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Original research article

Superior sulcus non-small cell lung carcinoma: A comparison of IMRT and 3D-RT dosimetry

Pierre Truntzer[a], *Delphine Antoni*[a,b], *Nicola Santelmo*[c], *Catherine Schumacher*[c], *Pierre-Emmanuel Falcoz*[c], *Elisabeth Quoix*[d], *Gilbert Massard*[c], *Georges Noël*[a,b,*]

[a] *Radiotherapy Department, Centre Paul Strauss, 3, rue de la Porte de l'Hôpital, BP 42, 67065 Strasbourg Cedex, France*

[b] *Radiobiology Laboratory EA 3430, Federation of Translational Medicine in Strasbourg (FMTS), Strasbourg University, Strasbourg, France*

[c] *Thoracic Surgery Department, Nouvel Hôpital Civil, 1, place de l'Hôpital, 67091 Strasbourg Cedex, France*

[d] *Pneumology Department, Nouvel Hôpital Civil, 1, place de l'Hôpital, 67091 Strasbourg Cedex, France*

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ABSTRACT

Aim: A dosimetric study comparing intensity modulated radiotherapy (IMRT) by TomoTherapy to conformational 3D radiotherapy (3D-RT) in patients with superior sulcus non-small cell lung cancer (NSCLC).

Background: IMRT became the main technique in modern radiotherapy. However it was not currently used for lung cancers. Because of the need to increase the dose to control lung cancers but because of the critical organs surrounding the tumors, the gains obtainable with IMRT is not still demonstrated.

Material and methods: A dosimetric comparison of the planned target and organs at risk parameters between IMRT and 3D-RT in eight patients who received preoperative or curative intent irradiation.

Results: In the patients who received at least 66 Gy, the mean V95% was significantly better with IMRT than 3D-RT ($p = 0.043$). IMRT delivered a lower D2% compared to 3D-RT ($p = 0.043$). The IH was significantly better with IMRT ($p = 0.043$). The lung $V_{5\,Gy}$ and $V_{13\,Gy}$ were significantly higher in IMRT than 3D-RT ($p = 0.043$), while the maximal dose (D_{max}) to the spinal cord was significantly lower in IMRT ($p = 0.043$). The brachial plexus D_{max} was significantly lower in IMRT than 3D-RT ($p = 0.048$). For patients treated with 46 Gy, no significant differences were found.

* *Corresponding author at*: Radiotherapy Department, Centre Paul Strauss, 3, rue de la Porte de l'Hôpital, BP 42, 67065 Strasbourg Cedex, France. Tel.: +33 388252471.

E-mail addresses: ptruntzer@strasbourg.unicancer.fr (P. Truntzer), dantoni@strasbourg.unicancer.fr (D. Antoni), Nicola.santelmo@chru-strasbourg.fr (N. Santelmo), cshumacher@strasbourg.unicancer.fr (C. Schumacher), pierre-emmanuel.falcoz@chru-strasbourg.fr (P.-E. Falcoz), elisabeth.quoix@chru-strasbourg.fr (E. Quoix), gilbert.massart@chru-strasbourg.fr (G. Massard), gnoel@strasbourg.unicancer.fr (G. Noël).

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Conclusion: Our study showed that IMRT is relevant for SS-NSCLC. In patients treated with a curative dose, it led to a reduction of the exposure of critical organs, allowing a better dose distribution in the tumor. For the patients treated with a preoperative schedule, our results provide a basis for future controlled trials to improve the histological complete response by increasing the radiation dose.

1. Background

Superior sulcus non-small cell lung cancer (SS-NSCLC) is a rare tumor, representing less than 5% of all NSCLC. By definition, these tumors invade the thoracic wall and are close to, abut or infiltrate the spinal cord, the brachial plexus and/or the esophagus. The tumor size, the respiratory motion in the irradiation fraction and the dose-constraints to reach a curative tumor dose are all limiting factors that prevent the delivery of safe and optimal irradiation with a radiation therapy conformal 3D (3D-RT) technique. Intensity modulated radiation therapy (IMRT) allows a homogeneous, high dose gradient to be delivered for cases of advanced NSCLC, leading to a better target volume coverage and a higher shielding of the surrounding critical organs.[1–5]

To improve the local and regional control rates, many centers have initiated dose escalation trials in stage III NSCLC patients to observe the feasibility and safety constraints of concurrent chemoradiotherapy at higher doses. Most concluded that 74 Gy was a tolerable dose in well-controlled setups of 3D-RT.[6–9] From a study including 106 NSCLC patients at the University of Michigan, Kong et al. reasoned that each 1 Gy increase in the dose administered improved the five-year local control rate by 1.25% and decreased the death risk by 3%.[7] This suggested that higher radiation doses were associated with better outcomes. However, in the RTOG 0617 trial, 74 Gy given in 2 Gy fractions with concurrent chemotherapy was not better than 60 Gy plus concurrent chemotherapy for patients with stage III non-small-cell lung cancer, and was considered to be potentially harmful.[10] The use of 3D-RT could be one of the reasons for the failure of this increased dose. In the case of SS-NSCLC, an increased dose could be relevant if it leads to increase the operability for otherwise inoperable patients or for those with pT0 tumors which should improve the patients outcomes.[11]

Because of the conformality, of its dramatic dose-gradient, IMRT requires a very precise set-up of the patient and strict control of the treated targets. Image-guided radiotherapy (IGRT) is the most secure system available that meets all of the required security controls. Tomotherapy combines IMRT and IGRT.[12]

2. Aim

IMRT is still not considered a reference treatment for SS-NSCLC. In the current study, we analyzed the dosimetric parameters by comparing Tomotherapy and 3D-RT in SS-NSCLC treated preoperatively or with curative intent.

3. Material and methods

Between January 2007 and January 2010, eight patients with a median age of 54.3 years (43–75) were treated with IMRT with TomoTherapy HiArt® device (Accuray Incorporated, Sunnyvale, CA). There were seven adenocarcinomas and one squamous cell carcinoma. The tumors were classified as IIB, IIIA, IIIB and IV stages in one, two, one and four patients, respectively. Six patients received chemoradiation alone, one received radiation alone and the last one received preoperative chemoradiation. The chemotherapy comprised a combination of cisplatin and vinorelbine.

3.1. Simulation

All patients underwent CT simulation using a General Electric (GE) light-speed scanner (General Electric, Milwaukee, WI) in the supine position. Injected and non-injected CT scans were both obtained. All but two patients underwent free-breath CT scans and the other two underwent a three-sequences CT scan (deep inspiration/expiration and free breath-hold). The slices depths were 2.5–3.75 mm.[13] ^{18}Fluoro Desoxy-Glucose PET-CT for delineation was performed in seven patients.

3.2. Target-volumes definition

The delineation of the target volumes was performed using the Focal software program (Elekta AB, Stockholm, Sweden). The gross tumor volume (GTV_{tumor}) was the tumor volume in the free-breath simulation CT scan or the combination of the three volumes in the three sequences simulation CT-scan (equivalent to an internal target volume). PET-CT images were matched with the simulation CT scan. The biological tumor volume represented 40% of the maximal standard unit value (SUV_{max}). All nodes $\leq$10 mm or $\geq$20 mm and ^{18}Fluoro Desoxy-Glucose avid, and all 10–19 mm nodes (avid or not) were considered to be metastatic and were included in a GTV_{node}.[14]

The clinical target volume for the tumor (CTV_{tumor}) was the GTV_{tumor} plus a margin of 6 or 8 mm according to Giraud et al.[15] and was corrected to the relevant anatomical border. The CTV for adenopathies ($CTV_{adenopathies}$) was the area where adenopathies developed and were delineated according to the report by Chapet et al.[16] No prophylactic node volume was defined.[17] The planning target volume for the tumor and nodes ($PTV_{tumor+adenopathies}$) was obtained by adding an isotropic 2 mm margin to the $CTV_{(tumor+node)}$ equal to ($CTV_{tumor} + CTV_{adenopathies}$) when a three-sequences CT-scan was used, and 10 mm cranio-caudal and 5 mm axial

margins for the eight other patients. The delineated organs at risk were the spinal cord, lungs, heart, esophagus and brachial plexus. No PRV was contoured.

3.3. *Treatment plan and dosimetric parameters*

The dose distribution was calculated with the Xio software program (Elekta AB, Stockholm, Sweden) and the TomoTherapy software program (Accuray Incorporated, Sunnyvale, CA). A comparison of the dose distribution was conducted using the Artiview software program (AQUILAB, Loos, France).

The total delivered dose was 70 Gy, 66 Gy and 46 Gy in one, three and four patients, respectively. The dose per fraction was always 2 Gy. Five weekly fractions were administered up to the completion of irradiation. According to the International Commission on Radiation Units and Measurements (ICRU) 50 and 62, the planning treatment delivered at least 95% of the prescribed dose in 95% of the PTV. To follow ICRU 83,[18] for each plan, the median dose (D50%), $D_{\text{near maximum}}$ (D2%) and $D_{\text{near maximum}}$ (D98%) were evaluated.

For each treatment planning, the following values were calculated:

- The conformal index (CI) defined as the ratio of the prescribed isodose volume and the PTV (ideal equal to 1).[19,20]
- The homogeneity index (HI) defined as the ratio of (D2%–D98%)/D50% (ideal equal to 0).[21]
- The coverage index (COI) defined as the ratio of the $D_{\text{near minimum}}$ and the reference D (ideal equal to 1).[18,22]

The lungs volume minus the PTV, $V_{5\,Gy}$, $V_{13\,Gy}$, $V_{20\,Gy}$, and $V_{30\,Gy}$, were restricted to 60%, 40%, 30% and 20%, respectively.[23] The lungs volume minus the PTV mean dose had to be <20 Gy. The heart $V_{35\,Gy}$ was restricted to 35%.[24] Spinal cord maximum dose was limited to 45 Gy, and the brachial plexus maximum dose was limited to 60 Gy.[25] The esophageal $V_{50\,Gy}$ was limited to 35%.[26]

The 3D-RT field's geometry used between two and four coplanar 6–25 MV X-photon beams. Concerning the Tomotherapy beam planning, for each plan the treatment slice width, pitch and modulation factor were 2.5 cm, 0.287 and 2.5, respectively. A MV-CT imaging was performed before treatment for IGRT control, acquisition, fusion and correction of positioning

3.4. *Statistics*

The dosimetric parameters of each patient were compared with the non-parametric equivalent in a paired *t*-test for matched observations (Wilcoxon test). The threshold for statistical significance was $p < 0.05$. All statistical analyses were performed using the IBM SPSS Statistics v20 software program (IBM Inc., Armonk, NY, USA).

4. Results

The mean GTV_{tumor}, CTV_{tumor} and $PTV_{(tumor+adenopathies)}$ were 155 mL (18–802), 267 mL (64–1130) and 391 mL (99–1489), respectively. Only one patient presented with metastatic lymph nodes, and $CTV_{adenopathies}$ was 67.7 mL.

4.1. *Dose distribution*

4.1.1. *Target volumes*

Concerning the patients who received at least 66 Gy (Table 1), the V95% was significantly higher with IMRT than with 3D-RT, (94.7% [91.3–99.7%] and 86.2% [72.8–97.1%]), respectively ($p = 0.043$; Figs. 1 and 2). One patient reached the constraint with IMRT compared to none with 3D-RT. The D2% was significantly lower with IMRT than with 3D-RT (102.4% [100.1–104.9%] vs. 105.6% [104.2–106.7%]; $p = 0.043$). The D98% and D50% were not significantly different between the two techniques. The HI was significantly better with IMRT compared to 3D-RT (0.24 [0.06–0.33] vs. 0.35 [0.26–0.44]); $p = 0.043$). The CI was 1.2 for IMRT and 1.7 for 3D-RT, but this difference was not significant ($p = 0.225$). There were no differences in the COI.

Table 1 – Dose distribution in the target-volumes.

Patient	Total dose	V95%		D98%		D50%		D2%		CI		HI		COI	
		3D-RT	IMRT	3D-RT	IMRT	3D-RT	IMRT	3D-RT	IMRT	3D-RT	IMRT	3D-RT	IMRT	3D-RT	IMRT
1	46 Gy	55.5	86.9	50.8	22.9	96.8	99.9	104.1	102.4	1.18	1.54	0.84	0.51	0.24	0.53
2	46 Gy	98.5	97.9	96.1	94.8	103.2	99.9	106.4	103.7	1.73	1.07	0.09	0.08	1	0.99
3	46 Gy	96.0	90.3	89.7	53.2	100.2	99.96	100.25	105.2	1.52	1.1	0.16	0.5	0.94	0.56
Mean		83.3	91.7	69.6	66.3	100.1	99.9	105.4	103.8	1.4	1.2	0.36	0.37	0.65	0.69
Median		95.9	90.3	89.7	53.2	100.3	99.9	105.8	103.7	1.5	1.1	0.16	0.5	0.94	0.56
p-value		NS		NS		NS		NS		NS		NS		NS	
4	66 Gy	86.2	94.7	71.1	73.8	102.6	100	101.9	105.9	1.96	1.1	0.34	0.28	0.75	0.78
5	70 Gy	89.5	92.5	74.4	70.4	100.3	99.9	101.8	106.7	2.9	1.1	0.32	0.32	0.78	0.74
6	66 Gy	72.8	91.3	64.2	69.2	100.6	100.6	102.4	104.2	1.4	1.2	0.39	0.33	0.68	0.73
7	66 Gy	94.1	99.7	79.4	99.3	104.3	102.2	104.9	106.4	1.8	1.5	0.26	0.06	0.83	1.05
8	66 Gy	80.6	94.9	62.5	81.0	99.8	M99.9	100.1	106.1	1.4	1.2	0.44	0.19	0.66	0.85
Mean		84.7	94.6	70.2	78.7	101.5	100.5	105.9	102.4	1.7	1.2	0.35	0.24	0.92	0.82
Median		86.2	94.7	71.1	73.8	100.6	100	106.2	101.9	1.8	1.2	0.34	0.28	1	0.78
p-value		**0.043**		NS		NS		**0.043**		NS		**0.043**		NS	

CI, conformal index; HI, homogeneity index; COI, coverage index; NS, non significant.

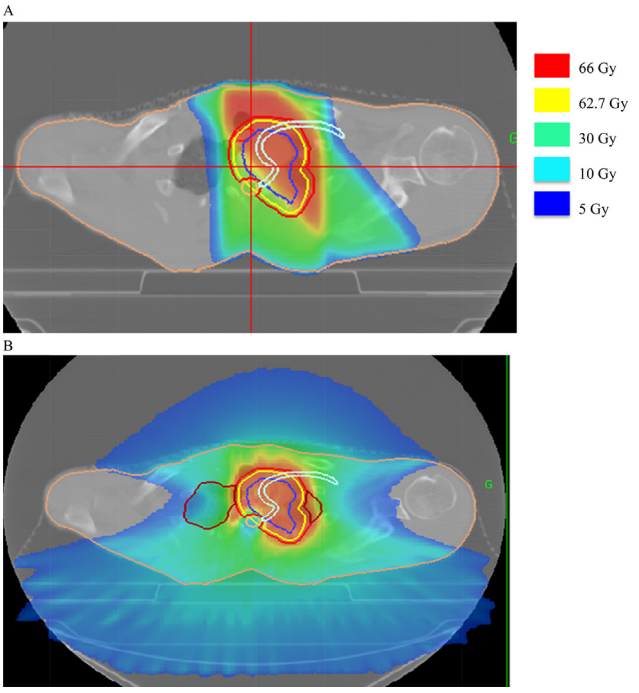

Fig. 1 – Treatment planning 3D-RT (A) and IMRT (B). Blue: GTV T; yellow: CTV T, red: PTV T; orange: spinal cord; light blue: brachial plexus.

For patients treated with 46 Gy, no significant differences were observed between the groups.

4.1.2. *Lungs minus PTV*

For patients treated with up to 70 Gy (Table 2 and Fig. 2), the $V_{5\,Gy}$ and $V_{13\,Gy}$ were significantly increased with IMRT compared to 3D-RT (20% vs. 11.9%; $p = 0.043$) and (12.2% vs. 8.3%, $p = 0.043$), respectively. The mean dose, $V_{20\,Gy}$ and $V_{30\,Gy}$ were not significantly different between the groups.

For patients treated with 46 Gy, none of the parameters were significantly different.

4.1.3. *Spinal cord*

For patients treated with up to 70 Gy, the D_{max} was significantly lower with IMRT compared to the dose delivered with 3D-RT (31.6 Gy vs. 45.5 Gy ($p = 0.043$; Table 2).

For patients treated with 46 Gy, there were no significant differences observed.

4.1.4. *Brachial plexus*

For the patients treated with up to 70 Gy irradiation, the D_{max} was significantly lower with IMRT compared to the dose delivered with 3D-RT (64.9 vs. 70.1 Gy ($p = 0.043$); Table 2 and Fig. 2).

There were no significant differences between the groups for the patients treated with 46 Gy irradiation.

4.1.5. *Esophagus and Heart*

There were no significant differences in any of the parameters or doses in the esophagus or heart (Table 2).

5. Discussion

SS-NSCLC treatment combines chemotherapy and/or radiation following by a surgery. The dose of irradiation is classically 46 Gy in 26 daily fractions. For lesions considered to be inoperable because of invasion of the bone or the spinal canal, chemoradiation is recommended, and the radiation dose is increased up to 66 Gy.[27,28] Because the development of this cancer occurs close to critical organs, the coverage of the volume with RT-3D over a dose of 46 Gy remains always challenging.

Murshed et al. reported a series of 41 patients with an inoperable stage IIIA-IV stage NSCLC irradiated up to a dose of 66 Gy in 33 fractions of 2 Gy delivered either by 3D-RT or IMRT. They found that IMRT delivered a more conformal dose distribution than 3D-RT, with a significant improvement of the median CI and HI, at 1.41 vs. 1.54 ($p = 0.004$) and 1.16 vs. 1.12,

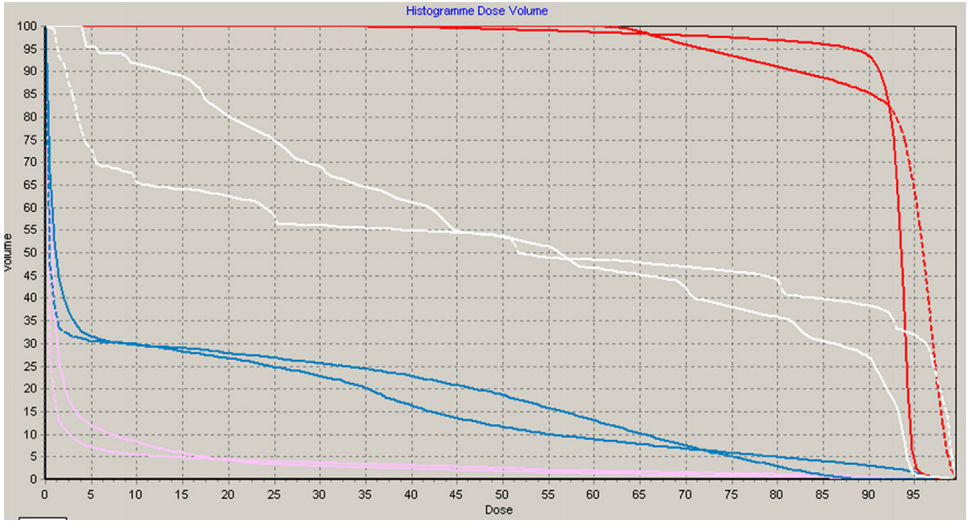

Fig. 2 – Dose-volume histogram (total dose 66 Gy). 3D-RT (dashed line) and IMRT (continuous line). Blue: lungs minus PTV; pink: spinal cord; red: PTV; white: brachial plexus.

Table 2 – Organs a risk parameters comparison.

Parameters/dose (Gy)		3D-RT		IMRT		*p*-value
		Median	Mean	Median	Mean	
Lungs minus PTV 46 Gy	D_{max} (Gy)	45.66	45.94	40.9	47.3	NS
	D_{min} (Gy)	0.003	0	0.037	0.12	NS
	D_{mean} (Gy)	0.98	3.03	2.043	3.27	NS
	$V_{5\,Gy}$ (%)	3.1	9.7	9.1	14.2	NS
	$V_{13\,Gy}$ (%)	2.0	7.1	4.4	6.8	NS
	$V_{20\,Gy}$ (%)	1.6	5.8	2.9	4.3	NS
	$V_{30\,Gy}$ (%)	1.0	4.6	1.9	2.6	NS
Lungs minus PTV 66 Gy	D_{max} (Gy)	69.4	70	68.6	68.4	NS
	D_{min} (Gy)	0	0.02	0.1	1.1	NS
	D_{mean} (Gy)	3	4.2	3.4	4.8	NS
	$V_{5\,Gy}$ (%)	11.4	11.9	13.5	20	0.043
	$V_{13\,Gy}$ (%)	7.5	8.6	8.3	12.2	0.043
	$V_{20\,Gy}$ (%)	4.6	7	5.2	7.9	NS
	$V_{30\,Gy}$ (%)	3.2	5.4	3	4.1	NS
Esophagus 46 Gy	D_{max} (Gy)	46.9	37.5	49.1	49.8	NS
	D_{min} (Gy)	0.1	0.3	0.65	0.63	NS
	D_{mean} (Gy)	16.1	15.7	18.8	19.5	NS
	$V_{20\,Gy}$ (%)	37.1	34.6	47.5	49.6	NS
	$V_{45\,Gy}$ (%)	6.3	9.1	7.3	9.1	NS
	$V_{50\,Gy}$ (%)	0	0.1	0	2.2	NS
Esophagus 66 Gy	D_{max} (Gy)	68.9	67	68.5	67.3	NS
	D_{min} (Gy)	0	5.25	0.3	7.1	0.043
	D_{mean} (Gy)	16.1	27	13.9	26.1	NS
	$V_{20\,Gy}$ (%)	28.1	49.5	26.3	27.8	NS
	$V_{45\,Gy}$ (%)	22.1	36.7	16	28.9	NS
	$V_{50\,Gy}$ (%)	20.7	31.6	14	24.4	NS
Spinal Cord 46 Gy	D_{max} (Gy)	32.2	30.4	40.7	32.8	NS
	D_{min} (Gy)	0.08	0.06	0.42	0.4	NS
	D_{mean} (Gy)	10.1	11.7	11.2	10.1	NS
Spinal Cord 66 Gy	D_{max} (Gy)	44.8	45.5	31.1	31.6	0.043
	D_{min} (Gy)	0	0.86	0.07	0.2	NS
	D_{mean} (Gy)	8	15.6	7.28	9	NS
Heart 46 Gy	D_{max} (Gy)	1	14	0.3	8.6	NS
	D_{min} (Gy)	0	0.01	0.04	0.16	NS
	D_{mean} (Gy)	0.36	0.5	0.15	1	NS
	$V_{35\,Gy}$ (%)	0	0	0	0	NS
Heart 66 Gy	D_{max} (Gy)	0.16	0.31	0.17	0.48	NS
	D_{min} (Gy)	0	0	0.1	0.1	NS
	D_{mean} (Gy)	0.02	0.04	0.27	0.25	NS
	$V_{35\,Gy}$ (%)	0	0	0	0	NS
Brachial Plexus 46 Gy	D_{max} (Gy)	47.6	41.6	46.5	42.9	NS
	D_{min} (Gy)	0.22	0.83	8.2	11.2	NS
	D_{mean} (Gy)	20.9	20.1	25.1	24.6	NS
Brachial Plexus 66 Gy	D_{max} (Gy)	70.1	70.6	68.8	64.9	0.043
	D_{min} (Gy)	0.26	1.5	1.6	1.4	NS
	D_{mean} (Gy)	36.8	36.1	37.9	36.1	NS

D_{min}, minimum dose; D_{max}, maximum dose; NS, non significant.

($p = 0.0004$), respectively.[29] Cattaneo et al. compared helical tomotherapy IMRT to 3D-RT for 13 patients with inoperable NSLC, with doses ranging between 61 and 70 Gy. IMRT significantly increased the PTV $V_{95\%}$ from 92% with 3D-RT to 97% with IMRT ($p < 0.002$).[30] In the current study, for the patients who received a dose >66 Gy, we showed that the V95% and HI were significantly improved for IMRT compared to 3D-RT. With regard to the CI, even if the difference was not significant, the values demonstrated a high level of conformality that can be reached with IMRT. However, the expected V95% constraint (i.e., >95% of the prescribed dose) was reached for only one patient who received IMRT. This result is likely to be attributable to the proximity of the spinal cord, the same reason for which the patients had been considered as inoperable. The limit of the dose into the tumor was the dose constraint in the spinal cord. The mean and the median maximum doses were close to the required threshold of 45 Gy. However, we were able to deliver 33 or 35 fractions that led to less than

1.8 or 2 Gy per fraction being given to the spinal cord; thus, the radiobiologically equivalent dose that reached the spinal cord was probably less than 45 Gy.

For patients with localized non-operable tumors (stage IIIA with N2 or IIIB), the reference treatment remains chemoradiotherapy. The total dose delivered to the tumor is a prognostic factor for local control and overall survival.[31] Vijayakumar et al. showed that a local control rate of 50% can be achieved if a dose of 53 Gy is delivered to the tumor, but this rate can reach 90% if a dose of 80 Gy is delivered.[32] Currently, the recommended dose is 66 Gy in 33 fractions of 2 Gy. Bari et al. prospectively evaluated, 14 patients treated with chemoradiotherapy with a median radiation dose of 72 Gy (64–74) in 2 Gy fractions.[27] The median OS was 20 months. Two patients initially considered to be inoperable, presented a partial response and were surgically treated. The pathological evaluation did not find any tumor. No complications were reported. An increase in the dose administered for all of the inoperable or limited operability patients may be possible using IMRT or proton therapy.[33] Our results showed that the dose constraints were not reached for almost critical organs; therefore dose escalation remains a relevant aim. The use of a PET scanner as a surrogate for a pathological response could also be relevant to personalize dose increase.[34,35]

In the patients who received 46 Gy in a preoperative schedule, there were no differences between IMRT and 3D-RT in terms of dose distribution. IMRT could thus be concluded to be non-superior to 3D-RT. However, if one considers that a histological complete response (pCR) can be a surrogate for overall survival, this may not be the case. In several studies, the pCR rate ranged between 16 and 36%.[11,28,36,37] In a previous publication, we showed that the overall survival was correlated to the pCR.[11] Previous studies have shown that the rate can be improved up to 40–47% by increasing the radiation dose.[38,39] However, the benefit of this dose escalation remains to be clearly proven by controlled studies.

In terms of critical organs, the doses reached in the different series have been variable. In the series reported by Murshed et al., the median $V_{10\,Gy}$ and $V_{20\,Gy}$, and mean dose in the lungs were significantly improved with IMRT.[29] In the series reported by Cattaneo et al. the median $V_{20\,Gy}$ and $V_{30\,Gy}$ were also significantly improved in patients irradiated with IMRT.[30] We did not conclude that the two approaches had equivalent results because we showed that lower doses were significantly decreased with IMRT. Some have argued that these low doses are associated with a higher risk of causing radio-induced pneumopathy in IMRT-treated patients than higher doses.[40] However, the differences between the results of the current series and the previously published articles are probably related to the location of the tumors because SS-NSCLC has less neighboring lung parenchyma. However, the high level of $V_{5\,Gy}$ retrieved in both series with 3D-RT is surprising and may explain the absence of a significant difference compared with IMRT, and may be related on the number of 3D-RT beams used.[29,30] In these series, the differences in the results for the esophagus and heart were also related to the same explanation, i.e., the proximity of the tumor to the organs at risk affecting the findings. It was expected that the doses were more important in 3D-RT than in the IMRT calculation.[29,30] In the current series, the distance of the tumor from the heart explains the low doses observed. More critical for SS-NSCLC is the brachial plexus, which is often included in the PTV (Figs. 1 and 2), and its maximum tolerated dose was close to the prescribed dose and ranged between 60 and 66 Gy in previous studies.[41,42] Even if we obtained a lower dose with IMRT, the risk is not low, especially for the long-term outcome of these patients with SS-NSCLC.[11,28,36,43] However, after a median follow-up of 9.8 months (3.1–26.3), no patients in the current series developed radiation-induced plexitis and this complication has been rarely reported in the treatment of SS-NSCLC. For the patients treated with 46 Gy, the dose distributions in the critical organs were favorable for the IMRT technique. Therefore, even if the difference between IMRT and 3D-RT was not significant, it is noteworthy that the difference, in terms of the maximum dose for the most critical organ, (i.e., spinal cord) was 8 Gy. This discrepancy could be used to increase the dose given to the tumors. Moreover, if the dose escalation in the tumor is not considered a relevant goal, this shielding of the critical organs can be deemed useful for the outcome of the patient because the risk of metastatic disease, which can appear in previously irradiated bone. Furthermore, dose reduction in other areas of the body is more rationally based on the ALARA (*as low as reasonably achievable*) principle.

Two more points could be disputable regarding the use of IMRT. First, the treatment duration of tomotherapy is longer than that with 3D-RT. The motion of the tumor during irradiation can affect the outcome. However, Giraud et al. analyzed the tumor position during respiratory cycle in ten different NSCLC patients and showed that for patients with SS-NSCLC, the median proximal-distal motion was 7 mm, and this was nearly zero in the other directions.[44] Thus, tomotherapy IMRT does not seem to be problematic for SS-NSCLC. The second point is more concerning because of the increase in the number of beams required to deliver the highly conformal dose, tomotherapy IMRT (and all IMRT modes) increases the low-dose distribution. These low doses have been questioned as an inductor of second cancers.[45–47] However, this risk remains relative in patients with other risk factors for cancer and because of the low life expectancy of these patients (regardless of the localization and stage). However, we have already shown that the integral dose was not increased by the use of tomotherapy IMRT.[48,49]

In conclusion, our study showed that IMRT is relevant in SS-NSCLC. In patients treated by a curative dose, it leads to a reduction of dose given to critical organs, allowing a better dose distribution in the tumor, and for patients treated with a preoperative schedule, our results provide the opportunity to increase the dose in future controlled trials to improve the pRC.

Authors' contribution

AT, GN: Conception and design of the study; AT, GN: Acquisition of data, analysis and interpretation of data; AT, AD, GN: Drafting the article; SN, CS, FPE, QE, MG: Acquisition of data. All authors read and approved the final manuscript.

Conflict of interests

None declared.

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