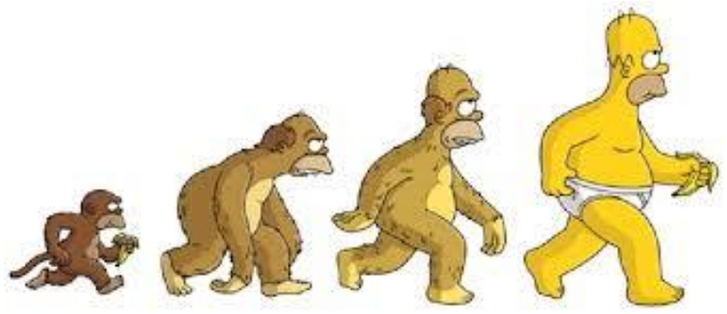
RADIOTHERAPIE ADJUVANTE CBNPC STADES III

L'évolution de la Radiothérapie



Réunion du 27 avril 2018

Dr Xavier Zasadny

Service d'Oncologie, de Radiothérapie et de Soins Palliatifs
Polycliniques Limoges

INTRODUCTION

1	1	1	1	-	-	-	-	N3	IIIB						IIIC	
0	0	0	0	1	1	-	-	N2	IIIA						IIIB	
0	0	0	0	0	0	1	1	N1	IIB						IIIA	
0	0	0	0	0	0	0	0	N0	IA1		IA2		IA3	IB	IIA	IIB	IIIA
Tumeur Primaire									T1a		T1b		T1c	T2a	T2b	T3	T4
Stade 0 TisN0M0		Taille (cm)							≤1		]1;2]		]2;3]	]3;4]	]4;5]	]5;7]	≥7
		Localisation							Pas d'extension proximale					Bronche souche Atélectasie		Bronche souche Atélectasie	Carène
		Invasion							Aucune					**Plèvre Viscérale**		Cage thoracique Péricarde Nerf phrénique	Trachée, Diaphragme, Médiastin, Cœur, Gros Vaisseaux, œsophage, Vertèbres, Nerf récurrent,
		Nodules Satellites							Aucun					Aucun		Même Lobe	Autres lobes ipsilatéraux

- 40% de cancers pulmonaires localement avancés
- Contrôle local < 50% à 5 ans
- Récidive locale corrélée à la progression métastatique

- Stades III opérés : Survie à 3 ans de 10 à 50%
- Groupe très hétérogène :
  - T3-4N0 vs T1-2N2
  - N2 vs Bulky N2
  - R0 vs R1 vs R2

PLAN

Ce dont on va parler :

- Résultats de la Radiothérapie adjuvante dans les Stades III
- Evolution des Techniques de Radiothérapie
- Recommandations NCCN / ESMO

Ce dont on ne parlera pas :

- Radiochimiothérapie pré- ou post-opératoire ?
- Radiochimiothérapie adjuvante séquentielle ou concomitante ?
- Quels territoires traiter par Radiothérapie ?
- Radiosensibilité tumorale
- …

CHIRURGIE N2 - RÉTRO - 1981

World J. Surg. 5, 663–666, 1981

World Journal of Surgery

Results of Surgical Treatment in N2 Lung Cancer

Nael Martini, M.D., Betty J. Flehinger, Ph.D., Muhammad B. Zaman, M.D., and Edward J. Beattie, Jr., M.D.

Thoracic Service, Department of Surgery, and Department of Pathology, Memorial Sloan-Kettering Cancer Center, New York, and Mathematical Sciences Department, IBM Thomas J. Watson Research Center, Yorktown Heights, New York, U.S.A.

Eighty patients were treated by resection for carcinoma of the lung with mediastinal lymph node metastases. Complete resection of the primary tumor and a mediastinal lymph node dissection were performed on all patients. The majority also received postoperative external radiation therapy to the mediastinum. Survival after resection was 47% at 3 years and 38% at 4 years. Survival was better when the histologic diagnosis was adenocarcinoma, when the primary tumor was small, and when the mediastinum appeared normal on regular chest roentgenograms.

majority also received postoperative external radiation

Table 1. Classification by pretreatment clinical stage.

	No. of patients
T1N0M0	21
T2N0M0	27
T1N1M0	2
T2N1M0	7
T3N0M0	9
T1N2M0	1
T2N2M0	9
T3N2M0	4
Total	80

Table 2. Classification by final stage after treatment.

	No. of patients
T1N2M0	17
T2N2M0	44
T3N2M0	19

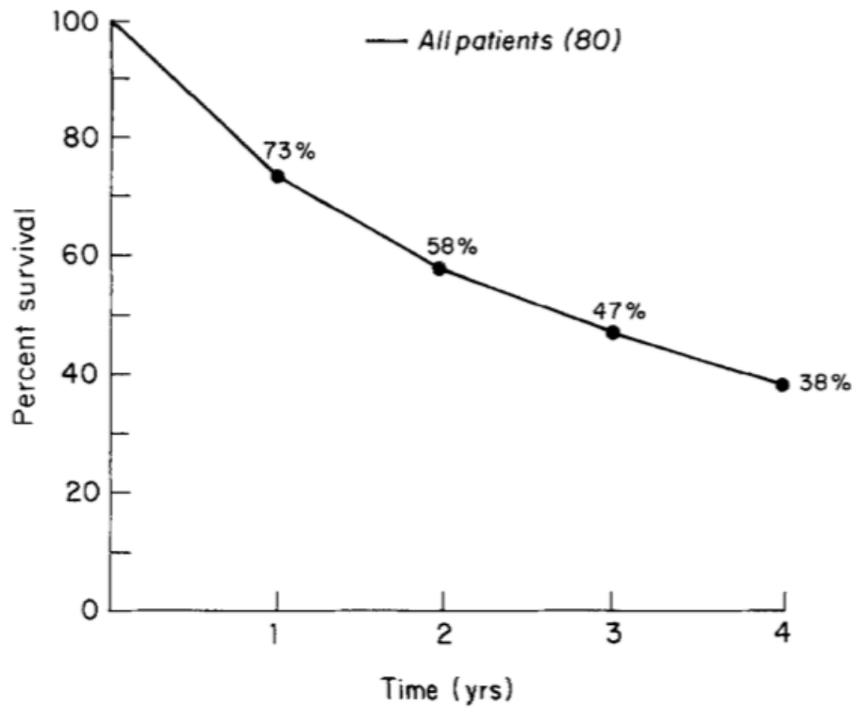


Fig. 1. Survival in 80 patients with complete resection.

RXTH ADJUVANTE - PHASE 3 - 1999

A Controlled Study of Postoperative Radiotherapy for Patients with Completely Resected Nonsmall Cell Lung Carcinoma

Bertrand Dautzenberg, M.D.
Rodrigo Arriagada, M.D.
Agnès Boyer Chammard, M.D.
Alina Jarema, M.D.
Maurizio Mezzetti, M.D.
Karin Mattson, M.D.
Jean L. Lagrange, M.D.
Cécile Le Pechoux, M.D.
Bernard Lebeau, M.D.
Claude Chastang, M.D., Ph.D.
for the Groupe d'Etude et de Traitement des Cancers Bronchiques

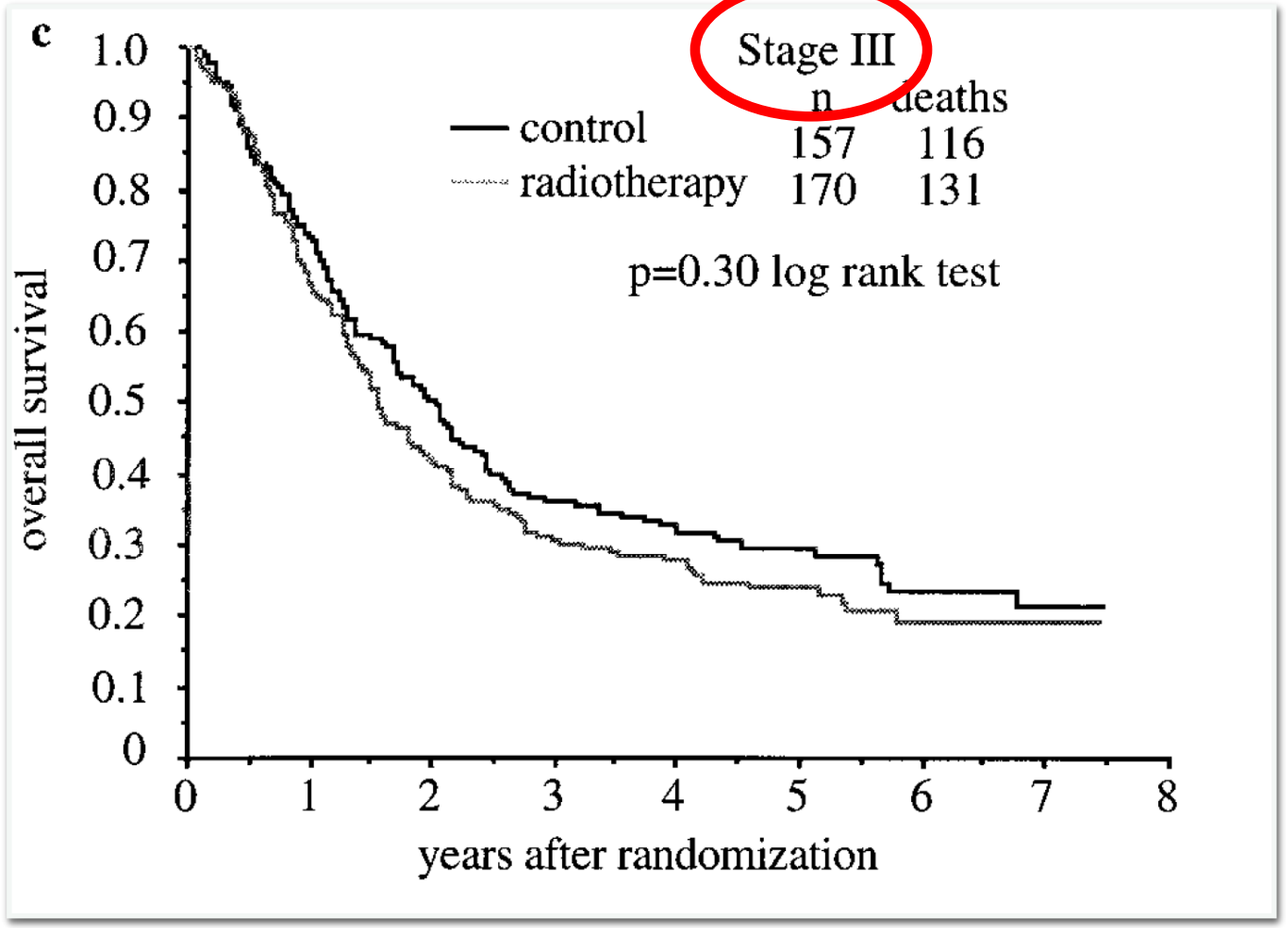
[1] Service de Pneumologie, Groupe Hospitalier Pitié-Salpêtrière, Paris, France.

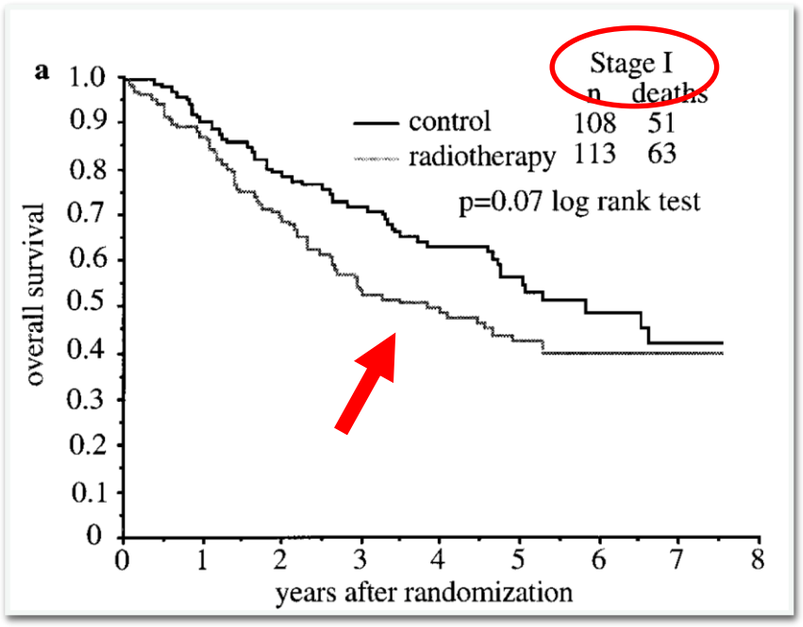
[2] Lung Cancer Unit, Institut Gustave Roussy, Villejuif, France.

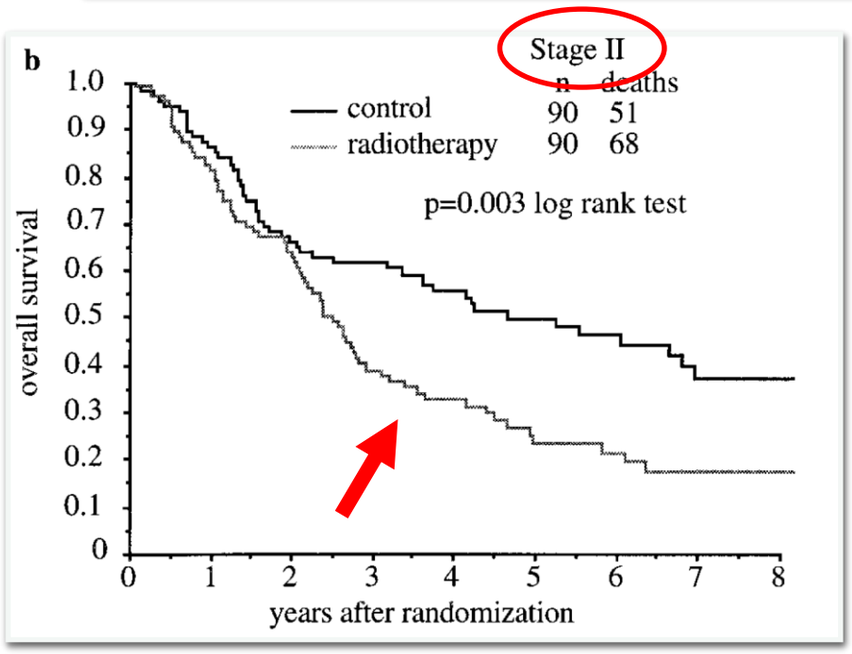
BACKGROUND. Postoperative radiotherapy is commonly used to treat patients with completely resected nonsmall cell lung carcinoma, but its effect on overall survival has not been established.

METHODS. After undergoing complete surgical resection, 728 patients with nonsmall cell lung carcinoma (221 Stage I, 180 Stage II, and 327 Stage III) were randomized to receive either postoperative radiotherapy at a total dose of 60 gray or observation only . The main end point was overall survival.

RESULTS. At the reference date, 218 of 355 patients in the control group had died and 262 of 373 in the radiotherapy group had died. Five-year overall survival was 43% for the control group and 30% for the radiotherapy group ($P = 0.002$, log rank test; relative risk [RR]: 1.33; 95% confidence interval [CI]: 1.11–1.59). This result was not modified by adjustment for potential prognostic factors. The excess mortality rate for the radiotherapy group was due to an excess of intercurrent deaths ($P = 0.0001$; RR: 3.47; the 5-year intercurrent death rate was 8% for the control group and 31% for the radiotherapy group). Radiotherapy had no significant effect on local recurrence (RR: 0.85; 95% CI: 0.64–1.14) and no effect on metastasis (RR: 1.06; 95% CI: 0.85–1.31). The rate of non-cancer-related death increased with the dose per fraction delivered.







RXTH ADJUVANTE - PHASE 3 - 1999

Causes of Death According to Treatment Group

Deaths	Control group (n = 355)	Radiotherapy group (n = 373)
Total no. of deaths	218	262
Cancer-related deaths		
Distant recurrence	122	127
Local recurrence	39	33
Both	33	30
Total cancer-related deaths	194	190
Intercurrent deaths[a]		
Toxic[b]	0	5
Cardiac	6	19
Infectious	1	10
Respiratory	1	5
Brain vascular disorder	2	5
Other primary malignancy	4	11
Others	12	17
Total intercurrent deaths	24	72

[a] Intercurrent deaths were all deaths unrelated to lung carcinoma (see end point definitions in text).
[b] Toxic deaths were sudden deaths during radiotherapy, hemoptysis during radiotherapy, radiation pneumonitis (2 cases), and paraplegy and radiation myelitis after radiotherapy.

Non-cancer-related death was clearly related to
the number of grays per fraction :

7% of patients in the control group

16% of patients who received less than 2 Gy per fraction

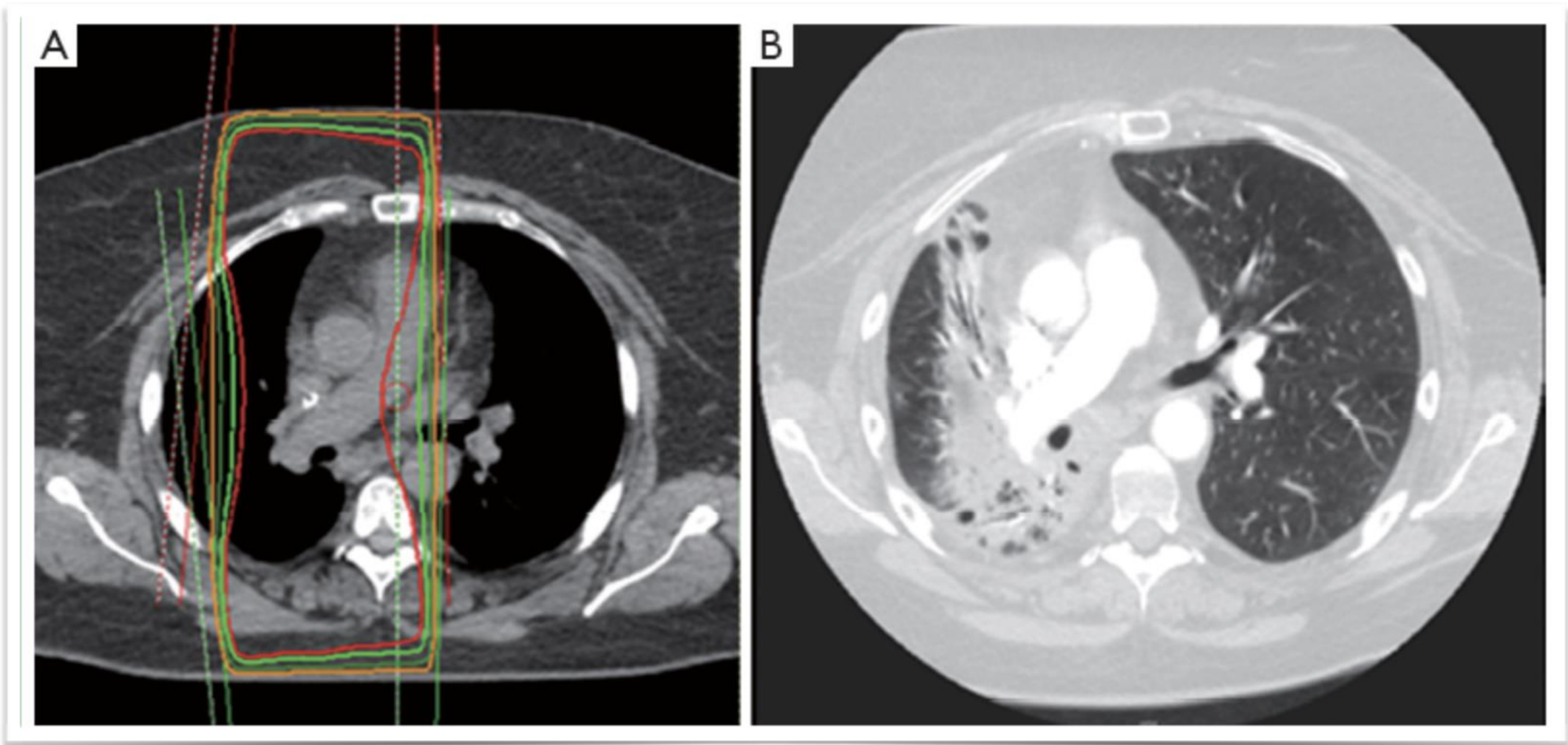
18% of patients who received 2 Gy per fraction

26% of patients who received more than 2 Gy per fraction

RXTH ADJUVANTE - PHASE 3 - 1999

The first 40 Gy were delivered by anteroposterior fields
to a target volume that included the bronchial
stump, the ipsilateral hilum, the upper and middle
mediastinum, and the supraclavicular areas.

An additional dose of 20 Gy
was then delivered by lateral and/or oblique fields,

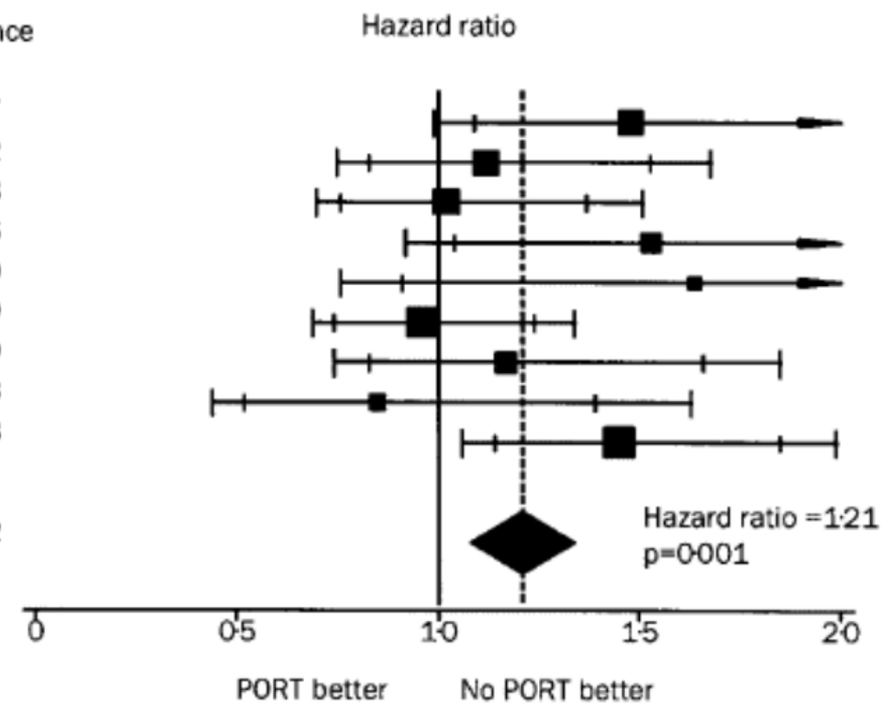


RXTH ADJUVANTE - MÉTAANALYSE OXFORD - 1998

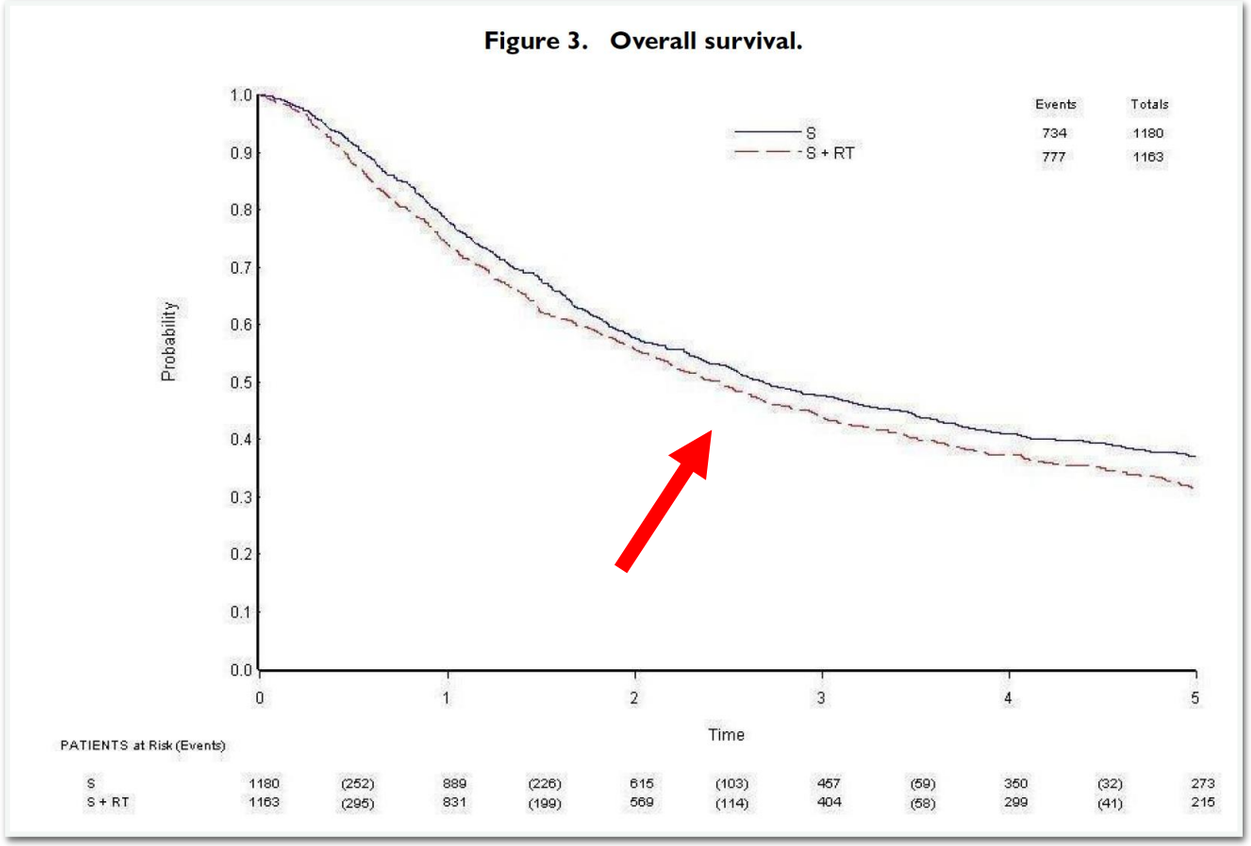
Méta-analyse PORT

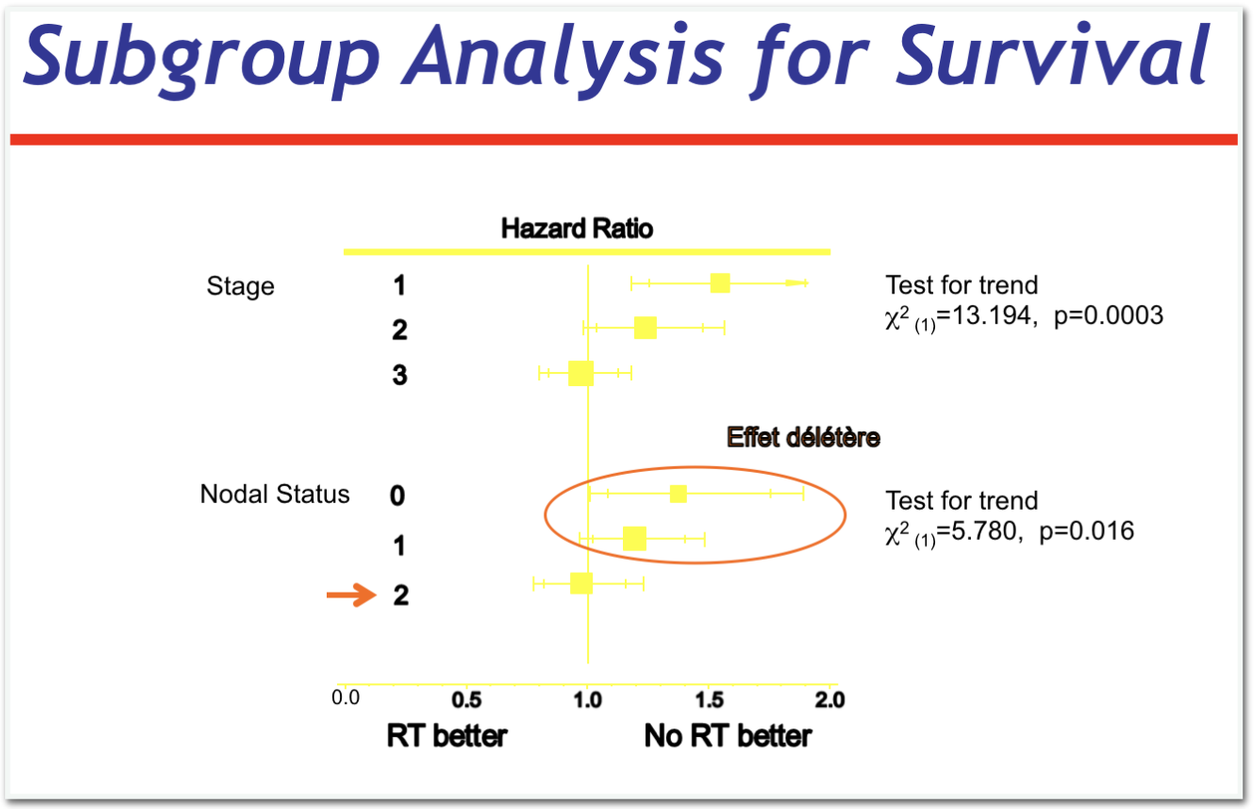
- 9 essais randomisés
- Entrée dans les essais de 1966 à 1988
- [74-539] patients par essais
- 2128 patients

Trial	Number of events/ number entered PORT	No PORT	O-E	Variance
Belgium (10)	88/98	80/104	16·04	40·67
LCSG 773 (11)	84/110	81/120	4·77	41·02
CAMS (12)	83/153	100/164	1·07	44·88
Lille (13)	59/81	45/82	10·87	25·66
EORTC 08861	26/52	20/54	5·53	11·20
MRC LU11 (14)	116/154	123/154	-2·48	59·39
GETCB 04CB86	69/99	59/90	4·95	31·59
Slovenia (15)	30/35	33/39	-2·56	15·63
GETCB 05CB88	152/274	120/265	25·13	67·08
Total	707/1056	661/1072	63·32	337·12



RXTH ADJUVANTE - MÉTAANALYSE OXFORD - 1998





REVIEWER'S CONCLUSIONS: PORT is detrimental to patients with early stage completely resected non-small cell lung cancer and should not be used in the routine treatment of such patients. The role of PORT in the treatment of N2 tumours is not clear and may justify further research.

RXTH ADJUVANTE - MÉTAANALYSE OXFORD - 1998

Technique de radiothérapie

Trial	Radiotherapy dose				Prescription technique	Machine used	Average field size (cm)	Clinical target volume	Technique
	Total dose (Gy)	Fractions	Duration (weeks)	Gy/day					
Belgium[10]	60	30	6	2	Isodose 90%	Co60	15x9	Bronchial stump, hilum, mediastinum	SCB,OF,LF
LCSG 773[11]	50	25·0–27·5	5·0–5·5	1·8–2·0	Central axis, at midplane	Co60 & linac	*	Bronchial stump, hilum, mediastinum	SCB,OF,LF
CAMS[12]	60	30	6	2	At midplane	Co60 & linac	6x12	Hilum, mediastinum	SCB,OF,LF
Lille[13]	45–60	22·5–30·0	6	2	Isodose 90%	Co60 & linac	12x12	Hilum, upper mediastinum	SCB,OF,LF
EORTC 08861	56	28	5·5	2	Central axis, at midplane	linac	15x10	Hilum, mediastinum	Composite plans
MRC LU11[14]	40	15	3	2·6	Central axis, at midplane	Co60 & linac	*	Hilum, mediastinum, supraclavicular fossae†	SCB,OF,LF
GETCB 04CB86	60	24–30	6	2·0–2·5	Isocentre	Co60 & linac	*	Bronchial stump, hilum, mediastinum	SCB,OF,LF
Slovenia[15]	30	10–12	2	2·5–3·0	Central axis, at midplane	linac	9x12	Hilum, mediastinum	OF,LF
GETCB 05CB88	60	24–30	6	2·0–2·5	Isocentre	Co60 & linac	*	Bronchial stump, hilum, mediastinum	SCB,OF,LF

4 études avec un fractionnement > 2 Gy/j

7 études utilisent le ^{60}Co

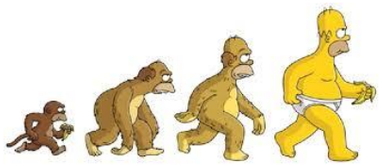
2 études avec correction d'hétérogénéité

1 étude utilise le scanner pour la délimitation

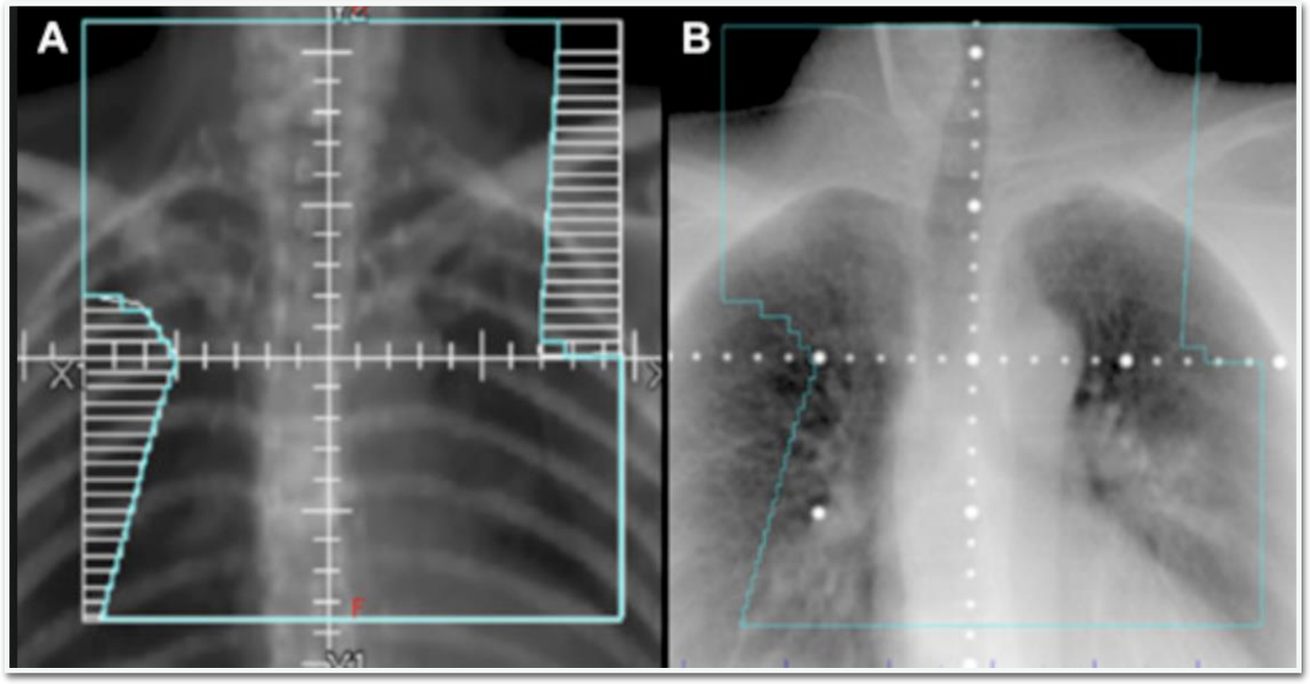
Toutes les études volume irradié > 200 cm^3

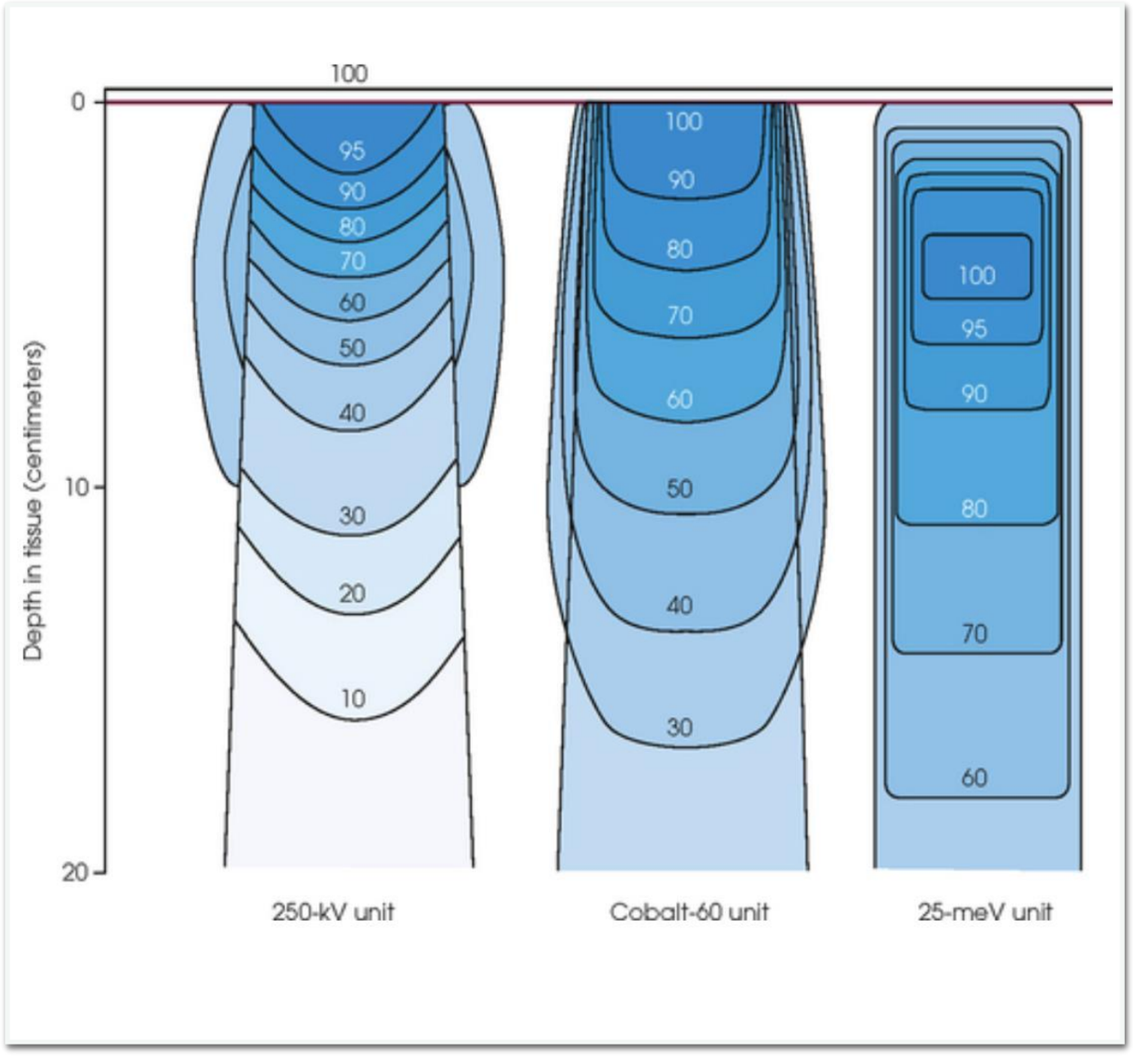
25% de pN0

RXTH 2D COBALT



RXTH 2D LINAC





RXTH ADJUVANTE - RÉTRO - 1993

POSTOPERATIVE RADIOTHERAPY AFTER PNEUMONECTOMY: IMPACT OF MODERN TREATMENT FACILITIES

PATRICIA PHLIPS, M.D.,[1] PIERRE ROCMANS, M.D.,[2] PATRICK VANDERHOEFT, M.D.[2] AND PAUL VAN HOUTTE, M.D., PH.D.[1]

[1]Department of Radiation Oncology, Institut Jules Bordet; and [2]Department of Thoracic Surgery, Hopital Erasme, Brussels, Belgium

Table 4. Staging and treatment

	T1,T2N0	T3N0	N1	N2	
Control	23	4			27
Co60	27	4	6	14	51
Linac		8	10	7	25
	50	16	16	21	103

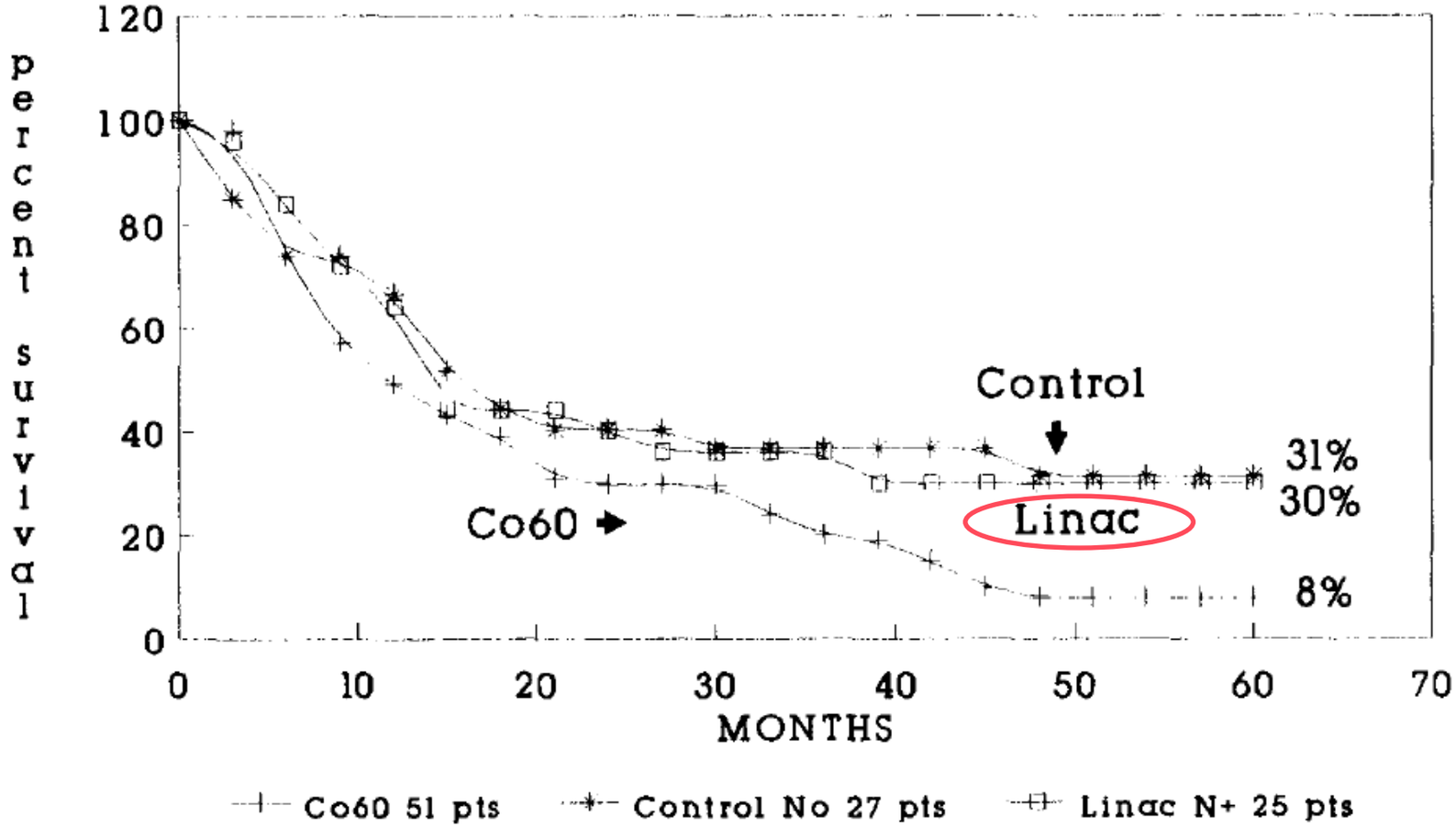
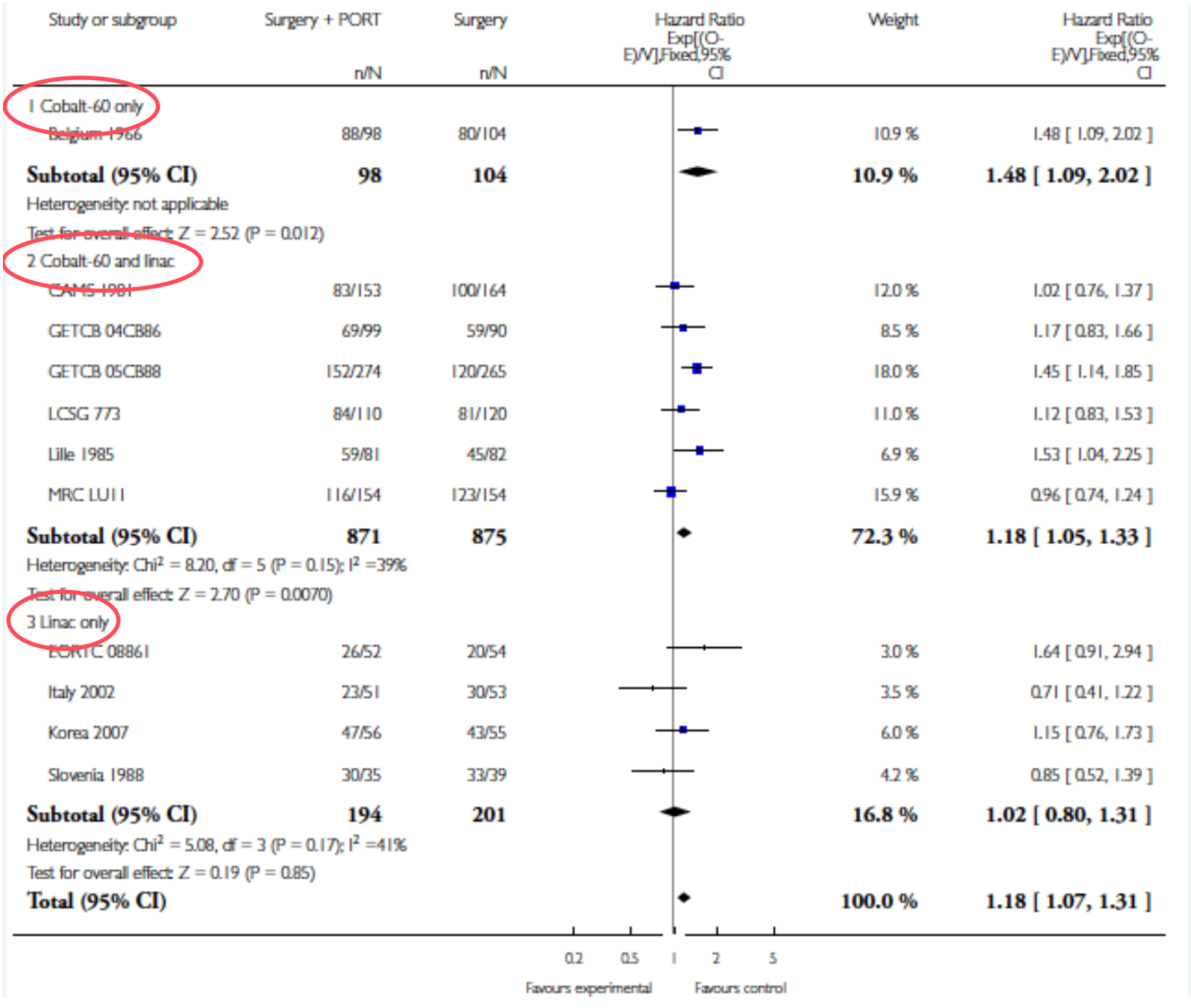
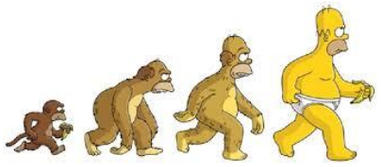


Fig. 1. Postop. RT and pneumonectomy: influence of radiation technique.

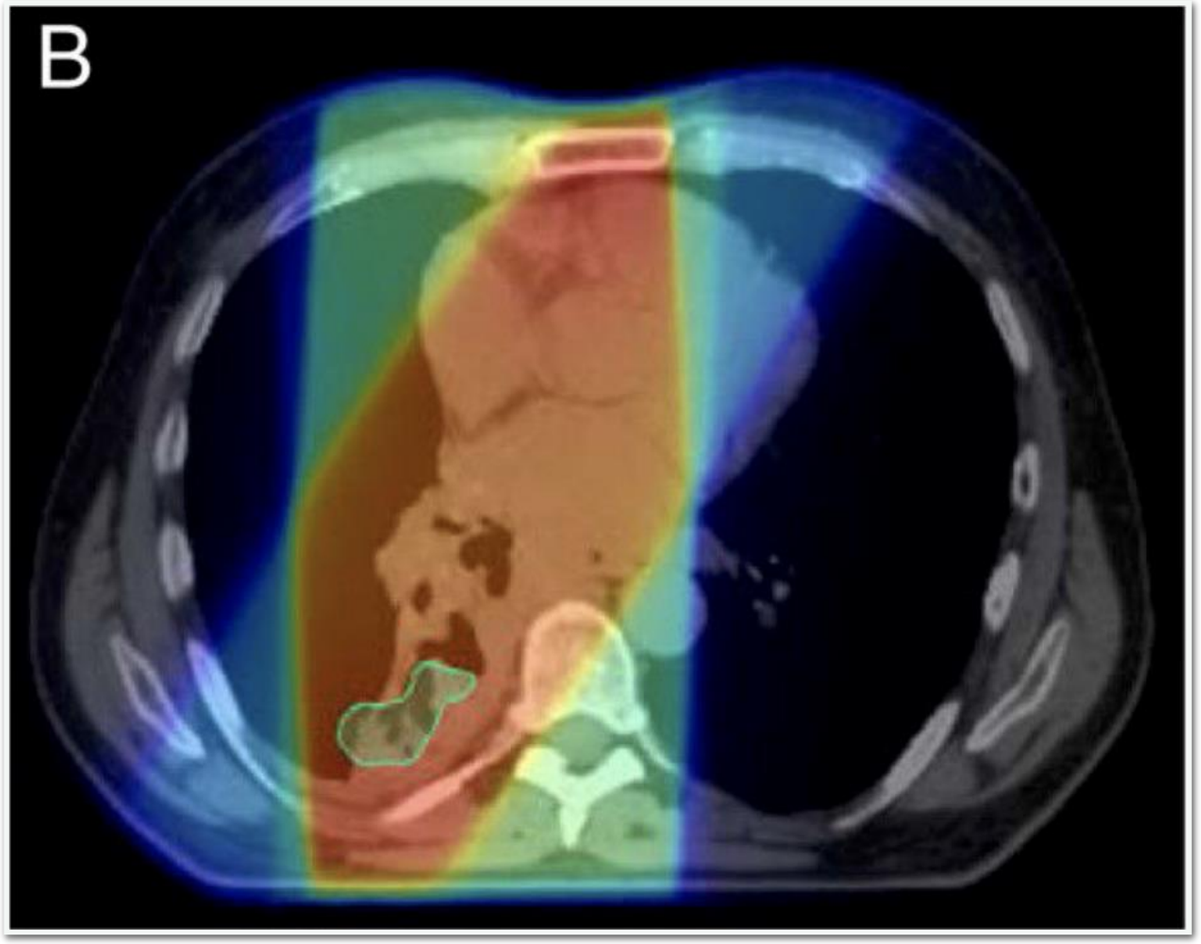
RXTH ADJUVANTE - MÉTAANALYSE OXFORD- MISE À JOUR 2016

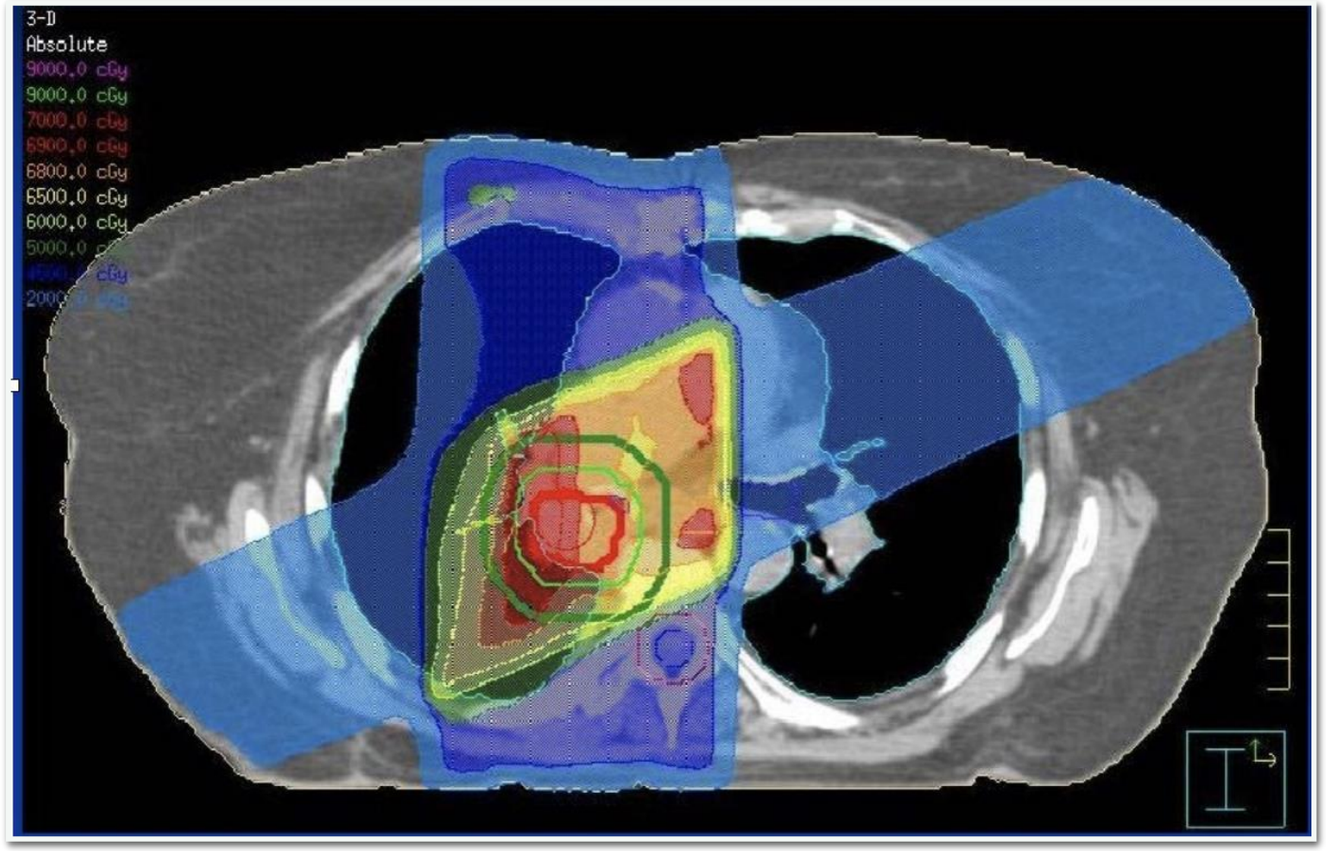


RXTH 2D

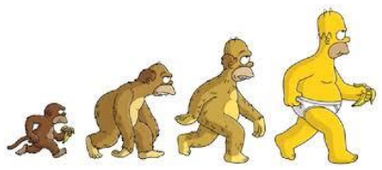


RXTH CONFORMATIONNELLE 3D

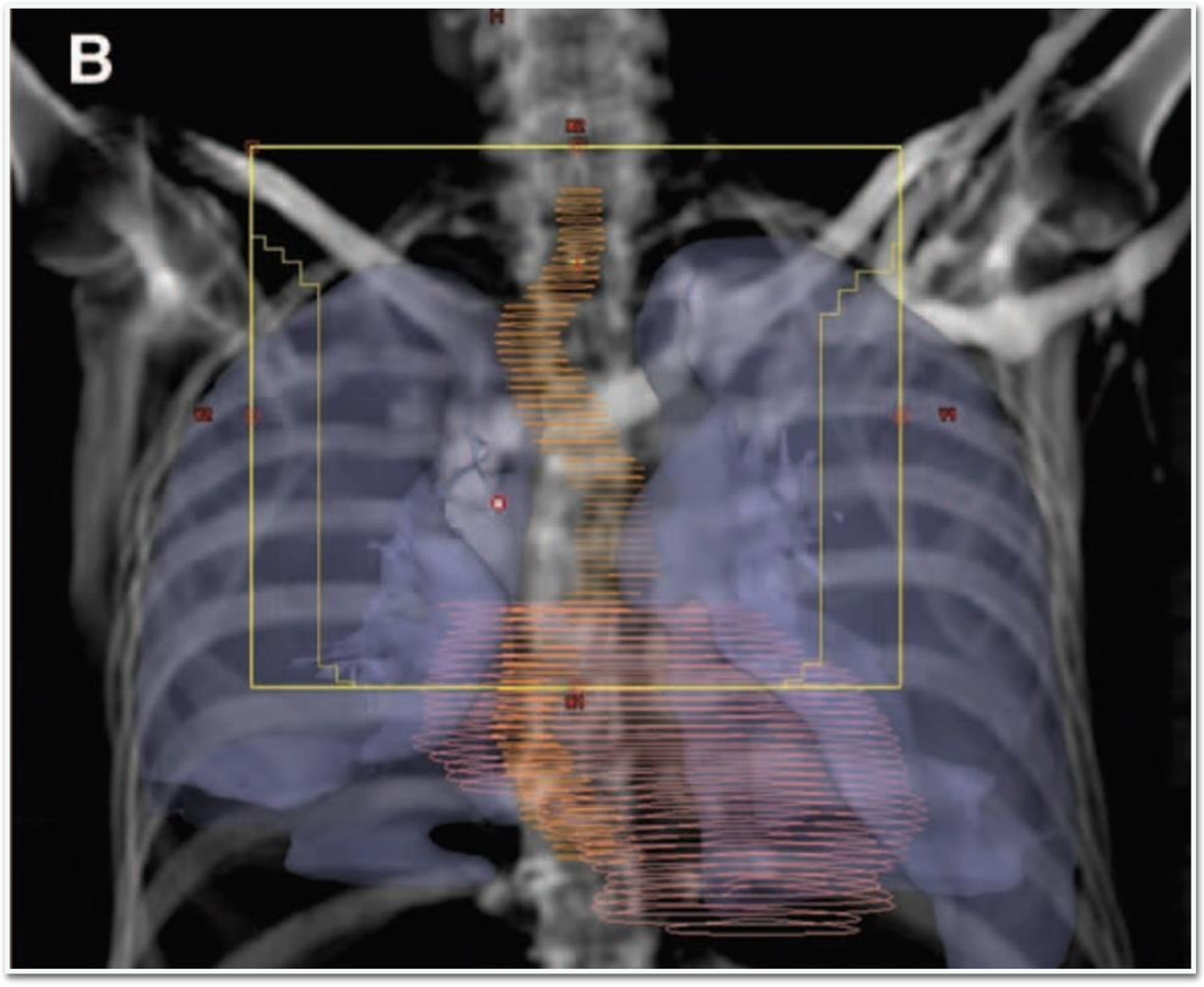


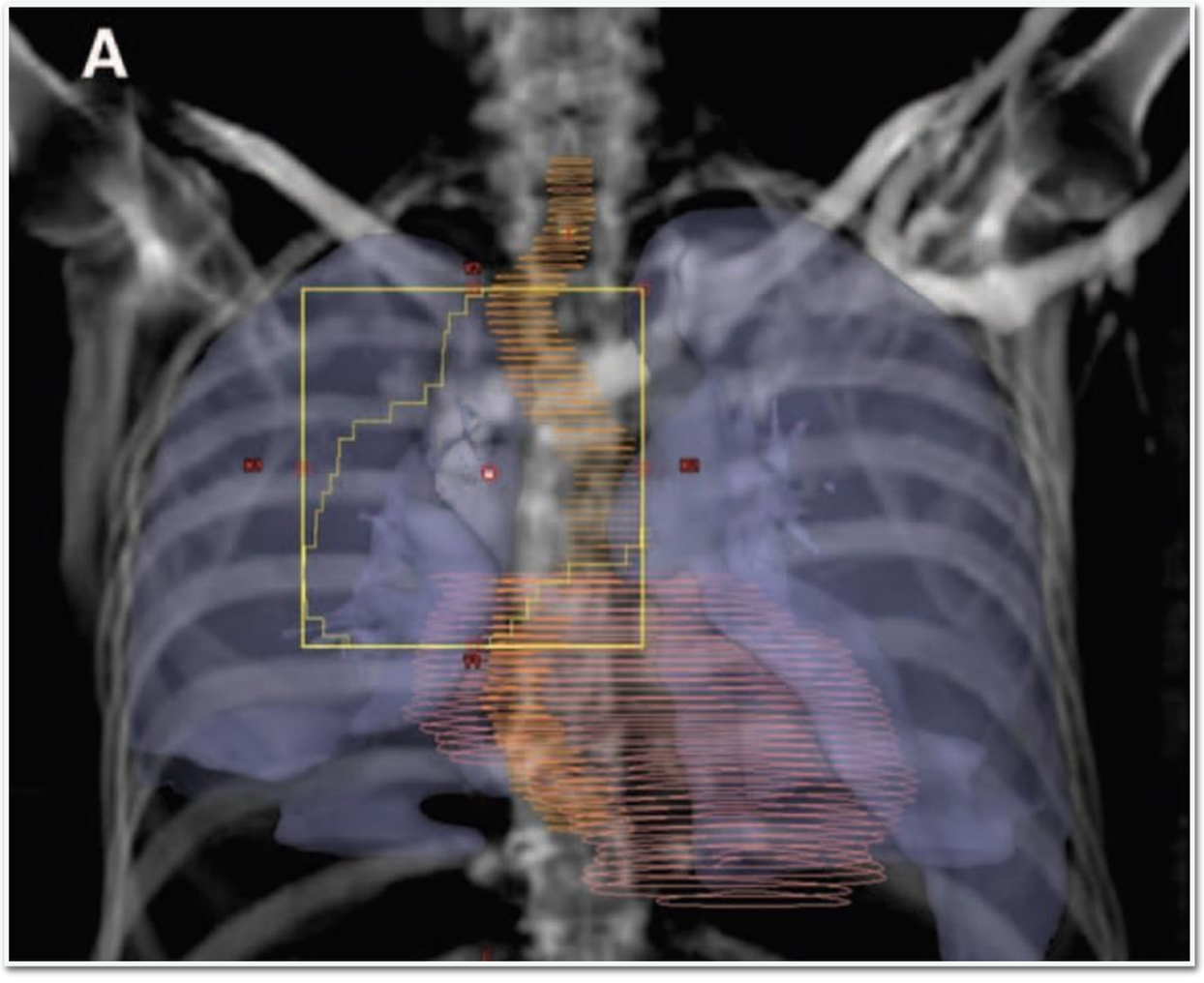


RXTH 2D



RXTH CONFORMATIONNELLE 3D





RXTH ADJUVANTE - RÉTRO - 1997/2001

Ann Thorac Surg. 1997 Nov;64(5):1402-7; discussion 1407-8.

Effectiveness of postoperative irradiation in stage IIIA non-small cell lung cancer according to regression tree analyses of recurrence risks.

Sawyer TE[1], Bonner JA, Gould PM, Foote RL, Deschamps C, Trastek VF, Pairolero PC, Allen MS, Lange CM, Li H.

J Clin Oncol. 2001 Oct 1;19(19):3912-7.

Risk of death from intercurrent disease is not excessively increased by modern postoperative radiotherapy for high-risk resected non-small-cell lung carcinoma.

Machtay M[1], Lee JH, Shrager JB, Kaiser LR, Glatstein E.

Both showed favorable overall survival and local control

All patients in these two studies underwent simulation and were treated on a linear accelerator using energies of 6 MV or higher

Risk of death from intercurrent disease
for patients receiving less than 54Gy of radiation was only 2%

RXTH ADJUVANTE N2 - RÉTRO SEER - 2006

VOLUME 24 · NUMBER 19 · JULY 1 2006

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Postoperative Radiotherapy for Stage II or III Non–Small-Cell Lung Cancer Using the Surveillance, Epidemiology, and End Results Database

Brian E. Lally, Daniel Zelterman, Joseph M. Colasanto, Bruce G. Haffty, Frank C. Detterbeck, and Lynn D. Wilson

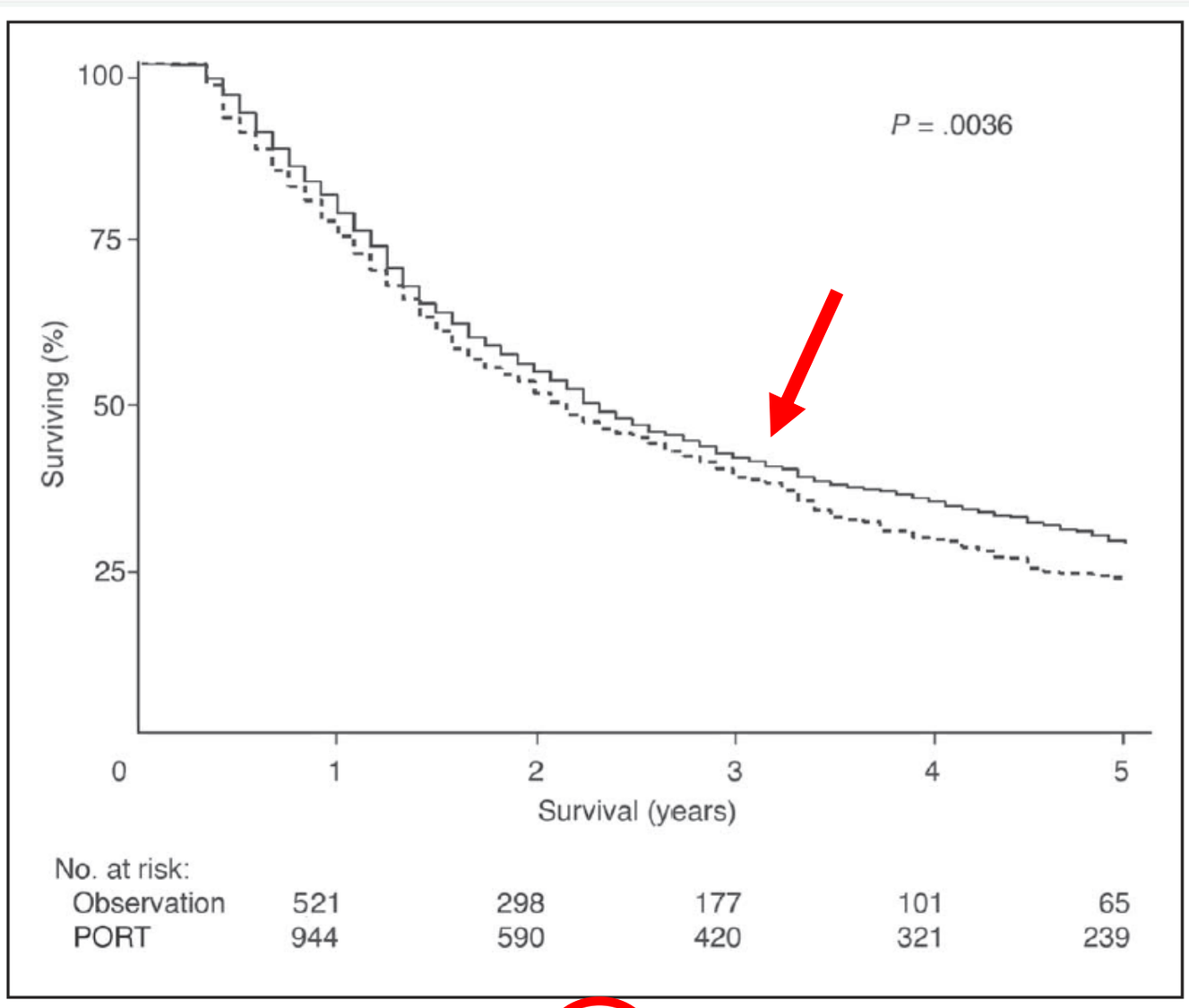
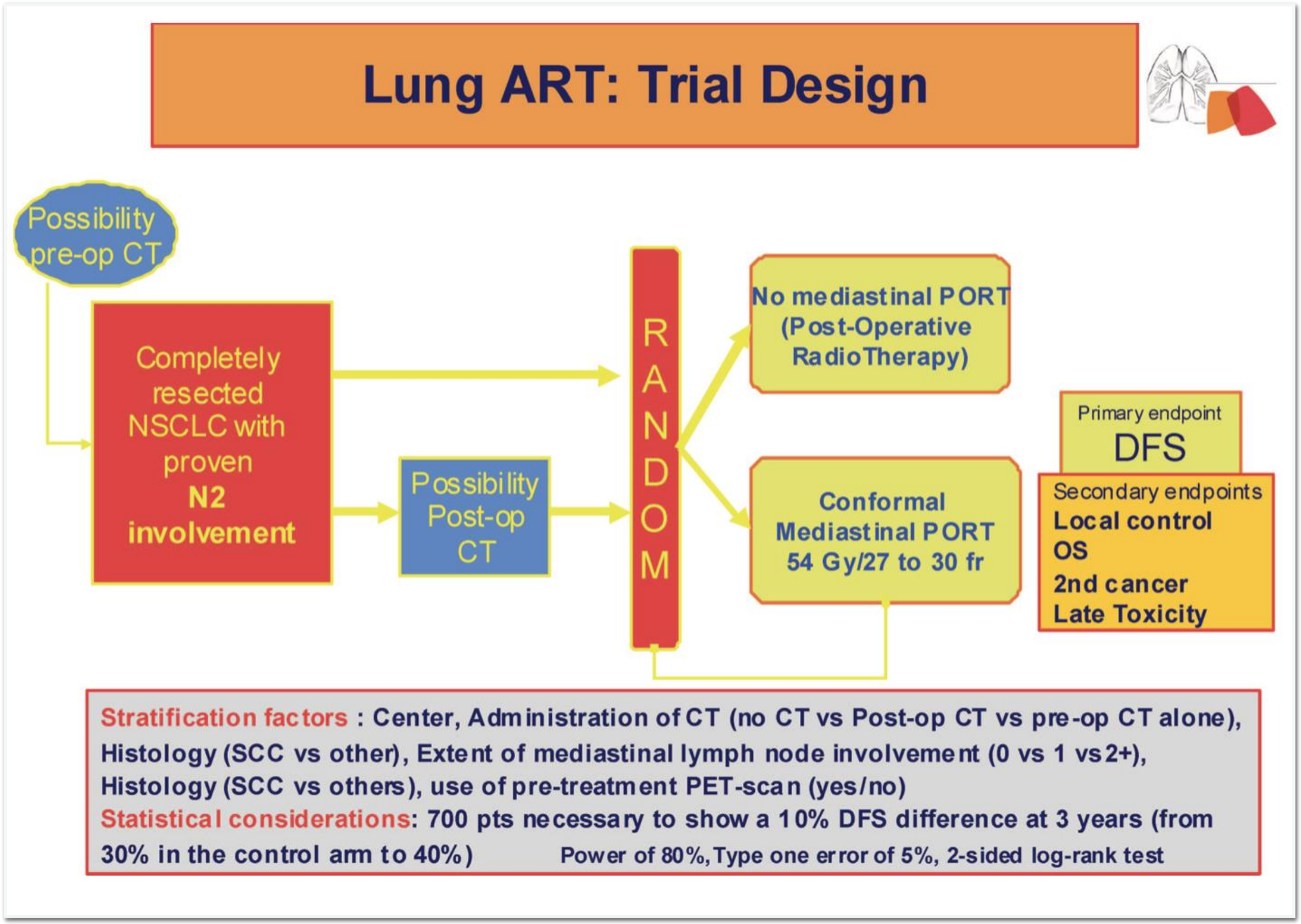


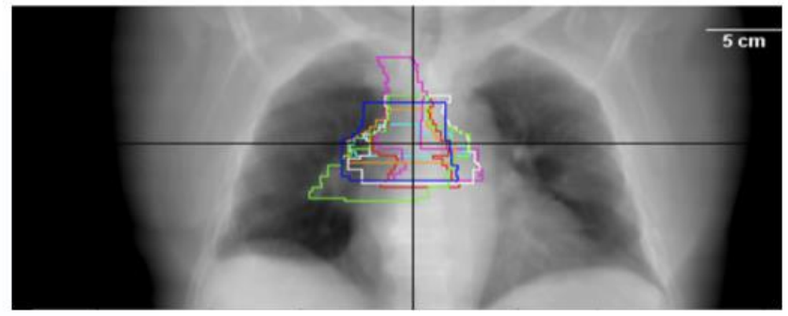
Fig 5. Plot of overall survival for N2 patients stratified by postoperative radiotherapy (PORT) use. The solid line represents patients who received PORT, and the dashed line represents patients who did not receive PORT.

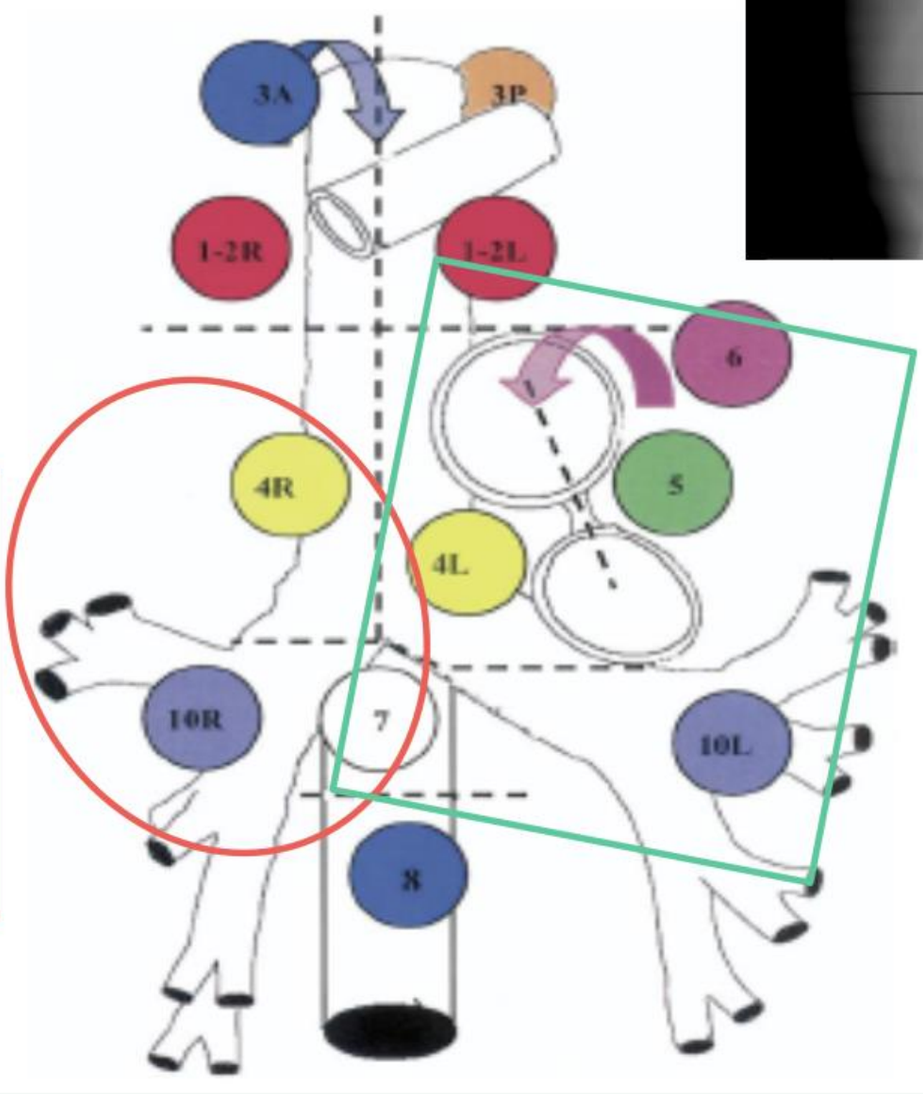
RXTH ADJUVANTE N2 - PHASE 3 - EN COURS …



RXTH ADJUVANTE N2 - PHASE 3 - EN COURS …

Respect du protocole dans la délinéation des volumes rCTV (ganglions réséqués et envahis) et CTV





CBNPC Dt
Ganglions
tjs irradiés
Inclus dans CTV
(4, 7 et 10)

CBNPC Gche
Ganglions
tjs irradiés
Inclus dans CTV
(4, 5, 6 ,7 et 10)

RXTH ADJUVANTE N2 - PHASE 3 - EN COURS …

Lung ART Newsletter N°12

IFCT-0503 – IGR 2006/1202 – UK 11/NW/0075 – EORTC 22055-08053

January 2015

We wish you all a

HAPPY NEW YEAR 2015

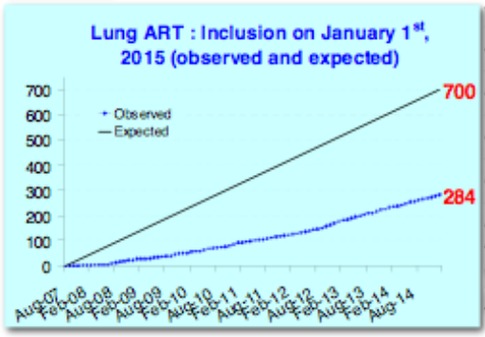
2015

May this New Year be our accrual record!

Congratulations to the centres with the best accruals in each group for 2014: Dijon, Marseille, Freiburg and Sheffield

Inclusions

Lung ART : Inclusion on January 1st, 2015 (observed and expected)



Inclusion up to January 1st 2015

Year	EORTC	FRANCE	UK	Total
2007		3		3
2008		25		25
2009		24		24
2010		41		41
2011		32		32
2012		49	4	53
2013	1	51	3	55
2014	*4*	*40*	*7*	*51*
Total	5	265	14	284
commitment for 2014+	*30*	*60*	*25*	*115*

Recommendations of the IDMC (held on January 16, 2015) to the Lung ART Coordinating Investigator:

"Lung ART is a very important trial. The management of the trial and the data presented did not reveal any problem. The trial should continue, but accrual should continue to improve. Accrual in 2015 will be of major importance for the future of the trial."

Steering Committee overview (held on January, 23 2015)

EORTC: Eleven centres are open. The projected accrual of 70 patients per year, was revised by EORTC to 30 patients per year in July 2014. Seven additional centres will open in 2015. A teleconference with EORTC investigators will be organized in the coming months, to help accrual.

In the UK, several centres (13) are still in the process of opening. 25 centres are open among which 7 centres are active. There are regularly teleconferences with UK investigators.

IFCT: Since the January 2014 Steering Committee, France has increased its target yearly accrual from 40 to 60 patients per year.

2015 is a pivotal year!

All participating groups are encouraged to improve the accrual!!
There have been several studies published recently exploring the role of mediastinal radiotherapy in completely resected NSCLC patients with N2 involvement. These studies have used historical data and are **not randomised**. Definitive conclusions therefore cannot be drawn from these studies. Lung ART is the only study that can adequately address this question and there are no other competitive trials open.

Lancement de l'étude : Février 2007

Fin estimée des inclusions : Janvier 2018

Nombre de patients à inclure : 400
(368 patients inclus au 20 décembre 2017)

RÉSULTATS DE LUNG ART …EN 2022 ?

RXTH ADJUVANTE N2 - « COMPILATION » - 2014

Lung Cancer 84 (2014) 156–160

Contents lists available at ScienceDirect

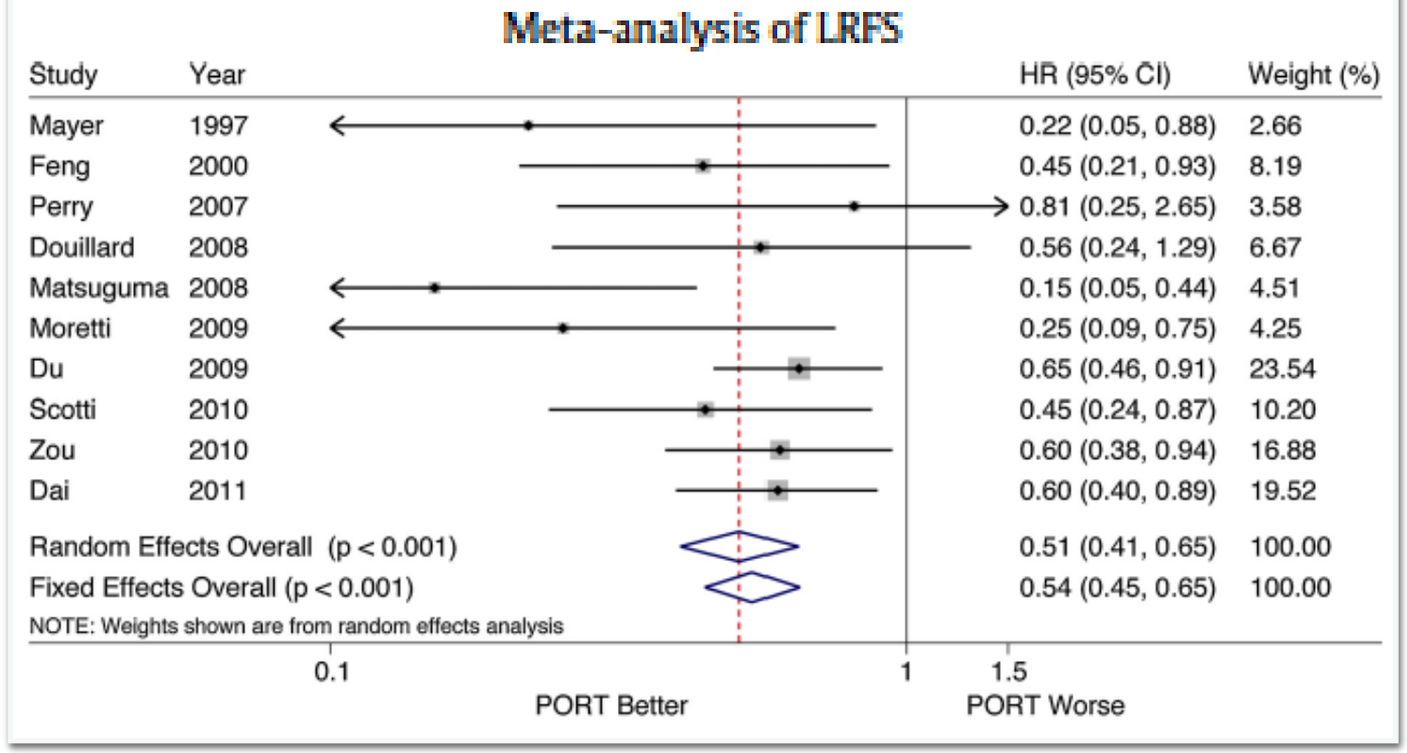
Lung Cancer

journal homepage: www.elsevier.com/locate/lungcan

Evidence supporting contemporary post-operative radiation therapy (PORT) using linear accelerators in N2 lung cancer

Suchit H. Patel[a], Yan Ma[b], A. Gabriella Wernicke[a], Dattatreyudu Nori[a], K.S.C. Chao[a], Bhupesh Parashar[a,*]

[a] Stich Radiation Center, New York Presbyterian Hospital/Weill Cornell Medical Center, 525 East 68th Street, New York, NY 10065, United States
[b] Division of Biostatistics and Epidemiology, Weill Cornell Medical College, 1300 York Avenue, New York, NY 10021, United States



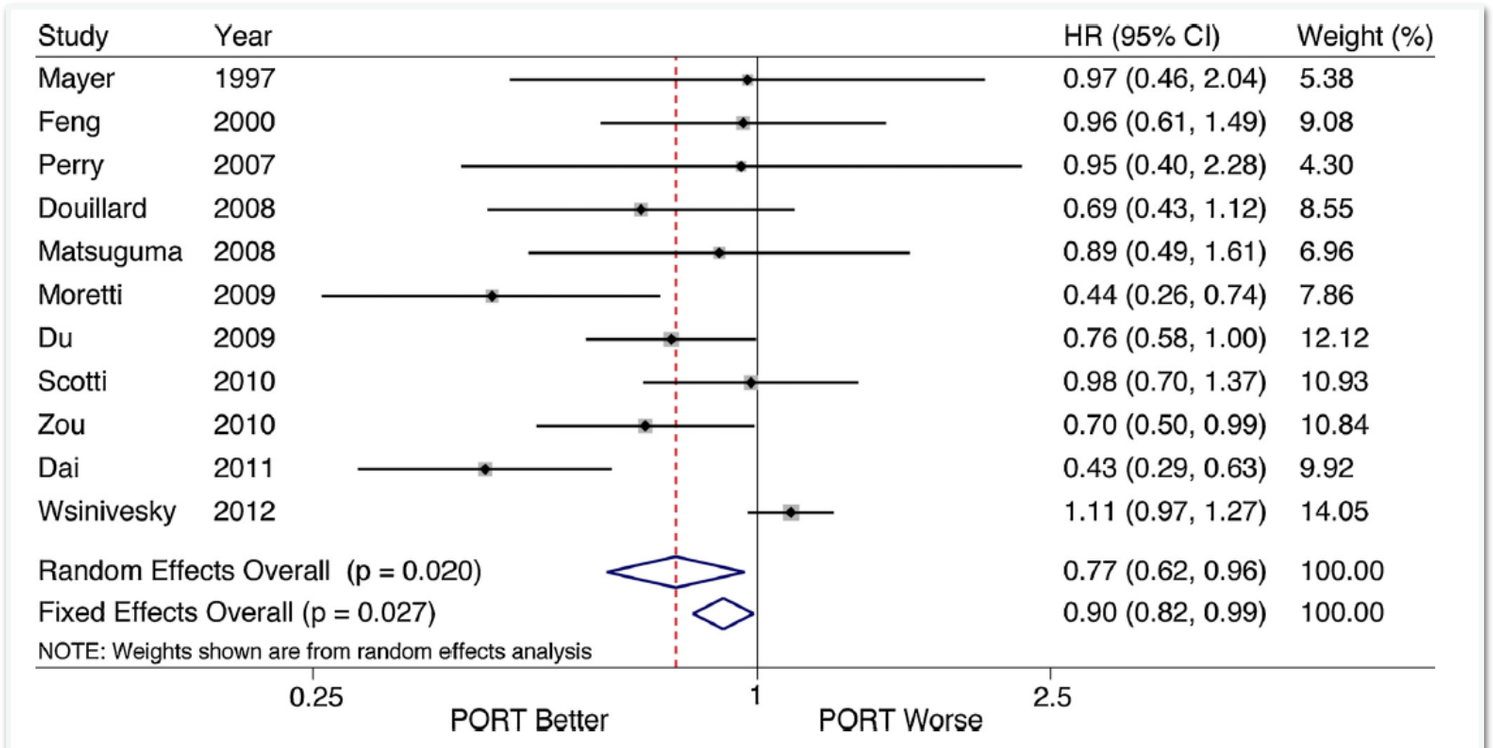
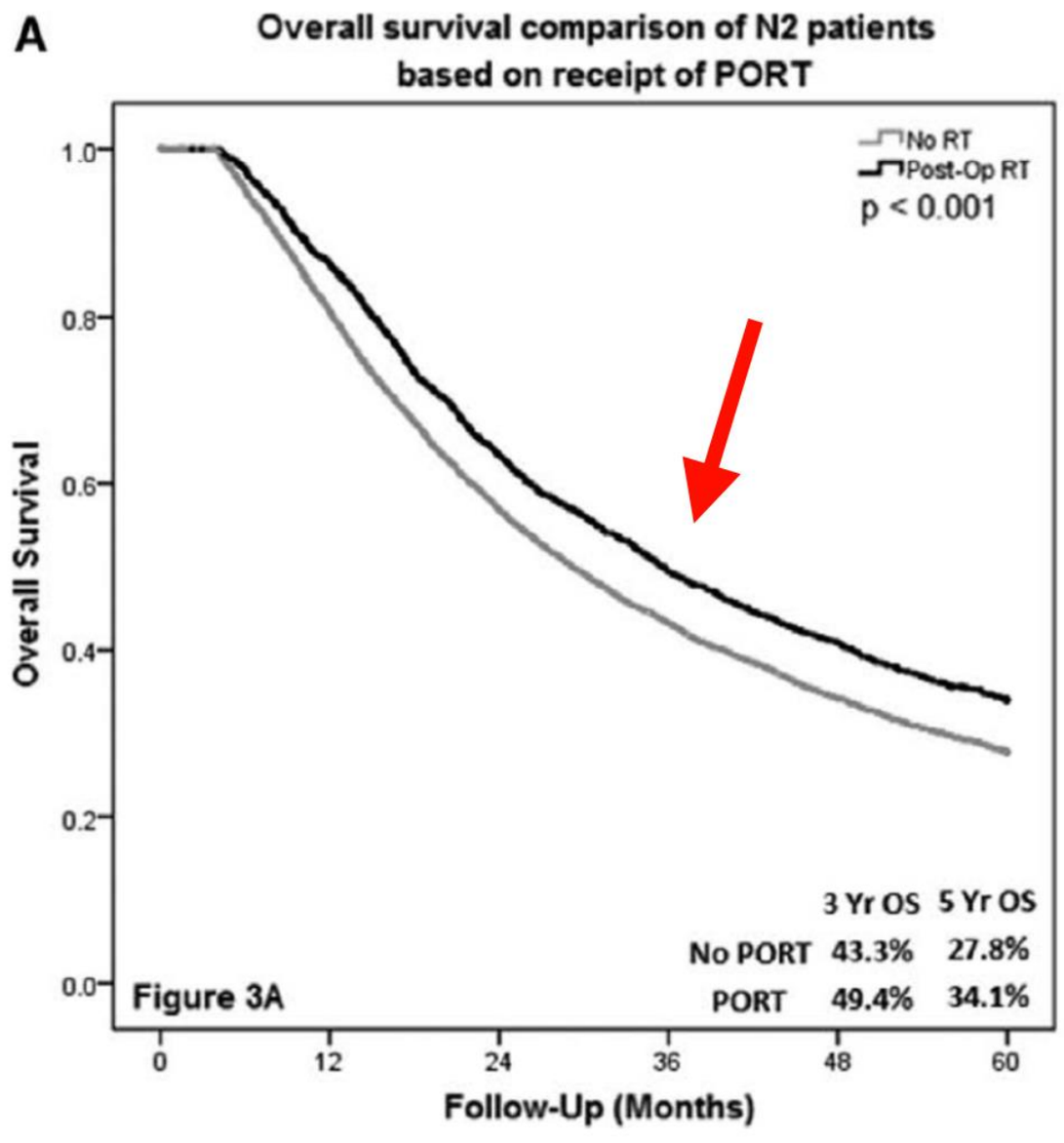


Fig. 1. Meta-analysis of OS outcomes of included studies.

2015 :
RXTH ADJUVANTE N2
3 ANALYSES RÉTROSPECTIVES
BASE DE DONNÉES NCDB

Re-evaluation of the Role of Postoperative Radiotherapy and the Impact of Radiation Dose for Non–Small-Cell Lung Cancer Using the National Cancer Database

Christopher D. Corso, MD, PhD,‡ Charles E. Rutter, MD,*‡ Lynn D. Wilson, MD,*‡ Anthony W. Kim, MD,†‡ Roy H. Decker, MD, PhD,*‡ and Zain A. Husain, MD*‡*



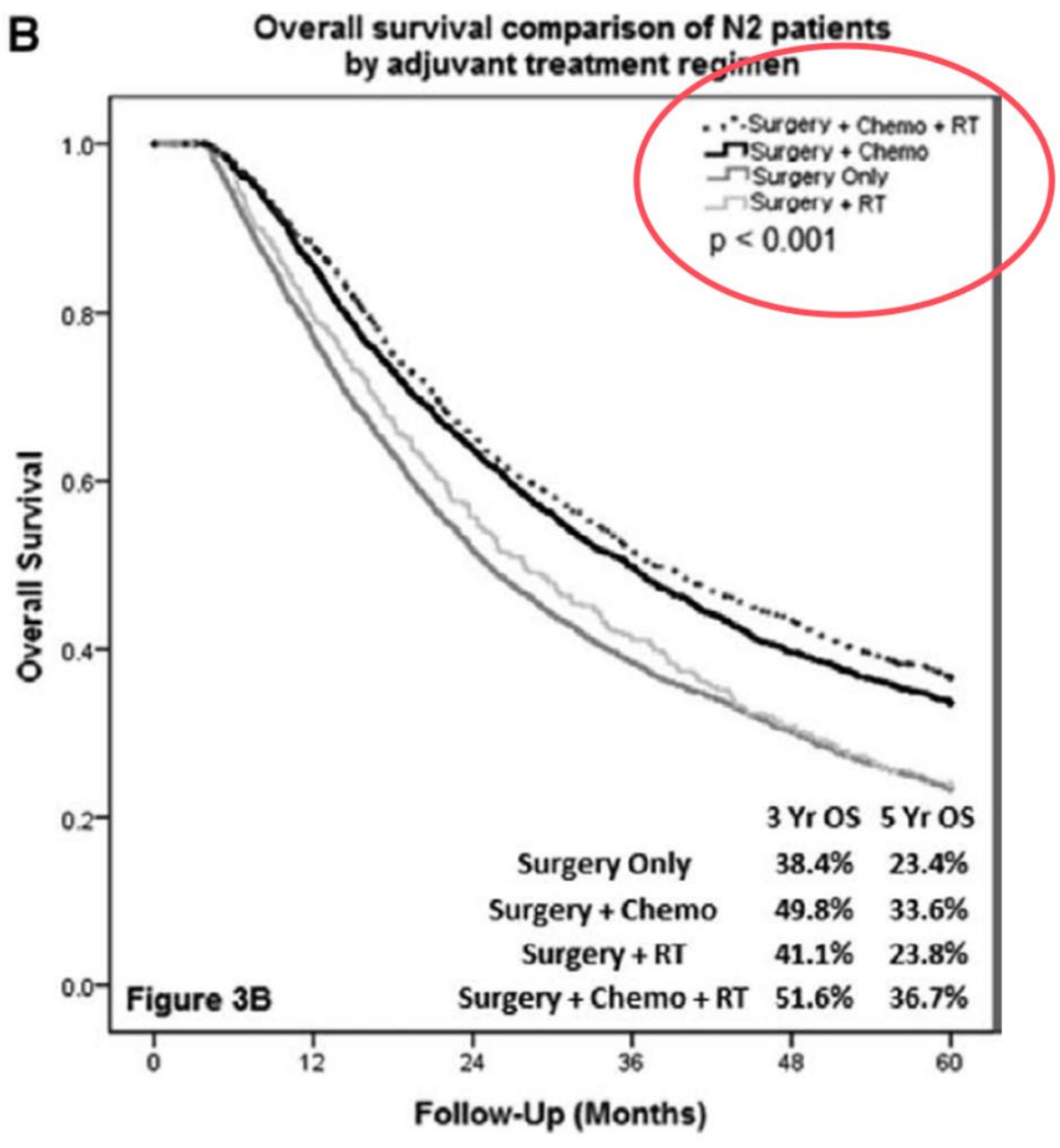


FIGURE 3. Comparison of OS in patients with N2 nodal disease based upon receipt of PORT (*A*) and by adjuvant treatment (*B*). OS, overall survival.

2015 :
RXTH ADJUVANTE N2
3 ANALYSES RÉTROSPECTIVES
BASE DE DONNÉES NCDB

Postoperative Radiotherapy is Associated with Better Survival in Non–Small Cell Lung Cancer with Involved N2 Lymph Nodes

Results of an Analysis of the National Cancer Data Base

John L. Mikell, MD,¶ Theresa W. Gillespie, PhD,†‡¶ William A. Hall, MD,*¶ Dana C. Nickleach, MA,§¶ Yuan Liu, PhD,§¶ Joseph Lipscomb, PhD,‖¶ Suresh S. Ramalingam, MD,†¶ Raj S. Rajpara, MD,*¶ Seth D. Force, MD,‡¶ Felix G. Fernandez, MD,‡¶ Taofeek K. Owonikoko, MD, PhD,†¶ Rathi N. Pillai, MD,†¶ Fadlo R. Khuri, MD,†¶ Walter J. Curran, MD,*¶ and Kristin A. Higgins, MD*¶*

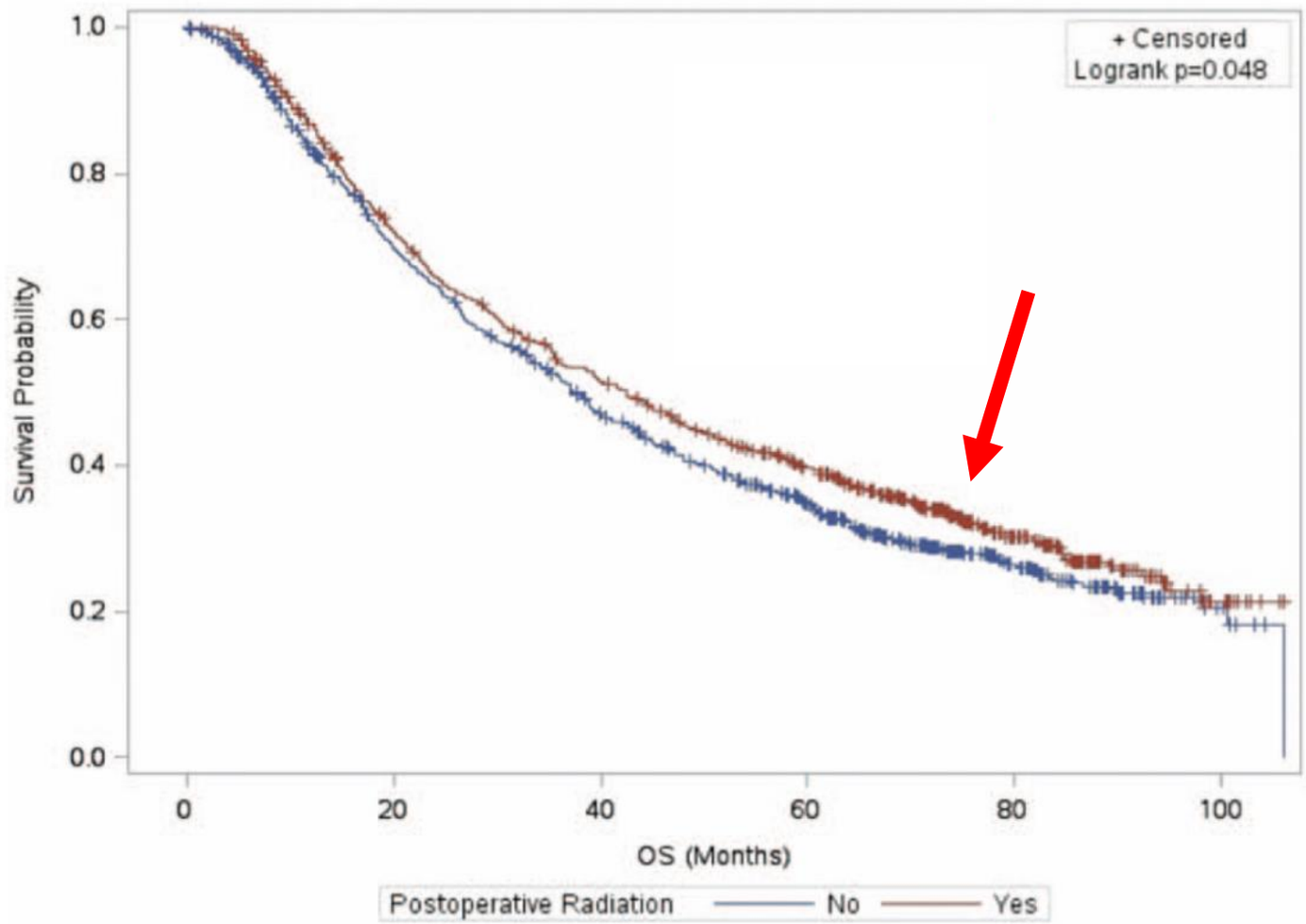


FIGURE 1. Adjusted Kaplan–Meier survival estimates and weighted log-rank test.

2015 :
RXTH ADJUVANTE N2
3 ANALYSES RÉTROSPECTIVES
BASE DE DONNÉES NCDB

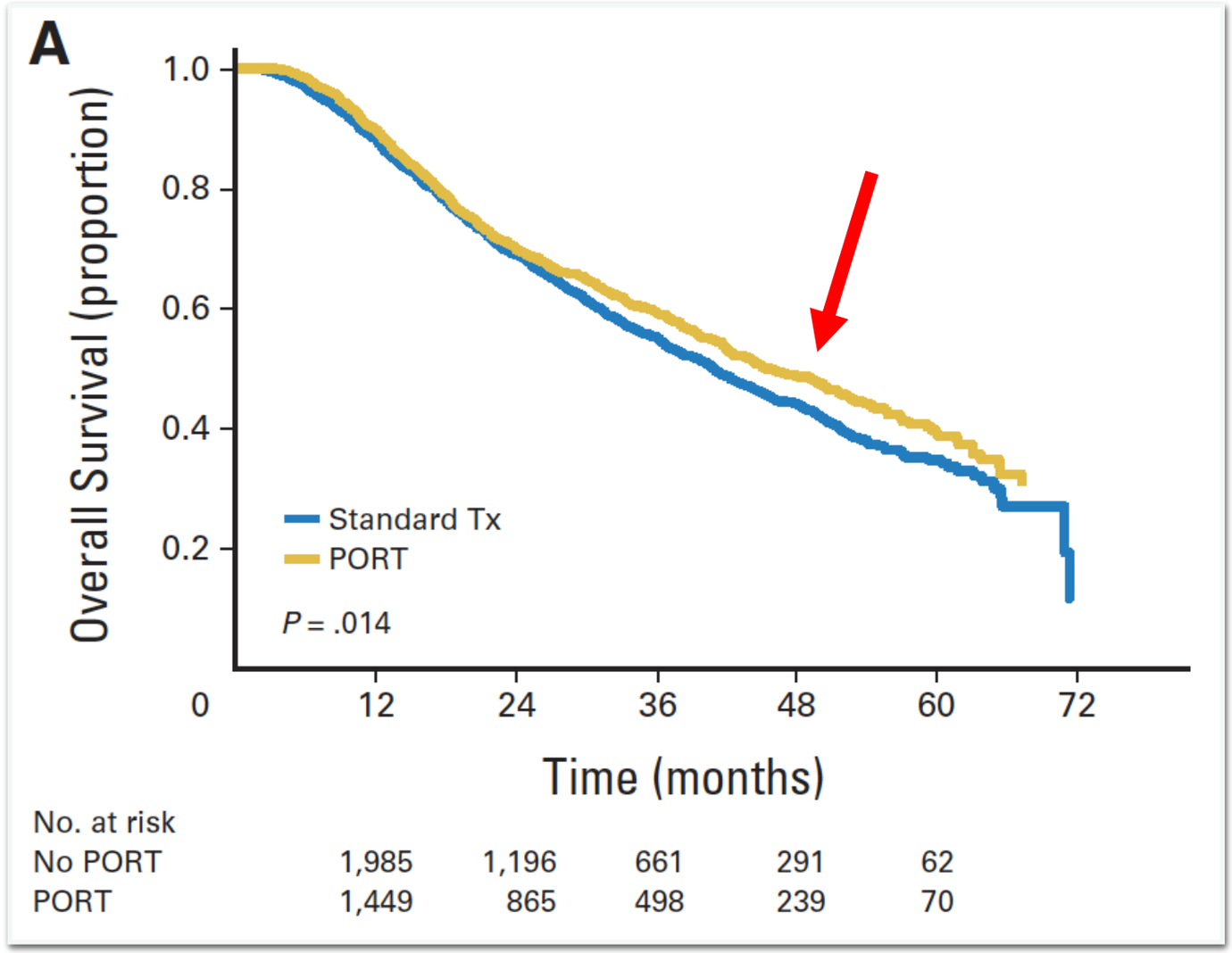
VOLUME 33 · NUMBER 8 · MARCH 10 2015

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Postoperative Radiotherapy for Pathologic N2 Non–Small-Cell Lung Cancer Treated With Adjuvant Chemotherapy: A Review of the National Cancer Data Base

Cliff G. Robinson, Aalok P. Patel, Jeffrey D. Bradley, Todd DeWees, Saiama N. Waqar, Daniel Morgensztern, Maria Q. Baggstrom, Ramaswamy Govindan, Jennifer M. Bell, Tracey J. Guthrie, Graham A. Colditz, Traves D. Crabtree, Daniel Kreisel, Alexander S. Krupnick, G. Alexander Patterson, Bryan F. Meyers, and Varun Puri



2015 :

RXTH ADJUVANTE N2

3 ANALYSES RÉTROSPECTIVES

BASE DE DONNÉES NCDB

Table 4. Studies of the NCDB in Patients With Resected Pathologic N2 NSCLC

Study (author, year)	Date of Diagnosis	Stage	Receipt of Chemotherapy	Median Follow-Up Time	Covariates in Multivariable Analysis	Intervention *v* Control Group	No. of Patients	Survival (intervention *v* control group)	
								OS	Median OS (months)
Mikell,[6] 2015	2004-2006	IIIA-N2	Adjuvant, 82%; neoadjuvant, 9.1%; unknown, 9.1%	NR	Sex, age, insurance, income, urban status, histology, T stage, No. of regional nodes positive, No. of regional nodes examined	EBRT with LINAC and 3D CRT *v*	918	HR, 0.89; 95% CI, 0.79 to 1.00; ***P* = .046**	42
						No PORT	1,197		38 ***P* = .048**
Robinson,[57] 2015	2006-2010	IIIA-N2	Yes (standard adjuvant chemotherapy)	22 months	Age, facility type, sex, income, urban status, comorbidity score, tumor size, multiagent chemotherapy, type of surgery, receipt of PORT	Assumed PORT (≥ 45 Gy) with CT simulation and at least LINAC-based 3D CRT *v*	1,850	HR, 0.888; 95% CI, 0.798 to 0.988; ***P* = .029**	45.2
						No PORT	2,633		40.7
Corso,[56] 2015	1998-2006	IIIA-N2	34.3% of overall sample received chemotherapy	7.5 years	Histology, age, sex, comorbidity score, type of surgery, receipt of chemotherapy, tumor site, tumor size, nodal stage, receipt of PORT	PORT ≥ 54 Gy *v*	1,444	HR, 0.96; 95% CI, 0.88 to 1.05; *P* = .337	NR
						No PORT	27,122		
						PORT 45 to 54 Gy *v*	1,985	HR: 0.85 (0.76-0.94, ***P* < 0.001**)	
						No PORT	27,122		

NOTE. Bold *P* values indicate a statistically significant difference between intervention and control groups.

Abbreviations: 3D, three dimensional; CRT, chemoradiotherapy; CT, computed tomography; HR, hazard ratio (HR < one indicates result favoring PORT); LINAC, linear accelerator; NCDB, National Cancer Database; NR, not reported; NSCLC, non–small-cell lung cancer; OS, overall survival; PORT, postoperative radiation therapy.

2017 :

RXTH ADJUVANTE N2

3 ANALYSES RÉTROSPECTIVES

BASE DE DONNÉES SEER

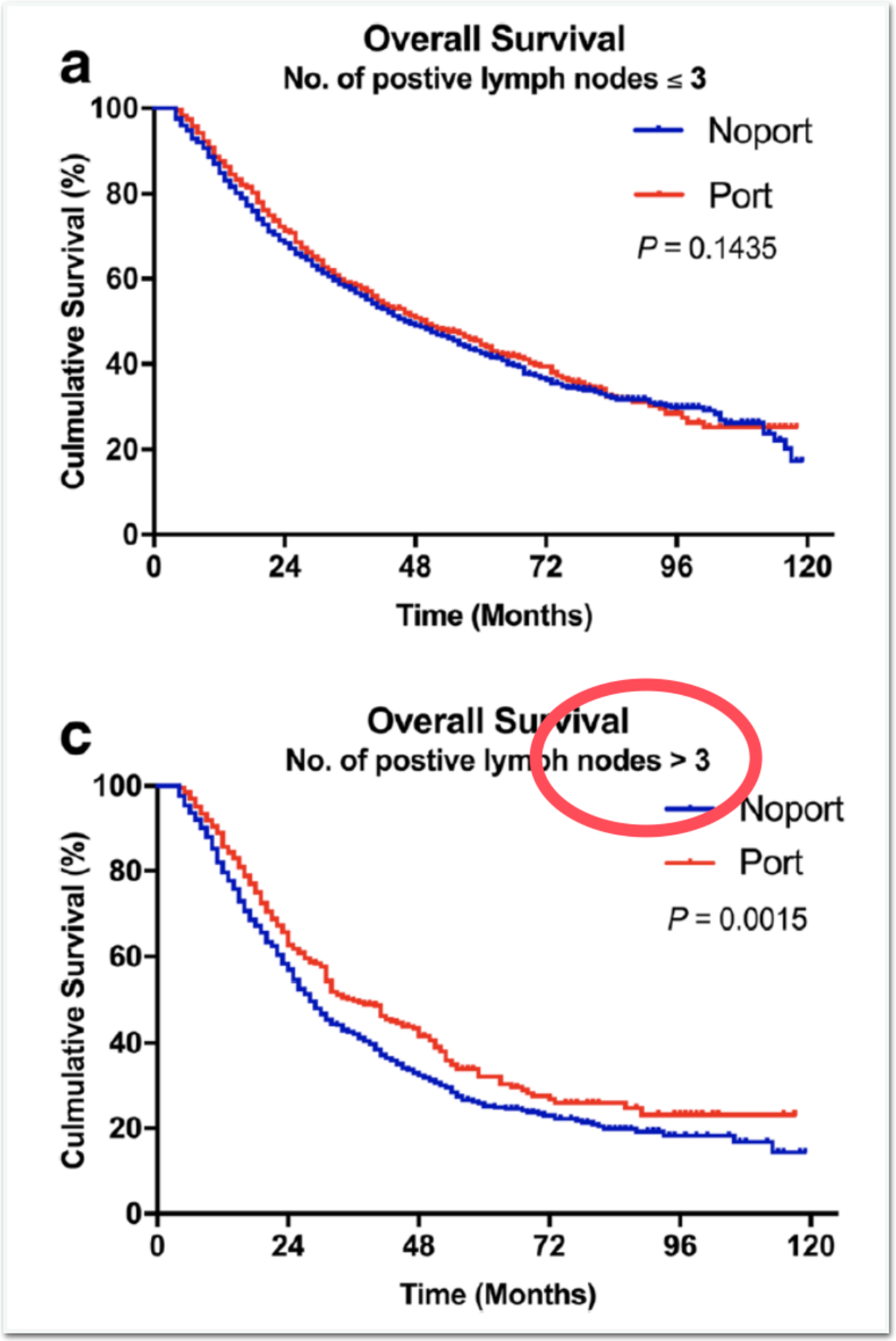
Wang *et al. Radiation Oncology* (2017) 12:207
DOI 10.1186/s13014-017-0946-1

Radiation Oncology

RESEARCH Open Access

Choice of postoperative radiation for stage IIIA pathologic N2 non-small cell lung cancer: impact of metastatic lymph node number

Siwei Wang[1,2†], Zhifei Ma[1,2†], Xiangbao Yang[3†], Yajing Wang[2], Youtao Xu[1], Wenjia Xia[1,2], Rui Chen[2,4], Mantang Qiu[1], Feng Jiang[1], Rong Yin[1], Lin Xu[1*] and Keping Xu[3*]



2017 :

RXTH ADJUVANTE N2

3 ANALYSES RÉTROSPECTIVES

BASE DE DONNÉES SEER

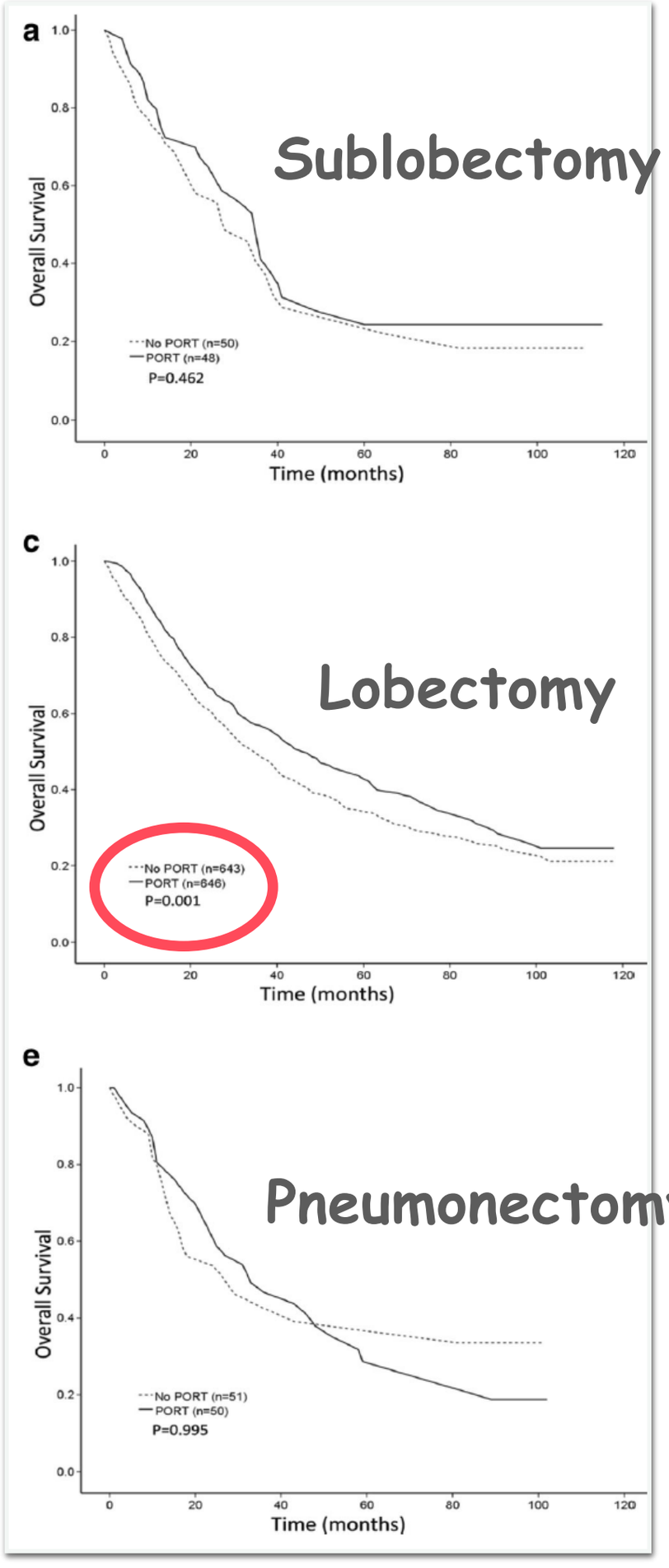
Wei *et al. Radiation Oncology* (2017) 12:96
DOI 10.1186/s13014-017-0836-6

Radiation Oncology

RESEARCH Open Access

Propensity score-matching analysis of postoperative radiotherapy for stage IIIA-N2 non-small cell lung cancer using the Surveillance, Epidemiology, and End Results database

Shenhai Wei[1], Mian Xie[2], Jintao Tian[1], Xiaoping Song[1], Bingqun Wu[1] and Limin Liu[3*]



2017 :

RXTH ADJUVANTE N2

3 ANALYSES RÉTROSPECTIVES

BASE DE DONNÉES SEER

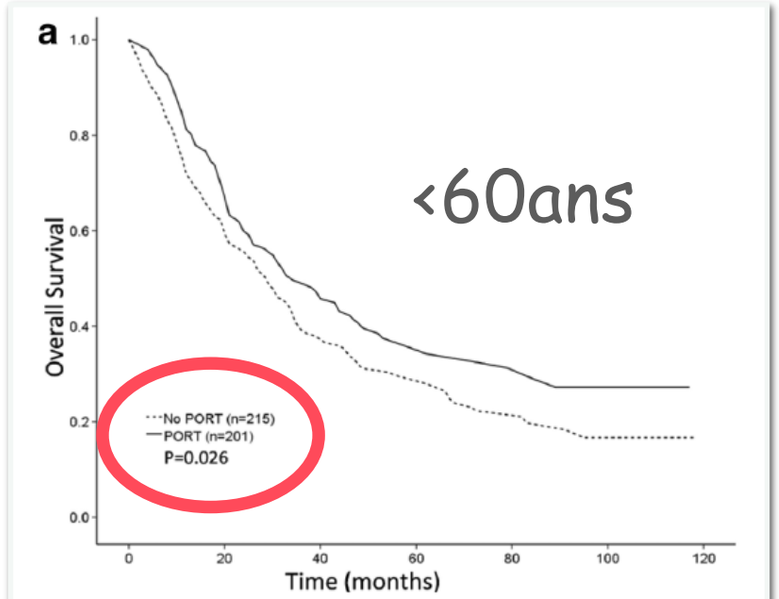
Wei *et al. Radiation Oncology* (2017) 12:96
DOI 10.1186/s13014-017-0836-6

Radiation Oncology

RESEARCH Open Access

Propensity score-matching analysis of postoperative radiotherapy for stage IIIA-N2 non-small cell lung cancer using the Surveillance, Epidemiology, and End Results database

Shenhai Wei[1], Mian Xie[2], Jintao Tian[1], Xiaoping Song[1], Bingqun Wu[1] and Limin Liu[3*]

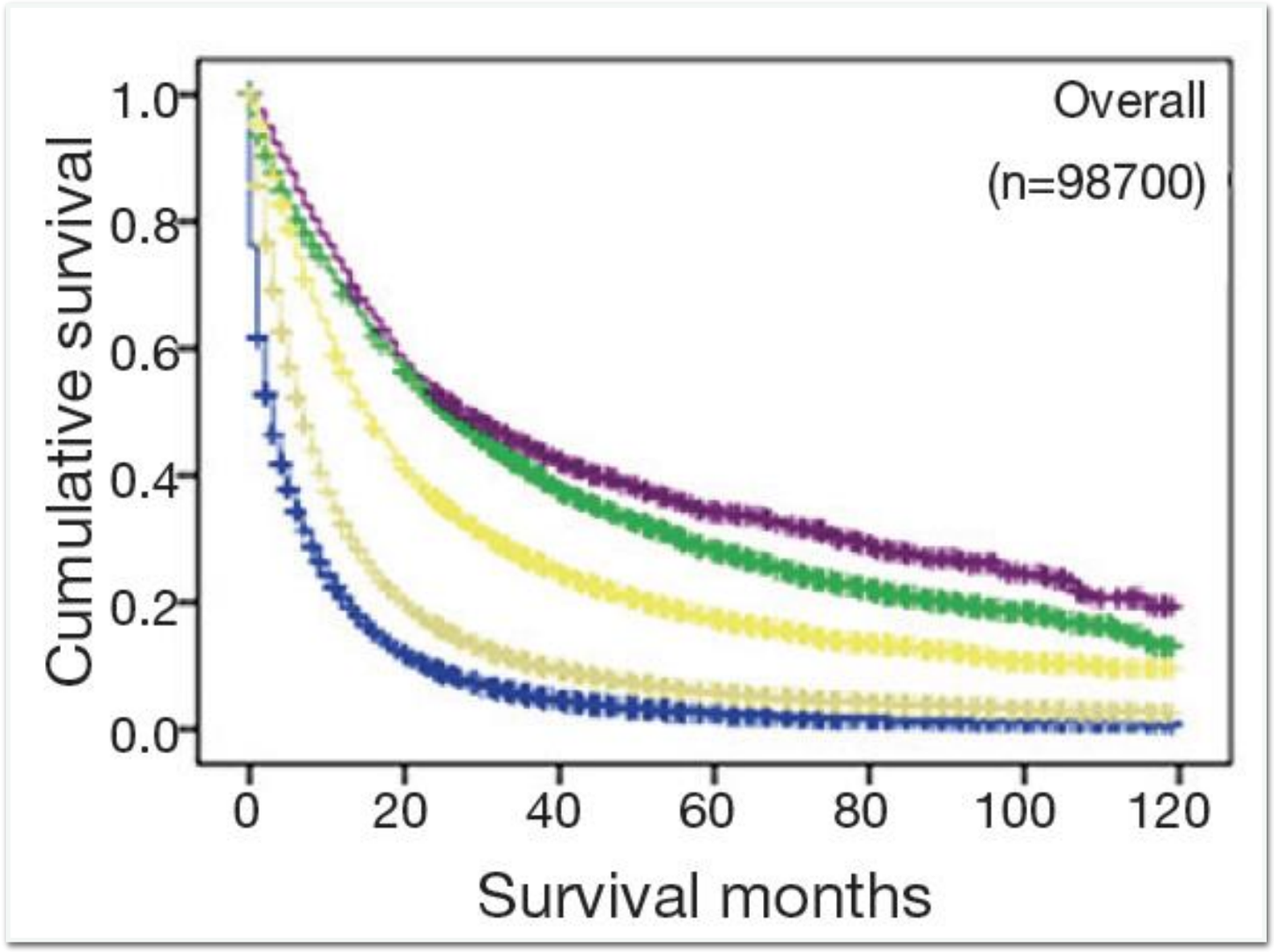


2017 :
RXTH ADJUVANTE N2
3 ANALYSES RÉTROSPECTIVES
BASE DE DONNÉES SEER

Original Article

Optimal managements of stage IIIA (N2) non-small cell lung cancer patients: a population-based survival analysis

Zhaofei Pang[1*], Yufan Yang[1*], Nan Ding[1], Cuicui Huang[1], Tiehong Zhang[2], Yang Ni[2], Jiajun Du[1,3], Qi Liu[1]



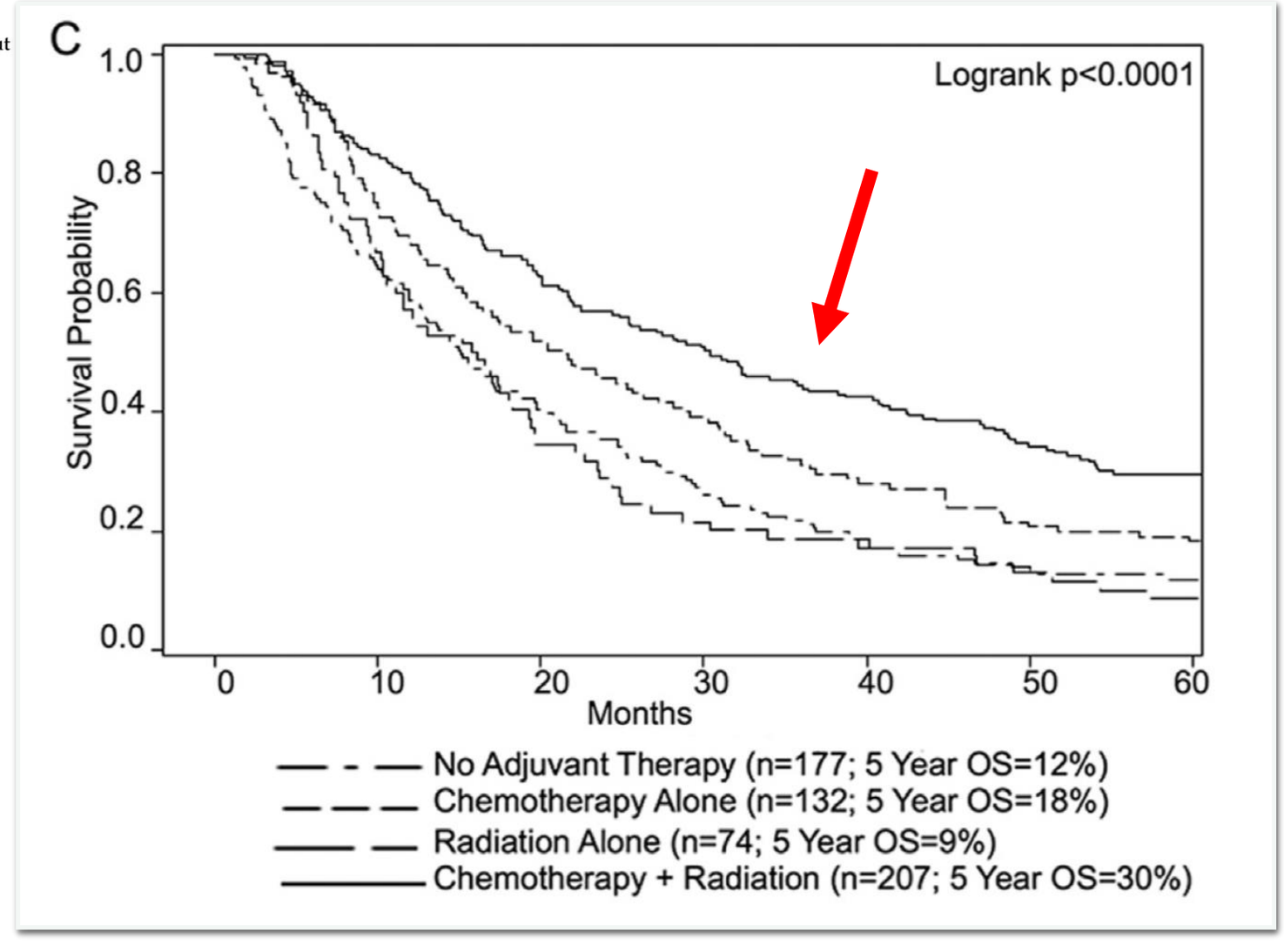
RXTH ADJUVANTE STADES III MARGES+ - RÉTRO - 2015

Impact of Adjuvant Treatment for Microscopic Residual Disease After Non-Small Cell Lung Cancer Surgery

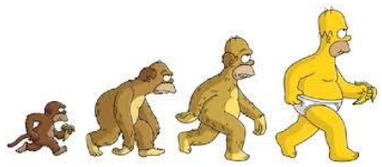
Jacquelyn G. Hancock, BS, Joshua E. Rosen, BAS, Alberto Antonicelli, MD, Amy Moreno, MD, Anthony W. Kim, MD, Frank C. Detterbeck, MD, and Daniel J. Boffa, MD

Section of Thoracic Surgery, Yale University School of Medicine, New Haven, Connecticut

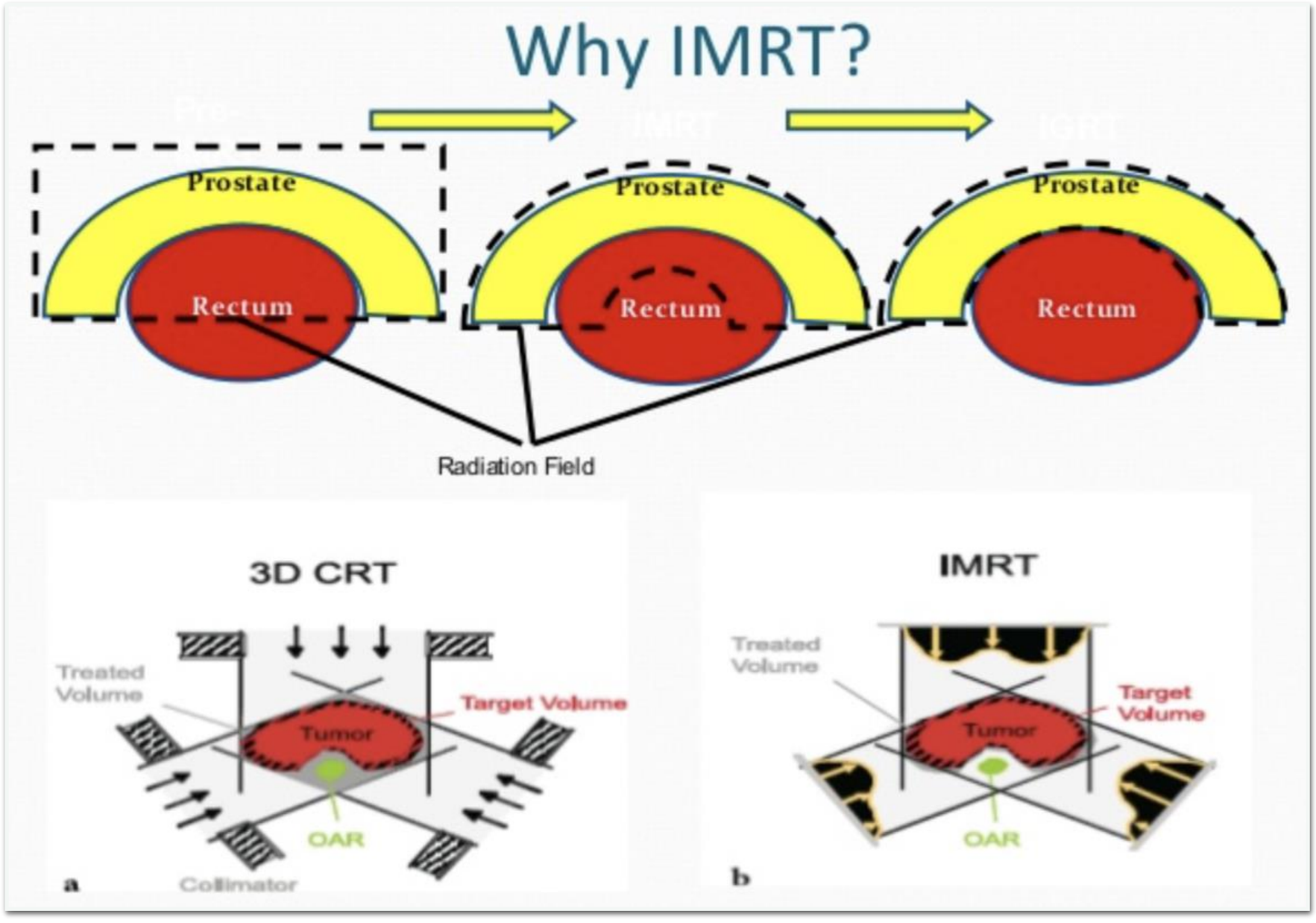
Stades III



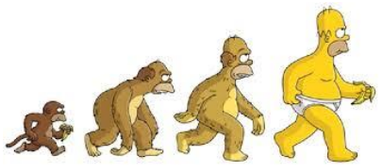
RXTH PAR MODULATION D'INTENSITÉ



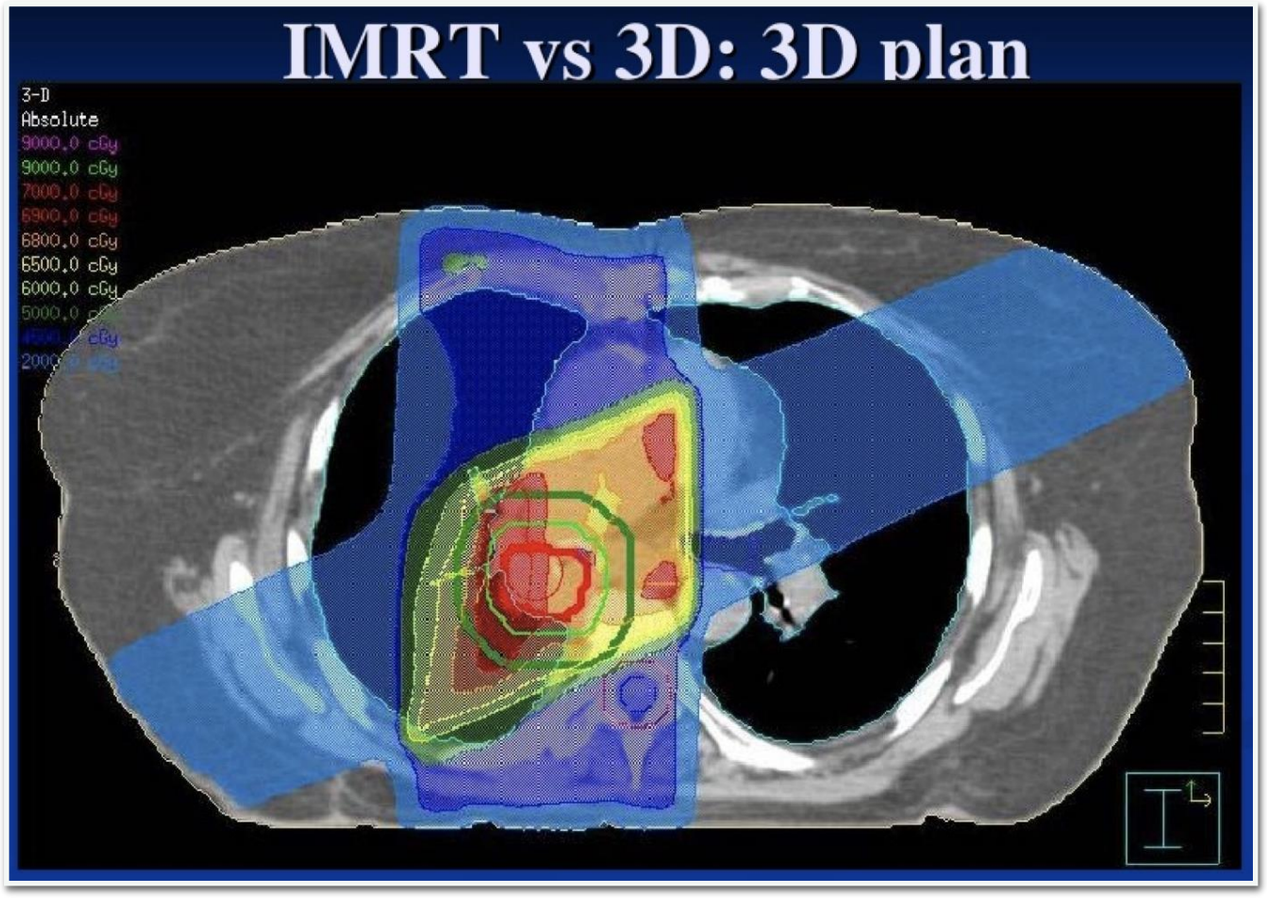
RXTH 3D

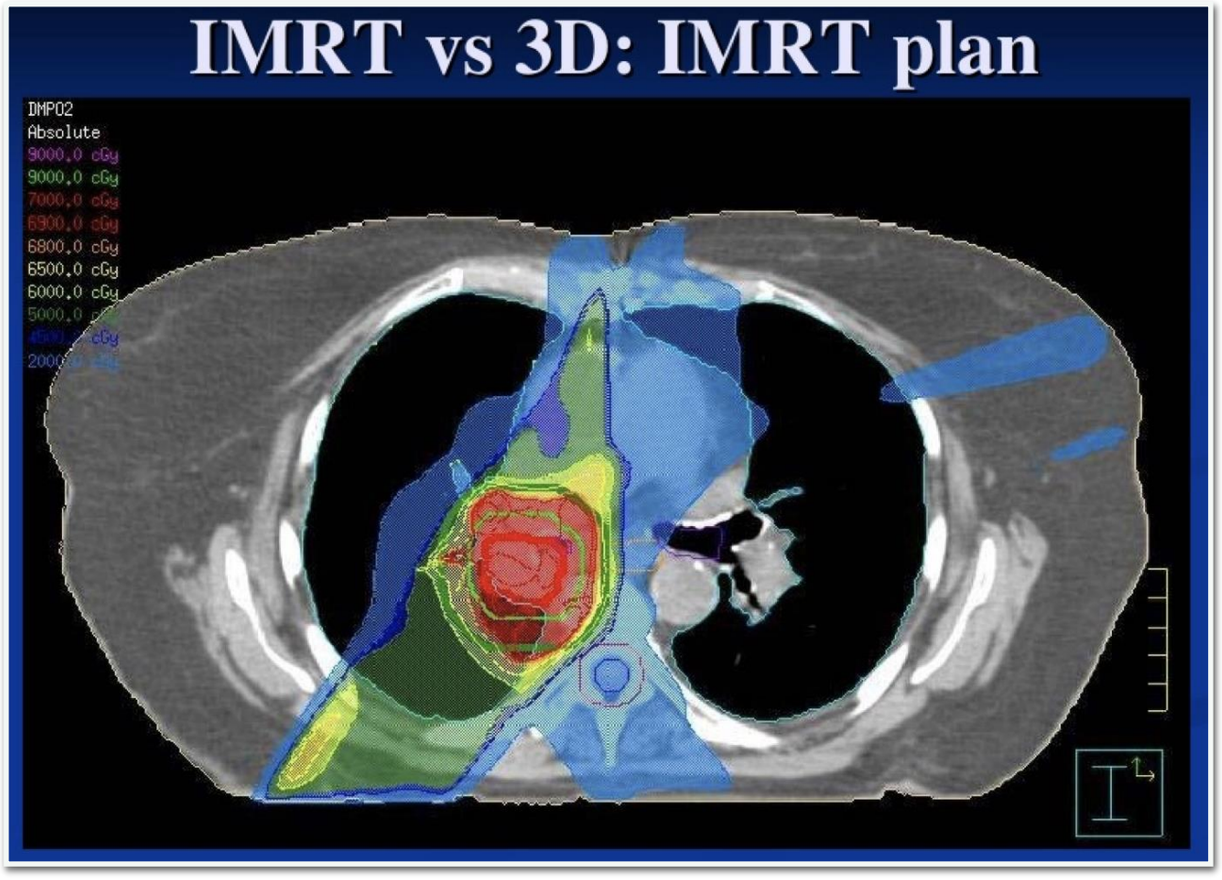


RXTH 3D



RXTH PAR MODULATION D'INTENSITÉ





RADIOCHIMIO EXCLUSIVE - PHASE 3 - 2017

VOLUME 35 · NUMBER 1 · JANUARY 1, 2017

JOURNAL OF CLINICAL ONCOLOGY | ORIGINAL REPORT

Impact of Intensity-Modulated Radiation Therapy Technique for Locally Advanced Non–Small-Cell Lung Cancer: A Secondary Analysis of the NRG Oncology RTOG 0617 Randomized Clinical Trial

Stephen G. Chun, Chen Hu, Hak Choy, Ritsuko U. Komaki, Robert D. Timmerman, Steven E. Schild, Jeffrey A. Bogart, Michael C. Dobelbower, Walter Bosch, James M. Galvin, Vivek S. Kavadi, Samir Narayan, Puneeth Iyengar, Clifford G. Robinson, Raymond B. Wynn, Adam Raben, Mark E. Augspurger, Robert M. MacRae, Rebecca Paulus, and Jeffrey D. Bradley

3D VS IMRT

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

RADIOCHIMIO EXCLUSIVE - PHASE 3 - 2017

- 2-year OS PFS LRFS DMFS were not different
- Less Pneumonitis ≥grade 3 (3,5% vs 7,9% P=.039)
- Lower heart doses (6,8% vs 11,4% P<.05) who was significantly associated with OS

but IMRT group had :

- larger treatment volumes (486ml vs 427ml P=.005)
- larger treatment volume/volume of lung (0,15 vs 0,13 P=.013)
- more stage IIIB disease (38,6% vs 30,3% P=.056)

Conclusion

IMRT was associated with lower rates of severe pneumonitis and cardiac doses in NRG Oncology clinical trial RTOG 0617, which supports routine use of IMRT for locally advanced NSCLC.

RADIOCHIMIO EXCLUSIVE - RÉTRO NCDB - 2017

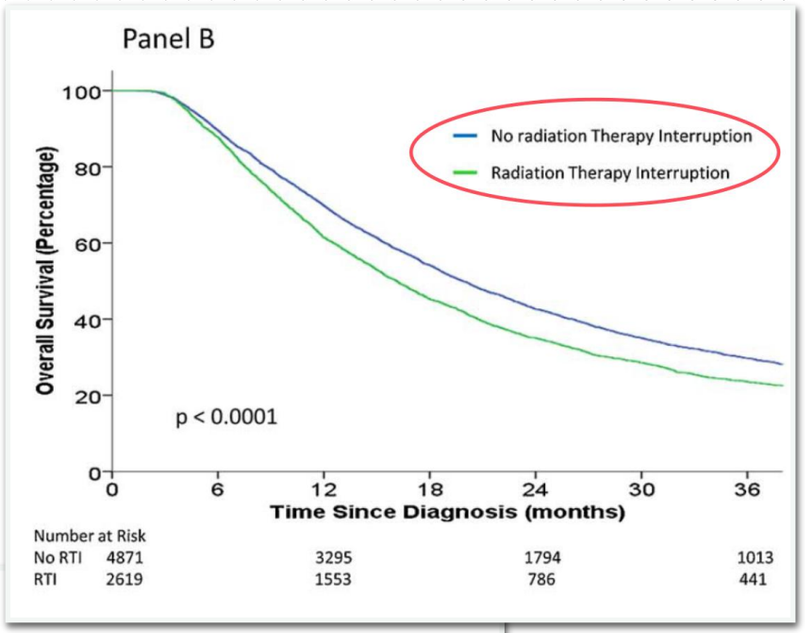
Contents lists available at ScienceDirect

Lung Cancer

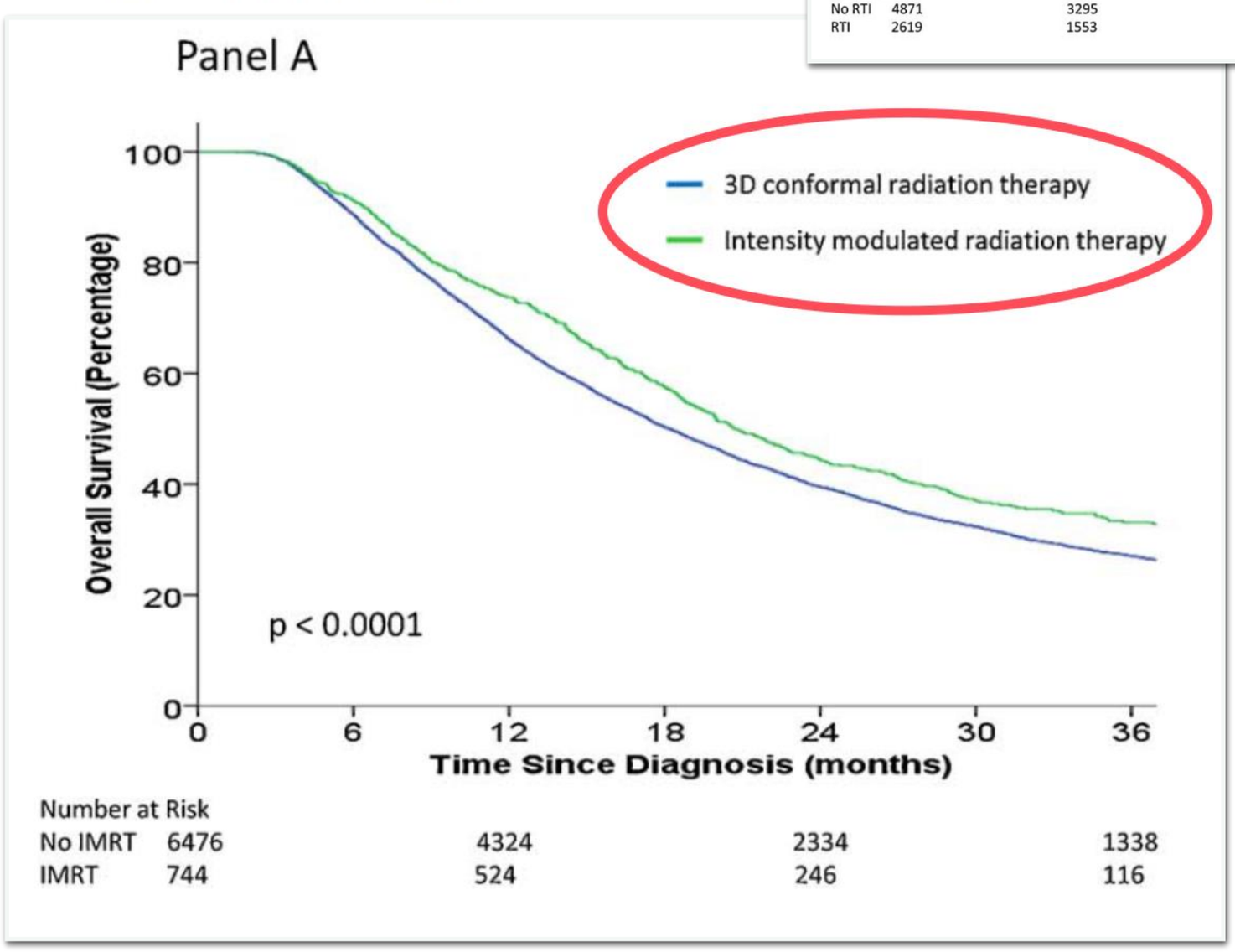
journal homepage: www.elsevier.com/locate/lungcan

Association between intensity modulated radiotherapy and survival in patients with stage III non-small cell lung cancer treated with chemoradiotherapy

Matthew Koshy[a,b,*], Renuka Malik[b], Michael Spiotto[a,b], Usama Mahmood[c], Chad G. Rusthoven[d], David J. Sher[e]

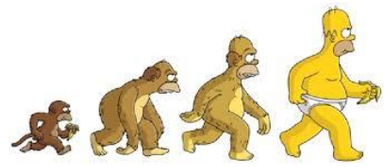


3D VS IMRT

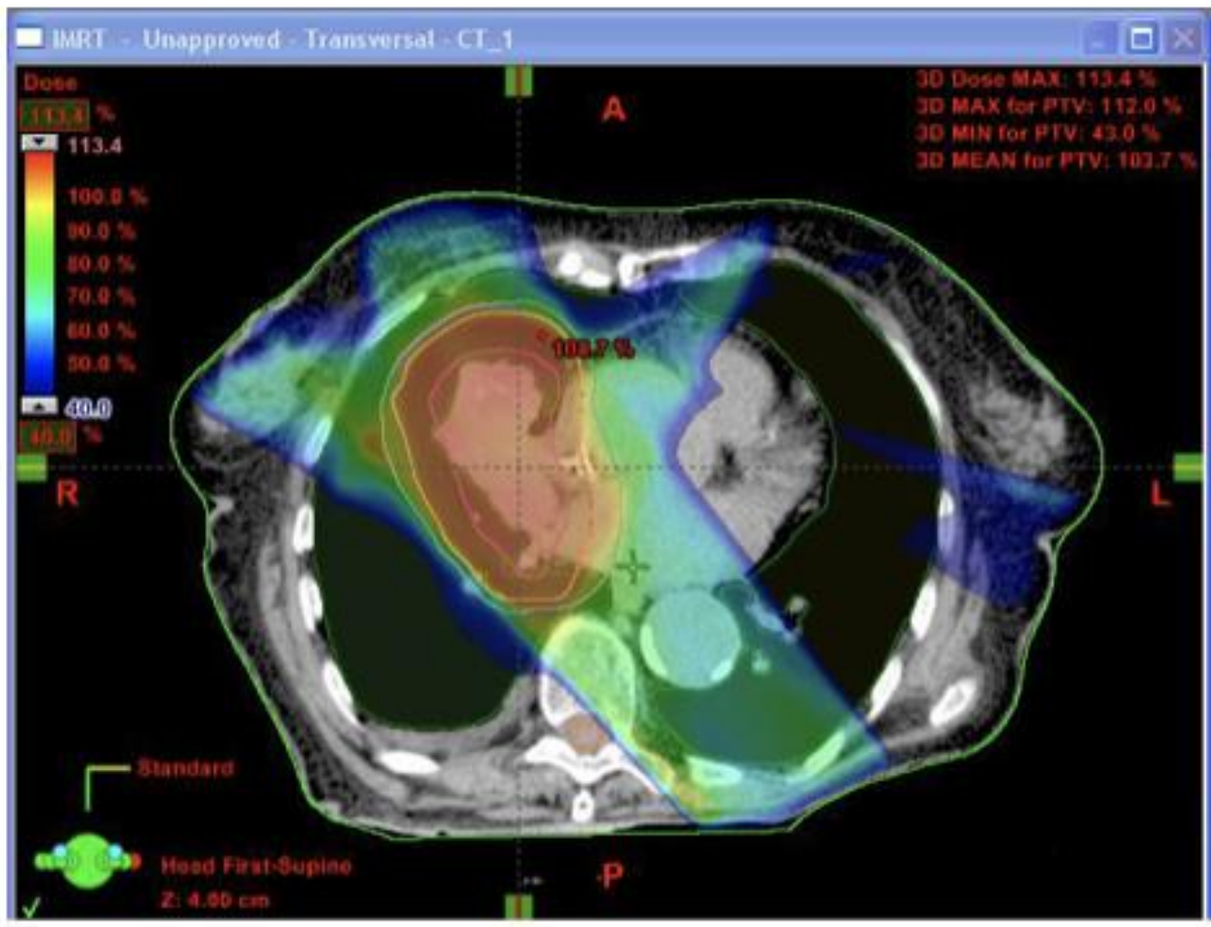


RXTH PAR MODULATION D'INTENSITÉ

VMAT

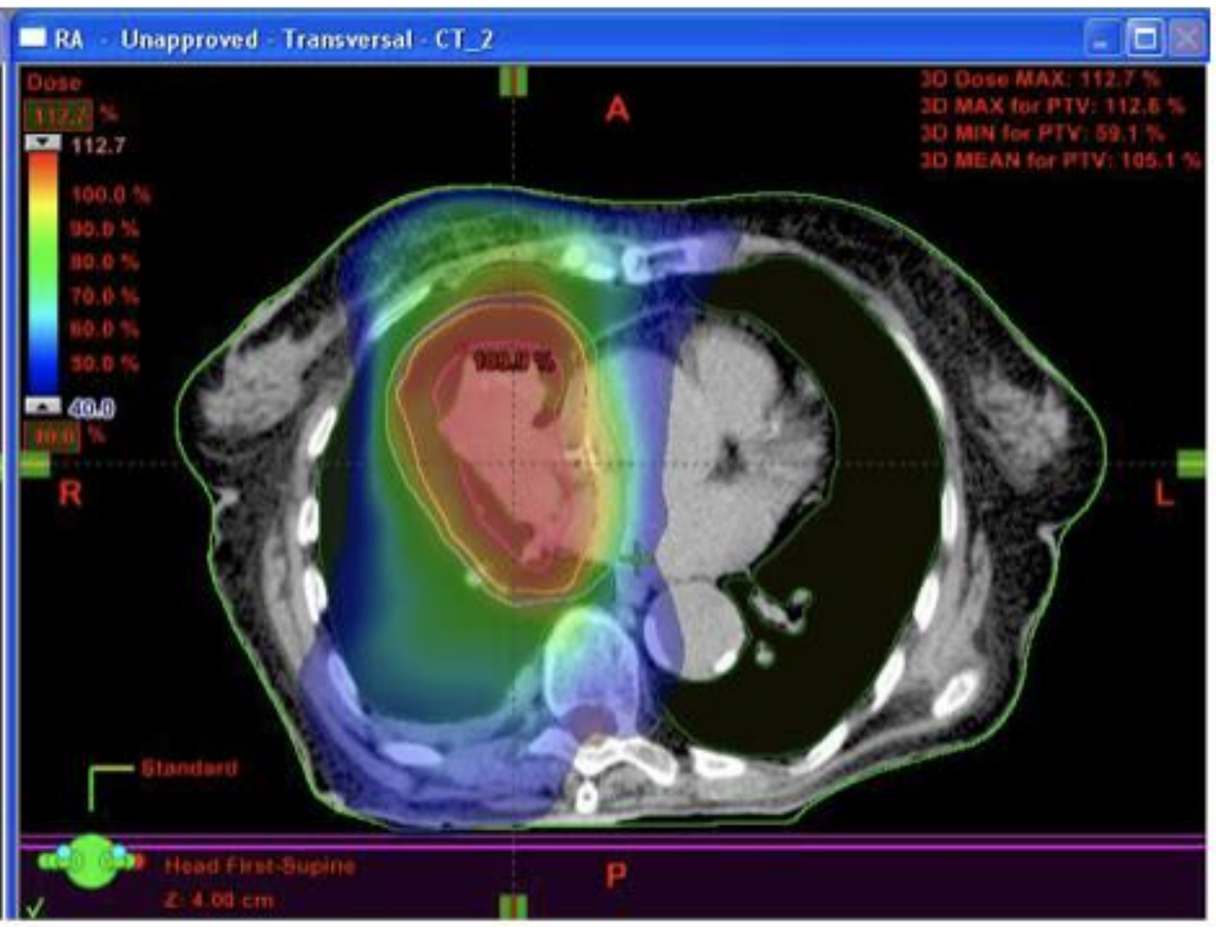


VMAT = Irradiation avec Modulation d'intensitéVolumétrique par ArcThérapie



1327 MUs
5.5 min

IMRT Plan



399 MUs
75 sec

RapidArc Plan

TECHNIQUES DE MODULATION D'INTENSITÉ - RÉTRO - 2017

SCIENTIFIC REPORTS

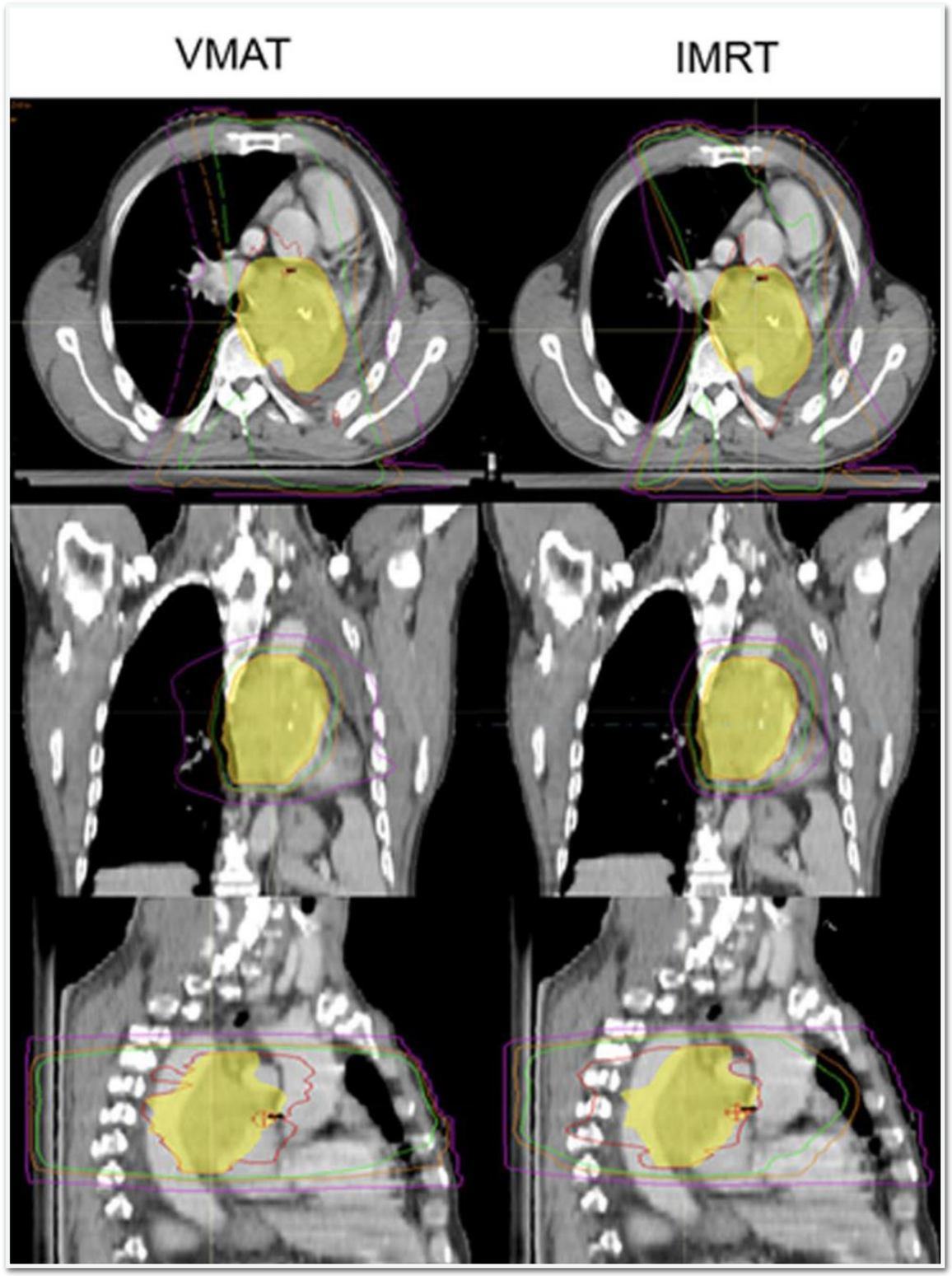
OPEN

Received: 1 June 2017
Accepted: 10 October 2017
Published online: 01 November 2017

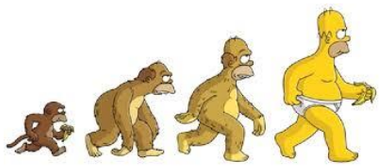
Dosimetric comparison of the helical tomotherapy, volumetric-modulated arc therapy and fixed-field intensity-modulated radiotherapy for stage IIB-IIIB non-small cell lung cancer

Yujin Xu[1,2], Weiye Deng[3], Shuangyan Yang[4], Pu Li[4], Yue Kong[2], Ye Tian[1], Zhongxing Liao[3] & Ming Chen[1,2]

					P value		
		TOMO	VMAT	IMRT	T vs. V	T vs. I	V vs. I
PTV	CI	0.76 ± 0.06	0.81 ± 0.07	0.75 ± 0.06	0.013	0.290	0.001
	HI	0.14 ± 0.04	0.10 ± 0.03	0.11 ± 0.02	0.002	0.003	0.070
	D_{mean}(Gy)	63.37 ± 1.08	62.41 ± 0.61	62.68 ± 0.66	0.000	0.002	0.047
	D_{max} (Gy)	66.39 ± 1.29	65.40 ± 1.02	65.66 ± 0.93	0.007	0.011	0.203
	D_1 (Gy)	65.61 ± 1.29	64.67 ± 0.90	64.95 ± 0.81	0.005	0.019	0.134
	D_2 (Gy)	65.43 ± 1.27	64.23 ± 1.65	64.79 ± 0.79	0.006	0.023	0.103
	D_{50} (Gy)	63.77 ± 1.18	62.60 ± 0.71	62.86 ± 0.54	0.000	0.000	0.062
	D_{95} (Gy)	59.82 ± 0.48	59.94 ± 0.25	59.91 ± 0.23	0.267	0.421	0.616
	D_{98} (Gy)	57.16 ± 1.99	58.41 ± 0.71	58.24 ± 0.61	0.004	0.011	0.265
	D_{99} (Gy)	54.94 ± 3.47	57.05 ± 1.20	56.65 ± 1.16	0.004	0.019	0.163
	V_{95} (%)	98.32 ± 0.89	99.03 ± 0.57	98.88 ± 0.49	0.001	0.006	0.224
	V_{100} (%)	94.63 ± 0.76	94.83 ± 0.65	94.73 ± 0.69	0.252	0.674	0.522
	V_{105} (%)	63.22 ± 19.24	35.05 ± 22.15	43.15 ± 16.45	0.000	0.000	0.054



RXTH DOSES STANDARDS



RXTH HAUTES DOSES

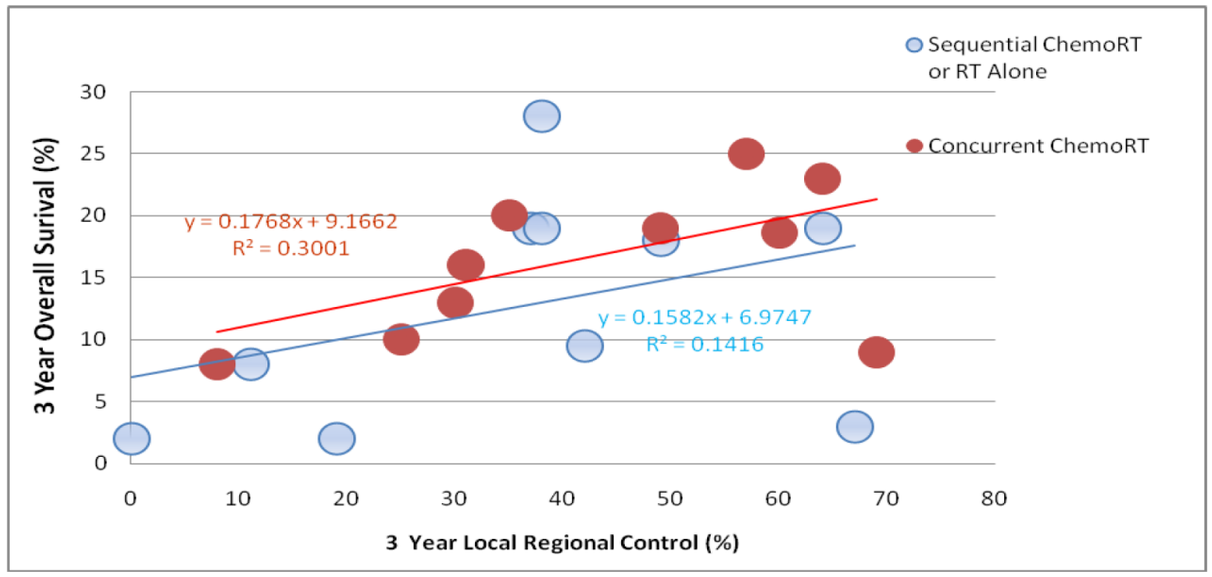


Figure 1: Correlation Between Local Regional Control And Overall Survival
Data presented are reported individual results from 10 phase III trials testing concurrent chemoradiation.

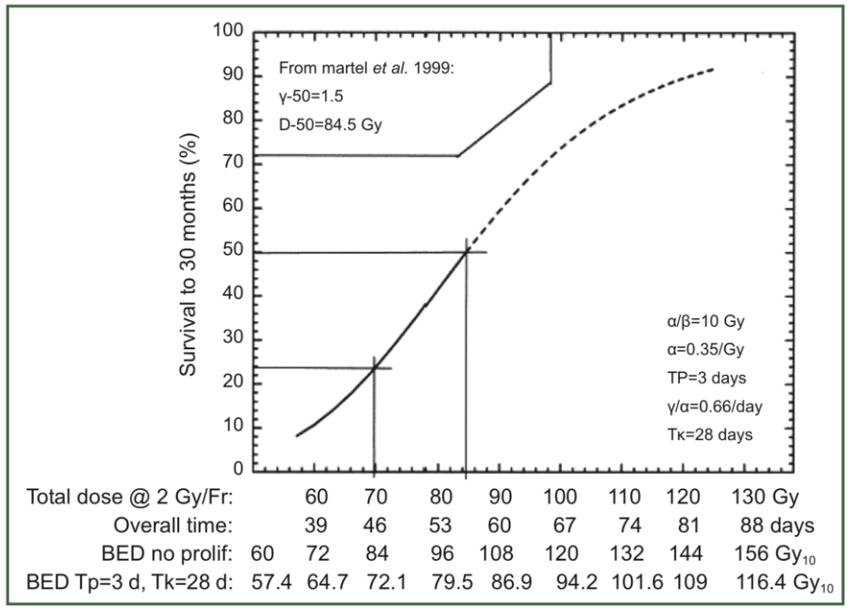


Figure 1. Tumor control probability and biological effective dose. The dose response relationship is sigmoidal in one of the early dose escalation studies of non-small cell lung cancer (NSCLC) performed in University of Michigan.

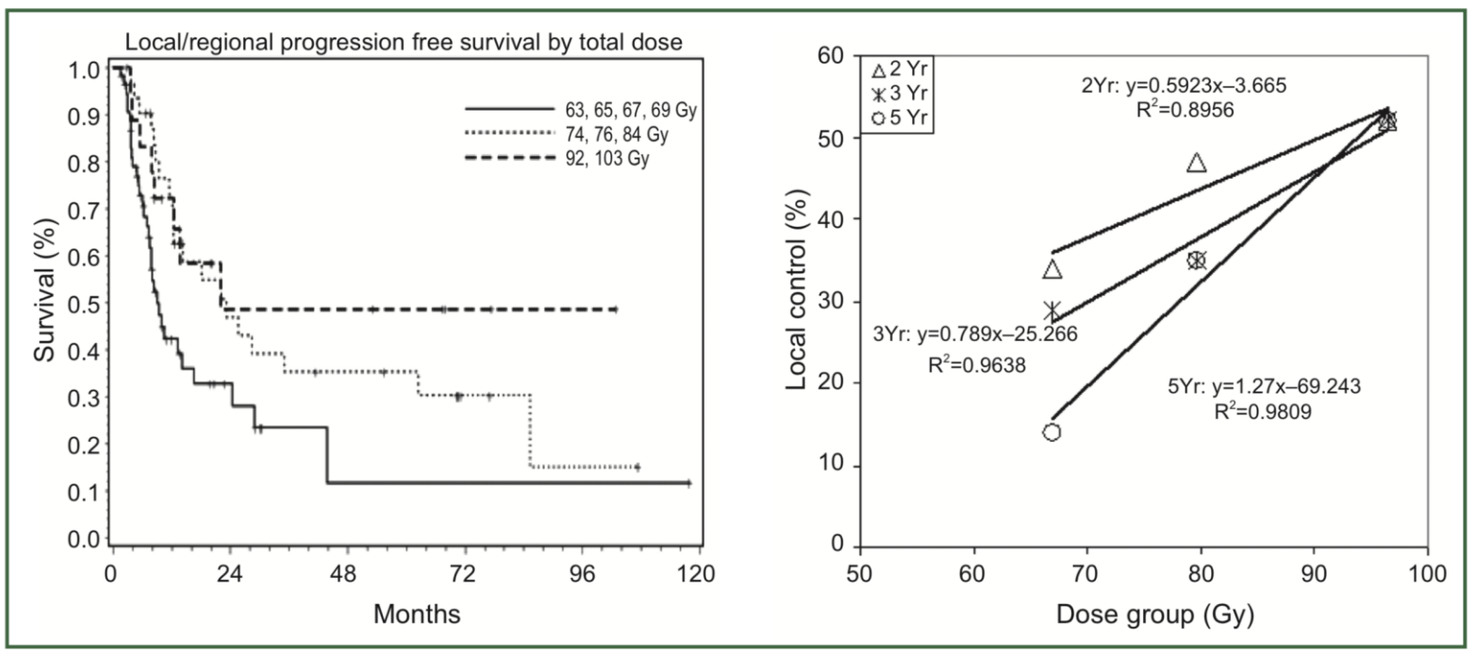


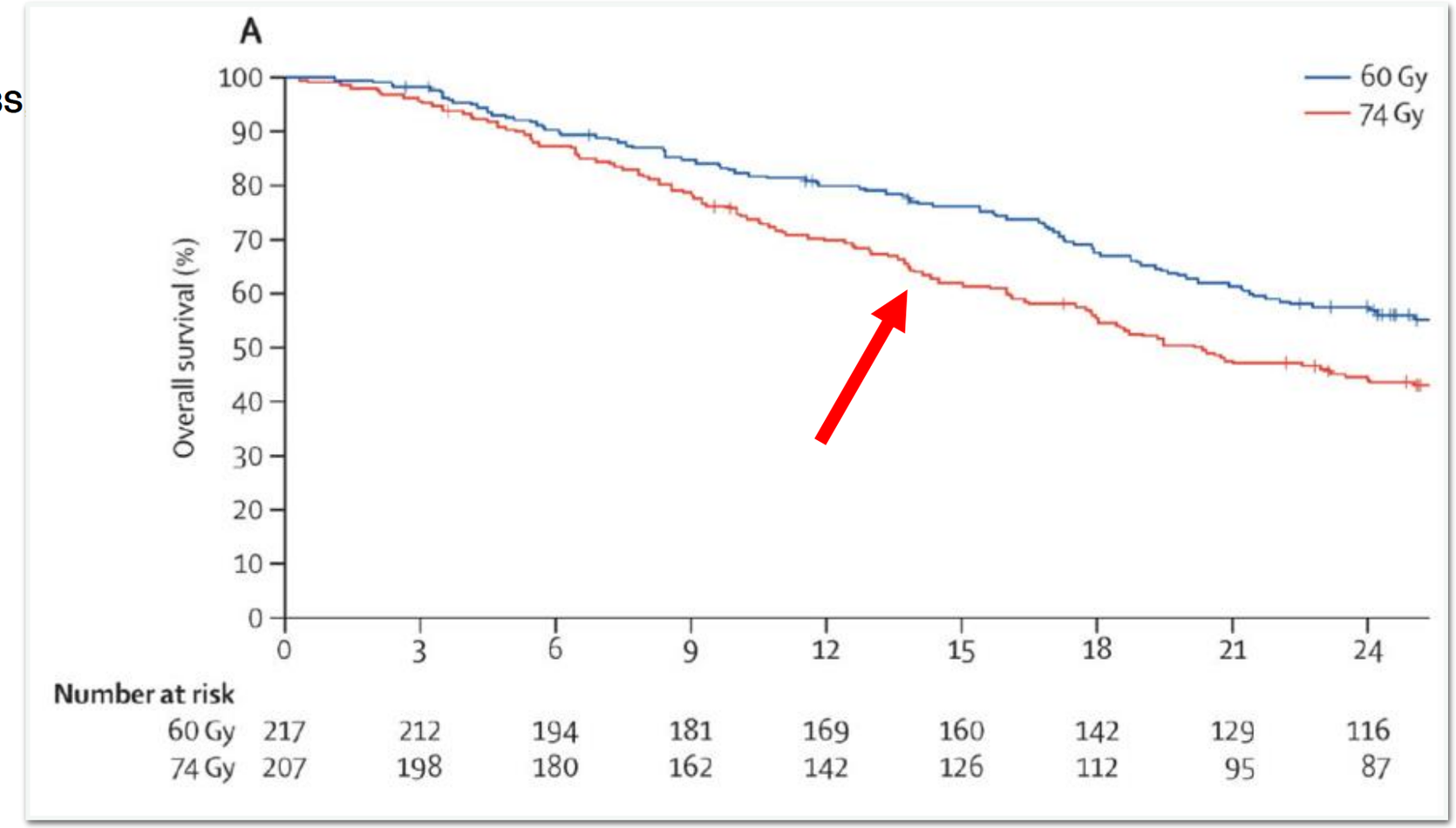
Figure 2. Local tumor control increases with higher dose radiation. Radiation dose is associated with long-term tumor control. Dose response relationship is steeper for longer follow-up.

RADIOCHIMIO EXCLUSIVE - PHASE 3 - 2015

Standard-dose versus high-dose conformal radiotherapy with concurrent and consolidation carboplatin plus paclitaxel with or without cetuximab for patients with stage IIIA or IIIB non-small-cell lung cancer (RTOG 0617): a randomised, two-by-two factorial phase 3 study

Prof. Jeffrey D Bradley, MD, Rebecca Paulus, BS

74Gy vs 60 Gy

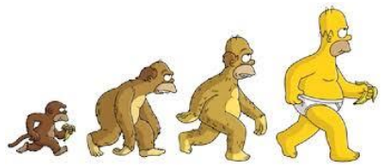


On multivariate analyses, factors predicting overall survival were :

Maximum oesophagitis grade

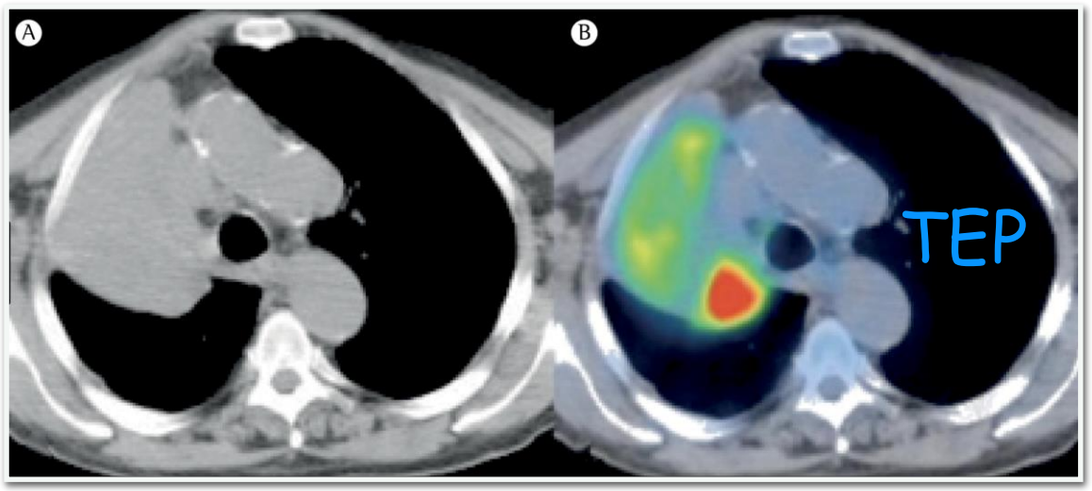
Heart V5 et V30

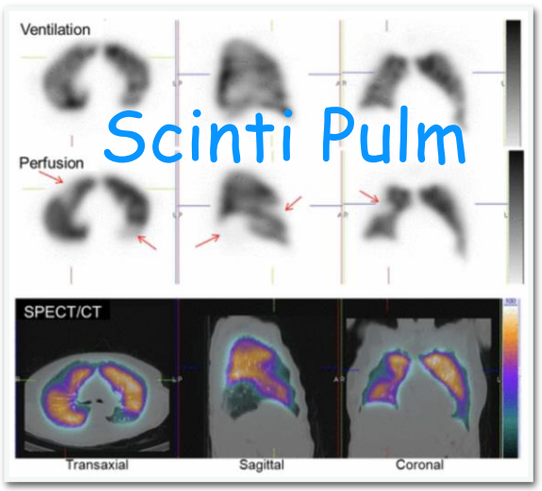
RXTH CLASSIQUE



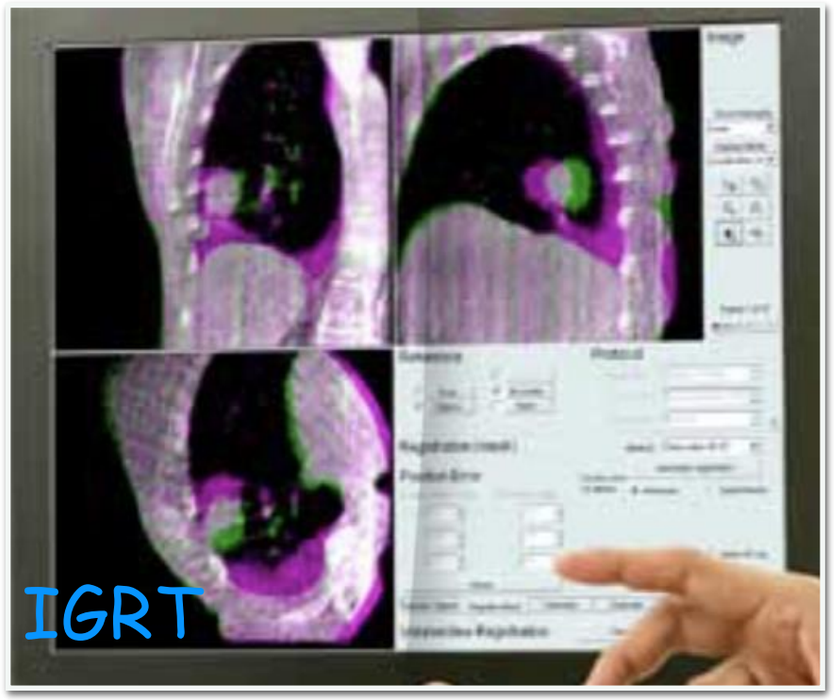
RXTH ADAPTATIVE

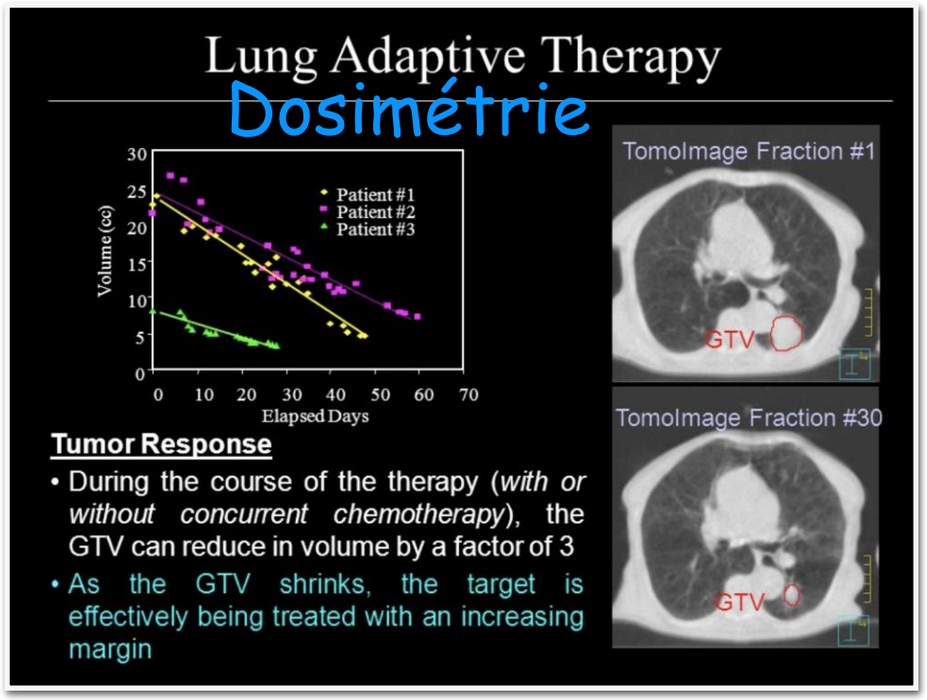
« Adaptation » pendant la préparation du Traitement



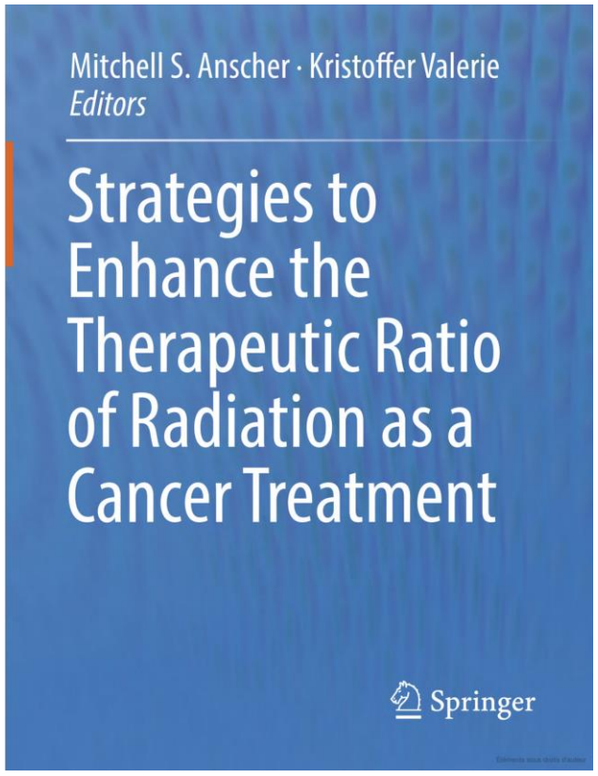


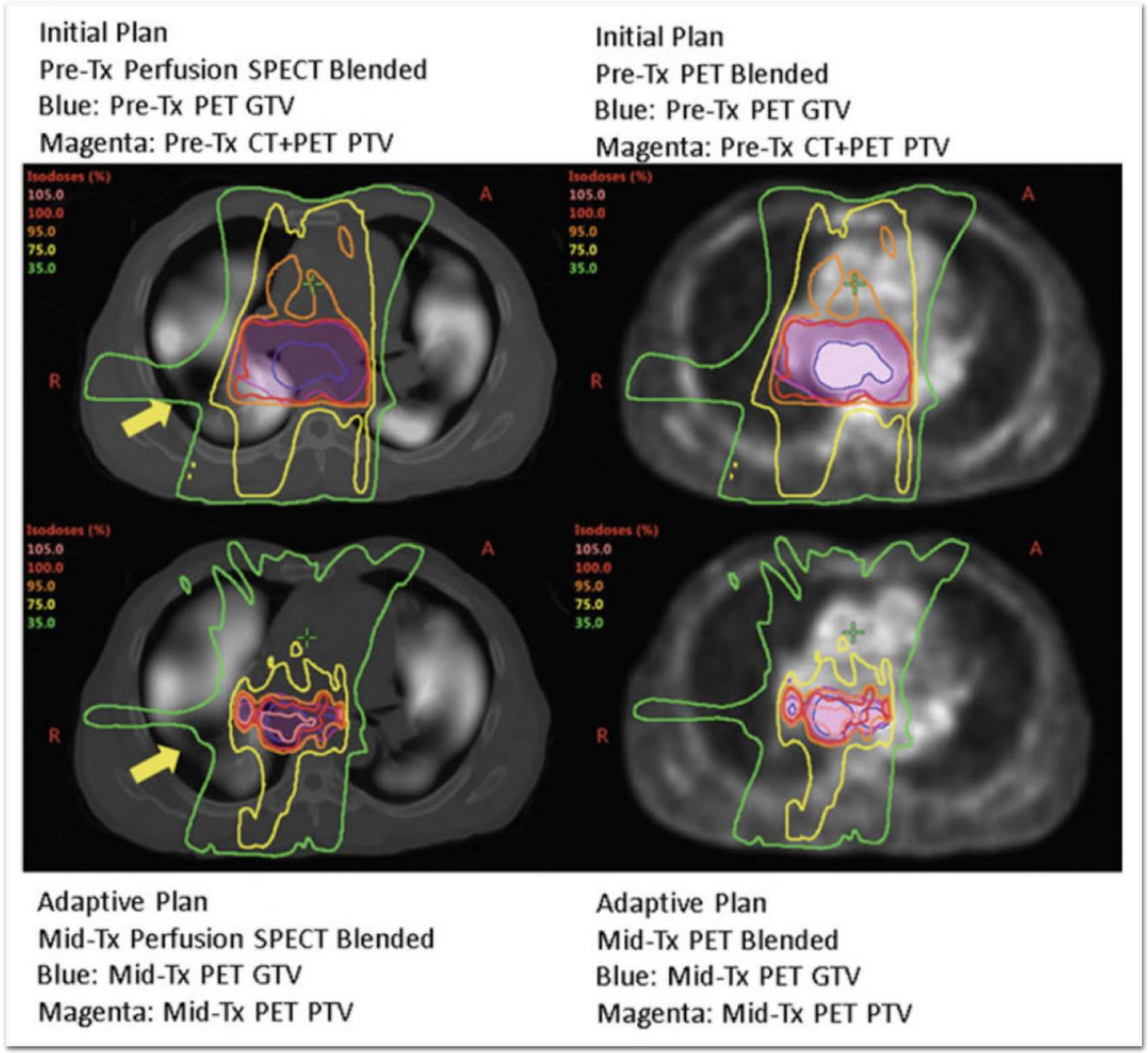
« Adaptation » pendant le Traitement





RADIOTHÉRAPIE ADAPTATIVE / SCANNER+TEP+SCINTI PULM - 2016





essai

en cours

RTOG 1106/ACRIN 6697

Randomized Phase II Trial of Individualized Adaptive Radiotherapy Using During-Treatment FDG-PET/CT and Modern Technology in Locally Advanced Non-Small Cell Lung Cancer (NSCLC)

SCHEMA (1/26/16)

[1]**All Patients**:	Baseline FDG-PET/CT scan within 4 weeks prior to registration
[2]**Subset of Patients**:	Baseline FMISO-PET/CT scan within 28 days prior to start of treatment, but not on same day as FDG-PET/CT scan. FMISO PET/CT must be done after subject has been registered. (FMISO sub-study closed to accrual on November 24, 2015)

STRATIFY	[3]RANDOMIZE
Stage 1. IIIA 2. IIIB **Primary Tumor Size** 1. > 5 cm 2. ≤ 5 cm **Histology** 1. Squamous 2. Non-Squamous	**Arm 1: Concurrent Chemoradiotherapy** RT to 50 Gy in 25 fractions (nominally 5 fx/week) [4]Carboplatin and paclitaxel weekly **Arm 2: Concurrent Chemoradiotherapy** RT to 46.2 Gy in 21 fractions (nominally 5 fx/week) [4]Carboplatin and paclitaxel weekly

ALL PATIENTS: During-RT FDG-PET/CT Scan between fractions 18 and 19 for Both Arms
For Arm 2, re-simulation with CT scan at fractions 18-19

Arm 1: Continuation of radiotherapy, per the initial plan, not based on during-RT FDG-PET/CT scan with carboplatin and paclitaxel for a total of 6 weekly cycles. No adaptation is allowed.

A total of 60 Gy in 30 daily fractions (nominally 5 fx/week)

Arm 2: Adaptive radiotherapy, based on during-RT FDG-PET/CT scan and resimulation with CT scan with carboplatin and paclitaxel for a total of 6 weekly cycles

19.8-34.2 Gy in 9 fractions; overall total of up to 80.4 Gy in 30 daily fractions
Individualized to MLD 20 Gy

ALL PATIENTS: Consolidative Chemotherapy

Arms 1 and 2: Carboplatin and paclitaxel q21 days X 3

IGRT is mandatory for this study. Each center must be credentialed for lung IGRT.

RECOMMANDATIONS ESMO 2017

- If N2 disease is only documented intra-operatively, surgery should be followed by adjuvant ChT [I, A]
- In case of complete resection, addition of PORT is not routinely recommended, but may be an option following individual risk assessment [V, C]

- If « single station N2 » disease can be demonstrated by preoperative pathological nodal analysis, resection followed by adjuvant ChT, induction ChT followed by surgery or induction CRT followed by surgery are options
- If induction ChT alone is given preoperatively, PORT is not standard treatment, but may be an option based on critical evaluation of locoregional relapse risks [IV, C]

- In « multistation N2 or N3 », concurrent definitive CRT is preferred [I, A]

- In potentially resectable superior sulcus tumours, concurrent CRT induction (with Cisplatin) followed by definitive surgery is the treatment of choice [III, A]
- The same strategy may be applied for potentially resectable T3 or T4 central tumours in highly selected cases and experienced centres [III, B]
- In both situations, surgery should be carried out within 4 weeks after the end of RT [III, B]

RECOMMANDATIONS US NCCN - 2018

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2018
Non-Small Cell Lung Cancer
NCCN Evidence Blocks™

- In patients with clinical stage I/II upstaged surgically to N2, PORT appears to improve survival significantly as an adjunction to postoperative chemotherapy in non-randomized analyses => « may be recommended »
- PORT is generally administered after postoperative chemotherapy
- PORT with concurrent chemotherapy can be administered safety in medically fit patients and is recommended for positive resection margins

1	1	1	1	-	-	-	-	N3	IIIB					IIIC	
0	0	0	0	1	1	-	-	N2	IIIA					IIIB	
0	0	0	0	0	0	1	1	N1	IIB					IIIA	
0	0	0	0	0	0	0	0	N0	IA1	IA2	IA3	IB	IIA	IIB	IIIA
Tumeur Primaire									T1a	T1b	T1c	T2a	T2b	T3	T4
								Taille (cm)	≤1	]1;2]	]2;3]	]3;4]	]4;5]	]5;7]	≥7
								Localisation	Pas d'extension proximale			Bronche souche Atélectasie		Bronche souche Atélectasie	Carène
Stade 0 TisN0M0								Invasion	Aucune			**Plèvre Viscérale**		Cage thoracique Péricarde Nerf phrénique	Trachée, Diaphragme, Médiastin, Cœur, Gros Vaisseaux, œsophage, Vertèbres, Nerf récurrent,
								Nodules Satellites	Aucun			Aucun		Même Lobe	Autres lobes ipsilatéraux

National Comprehensive Cancer Network®

APRES CHIRURGIE

1	1	1	1	-	-	-	-	N3	IIIB					IIIC	
0	0	0	0	1	1	-	-	N2	IIIA					IIIB	
0	0	0	0	0	0	1	1	N1	IIB					IIIA	
0	0	0	0	0	0	0	0	N0	IA1	IA2	IA3	IB	IIA	IIB	IIIA
Tumeur Primaire									T1a	T1b	T1c	T2a	T2b	T3	T4
								Taille (cm)	≤1	]1;2]	]2;3]	]3;4]	]4;5]	]5;7]	≥7
								Localisation	Pas d'extension proximale			Bronche souche Atélectasie		Bronche souche Atélectasie	Carène
Stade 0 TisN0M0								Invasion	Aucune			**Plèvre Viscérale**		Cage thoracique Péricarde Nerf phrénique	Trachée, Diaphragme, Médiastin, Cœur, Gros Vaisseaux, œsophage, Vertèbres, Nerf récurrent,
								Nodules Satellites	Aucun			Aucun		Même Lobe	Autres lobes ipsilatéraux

FINDINGS AT SURGERY

ADJUVANT TREATMENT

Stage IA (T1abc, N0)
- Margins negative (R0)[r] → Observe
- Margins positive (R1, R2)[r] → Reresection (preferred) or RT[l] (category 2B)

Stage IB (T2a, N0); Stage IIA (T2b, N0)
- Margins negative (R0)[r] → Observe or Chemotherapy[o] for high-risk patients[p]
- Margins positive (R1, R2)[r] → Reresection (preferred) ± chemotherapy[o,s] or RT[l] ± chemotherapy[o] (chemotherapy for stage IIA)

Stage IIB (T1abc-T2a, N1); Stage IIB (T3, N0; T2b, N1)
- Margins negative (R0)[r] → Chemotherapy[o] (category 1)
- Margins positive
  - R1[r] → Reresection + chemotherapy[o] or Chemoradiation[l] (sequential[o] or concurrent[q])
  - R2[r] → Reresection + chemotherapy[o] or Concurrent chemoradiation[l,q]

Stage IIIA (T1-2, N2; T3, N1); Stage IIIB (T3, N2)
- Margins negative (R0)[r] → Chemotherapy[o] (category 1) or Sequential chemotherapy[o] + RT[l] (N2 only)
- Margins positive
  - R1[r] → Chemoradiation[l] (sequential[o] or concurrent[q])
  - R2[r] → Concurrent chemoradiation[l,q]

APRES BILAN PRÉ-THÉRAPEUTIQUE

IIIA cT4N0 NS

IIIA cT3-4N1 NS

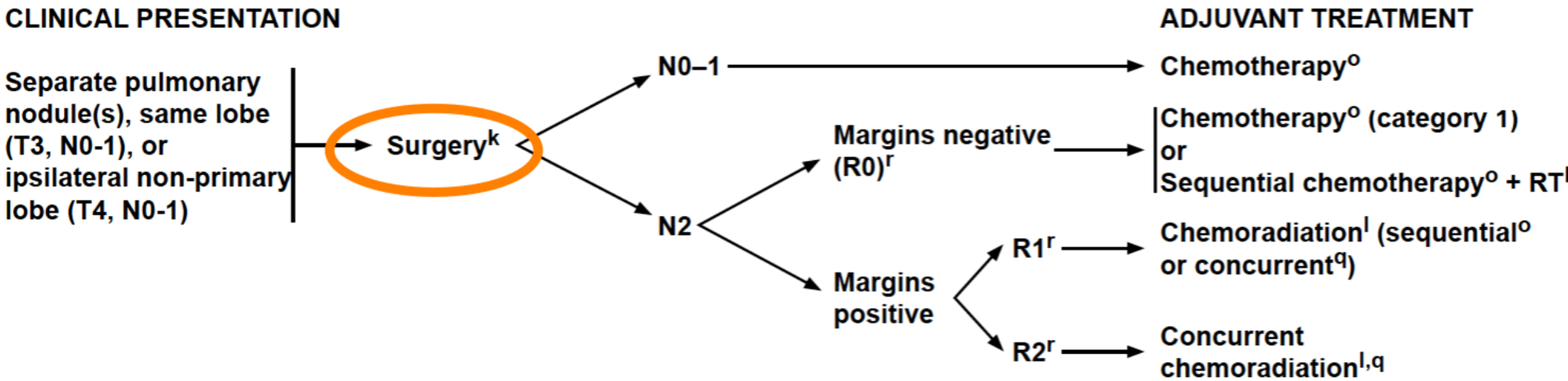
IIIA cT1-2N2

IIIB cT3N2

IIIB cT4N2

IIIB cT1-2N3

IIIC cT3-4N3



1	1	1	1	-	-	-	-	N3	IIIB						IIIC	
0	0	0	0	1	1	-	-	N2	IIIA						IIIB	
0	0	0	0	0	0	1	1	N1	IIB						IIIA	
0	0	0	0	0	0	0	0	N0	IA1	IA2	IA3	IB	IIA	IIB	IIIA	
Tumeur Primaire									T1a		T1b	T1c	T2a	T2b	T3	T4
Stade 0 TisN0M0	Taille (cm)								≤1		]1;2]	]2;3]	]3;4]	]4;5]	]5;7]	≥7
	Localisation								Pas d'extension proximale				Bronche souche Atélectasie		Bronche souche Atélectasie	Carène
	Invasion								Aucune				**Plèvre Viscérale**		Cage thoracique Péricarde Nerf phrénique	Trachée, Diaphragme, Médiastin, Cœur, Gros Vaisseaux, œsophage, Vertèbres, Nerf récurrent,
	Nodules Satellites								Aucun				Aucun		Même Lobe	Autres lobes ipsilatéraux

APRES BILAN PRÉ-THÉRAPEUTIQUE

IIIA cT4N0
Hors NS

IIIA cT3-4N1
Hors NS

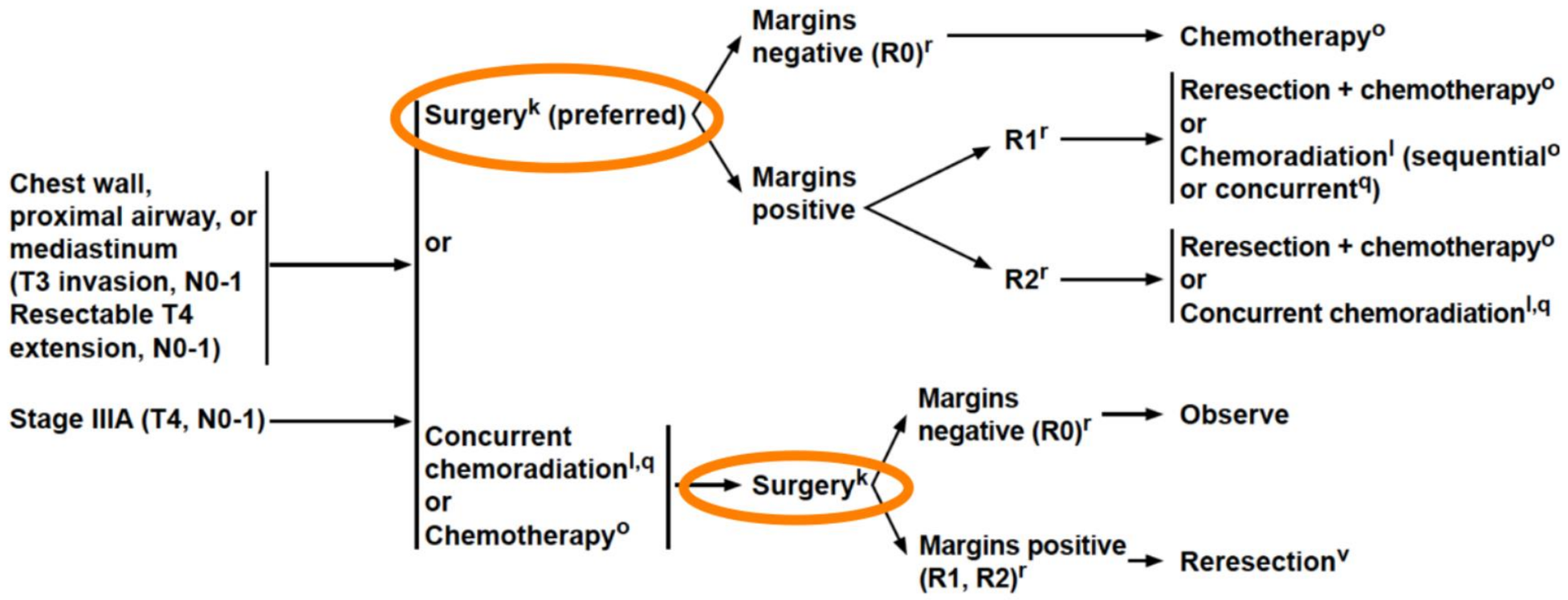
IIIA cT1-2N2

IIIB cT3N2

IIIB cT4N2

IIIB cT1-2N3

IIIC cT3-4N3



1	1	1	1	-	-	-	-	N3	IIIB					IIIC	
0	0	0	0	1	1	-	-	N2	IIIA					IIIB	
0	0	0	0	0	0	1	1	N1	IIB					IIIA	
0	0	0	0	0	0	0	0	N0	IA1	IA2	IA3	IB	IIA	IIB	IIIA
Tumeur Primaire									T1a	T1b	T1c	T2a	T2b	T3	T4
Stade 0 TisN0M0	Taille (cm)								≤1	]1;2]	]2;3]	]3;4]	]4;5]	]5;7]	≥7
	Localisation								Pas d'extension proximale			Bronche souche Atélectasie		Bronche souche Atélectasie	Carène
	Invasion								Aucune			**Plèvre Viscérale**		Cage thoracique Péricarde Nerf phrénique	Trachée, Diaphragme, Médiastin, Cœur, Gros Vaisseaux, œsophage, Vertèbres, Nerf récurrent,
	Nodules Satellites								Aucun			Aucun		Même Lobe	Autres lobes ipsilatéraux

APRES BILAN PRÉ-THÉRAPEUTIQUE

IIIA cT4N0

IIIA cT3-4N1

IIIA cT1-2N2

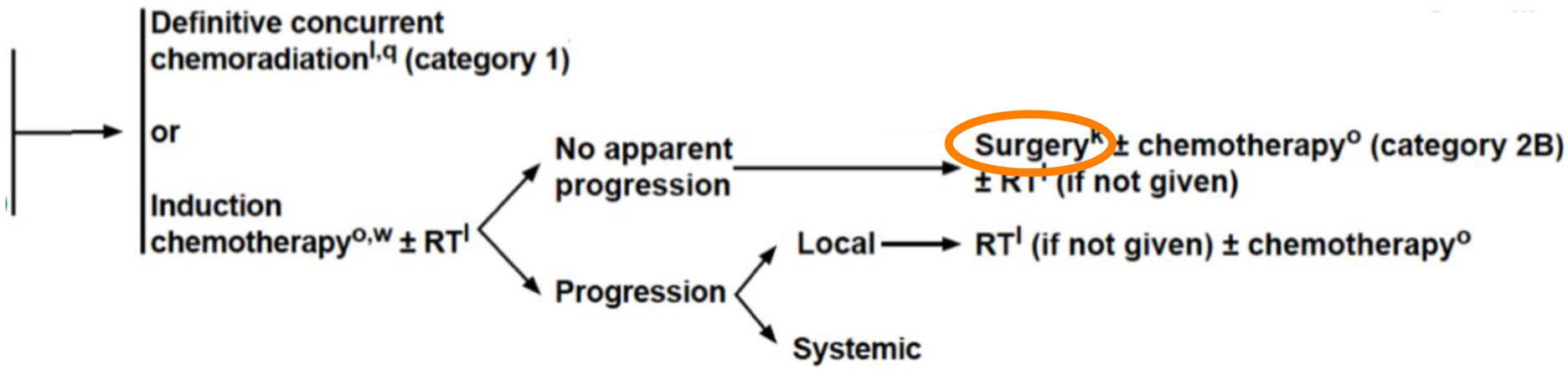
IIIB cT3NS N2

IIIB cT3INV N2

IIIB cT4N2

IIIB cT1-2N3

IIIC cT3-4N3



1	1	1	1	-	-	-	-	N3	IIIB					IIIC	
0	0	0	0	1	1	-	-	N2	IIIA					IIIB	
0	0	0	0	0	0	1	1	N1	IIB					IIIA	
0	0	0	0	0	0	0	0	N0	IA1	IA2	IA3	IB	IIA	IIB	IIIA
Tumeur Primaire									T1a	T1b	T1c	T2a	T2b	T3	T4
	Taille (cm)								≤1	]1;2]	]2;3]	]3;4]	]4;5]	]5;7]	≥7
	Localisation								Pas d'extension proximale			Bronche souche Atélectasie		Bronche souche Atélectasie	Carène
Stade 0 TisN0M0	Invasion								Aucune			Plèvre Viscérale		Cage thoracique Péricarde Nerf phrénique	Trachée, Diaphragme, Médiastin, Cœur, Gros Vaisseaux, œsophage, Vertèbres, Nerf récurrent,
	Nodules Satellites								Aucun			Aucun		Même Lobe	Autres lobes ipsilatéraux

APRES BILAN PRÉ-THÉRAPEUTIQUE

IIIA T4N0

IIIA T3-4N1

IIIA T1-2N2

IIIB T3NS N2

IIIB T3INV N2

IIIB T4N2

IIIB T1-2N3

IIIC T3-4N3

									IIIB					IIIC	
0	0	0	0	1	1	-	-	N2	IIIA					IIIB	
0	0	0	0	0	0	1	1	N1	IIB					IIIA	
0	0	0	0	0	0	0	0	N0	IA1	IA2	IA3	IB	IIA	IIB	IIIA
Tumeur Primaire									T1a	T1b	T1c	T2a	T2b	T3	T4
Stade 0 TisN0M0	Taille (cm)								≤1	]1;2]	]2;3]	]3;4]	]4;5]	]5;7]	≥7
	Localisation								Pas d'extension proximale			Bronche souche Atélectasie		Bronche souche Atélectasie	Carène
	Invasion								Aucune			Plèvre Viscérale		Cage thoracique Péricarde Nerf phrénique	Trachée, Diaphragme, Médiastin, Cœur, Gros Vaisseaux, œsophage, Vertèbres, Nerf récurrent,
	Nodules Satellites								Aucun			Aucun		Même Lobe	Autres lobes ipsilatéraux

Definitive concurrent chemoradiation

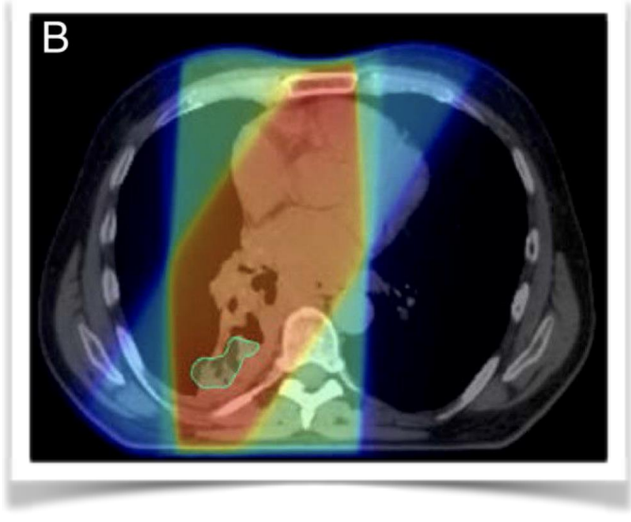
PRINCIPLES OF RADIATION THERAPY

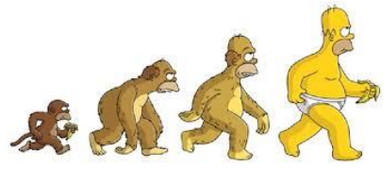
Preoperative RT	**45–54 Gy**	**1.8–2 Gy**	**5 weeks**
Postoperative RT			
• Negative margins	**50–54 Gy**	**1.8–2 Gy**	**5–6 weeks**
• Extracapsular nodal extension or microscopic positive margins	**54–60 Gy**	**1.8–2 Gy**	**6 weeks**
• Gross residual tumor	**60–70 Gy**	**2 Gy**	**6–7 weeks**

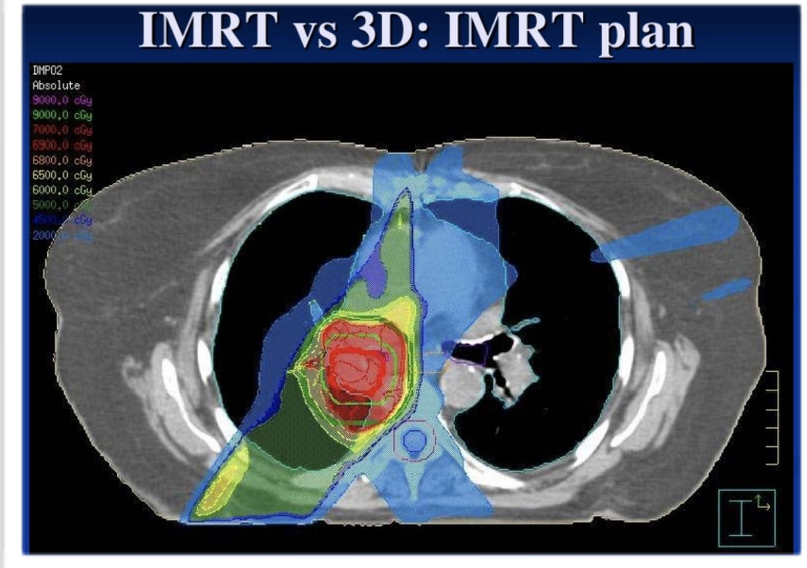
Radiation Therapy Simulation, Planning, and Delivery

- **Simulation should be performed using CT scans obtained in the RT treatment position with appropriate immobilization devices. IV contrast with or without oral contrast is recommended for better target/organ delineation whenever possible in patients with central tumors or nodal disease. Because IV contrast can affect tissue heterogeneity correction calculations, density masking or use of a pre-contrast scan may be needed when intense enhancement is present.**
- **PET/CT significantly improves targeting accuracy,[92] especially for patients with significant atelectasis and when IV CT contrast is contraindicated. A randomized trial of PET/CT versus CT-only RT planning demonstrated improved preemption of futile radical RT, decreased recurrences, and a trend toward improved overall survival with PET/CT RT planning.[93] Given the potential for rapid progression of NSCLC,[94,95] PET/CT should be obtained preferably within 4 weeks before treatment. It is ideal to obtain PET/CT in the treatment position.**
- **Tumor and organ motion, especially owing to breathing, should be assessed or accounted for at simulation. Options include fluoroscopy, inhale/exhale or slow scan CT, or, ideally, 4D-CT.**
- **Photon beam energy should be individualized based on the anatomic location of the tumors and beam paths. In general, photon energies between 4 to 10 MV are recommended for beams passing through low-density lung tissue before entering the tumor. When there is no air gap before the beam enters the tumor (such as for some large mediastinal tumors or tumors attached to the chest wall), higher energies may improve the dose distribution, especially when using a smaller number of fixed beam angles.**
- **Tissue heterogeneity correction and accurate dose calculation algorithms that account for buildup and lateral electron scatter effects in heterogeneous density tissues are recommended. Heterogeneity correction with simple pencil beam algorithms is not recommended.[60]**
- **Respiratory motion should be managed when motion is excessive. This includes (but is not limited to) forced shallow breathing with abdominal compression, accelerator beam gating with the respiratory cycle, dynamic tumor tracking, active breathing control (ABC), or coaching/biofeedback techniques. If motion is minimal or the ITV is small, motion-encompassing targeting is appropriate. A useful resource for implementation of respiratory motion management is the report of AAPM Task Group 76.[96]**
- **IGRT—including (but not limited to) orthogonal pair planar imaging and volumetric imaging (such as CBCT or CT on rails)—is recommended when using SABR and 3D-CRT/IMRT with steep dose gradients around the target, when OARs are in close proximity to high-dose regions, and when using complex motion management techniques.**

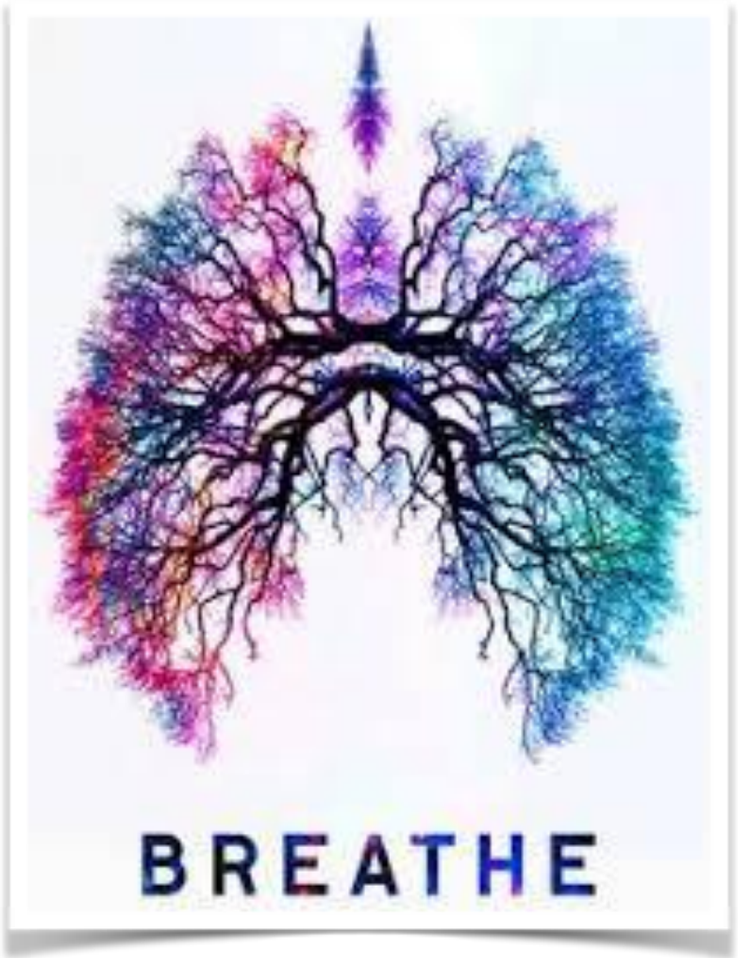
CONCLUSIONS

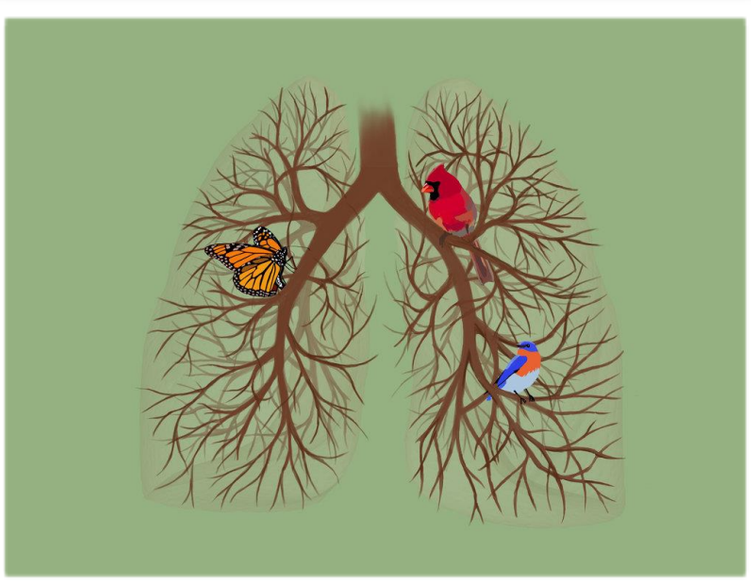






- ***Quoi attendre de LungArt ? … résultats en 2022 !***
  … sur une technique 3D … sans TEP ni IGRT obligatoires
- ***Données sur techniques récentes encourageantes car morbidité moindre***
- ***IMRT nouveau standard ? … nouvel essai randomisé nécessaire ?***
- ***Place de la radiothérapie adjuvante chez les … N0/N1 R0 ?***
- ***Intérêt de la Radiochimiothérapie Néoadjuvante vs Adjuvante ?***
- ***Intérêt de la Chimiothérapie séquentielle ou concomitante ?***
- ***Intérêt de l'Immunothérapie chez les M0 ? (essai MSD K671 …)***


BREATHE



RXTH VS CHIR APRÈS CHIMIO NEOADJ – PHASE 3 – 2007

Randomized Controlled Trial of Resection Versus Radiotherapy After Induction Chemotherapy in Stage IIIA-N2 Non–Small-Cell Lung Cancer

Jan P. van Meerbeeck, Gijs W. P. M. Kramer, Paul E. Y. Van Schil, Catherine Legrand, Egbert F. Smit, Franz Schramel, Vivianne C. Tjan-Heijnen, Bonne Biesma, Channa Debruyne, Nico van Zandwijk, Ted A. W. Splinter, Giuseppe Giaccone

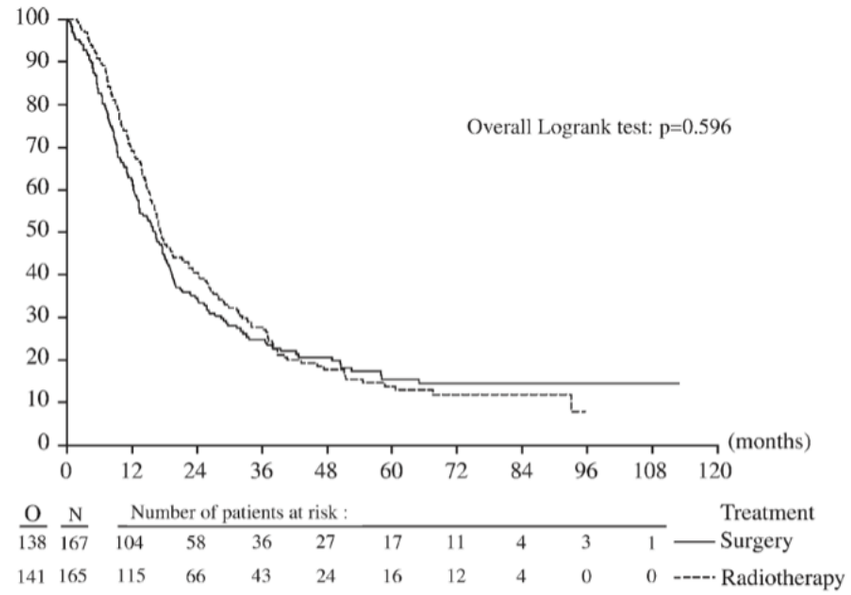


Fig. 2. Overall survival rates estimated from time of randomization using Kaplan–Meier analyses. *P* value (two-sided) was calculated using the log-rank test. O = number of deaths; N = number of patients. Hazard ratio = 1.06, 95% confidence interval = 0.84 to 1.35; *P* = .596.

Table 5. Exploratory analyses in 154 patients in the resection surgery arm*

Subgroup	N	Median OS, months (95% CI)	5-year OS, %	*P*, Univariate analysis	*P*, Multivariable analysis
Extent of resection				.009	.03
(Bi-)lobectomy	58	25.4 (17.7 to 48.9)	27		
Pneumonectomy	72	13.4 (11.1 to 19.5)	12		
Mediastinal status				<.001	.04
ypN0–1	64	22.7 (17.6 to 42.7)	29		
ypN2	86	14.9 (11.2 to 18.5)	7		
Type of resection				<.001	.01
Complete	77	24.1 (16.7 to 42.4)	27		
Incomplete	76	12.1 (9.5 to 17.1)	7		
No PORT	92	14.1 (11.2 to 19.9)	19	.6	.004
PORT	62	18.0 (15.0 to 25.9)	13		

* OS = overall survival; PORT = postoperative radiotherapy; CI = confidence interval; ypN = pathologic N after induction therapy. *P* values were calculated using a two-sided log-rank test.

RADIOCHIMIO +/- CHIR - PHASE 3 - 2009

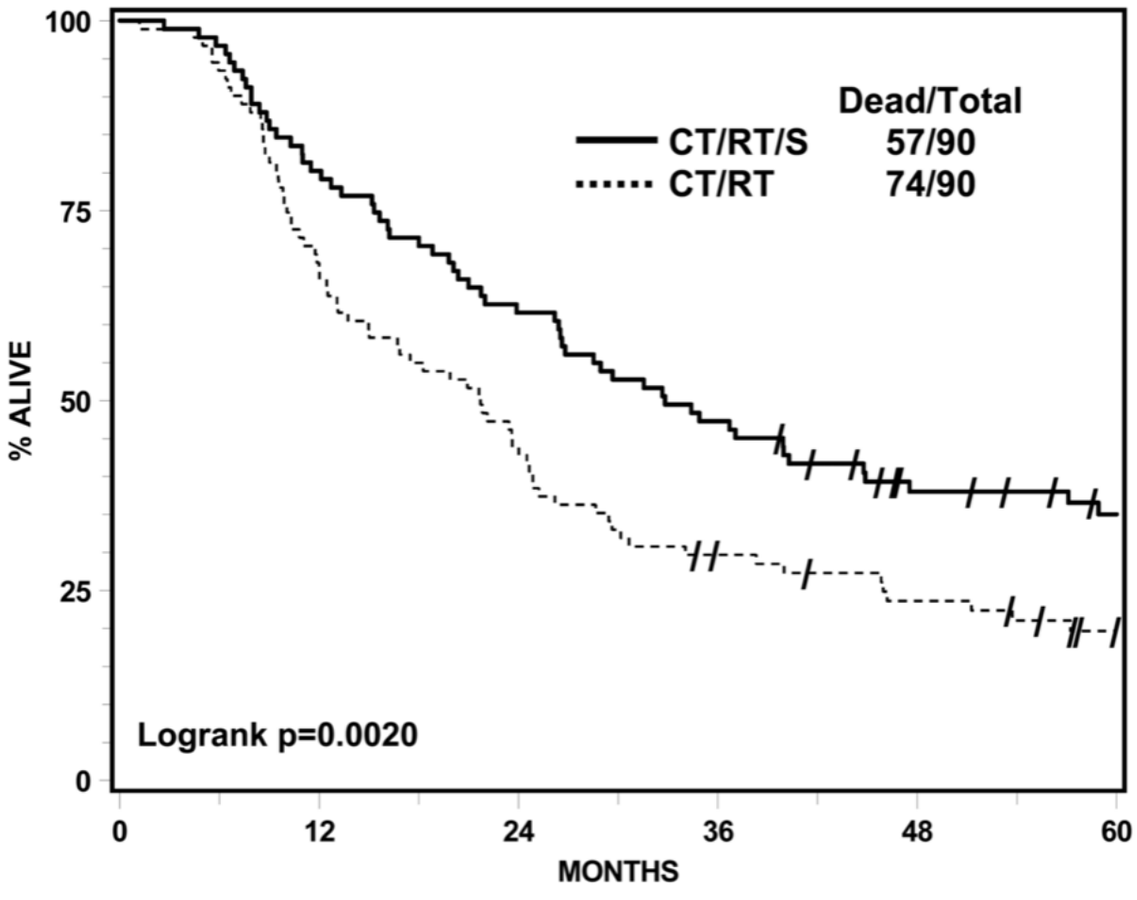
Radiotherapy plus Chemotherapy with or without Surgical Resection for Stage III Non-Small Cell Lung Cancer

Kathy S. Albain, MD[1], **R. Suzanne Swann, PhD**[2], **Valerie R. Rusch, MD**[3], **Andrew T. Turrisi III, MD**[4], **Frances A. Shepherd, MD**[5], **Colum Smith, MD**[6], **Yuhchyau Chen, MD**[7], **Robert B. Livingston, MD**[8], **Richard Feins, MD**[9], **David R. Gandara, MD**[10], **Willard A. Fry, MD**[11], **Gail Darling, MD**[12], **David H. Johnson, MD**[13], **Mark R. Green, MD**[14], **Robert C. Miller, MD**[15], **Joanne Ley, RN, CCRP**[2], **Willliam T. Sause, MD**[16], and **James D. Cox, MD**[17]

Methods—Patients with stage T1-3pN2M0 NSCLC were randomized before induction chemoRT (2 cycles of cisplatin and etoposide [PE] concurrent with 45 Gy RT). If no progression, arm 1 underwent resection, and arm 2 continued RT uninterrupted to 61 Gy. Two additional cycles of PE were given. The primary endpoint was overall survival (OS).

Findings—Progression-free survival for 396 eligible patients was superior in arm 1: median 12.8 versus 10.5 months, p=0.017, hazard ratio (HR) 0.77 (0.62,0.96); 5-yr 22.4% versus 11.1%. Median OS was 23.6 versus 22.2 months, p=0.24, HR 0.87 (0.70,1.10). Five-year survivals were arm 1, 27.2% and arm 2, 20.3%; odds ratio 0.63 (0.36,1.10, p=0.10). N0 status at thoracotomy predicted median OS of 33.5 months (5-year, 41.8%). Major chemoRT toxicities were neutropenia and esophagitis. Treatment-related death occurred in 16 (7.9%) patients on arm 1, of which 14 were post-pneumonectomy; and in 4 (2.1%) on arm 2. An exploratory analysis showed improved OS for patients who underwent lobectomy versus a matched cohort on chemoRT alone, but not for those undergoing pneumonectomy (matched similarly).

Interpretation—There was no significant survival advantage to surgery after chemoRT, despite improved PFS. Both chemoRT with definitive RT and chemoRT followed by resection (preferably lobectomy) are options for patients with stage IIIA(N2) NSCLC.



Résumé étude MSD 671 POUMON Non M+

S'adresse aux patients avec un CBNPC IIB ou IIIA (cT1-2 N1-2 ou cT3-4 N0-N1) opérables / PS 0-1

Phase 3

CHIMIO néoadj (au moins 1 cure et max 4 cures)

Cisplatine uniquement (75mg/m2) + GMZ 1000 (épider) ou ALIMTA 500 (adénoca)

+ **PEMBRO (Keytruda) ou PLACEBO en double aveugle ttes les 3 sem**

Puis CHIR (mais si finalement pas de chir peuvent rester inclus mais à traiter par RADIOTHERAPIE seule sans chimio conco +++)

Puis RADIOTH adj si masse résiduelle ou marges non saines ou N+ avec RC uniquement (pas de facteur de croissance ni de chimio pdt la radioth)

Puis **PEMBRO ou PLACEBO adjuvant pour 13 cures (10 mois) ttes les 3 sem**