Dose-volume effects in lung radiotherapy

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Introduction

Acute pulmonary toxicity from radiation therapy is often a dose-limiting factor for irradiation of lung cancer to high doses

Acute pulmonary toxicity is generally analyzed by the incidence of radiation pneumonitis

Ideally: prediction of the incidence of radiation pneumonitis as a function of dose-volume parameters

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Introduction

The incidence and severity of radiation pneumonitis depend on a number of factors:

Total dose

Dose per fraction

Volume and region of irradiated lung

Use of concomitant chemotherapy

Radiation dose to the heart

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Difficulties in scoring radiation pneumonitis

Follow-up times of at least 6 months

Incidence of radiation pneumonitis is low

Reliable measurements of dose-volume effects require large patient groups

Diversity (and subjectivity) in scoring systems for the severity of radiation pneumonitis (SWOG/RTOG/CTC)

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Scoring radiation pneumonitis

Grade	CTC	SWOG	RTOG
1	Asymptomatic, radiographic findings only	Normal radiographic changes, symptoms do not require steroids (non-infectious)	Mild symptoms of dry cough or dyspnea on exertion
2	Symptomatic, not interfering with activities of daily living	Steroids required or tap of effusion	Persistent cough requiring narcotic, anti-tussive agents/dyspnea with minimal effort but not at rest
3	Symptomatic , interfering with activities of daily living, oxygen indicated	Oxygen required	Severe cough unresponsive to narcotic anti-tussive agent or dyspnea at rest/clinical or radiologic evidence of acute pneumonitis; intermittent oxygen or steroids may be required
4	Life threatening, ventilatory support indicated	Requires assisted ventilation	Severe respiratory insufficiency/continuous oxygen or assisted ventilation
5	Fatal	Fatal	Fatal

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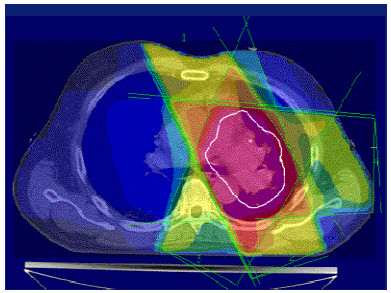
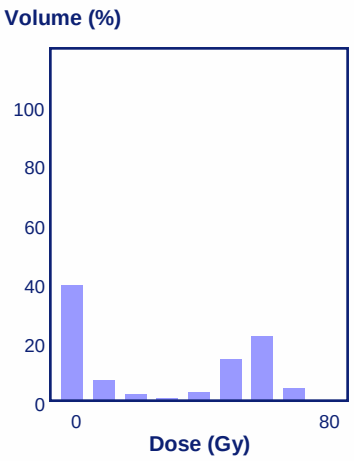
Dose-volume effects

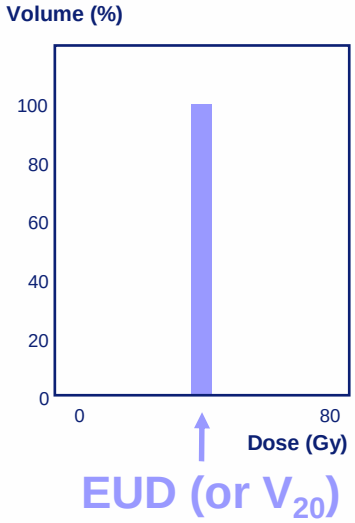
- Reduction 3D dose distribution to single parameter
- Relation between single parameter and complication



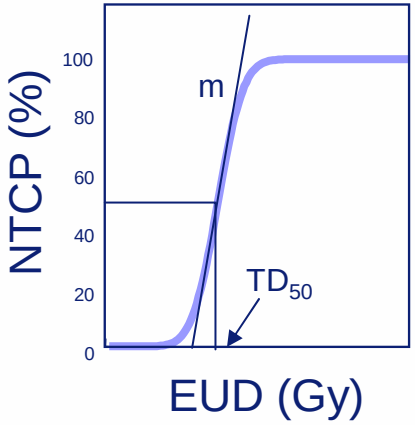
3D dose distribution



Dose volume histogram



Single parameter



NTCP TD_{50} and m

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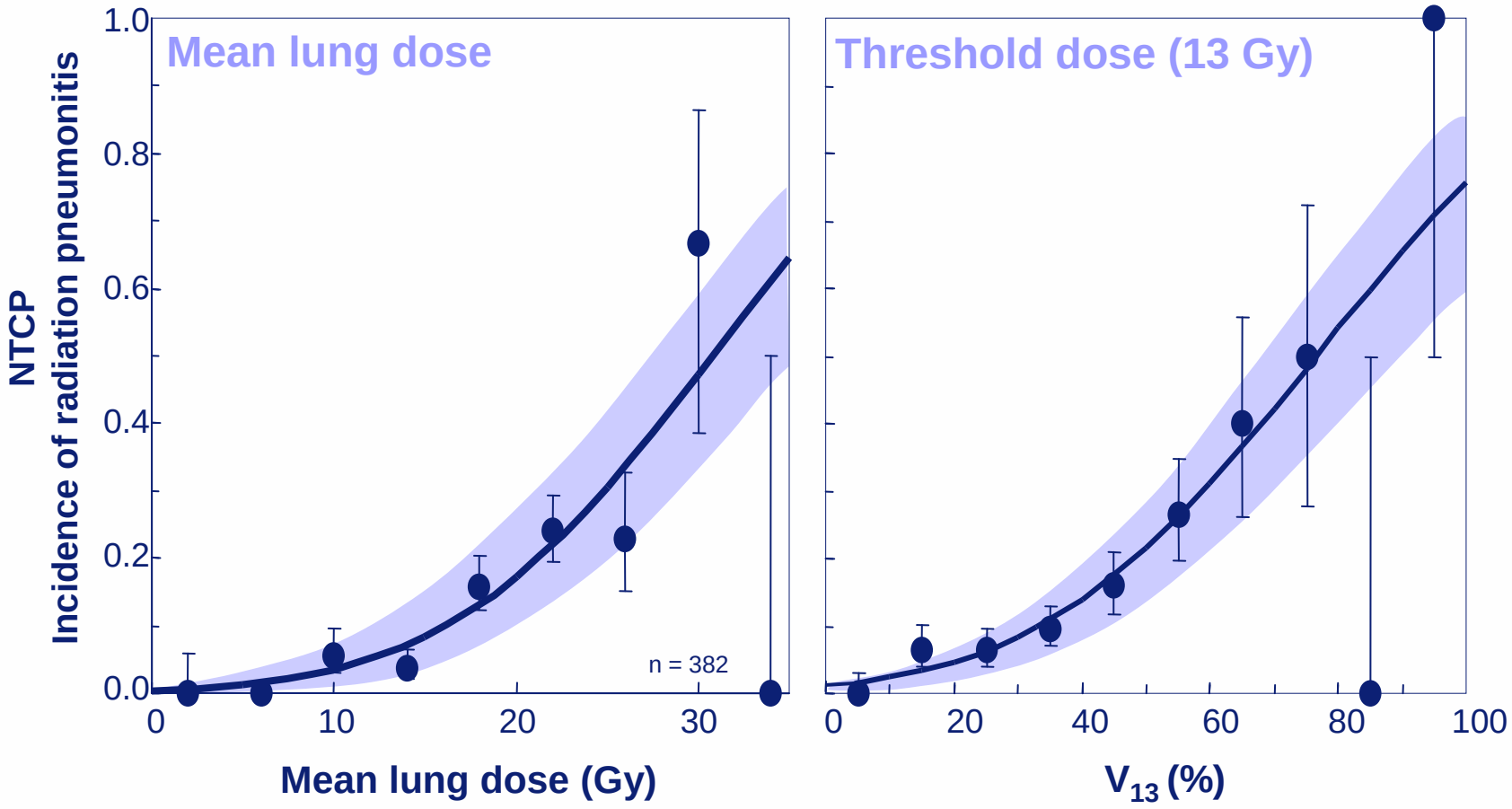
Dose-volume effects



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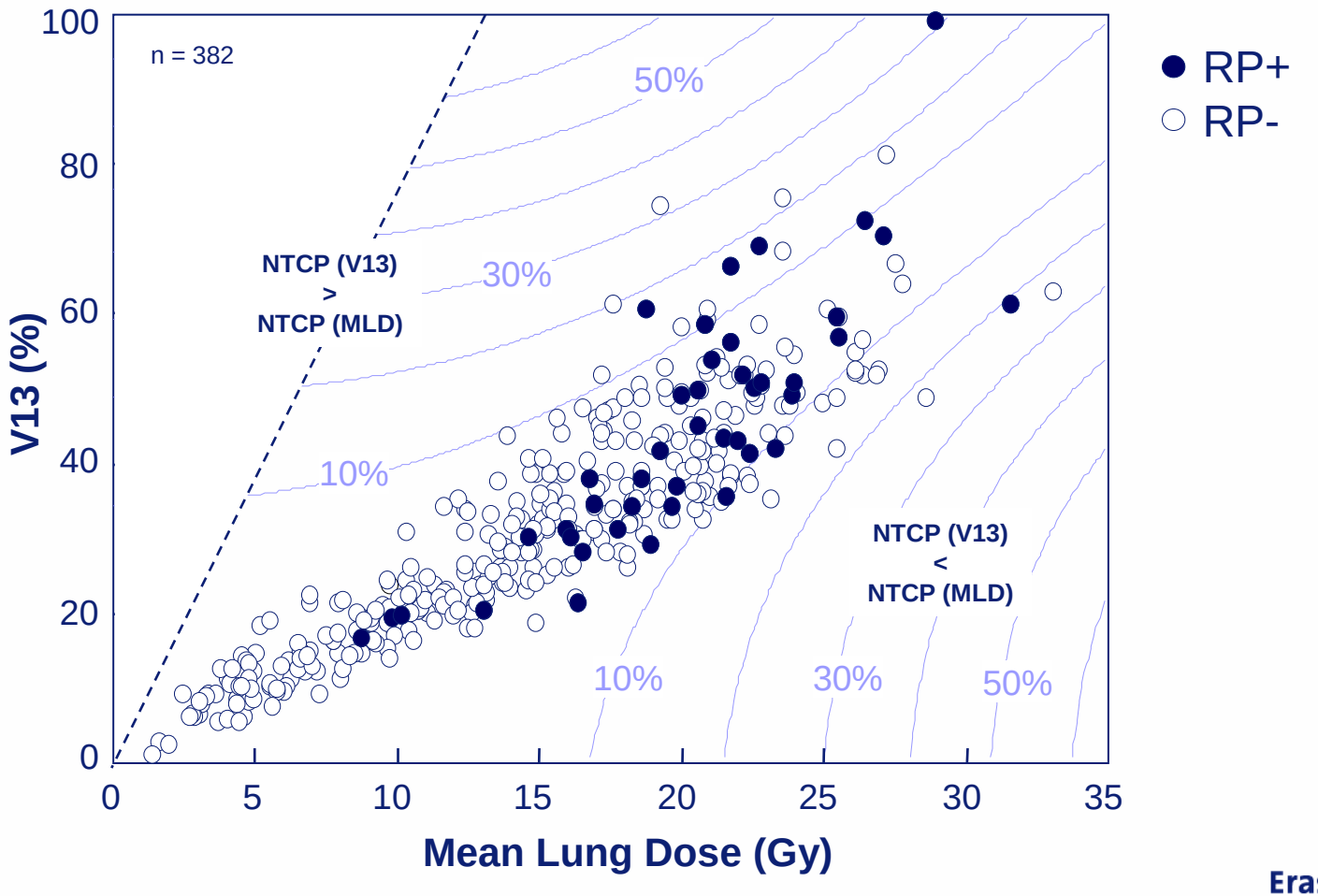
Dose-volume parameters are highly correlated



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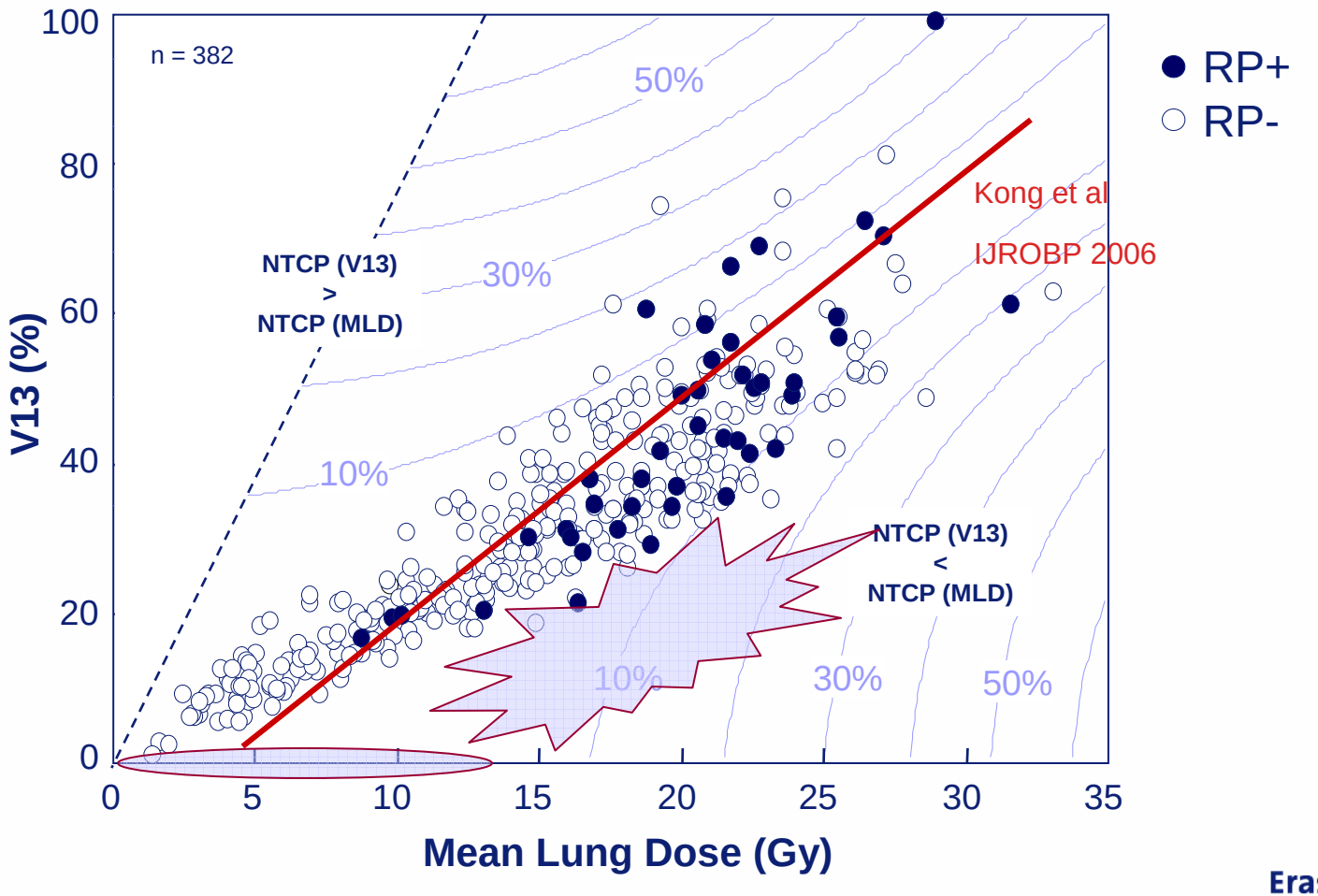
New treatment techniques



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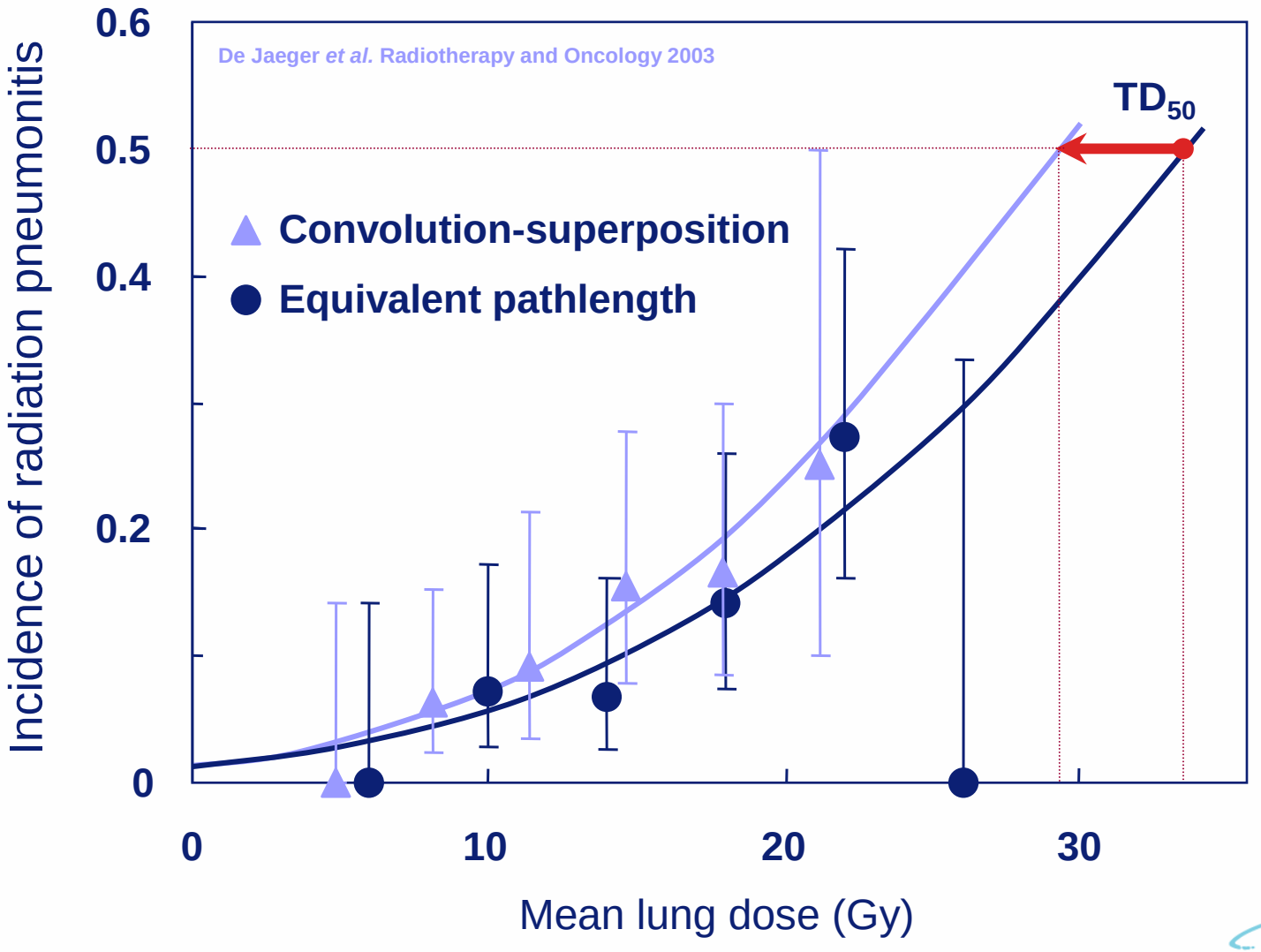
Influence of dose-calculation algorithm on TD_{50}



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(Hypo) fractionation

Total dose	fractionation scheme	EQD_2 tumor	EQD_2 normal tissue @ 80%	@ 20%
60	30 x 2	60	45	9
75	30 x 2.5	78	60	11
60	3 x 20	150	160	16
		$\alpha/\beta = 10$	$\alpha/\beta = 4$ Bentzen et al. 2000	

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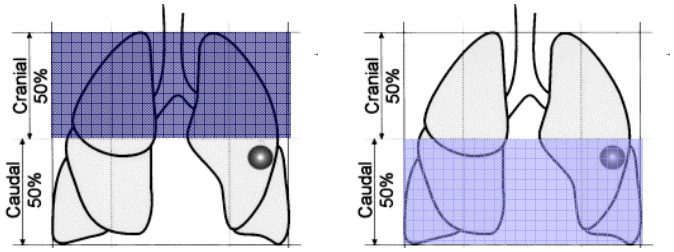
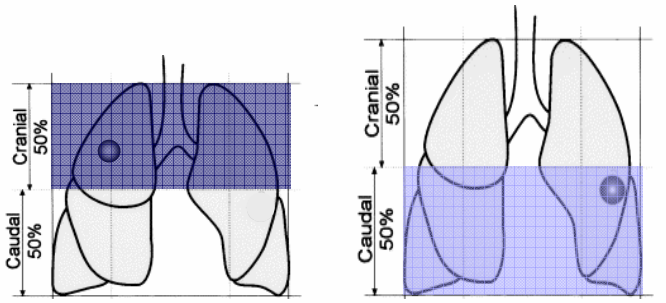
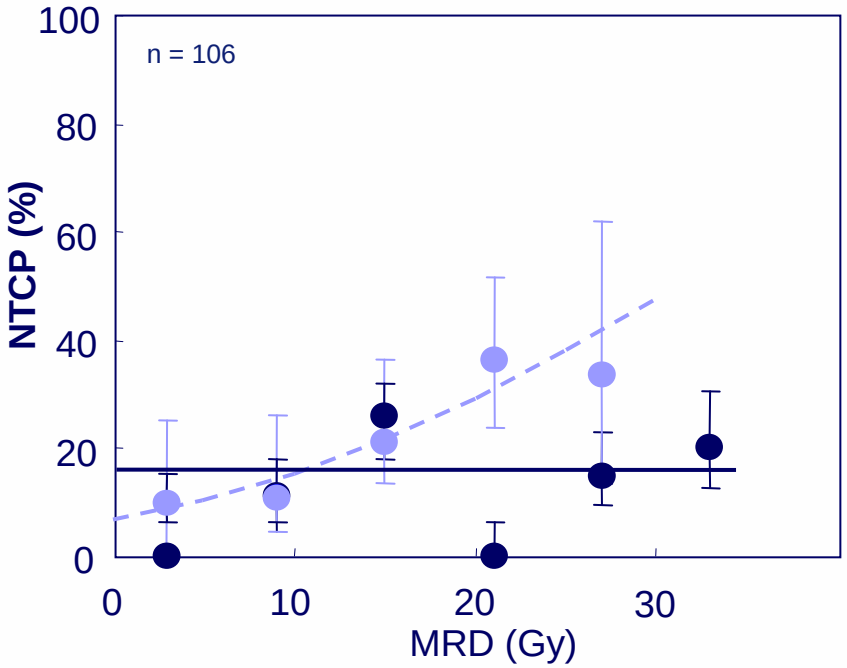
Regional sensitivity

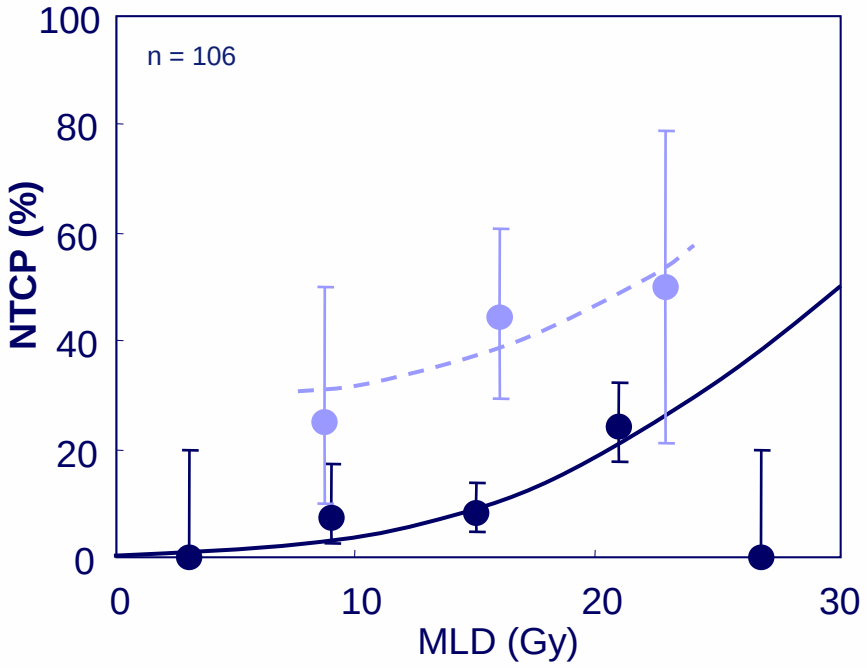


● Mean cranial **dose** ● Mean caudal **dose**



● Cranial **tumors** ● Caudal **tumors**





Higher incidence of RP for lower lobe tumors

YES Graham 1995, Yorke 2002, Seppenwoolde 2004, Bradley 2005

NO Yu 2003 (superior and inferior regions)

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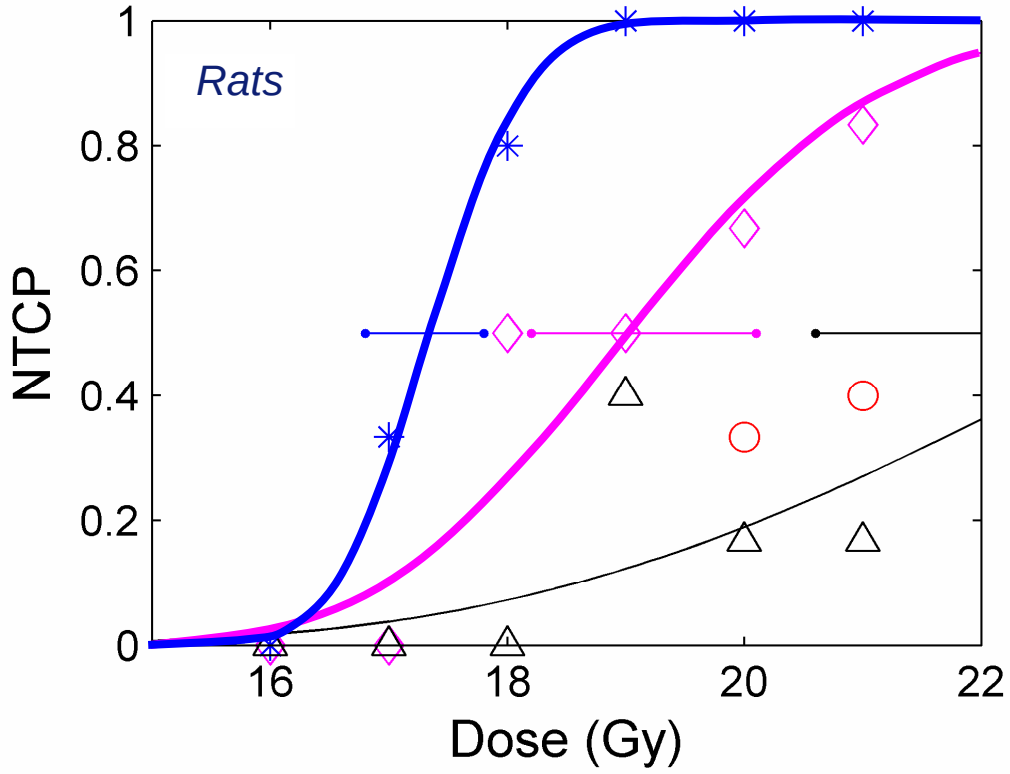
Irradiation of the heart

Van Luijk *et al.* Cancer Reseach 2005



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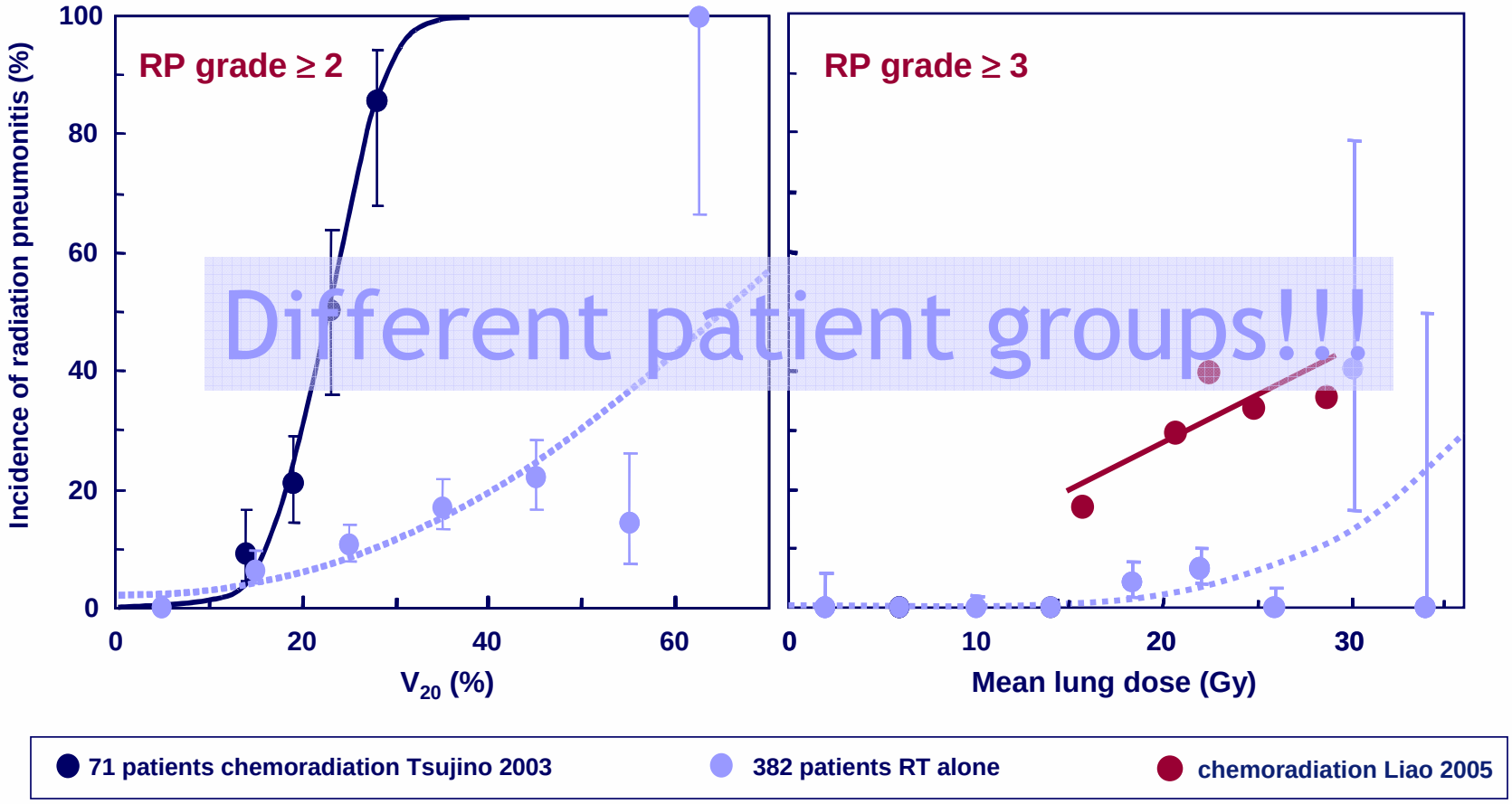
Concurrent chemotherapy Cisplatin/carboplatin plus taxane



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Conclusion

Many factors influence dose-volume effects in lung

⇨ Unambiguous systems for scoring RP and registration of treatment parameters are required

Current NTCP models should be used with caution in case of unconventional dose distributions / calculation algorithms

Multivariate analyses with large patient groups are necessary

⇨ Recalculation of dose distributions might be essential to compare patient groups

Ongoing research and dose-escalation studies will provide valuable new data that will enable further improvement of prediction models

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