Original Research Article

Volumetric-modulated arc therapy as an alternative to intensity-modulated radiotherapy for primary tumors of advanced non–small-cell lung cancer: A multicenter retrospective analysis based on propensity score matching

Jie Liu¹-³, Tao Li⁴, Xiaohu Wang⁵, Shengfa Su¹,⁶, Qingsong Li¹,⁶, Yichao Geng¹,⁶, Wengang Yang¹,⁶, Xiaxia Chen¹,⁶, Welwei Ouyang¹,⁶, Wei Zhang¹,², Bing Lu¹,⁶*,

¹Department of Thoracic Oncology, Affiliated Hospital, ²Teaching and Research Section of Oncology, ³The Fourth People’s Hospital of Guiyang, Guiyang, China, ⁴Sichuan Cancer Hospital and Institute, Sichuan, ⁵The First Clinical Medical College of Lanzhou University, Gansu Provincial Cancer Hospital, ⁶Affiliated Cancer Hospital of Guizhou Medical University, Guizhou, China

*For correspondence: Email: liuygmaaaaa@163.com

Sent for review: 21 June 2022 Revised accepted: 29 September 2022

Abstract

Purpose: To investigate the effect of volumetric-modulated arc therapy (VMAT) versus intensity-modulated radiotherapy (IMRT) for advanced non–small-cell lung cancer (NSCLC).

Methods: Cases in which the primary tumors were treated with IMRT or VMAT as initial intervention in stages III and IV NSCLC patients from September 2008 to March 2020 were retrospectively analyzed. Propensity Score Matching (PSM) was used to assess the efficacy and toxicity of the two radiotherapy techniques.

Results: A total of 637 patients were included, out of which 483 cases were treated with IMRT, while 154 received VMAT. A total of 308 patients were selected after PSM. Patients who were having acute radiation esophagitis and pneumonia treated with VMAT had a lower percentage than those treated with IMRT (p < 0.05) before PSM. However, there was no significant difference in grades 3-4 toxicity (χ² = 2.77, p = 0.096). There were also no significant differences in the primary endpoints between the two groups after PSM (p > 0.05), while for secondary endpoints, all lung V5, V20, mean lung dose and heart V40, mean heart dose in all patients and stage N2 patients in VMAT after PSM were significantly lower than those of IMRT (p < 0.05).

Conclusion: Radiation therapy of A-NSCLC primary tumors using VMAT and IMRT seem to produce similar efficacy. The volume parameters of normal tissues and organs is significantly lower in VMAT, especially in patients with stage N2. Therefore, VMAT may be more beneficial for reducing radiation damage in normal tissues and organs.

Keywords: Non–small-cell lung cancer, Volumetric-modulated arc therapy, Survival, Local progression-free survival, Radiation damage, Dose-volume parameter

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0) and the Budapest Open Access Initiative (http://www.budapestopenaccessinitiative.org/read), which permit unrestricted use, distribution, and reproduction in any medium, provided the original work is properly credited.

Tropical Journal of Pharmaceutical Research is indexed by Science Citation Index (SciSearch), Scopus, Web of Science, Chemical Abstracts, Embase, Index Copernicus, EBSCO, African Index Medicus, JournalSeek, Journal Citation Reports/Science Edition, Directory of Open Access Journals (DOAJ), African Journal Online, Bioline International, Open-J-Gate and Pharmacy Abstracts

© 2022 The authors. This work is licensed under the Creative Commons Attribution 4.0 International License
INTRODUCTION

A lot of studies have shown that chemotherapy and molecular targeted therapy, combined with three-dimensional conformal radiotherapy (3D-CRT), intensity-modulated radiotherapy (IMRT), and stereotactic body radiotherapy (SBRT), can prolong overall survival (OS) [1–4], especially in patients with cancer oligometastases. But two phase II prospective studies confirmed that randomization to 3D-CRT or IMRT for stage IV non–small-cell lung cancer (NSCLC) prolonged survival. The characteristics of 3D-CRT or IMRT were not analyzed [5,6].

A study showed that the cases after chemotherapy combining molecular targeted therapy with no disease progression in oligometastatic NSCLC, which then had SBRT therapy versus drug therapy alone, showed that the PFS and OS were significantly prolonged in patients treated with radiotherapy. However, which radiotherapy technique had better efficacy is still unclear, because the therapy plan was determined by the radiotherapists participating in the study, and there was no choice of radiotherapy technology or divided dose administration [7].

Iyengar et al [8] indicated that chemotherapy combined with radiotherapy significantly prolonged PFS in EGFR wild-type stage IV non-small cell lung cancer compared with chemotherapy alone. Although the segmented dose was described in the study, there was no analysis of the use of different three-dimensional radiotherapy modalities. A meta-analysis by Petrelli et al [9] confirmed that radiotherapy of primary tumors significantly prolonged OS and PFS.

This study included the analysis of using 3D-CRT, IMRT, SBRT, etc., but also did not have radiotherapy techniques comparison. Advanced NSCLC is characterized by late stage (T3-4 accounts for 64 %, N2-3 accounts for 83 %), large size, spatial diversity, and high primary tumor failure rate [5,10-11].

Studies have shown that improving the primary tumor control rate can prolong survival. In order to improve the primary tumor control rate, this study compared IMRT with Volumetric Modulated Arc Therapy (VMAT), which has more optimized conformation, composite lung V20 and dose monitor unit (MU), and better radiophysical quality assurance [12-14]. The clinical value of VMAT technology was evaluated in the treatment of primary tumors of A-NSCLC by propensity score matching.

METHODS

Inclusion criteria

The case selection criteria were as follows: (1) pathologically diagnosed untreated stage III – IV non-small cell lung cancer patients; (2) between 18 and 80 years old; (3) Karnofsky performance status (KPS) score ≥ 70 %; (4) primary tumor radiation therapy using IMRT or VMAT techniques; (5) primary tumor irradiation total dose ≥ 40 Gy, fractionated dose ≥ 2 Gy; (6) patients with no driver gene mutation received more than 2 cycles of chemotherapy; (7) patients with EGFR-sensitive mutations receive primary recommended treatment; (8) patients have accepted recent efficacy and acute radiation toxicity evaluation; (9) follow-up information is complete. In this study, oligometastases were defined as 1 - 5 distant metastases [15,16].

Approval for this study was received from the institutional ethical committee, and the study followed international guidelines for human studies.

Radiotherapy protocol

A 6-MV X-ray from Elekta Infinity linear accelerator was first selected. Computed tomography was simulated with a 5-mm-layer thickness enhancement scan. The treatment was planned using Pinnacle [14]. The gross tumor volume (GTV) was defined as primary lesion and regional lymph nodes (The single lymph node with a short diameter of ≥ 1.0 cm or at least three lymph nodes with a diameter of ≥ 0.5 cm).

The clinical target volume (CTV) was defined as a three-dimensional expansion of the GTV edge by 0.6 cm and combined with anatomical barriers, and the planning target volume (PTV) was defined as a three-dimensional expansion of the CTV edge by 0.5 to 1 cm. The Pinnacle system [14] was used to complete the radiotherapy plan design. The IMRT of the primary tumor employed four to eight coplanar or non-coplanar fields, and VMAT required two to four arcs. The plan evaluation required that the prescribed dose covered 100 % of the GTV volume; 95 % of the prescribed dose included 95 % or more of the PTV volume for stage III cases, and 90 % of the prescribed dose included 98 % or more of the PTV volume for stage IV patients. In this case mean lung dose (MLD) ≤ 20 Gy and all lung V20 ≤ 32 %. Primary tumor radiotherapy using IMRT or VMAT techniques. The first course of radiotherapy was given in 1.8 - 2 Gy fractions for 5 days a week at a total dose of 36 – 40 Gy, whereas late-course of radiotherapy was
given in 1.5 Gy fractions for 5 days a week at a total dose of 21 – 30 Gy.

**Systemic therapy protocol**

Platinum-based two-drug combination regimen was used in this study [17]. Platinum drugs refer to cisplatin or carboplatin, and platinum combined with docetaxel, paclitaxel, pemetrexed or vinorelbine were used, 21 - 28 days as a cycle, and 2 - 6 cycles of the treatment. Molecular targeted therapy selects drugs based on the type of sensitive mutations in driver genes.

**Evaluation of therapeutic efficacy and acute toxicity**

The responses of the primary tumors, including complete response (CR), partial response (PR), stable disease (SD), and progressive disease (PD), were evaluated according to the RECIST 1.1 standard [18]. The CR + PR was defined as response rate (RR), CR + PR + SD was defined as disease control rate (DCR). Radiation damage to the lungs, esophagus, and heart was assessed according to the Radiotherapy Oncology group (RTOG) radiation damage grading criteria.

**Outcomes**

The primary endpoints were response, local control rate (LCR), local-regional progress-free survival (LRPFS) of primary tumor, acute radiation pneumonitis (RP) and esophagitis (RE). The secondary endpoints were all lung (V5, V20) MLD; heart (V30, V40) MHD; V50 of esophagus, two-years overall survival (OS) and other dose-volume parameters.

**Statistical analysis**

Statistical tests were done with Statistical Package for the Social Sciences version 26.0 software (Chicago, IL). The PSM characteristics including sex, age, pathological type, T/N/M staging, GTV, primary lesion location, clinical stage, metastasis status, targeted therapy, chemotherapy cycle, prescription dose, and other factors for IMRT and VMAT and the matching tolerance was 0.02. Survival analysis used Kaplan–Meier and log-rank methods; local control rate was calculated by the life table method; and recent measurements, radiation injury, and dose-volume parameters were determined using chi-squared test. P-value of 0.05 or less was considered statistically significant.

**RESULTS**

**Clinical characteristics**

From September 2008 to March 2020, 637 cases met the case selection criteria. In the study population, the male to female ratio was 2.5:1; the median age was 56 years (range 22 – 79 years); and there were 51, 91, 68, and 427 patients in stages IIIA, IIIB, IIIC, and IV, respectively. Of the 637 cases, 102 cases of driver gene-sensitive mutations were detected before treatment (including 83 cases of EGFR mutations and 19 cases of ALK mutations), and only 10.20 % of patients received molecular targeted therapy (including Gefitinib in 28 cases, Icotinib in 22 cases, Ositinib in two cases, and Crizotinib in 13 cases), while chemotherapy was used in 89.80 % of the total 637 cases. Before PSM, the proportions of N2–3 and IV stages among IMRT patients was higher than that in VMAT (p < 0.05), the radiation therapy dose and GTV were also similar before PSM (p > 0.05). After PSM, there were 308 patients (154 pairs) with a median age of 58 years. The clinical baseline conditions of the two groups were similar (p > 0.05) Table 1.

**Response to radiotherapy with different techniques for primary tumors**

Before PSM, the response of treatment with IMRT showed that CR, PR, SD, and PD were 1.7, 69.4, 18.2, and 10.8 %, respectively. The response of treatment with VMAT showed CR, PR, SD, and PD were 1.3, 72.1, 21.4, and 5.2 %, respectively. The RR of IMRT was 71.01 % and RR of VMAT was 73.37 % (χ² = 1.037, P = 0.370, P=0.197) Table 2. After PSM, the response of treatment with IMRT showed that CR, PR, SD, and PD were 1.3, 72.7, 19.5, and 6.5 %, respectively. The response of treatment with VMAT showed CR, PR, SD, and PD were 1.3, 72.1, 21.4, and 5.2 %, respectively. The RR of IMRT was 72.72 % and RR of VMAT was 73.72 % (χ²=1.662, P=0.197), the DCR of IMRT was 93.50 % and of VMAT was 94.08 % (χ²=2.781, P=0.427). After PSM, the response of treatment with IMRT showed that CR, PR, SD, and PD were 1.3, 72.7, 19.5, and 6.5 %, respectively. The response of treatment with VMAT showed CR, PR, SD, and PD were 1.3, 72.1, 21.4, and 5.2 %, respectively. The RR of IMRT was 72.72 % and RR of VMAT was 73.37 % (χ²=0.370, P=0.197) (Table 2). Before PSM, the 1- year local control rates with IMRT and VMAT were 93.2 % vs. 93.3 %, and the 2-year local control rates with IMRT and VMAT were 76.2 % vs. 86.1 % (χ²=0.292, P = 0.589). After PSM, the 1- year local control rates with IMRT and VMAT were 93.50 vs. 93.3 %, and the 2-year local control rates with IMRT and VMAT were 76.1 vs. 86.1 % (χ²= 0.467, P = 0.490).
Table 1: Clinical characteristics of 637 patients for A-NSCLC with IMRT or VMAT before and after PSM

| Variable                  | Before PSM | P-value | After PSM | P-value |
|---------------------------|------------|---------|-----------|---------|
|                           | IMRT (n = 483) | VMAT (n = 154) |           |          |
| Sex (Male/female)         | 344/139    | 113/41  | 0.606     | 113/41  | 1.000   |
| Age (years)               | 22–79      | 28–78   | 0.717     | 30–77   | 0.680   |
| Median age (years)        | 58         | 58      |           | 58      |         |
| Pathological type         |            |         | 0.179     |         | 0.426   |
| Squamous cell carcinoma   | 180        | 64      |           | 73      |         |
| Adenocarcinoma            | 273        | 84      |           | 74      |         |
| Other                     | 30         | 6       |           | 7       |         |
| Primary lesion site       |            |         | 0.404     |         | 0.458   |
| Right upper lung          | 125        | 43      | 0.606     | 48      | 0.43    |
| Right middle lung         | 50         | 12      | 0.717     | 17      | 0.12    |
| Right lower lung          | 87         | 39      | 0.542     | 29      | 0.39    |
| Upper left lung           | 129        | 34      | 0.717     | 38      | 0.34    |
| Lower left lung           | 92         | 26      | 0.857     | 22      | 0.26    |
| Gene mutation             | 54         | 48      | 0.857     | 47      | 0.48    |
| Targeted therapy          | 50         | 15      | 0.827     | 20      | 0.15    |
| Chemotherapy              | 433        | 139     | 0.260     | 134     | 0.139   |
| Transfer situation        |            |         | 0.058     |         | 0.831   |
| Oligo transfer            | 302        | 63      |           | 69      | 0.63    |
| Non-oligo transfer        | 45         | 17      |           | 19      | 0.17    |
| T stage                   |            |         | 0.998     |         | 0.324   |
| T1–2                     | 160        | 51      | 0.305     | 43      | 0.51    |
| T3–4                     | 323        | 103     | 0.035     | 111     | 0.103   |
| N stage                   |            |         |           |         | 0.874   |
| N0–1                     | 61         | 10      |           | 10      | 0.10    |
| N2                       | 157        | 53      |           | 51      | 0.53    |
| N3                       | 265        | 91      |           | 93      | 0.91    |
| M stage                   |            |         |           |         | 0.437   |
| M0                       | 136        | 74      |           | 66      | 0.74    |
| M1a                      | 57         | 20      |           | 17      | 0.20    |
| M1b                      | 203        | 23      |           | 36      | 0.23    |
| M1c                      | 87         | 37      |           | 35      | 0.37    |
| Stage (III/IV)            | 136/347    | 74/80   | 0.000     | 66/88   | 0.491   |
| GTV (cm³)                 |            |         | 0.335     |         | 0.104   |
| III                      | 205 ± 185  | 212 ± 193 | 0.000   | 216 ± 190 | 212 ± 193 |
| IV                       | 224 ± 179  | 194 ± 169 |          | 239 ± 151 | 194 ± 169 |
| III+IV                   | 216 ± 181  | 200 ± 175 |          | 228 ± 167 | 200 ± 175 |
| Prescribed dose/median (Gy) | 40–76.5/63 | 40–71/64   | 0.056   | 40–76/63  | 40–71/64   |

Table 2: The recent results of IMRT and VMAT before and after PSM in the treatment of primary tumors

| Group       | Technology | Cases | CR | PR | SD | PD | RR (%) | χ² | P-value | DCR (%) | χ² | P-value |
|-------------|------------|-------|----|----|----|----|--------|-----|---------|---------|----|---------|
| Before PSM  | IMRT       | 483   | 8  | 335| 88 | 52 | 71.01  | 1.037| 0.309   | 89.23   | 0.271| 0.427   |
|             | VMAT       | 154   | 2  | 111| 33 | 8  | 73.37  |     |         | 94.8    |    |         |
| After PSM   | IMRT       | 154   | 2  | 112| 30 | 10 | 72.72  | 1.662| 0.197   | 93.50   | 0.370| 0.946   |
|             | VMAT       | 154   | 2  | 111| 33 | 8  | 73.37  |     |         | 94.80    |    |         |

LRPFS after PSM

The 1-year LDFS with IMRT and VMAT radiotherapy were 67.5 vs. 68.8%. The 2-year LDFS with IMRT and VMAT radiotherapy were 29.9 vs. 51.2%, and the median LDFS of IMRT and VMAT was 19 months vs. 29 months respectively (χ² = 1.525, P = 0.217). Stratified analysis showed that stage III patients under the 1-year LDFS with IMRT and VMAT radiotherapy were 80.3 vs. 73.4%. The 2-year LDFS with IMRT and VMAT radiotherapy were 42.9 vs. 63.1% (χ² = 0.023, P = 0.880). In stage IV patients, the 1-year LDFS with IMRT and VMAT radiotherapy were 57.9 vs. 65.0%. The 2-year LDFS with IMRT and VMAT radiotherapy were 20.4 vs. 41.8% (χ² = 2.242, P = 0.119), and the median LDFS of IMRT and VMAT was 14 months vs. 18 months, respectively (χ² = 2.242, P = 0.119) Figure 1 A–C.
The 1- and 2-year OS after PSM

The 1-year OS with IMRT and VMAT radiotherapy were 70.1 vs. 69.9 %, the 2-year OS with IMRT and VMAT radiotherapy were 31.3 vs. 50.1 %, respectively (χ² = 1.543, P = 0.214). Stratified analysis showed that in stage III patients, the 1-year OS with IMRT and VMAT radiotherapy were 81.8 vs. 74.1 %. The 2-year OS with IMRT and VMAT radiotherapy were 44.7 vs. 67.5 % (χ² = 0.076, P = 0.782). In stage IV patients, the 1-year OS with IMRT and VMAT radiotherapy were 61.3 vs. 66.4 %, and the 2-year OS with IMRT and VMAT radiotherapy were 21.4 vs. 37.1%, respectively (χ² = 2.023, P = 0.155) Figure 2 A–C.

RP and RE treated with different techniques

There was no grade 5 damage in the all patients. Before PSM, the incidences of RE and RP in

| Group       | Acute toxicity | IMRT | VMAT | χ² | p-value |
|-------------|----------------|------|------|----|---------|
| Before PSM  | RE             | 127  | 50   | 0  | 1.336   | .721   |
|             | RP             | 209  | 109  | 0  | .533    | .912   |
| After PSM   | RE             | 60   | 30   | 0  | 0.533   | .912   |
|             | RP             | 109  | 21   | 0  | .533    | .912   |

Figure 1: IMRT or VMAT radiotherapy for primary tumor LPFS after PSM. (A) Stages III through IV, (B) stage III, and (C) stage IV

Figure 2: (A) The OS of IMRT or VMAT primary tumor radiotherapy after PSM. All patients; (B) The OS of IMRT or VMAT primary tumor radiotherapy after PSM. stage III, and (c) stage IV. (C) The OS of IMRT or VMAT primary tumor radiotherapy after PSM. stage IV
DISCUSSION

The results of this study showed that male to female ratio was 2.5 vs. 1, the median age was 58 years. This research also found adenocarcinoma and squamous cell carcinoma cases to be about 94.3% of the study population, which is similar to the epidemiological characteristics of the incidence of NSCLC [19]. The T3–4 and N2–3 cases were 67 and 88.9%, respectively. The average volume of GTV was 200 cm³. There was no significant difference in the distribution of primary lesions between patients who received VMAT or IMRT, respectively. The disease stage was late, and mediastinal lymph node metastasis was obvious [5, 20]. The proportions of N2–3 and stage IV patients in the pre-PSM IMRT group were relatively high, regardless of stage III or oligometastasis of more than 50% among stage IV NSCLC patients. Research by Yang Y et al [21], also indicated that when the primary tumor is large in size, it is difficult to obtain the local control rate by increasing the dose under the premise of controlling the damage. It is necessary to use the physical characteristics of different three-dimensional radiotherapy techniques to explore the clinical value.

The difference between VMAT and IMRT is that, during the accelerator irradiation process of VMAT, the rotating irradiation is realized by continuous changes in the gantry speed, collimator angle, and dose rate, it has the characteristic of a short irradiation time. Studies on head and neck tumors in elderly patients over 80 years old with irregular target volume and need more protection of organs at risk showed that because VMAT has better conformal degree, when using the same target dose-volume as IMRT, it can significantly reduce the dose of organs at risk and obtain the same disease-free survival rate as young patients. A small sample of A-NSCLC radiation therapy plan dose-volume parameter study showed that VMAT increased the V95% and conformity of the planned target area, and reduced the average dose to the lungs, esophagus, and heart as well. Therefore, in this multicenter and retrospective analysis of VMAT and IMRT treatment, results through PSM showed that the RR, DCR, and LCR were similar both before and after PSM (p > 0.05), suggesting that when VMAT and IMRT have similar primary tumor volume and radiation dose, the efficacy of VMAT in A-NSCLC patients is not lower than that of IMRT. There was no significant difference in LRPFS in the whole group nor during stratified analysis under the premise of the same baseline conditions after PSM, indicating that VMAT combined with drugs can be used in the first-line treatment of A-NSCLC with a long-term efficacy similar to that of IMRT. Moreover, the 1-, and 2-year OS rates of VMAT combined with chemotherapy in the first-line treatment of stage IV NSCLC patients were 66.4 and 37.1%, respectively, which it is higher than the 1-, and 2-year OS rates of 35 and 10%, respectively. This is associated with platinum-containing two-drug regimen first-line chemotherapy, suggesting a prolonged survival rate [4].

In summary, the effect of VMAT in the treatment of A-NSCLC was similar to that of IMRT, which can improve recent efficacy and OS. The

Table 4: Normal tissue dose-volume parameters of IMRT and VMAT radiotherapy for primary tumor after PSM

| Variable | Staging | IMRT | VMAT | P-value |
|----------|---------|------|------|---------|
| All lung | All patients | 67.06 ± 13.36 | 56.90 ± 16.28 | 0.000 |
|          | N2      | 63.74 ± 14.41 | 48.22 ± 15.84 | 0.000 |
|          | N3      | 70.55 ± 13.66 | 62.50 ± 13.72 | 0.000 |
| All lung | All patients | 28.10 ± 6.17 | 25.71 ± 6.88 | 0.001 |
|          | N2      | 27.02 ± 6.30 | 22.36 ± 7.76 | 0.000 |
|          | N3      | 29.29 ± 4.95 | 23.98 ± 4.84 | 0.154 |
| MLD      | All patients | 17.82 ± 3.54 | 16.21 ± 4.34 | 0.001 |
|          | N2      | 17.30 ± 4.18 | 14.30 ± 4.95 | 0.000 |
|          | N3      | 18.30 ± 3.27 | 17.88 ± 3.20 | 0.312 |
| Heart    | All patients | 25.36 ± 12.88 | 21.58 ± 11.80 | 0.010 |
|          | N2      | 25.29 ± 13.44 | 17.04 ± 11.91 | 0.000 |
|          | N3      | 26.99 ± 14.73 | 24.89 ± 10.82 | 0.230 |
| V30      | All patients | 17.09 ± 9.77 | 14.71 ± 8.99 | 0.017 |
|          | N2      | 17.52 ± 10.85 | 11.98 ± 8.41 | 0.001 |
|          | N3      | 17.82 ± 10.91 | 16.85 ± 8.90 | 0.463 |
| MHD      | All patients | 19.77 ± 8.65 | 17.22 ± 8.09 | 0.019 |
|          | N2      | 19.63 ± 8.62 | 13.74 ± 8.23 | 0.000 |
|          | N3      | 20.36 ± 8.77 | 19.66 ± 7.38 | 0.515 |
| Esophagus| All patients | 32.95 ± 20.03 | 32.37 ± 19.99 | 0.800 |
|          | N2      | 34.84 ± 18.33 | 28.60 ± 18.02 | 0.046 |
|          | N3      | 36.80 ± 20.05 | 35.22 ± 21.05 | 0.545 |

Trop J Pharm Res, October 2022; 21(10): 2238
proportion of primary tumor volume shrinkage is also negatively correlated with the risk of progression failure, and OS is prolonged through radiotherapy, as well as an increased dose and local control rate [5].

It is well known that acute radiation injury caused by the dose-limiting toxicity of radiotherapy, RE and RP over grade 3 are unfavorable factors for the prognosis of NSCLC, and the volume of normal lung low-dose radiation is related to the occurrence of RP. VMAT irradiation needs to be performed through a rotating arc of the gantry, but the low dose volume of normal tissues does not necessarily increase. This study showed that the incidence rates of RP and RE of primary A-NSCLC tumors with a median dose of 64 Gy and an average volume of more than 200 cm³ after VMAT treatment were lower than that of IMRT before PSM. There was no significant difference in grades 3 and 4 acute radiation damage between groups and no significant difference after PSM.

There were suggestions that the rotating irradiation mode of VMAT did not increase the acute radiation injury which was caused by the low dose volume of normal tissue in clinical practice. This study analyzed MHD and the important indicators of RE and RP (esophageal V50 and all lung V5, V20, MLD), showing that VMAT has more advantages. After PSM, the dose-volume parameters of VMAT technology were more advantageous, especially for N2 cases in stratified analysis, suggesting that radiotherapy with VMAT technology may be a better choice for N2 patients. While N3 patients with only normal whole-lung V5 had parameters significantly lower than IMRT group (p = 0.000), further suggesting that the VMAT rotary irradiation method has a more reasonable dose distribution and maintains the low dose volume to reduce radiation damage.

The VMAT rotary irradiation method has the advantage of a more reasonable dose distribution and better control of low dose volume to reduce radiation damage, especially in patients with mediastinal lymph node metastasis only on the same side. More importantly, the reduction in dose volume may reduce the damage to normal tissues, especially heart tissue damage.

CONCLUSION

The application of VMAT for primary tumor radiotherapy in A-NSCLC achieves similar efficacy to IMRT, but it may be more advantageous to use this approach to reduce acute radiation injury, especially for late cardiac damage. Further research will be required to establish this.

DECLARATIONS

Acknowledgements

This work was supported by Science and Technology Office of Guizhou Province, China (grant Qian ke He Support (2019) no. 2795).

Funding

None provided.

Ethical approval

None provided.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

The authors declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by them.

Open Access

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0) and the Budapest Open Access Initiative (http://www.budapestopenaccessinitiative.org/road), which permit unrestricted use, distribution, and reproduction in any medium, provided the original work is properly credited.

REFERENCES

1. Kunitoh H, Kato H, Tsuboi M, Shibata T, Asamura H, Ichinose Y, Kakizaki N, Nagai K, Mitsudomi T, Matsumura A, et al. Phase II trial of preoperative chemoradiotherapy followed by surgical resection in patients with superior sulcus non-small-cell lung Trop J Pharm Res, October 2022; 21(10): 2239
2. Cong Z, Jiang T, Liu X, Jiao X, Wang W, Liu X, Zhao L. Safety and clinical outcomes of regional anaesthesia in Chinese patients with non-small cell lung cancer undergoing non-intubated lobectomy. Trop J Pharm Res 2021; 20(10): 2149-2154 doi: 10.4314/tjpr.v20i10.19.

3. Qin Y, Xie J, Wang H. Efficacy and safety of combined use of docetaxel-gemcitabine chemotherapy and 5-fluorouracil targeted therapy in the treatment of advanced non-small cell lung cancer. Trop J Pharm Res 2022; 21(7):1523-1529 doi: 10.4314/tjpr.v21i7.24.

4. Su S, Hu Y, Ouyang W, Ma Z, Lu B, Li Q, Li H, Wang Z, Wang Y. The survival outcomes and prognosis of stage IV non-small-cell lung cancer treated with thoracic three-dimensional radiotherapy combined with chemotherapy. Radiat Oncol 2014; 9: 290.

5. Lu J, Qiang H, Chu T. Atorvastatin suppressed proliferation and facilitated apoptosis of A549 cells through mediating recruitment of Fas and CD59 in lipid raft. Trop J Pharm Res 2022; 21(2):237-244 doi: 10.4314/tjpr.v21i2.4.

6. Su S, Li T, Lu B, Wang X, Li J, Chen M, Lu Y, Bai Y, Hu Y, Ouyang W, et al. three-dimensional radiation therapy to the primary tumor with concurrent chemotherapy in patients with stage IV non-small cell lung cancer: results of a multicenter phase 2 study from PPRA-RTOG, China. Int J Radiat Oncol Biol Phys 2015; 93(4): 769-777.

7. Gomez DR, Blumenschein GJ, Lee JJ, Hernandez M, Ye R, Camidge DR, Doebele RC, Skoulidas F, Gaspar LE, Gibbons DL, et al. Local consolidative therapy versus maintenance therapy or observation for patients with oligometastatic non-small-cell lung cancer without progression after first-line systemic therapy: a multicentre, randomised, controlled, phase 2 study. Lancet Oncol 2016; 17(12): 1672-1682.

8. Iyengar P, Wardak Z, Gerber DE, Tumati V, Ahn C, Hughes RS, Dowell JE, Chedella N, Nedzi L, Westover KD, et al. Consolidative radiotherapy for limited metastatic non-small-cell lung cancer: A Phase 2 Randomized Clinical Trial. Jama Oncol 2018; 4(1): e173501.

9. Petrelli F, Ghidini A, Cabiddu M, Tomasello G, De Stefani A, Bruschieri L, Vitali E, Ghiardi M, Borgonovo K, Barni S, et al. Addition of radiotherapy to the primary tumour in oligometastatic NSCLC: A systematic review and meta-analysis. Lung Cancer 2018; 126: 194-200.

10. Xie M, Liu H, Houwing-Duistermaat J. Nonparametric clustering for longitudinal functional data with the application to H-NMR spectra of kidney transplant patients. Longitudinal functional data clustering. Theor Biol Forum 2021; 114(1-2): 15-28.

11. Wang B, Zhang X, Lin L, Hao X, Zhang X, Li J, Shi Y. Progressive patterns of gifitinib treating advanced non-small cell lung cancer after obtained resistance. Zhongguo Fei Ai Za Zhi 2013; 16(10): 510-513.

12. Abbas AS, Moseley D, Kassam Z, Kim SM, Cho C. Volumetric-modulated arc therapy for the treatment of a large planning target volume in thoracic esophageal cancer. J Appl Clin Med Phys 2013; 14(3): 4269.

13. Yadav G, Bhushan M, Dewan A, Saxena U, Kumar L, Chauhan D, Raman K, Mitra S, Suhail M. Dosimetric influence of photon beam energy and number of arcs on volumetric modulated arc therapy in carcinoma cervix: A planning study. Rep Pract Oncol Radiother 2017; 22(1): 1-9.

14. Young LA, Yang F, Cao N, Meyer J. Rounded leaf end modeling in Pinnacle VMAT treatment planning for fixed jaw linacs. J Appl Clin Med Phys 2016; 17(6): 149-162.

15. Kang X, Chen K. The conceptual oligometastatic non-small cell lung cancer and therapeutic strategies. Zhongguo Fei Ai Za Zhi 2012; 15(4): 242-245.

16. Rusthoven CG, Yeh N, Gaspar LE. Radiation therapy for oligometastatic non-small cell lung cancer: theory and practice. Cancer J 2015; 21(5): 404-412.

17. Delbaldo C, Michiels S, Syz N, Sonia JC, Le Chevalier T, Pignon JP. Benefits of adding a drug to a single-agent or a 2-agent chemotherapy regimen in advanced non-small-cell lung cancer: a meta-analysis. JAMA 2004; 292(4): 470-484.

18. Eisenhauer EA, Therasse P, Bogaerts J, Schwartz LH, Sargent D, Ford R, Dancey J, Arbuck S, Gwyther S, Gwyther, S, Mooney M, et al. New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). Eur J Cancer 2009; 45(2): 228-247.

19. Fuady AM, El Bouhaddani S, Uh HW, Houwing-Duistermaat J. Estimation of the effect of surrogate multi-omic biomarkers. Theor Biol Forum 2021; 114(1-2): 59-73.

20. Morgensztern D, Ng SH, Gao F, Govindan R. Trends in stage distribution for patients with non-small cell lung cancer: a National Cancer Database survey. J Thorac Oncol 2010; 5(1): 29-33.

21. Yu Y, Guan H, Xing LG, Xiang YB. Role of gross tumor volume in the prognosis of non-small cell lung cancer treated with 3D conformal radiotherapy: a meta-analysis. Clin Ther 2015; 37(10): 2256-2266.