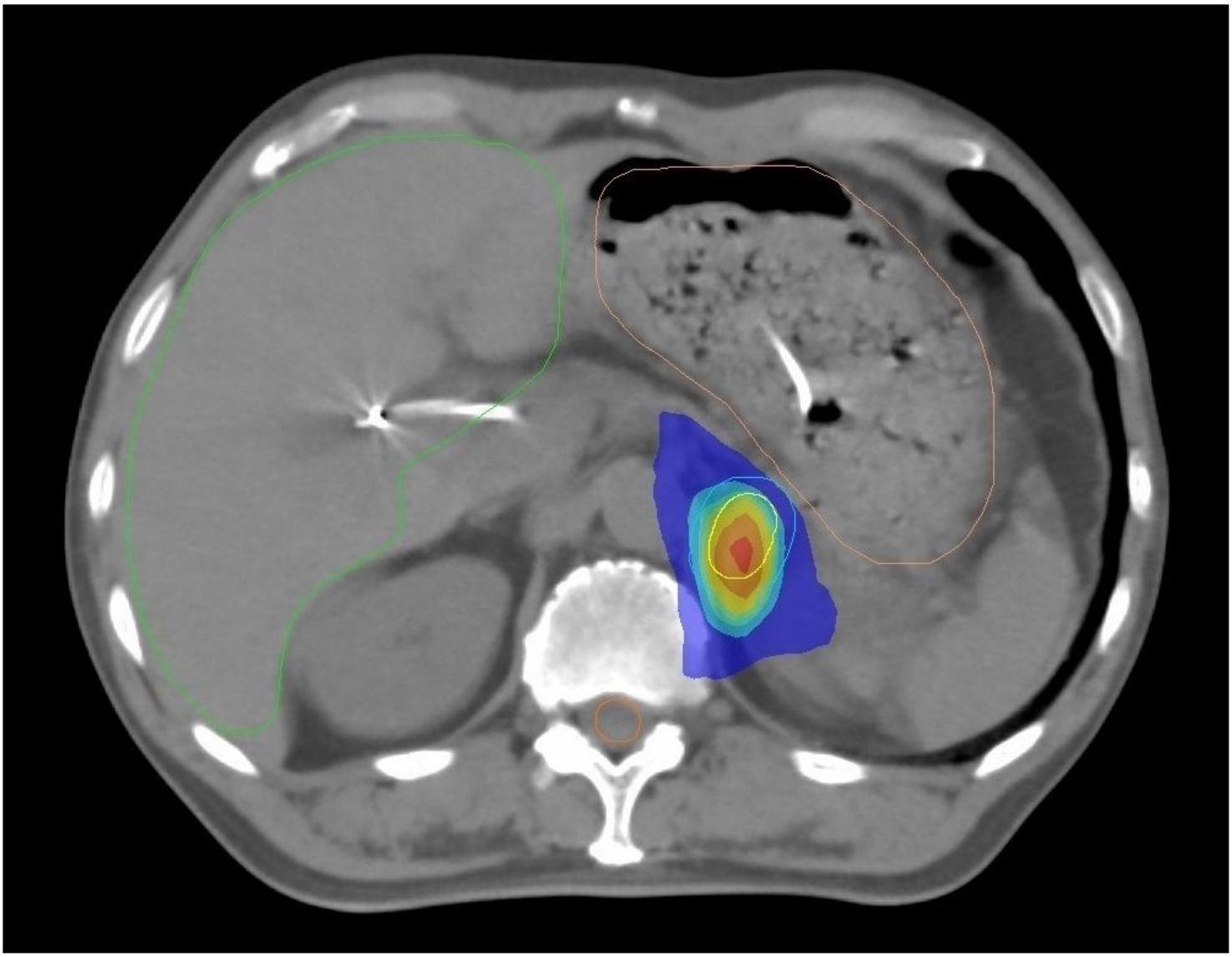

Figure 1

An example of adrenal SBRT administered in the setting of a large stomach. The pancreas was not shown in this slice. CTV coverage is good Yellow line; adrenal CTV (2 mm margin from GTV) OAR: Liver (green line), Stomach (orange line)

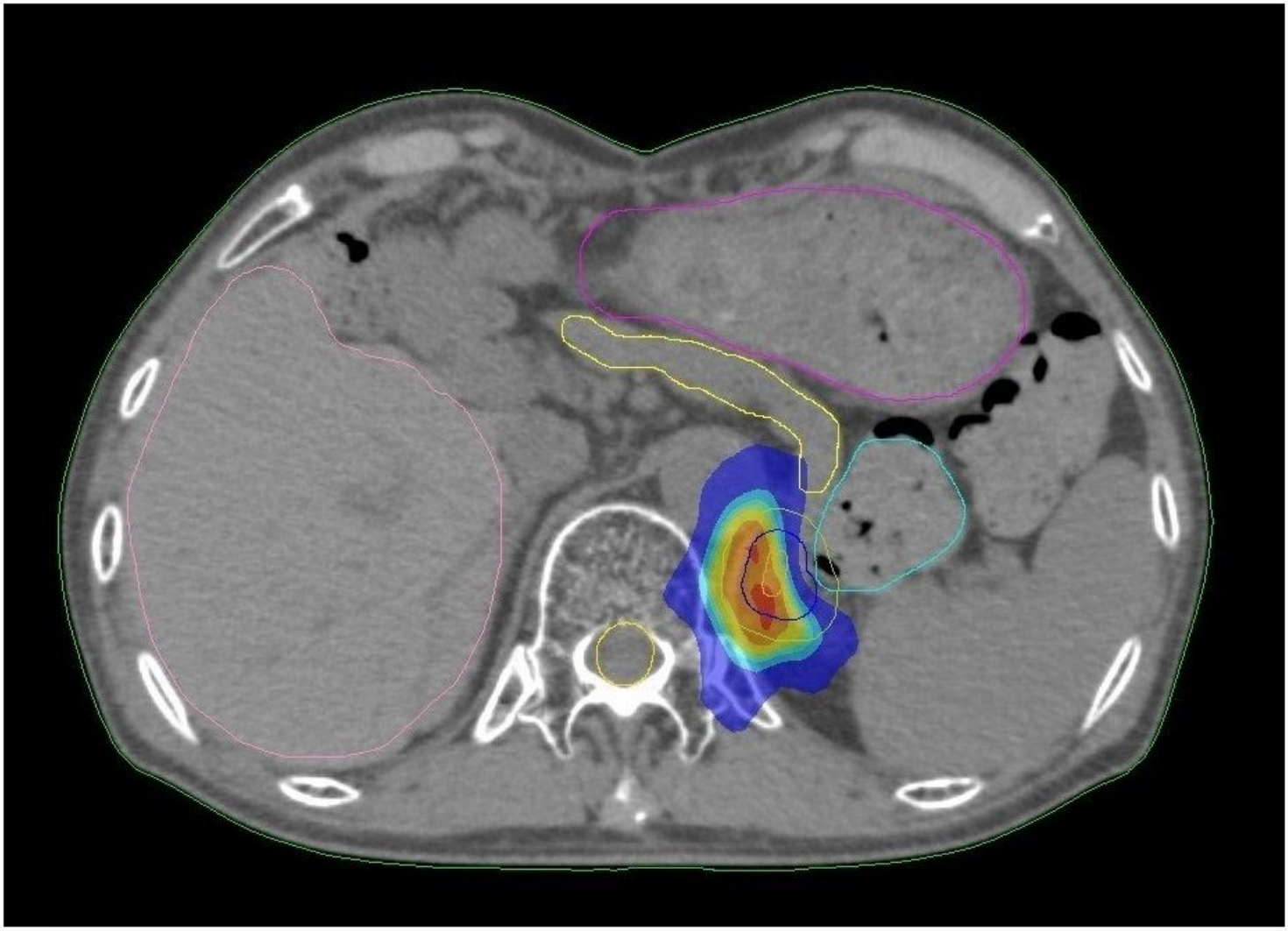

Figure 2

An example of adrenal SBRT in the setting of a large stomach. The intestine is close to the left adrenal ground. CTV coverage is not good due to the intestine. Blue line; adrenal CTV (2 mm margin from GTV) OAR: Liver (pink line), Stomach (purple line), Pancreas (yellow line) and Intestine (light blue line).

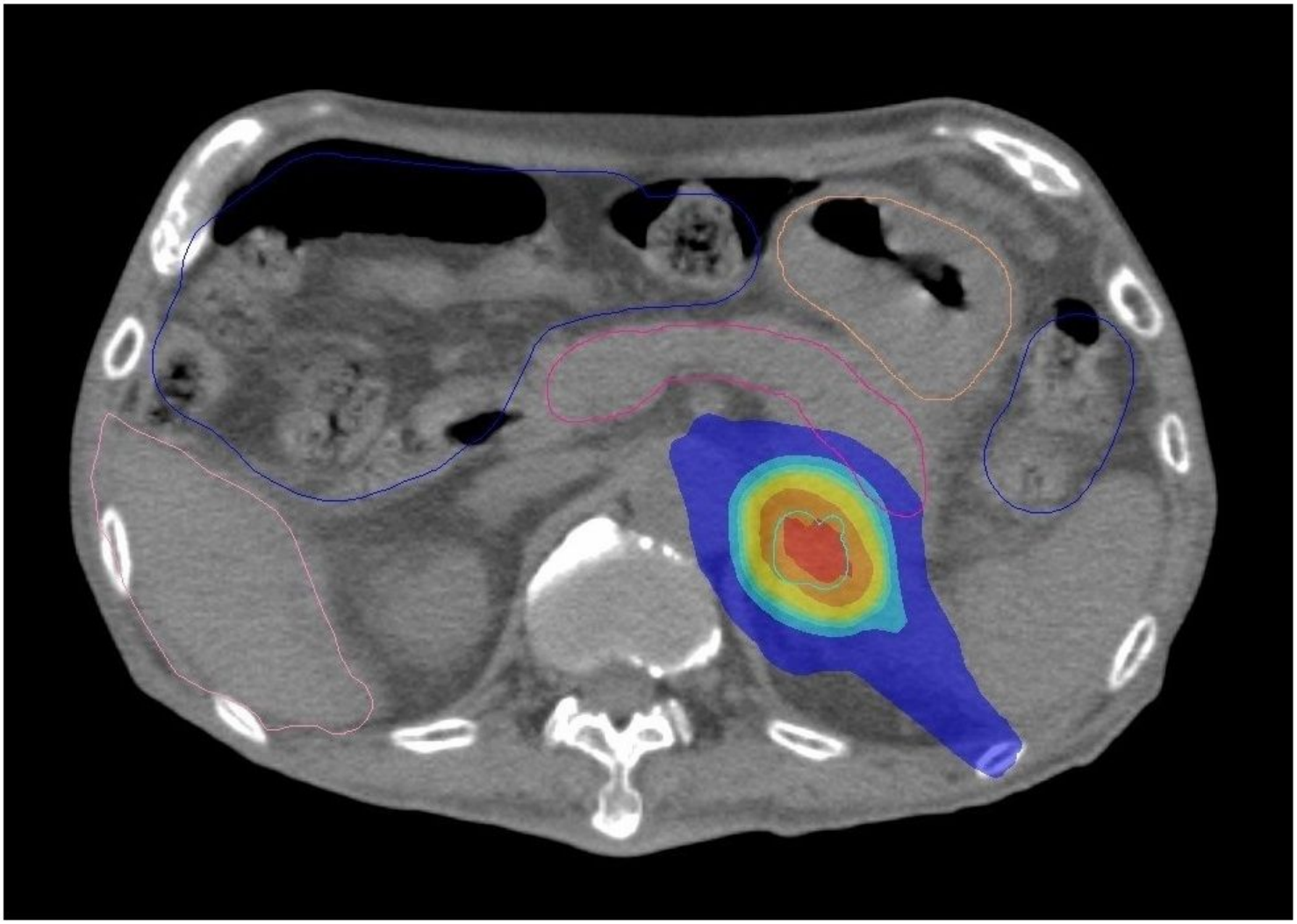

Figure 3

An example of adrenal SBRT in the setting of a small stomach. The pancreas is close to the left adrenal ground. CTV coverage is good. Light blue line; adrenal CTV (2 mm margin from GTV) OAR: Liver (pink line), Stomach (light orange line), Pancreas (light red line) and Intestine (blue line).

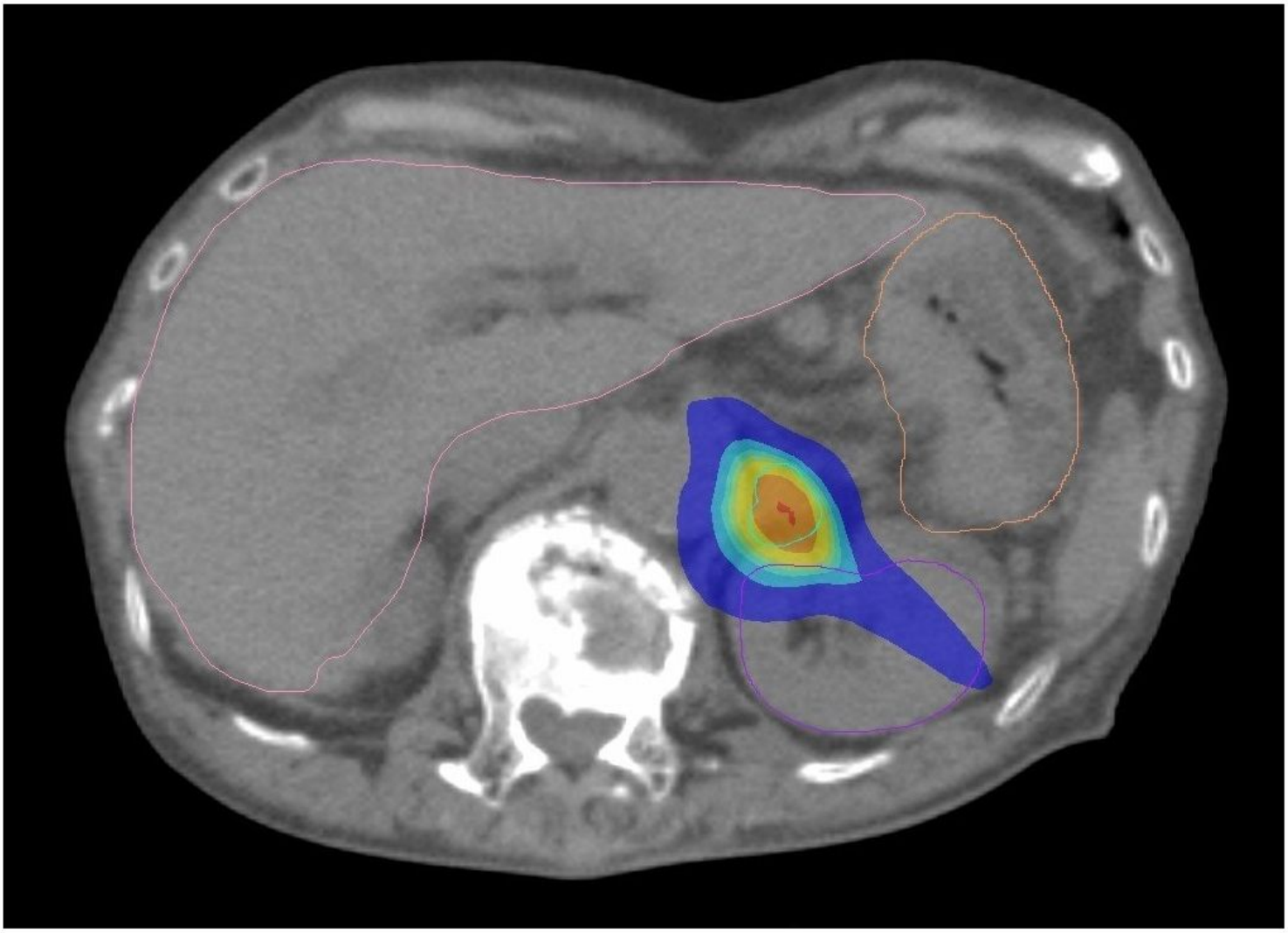

Figure 4

An example of adrenal SBRT in the setting of a small stomach. The left kidney is close to the left adrenal ground. However, left adrenal CTV coverage is good. Light blue line; adrenal CTV (2 mm margin from GTV) OAR: Liver (pink line), Stomach (light orange line), Pancreas (disappeared in this slide) and Intestine (disappeared in this slide).

Figure 5

Color dose wash list (Dose distribution of Figure 1 to 4) Prescribed dose is 54 Gy / 6 fractions When the area irradiated with 54 Gy is 100% (yellow), the percentage is expressed by color.