Radiotherapy in rare Tumors: Thymic Epithelial Tumors

FOCUS ON: Technique

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Today's Agenda

Dose

Volume

Technological advances

In adjuvant and radical setting

Review published in 2009-2010

ITMIG Definitions and Policies

(J Thorac Oncol. 2011;6: S1743–S1748)

Radiation Therapy Definitions and Reporting Guidelines for Thymic Malignancies

Daniel Gomez, MD,* Ritsuko Komaki,* James Yu, MD,† Hitoshi Ikushima, MD, PhD,‡ and Andrea Bezjak, MSc, FRCPC, MD§

State of the Art: Concise Review

(J Thorac Oncol. 2009;4: 119–126)

Thymoma

A Focus on Current Therapeutic Management

Nicolas Girard, MD,*† Françoise Mornex, MD, PhD,* Paul Van Houtte, MD,‡ Jean-François Cordier, MD,† and Paul van Schil, MD, PhD§

State of the Art: Concise Review

(J Thorac Oncol. 2009;4: 911–919)

The Management of Thymoma: A Systematic Review and Practice Guideline

Conrad B. Falkson, MBChB,* Andrea Bezjak, MD, MSc,† Gail Darling, MD,‡ Richard Gregg, MD,* Richard Malthaner, MD,§ Donna E. Maziak, MDCM,‖ Edward Yu, MD,¶ Christopher A. Smith, MSc,# Shetla McNatr, PhD,# Yee C. Ung, MD,** William K. Evans, MD,†† and the Lung Cancer Disease Site Group of Cancer Care Ontario's Program in Evidence-Based Care

Malignancies of the Thymus

(J Thorac Oncol. 2010;5: S327–S335)

Radiotherapy for Thymic Neoplasms

Clifton D. Fuller, MD,*†‡ Emma H. Ramahi, BA,* Noel Aherne, MD,§ Tony Y. Eng, MD,* and Charles R. Thomas, Jr., MD‡

Malignancies of the Thymus

(J Thorac Oncol. 2010;5: S336–S343)

Technical Advances of Radiation Therapy for Thymic Malignancies

Daniel Gomez, MD,* and Ritsuko Komaki, MD*

Adjuvant setting

Dose

Which is the minimal effective dose ?

Volume

Must we include tumor bed and entire mediastinum, and/or supraclavicular fossa ?

Adjuvant setting

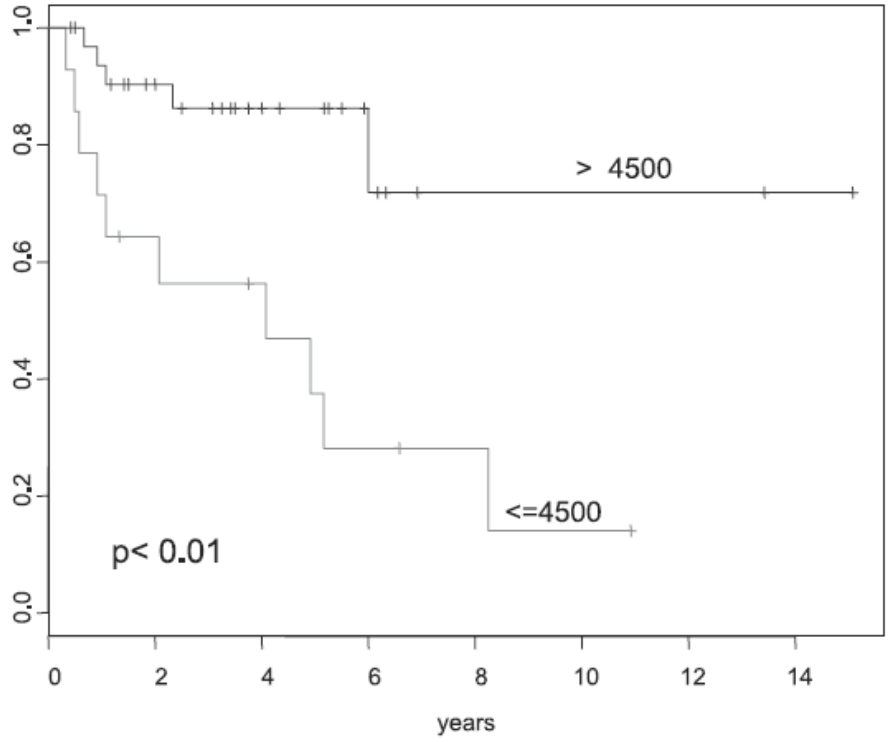
Study	# pts	End-point	Total dose	
			45-50 Gy	> 50 Gy
Zhu '04	128	LC 5yr	71.8%	65.1%
Chen '10	66	DFS 5-yr	92.9%	91.9%

Zhu et al, Int. J. Radiation Oncology Biol. Phys 2004;60:1113-9
Chen et al, Int. J. Radiation Oncology Biol. Phys 2010;78:1400-6

Adjuvant setting

47 Resected patients
Stage II-IVa
Margin
- Positive: 12 (26%)
- Negative: 35 (74%)

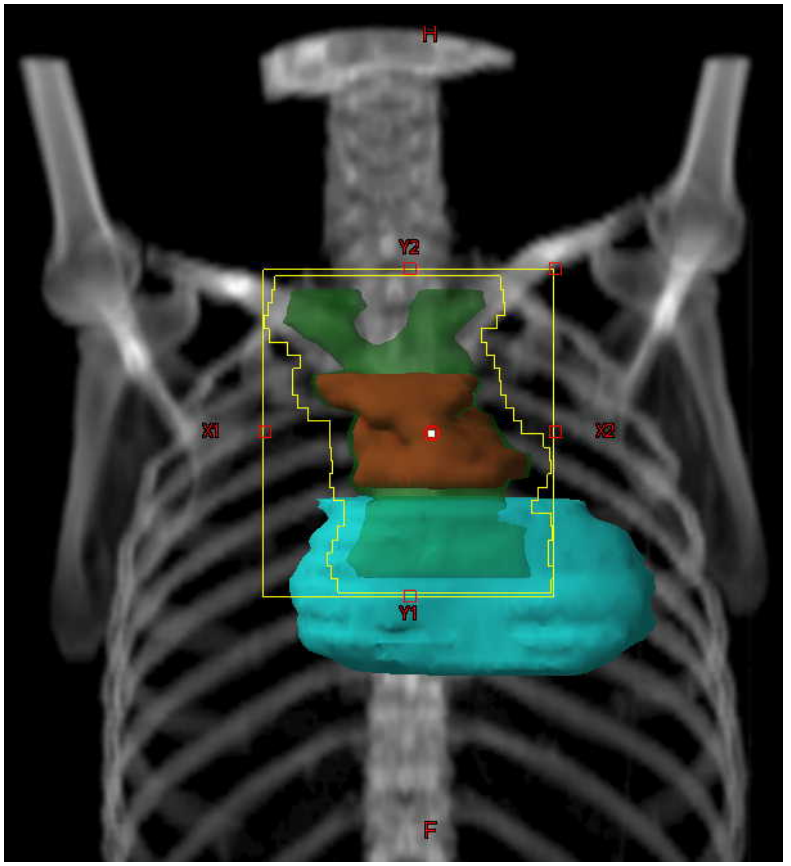
Total Dose
- ≤ 45 Gy: 14 (30%)
- > 45 Gy: 33 (70%)



Kundel Y et al, Am J Clin Oncol 2007;30: 389–394

Adjuvant setting

Study	# pts	End-point	Volume	
			IF	EF
Zhu '04	128	LC 5yr	68.2%	66.6%
Chen '10	66	DFS 5-yr	94.2%	83.3%



Zhu et al, Int. J. Radiation Oncology Biol. Phys 2004;60:1113-9
Chen et al, Int. J. Radiation Oncology Biol. Phys 2010;78:1400-6

Adjuvant setting

Series with: CTV = Tumor bed; Total dose = 50 Gy

Study	# pts	Local recurrence
Kim '07	100	2%
D'Angelillo '08	98	1%
Chang '11	76	3%
Berman '11	62	0%

Kim et al, ONCOLOGY REPORTS 19: 1525-1531, 2008
D'Angelillo et al, Int. J. Radiation Oncology Biol. Phys 2008;71:420-7
Chang et al, J Thorac Oncol. 2011;6: 1282–1286
Berman et al, Cancer 2011;117:3502–8

Adjuvant setting

Series with: CTV = Tumor bed; Total dose = 50 Gy

Study	# pts	Acute Toxicity	
		Grade1-2	**Grade 3-4**
Kim '07	100	---	**0%**
D'Angelillo '08	98	12.2%	**0%**
Chang '11	76	---	**0%**
Berman '11	62	50.9%	**0%**

Kim et al, ONCOLOGY REPORTS 19: 1525-1531, 2008
D'Angelillo et al, Int. J. Radiation Oncology Biol. Phys 2008;71:420-7
Chang et al, J Thorac Oncol. 2011;6: 1282–1286
Berman et al, Cancer 2011;117:3502–8

Adjuvant setting

Series with 2D Technique

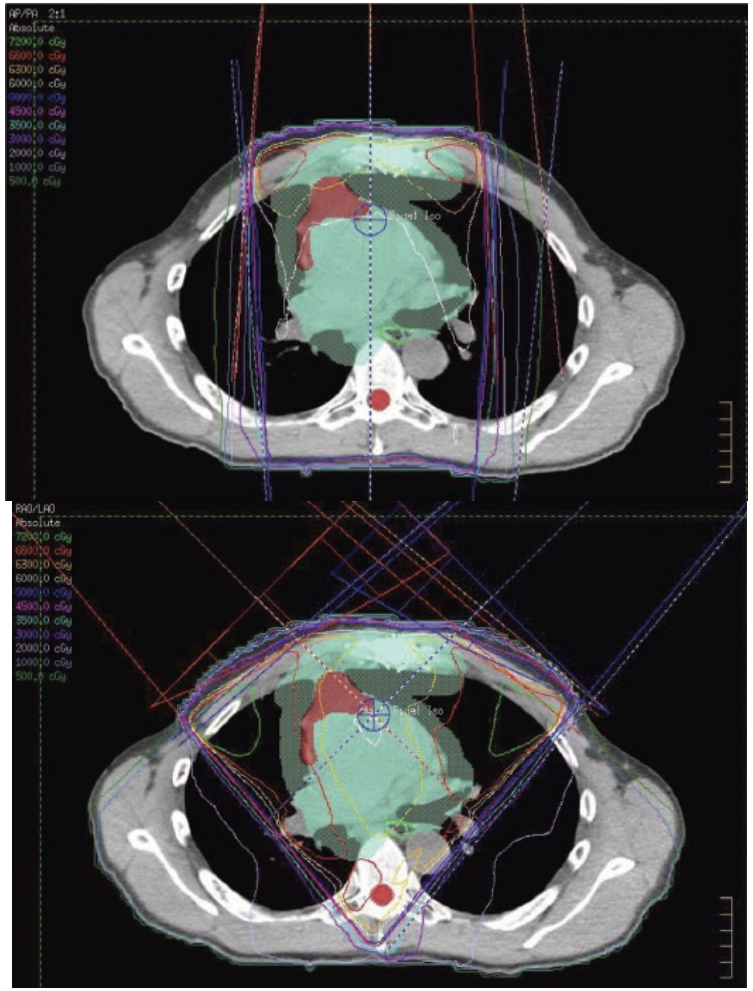
Grade 3-4 toxicity: 5-15%

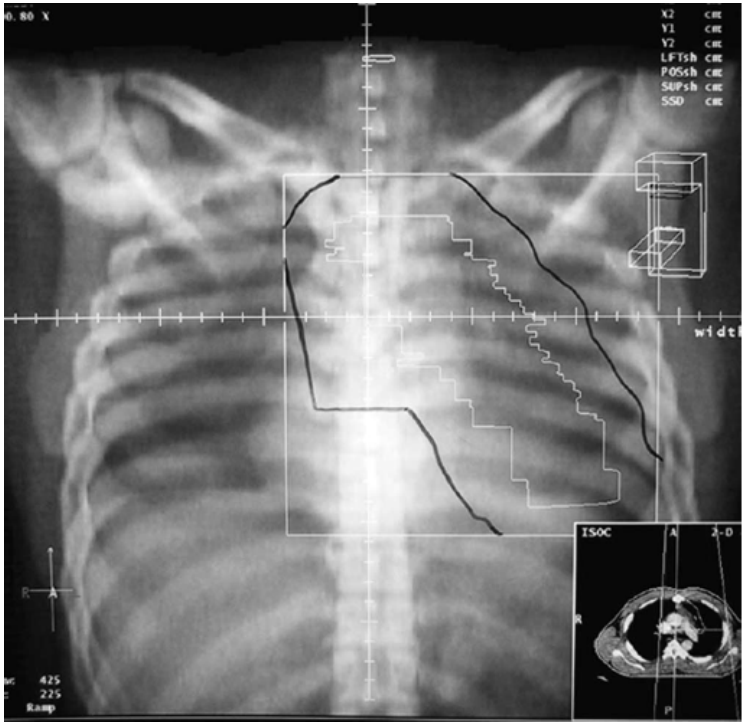
Nakao et al, Jpn J Med 29:104-410, 1990
Latz et al, Radiology 1997;204:859-64

Pericarditis and lung fibrosis: 7.7%

Mornex et al, Int. J. Radiation Oncology Biol. Phys 32:651-659, 1995

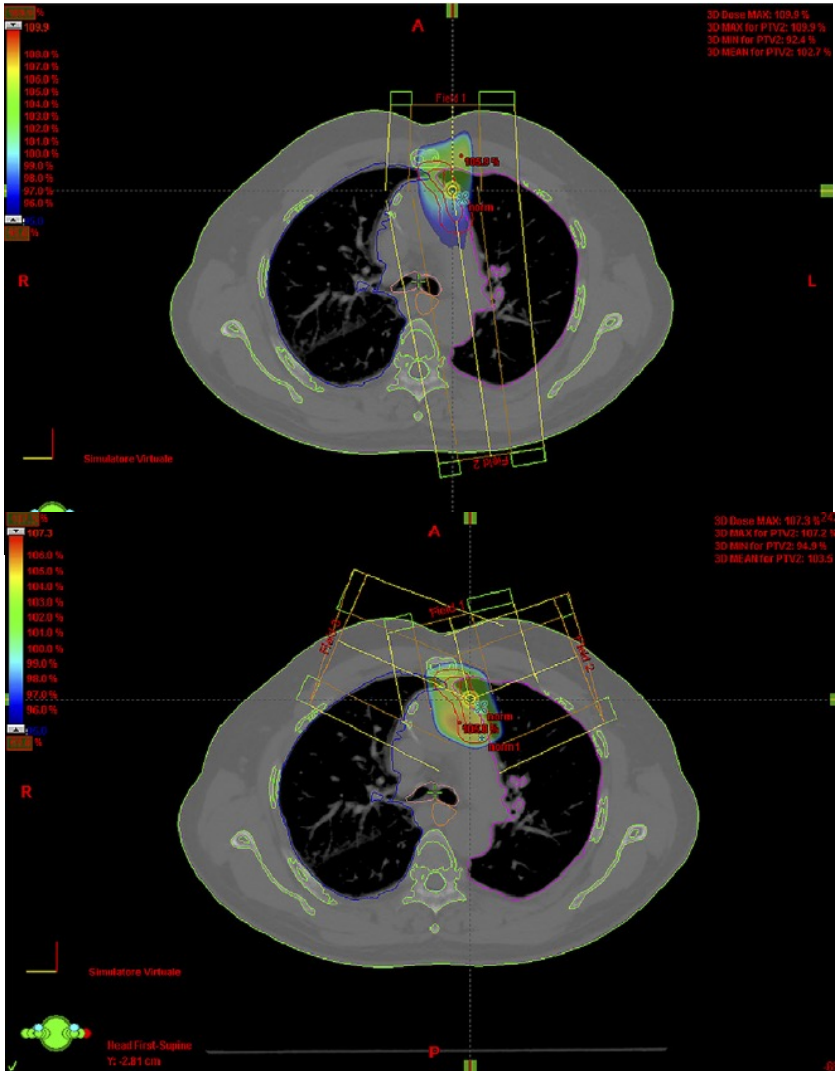
2D Technique

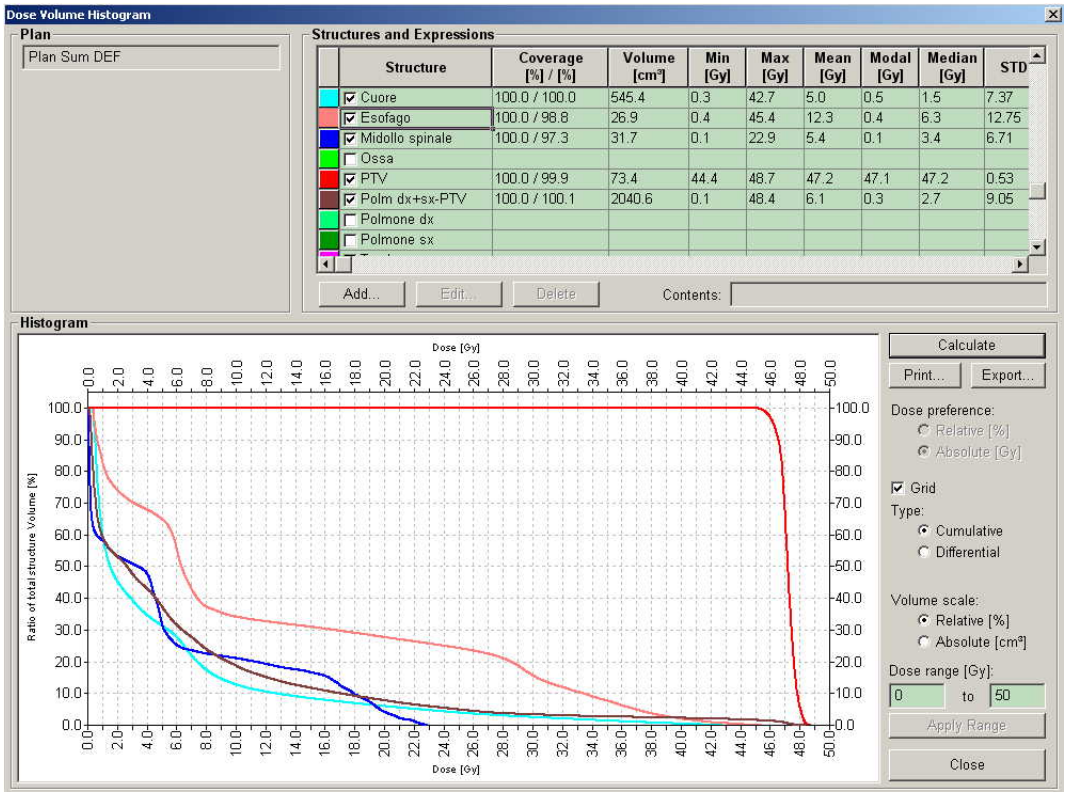




Eng, Thomas, Semin Thorac Cardiovasc Surg 2005
Gomez, Komaki, J Thorac Oncol. 2010;5: S336–S343

3D Technique

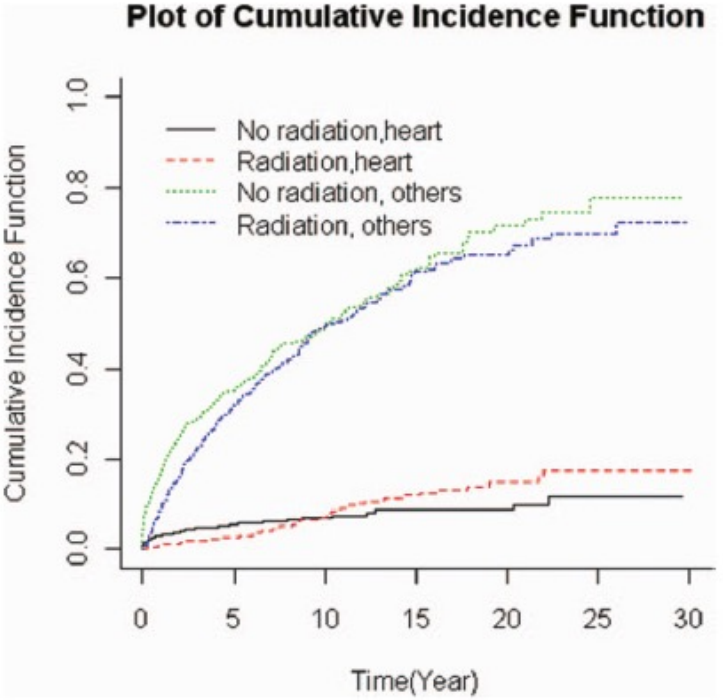




Late Effects

Cardiac events

Treatment	# pts	Mortality
Radiotherapy	706	14.4%
No RT		12%
	p=	***0.4***



Fernandes et al, J Thorac Oncol. 2010;5: 1454–1460

Late Effects

Second malignancies

Treatment	# pts	Thoracic
Radiotherapy	824	3.4%
No RT	510	4.3%
	p=	***0.31***

TABLE 4. Secondary Malignancies Among Patients with Thymoma After Treatment with or without Radiation ($N = 1334$)

	Radiation ($n = 824$)	No Radiation ($n = 510$)
Thyroid	1 (0.12%)	4 (0.78%)
Breast	12 (1.46%)	7 (1.37%)
Esophagus	3 (0.36%)	2 (0.39%)
Lung and bronchus	12 (1.46%)	9 (1.76%)
Lymphoma	10 (1.21%)	1 (0.20%)
Leukemia	7 (0.85%)	2 (0.39%)
All other malignancies	51 (6.19%)	38 (7.45%)
All sites	96 (11.65%)	63 (12.35%)
Overall p value = 0.22		

Fernandes et al, J Thorac Oncol. 2010;5: 1454–1460

Adjuvant setting

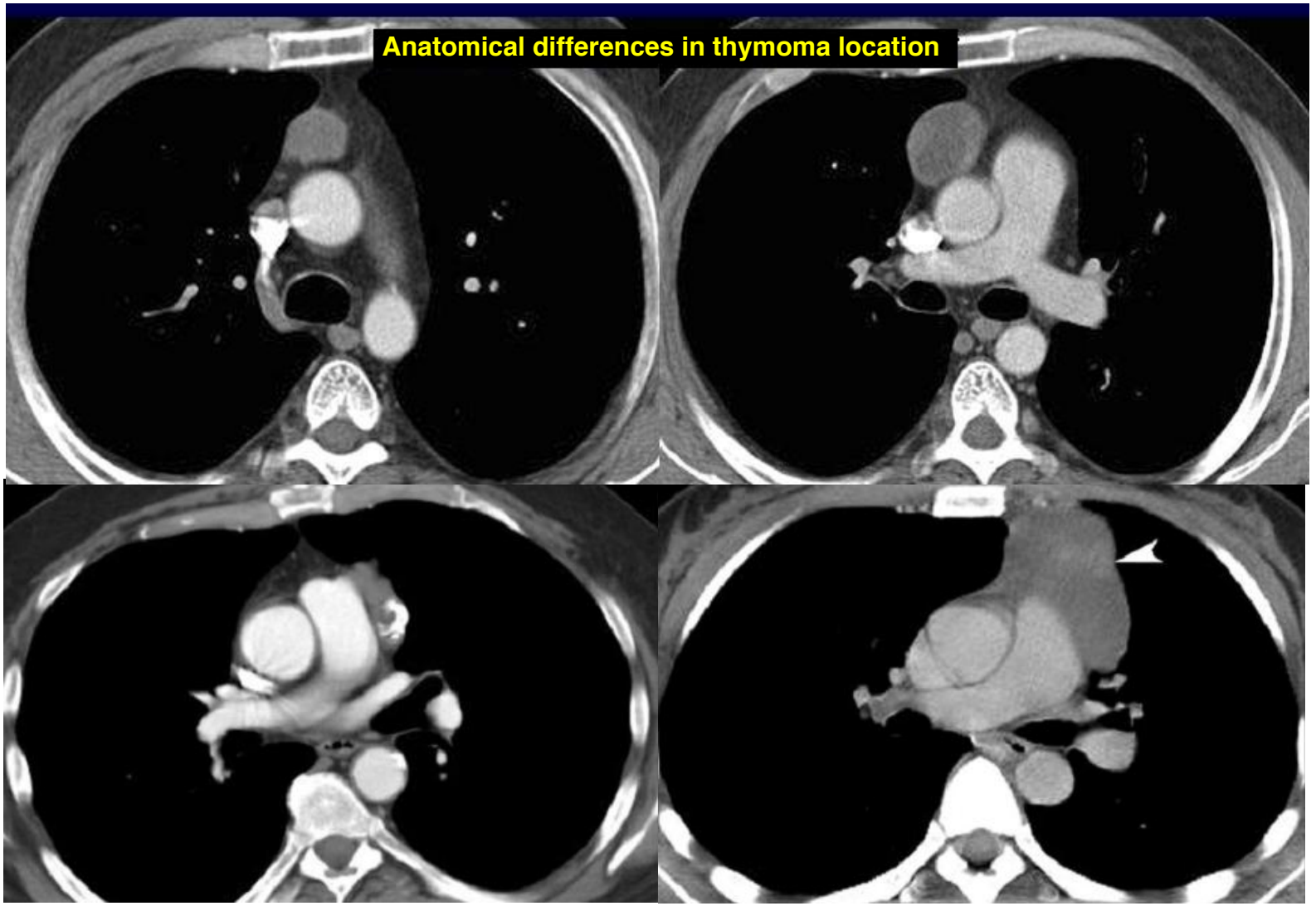
Summary

Dose: 45-50 Gy

CTV: ***Tumor Bed***

Technique: 3D-conformal treatment is enough

Delineation of Tumor Bed



Adjuvant setting

Summary

Dose: 45-50 Gy

CTV: Tumor Bed

Technique: 3D-conformal treatment is enough

Should we modulate treatment according to tumor histology ?

	Oncogenes	Tumor suppressor genes
Type A (n=11)	APP ITGA6 ATF4 CX3CR1 Wnt-Pathway	SDC4 VDUP1 NET1 CD81 ANXA7 CD164
Type B3 (n=21)	MAF DIAPH2 POLB GOT1 EGFR MAP3K8	PIK3R1 (p85)

Courtsey of P Ströbel

	Oncogenes	Tumor suppressor genes
Typ B3 (n=21)	MAF DIAPH2 POLB GOT1 EGFR MAP3K8	PIK3R1 (p85)
TSCC (n=14)	ErbB3 KIT FGFR3 MYC ARNT2 ATF4	-----

Courtesy of P Ströbel

Gruppo AIRO

Partecipate in creating an Italian Database

To Assess the benefit of RT

The Impact of Histology & Stage

Evaluation of prognostic classes

Radical setting

Radiotherapy in a multimodality approach

Radiotherapy in unresectable disease

Radical setting

Radiotherapy in a multimodality approach

Radiotherapy in unresectable disease

Radical setting

Radiotherapy in a multimodality approach @ MDACC

Induction Chemotherapy: 3 courses of CAPP

Re-evaluation and then Surgery

RT: CR and 80% necrotic tumors 50 Gy

otherwise 60 Gy

Consolidation CT: 3 courses of CAPP

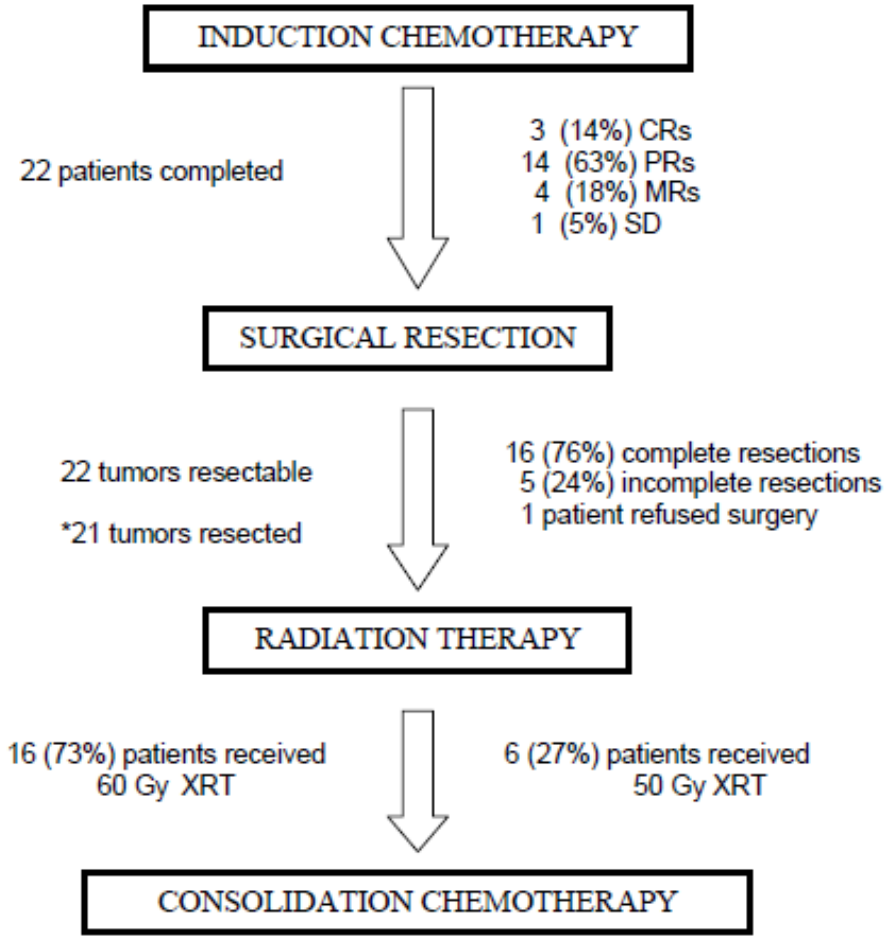
Kim et al, Lung Cancer. 2004; 44, 369—379

Radical setting

Study design

22 pts

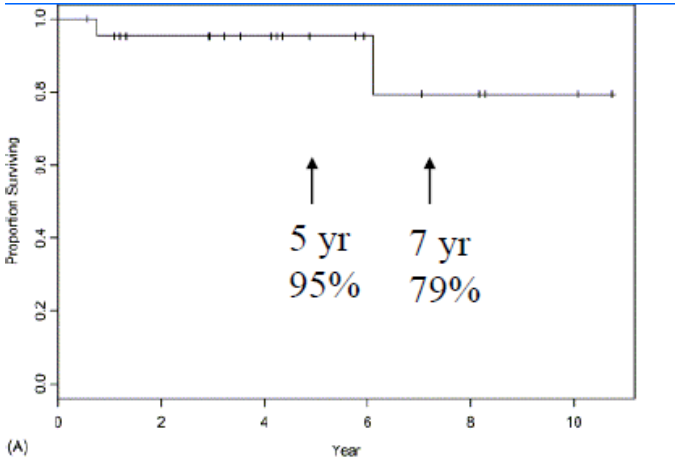
Stage III-IV



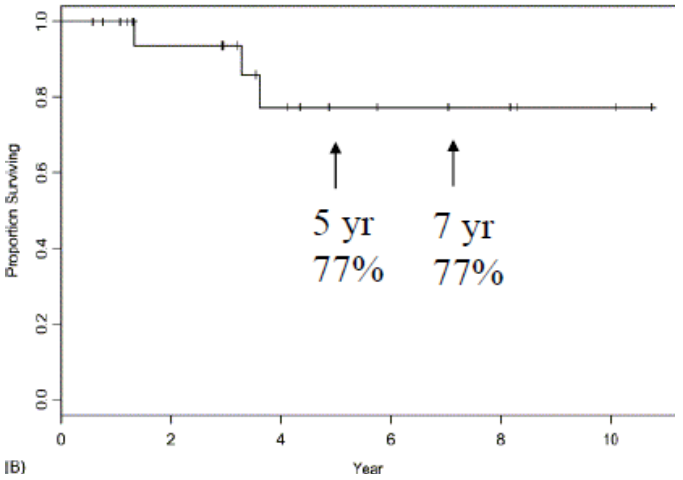
Kim et al, Lung Cancer. 2004; 44, 369—379

Radical setting

Overall Survival



Progression Free Survival



Kim et al, Lung Cancer. 2004; 44, 369—379

Radical setting

Radiotherapy in a multimodality approach

Increase total dose up to 60 Gy

Radiotherapy in unresectable disease

Radical setting

Radiotherapy in a multimodality approach

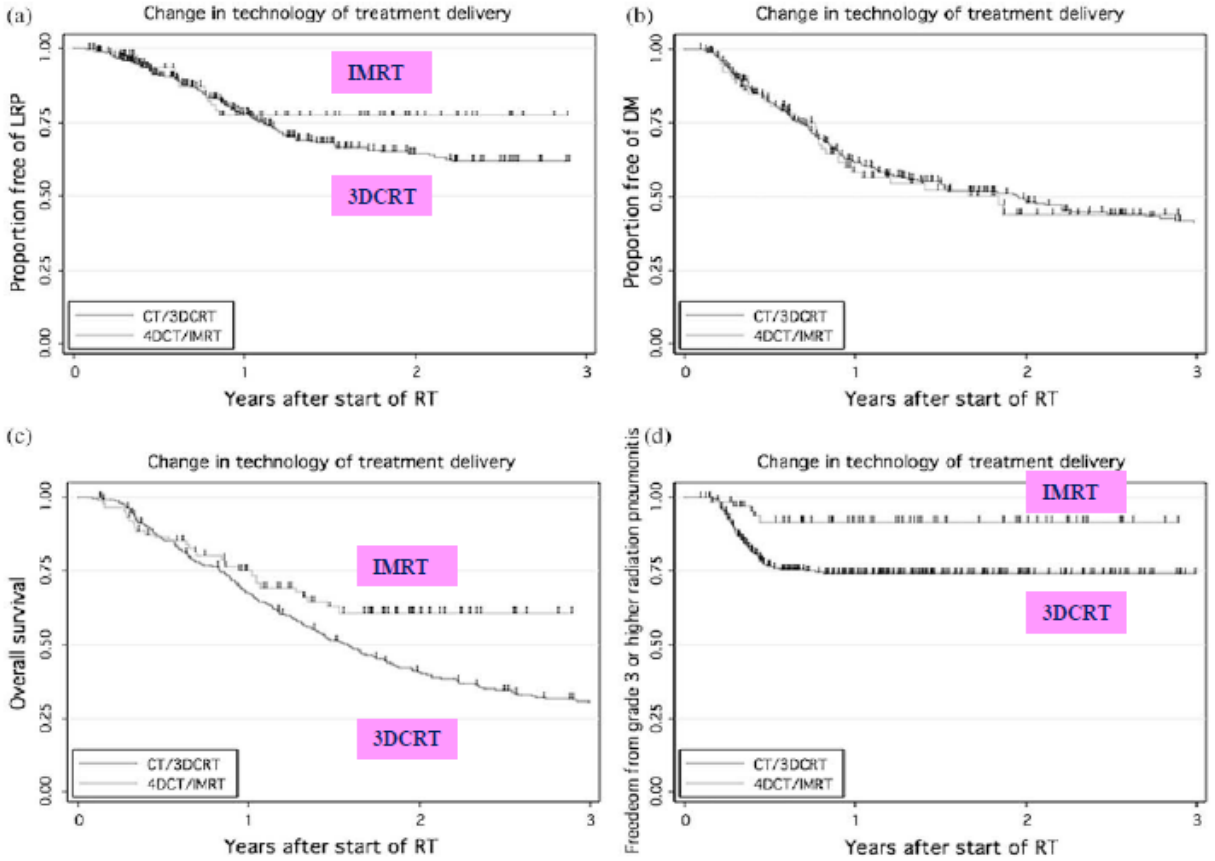
Increase total dose up to 60 Gy

Radiotherapy in unresectable disease

May we improve RT results with new technologies ?

Radical setting

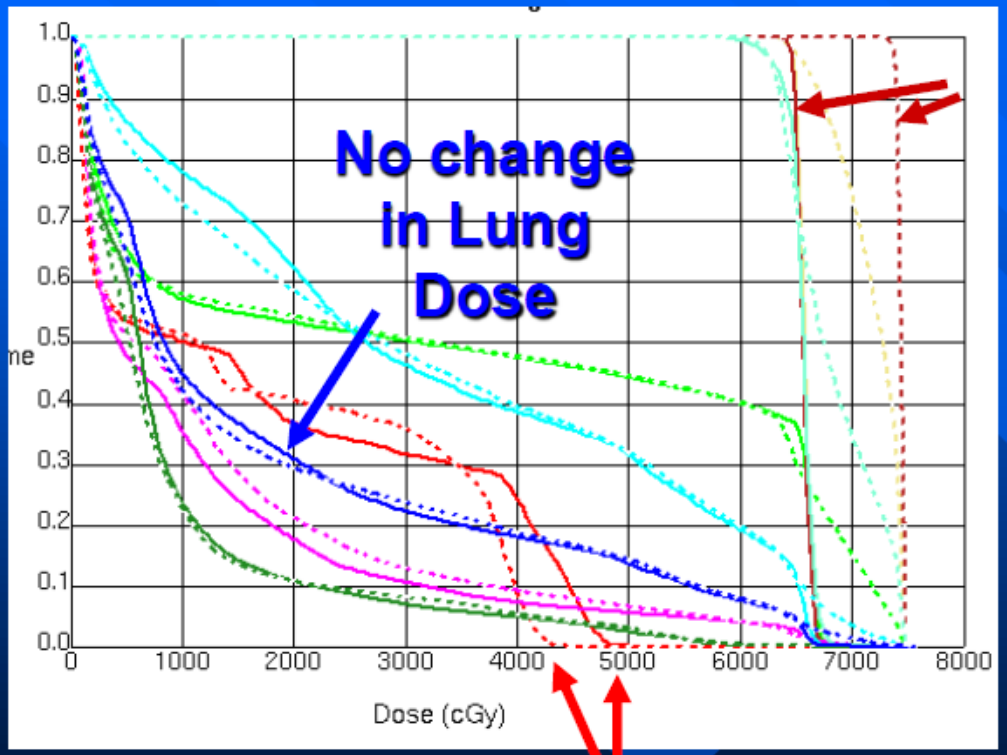
3D vs. IMRT in LA-NSCLC



Liao et al, Int. J. Radiation Oncology Biol. Phys 2010;76:775-81

3D-CRT vs. IMRT DVH

Solid Lines = 3D-CRT **Dashed Lines = IMRT**



No change in Lung Dose

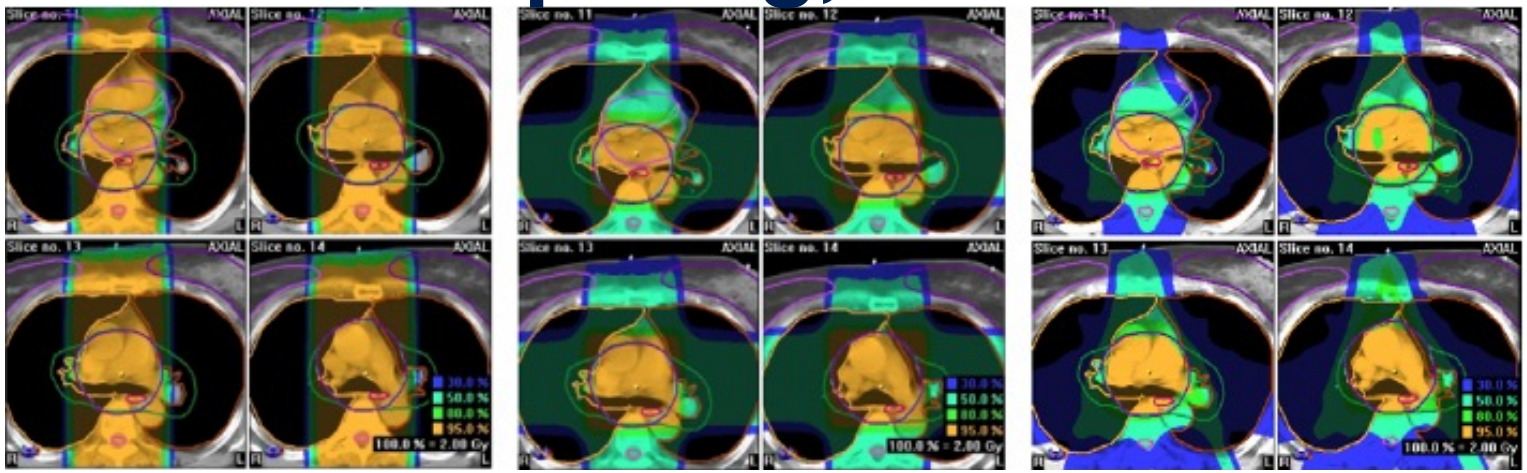
↑er GTV Dose

↓er Cord Dose

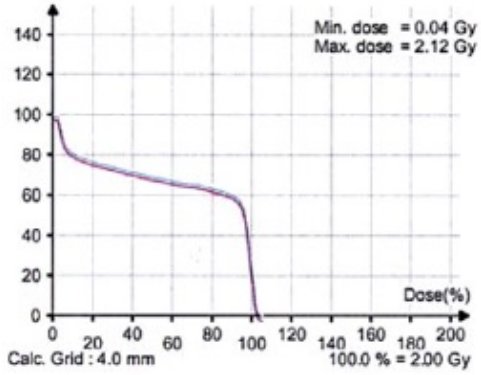
FTCR
FOUNDATION FOR THYMIC CANCER RESEARCH

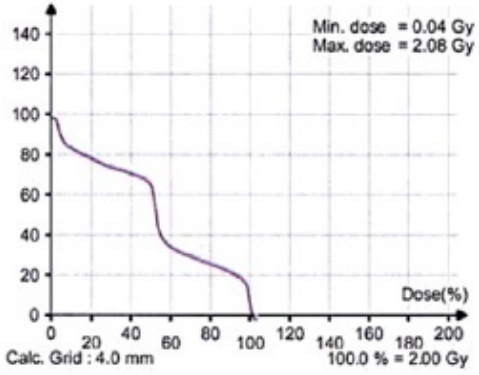
Courtsey of R. Komaki

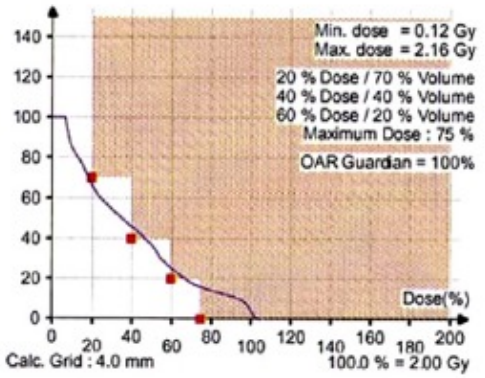
Hearth Sparing, median dose



AP-PA: 98% **4Field-3D: 56%** **IMRT: 39%** p=<0.05







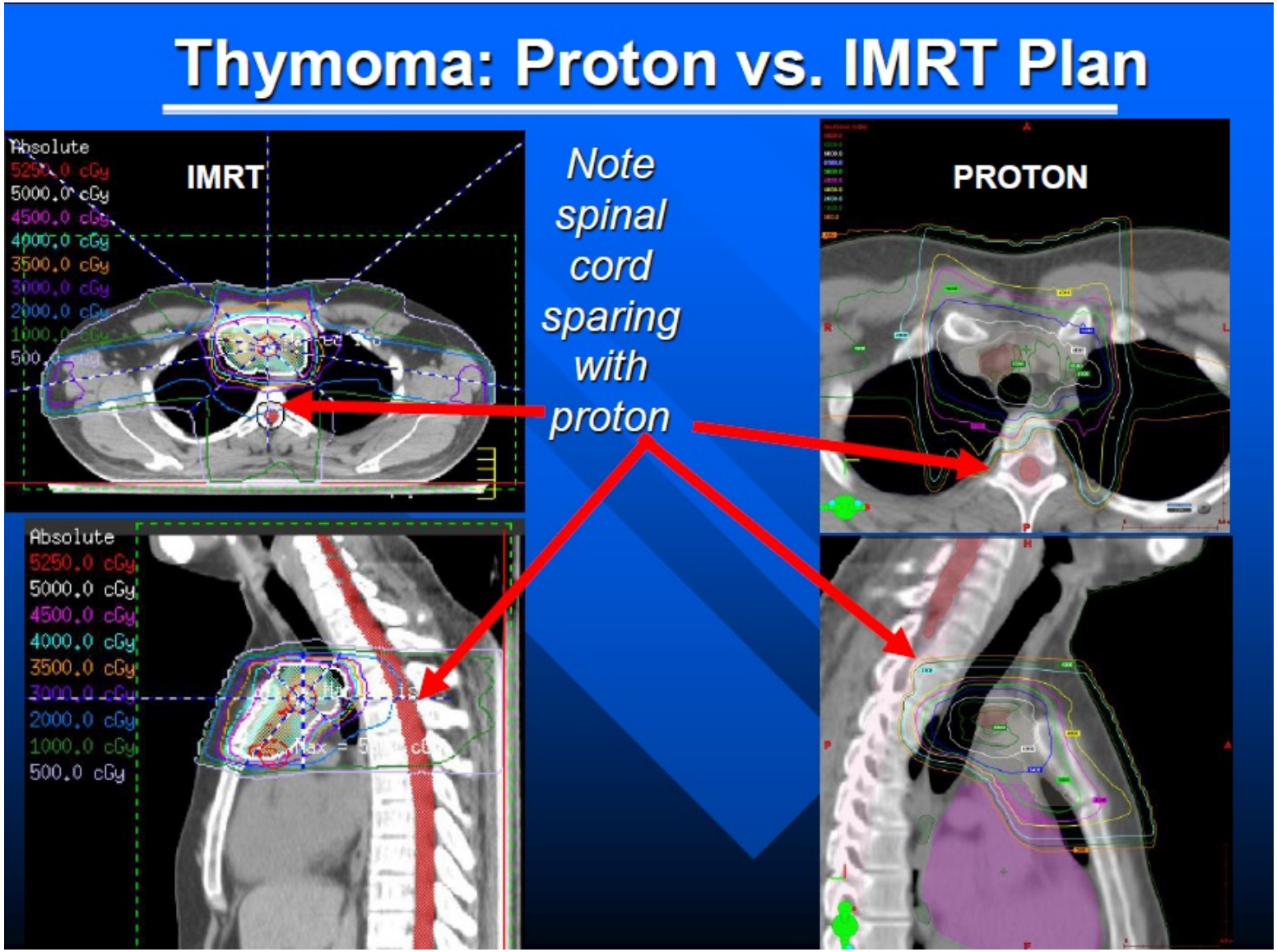
Nieder et al, Radiotherapy and Oncology 82 (2007) 301–307

Dosimetric constraints

TABLE 2. Dosimetric Constraints to be Used and Reported in the Treatment of Thymic Malignancies[5]

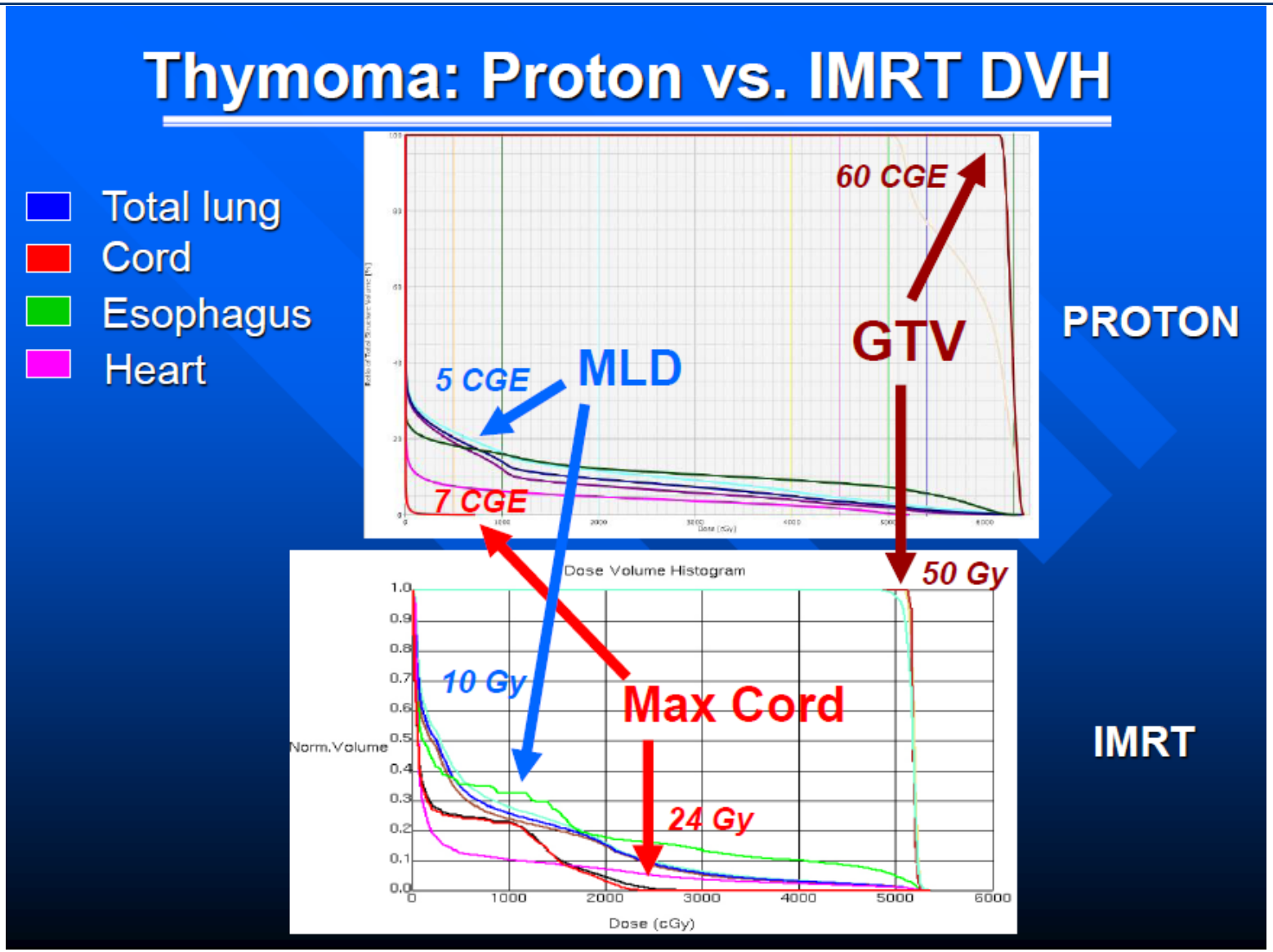
	RT Alone	Chemotherapy and RT	Chemotherapy and RT Before Surgery
Spinal cord[a]	D_{max} <45 Gy	D_{max} <45 Gy	D_{max} <45 Gy
Lung[b]	MLD ≤20 Gy	MLD ≤20 Gy	MLD ≤20 Gy
	V_{20} ≤40%	V_{20} ≤35%	V_{20} ≤30%
		V_{10} ≤45%	V_{10} ≤40%
		V_5 ≤65%	V_5 ≤55%
Heart	V_{30} ≤45%	V_{30} ≤45%	V_{30} ≤45%
	Mean dose <26 Gy	Mean dose <26 Gy	Mean dose <26 Gy
Esophagus	D_{max} ≤80 Gy	D_{max} ≤80 Gy	D_{max} ≤80 Gy
	V_{70} <20%	V_{70} <20%	V_{70} <20%
	V_{50} <50%	V_{50} <40%	V_{50} <40%
	Mean dose <34 Gy	Mean dose <34 Gy	Mean dose <34 Gy
Kidney[c]	20 Gy <32% of bilateral kidney	20 Gy <32% of bilateral kidney	20 Gy <32% of bilateral kidney
Liver	V30 ≤40%	V30 ≤40%	V30 ≤40%
	Mean dose <30 Gy	Mean dose <30 Gy	Mean dose <30 Gy

ITMIG - Gomez et al, J Thorac Oncol. 2011;6: S1743–S1748



Courtesy of R. Komaki

Thymoma: Proton vs. IMRT DVH



Courtesy of R. Komaki

Radical Treatment

Summary

Dose: 60 Gy or over

CTV: Tumor bed or Macroscopic Disease

Technique: improving delivered dose by means of IMRT or other technologies

Gomez, Komaki, J Thorac Oncol. 2010;5: S336–S343

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