Research Letter

Cone Beam CT-Based Daily Adaptive Planning or Defined-Filling Protocol for Neoadjuvant Gastric Cancer Radiation Therapy: A Comparison

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Abstract

Purpose: This study aimed to investigate, in the setting of neoadjuvant gastric irradiation with integrated boost, whether cone beam computed tomography (CBCT)-based adaptive radiation therapy compared with a defined-filling protocol would be beneficial in terms of feasibility and achieving daily reproducible dose volume indexes of the planning target volume (PTV) and organs at risk (OARs) and workflow.

Methods and materials: Planning computed tomography (PCT) and 25 CBCT scans of a previously treated patient were used, and neoadjuvant therapy of gastric carcinoma was simulated offline. PTVs and OARs were defined per the TOPGEAR protocol (PTV: 45 Gy/1.8 Gy), and an integrated boost (gross tumor volume [GTV]: 50.4 Gy/2.016 Gy) was added. The patient followed a filling regimen consisting of 12-hour fasting followed by 200 mL of water intake (2 glasses of water) immediately before irradiation. OARs and PTVs were newly contoured on each CBCT. Nonrigid registration of PCT and CBCT scans was performed. Nonadapted plans were recalculated on each CBCT (R-CBCT). Furthermore, an adapted plan was created for the new anatomy (A-CBCT). Dose parameters and comparison of R-CBCT and A-CBCT for the kidneys, liver, and heart were analyzed using a paired t test.

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Data-sharing statement: The data used and generated in this work may be available under ethical and data protection considerations upon request on an individual basis.

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Results: A total of 200 plans for R-CBCT and A-CBCT were obtained. Mean gastric volumes were 277.32 cm³ (±54.40 cm³) in CBCT scans and 519.2 cm³ in PCT. Mean doses to the PTV did not differ meaningfully within the CBCT scans, with an average of 1.54%. The D95 improved in GTV coverage by 5.26% compared with the R-CBCT plan. Mean heart, liver, and right kidney doses were reduced with the A-CBCT plan by 35.74%, 10.71% and 29.47%, respectively. The R- and A-CBCT comparison for GTV and OARs was significantly different in all cases (P < .0001).

Conclusions: Adaptive radiation therapy through deformable registration represents an important tool in neoadjuvant gastric irradiation, encompassing daily variability and organ motion, compared with the defined-filling protocol while improving OAR sparing.

Introduction

One of the main problems radiation oncologists have to overcome in a neoadjuvant setup is the daily planning target volume (PTV) motion, which is an inherent feature for this organ. Although the defined-filling protocol has been widely applied, this approach might not represent a reliable alternative for achieving daily similar volumes throughout the treatment, as confirmed by previous experiences.

Therefore, a comparison between a novel cone beam–based adaptive radiation therapy approach and a defined-filling protocol is presented herein, accounting for daily changes in the PTV, organs-at-risk (OARs) sparing, and potential workflow benefit.

Methods and Materials

Imaging of a previously treated patient was used and a neoadjuvant treatment simulation of gastric carcinoma was performed retrospectively (planning computed tomography [PCT]; Brilliance Big Bore, Philips Healthcare, Best, The Netherlands; and cone beam computed tomography [CBCT]; XVI/Versa HD, Elekta AB, Stockholm, Sweden). PTVs and OARs (heart, lungs, kidneys, liver, spinal cord) were defined on the PCT per the TOPGEAR study protocol (PTV 45 Gy/1.8 Gy) with an additional integrated boost (gross tumor volume [GTV]: 50.4 Gy/2.016 Gy) localized on the greater curvature and including nodal areas. For each fraction, the patient followed a defined gastric filling regimen of a fasting period of 12 hours, followed by an intake of 200 mL of water shortly before daily irradiation. Daily CBCT images (n = 25) were exported to an image registration platform (Velocity V3.2.1, Varian Medical Systems, Palo Alto, CA), and OARs and PTVs were recontoured on each data set. Registration of the PCT and daily CBCT scans were performed throughout organ-guided deformable matching and controlled through the spyglass function and warp map (voxel migration map). CBCT imaging does not support Hounsfield units (HU); thus, a resampled PTV was created (based on the registration and anatomy of the CBCT). The treatment plan without adaptation was recalculated this way on each CBCT (R-CBCT). Furthermore, an adapted treatment plan was created and optimized for the modified anatomy (A-CBCT). All plans were calculated with a Monte Carlo-based algorithm (Monaco V5.11, Elekta AB).

The paired t test was employed for statistical significance assessment with the R-project software (R Core Team, R Foundation for Statistical Computing, Vienna, Austria).

Results

Complete abdominal imaging was obtained from daily CBCT images (n = 25). In total, 200 plans were performed for R-CBCT (n = 100) and A-CBCT (n = 100). In the PCT, the stomach volume was 519.2 cm³, which was found to differ in CBCT images (277.32 ± 54.4 cm³ average; Vmin 193.7; Vmax 365.7). The GTV in the PCT was 7.9 cm³ (Fig 1).

The PTV Dmean distributions were 45.23 Gy, 45.79 Gy, and 45.09 Gy for PCT, R-CBCT, and A-CBCT, respectively, yielding a difference of −1.54% between A-CBCT and R-CBCT, 1.25% between R-CBCT and PCT, and −0.32% between A-CBCT and PCT. As for the D95, 43.39 Gy, 42.96 Gy, and 43.40 Gy were found for PCT, R-CBCT, and A-CBCT, respectively. The difference rates were 1.02%, −0.98, and 0.03 between A-CBCT and R-CBCT, R-CBCT and PCT, and A-CBCT and PCT, respectively. Other parameters are shown in Table 1. The PTV covered by 45 Gy (V45) was 60.47%, 81.20%, and 53.50% for PCT, R-CBCT, and A-CBCT, respectively (Fig 2).

The GTV Dmean was 50.36 Gy, 49.47 Gy, and 50.30 Gy for PCT, R-CBCT, and A-CBCT, respectively. The differences between the plans were 1.68% between A-CBCT and R-CBCT, −1.76% for R-CBCT and PCT, and −0.11% for A-CBCT and PCT. The D95 profile was 49.48 Gy, 46.79 Gy, and 49.26 Gy, respectively, with absolute differences of 5.26% between A-CBCT and R-CBCT, −5.43% for R-CBCT and PCT, and −0.45% for A-CBCT and PCT. Additional characteristics are shown in Table 1.
The mean dose to the heart, liver, and right kidney could be reduced with the A-CBCT plan by $-35.74\%$, $-10.71\%$, and $-29.47\%$, respectively, compared with the R-CBCT (Fig 3). No differences were found in the left kidney, spinal cord, or overdosing ($V > 110\%$) parameters. Further dose-distribution details are shown in Table 2.

The comparison for R-CBCT and A-CBCT differences regarding GTV $D_{\text{min}}$ and $D_{95}$; right kidney $D_{\text{mean}}, D_{30},$ and $D_{60};$ liver $D_{\text{mean}};$ and heart $D_{\text{mean}},$ were significant according to the paired $t$ test ($P < .0001$). Additional details are shown in Table 3.

**Discussion**

According to the results presented herein, with a wide range of volume variability ($V_{\text{min}}: 193.7; \ V_{\text{max}}: 365.7$),

### Table 1 Planning and gross tumor volume dose parameters

|                      | $D_{\text{min}}$ | $D_{\text{mean}}$ | $D_{\text{max}}$ | $D_{99}$ | $D_{95}$ | $D_{90}$ | $D_{50}$ |
|----------------------|------------------|------------------|------------------|----------|----------|----------|----------|
| PCT                  | 34.28            | 45.23            | 51.6             | 41.37    | 43.39    | 43.94    | 45.24    |
| Recalculated         | 27.88            | 45.79            | 53.28            | 37.70    | 42.69    | 44.31    | 45.94    |
| Adapted              | 33.22            | 45.09            | 52.02            | 41.99    | 43.40    | 43.88    | 45.06    |
| Difference, %        |                  |                  |                  |          |          |          |          |
| A – R                | 19.16            | -1.54            | -2.38            | 11.38    | 1.02     | -0.98    | -1.92    |
| R – PCT              | -18.67           | 1.25             | 3.26             | -8.88    | -0.98    | 0.85     | 1.55     |
| A – PCT              | -3.08            | -0.32            | 0.81             | 1.49     | 0.03     | -0.14    | -0.41    |
| Gross target volume dose, Gy |
| PCT                  | 48.42            | 50.36            | 51.6             | 48.79    | 49.48    | 49.67    | 50.37    |
| Recalculated         | 45.30            | 49.47            | 52.99            | 46.07    | 46.79    | 47.32    | 49.53    |
| Adapted              | 48.17            | 50.30            | 52.02            | 48.83    | 49.29    | 49.49    | 50.35    |
| Difference, %        |                  |                  |                  |          |          |          |          |
| A – R                | 6.35             | 1.68             | -1.83            | 6.0      | 5.26     | 4.59     | 1.65     |
| R – PCT              | -6.45            | -1.76            | 2.69             | -5.58    | -5.43    | -4.73    | -1.67    |
| A – PCT              | -0.51            | -0.11            | 0.81             | 0.08     | -0.45    | -0.35    | -0.05    |

Abbreviations: A = new anatomy; PCT = planning computed tomography; R = recalculated
the adaptive radiation therapy approach emerges as a solid alternative option to overcome this problem.\textsuperscript{5} Previously published experiences have pointed out the value of this concept, due to the inherent motion of this organ, which could exceed the established margins according to most guidelines.\textsuperscript{1,6-8}

The advantage of deformable registration lies with improved OARs sparing while assuring an accurate PTV delimitation.\textsuperscript{9,10} The results obtained herein regarding doses reaching critical structures, such as the heart, kidney, or liver, confirm the value of this procedure, because rigid matching might result in inaccurate structure dosimetry. Despite the low intended doses, sparing of large abdominal areas due to variable daily volumes could also translate into better intestine sparing, therefore diminishing potential clinically acute toxicity, which tends to impair treatment compliance in this set of patients.\textsuperscript{11,12} Part of the limitations of this study encompasses the variability of registered PTV sizes from the PCT and the subsequent CBCT images, which could result in biased outcomes due to the nature of these organs and the single-patient design; however, these results should not be disregarded because they show the same trend toward potential benefits of plan adaptation as previous publications and describe the feasibility of a workflow not previously reported. Although not measured, the entire process, from image acquisition, recontouring, deformable registration, and computed tomography resampling to completed treatment planning, required approximately 40 to 60 minutes, which is not

Figure 2  Planning target volume (red), stomach (blue), and gross tumor volume (red) dose distribution and anatomic and contour variations between planning, recalculated cone beam, and new anatomy cone beam computed tomography in (A, B, C) axial, (D, E, F) coronal, and (G, H, I) sagittal representative views, respectively.
suitable in this form for daily routine. A proposed alternative to overcome the timing problem could be limiting the workflow days. This plan-of-the-day strategy, selecting the most accurate plan according to daily imaging, has been already reported in the setting of bladder and uterine cervix irradiation and published by different groups worldwide.13,14

Conclusions

Adaptive radiation therapy through deformable registration represents an important tool in neoadjuvant gastric irradiation, encompassing daily volume variability, compared with daily defined-filling protocol. OAR sparing could be significantly improved with this approach.

Table 2  Organ-at-risk dose parameters

| Structure | Dose, Gy | D_{30} | D_{60} | D_{30} | D_{60} | D_{mean} | D_{mean} | D_{mean} |
|-----------|---------|--------|--------|--------|--------|----------|----------|----------|
|           | Left kidney | Right kidney | Liver | Spinal cord | Heart |
| PCT       | 3.02     | 1.44   | 13.66  | 3.32   | 21.23  | 40.06    | 8.97     |
| Recalculated | 2.67 | 1.35   | 13.84  | 2.59   | 22.87  | 38.27    | 12.20    |
| Adapted   | 2.66     | 1.24   | 10.58  | 2.14   | 20.42  | 37.25    | 7.84     |
| Difference, % | | | | | | | |
| A − R     | −6.62   | −8.15  | −23.55 | −17.37 | −10.71 | −2.67    | −35.74   |
| R − PCT   | −4.97   | −6.25  | −0.14  | −21.99 | 7.72   | −4.52    | 36.01    |
| A − PCT   | −11.26  | −13.89 | −23.67 | −35.54 | −3.82  | −7.06    | −12.60   |

Abbreviations: A = new anatomy; PCT = planning computed tomography; R = recalculated.
Table 3  Dose-distribution difference between recalculated and new anatomy cone beam computed tomography for GTV and organs at risk

| Recalculated – adapted difference | Paired differences | t    | dF | Significance       |
|----------------------------------|--------------------|------|----|--------------------|
|                                  | Mean  | SD   | Mean standard error | 95% confidence interval | Lower | Upper |
| GTV $D_{\text{mean}}$            | -0.11484 | 0.05177 | 0.01035 | -0.13621 | -0.09347 | 11.092 | 24 | < .0001 |
| GTV $D_{95}$                     | -0.9840  | 0.04930 | 0.00986 | -0.11875 | -0.07805 | -9.980 | 24 | < .0001 |
| Right kidney $D_{\text{mean}}$  | 0.12064  | 0.06702 | 0.01340 | 0.09297  | 0.14831  | 9.000  | 24 | < .0001 |
| Right kidney $D_{30}$           | 0.12644  | 0.13011 | 0.02602 | 0.07273  | 0.18015  | 4.859  | 24 | < .0001 |
| Right kidney $D_{60}$           | 0.02056  | 0.02488 | 0.00498 | 0.01209  | 0.03083  | 4.131  | 24 | < .0001 |
| Liver $D_{\text{mean}}$         | 0.09836  | 0.05890 | 0.01178 | 0.07405  | 0.12267  | 8.349  | 24 | < .0001 |
| Heart $D_{\text{mean}}$         | 0.18200  | 0.08940 | 0.01788 | 0.14510  | 0.21890  | 10.179 | 24 | < .0001 |

Abbreviations: GTV = gross tumor volume; SD = standard deviation.

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