

References

40. Yom SS, Liao Z, Liu HH, et al. Initial evaluation of treatment-related pneumonitis in advanced-stage non-small-cell lung cancer patients treated with concurrent chemotherapy and intensity-modulated radiotherapy. *Int J Radiat Oncol Biol Phys* 2007;68:94-102.
41. Sura S, Gupta V, Yorke E, et al. Intensity-modulated radiation therapy (IMRT) for inoperable non-small cell lung cancer: the Memorial Sloan-Kettering Cancer Center (MSKCC) experience. *Radiother Oncol* 2008;87:17-23.
42. Govaert SL, Troost EG, Schuurbiens OC, et al. Treatment outcome and toxicity of intensity-modulated (chemo) radiotherapy in stage III non-small cell lung cancer patients. *Radiat Oncol* 2012;7:150.
43. Palma DA, Senan S, Tsujino K, et al. Predicting radiation pneumonitis after chemoradiation therapy for lung cancer: an international individual patient data meta-analysis. *Int J Radiat Oncol Biol Phys* 2013;85:444-50.
44. Ma L, Ye W, Li Q, et al. Subjective Global Assessment (SGA) Score Could Be a Predictive Factor for Radiation Pneumonitis in Lung Cancer Patients With Normal Pulmonary Function Treated by Intensity-Modulated Radiation Therapy and Concurrent Chemotherapy. *Clin Lung Cancer* 2018;19:e211-7.
45. Huang J, He T, Yang R, et al. Clinical, dosimetric, and position factors for radiation-induced acute esophagitis in intensity-modulated (chemo)radiotherapy for locally advanced non-small-cell lung cancer. *Onco Targets Ther* 2018;11:6167-75.
46. Appel S, Bar J, Ben-Nun A, et al. Comparative effectiveness of intensity modulated radiation therapy to 3-dimensional conformal radiation in locally advanced lung cancer: pathological and clinical outcomes. *Br J Radiol* 2019;92:20180960.
47. Zhou Y, Yan T, Zhou X, et al. Acute severe radiation pneumonitis among non-small cell lung cancer (NSCLC) patients with moderate pulmonary dysfunction receiving definitive concurrent chemoradiotherapy: Impact of pre-treatment pulmonary function parameters. *Strahlenther Onkol* 2020;196:505-14.
48. Grambozov B, Wolf F, Kaiser J, et al. Pulmonary function decreases moderately after accelerated high-dose irradiation for stage III non-small cell lung cancer. *Thorac Cancer* 2020;11:369-78.

Table S1 Dose-volume histogram parameters

DVH parameter	Homolateral lung	Contralateral lung	Bilateral lungs	Heart	Esophagus
V5Gy	61.8 (48.8–74.6)	51.6 (42–64.9)	58.2 (47.1–69.1)	–	54.7 (42.9–65.2)
V10Gy	52.7 (41.3–65.2)	31.2 (19.8–40.3)	42.1 (30.3–51.6)	–	49.0 (38.2–59.2)
V13Gy	48.5 (36.9–60.1)	20.7 (10.1–30.3)	34.2 (25.5–41.2)	–	–
V20Gy	36.7 (27.4–46.7)	7.3 (2.0–14.1)	23.0 (18.3–28.0)	–	43.2 (31.8–54.0)
V30Gy	25.4 (16.7–33.9)	1.4 (0.1–5.4)	14.4 (9.7–18.3)	7.4 (1.2–15.9)	37.2 (24.7–47.7)
V40Gy	–	–	–	4.65 (0.6–9.4)	30.9 (18.1–40.9)
V50Gy	–	–	–	–	28.4 (10.4–32.6)
V60Gy	–	–	–	–	8.6 (1.3–20.7)
Mean dose (Gy)	18.6 (11.7–25.5)	8.1 (4.8–11.4)	13.5 (9.2–17.8)	8.5 [1–16]	23.0 (13.6–32.4)
Max dose (Gy)	67.8 (62.9–69.4)	52.0 (34.7–64.0)	–	–	64.4 (61.0–67.6)
L40Gy (cm)	–	–	–	–	9.70 (4.5–19.3)

Data are shown as median (IQR). VxGy, volume of the organ receiving xGy; IQR, inter quartile range; L40Gy, length of oesophagus receiving 40 Gy.

Table S2 Radiologic toxicity occurring after radiotherapy

Variables	3 months		12 months	
	n=167	%	n=95	%
Alveolar opacities				
Around the tumor	65	38.9	9	9.5
Same lobe	20	12.2	1	1.0
Homolateral lung	11	6.7	1	1.0
Contralateral lung	6	3.3	0	0
Bilateral lungs	4	2.2	0	0
Not reported	61	36.7	84	88.5
Ground glass				
Around the tumor	57	34.4	5	5.3
Same lobe	19	11.1	2	2.1
Homolateral lung	17	10	0	0
Contralateral lung	7	4.4	1	1.0
Bilateral lungs	6	3.3	2	2.1
Not reported	61	36.7	85	89.5
Fibrosis				
Around the tumor	74	44.3	5	5.3
Same lobe	17	10	2	2.#
Homolateral lung	7	4.2	2	2.#
Contralateral lung	0	0	0	0
Bilateral lungs	7	4.2	1	1.0
Not reported	62	37.1	85	89.5
All RILD				
Around the tumor	24	14.4	2	2.1
Same lobe	37	22.2	1	1.0
Homolateral lung	20	12.0	3	3.2
Contralateral lung	9	5.4	1	1.0
Bilateral lungs	15	9.0	3	3.2
Not reported	62	37.1	85	89.5

RILD, radiation induced lung disease.

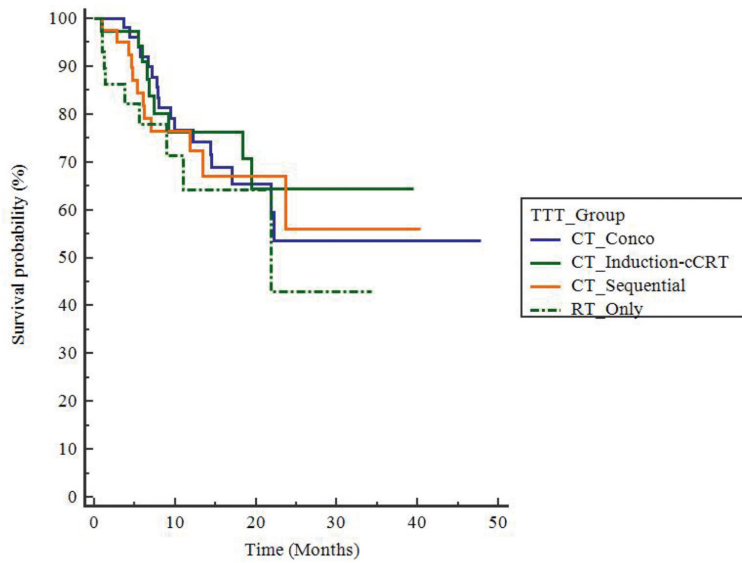


Figure S1 Kaplan-Meier estimate of in field local control in patient receiving radiotherapy only or combined with chemotherapy.

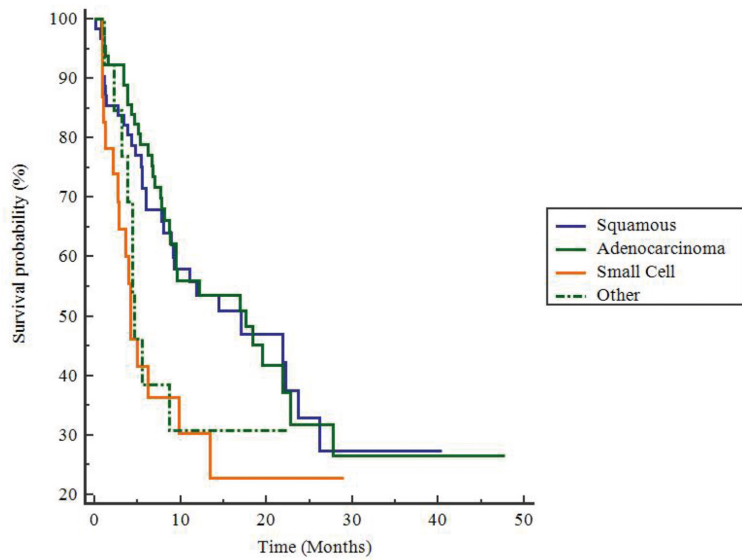


Figure S2 Kaplan-Meier estimate of progression-free survival in patient depending on the histology. Other, large cell undifferentiated carcinoma and giant-cell carcinoma.

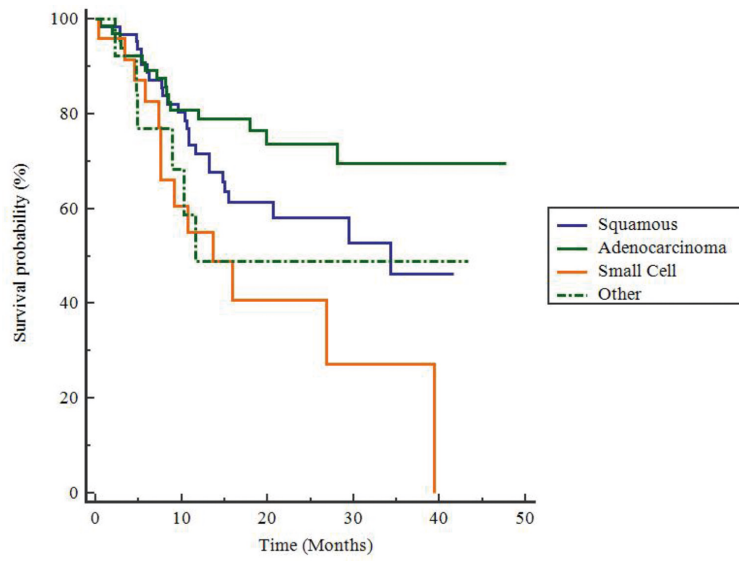


Figure S3 Kaplan-Meier estimate of overall survival in patient depending on the histology. Other, large cell undifferentiated carcinoma and giant-cell carcinoma.

Table S3 Literature data reporting on VMAT and IMRT in lung cancer

Author	n	RT technique	Pulmonary toxicity	Esophageal toxicity	Median FU	Local control
Yom (40), 2007	151	IMRT: n=151	APT: G ≥3: 8%	N/A	8.5 mo	NR
Sura (41), 2008	55	IMRT	APT: G2: 18%, G ≥3: 11%; LPT: G2:16%, G 3-4: 2%, G5:2%	AET: G2: 22%, G ≥3: 4%; LET: G2: 6%, G ≥ 3: 0%	26 mo	2 y: 50%
Govaert (42), 2012	86	IMRT: n=86	APT: G 1: 59%, G 2: 23%	APT: G 1: 50%, G2: 35%	N/A	N/A
Jiang (17), 2011	165	IMRT: n=165	APT: G ≥3: 11%; LPT: G ≥3: 1%	AET: G2: 70%; LET: G3: 17.6%	16.5 mo	2 y: 57%
Palma (43), 2013	836	IMRT or 3D-CRT	APT: G ≥2: 29.8%, G5: 1.9%	N/A	2.3 y	N/A
Khalil (9), 2015	87	IMRT: A: 12:V20 <40%; B: 25:V20 <40% + MLD <20 Gy; C: 50: V5 <60%	APT: A: G ≥3: 42%, G5: 17%; B: G ≥3: 24%, G5: 16%; C: G ≥3: 30%, G5: 4%	N/A	18.1 mo	
Wang (32), 2016	327	IMRT: n=152	APT: G ≥2: 11%, G ≥3: 3%	AET: G ≥2:37%, G ≥3:8%	72.1 mo	5 y: 43%
Wijsman (18), 2017	188	IMRT: n=92; VMAT: n=96	APT: G2: 23.9% vs. 18.8%, G3: 1.1% vs. 0%; LPT: G ≥3: 9.8% vs. 17.7%	AET: G2: 23.9% vs. 41.7%*, G3:6.5% vs. 17.7%*; LET: G ≥3: 1.1 vs. 3.1	18.4 mo	
Ling (28), 2016	145	IMRT+IFRT: n=37	APT G ≥2: 5.4%	AET G ≥2: 21.6%	13.1 mo	6 mo:76.5%; 1 y:65.8%; 2 y:57.1%
Chun (29), 2017	482	IMRT: n=228	APT G ≥3: 3.5%	AET: G ≥3: 13.2 %	21.3 mo	2 y: 30.8%
Ma (44), 2018	150	IMRT n=150	APT: G2: 16%, G ≥3: 8%	AET: G2: 47.3%, G ≥3: 24.6%	N/A	N/A
Jaksic (12), 2018	73	IMRT: n=73	APT: G2: 7%, G ≥3: 6%	AET: G2: 34%, G ≥3: 1%	44 mo	2 y: 62%
Huang (45), 2018	193	IMRT: n=152; VMAT: n=41		AET: G2: 22.8%, G ≥3: 4.7%		
Wu (30), 2018	77	VMAT	APT: G2: 16.9%, G ≥3: 9.1%, G5: 2.6%	AET: G2: 13.0%, G ≥3: 5.2%	14.8 mo	N/A
Appel (46), 2019	73	IMRT/VMAT (n=22)	APT: ≥ G3: 5%	AET: G2-3: 32%, G4: 0%	3.6y	N/A
Rades (31), 2019	278	VMAT	APT: G3: 7.6%			
Zhou (47), 2020	122	IMRT	APT: G3: 20.5%, G4: 3.3%, G5: 1.6%			
Grambozov (48), 2020	72	IMRT	APT: G2: 4.2%, G3-4: 4.2%, G5: 2.8%	AET: G2: 27.8%, G3-4: 11.1%	15.8 mo (0.3–50.5 mo)	1 y: 70%

*, P<0.05. 3D-CRT, 3-dimensional conformal radiation therapy; IMRT, intensity-modulated radiation therapy; VMAT, volumetric modulated arc therapy; G, Grade; ENI, elective nodal irradiation; IFRT, involved-field radiotherapy; mo, months; y, years; FU, follow-up; AET, acute esophageal toxicity; APT, acute pulmonary toxicity; MLD, mean lung dose; N/A, not available; RP, radiation pneumonitis.