

INTEGRATE 7.0

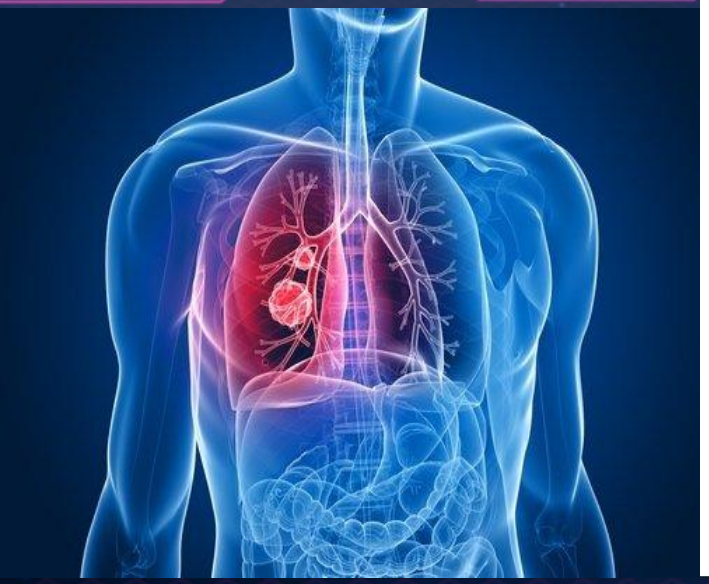
QUALI ‘REGOLE’ NELLA GESTIONE INTEGRATA DELLA NEOPLASIA POLMONARE?

GAMES

VERONA

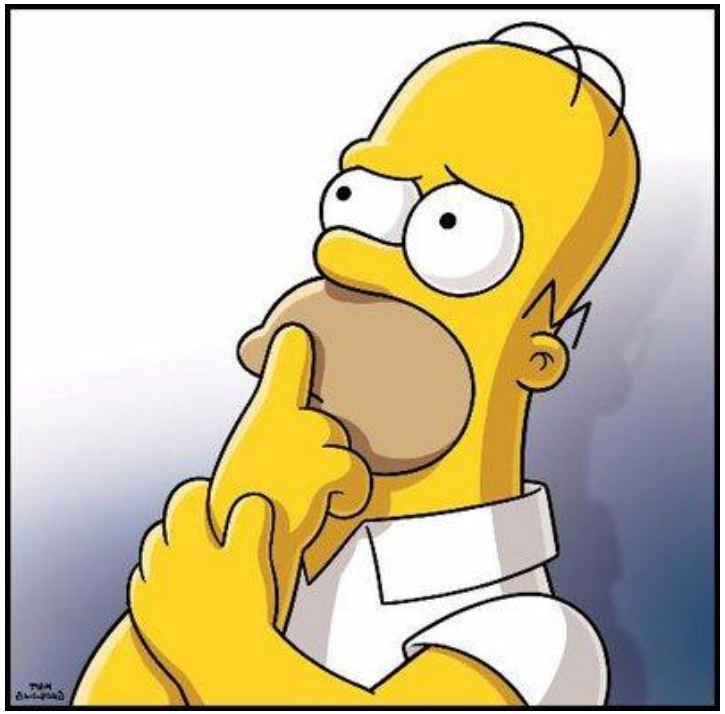
13-14 OTTOBRE 2025





V SESSIONE
Radioterapia nella malattia «più che» localmente avanzata

Non irradiabile, può esistere un criterio di definizione?



Matteo Sepulcri
Radio-oncologo
IOV-IRCCS Padova

Irradiabile o non irradiabile?





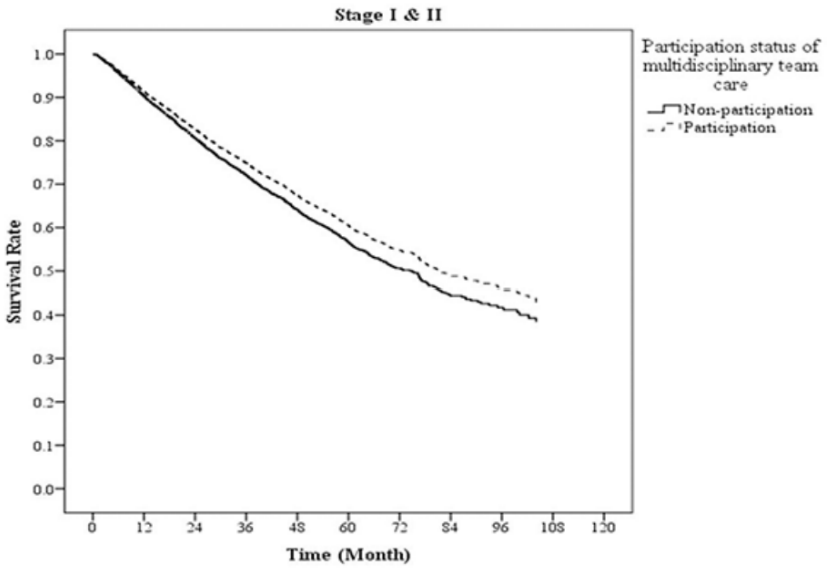


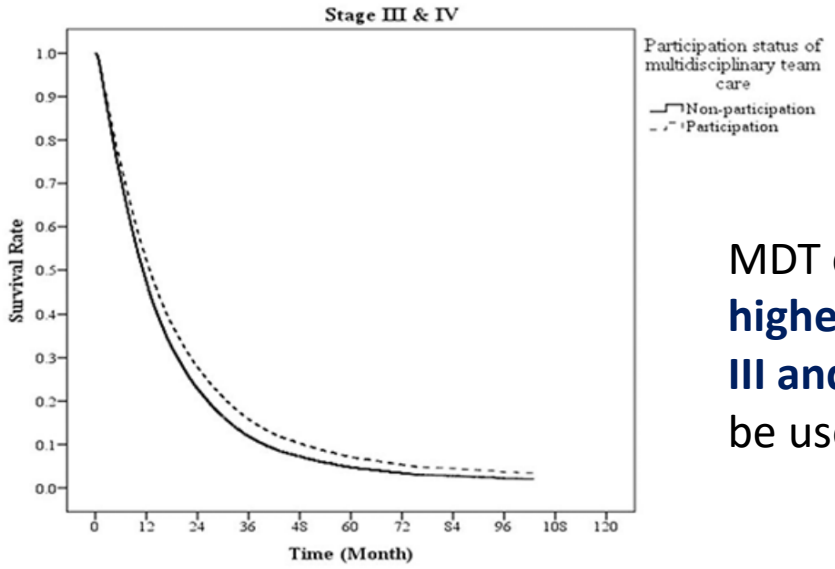
Cosa significa «non resecabile»?

"Unresectable in this situation refers to the situation that, even after induction therapy, a **complete resection (R0) would not be possible**, based on evaluation within a **multidisciplinary team**, including an experienced thoracic surgeon."

Early and locally advanced NSCLC, ESMO Guidelines 2017





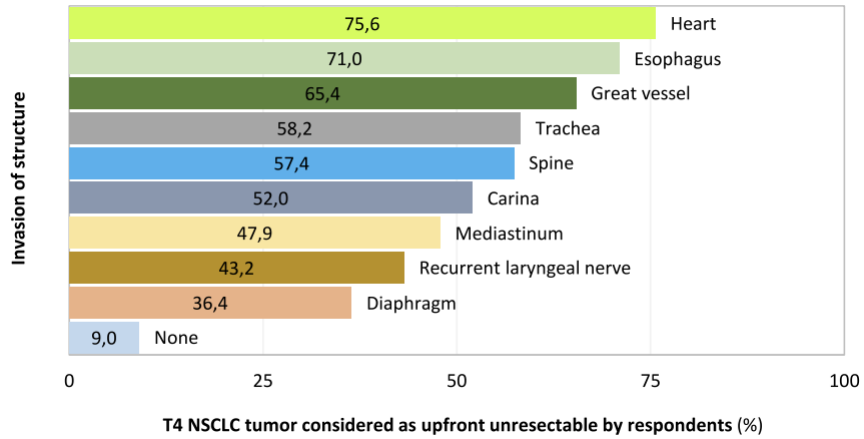


MDT care are significantly associated with **higher survival rate of patients with stage III and IV NSCLC**, and thus MDT care should be used in the treatment of these patients.

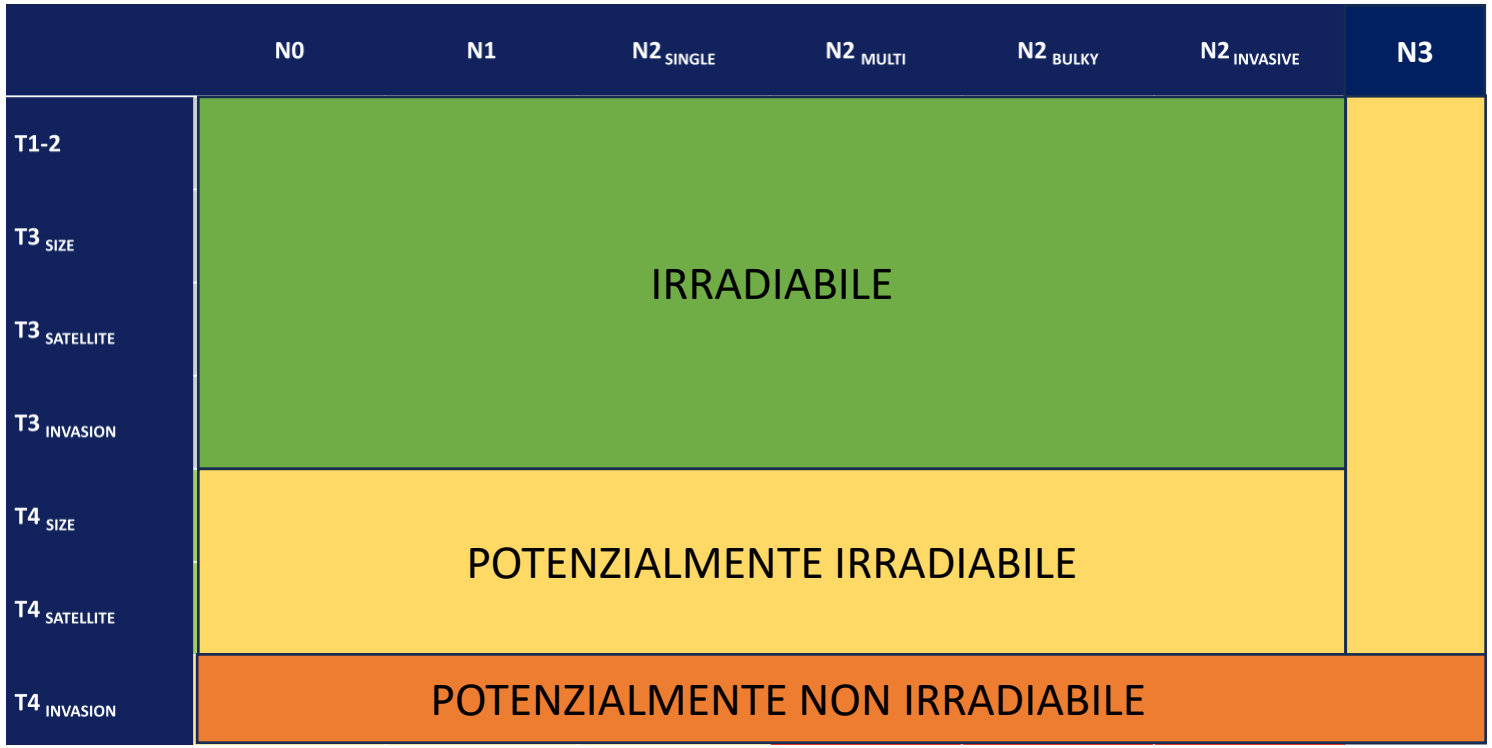
Pan CC, Plos One 2015

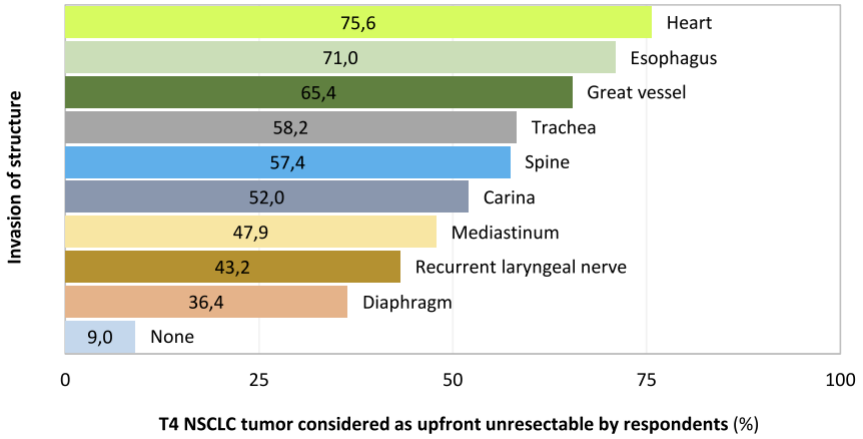
Consensus EORTC

	N0	N1	N2 SINGLE	N2 MULTI	N2 BULKY	N2 INVASIVE
T1-2	N/A	N/A	POTENTIALLY RESECTABLE (95%)	NO AGREEMENT (50%)	UNRESECTABLE (75%)	UNRESECTABLE (84%)
T3 SIZE	N/A	RESECTABLE (83%)[a]	POTENTIALLY RESECTABLE (87%)	NO AGREEMENT (39%)	UNRESECTABLE (80%)	UNRESECTABLE (88%)
T3 SATELLITE	N/A	POTENTIALLY RESECTABLE (94%)	POTENTIALLY RESECTABLE (79%)	NO AGREEMENT (34%)	UNRESECTABLE (84%)	UNRESECTABLE (91%)
T3 INVASION	N/A	POTENTIALLY RESECTABLE (89%)	NO AGREEMENT (71%)[b]	NO AGREEMENT (28%)[c]	UNRESECTABLE (87%)	UNRESECTABLE (92%)
T4 SIZE	POTENTIALLY RESECTABLE (94%)	POTENTIALLY RESECTABLE (90%)	NO AGREEMENT (66%)	UNRESECTABLE (77%)	UNRESECTABLE (88%)	UNRESECTABLE (93%)
T4 SATELLITE	POTENTIALLY RESECTABLE (78%)	NO AGREEMENT (71%)[b]	NO AGREEMENT (44%)	UNRESECTABLE (85%)	UNRESECTABLE (92%)	UNRESECTABLE (94%)
T4 INVASION	NO AGREEMENT (62%)[b]	NO AGREEMENT (57%)[b]	NO AGREEMENT (34%)[c]	UNRESECTABLE (90%)	UNRESECTABLE (95%)	UNRESECTABLE (94%)



Ragionando in termini di irradiabilità…





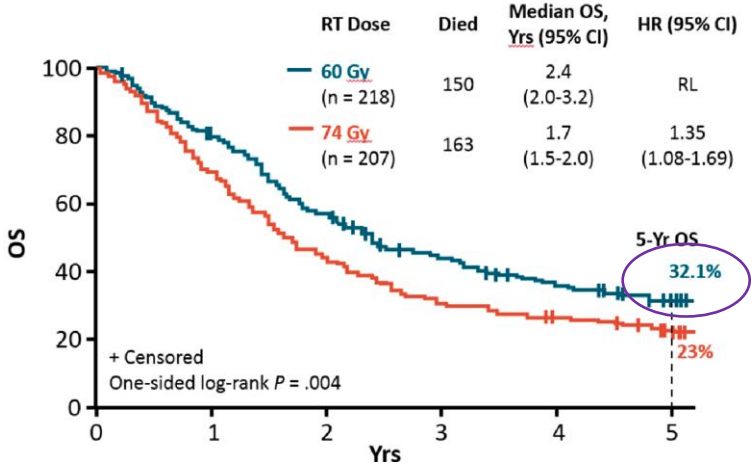


Invasione:

- Cuore
- Esofago
- Trachea/carena

CT-RT: trattamento potenzialmente curativo

RTOG 0617



PACIFIC

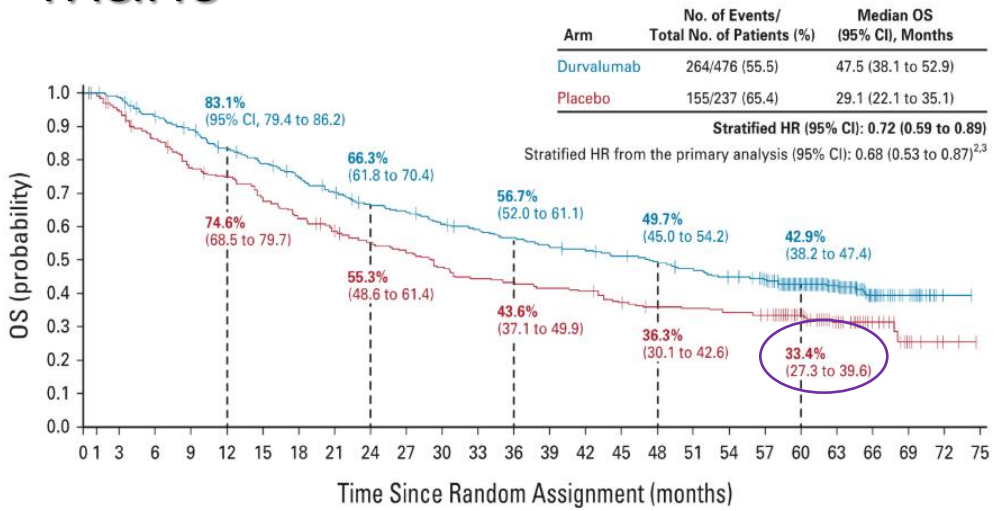
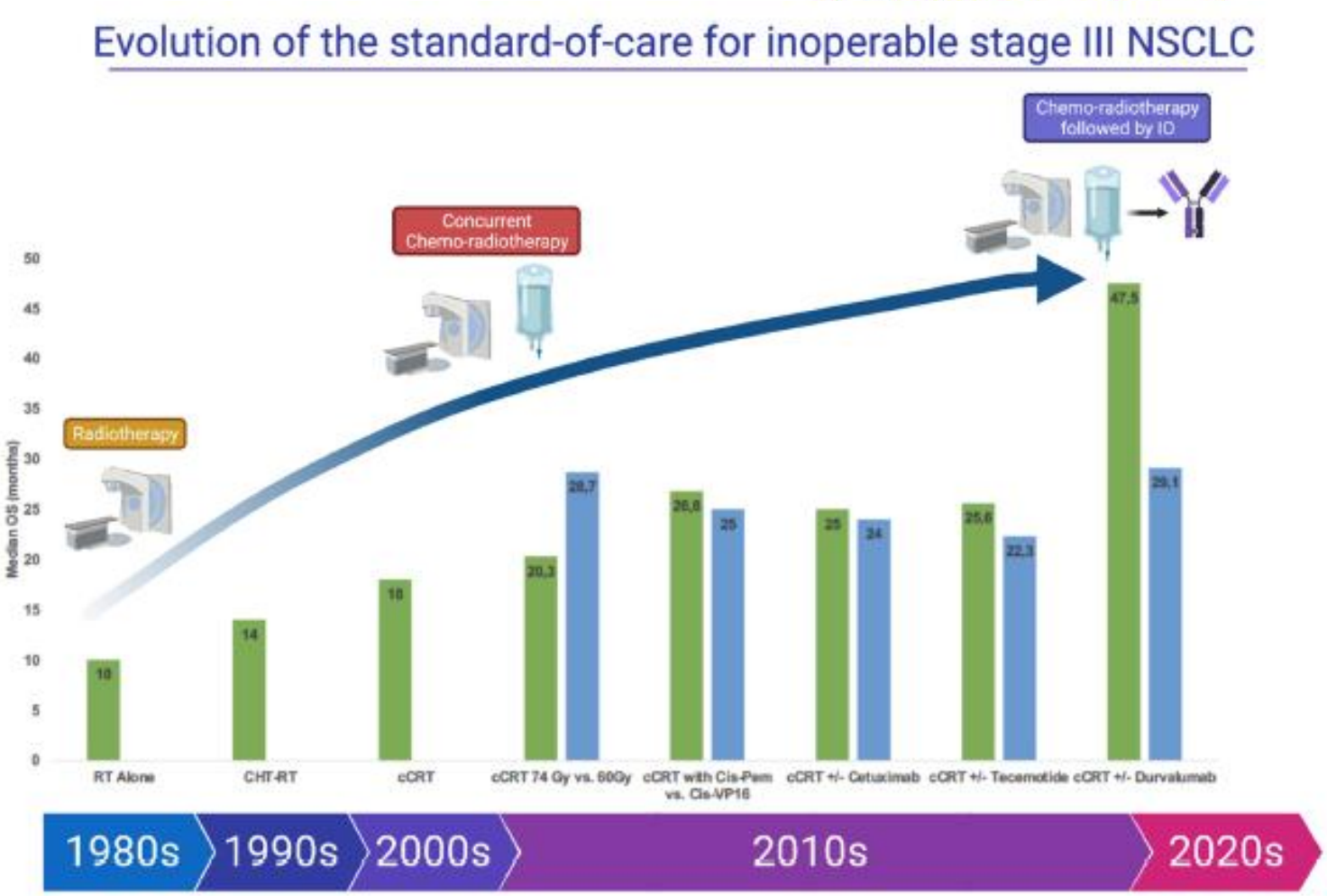


Table 1. Baseline Characteristics, Stratification Factors, and Prior Therapy in the Intention-to-Treat Population.*

Characteristic	Durvalumab (N=476)	Placebo (N=237)	Total (N=713)
Age — yr			
Median	64	64	64
Range	31–84	23–90	23–90
Sex — no. (%)			
Male	334 (70.2)	166 (70.0)	500 (70.1)
Female	142 (29.8)	71 (30.0)	213 (29.9)
Race — no. (%)†			
White	337 (70.8)	157 (66.2)	494 (69.3)
Black	12 (2.5)	2 (0.8)	14 (2.0)
Asian	120 (25.2)	72 (30.4)	192 (26.9)
Disease stage — no. (%)			
IIIA	252 (52.9)	125 (52.7)	377 (52.9)
IIIB	212 (44.5)	107 (45.1)	319 (44.7)
Other‡	12 (2.5)	5 (2.1)	17 (2.4)
WHO performance-status score — no. (%)§			
0	234 (49.2)	114 (48.1)	348 (48.8)
1	240 (50.4)	122 (51.5)	362 (50.8)
Tumor histologic type — no. (%)			
Squamous	224 (47.1)	102 (43.0)	326 (45.7)
Nonsquamous	252 (52.9)	135 (57.0)	387 (54.3)
Smoking status — no. (%)			
Current smoker	79 (16.6)	38 (16.0)	117 (16.4)
Former smoker	354 (74.4)	178 (75.1)	532 (74.6)
Never smoked	43 (9.0)	21 (8.9)	64 (9.0)
Previous radiotherapy — no. (%)¶			
<54 Gy	3 (0.6)	0	3 (0.4)
≥54 to ≤66 Gy	442 (92.9)	217 (91.6)	659 (92.4)
>66 to ≤74 Gy	30 (6.3)	19 (8.0)	49 (6.9)
Previous chemotherapy — no. (%)‖			
Induction	123 (25.8)	68 (28.7)	191 (26.8)
Concurrent with radiation therapy	475 (99.8)	236 (99.6)	711 (99.7)
Best response to previous chemoradiotherapy — no. (%)			
Complete response	9 (1.9)	7 (3.0)	16 (2.2)
Partial response	232 (48.7)	111 (46.8)	343 (48.1)
Stable disease	222 (46.6)	114 (48.1)	336 (47.1)

Anche senza consolidamento con durvalumab,
un terzo dei pazienti è vivo a 5 anni

CT-RT: trattamento potenzialmente curativo



9th Ed TNM Categories and Stages

9th Ed TNM Categories						
T/M	Description	N0	N1	N2		N3
				N2a	**N2 b**	
T1	T1a ≤1 cm	IA1	IIA	IIB	IIIA	IIIB
	T1b >1 to ≤2 cm	IA2	IIA	IIB	IIIA	IIIB
	T1c >2 to ≤3 cm	IA3	IIA	IIB	IIIA	IIIB
T2	T2a Visceral pleura / central invasion	IB	IIB	IIIA	IIIB	IIIB
	T2a >3 to ≤4 cm	IB	IIB	IIIA	IIIB	IIIB
	T2b >4 to ≤5 cm	IIA	IIB	IIIA	IIIB	IIIB
T3	T3 >5 to ≤7 cm	IIB	IIIA	IIIA	IIIB	IIIC
	T3 Invasion	IIB	IIIA	IIIA	IIIB	IIIC
	T3 Same lobe tumor nodule	IIB	IIIA	IIIA	IIIB	IIIC
T4	T4 >7 cm	IIIA	IIIA	IIIB	IIIB	IIIC
	T4 Invasion	IIIA	IIIA	IIIB	IIIB	IIIC
	T4 Ipsilateral tumor nodule	IIIA	IIIA	IIIB	IIIB	IIIC
M1	M1a Pleural / pericardial dissemination	IVA	IVA	IVA	IVA	IVA
	M1a Contralateral tumor nodule	IVA	IVA	IVA	IVA	IVA
	M1b Single extrathoracic lesion	IVA	IVA	IVA	IVA	IVA
	M1c1 Multiple lesions, 1 organ system	IVB	IVB	IVB	IVB	IVB
	M1c2 Multiple lesions, >1 organ system	IVB	IVB	IVB	IVB	IVB

Cosa significa «non irradiabile»?

- Assenza di una definizione standardizzata
- Criteri clinici e/o tecnici
- Concetto relativo che può variare in relazione all’expertise del centro
- Ruolo del team multidisciplinare nella decisione



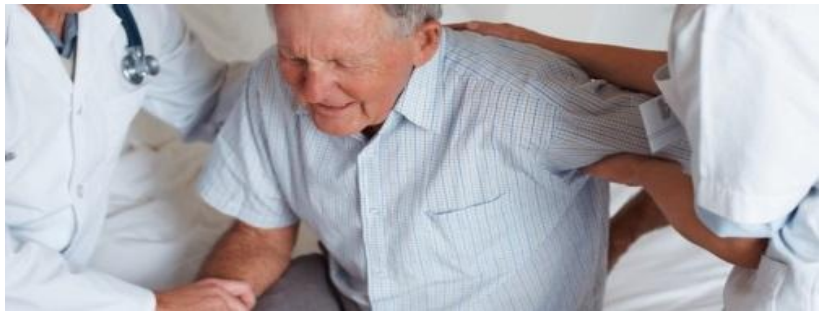
Linee guida internazionali

- NCCN: nessun criterio rigido per non irradiabilità
- ESMO, ASTRO, AIRO: valutazione individuale
- Importanza della valutazione dosimetrica personalizzata
- Ruolo dell’evoluzione tecnologica

Possibili criteri di non irradiabilità

CLINICI:

- Funzionalità respiratoria (BPCO severa, ILD)
- Comorbidità CV (SCC, pregressi IMA), fumo
- Performance status (ECOG PS ≥ 2)
- Presenza di cancro-ascesso



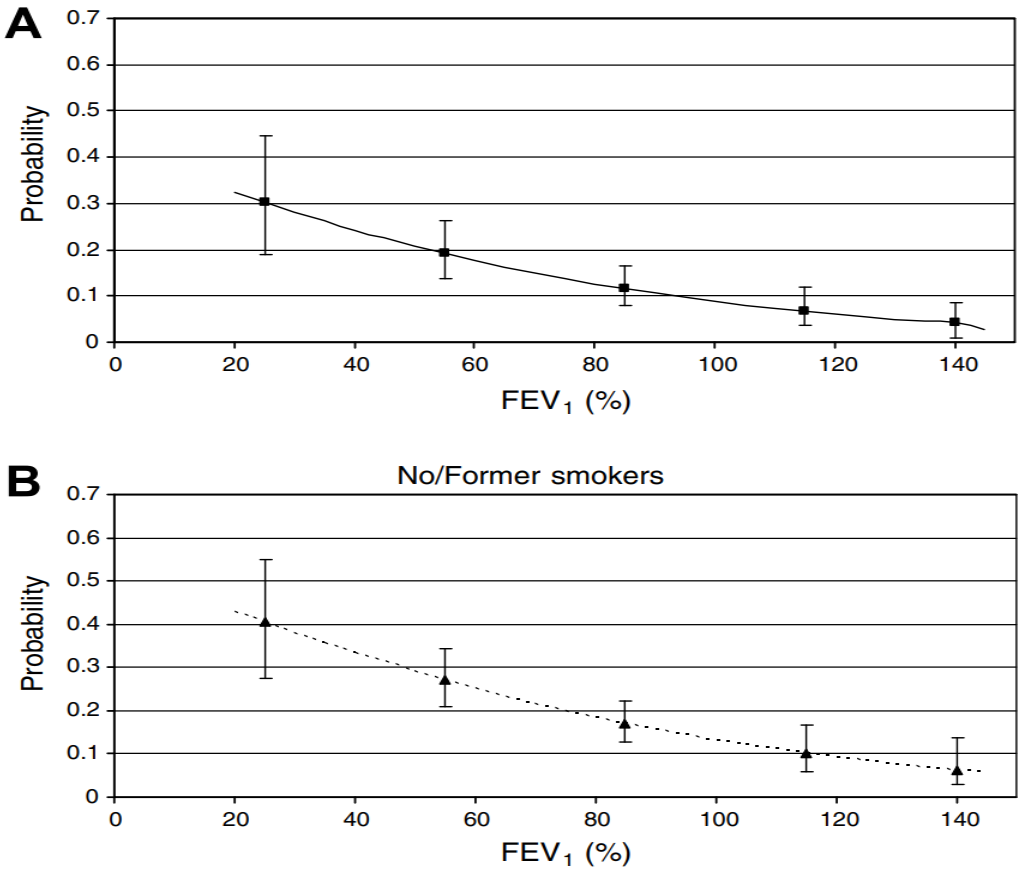


Funzionalità respiratoria: FEV1

Radiother Oncol. 2009 Jun;91(3):421-6. doi: 10.1016/j.radonc.2008.12.002. Epub 2009 Jan 13.

The importance of patient characteristics for the prediction of radiation-induced lung toxicity

Cary Dehing-Oberije [1], Dirk De Ruysscher, Angela van Baardwijk, Shipeng Yu, Bharat Rao, Philippe Lambin



Valori bassi di FEV1 correlano con il rischio di sviluppare dispnea grave dopo la RT, ma non è possibile definire un valore predittivo di FEV1.

Funzionalità respiratoria: BPCO vs ILD

Outcomes of curative-intent radiotherapy in non-small cell lung cancer (NSCLC) patients with chronic obstructive pulmonary disease (COPD) and interstitial lung disease (ILD)

Celion Tang [a], Hitesh Mistry [b,c], Neil Bayman [d], Clara Chan [d], David Cobben [b,d], Corinne Faivre-Finn [b,d], Margaret Harris [d], Jason Kennedy [b], Laura Pemberton [d], Gareth Price [b,d], Hamid Sheikh [d], David Woolf [b,d], Joanna Coote [d], Ahmed Salem [b,d,*]

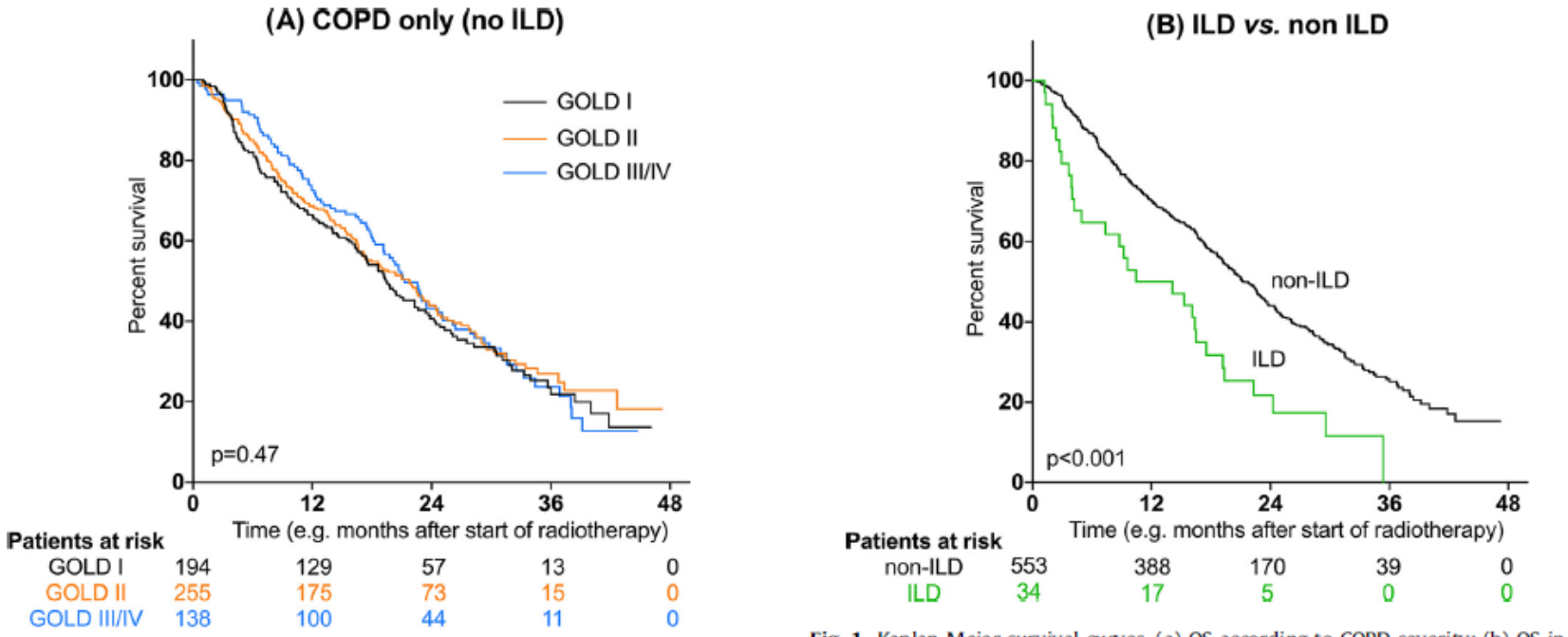


Fig. 1. Kaplan-Meier survival curves. (a) OS according to COPD severity; (b) OS in ILD (n = 34) *vs* non-ILD COPD (n = 553) patients.

Funzionalità respiratoria: ILD

G. RT for locally advanced disease and ILD	10. Chemoradiotherapy in patients with locally advanced disease and ILD should be proposed only after careful assessment of the benefit/harm ratio within a multidisciplinary context in which the type of ILD, the presence of symptoms related to respiratory comorbidity, the patient's life expectancy, the presentation characteristics of the lesion to be treated, the possible toxicities (including fatal ones) are evaluated. However, the use of the highest technological standards is essential.	9 (7-9)

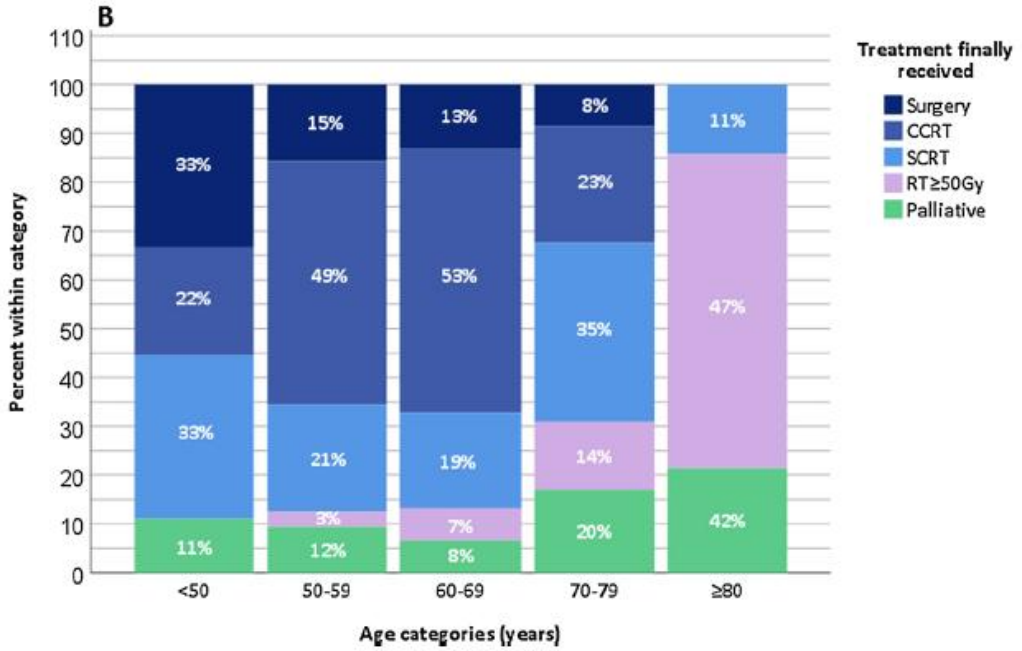
Borghetti P, et al. 2025 *in press*

Funzionalità respiratoria: ILD

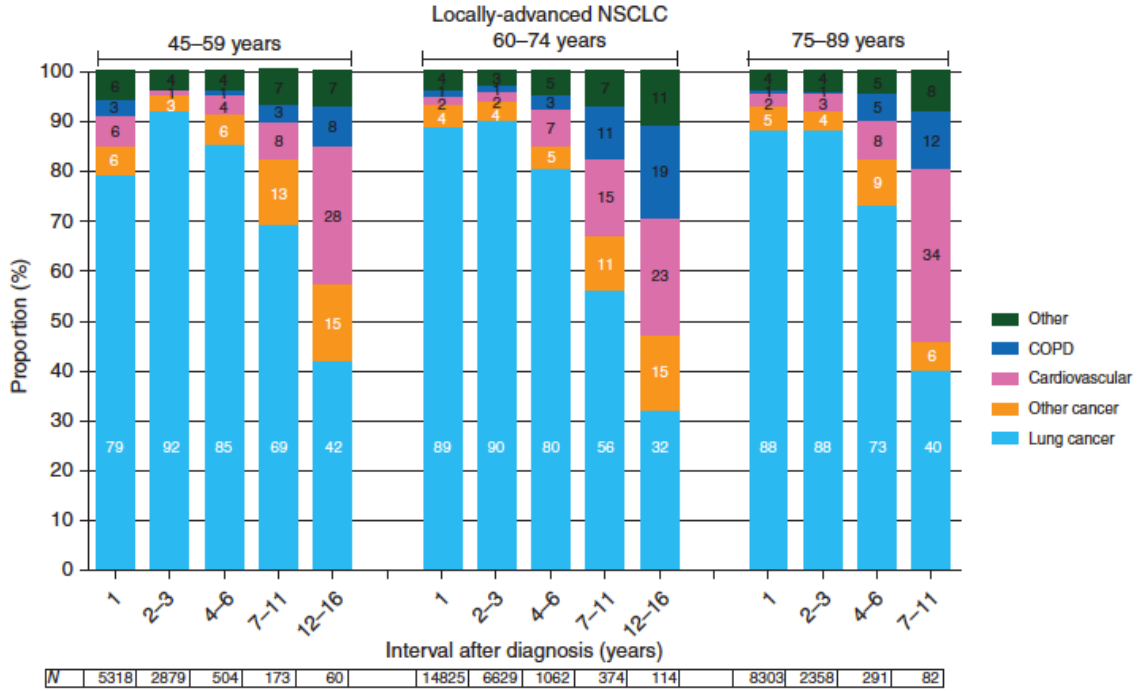
H. RT combined with systemic treatment and ILD	11. In case of combined treatment with chemotherapy and RT in NSCLC patients with ILD, cytotoxic drugs that could be considered are cisplatin, carboplatin, vinorelbine, weekly (nab-) paclitaxel. Gemcitabine and docetaxel should be avoided	9 (6-9)
	12. Maintenance immunotherapy after curative chemo-radiotherapy should not be always excluded upfront in patients with suspected ILD., Immunotherapy could be an option in patients with advanced NSCLC and concomitant ILD with a close monitoring of respiratory function.	8.5 (6-9)
	13. Thoracic RT for patients with ILD, treated with targeted therapy (TKI or ADC), is limited from the risk of pneumonitis related to these treatments.	8 (5-9)

Borghetti P, et al. 2025 *in press*

Età, comorbidità e cause di morte



Ronden MI, Lung Cancer 2021

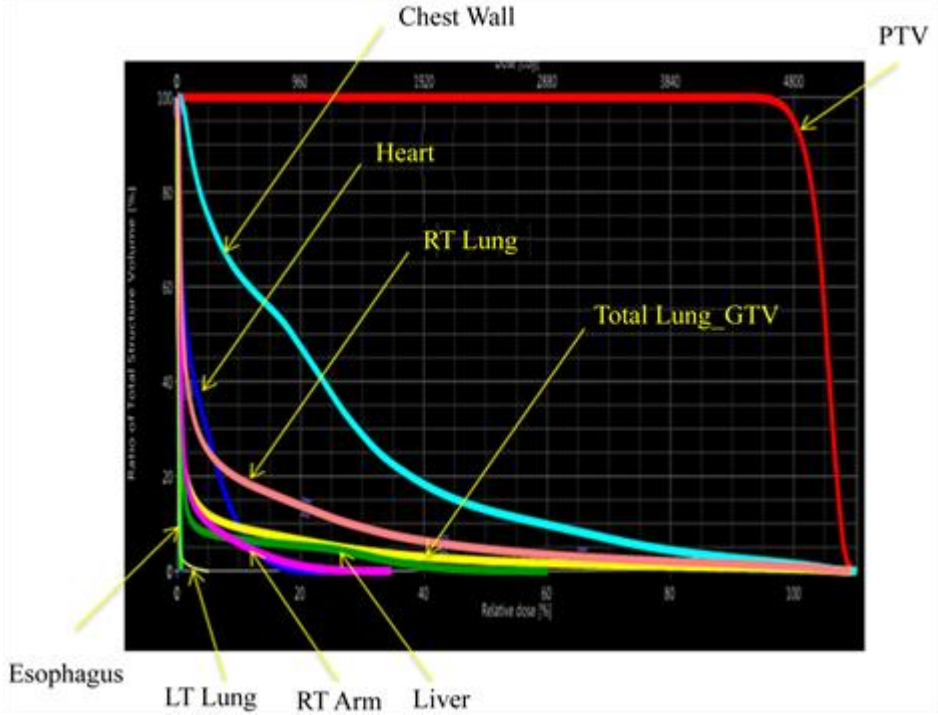


Janssen-Heijnen ML, Ann Oncol. 2015

Possibili criteri di non irradiabilità

TECNICI:

- Lung V20 > 35% o V5 > 60%
- Dose media cardiaca > 16 Gy o V40 > 10%
- Linfopenia radio-indotta
- Volume di malattia > 500 cc (?)



Fattori di rischio per polmonite attinica

Clinical Investigation: Thoracic Cancer

Predicting Radiation Pneumonitis After Chemoradiation Therapy for Lung Cancer: An International Individual Patient Data Meta-analysis



Table 5 Risk of radiation pneumonitis based on V_{20} (volume of lung receiving 20 Gy or more) in the whole cohort of patients (training and validation set combined)

Lung volume receiving ≥20 Gy	Symptomatic pneumonitis (% of patients)	Fatal pneumonitis (% of patients)
<20%	18.4%	0.0%
20%-29.99%	30.3%	1.0%
30%-39.99%	32.6%	2.9%
≥40%	35.9%	3.5%

Il rischio di polmonite attinica è associato a:

- Schema di chemioterapia (carbo-paclitaxel)
- Parametri dosimetrici (Lung V20)
- Età del paziente (>65)
- Localizzazione del tumore (basi polmonari)

Constraints

Consensus Quality Measures and Dose Constraints for Lung Cancer From the Veterans Affairs Radiation Oncology Quality Surveillance Program and ASTRO Expert Panel

Lindsay L. Puckett, MD [a] · Mohammad Titi, BS [a] · Ksenija Kujundzic, BS [b] · ... · Randi Kudner, MA [b] · Emily Wilson, BS [b] · Charles B. Simone, II, MD, FACRO [o] ... Show more

Fractionation Regimen	OAR	Metric	Tolerance Dose limit	Minor Deviation	Major deviation	Metric Type	Expected Performance Rate	Source
Standard (1.8-2Gy/Fx to 59.4-70Gy)	SpinalCord	Dmax*	≤ 50.5 Gy	>50 Gy ≤ 52 Gy	> 52 Gy	Constraint	100%	RTOG 0617
	Lungs (whole lung - iGTV)	V20 Gy	≤ 33%	> 33% ≤ 37%	> 37%	Constraint	95%	QUANTEC/RTOG 0617
		V5 Gy	≤ 60%	> 60% ≤ 70%	> 70%	Informational	N/A	RTOG 1308(min)/LU004 (max)
		Dmean	≤ 18 Gy	> 18 Gy ≤ 22 Gy	> 22 Gy	Constraint	95%	QUANTEC/RTOG 0617/NCCN
	Lung (single lung - iGTV) ^	V20 Gy	≤ 6.3%	> 6.3% ≤ 7%	> 7%	Constraint	95%	Rice et al, IJROBP 2007
		V5 Gy	≤ 42%	> 42% ≤ 60%	> 60%	Informational	N/A	Panel consensus
		Dmean	≤ 7.7 Gy	> 7.7 Gy ≤ 8.5 Gy	> 8.5 Gy	Constraint	95%	Rice et al, IJROBP 2007
	BrachialPlex	Dmax*	≤ 66 Gy	> 66Gy ≤70 Gy	> 70 Gy	Constraint	100%	RTOG 1308
	Esophagus	Dmax*	≤ 105% Rx	> 105% Rx ≤74 Gy	> 74 Gy	Constraint	95%	RTOG 1308
		V60 Gy	≤ 15.3 %	> 15.3% ≤ 17 %	> 17%	Informational	N/A	Palma et al, IJROBP 2014/NCCN
		Dmean	≤ 30.6 Gy	> 30.6 Gy ≤ 34 Gy	> 34 Gy	Informational	N/A	QUANTEC/RTOG 0617/NCCN
	Heart	V45Gy	≤ 35%	> 35% ≤ 40%	> 40 %	Constraint	95%	RTOG 1308

Constraints

Open Access Full Text Article

ORIGINAL RESEARCH

Dose-Volume Constraints Parameters for Lung Tissue in Thoracic Radiotherapy Following Immune Checkpoint Inhibitor Treatment

Kang Wang[1], Fengchang Yang[1], Changxing Feng[1], Fuhao Xu[1], Li Li[1], Jinghao Duan[1], Shuanghu Yuan[1,2]

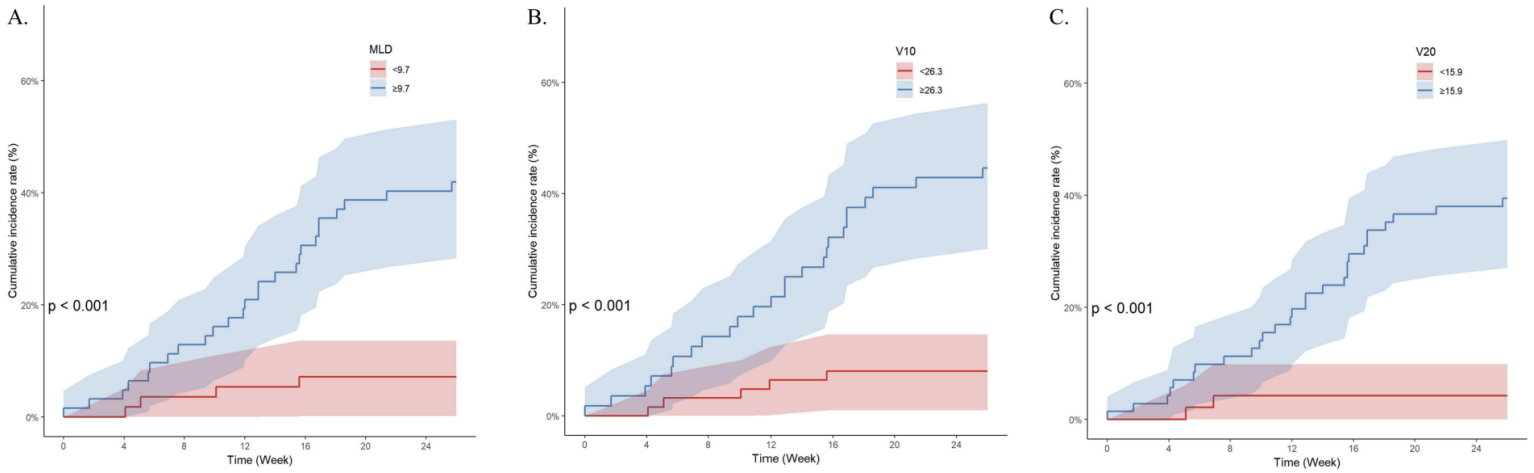
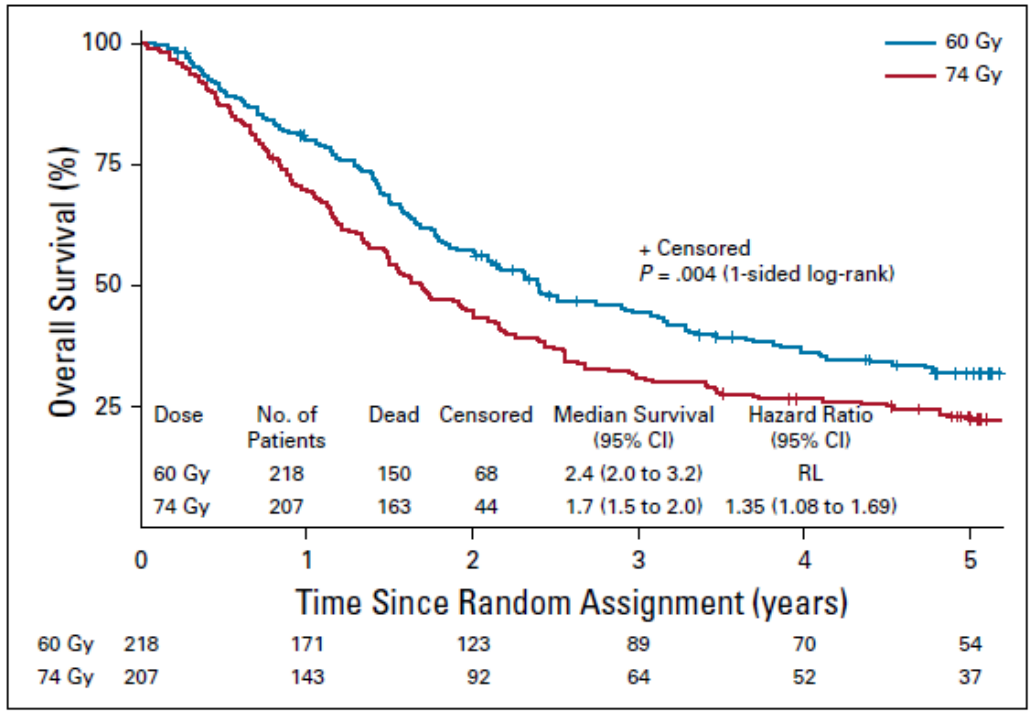


Table 3 Patient and Tumor Characteristics Correlate with Grade ≥2 Radiation Pneumonitis

Characteristics	Patients N (%)	Grade ≥2 RP		
		N (%)	OR (95% CI)	p
Age (years)				0.590
<62	54 (45.8)	15 (27.8)	1.000 (reference)	
≥62	64 (54.2)	15 (23.4)	0.796 (0.347–1.826)	
Gender				0.803
Female	18 (15.3)	5 (27.8)	1.000 (reference)	
Male	100 (84.7)	25 (25.0)	0.867 (0.281–2.673)	
Smoking History				0.531
No	53 (44.9)	12 (22.6)	1.000 (reference)	
Yes	65 (55.1)	18 (27.8)	1.309 (0.564–3.037)	
History of ILD/COPD				0.140
No	95 (80.5)	27 (28.4)	1.000 (reference)	
Yes	23 (19.5)	3 (13.0)	0.378 (0.104–1.376)	
Pathology				0.564
Squamous cell carcinoma	59 (50.0)	13 (22.0)	1.000 (reference)	
Adenocarcinoma	57 (48.3)	16 (28.1)	3.538 (0.207–60.524)	
Others	2 (1.7)	1 (50.0)	1.381 (0.594–3.212)	
Tumor location (lobes)				0.023
Upper or middle lobes	86 (72.9)	17 (19.8)	1.000 (reference)	
Lower lobe	32 (27.1)	13 (40.6)	2.777 (1.149–6.714)	
T stage				0.516
T1	16 (13.6)	6 (37.5)	1.000 (reference)	
T2	32 (27.1)	9 (28.1)	0.652 (0.183–2.327)	
T3	23 (19.5)	6 (26.1)	0.588 (0.149–2.326)	
T4	47 (39.8)	9 (19.1)	0.395 (0.114–1.372)	
N stage				0.890
N0	10 (8.5)	0 (0.0)	1.000 (reference)	
N1	18 (15.3)	4 (22.2)	–	
N2	41 (34.7)	13 (31.7)	–	
N3	49 (41.5)	13 (26.5)	–	
M stage				0.761
M0	50 (42.4)	12 (24.0)	1.000 (reference)	
M1	68 (57.6)	18 (26.5)	1.140 (0.490–2.650)	
Time interval of Radioimmunotherapy (days)				0.003
≤21	66 (55.9)	24 (36.4)	1.000 (reference)	
>21	52 (44.1)	6 (11.5)	0.228 (0.085–0.613)	
Radiation Prescription Dose (Gy)				0.849
<54	28 (23.7)	6 (21.4)	1.000 (reference)	
54–60	78 (66.1)	21 (26.9)	1.351 (0.481–3.792)	
>60	12 (10.2)	3 (25.0)	1.222 (0.250–5.982)	

RTOG 0617: 3D-CRT vs IMRT

Stage III NSCLC 74 Gy vs 60 Gy (2 Gy/fraction)



Bradley JD, Lancet 2015

Table 3. Outcomes at 2 Years by Radiation Therapy Technique

Outcome	3D-CRT, % (95% CI)	IMRT, % (95% CI)	*P*
Overall survival	49.4 (42.9 to 55.5)	53.2 (46.4 to 59.6)	.597
Progression-free survival	27.0 (21.5 to 32.7)	25.2 (19.7 to 31.1)	.595
Local failure	37.1 (31.0 to 43.1)	30.8 (24.8 to 36.9)	.498
Distant metastases	49.6 (43.2 to 55.8)	45.9 (39.2 to 52.3)	.661

Table 4. CTCAE ≥ Grade 3 Radiation-Related Adverse Events of 3D-CRT and IMRT

≥ Grade 3 Toxicity	3D-CRT, % (No.)	IMRT, % (No.)	*P*
No. of patients	254	228	
Pneumonitis	7.9 (20)	3.5 (8)	.039
Esophagitis/dysphagia	15.4 (39)	13.2 (30)	.534
Weight loss	2.8 (7)	3.9 (9)	.419
Cardiovascular	8.3 (21)	4.8 (11)	.131

Table 2. Dosimetric Factors of 3D-CRT Versus IMRT

Dosimetric Factor	3D-CRT Median	3D-CRT Q1-Q3	IMRT Median	IMRT Q1-Q3	*P*
Volume of heart, %					
V20	23.5	7.8-46.0	19.3	5.2-36.5	.049†
V40	11.4	1.7-25.9	6.8	0.6-15.5	.003†
V60	2.4	0.0-8.3	1.4	0.0-5.0	.045†

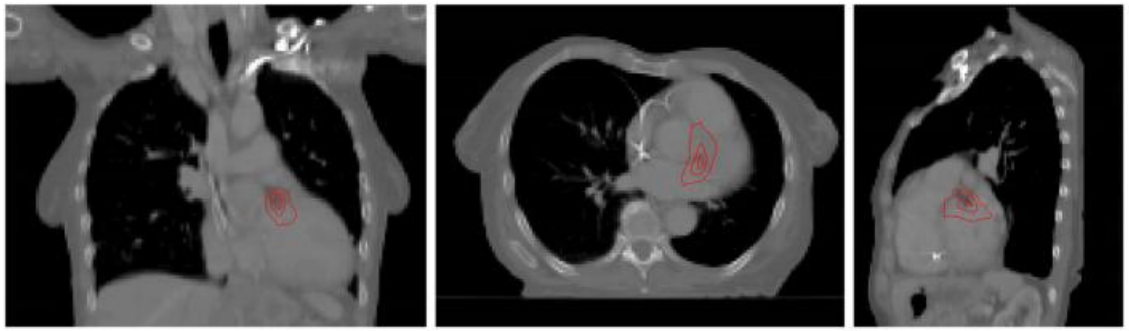
V40 cardiaca correla con OS in analisi multivariata

Chun SG, JCO 2017

Importanza delle substrutture cardiache

Demystifying the Results of RTOG 0617: Identification of Dose Sensitive Cardiac Subregions Associated With Overall Survival

Alan McWilliam, PhD,[a,b,*] Azadeh Abravan, PhD,[a,b] Kathryn Banfill, PhD,[a,b] Corinne Faivre-Finn, PhD,[a,b] Marcel van Herk, PhD[a,b]



Region of the heart identified in the voxel-based analysis in which a higher dose is associated with excess mortality

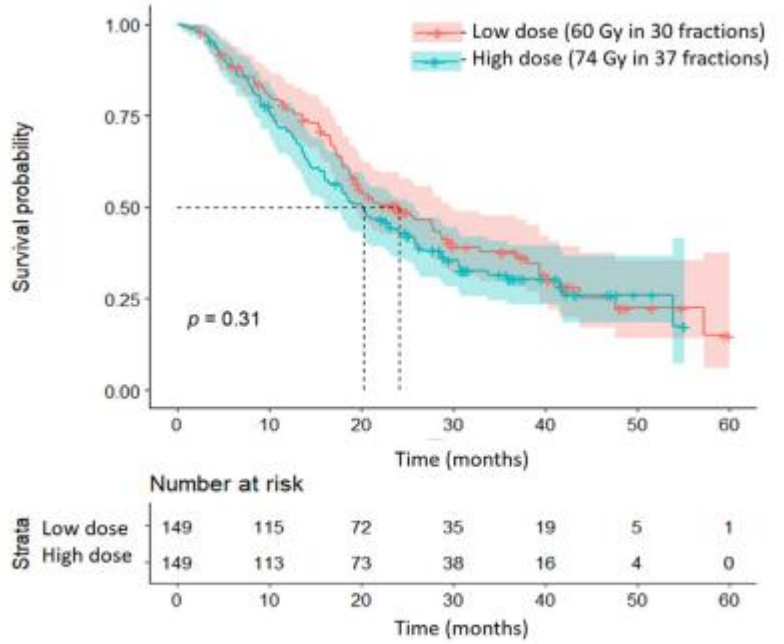


Figure 2. Kaplan-Meier curves after propensity matching. No survival difference was seen between radiation levels.

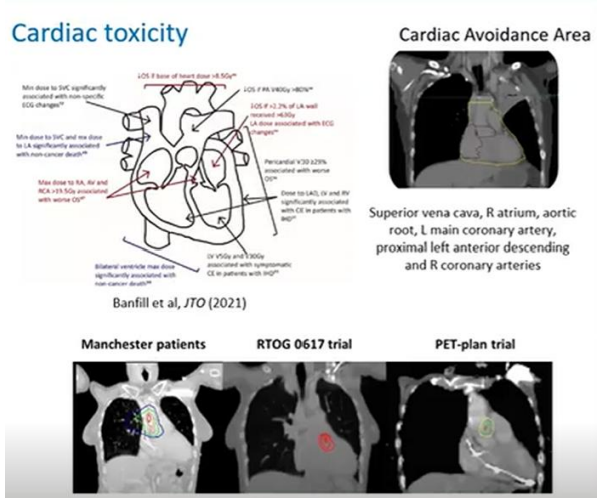
McWilliam A, JTO 2023

Results suggest that the worse survival of the high-dose arm in RTOG 0617 is strongly influenced by the dose delivered to the base of the heart

RWD e prossimi step

Role of Real-World Data in Assessing Cardiac Toxicity After Lung Cancer Radiotherapy

Azadeh Abravan [1,2], Gareth Price [1,2], Kathryn Banfill [1], Tom Marchant [2], Matthew Craddock [1,2], Joe Wood [3], Marianne C. Aznar [1,2], Alan McWilliam [1,2], Marcel van Herk [1,2] and Corinne Faivre-Finn [1,2]*



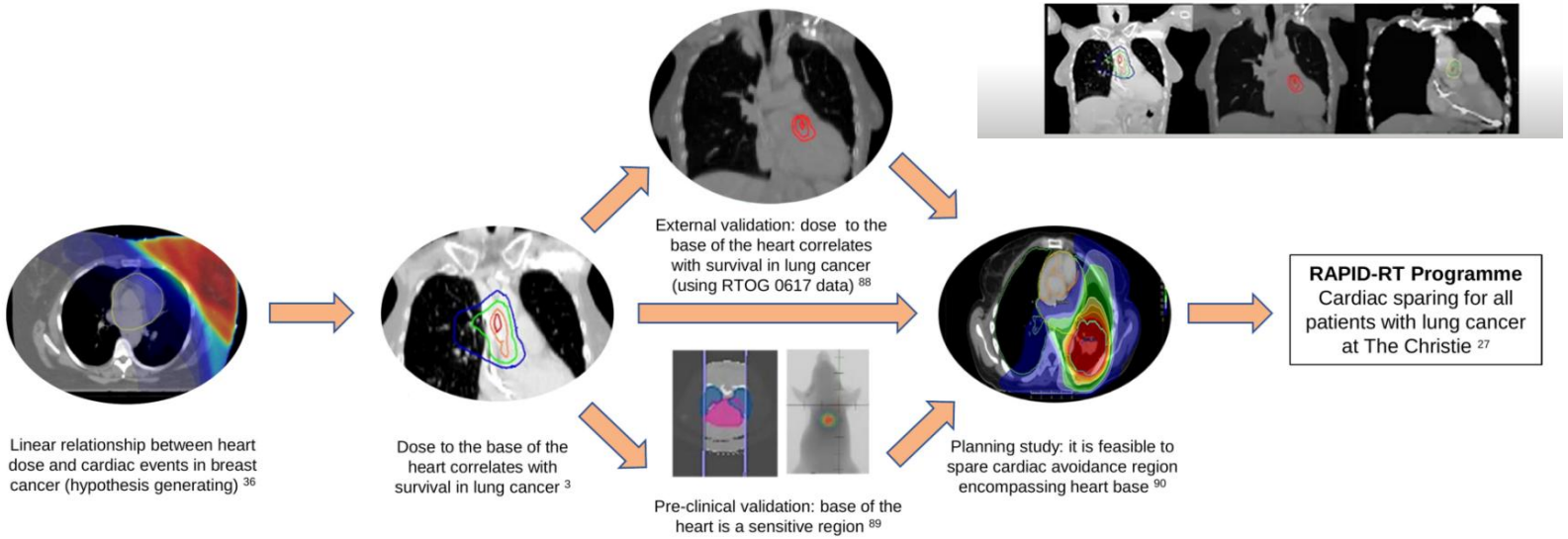
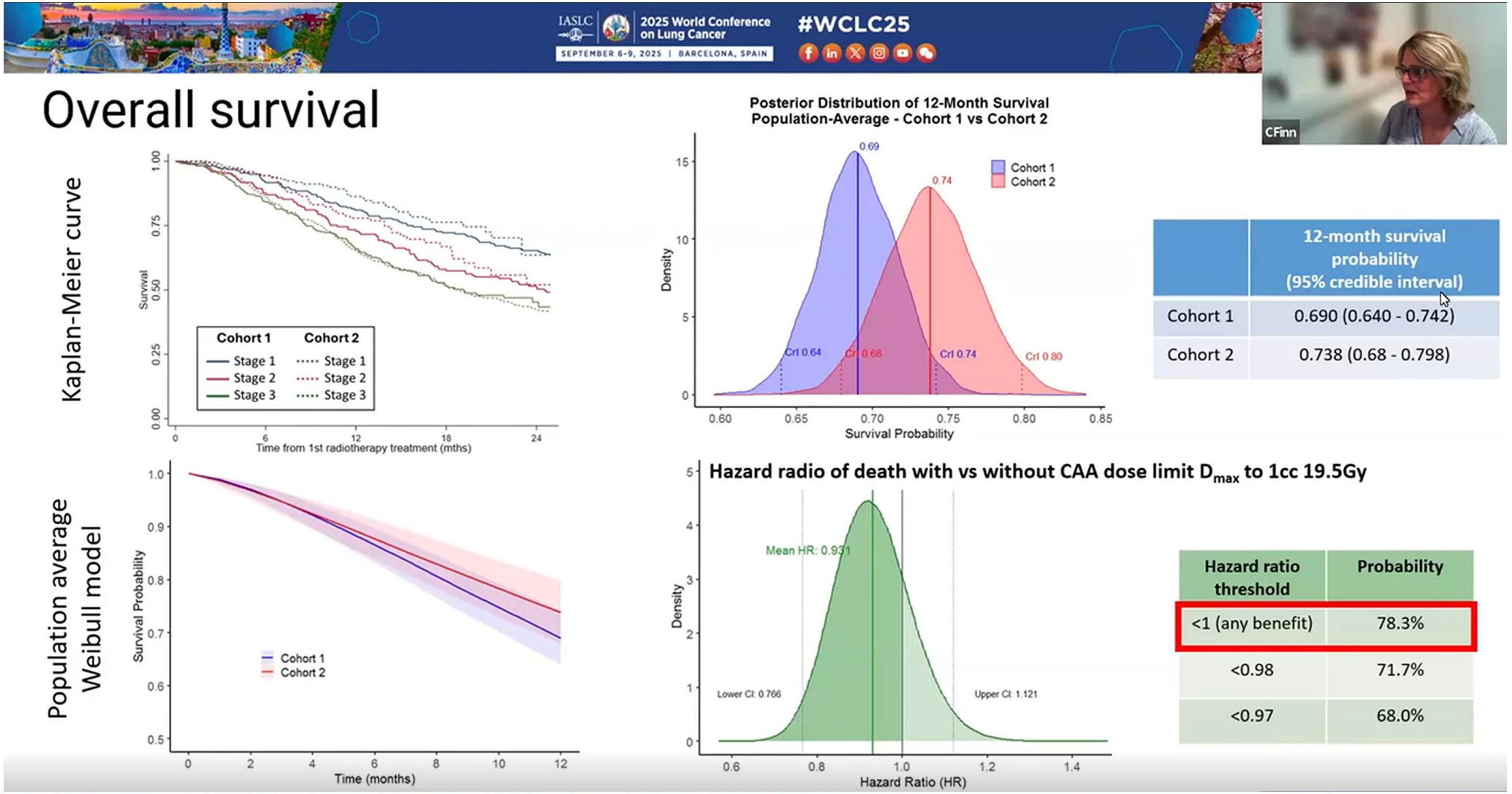


TABLE 1 | Summarizing RWD studies suggesting associations between heart dosimetric factors and outcome of patients with lung cancer in multivariable models.

Authors, year	Patient stage, population (n)	Study Institution	Correlation between heart dosimetric factors, other heart related factors and outcome in multivariable analysis
Speirs et al, 2016 (2)	Stage II-III NSCLC (416)	Single institution, Siteman Cancer Center/ Barnes Jewish Hospital	Heart V_{50} associated with OS and cardiac toxicity
Mcwilliam et al, 2017 (3)	Stage I-IV Lung cancer (1101)	Single institution, The Christie	Mean dose to the identified region located in the base of the heart associated with OS
Stam et al, 2017 (13)	Stage I-II NSCLC (803)	Multi-institutional	Maximum dose on the left atrium and dose to 90% of the superior vena cava associated with non-cancer death
Stam et al, 2017 (4)	Stage II-III NSCLC (469)	Single institution, NKI	Heart V_2 associated with OS
Wang et al, 2017 (15)	Stage III NSCLC (112)	Multi-institutional	MHD, heart V_5, heart V_{30}, and left ventricle V_5 associated with CE in patients with IHD or high WHO/ ISH risk scores. MHD ≥ 20 Gy higher rate of CE No association between OS and heart dose
Dess et al, 2017 (16)	Stage II-III NSCLC (125)	Multi-institutional	MHD and PCD associated with higher CE
Vivekanandan et al, 2017 (5)	Stage IIB-III NSCLC (78)	University of Oxford	ECG changes at 6 month and left atrium dose > 64 Gy associated with OS
Ning et al, 2017 (17)	Stage I-IV NSCLC (201)	Single institution, MD Anderson Cancer Center	Heart V35 >10% and PCD associated with PCE
Chun et al, 2017 (6)	Stage III NSCLC (482)	Multi-institutional	Heart V40 associated with OS
Yegya-Raman et al, 2018 (18)	Stage II-IV NSCLC (140)	Single institution, Rutgers Cancer Institute	MHD and baseline coronary artery disease associated with symptomatic CE
Wong et al, 2018 (14)	Stage I-II NSCLC (189)	Single institution, Princess Margaret Cancer Centre	Max dose (per 100 Gy) to left and right ventricle associated with non-cancer deaths
Xue et al, 2019 (7)	Stage I-III NSCLC (94)	Multi-institutional	MHD, hart V5, V55, pericardial mean dose, V5, V30, and V55 associated with PCE Pericardial V30 and V55 associated with OS
Atkins et al, 2019 (8)	Stage II-IIIB NSCLC (748)	Single institution, Dana-Farber Cancer Institute/ Brigham and Women's Hospital	MHD (≥10 Gy) associated with MACE and OS
Mcwilliam et al, 2020 (9)	Stage I-IV Lung cancer (978)	Single institution, The Christie	Max dose to the combined cardiac region including right atrium, right coronary artery, and ascending aorta associated with OS
Abravan et al, 2020 (19)	Stage II-III Lung cancer (1243)	Single institution, The Christie	Mean dose to the identified region overlapping with right atrium (≥10 Gy) associates with cardiac related death in patients without PCD
Atkins et al, 2021 (10)	Stage II-III NSCLC (701)	Single institution, Dana-Farber Cancer Institute/ Brigham and Women's Hospital	LAD coronary artery V15≥ 10% associated with MACE and OS, particularly in patients without CHD. Left ventricle V15 ≥ 1% associated with MACE in patients with CHD.
Shepherd et al, 2021 (11)	Stage I-III NSCLC (285)	Single institution, MSKCC	Heart V8 associated with OS
Abravan et al, 2021 (20)	Stage II-III Lung cancer (1218)	Single institution, The Christie	Mean dose to LAD associated with cardiac hospital admission and cardiac related death in patients without diagnosed PCD
Abravan et al, 2022 (43)	Stage II-III Lung cancer (2488)	Single institution, The Christie	Mean dose to cardiac avoidance region (superior vena cava, right atrium, aortic root, and proximal segments of the coronary arteries) linearly associated with the increase in the risk of cardiac related death

Abravan A, Frontiers Onc 2022

RAPID-RT trial



	12-month survival probability (95% credible interval)
Cohort 1	0.690 (0.640 - 0.742)
Cohort 2	0.738 (0.68 - 0.798)

Hazard ratio threshold	Probability
<1 (any benefit)	78.3%
<0.98	71.7%
<0.97	68.0%

Linfopenia radio-indotta

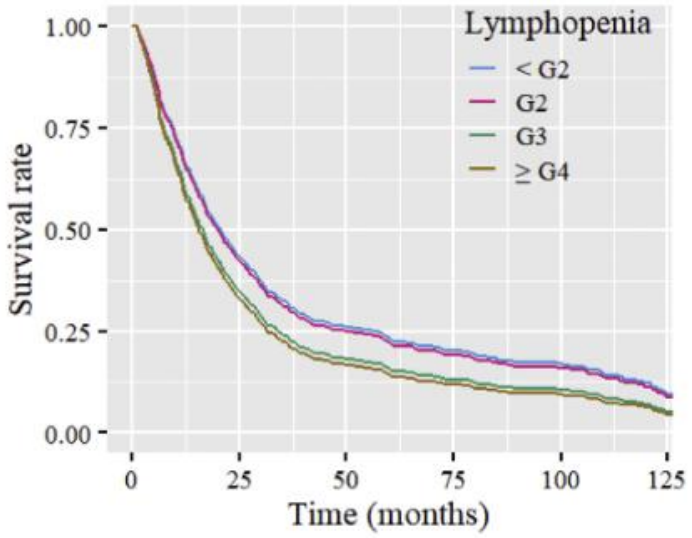
ORIGINAL ARTICLE

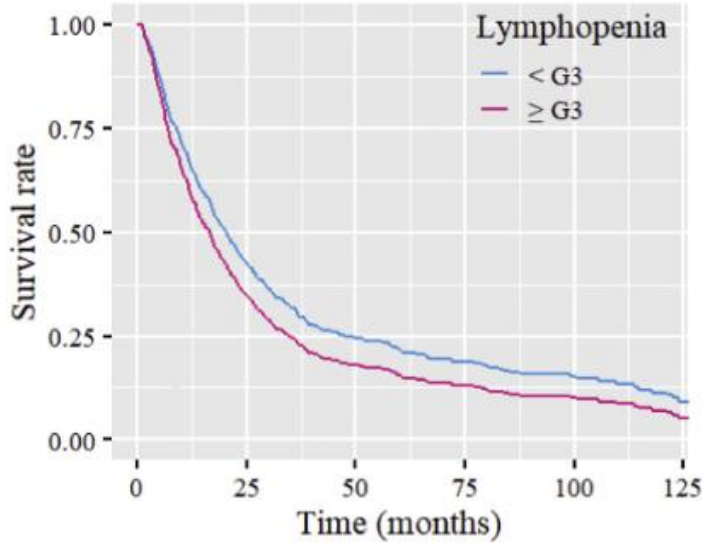
Radiotherapy-Related Lymphopenia Affects Overall Survival in Patients With Lung Cancer

Azadeh Abravan, PhD,[a,b,*] Corinne Faivre-Finn, PhD,[a,b] Jason Kennedy, MSc,[b] Alan McWilliam, PhD,[a,b] Marcel van Herk, PhD[a,b]

Journal of Thoracic Oncology
IASLC INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER

JTO, 2022





Linfopenia rappresenta un fattore prognostico sfavorevole per la sopravvivenza generale

Linfopenia radio-indotta

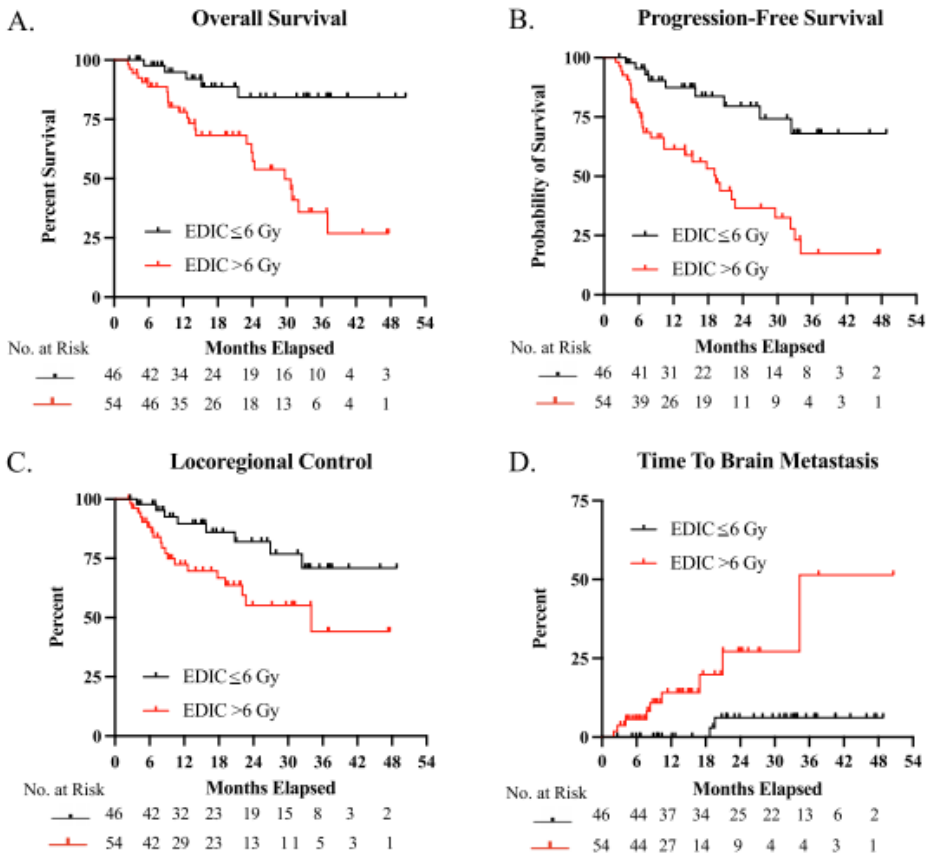
Original Article

Impact of radiation dose to the immune cells in unresectable or stage III non-small cell lung cancer in the durvalumab era

Neal S. McCall [a,*], Hamilton S. McGinnis [a], James R. Janopaul-Naylor [a], Aparna H. Kesarwala [a], Sibo Tian [a], William A. Stokes [a], Joseph W. Shelton [a], Conor E. Steuer [b], Jennifer W. Carlisle [b], Ticiana Leal [b], Suresh S. Ramalingam [b], Jeffrey D. Bradley [a], Kristin A. Higgins [a]

$$EDIC = 0.12 * MLD + 0.08 * MHD + \left[0.45 + 0.35 * 0.85 * \left(\frac{\#fractions}{45}\right)^{\frac{1}{2}}\right] * ITDV/(61.8 * 10^3)$$

EDIC: Estimated radiation Doses to Immune Cells



Alto valore EDIC è un fattore indipendente per peggior OS, PFS e LC

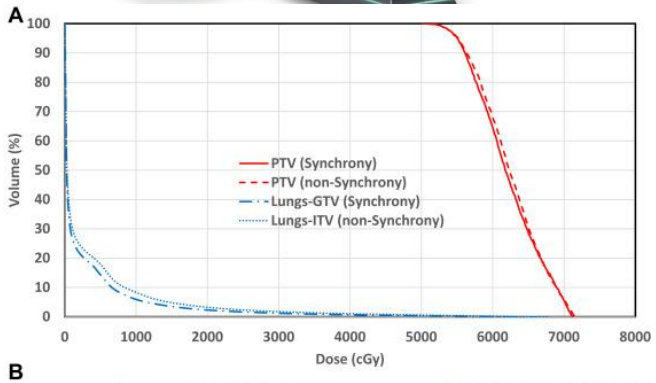
Evoluzione tecnologica

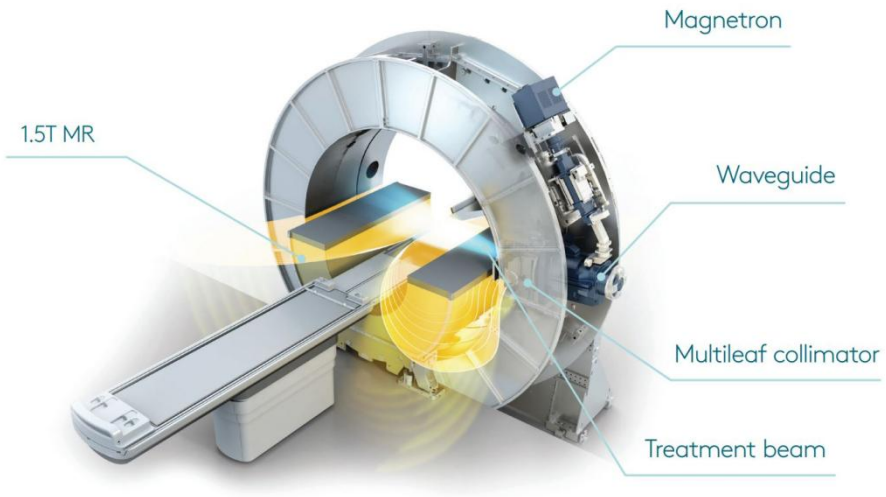
- IMRT, VMAT, protonterapia → maggiore conformazione
- Radioterapia adattativa (ART) → MR-Linac (ma non solo…)
- Imaging avanzato per definizione GTV/CTV → PET, simTC con mdc
- AI e algoritmi predittivi in pianificazione RT

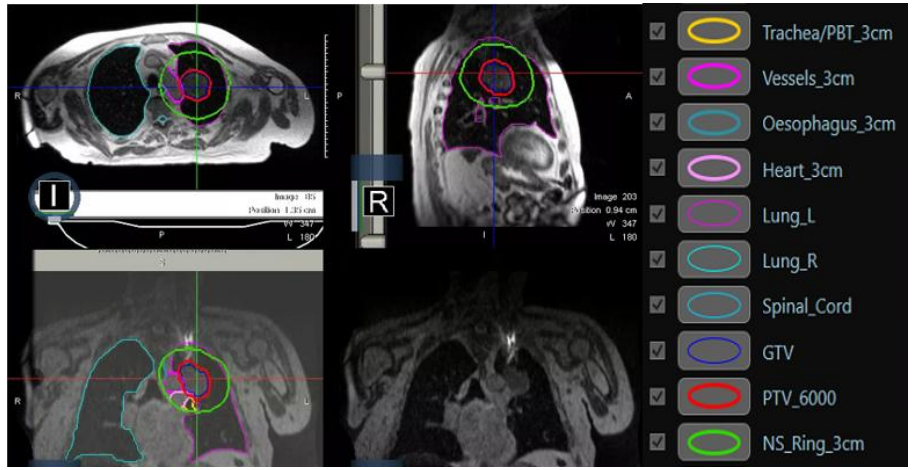


Radioterapia moderna

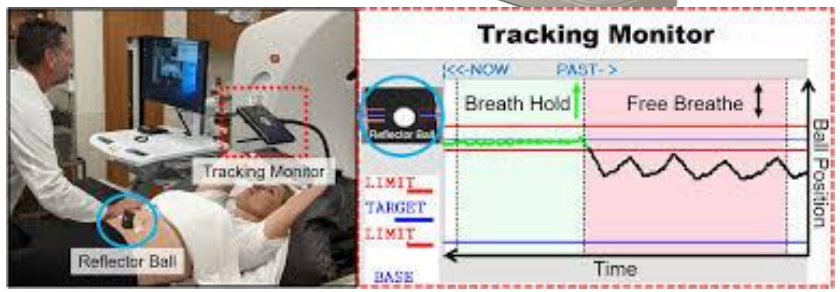


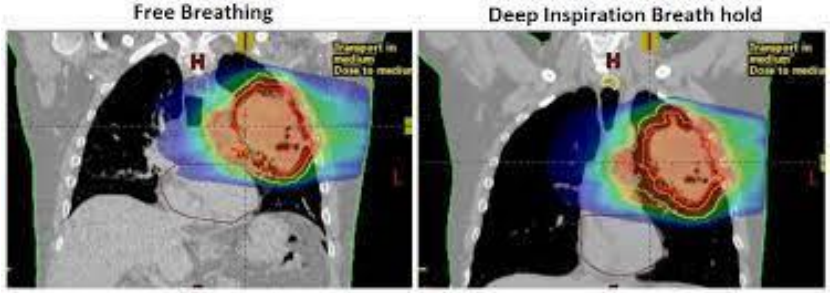












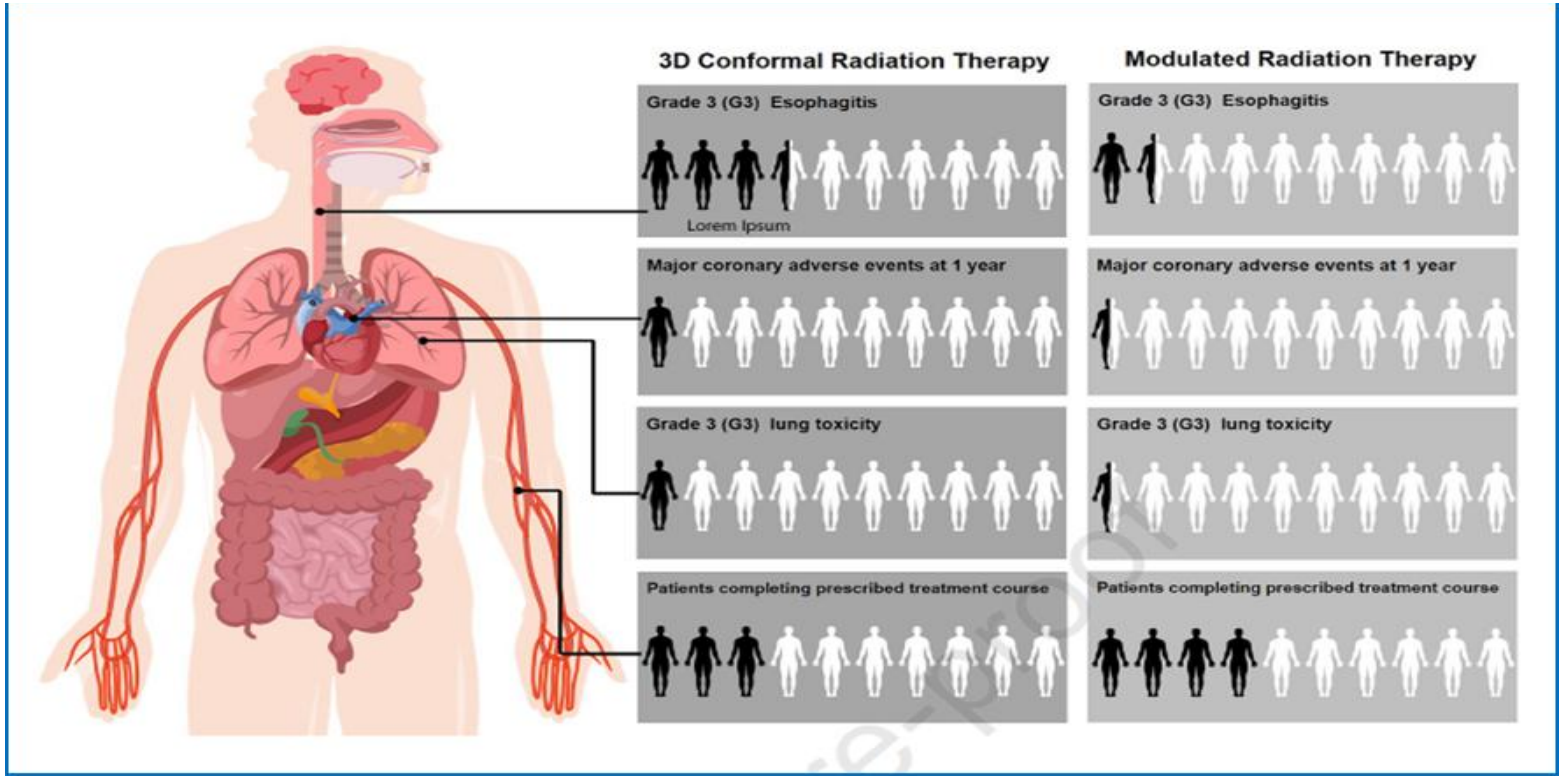
Radioterapia moderna

STATE OF THE ART: CONCISE REVIEW

IASLC

Avoiding Toxicity With Lung Radiation Therapy: An IASLC Perspective

Check for updates

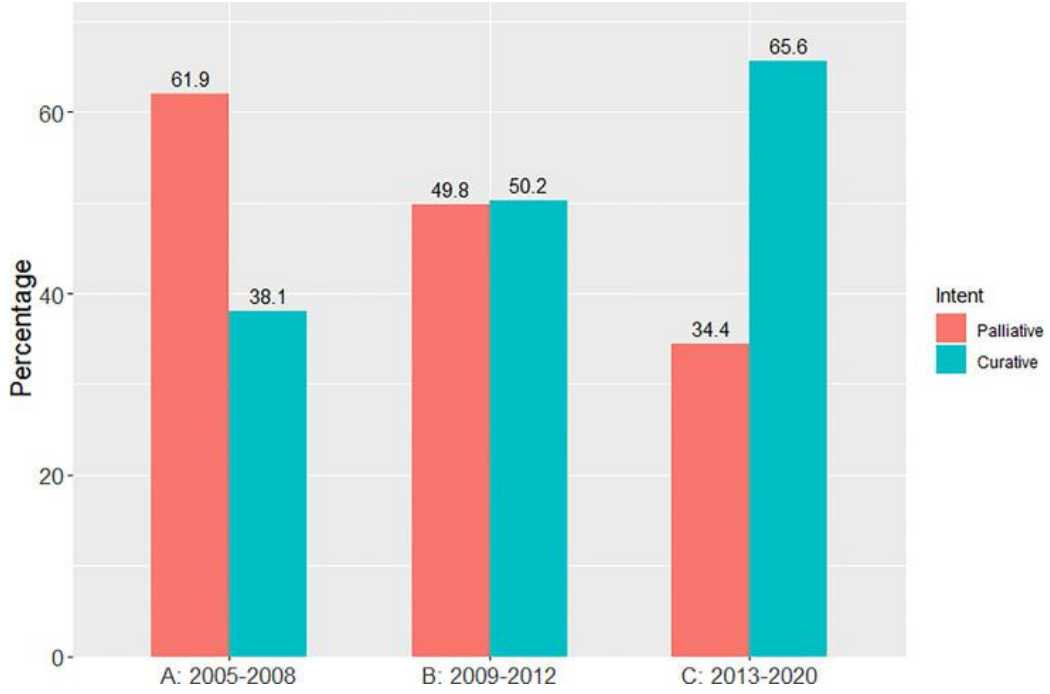


Tecnica radioterapica

frontiers | Frontiers in Oncology

ORIGINAL RESEARCH
published: 31 May 2022
doi: 10.3389/fonc.2022.835844

Impact of Introducing Intensity Modulated Radiotherapy on Curative Intent Radiotherapy and Survival for Lung Cancer

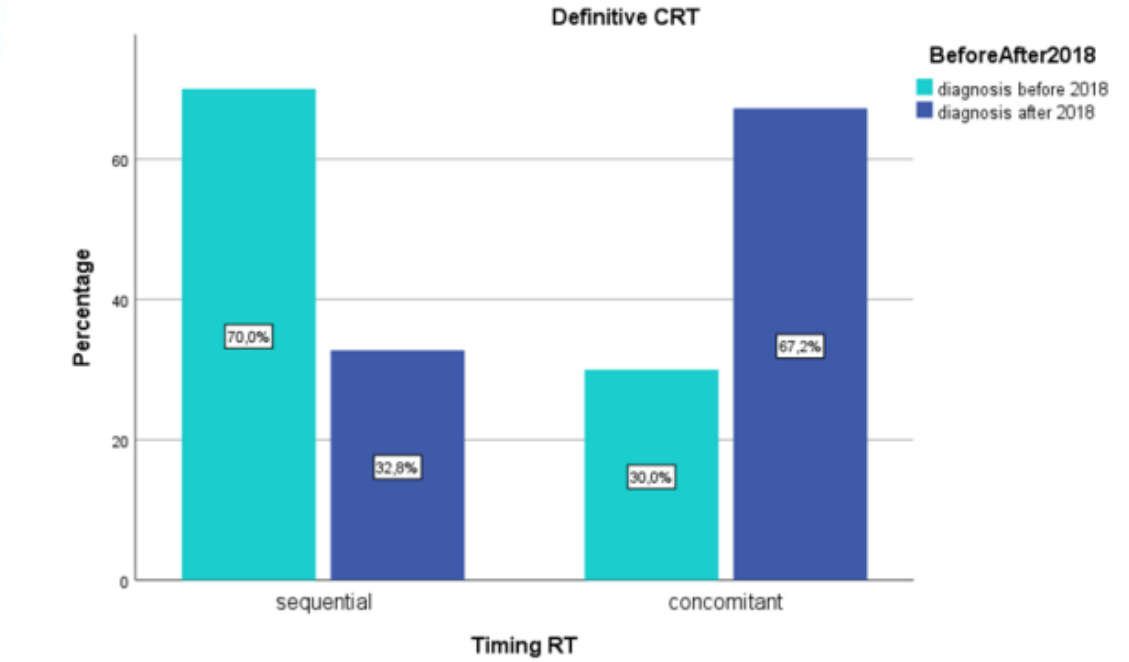


cancers

MDPI

Article

The Multidisciplinary Approach in Stage III Non-Small Cell Lung Cancer over Ten Years: From Radiation Therapy Optimisation to Innovative Systemic Treatments



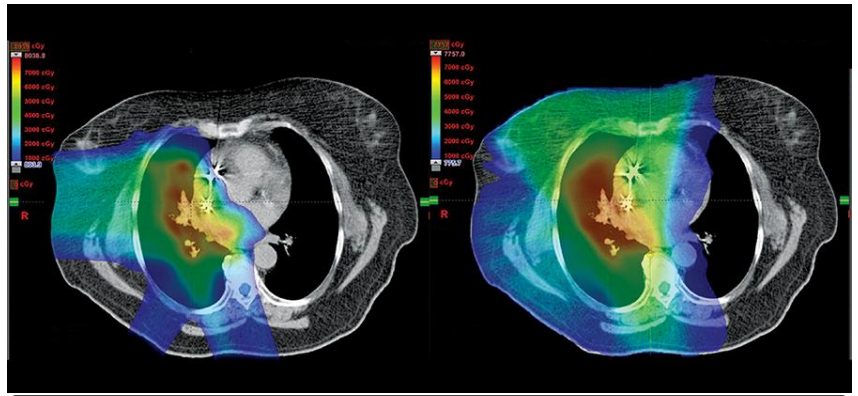
Protons vs Photons

RTOG 1308 Schema

STRATIFY	Stage 1.II 2.IIIA 3.IIIB Histology 1.Squamous 2.Non-Squamous Concurrent Chemotherapy Doublet Type 1.Carboplatin/paclitaxel 2.Cisplatin/etoposide 3. carboplatin/ pemetrexed	RANDOMIZE	Arm 1: Photon dose—70 Gy*, at 2 Gy (RBE) once daily plus platinum-based doublet chemotherapy** Arm 2: Proton dose—70 Gy (RBE), at 2 Gy once daily plus platinum-based doublet chemotherapy**	Both Arms: Durvalumab or Consolidation chemotherapy x 2 cycles required for patients who receive concurrent carboplatin and paclitaxel***

Primary Objectives:

1. Overall survival (OS)
2. Cardiac AE and lymphocyte reduction (lymphopenia)



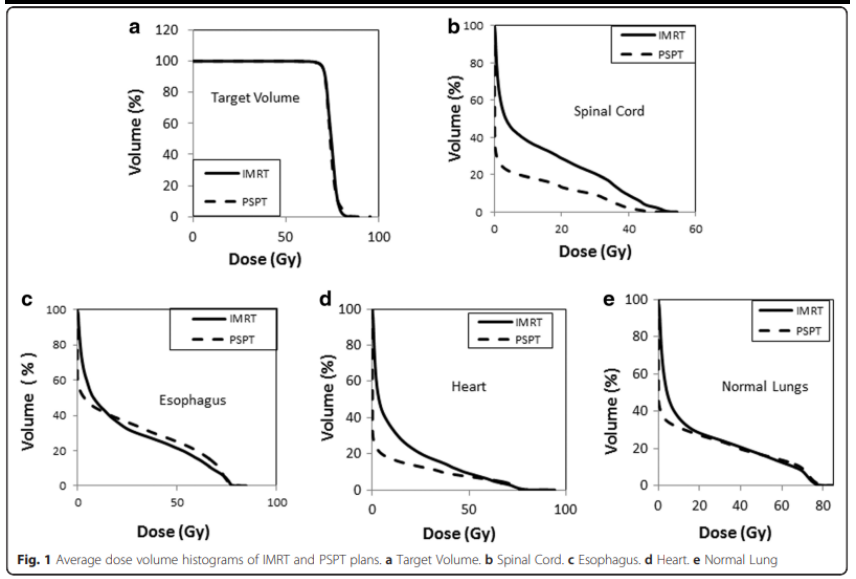


Fig. 1 Average dose volume histograms of IMRT and PSPT plans. **a** Target Volume. **b** Spinal Cord. **c** Esophagus. **d** Heart. **e** Normal Lung

Accrual complete (330 patients), primary end-point results expected to late 2026

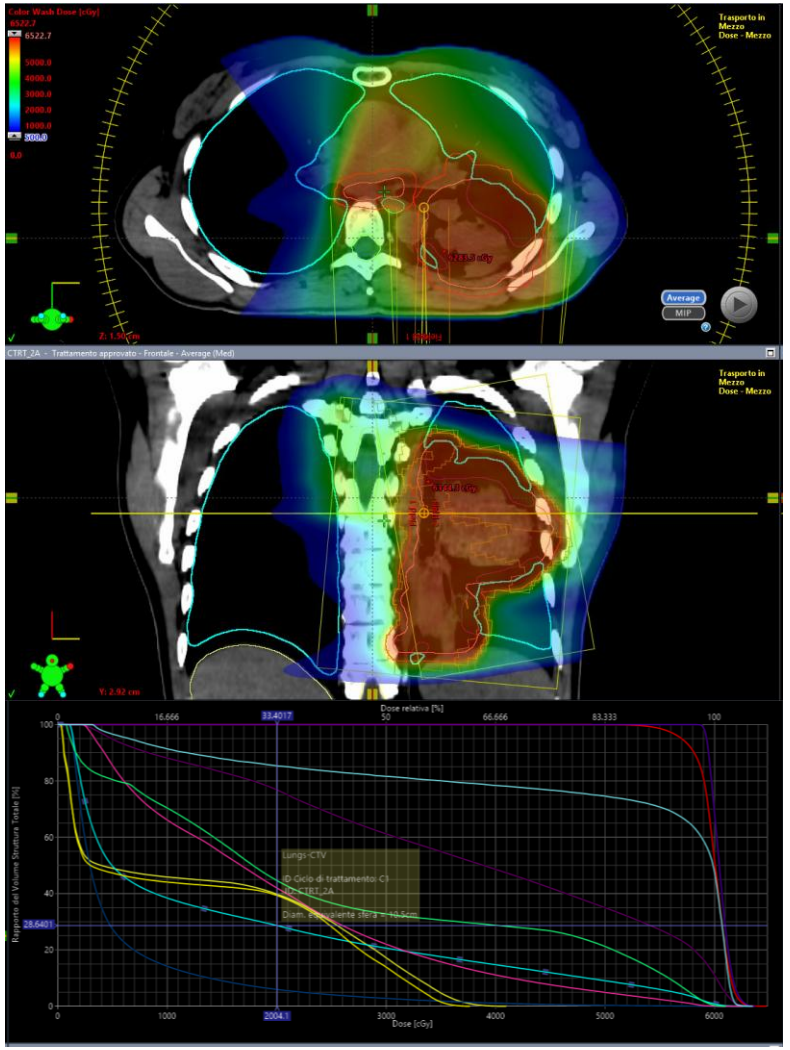
Variabilità tra centri

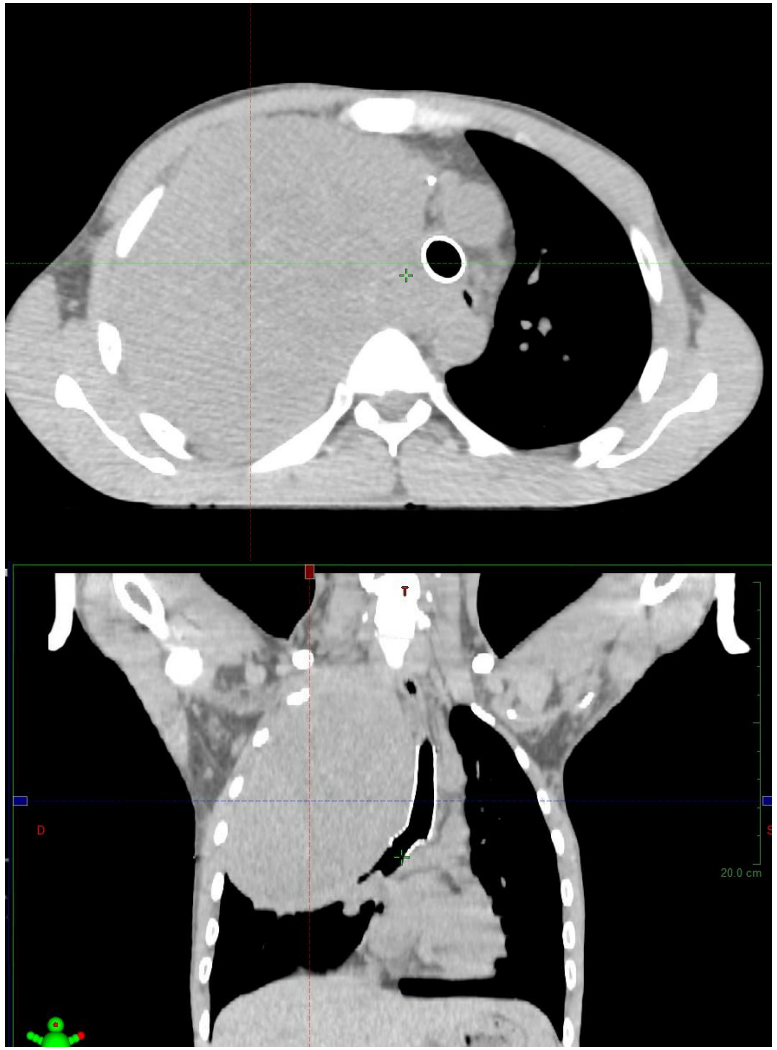
- Discrepanze nell'accesso a tecnologie avanzate
- Diversa esperienza nel gestire casi borderline
- Possibili differenze nel rischio accettabile per OAR
- Mancanza di criteri uniformi → necessità di standardizzazione



Irradiabile o non irradiabile?







Conclusioni



- Non esiste definizione universale di «non irradiabile»
- Attenzione al parametro T in relazione all’invasione
- Volumi di trattamento non rappresentano controindicazione assoluta
- Selezione del paziente in relazione ad età, comorbidità e storia di malattia
- Importanza del team multidisciplinare per condivisione e collaborazione

Grazie per l’attenzione



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