



Case Presentation: The Effect of Volumetric Image Guidance & Adaptive Radiotherapy on Cardiac Dose in A Patient with Esophageal Cancer

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SUMMARY

We present the case of a patient with esophageal cancer whose tumor size regression prompted re-planning to decrease the cardiac dose. A 68-year-old male presented at our outpatient clinic with dysphagia. He was diagnosed with clinical T3N1M0 adenocarcinoma located at the distal esophagus–esophagogastric junction. He was decided to have surgery after receiving neoadjuvant chemoradiotherapy. Following 4-D CT simulation, IG-IMRT with SIB technique was planned as 50 Gy in 25 fractions to iGTV and as 45 Gy to the area identified as the CTV. Daily kV and weekly CBCT were planned at the beginning of the treatment. Concurrent CT with weekly paclitaxel–carboplatin was administered. At the simulation and start of the treatment, the heart was pushed anteriorly due to the mass effect and dilatation in the mid-lower esophagus. The mass and dilatation regressed at the weekly CBCT of the patient. The third-week CBCT evaluation revealed the movement of the heart posteriorly into the PTV. Re-simulation was performed to continue with the adaptive planning for the last 10 treatment fractions. The cumulative dose received by the heart was reduced from 96% to 93% for V5Gy, from 79% to 60.8% for V10Gy, from 60% to 43.2% for V15Gy, from 35% to 21% for V20Gy, and from 29.6 to 28 Gy for the mean cardiac dose with the volumetric image-guided adaptive planning. If tumor regression is predicted during radiotherapy to possibly change doses of organs at risk, volumetric image guidance should be encouraged once per week, at least, to consider adaptive treatment when required to ensure the critical organ doses within safe limits.

Keywords: Adaptive radiotherapy; esophageal cancer; volumetric image guidance.

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Introduction

Neoadjuvant or definitive chemoradiotherapy constitutes the main approach in the treatment of locally advanced esophageal cancer.[1-3] We present a patient with esophageal cancer whose tumor size regression prompted re-planning to decrease the cardiac dose.

Case Report

A 68-year-old male with no significant past medical history presented at our outpatient clinic with gradually aggravated dysphagia mainly to solids and loss of appetite. He had a history of social alcohol consumption for nearly 40 years but no history of cigarette smoking.

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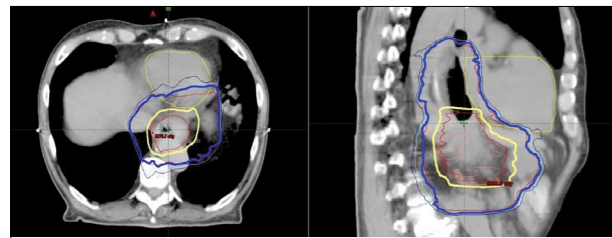


Fig. 1. Initial treatment plan.

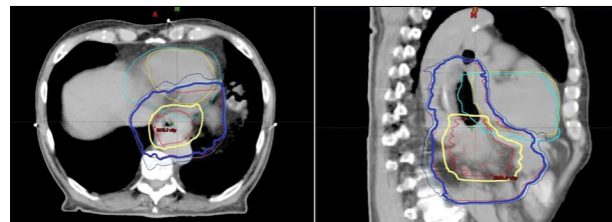


Fig. 2. Initial treatment plan. Pretreatment position of the heart (yellow contour) and replacement of the heart in the third week of the treatment (blue contour).

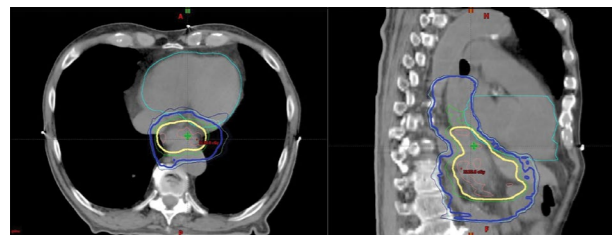


Fig. 3. Adaptive plan on computed tomography re-simulation.

He had a good physical status, with a body mass index of 22 kg/m², but he also complained of weight loss of approximately 20 kg over the last 6 months. He denied any history of nausea, vomiting, abdominal pain, hematemesis, or melena.

His physical examination was unremarkable. There were no lesions in the gingiva, buccal mucosa, floor of the mouth, oral tongue, base of the tongue, hard palate, soft palate, tonsillar fossa, or posterior oropharyngeal wall by visualization. On routine investigation, the hemoglobin level was 11.9 g/dL, white blood cell count was 4.7 K/uL, platelet count was 219 K/uL, serum creatinine level was 0.92 mg/dL, alanine transaminase level was 56 U/L, and aspartate transaminase level was 13 U/L.

A contrast-enhanced computed tomography (CT) of the thorax and upper abdomen revealed circumferential wall thickening in the lower one-third of the esophagus, causing near-complete lumen occlusion

with proximal dilatation as well as enlarged perigastric lymph nodes.

Upper gastrointestinal tract endoscopy revealed an ulcerovegetative tumor of 36 cm starting from the incisors and extending distally to the inside of the stomach while surrounding the cardia. The upper and middle esophagi were reported to be dilated secondary to the mass. A biopsy of the lesion confirmed moderately differentiated adenocarcinoma.

Staging positron emission tomography with CT defined avid uptake in delayed images extending between the distal part of the esophagus and lesser curvature with a maximum standard uptake value (SUV_{max}: 26.75). Multiple hypermetabolic lymph nodes were observed adjacent to the cardia and lesser curvature side of the junction, the greatest of which measured 10×15 mm, whereas metastases to other organs were not detected.

Taking all these findings into consideration, our patient was diagnosed with clinical T3N1M0 adenocarcinoma located at the distal esophagus–esophago-gastric junction. His case was discussed in a meeting of the Multidisciplinary Oncology Board, and it was decided that he would undergo surgery after receiving neoadjuvant concomitant chemoradiotherapy. He was also referred to a dietetic team because of his weight loss and was advised to modify his diet. Following 4-dimensional CT simulation, image-guided intensity-modulated radiotherapy (IG-IMRT) with simultaneous integrated boost technique was planned as 50 Gy in 25 fractions (2 Gy/day) to the primary disease, defined as the internal gross tumor volume, and as 45 Gy (1.8 Gy/day) to the area identified as the clinical tumor volume. The plan was generated with 0°, 40°, 80°, 120°, 160°, and 200° beam arrangements. The simulation and administration of each treatment fraction were performed after 3 hours of fasting in order to provide similar gastric dimensions. Daily kV and weekly cone beam CT (CBCT) was planned at the beginning of the treatment. Concurrent chemotherapy with weekly paclitaxel 60 mg/m²–carboplatin AUC 2 was administered by the medical oncology department.

At the simulation and start of the treatment, the heart was pushed anteriorly due to the mass effect and dilatation in the mid-lower esophagus. The mass and dilatation regressed at the weekly volumetric image-guided evaluation (CBCT) of the patient during the treatment process. The third-week CBCT evaluation revealed the movement of the heart posteriorly into the planning treatment volume (PTV). The magnitude of the regression was <0.2 cm in the first week, but the largest regression occurred in the anterior–posterior dimension from the second to the third week as 1.4

cm in total due to the regression of the esophagus mass and dilatation.

In light of this major finding, re-simulation and re-planning were performed to continue with the adaptive planning for the last 10 treatment fractions without any treatment break. Compared with the previously planned values, the dose received by the heart for the last 10 fractions was decreased from 96% to 90% for V5Gy, from 60% to 47% for V10Gy, from 30% to 18% for V15Gy, from 8% to 0% for V20Gy, and from 11.82 to 10.38 Gy for the mean cardiac dose. The heart V5Gy value was 100%, V10Gy value was 70%, V15Gy value was 60%, V20Gy value was 35%, and the mean cardiac dose was 17.72 Gy for the initial 15 fractions. Within this framework, the cumulative dose received by the heart, calculated in the composite plan, was reduced from 96% to 93% for V5Gy, from 79% to 60.8% for V10Gy, from 60% to 43.2% for V15Gy, from 35% to 21% for V20Gy, and from 29.6 to 28 Gy for the mean cardiac dose with the volumetric image-guided adaptive planning (Figs.).

At the end of the radiotherapy, his dysphagia was partially relieved. The treatment was completed without any unexpected complications or acute side effects.

Discussion

Radiotherapy has an important role in both operable and inoperable esophageal cancer. However, radiotherapy planning for esophageal cancer has difficulties due to the central location of the esophagus; large treatment volumes concerning the risk of transmural and lymphatic spread; and the proximity of critical organs, such as the heart, lungs, and spinal cord.

Advances in radiation techniques have resulted in higher treatment response rates, more normal tissue sparing, and less treatment time. Recently, IG-IMRT has replaced 3-dimensional conformal radiotherapy for esophageal cancer owing to relatively preferable dose distributions as well as significant dose reductions in critical organs. The current literature rationalizes the increasing use of IMRT.[4-6] In contrast, IMRT requires more precise mechanisms in the planning and treatment process with regard to smaller safety margins. Thus, 4-dimensional CT is useful to consider movements secondary to respiration, circulation, or peristalsis.[7-9] Volumetric-modulated arc treatment is also advantageous with shorter treatment times that may decrease the risk of intrafractional positional shifts.[10]

In addition to intrafractional changes, interfractional differences may occur due to tumor regression, progression, or displacement. In this context, CBCT

is an inevitable component of modern radiotherapy procedures. Planar kV imaging remains incapable in organs without bony structures, such as the esophagus. Martins et al. compared planar kV imaging versus CBCT in the evaluation of setup errors in esophagus carcinoma radiotherapy [11]; sixteen patients, 212 kV images, and 116 CBCT images were reviewed in that study, revealing superiority of CBCT over planar kV imaging due to the soft tissue structure of the esophagus and a decrease in the number of possible setup errors with CBCT. There was no additional significant relationship between setup errors and immobilization system or tumor location. Although a small sample size was a limitation of that study, routine-use CBCT was encouraged by the authors.[11]

To date, there have been limited studies addressing esophageal displacement as a numerical value during radiotherapy. Yamashita et al. analyzed the shift of the esophagus in 20 patients treated with radiotherapy for esophageal cancer.[12] CBCT was performed for each patient twice a week. According to the results, the authors suggested the use of target margins of 9 mm for day-to-day esophageal motion and 8 mm for patient setup in all directions, respectively [12]; if CBCT is a standard procedure for daily imaging, setup errors may be neglected and only day-to-day esophageal motion of 9 mm may be taken into account. Although the results of the present study are consistent with those of previous studies [13], mentioned margins raise the question of whether we need to use CBCT more frequently than twice a week.

Online volumetric images of the patient in the treatment position provide further information about current status, and regular volumetric imaging during the treatment process enables the evaluation of the necessity of adaptive planning. Hawkins et al. evaluated the organs at risk for 14 cases by creating a patient-specific PTV with CBCTs acquired on days 1–4 and then weekly.[14] Heart mean dose and V20 value for lungs were significantly reduced for the adaptive plans that were created with this PTV. They concluded that a decreased planning volume can be constructed within the first week of treatment using CBCT. In a similar trial, adaptive plans were created based on CBCTs that were acquired daily for the first week and then weekly. [15] Adaptive plans revealed significantly reduced V10Gy, V20Gy, and mean lung dose values as well as smaller D35% and mean heart doses compared with the initial plans.[15] In another study from Denmark, 29 patients with esophageal cancer were evaluated with daily CBCT and an additional CT at medial fraction 10 (range, 9–14).[16] After the contouring and re-planning processes, two CTs were compared whether there

was a decrease <1% in CTV or < 3% in PTV coverage that was accepted. In case of a larger decrease, previous CBCTs were reviewed in terms of adaptive planning requirements. Nine of the 29 patients underwent adaptive radiotherapy, and an increased V30Gy dose to the heart of >2% was observed in nine (31%) patients (maximum 5% increase). Although this result is consistent with that of the presented case, there also exists conflicting data regarding the heart dose.[17]

As adaptive planning has become widespread, questions have been raised regarding the incidence of local recurrence of the adaptive treatment and particularly the risk for failure in the area excluded with subsequent planning. The limited number of publications has thus far investigated the effect of local failure patterns concerning thoracic tumors, and the greater part of them is related to lung cancer. Ramella et al. prospectively analyzed 50 patients with locally advanced non-small-cell lung cancer treated with concomitant chemoradiotherapy.[18] The patients underwent weekly CT simulation during treatment. Adaptive planning was outlined in cases of tumor regression. Patterns of failure were classified as in-field (progression within the re-planning PTV), marginal (recurrence in the initial PTV excluded from the re-planning PTV), and out-of-field (recurrence outside of the initial PTV). Marginal relapse was recorded in 6% of the patients, whereas 20% and 4% of the patients showed in-field and out-of-field local failure, respectively. Ramella et al. deserves appreciation for drawing attention to the failure patterns after adaptive radiotherapy.

Conclusion

In the evolution of radiation oncology, there is an ongoing effort to increase the treatment efficiency without any major acute and long-term toxicity. The current literature supports the use of IMRT, including 4-D imaging, for esophageal cancer. Nevertheless, target and organs at risk motion might be a major problem in esophageal radiotherapy, and the importance of volumetric image guidance and adaptive planning, if necessary, sound to be critical. Overall, if tumor regression is predicted during radiotherapy to possibly change doses of organs at risk, volumetric image guidance should be encouraged once per week, at least, to consider adaptive treatment when required to ensure critical organ doses within safe limits.

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