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Treatment planning for non-small cell lung tumours: VMAT versus 3DCRT a quantitative dosimetric study

Ahmed Hadj Henni, Yann Lauzin, Nicolas Pirault, Brian Dubos, Maximilien Roge, Perrine Clarisse, David Gensanne and Sebastien Thureau

Centre Henri Becquerel, Rouen, France

Original Article

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Author for correspondence:
Ahmed Hadj Henni, Centre Henri Becquerel, 1 rue d'Amiens 76000, Rouen, France.
Tel: +33(0)2 32 08 25 85.
E-mail: ahmed.hadj-henni@chb.unicancer.fr

Abstract

Purpose: The dosimetric impact of volumetric modulated arc therapy (VMAT) in lung cancer compared with 3D conformal radiotherapy (3DCRT) is well known. However, this improvement is often associated with an increase in low doses. The aim of this study is to quantify these results more accurately.
Methods: For each patient treated with 3DCRT, a second VMAT treatment plan was calculated. Usual dosimetric parameters such as target coverage or dose to the organs at risk were used to achieve the comparisons.
Results: For planning target volume, homogeneity and conformity indices showed superiority of VMAT (respectively 0·07 and 0·87) compared to 3DCRT (0·11 and 0·57). For spinal cord planning organ at risk volume, the median maximum dose was 45·6 Gy in 3DCRT against 19·3 Gy in VMAT. Heart volume receiving at least 35 Gy (V_{35}) decreased from 15·64% in 3DCRT to 8·28% in VMAT. Oesophagus V_{50} was higher in 3DCRT (25·45%) than in VMAT (14·03%). The mean lung dose was 17·9 Gy in 3DCRT versus 15·5 Gy in VMAT. Moreover, volumes receiving 5, 10 and 15 Gy were not significantly different between the two techniques when VMAT was performed with partial arcs.
Conclusion: All the dosimetric parameters were improved with VMAT compared to the 3DCRT without increasing low doses when using partial arcs.

Background

The objective of external radiotherapy is to deliver the most ablative dose to the target volume while sparing the surrounding healthy tissues. For this purpose, irradiation techniques developed to be delivered by linear accelerators are the 3D conformal radiotherapy (3DCRT) and the intensity modulated radiotherapy (IMRT).

Compared with 3DCRT, the expected benefits of intensity modulation are a better conformation to planning target volume (PTV), especially for complex forms, and a better savings of organs at risk (OAR).[1]

Today, validated indications in France for IMRT are the head and neck cancers, prostate, spine, base of the skull and recently the anal canal and cervical cancer with lymph node invasion.[2] This is not yet the case for non-small cell lung cancer (NSCLC).

However, lung cancer is one of the most important cancer sites in the world with a largely unfavourable prognosis. Five-year survival rates for stage IIIA and IIIB diseases do not exceed 6–8%.[3] Recent studies show that the prognosis of patients can be improved by immunotherapy which makes it important to manage the toxicities induced by treatments (heart and lung).[4] The impact of the dose remains adverse to OAR; however, the majority of the studies are in favour of an increase in the dose.[5,6] The study RTOG0617 is negative for the arm with high-dose of 74 Gy compared to the arm with standard-dose of 60 Gy both with conventional fractionation schemes (2 Gy fractions). The higher dose might increase toxicity in critical organs.[7]

Several studies[8,9] have compared the 3DCRT and volumetric modulated arc therapy (VMAT), which confirm a dosimetric improvement of the latter in terms of conformation to the target volume and reduction in the dose delivered to the OAR. This problem is all the more true since the dose of radiotherapy to OAR can limit therapeutic indications or lead to significant radiotoxicities, which can be increased by the addition of immunotherapy in maintenance. These modern techniques could allow higher and heterogeneous doses to be delivered (dose painting).

Some questions are however raised by some publications concerning low doses to the healthy tissues (V_{5Gy} and V_{10Gy}) due to the multiplication of the number of beam entries during irradiation. Solutions are proposed such as partial arcs or hybrid techniques associating VMAT and 3DCRT.[10,11] Considering that the results are closely related to the way of calculating the

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Table 1. Patient characteristics ($n = 36$)

Age	
Average (years)	61
Sex	
Male	26
Female	10
Histology	
Squamous carcinoma	18
Adenocarcinoma	10
others	6
Clinical stage	
II	6
IIIA	16
IIIB	14
GTV volume (cm^3)	
Median	39·0
Range	0·8–235·5
PTV volume (cm^3)	
Median	352·5
Range	58·1–1363·9
Lungs volume (cm^3)	
Median	3865·6
Range	1909·7–5669·8
Ratio PTV volume/Lungs volume	
Median	0·107
Range	0·019–0·321
Prescription	33 × 2 Gy

Table 2. Dosimetric comparison of both techniques. Median accompanied by the minimum–maximum extreme values for HI and PCI for PTV of 3DCRT and VMAT (up). Constraint and median [min-max] values for the OARs of the two techniques (down)

Volumes	Indices	3DCRT	VMAT	*p*
PTV	PCI	0·57 [0·14; 0·80]	0·87 [0·78; 0·95]	<0·001
PTV	HI	0·11 [0·07; 0·47]	0·07 [0·04; 0·27]	<0·001
OAR	**Constraints**	**3DCRT**	**VMAT**	***p***
Spinal cord PRV	Dmax < 46 Gy	45·59 Gy (15.68; 46·44)	19·30 Gy (10·05; 46·42)	<0·001
Heart	V35 < 30%	15·64% (0; 37·77%)	8·28% (0; 28·86%)	<0·001
Oesophagus	V50 < 35%	25·45% (0; 52·96%)	14·03% (0; 40·40%)	0·001
Lungs	Dmean < 20 Gy	17·9 Gy (3·33; 20·93)	15·5 Gy (5·47; 20·11)	0·002
	V30 < 20%	23·6% (0·78%; 29·10%)	18·8% (1·30%; 26·56%)	<0·001
	V20 < 30%	29·0% (1·26%; 38·31%)	24·8% (2·88%; 37·77%)	0·02

treatment plan, we decided in addition to the bibliographical study to undertake a dosimetric comparison of the two irradiation techniques, 3DCRT and VMAT. We will also study the possibility to optimise treatment plans to achieve the best planning option.

Finally, our aim is to evaluate precisely for lung cancer the dosimetric impact that would result from the switching between planning techniques.

Patients and Methods

Patients

This was a retrospective study that included 36 patients treated in our centre with 3DCRT for NSCLC between 2015 and 2017. All these patients had their plans delineated and validated by the same experienced physician. This study did not need ethical approval.

The group consisted in 26 men and 10 women mainly clinical stage IIIA and IIIB. The more detailed characteristics of pathologies and irradiated target volumes are summarised in Table 1. For each patient treated with 3DCRT, a second VMAT treatment plan was calculated using either two complete arcs (VMAT-CA, 5 patients) or two partial arcs (VMAT-PA, 31 patients), depending on the location of the volume to be irradiated. Moreover, to investigate whole-body irradiation at low doses, 14 additional treatment plans initially in VMAT-PA have been re-optimised in VMAT-CA and were used to compare the V_{5Gy}, the V_{10Gy} and the V_{15Gy} to the 3DCRT. All the patients in this study received a total dose of 66 Gy in 33 fractions to PTV.

During the scanner acquisition (GE Optima580RT, Milwaukee, WI, USA) with a 2·5 mm slice thickness, the patient was positioned on a Posirest™ supine head position, with both arms above the head and knees resting on a Kneefix™ wedge (CIVCO Radiotherapy, Orange City, IA, USA). The acquisition area extended from the base of the neck to the lower abdomen.

From the GTVn (gross tumour volume—nodal) and/or GTVt (gross tumour volume—tumour) and then CTVn (clinical target volume—nodal) and/or CTVt (clinical target volume—tumour) volumes delineated by the physician, a margin of 1 cm is added to create the PTV. The objectives of the 3DCRT treatment plans were, in accordance with ICRU (International Commission on Radiation Units and Measurements) recommendations,[12,13] that at least 95% of the dose covers 95% of the volume with a maximum dose of 107%.

The OAR that have been taken into account are the spinal cord planning organ at risk volume (SC PRV), created by adding a symmetrical margin of 5 mm around the spinal cord, lungs, oesophagus and heart. The dose constraints used in clinical routine are those described in Table 2.

Planning treatment techniques

Patients were treated on Varian Linear Accelerators Clinac iX with MLC120 or Truebeam STX MLC120HD (Varian Medical Systems, Palo Alto, CA, USA) with daily kV-CBCT imaging (Figure 1). The dosimetric calculation was performed using the Eclipse treatment planning system (AAA 13.6.23, 0·25 cm grid; Varian Medical Systems).

3DCRT

All of the 36 patients were treated using 3DCRT technique. The treatment plan was based on three beams, 'Y-technique or inverted

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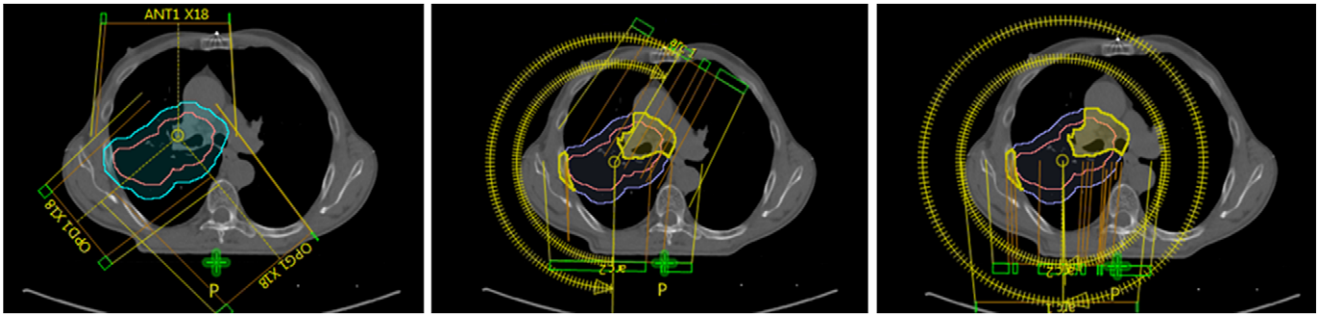


Figure 1. From the left to the right the three treatment plans compared in this study, 3DCRT, VMAT-PA and VMAT-CA. CTV (pink), PTV (blue), PTVair (purple), PTVdense (yellow) volumes are also represented.

Y-technique', with at least one beam that avoided the spinal cord. If necessary a weakly weighted fourth beam was added. The beam energy used was preferentially 6 MV with the possibility of using an 18 MV beam in the case of over-dose in the muscles.[14,15] Normalisation was done at the main reference point centred in the target volume.

Volumetric modulated arc therapy

Treatment plan was performed either with 2 complete arcs (5 plans) or with 2 partial arcs (31 plans), according to the localisation of the volume to be irradiated. The PRO v13.6.23© (Varian Medical Systems) is used for optimisation.

To compare VMAT-PA and VMAT-CA techniques, 14 VMAT-PA plans were re-optimised using complete arcs, in order to obtain 19 VMAT-PA plans. We then compared the low doses of these 19 VMAT-CA plans and the 31 VMAT-PA plans with the 3DCRT technique taken as reference.

The normalisation, 100% of the prescription dose covers 50% of PTV, was following the recommendations of ICRU.[13]

To improve dose gradients, several optimisation rings around the PTV were used. PTVair and PTVdense volumes, respectively, corresponding to the portion of PTV in the parenchyma and in the dense part of the tissue, facilitate the target volume coverage. The volumes OAR—(PTV + 2 mm) also helped to better optimise on the OAR especially for lung—PTV, SC PRV—PTV and heart—PTV.

In all cases, the treatment plan is based on a pair of arcs, one clockwise and the other counterclockwise with collimators set at 30 and 330° to encompass the entire target volume and minimise the tongue and groove effect specific to Varian MLC.[16] The maximum dose rate is set at 600 MU/minutes.

Criteria for comparing 3DCRT and VMAT

Planning target volume

The doses delivered to PTV were obtained with the dose–volume histograms (DVHs). From these DVHs, we compared the Paddick conformity index (PCI)[17] defined by:

$$PCI = \frac{(PTV \cap V_{95\%})^2}{(\mathrm{PTV} \cup \mathrm{V}_{95\%})} \quad (1)$$

The $V_{95\%}$ value corresponding to the volume received at least 95% of the prescribed dose. We also use the homogeneity index (HI) defined by ICRU report 83[13]:

$$HI = \frac{(D_{2\%} - D_{98\%})}{D_{50\%}} \quad (2)$$

The $D_{x\%}$ value is the minimum dose received by x% of PTV. The best plan will be characterised by a PCI closest to 1 and an HI closest to 0.

Organs at risk

Doses to OAR were evaluated using their DVHs and the constraints used in our centre (Table 2).

Statistical study of the data

The comparison of the different techniques is based on non-Gaussian data distributions. It was therefore performed using the non-parametric Wilcoxon test and using the statistical study software R (version 3.4.4). Median, minimum and maximum values were calculated, associated with a p-value with a threshold of 0·05 below which the difference is considered significant.

Results

PTV results

The median DVH of the PTV for both VMAT and 3DCRT techniques shows qualitatively a clear improvement in dose coverage for the intensity modulation (Figure 2).

The PCI as defined in the previous paragraph (1) is greater in VMAT (0·87) compared to the 3DCRT (0·57) ($p < 0{\cdot}001$). The HI (2) is better in VMAT than in 3DCRT, the HI being, respectively, 0·07 and 0·11 ($p < 0{\cdot}001$), see Table 2.

Moreover, for these conformity and homogeneity indices, the interquartile gap is 44 and 50% lower, respectively, in VMAT compared to the 3DCRT, which clearly indicates a lower dispersion in favour of the VMAT and therefore a better reproducibility in treatments (Figure 3).

OAR study

The results of doses to the OAR are summarised in Table 2.

Spinal cord PRV

For the SC PRV, the difference between the median DVHs of VMAT and 3DCRT is clearly visible (Figure 2).

The median maximum dose (Dmax) decreases by 58% in VMAT compared to 3DCRT (19·30 and 45·59 Gy, respectively, $p < 0{\cdot}001$), which represents a difference of more than 25 Gy.

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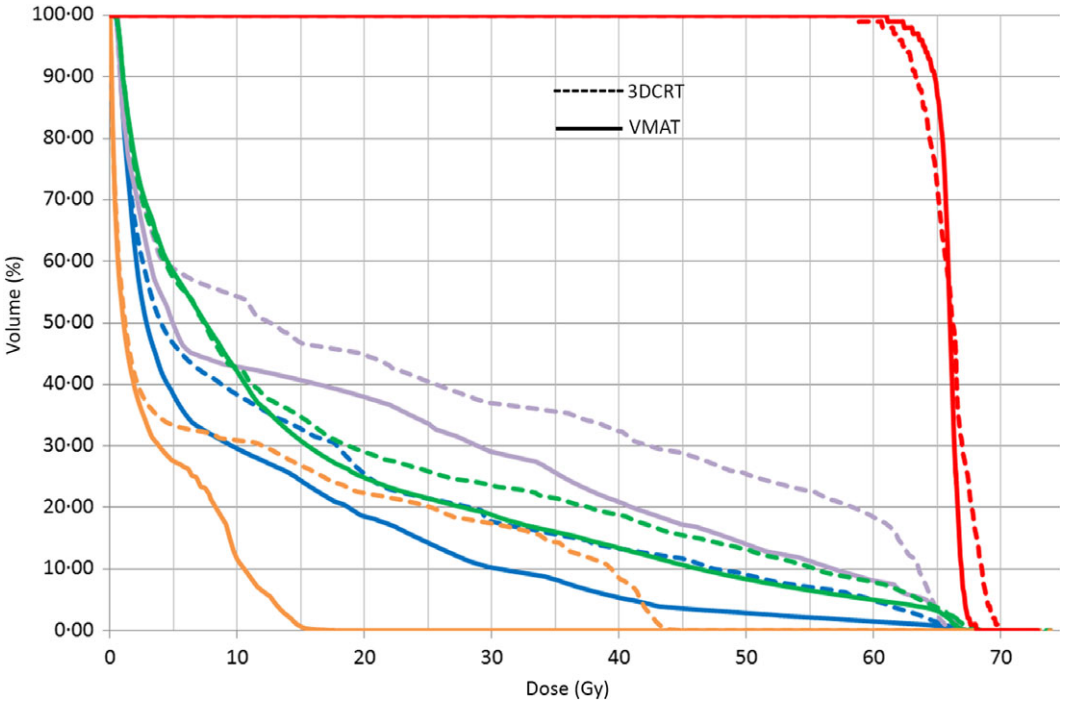


Figure 2. The median DVH for PTV (red) and OARs (oesophagus: purple, lungs: green, heart: blue, SC PRV: orange) of the 3DCRT (dashed curves) and VMAT (solid curves) treatment plans.

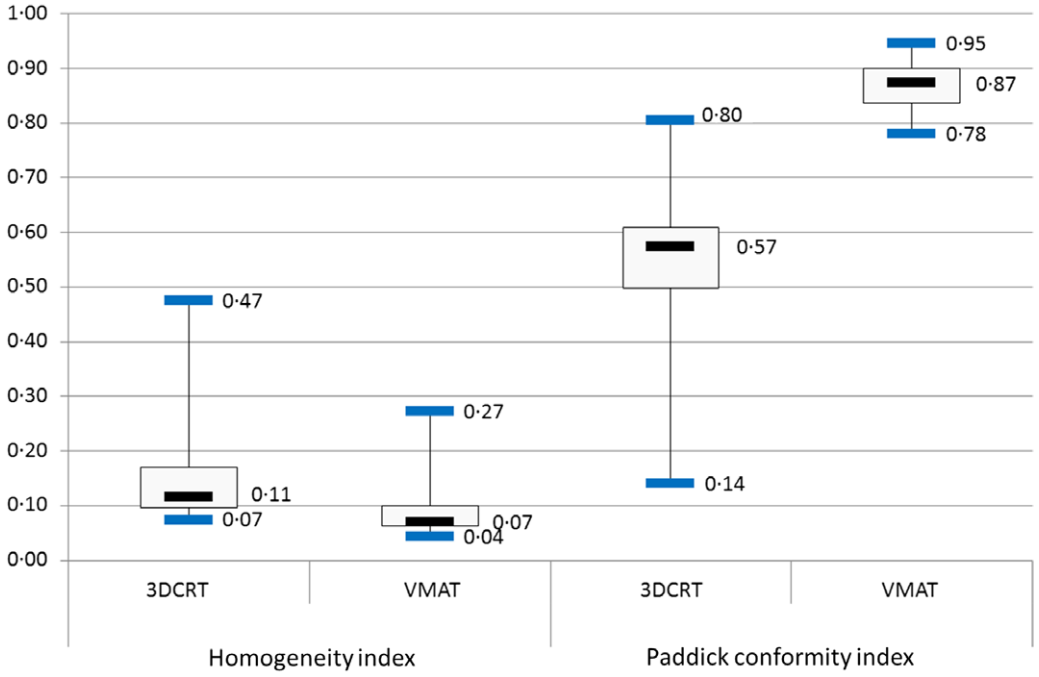


Figure 3. Boxplots for homogeneity index (left) and Paddick conformity index (right) for the two treatment plans.

Heart

Like the spinal cord, a decrease in the doses received by the heart in VMAT compared to the 3DCRT is visible on the median DVH (Figure 2).

The median heart volume receiving at least 35 Gy (V_{35}) decreased by 47%, from 15·64% in 3DCRT to 8·28% in VMAT ($p < 0·001$). The maximum value for the latter technique (28·86%) is lower than the dose constraint set at 30%, unlike the 3DCRT for which the maximum value is 37·77% (Table 2).

Oesophagus

DVH also shows a decrease in doses received by this organ. The V_{50} is significantly higher in 3DCRT than in VMAT (25·45 and 14·03%, with $p < 0·001$, Table 2).

Lungs

The median DVH for the lungs follows the same tendency observed for the other OAR (Figure 2).

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Table 3. Volumes of the low doses to the healthy tissues. Median accompanied by the minimum–maximum extreme volumes for the isodose lines of the 3DCRT versus VMAT-PA techniques (up). The same for the 3DCRT versus VMAT-CA techniques (down)

Isodose lines (Gy)	3DCRT (cm^3)	VMAT-PA (cm^3)	Variation (%)	p
5	6204·2 (3039·2; 11283·7)	6633·8 (2846·7; 10982·0)	6·9	0·379
10	5014·2 (2564·3; 8216·0)	4511·2 (1721·5; 7822·8)	−10·1	0·098
15	3806·3 (1793·8; 6860·8)	3573·4 (994·4; 6241·4)	−6·1	0·061
20	3693·0 (1380·5; 6212·4)	2726·0 (574·4; 5412·2)	−26·2	0·006
Isodose lines (Gy)	**3DCRT (cm^3)**	**VMAT-CA (cm^3)**	**Variation (%)**	**p**
5	6204·2 (3593·2; 10820·4)	7633·9 (4504·1; 14021·7)	23	0·0482
10	4809·4 (2927·0; 8767·6)	5774·7 (2971·9; 11360·5)	20·1	0·0453
15	3806·3 (2225·7; 7189·3)	4319·9 (1473·3; 8626·4)	13·5	0·3118

The mean lungs dose is 17·9 Gy in 3DCRT against 15·5 Gy in VMAT ($p = 0·002$), a decrease of 13%.

The minimum value is higher in VMAT (5·47 Gy) than in 3DCRT (3·33 Gy, Table 2) and the maximum values for the two techniques remain close to the constraint of 20 Gy.

The lungs volume receiving more than 30 Gy (V_{30}) is 23·6% in 3DCRT against 18·8% in VMAT ($p < 0·001$), a decrease of 20%. This latter value meets the 20% constraint used in clinical routine, unlike 3DCRT (Table 2).

For lungs volume receiving more than 20 Gy (V_{20}), the decrease from 29·0% in 3DCRT to 24·8% in VMAT is statistically significant ($p = 0·02$). However, the maximum values for both techniques are very close, respectively, 38·31 and 37·77% (Table 2).

Low doses to the healthy tissue

The isodose lines volumes 5, 10, 15 and 20 Gy (V_{5Gy}, V_{10Gy}, V_{15Gy}, V_{20Gy}) for 31 VMAT-PA plans and the corresponding 31 3DCRT plans are summarised in Table 3. This table also gives the results for 19 VMAT-CA plans and the 19 corresponding 3DCRT plans.

VMAT-PA versus 3DCRT

The median V_{5Gy} of the VMAT-PA plans is 6633·8 cm^3 against 6204·2 cm^3 for the 3DCRT ($p = 0·379$), a decrease of 7% which is not significant.

The median V_{10Gy} of the VMAT-PA plans is 4511·2 cm^3 against 5014·2 cm^3 for the 3DCRT ($p = 0·098$). This decrease of 10% is also not significant.

For the median V_{15Gy}, we find the same tendency with a non-significant 6% decrease in VMAT-PA compared to the 3DCRT (3573·4 and 3806·3 cm^3, respectively, $p = 0·061$).

The difference becomes significant for the V_{20Gy} with a 26% decrease in favour of the VMAT-PA compared to the 3DCRT (2726·0 and 3693·0 cm^3, respectively, $p = 0·006$).

VMAT-CA versus 3DCRT

The median V_{5Gy} of the VMAT-CA plans is 7633·9 cm^3 against 6204·2 cm^3 for the 3DCRT ($p = 0·048$), a decrease of 23% which is this time significant.

We find a similar result for the V_{10Gy} where the VMAT-CA has a median volume significantly higher than 20% of the 3DCRT (5774·7 and 4809·4 cm^3, respectively, $p = 0·045$).

On the other hand, the 13% increase in the median V_{15Gy} volume in VMAT-CA compared to the 3DCRT is no longer significant (4319·9 and 3806·3 cm^3, $p = 0·312$).

Discussion

This study, using a cohort of patients covering a broad spectrum of possible cases, allows us to show a superiority of the dosimetric results obtained by VMAT to the detriment of the 3DCRT.

The homogeneity and conformity indices at the PTV are in favour of the VMAT with a significant improvement.

The gain is also clear for all OAR, for instance, the median maximum dose decrease for the SC PRV from 45·6 Gy for the 3DCRT to 19·3 Gy for the VMAT. This difference of more than 25 Gy could be beneficial in anticipation of a patient re-irradiation. VMAT also spares the heart, oesophagus and lungs better than the 3DCRT.

The V_{20} dose for the lungs in particular is of great importance to our radiation oncologists to prevent the risk of radiation pneumonitis.

The VMAT could finally allow a wider recruitment of patients whose tumour volumes are much larger and could not have been supported by a technique in 3DCRT.

The low doses are the reproach that is commonly addressed to VMAT compared to the 3DCRT. This study confirms quantitatively that it is possible to not increase the low doses compared to 3DCRT if the treatment plan is done with two partial arcs. This strategy is simpler to perform than other proposals such as the hybrid-arc mixing VMAT and 3DCRT.[11] VMAT-PA is therefore the recommended technique in our centre when planning treatment plans for NSCLCs.

Nevertheless, the dosimetric study and the results obtained were a first step in the VMAT set-up for pulmonary tumours, it is not the only point to validate in the patient's care process.

The implementation of this technique requires the validation of other points in the patient's care process. Problems of mobile tumours,[18] doses received by a four-dimensional CT,[19] the use of image-guided radiation therapy[20] and interplay effects are the main ones.[21]

This study is limited to 36 patients and is based on our own treatment planning system and our own consideration of tumour mobility. The IMRT problem is largely related to tumour movements, which must be analysed by each team before the technique is implemented. The risk would be an increase in local recurrences due to isodoses closer to the target volume. Moreover, a study which evaluates the clinical benefits would strengthen the contribution of VMAT for patients treated for NSCLC.

Conclusion

The dosimetric comparison achieved in this study allows us to conclude that VMAT is clearly superior to 3DCRT. The use of partial arcs also keeps the order of magnitude of the low doses at the same level as the 3DCRT.

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The management of NSCLC by VMAT in our centre has evolved from 2% in the first trimester of 2017 to 92% in the last trimester. To date, all of our patients treated for NSCLC benefit from this technique.

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Conflicts of interest. None.

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