# Re-irradiation of lung tumours

CRPR Workshop on re-irradiation

Judith van Loon M.D., PhD.

Radiation Oncologist Maastro Clinic/ZON-PTC
Maastricht University Medical Center
Maastricht The Netherlands

# Disclosures

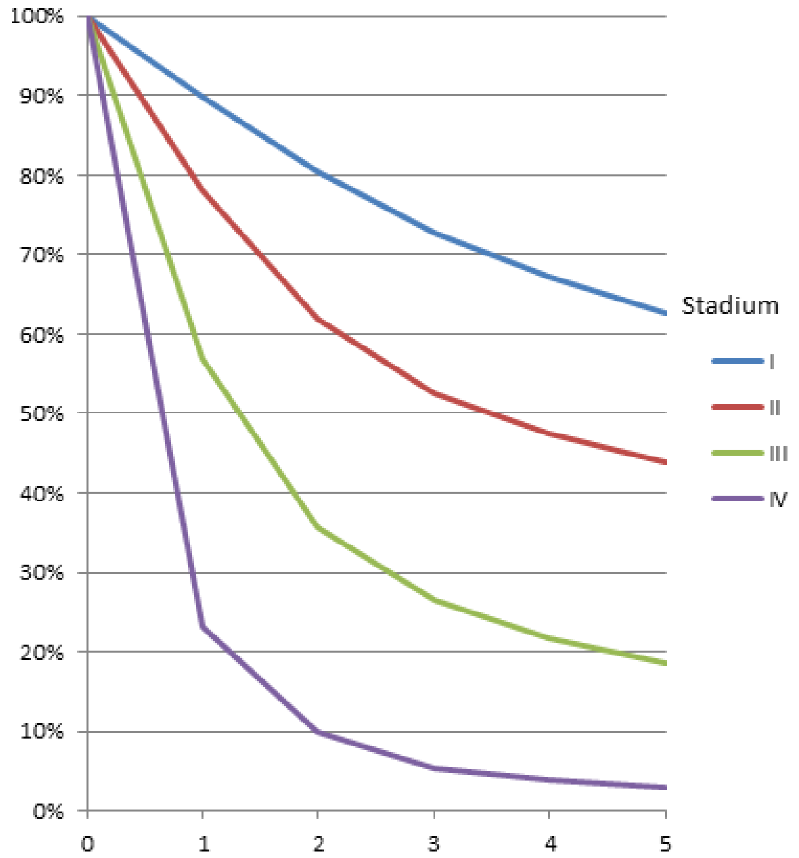
- None

MAASTRO CLINIC

# Re-irradiation of lung tumours

- Background
- Key questions
  - Is it worthwhile?
  - Is it safe?
  - Dose constraints
- New techniques and future developments
- Guidelines for clinical practice

# Background



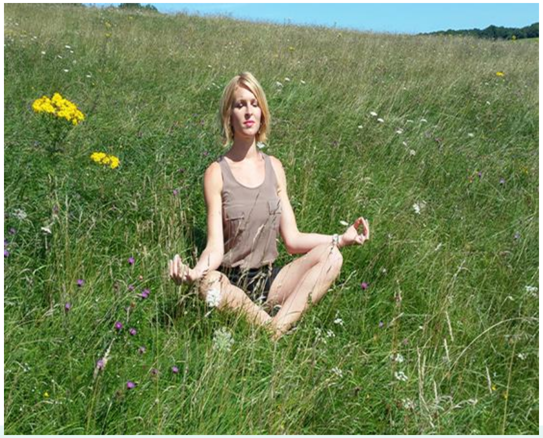

Overall survival

# Background

- High local recurrence rates
  - PD on imaging: 30-40 % after (chemo)RT
  - Potential increase with better prognosis (immunotherapy)
- Most recurrences are irresectable
- Low success rates with 2nd line systemic treatment
  - 15-25 % (local) remissions
  - Median OS up to 12 months (comparable stage V)

MAASTRO CLINIC

# Changing patient population



# Background

- Technological improvements
  - RT techniques (SABR, IMRT, VMAT)
  - Imaging
    - Dose accumulation
    - Image guidance

↓

High dose ReRT technologically feasible

MAASTRO CLINIC

# Key Questions

- Is it worthwhile?
- Is it safe?

## High-dose re-irradiation following radical radiotherapy for non-small-cell lung cancer

THE LANCET Oncology **2014**

- "High dose reirradiation"
- 24 studies, 14 radical dose (rest excluded)

## Re-irradiation for Locally Recurrent Lung Cancer: Evidence, Risks and Benefits

clinical ONCOLOGY **2018**

- "Reirradiation"
- 23 studies, 17 radical dose

MAASTRO CLINIC

# Buts..

- Retrospective (except 1) , small series
- Different RT treatments (primary and re-RT)
- Non- and small cell lung cancer
- Short follow-up
- Different second-line therapy
- Different endpoints
- Rarely detailed DVH parameters available

# Re-irradiation: is it worthwhile?

High-dose re-irradiation following radical radiotherapy for non-small-cell lung cancer

| | | | |
|---|---|---|---|
| Wu et al[28] | Prospective | 3DCRT | 13 (radical) |
| Okamoto et al[29] | Retrospective | 3DCRT | 18 (radical) |
| Peulen et al[30]‡ | Retrospective | SABR | 29 |
| Coon et al[31] | Retrospective | SABR | 12 |
| Kelly et al[32] | Retrospective | SABR | 36 |
| Evans et al[33] | Retrospective | SABR | 35 |
| Liu et al[34] | Retrospective | SABR | 72 |
| Meijneke et al[35] | Retrospective | SABR | 20 |
| McAvoy et al[36] | Retrospective | Protons | 33 |
| Reyngold et al[37] | Retrospective | SABR | 39 |
| Kilburn et al[38] | Retrospective | SABR/conv | 34/3 |
| Yoshitake et al[39] | Retrospective | 3DCRT | 17 |
| Trovo et al[40] | Retrospective | SABR | 17 |
| Griffioen et al[41] | Retrospective | 3DCRT | 24 |

MAASTRO

| | Number of patients | Median follow-up (months) | Median interval first RT and re-RT (months) | Median overall survival (months) | Median time to progression (months) |
|---|---|---|---|---|---|
| Wu et al[28] | 23 | 15 | 13 | 14 | Not stated |
| Okamoto et al[29] | 18 (radical) | Not stated | 23 | 15 | Not stated |
| Peulen [illegible] | [illegible] | [illegible] | [illegible] | 19 | Not stated |
| Coon et [illegible] | [illegible] | [illegible] | [illegible] stated | Not stated | 7·7 |
| Kelly et [illegible] | [illegible] | [illegible] | [illegible] | 24 | 12 |
| Evans e[illegible] | [illegible] | [illegible] | [illegible] stated | Not stated | Not stated |
| Liu et al[34] | 72 | 16 | 21 | Not stated | Not stated |
| Meijneke et al[35] | 20 | 12 | Not stated | 15 | 10 |
| McAvoy et al[36] | 33 | 11 | 36 | 11·1 | 4·5 |
| Reyngold et al[37] | 39 | 12·6 | 37 | 22 | 13·8 |
| Kilburn [illegible] | [illegible] | [illegible] | [illegible] | 21 | 16 |
| Yoshitake et al[39] | 17 | 12·6 | Not stated | 18 | 8 |

RT=radiotherapy. Re-RT=re-irradiation. OS=overall survival.

**Table 4: Efficacy of high-dose re-irradiation**

Time to progression 10 mnths

Med OS 17 mnths

OS after palliative reRT: 5 mnths

*De Ruysscher et al; Lancet oncol 2014*

## Conventional

| Author | Med OS | LC |
|---|---|---|
| Wu | 14 mnths | 51% 1yr |
| Tada | 7 mnths | NR |
| Kruser | 12 mnths | NR |
| Sumita | 31 mnths | 57% 1 yr |
| Griffioen/ Tetar | 14 mnths | 63% x yr |
| **Average** | **12 mnths** | **50-65%** |

## SBRT

| Author | Med OS | LC |
|---|---|---|
| Reyngold | 22 mnths | 77% 1yr |
| Trovo | 19 mnths | 86% 1 yr |
| Ceylan | 21 mnths | 69% 1 yr |
| Kilburn | 21 mnths | 80% 1 yr |
| Patel | 14 mnths | 79% 1 yr |
| Kelly | NR | 92% 2 yr |
| **Average** | **20 mnths** | **70-90%** |

MAASTRO CLINIC

*Rulach et al; Clin Oncol 2018*

## High-dose re-irradiation following radical radiotherapy for non-small-cell lung cancer

THE LANCET Oncology **2014**

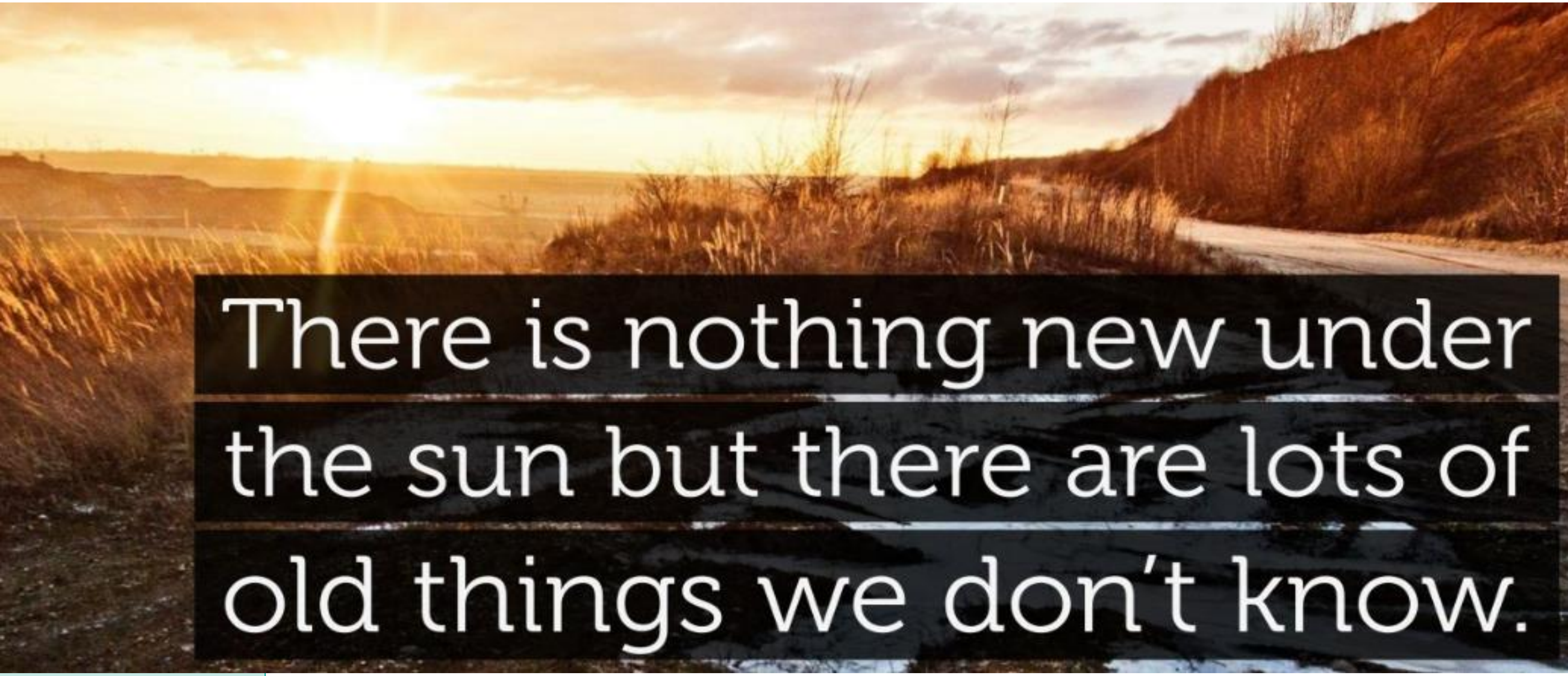
- "High dose reirradiation"
- 24 studies, 14 radical dose (rest excluded)

## Re-irradiation for Locally Recurrent Lung Cancer: Evidence, Risks and Benefits

clinical ONCOLOGY **2018**

- "Reirradiation"
- 23 studies, 17 radical dose

# 2014 to 2018.. No news?



# 2014 to 2018.. No news?


MAASTRO CLINIC

**Long-Term Outcomes of Salvage Stereotactic Ablation Radiotherapy for Isolated Lung Recurrence of Non-Small-Cell Lung Cancer: A Phase II Clinical Trial**

Bing Sun, MD[a,1], Eric D. Brooks, MD, MHS[a], Ritsuko Komaki, MD[a], Zhongxing Liao, MD[a],

- N=59, '05-'13
  - Isolated local recurrence ≤ 3 cm
- Median FU: 58 mnths

*Sun et al; J Thor Oncol '17*

MAASTRO CLINIC

Long-Term Outcomes of Salvage Stereotactic Ablation Radiotherapy for Isolated Lung Recurrence of Non-Small-Cell Lung Cancer: A Phase II Clinical Trial

Bing Sun, MD[a,1], Eric D. Brooks, MD, MHS[a], Ritsuko Komaki, MD[a], Zhongxing Liao, MD[a],

*But…*

- Initial stage: 78% stage I or II
- Only 56% initial RT (15% SABR, 85% conventional)
  - 2 patients with overlapping PTV

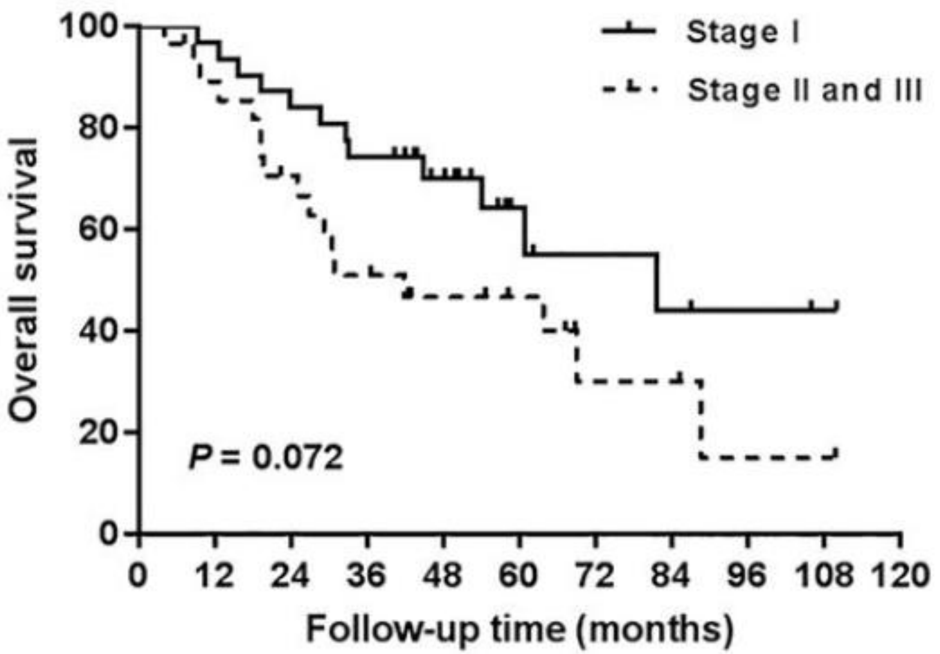
MAASTRO CLINIC

*Sun et al; J Thor Oncol '17*

**Long-Term Outcomes of Salvage Stereotactic Ablation Radiotherapy for Isolated Lung Recurrence of Non-Small-Cell Lung Cancer: A Phase II Clinical Trial**

Bing Sun, MD[a,1], Eric D. Brooks, MD, MHS[a], Ritsuko Komaki, MD[a], Zhongxing Liao, MD[a],

- Median OS: 64 mnths
- 5 yr cumulative
  - LR: 5%
  - RR: 10%
  - M+: 22%




*Sun et al; J Thor Oncol '17*

# Is it worthwhile? - Conclusions

- OS: Unknown
  - Better than palliative RT (17 vs 5 months)
  - Selection "bias": interval > 1 yr
- Postpone systemic therapy: probably
  - No uniform measurement of LC or time to progression
- Quality of life: Unknown
- Symptom control: Unknown
  - Palliative RT*: 35% (dyspnea) to 100% (hemoptysis)

**Rulach et al; Clin Oncol 2018*

# Worthwhile for whom?- Predictive factors

- Performance status
  - WHO, KPS
- PTV volume
  - 75-300 cc
- Interval
  - > 12 mnths, > 18 months
- EQD2
  - 60 Gy? 100 Gy?

# Worthwhile for whom?- Predictive factors

- Performance status
  - WHO, KPS
- PTV volume
  - 75-300 cc
- Interval
  - > 12 mnths, > 18 months
- EQD2
  - 60 Gy? 100 Gy?

*No clear cut off points*

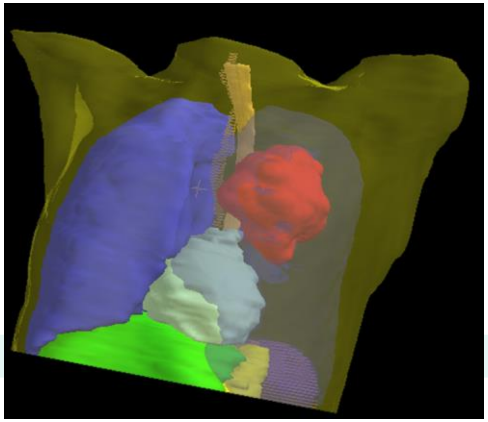
MAASTRO CLINIC

# Is it Safe?: Challenges

- Organs at risk
  - Lung — Pneumonitis/fibrosis
  - Trachea/bronchus — Fistula, stenosis
  - Esophagus — Fistula, stenosis
  - Great vessels — Stenosis, hemorrhage
  - Heart — Cardiac failure
  - Spinal cord — Myelopathy

- Predictive factors for adverse events
  - Cumulative dose
  - Area of overlap

*Not/incompletely recorded*



MAASTRO CLINIC

# Is it safe?

**High-dose re-irradiation following radical radiotherapy for non-small-cell lung cancer**

THE LANCET Oncology **2014**

Re-irradiation for Locally Recurrent Lung Cancer: Evidence, Risks and Benefits

clinical ONCOLOGY **2018**

# Overall grade 3-4 toxicity: low

- Esophagitis ≥ G3: 2% (0-9%)
- Lung ≥ G3: 10% (0-21%)
  - Baseline dyspnea not accounted for
- Lung G5: 0.5%

*De Ruysscher et al; Lancet oncol 2014*
*Rulach et al; Clin Oncol 2018*

# Overall grade 3-4 toxicity: low

- Esophagitis ≥ G3: 2% (0-9%)
- Lung ≥ G3: 10% (0-21%)
  - Baseline dyspnea not accounted for
- Lung G5: 0.5%
- Bleeding G5: centrally located: up to 20%

*De Ruysscher et al; Lancet oncol 2014*
*Rulach et al; Clin Oncol 2018*

MAASTRO CLINIC

Morbidity of lung SBRT

# Toxicity after reirradiation of pulmonary tumours with stereotactic body radiotherapy

Heike Peulen [d], Kristin Karlsson [b,c], Karin Lindberg [a,c], Owe Tullgren [a,c], Pia Bauman …,
Rolf Lewensohn [a,c], Peter Wersäll [a,c,*]

- Re-RT with SBRT, N=32 (11 central)
  - >50% overlap PTVs
- Median FU 1 yr
- 1/11 G4 fistula/stenosis
- 3/11 (central) G5 bleeding
  - Interval 6 wks-11 mnths

# High-dose, conventionally fractionated thoracic reirradiation for lung tumors

Gwendolyn H.M.J. Griffioen[a,*],
Ben J. Slotman[a], Suresh Senan

Letter to the Editor

**High-dose conventional thoracic re-irradiation for lung cancer: Updated results**

- Median follow-up: 25 months
- N=30
  - 29/30 centrally located (2nd RT)
  - ChemoRT: 67%
  - Median interval: 29.7 mnths (5-189)

*Griffioen et al; Lung Cancer 2014*
*Tetar et al; Lung Cancer 2015*

High-dose, conventionally fractionated thoracic reirradiation for lung tumors

Gwendolyn H.M.J. Griffioen[a,*],
Ben J. Slotman[a], Suresh Senan

Letter to the Editor

**High-dose conventional thoracic re-irradiation for lung cancer: Updated results**

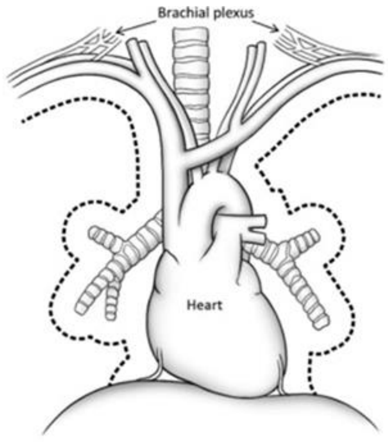
- 6/30 fatal bleeding (12⟶20%)
  - All central, 5/6: overlap high dose areas
  - Median interval: 7 months
- 2/30 grade 5 respiratory failure
- 1/30 grade 4 bronchial stenosis

MAASTRO CLINIC

*Griffioen et al; Lung Cancer 2014*
*Tetar et al; Lung Cancer 2015*

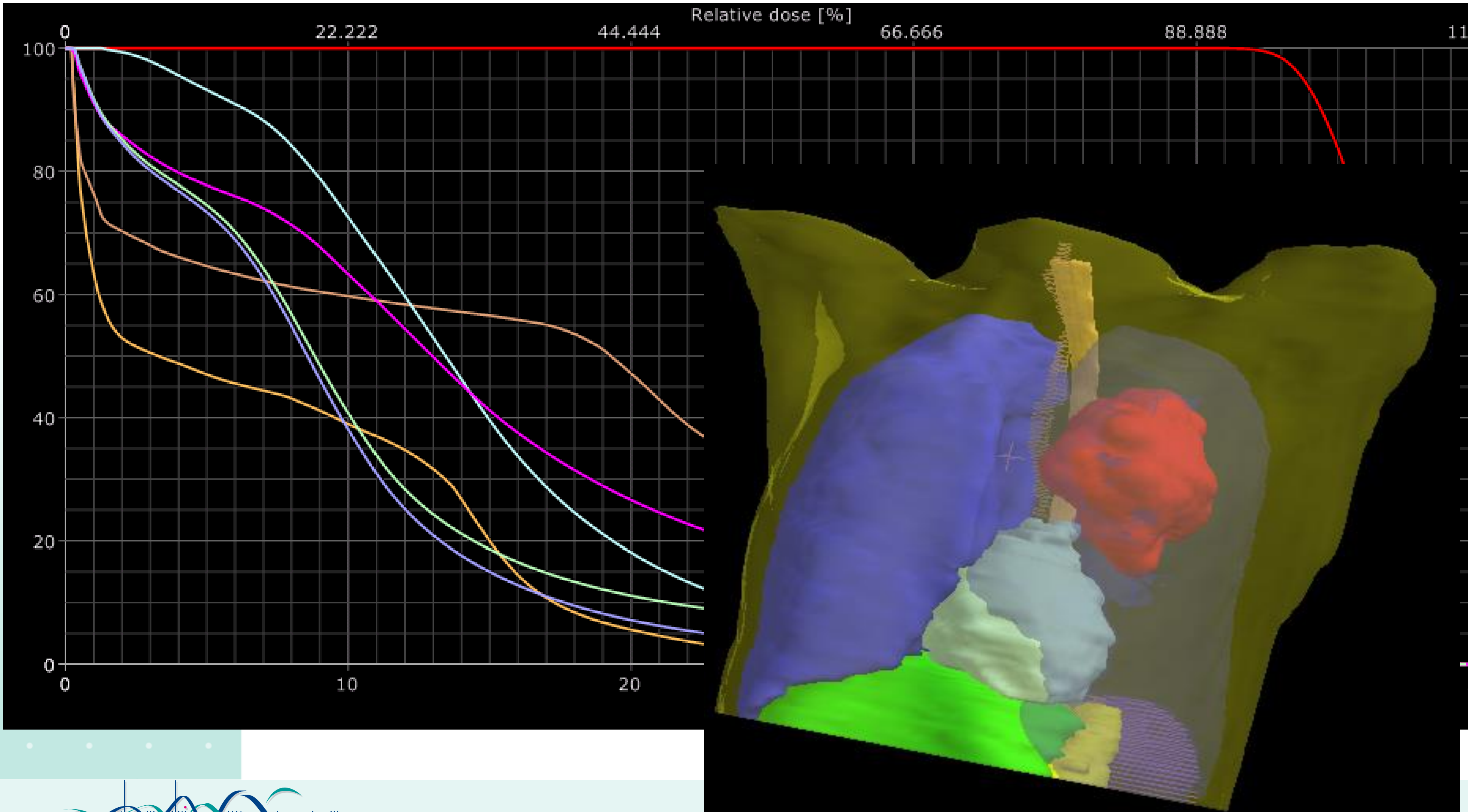
# Conclusions: Is it safe?

- Centrally..?
  - Dose accumulation
- Lung: remarkably low toxicity
  - Small volumes
  - Lung G5: 0.5%

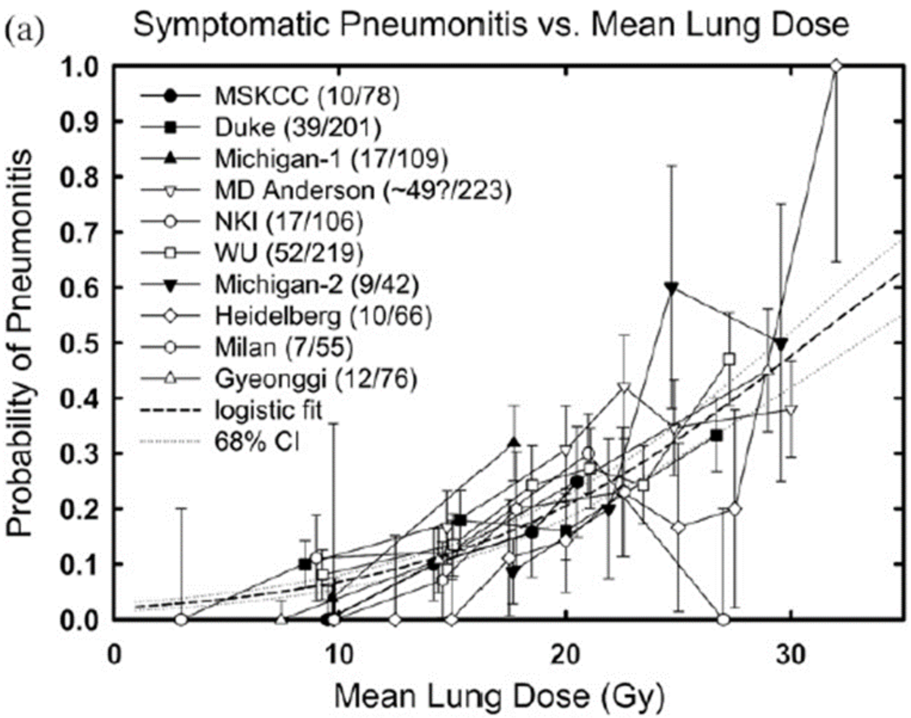



*De Ruysscher et al; Lancet oncol 2014*
*Rulach et al; Clin Oncol 2018*

# Safety: Dose constraints?



# Already large uncertainty for primary RT!

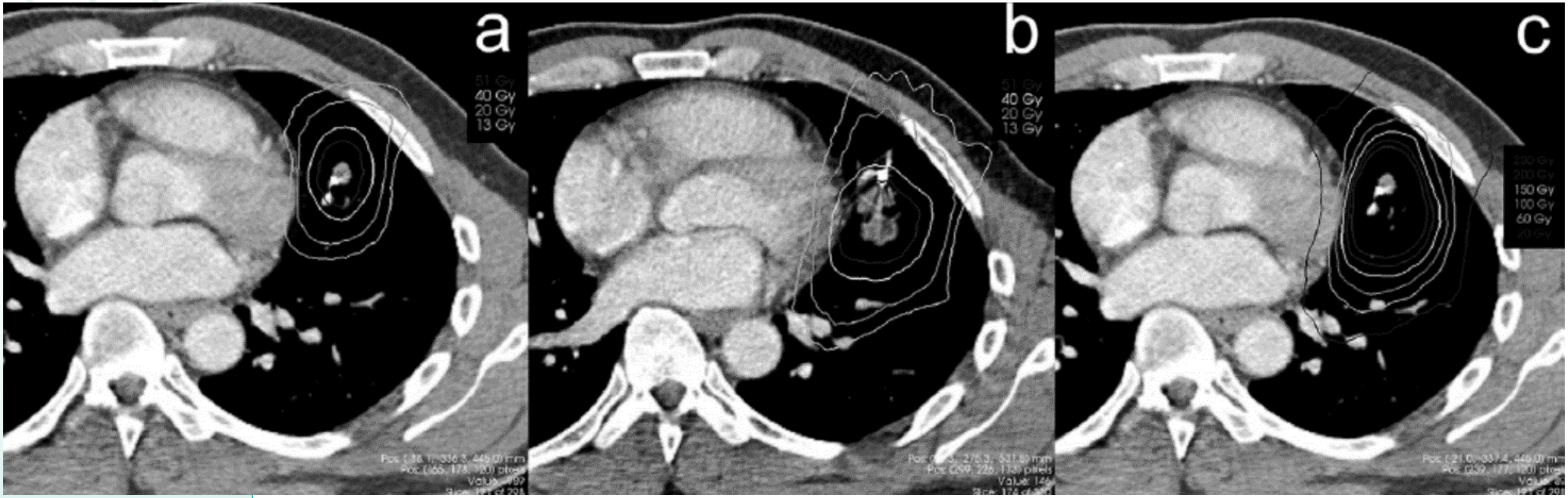



- Repair? Initial dose?
- α/β ?
- Radiosensitivity?

Reirradiation and stereotactic radiotherapy for tumors in the lung: Dose summation and toxicity

Thomas R. Meijneke, Steven F. Petit, Davy Wentzler, Mischa Hoogeman, Joost J. Nuyttens *

*Department of Radiation Oncology, Erasmus MC-Daniel den Hoed Cancer Center, Rotterdam, The Netherlands*




- Rigid followed by deformable registration
- Accumulated dose ≥ 70 $Gy_3$
  - N=7 trachea/heart
  - N=8 esophagus

*Meijneke, Radiother Oncol 2013*


MAASTRO CLINIC

# Summed dose ≥ 70 Gy

| | Median ($Gy_3$) |
|---|---|
| *Heart (n = 7)* | |
| Summed plan | 114.5 |
| First plan | 71.3 |
| Second plan | 95.6 |
| *Esophagus (n = 8)* | |
| Summed plan | 85.2 |
| First plan | 60.7 |
| Second plan | 37.1 |
| *Trachea (n = 7)* | |
| Summed plan | 89.2 |
| First plan | 49.8 |
| Second plan | 65.1 |

*Meijneke, Radiother Oncol 2013*

# Accumulated dose ≥ 70 Gy

| | Median ($Gy_3$) |
|---|---|
| *Heart (n = 7)* | |
| Summed plan | 114.5 |
| First plan | 71.3 |
| Second plan | 95.6 |
| *Esophagus (n = 8)* | |
| Summed plan | 85.2 |
| First plan | 60.7 |
| Second plan | 37.1 |
| *Trachea (n = 7)* | |
| Summed plan | 89.2 |
| First plan | 49.8 |
| Second plan | 65.1 |

- No grade 3-4 toxicity
- Safe if
  - Accumulated Dmax to the heart < 115 $Gy_3$
  - Accumulated Dmax to the trachea < 89 $Gy_3$
  - Accumulated Dmax to the oesofagus < 85 $Gy_3$

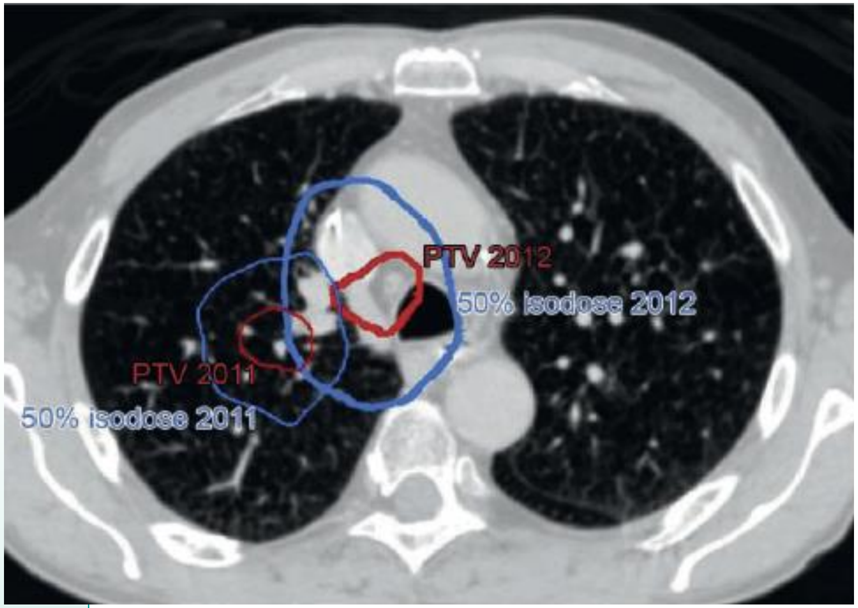
*Meijneke, Radiother Oncol 2013*

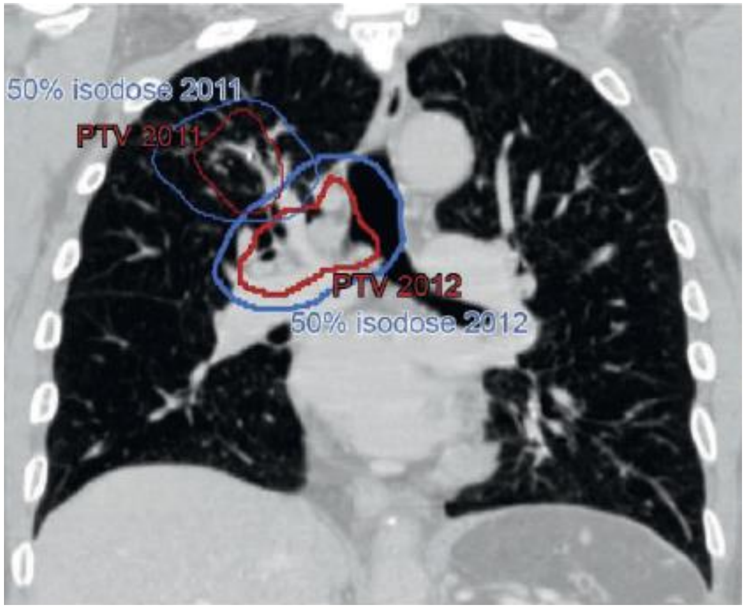


MAASTRO CLINIC

# Dosimetric Factors and Toxicity in Highly Conformal Thoracic Reirradiation

Michael S. Binkley, BA,* Susan M. Hiniker, MD,*

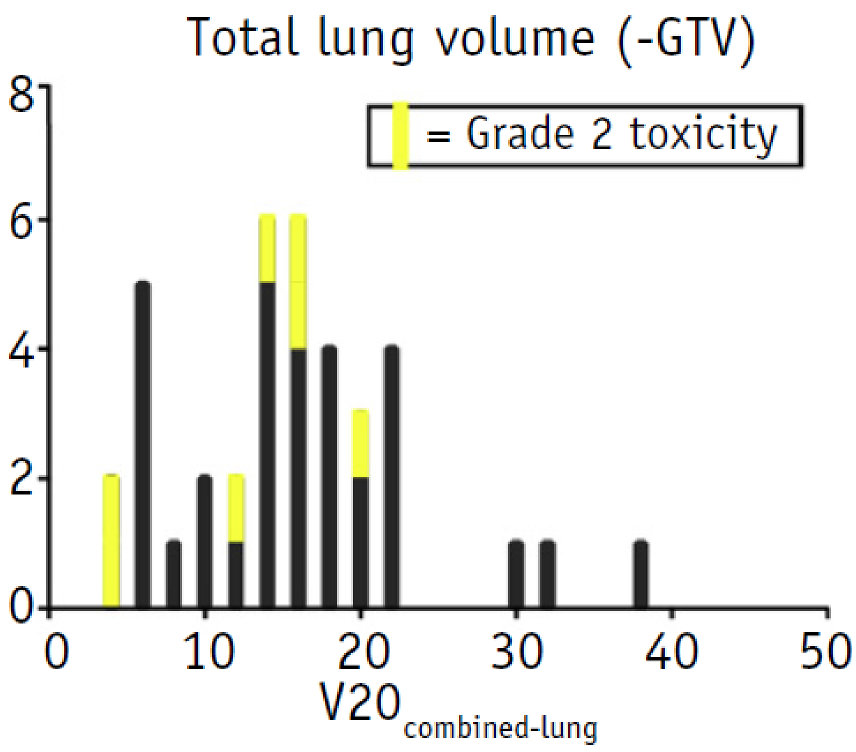


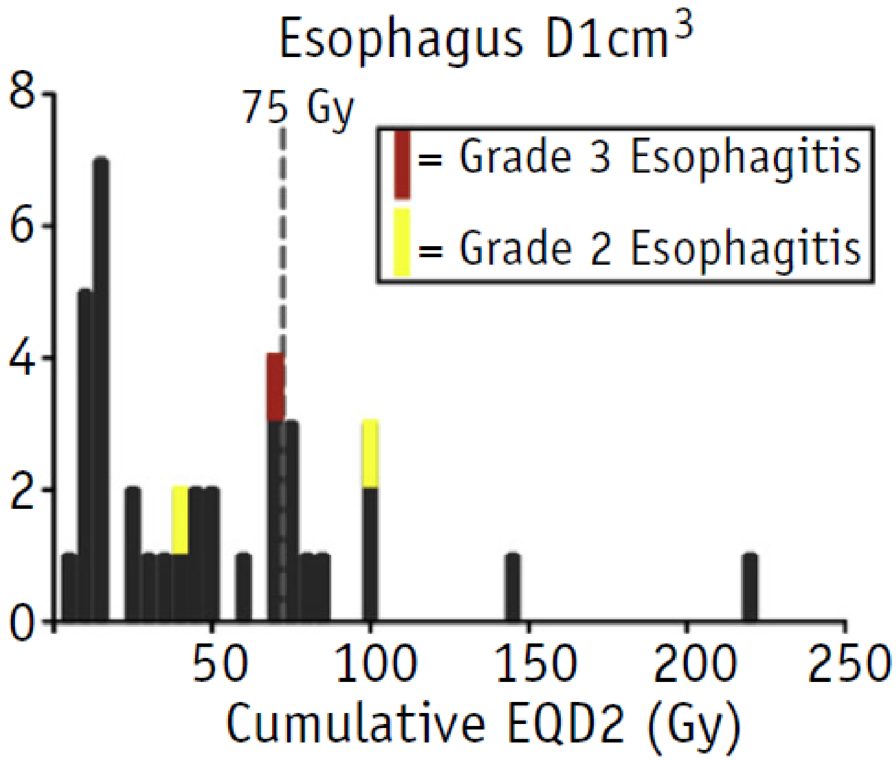




- Deformable registration
- Accumulated EQD2

*Binkley et al , Int J Rad Oncol Biol Phys 2016*

# Cumulative DVHs



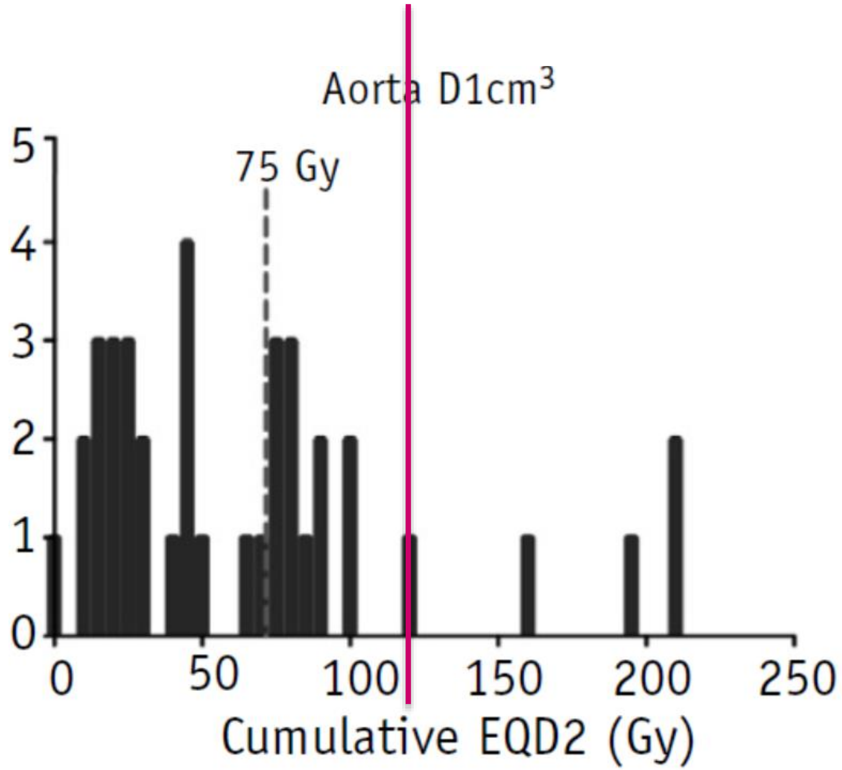




V20: 4.7-21.7%

D1cc: 41-101 Gy

*Binkley, Int J Rad Oncol Biol Phys 2016*

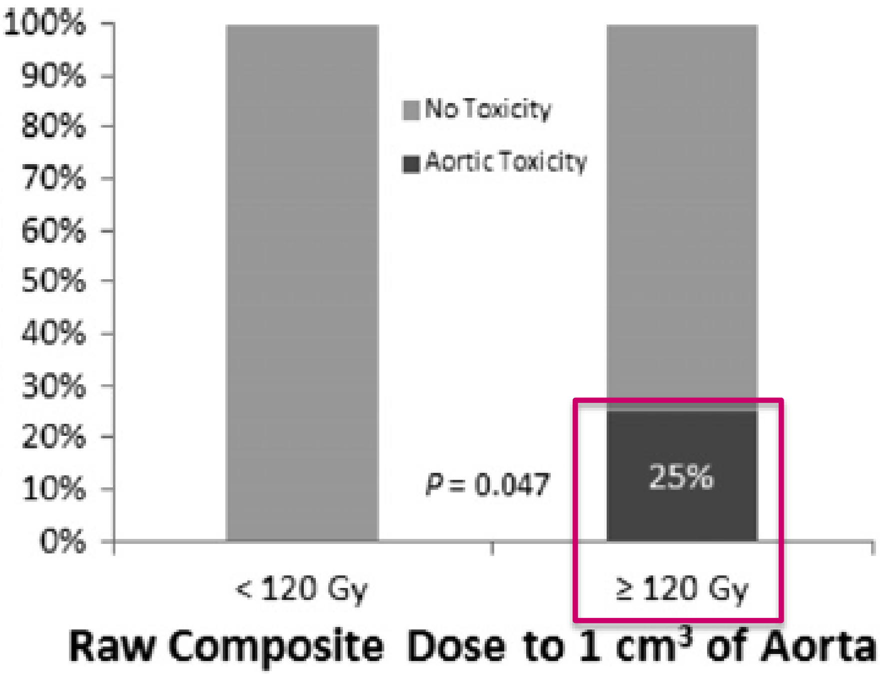
# Cumulative DVHs




D1cc >120 Gy: 0/5

*Binkley, Int J Rad Oncol Biol Phys 2016*

# Large vessels- Aorta: Evans et al


*Evans et al; Radiother Oncol 2014*

# DVH constraints

- Accumulated Dmax to the aorta is < 120 Gy?
- Accumulated V20 of the lungs is < 16 %
- Accumulated Dmax to the heart < 115 $Gy_3$
- Accumulated Dmax to the trachea < 89 $Gy_3$
- Accumulated Dmax to the esophagus <75 or 85 $Gy_3$ to the oesophagus

# DVH constraints

- Accumulated Dmax to the aorta is < 120 Gy?
- Accumulated V20 of the lungs is < 16 %
- Accumulated Dmax to the heart < 115 Gy[3]
- Accumulated Dmax to the trachea < 89 Gy[3]
- Accumulated Dmax to the esophagus <75 or 85 Gy[3] to the oesophagus

→ More evidence needed for rigorous constraints

MAASTRO CLINIC

# Re-irradiation of lung tumours

- Background
- Key questions
  - Is it worthwhile?
  - Is it safe?
  - Dose constraints
- New techniques and future developments
- Guidelines for clinical practice

# New techniques and future developments

- NTCP models
- Technological advances
- Role of systemic treatment?

THERE IS NOTHING NEW
UNDER THE SUN, BUT
THERE ARE NEW SUNS.

# NTCP models: classical lung

## NL: model based selection proton therapy

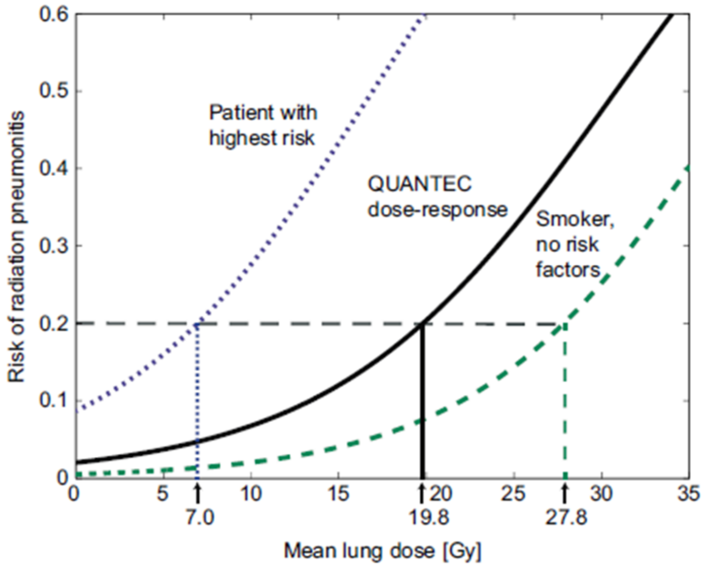
Dyspnea

Appelt 2014

Dysphagia

Zhu 2010

Gomez 2010



# NTCP models: classical lung

## NL: model based selection proton therapy

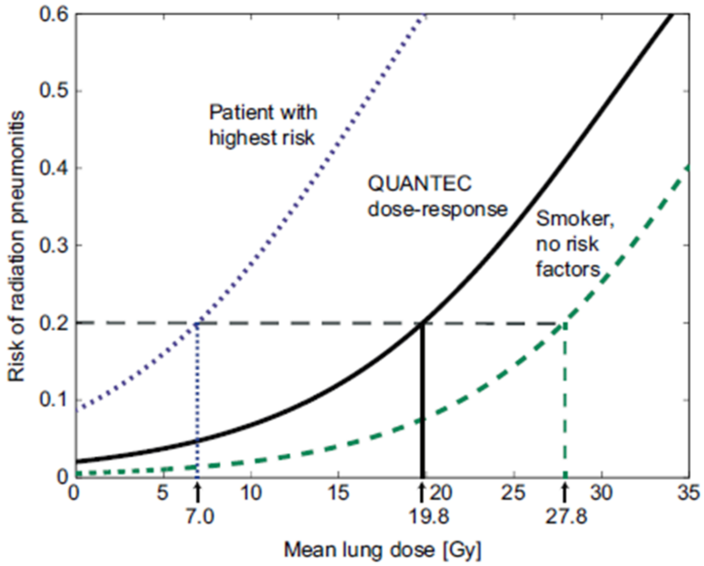
Dyspnea

Appelt 2014

Dysphagia

Zhu 2010

Gomez 2010




Delta dyspnea!

# NTCP models: cardiac toxicity: paradigm shift

Cardiac Toxicity After Radiotherapy for Stage III Non–Small-Cell Lung Cancer: Pooled Analysis of Dose-Escalation Trials Delivering 70 to 90 Gy

*Kyle Wang, Michael J. Eblan, Allison M. Deal, Matthew Lipner, Timothy M. Zagar, Yue Wang, Panayiotis Mavroidis, Carrie B. Lee, Brian C. Jensen, Julian G. Rosenman, Mark A. Socinski, Thomas E. Stinchcombe, and Lawrence B. Marks*

New Era in Radiation Oncology for Lung Cancer: Recognizing the Importance of Cardiac Irradiation

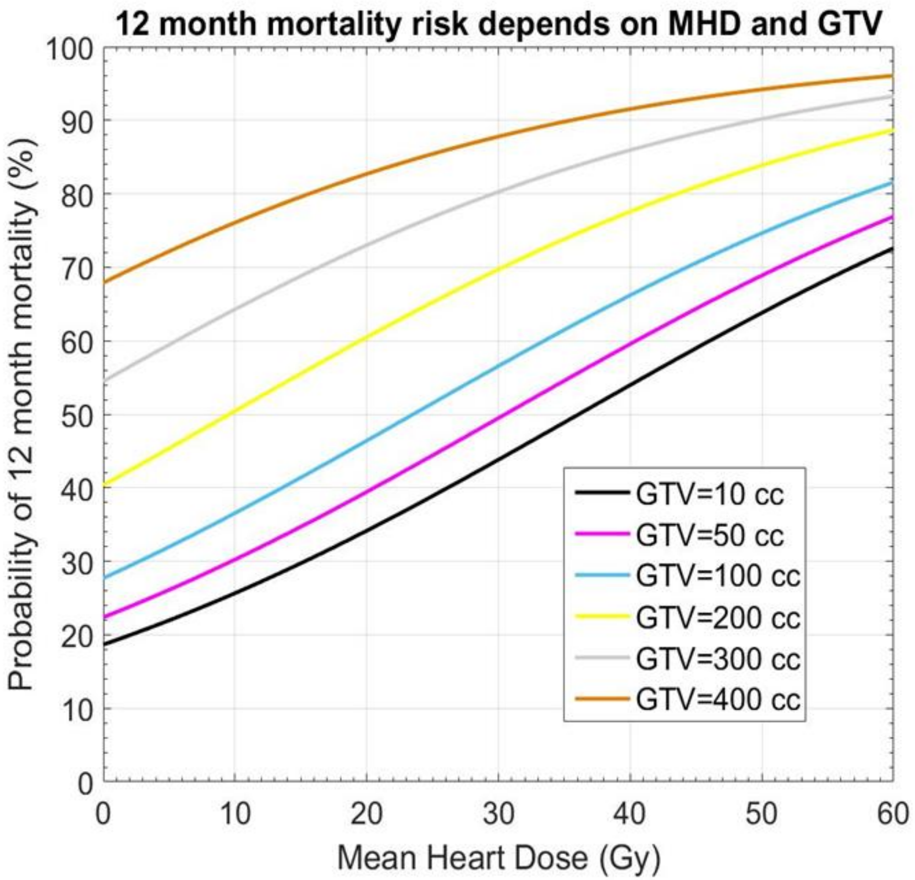
Charles B. Simone II, *University of Maryland Medical Center, Baltimore, MD*

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

MAASTRO CLINIC

# Heart: NTCP model for 1- and 2 year mortality

## GTV (tumor and nodes) + MHD




*Defraene/De Ruysscher, WCLC 2017*
*Defraene et al, submitted*

MAASTRO CLINIC

# Sublocations within the heart?

## Dose to cardiac substructures predicts survival in non-small cell lung cancer chemo-radiotherapy

Maria Thor, Alexandra Hotca, Andrew Jackson, Ellen Yorke, Andreas Rimner, and Joseph O Deasy

*Memorial Sloan Kettering Cancer Center, USA*

MANCHESTER 1824 The University of Manchester

The Christie NHS Foundation Trust

## Correlation between coronary artery doses and overall survival in locally advanced lung cancer patients

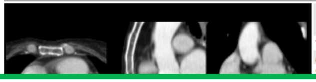
Marianne C Aznar[1,2], Eliana M. Vasquez Osorio[1,] Jason Kennedy[3], Jasmin Mahil[1], Martin Swinton[1], Corinne Faivre-Finn[1,3], Marcel van Herk[1,] Alan McWilliam[1,2]
[1]The University of Manchester, Division of Cancer Sciences, [2]The Christie NHS Foundation Trust, Christie Medical Physics and Engineering, [3]The Christie NHS Foundation Trust, Clinical Oncology

**INTRODUCTION:**

- Irradiating the base of the heart has been linked to poorer overall survival (OS) in both early stage non-small cell lung cancer (NSCLC) patients treated with SABR and locally advanced NSCLC patients treated with standard fractionated RT [1,2].
- We hypothesized that the origin of both coronary arteries are the dose-sensitive structures driving this increased mortality.
- We therefore investigated the correlation between overall survival (OS) and the dose to the origin of the left and right coronary arteries (LCA and RCA) in a large, single-institution cohort.

**MATERIALS AND METHODS:**

- Two observers identified the origin of the LCA and RCA on contrast enhanced CT scans (Figure 1) from a total of 804 NSCLC patients treated between 2010 and 2013 with curative-intent radiotherapy (55 Gy in 20 fractions).
- For 167 of 804 patients, LCA and RCA were identified by both observers, allowing intra-observer variation to be calculated.
- The mean lung dose (MLD) and dose to the root of RCA and LCA ($D_{RCA}$, $D_{LCA}$) were extracted from the radiotherapy plan. These were used in a multivariate survival analysis including patient and tumour characteristics (age, sex, tumour size, TNM stage, induction chemotherapy and performance status).



| | | Multivariate analysis | |
|---|---|---|---|
| | | HR (95% CI) | p |
| Tumour volume | (median 27 cm3) | 1.004 (1.002-1.005) | <0.001 |
| Age | (median 74 years) | | |
| Sex | (421 M, 383 F) | 1.46 (1.20-1.78) | <0.001 |

**CONCLUSIONS:**

- Even though dose to the base of the heart has been linked with survival, in this cohort, the dose to the roots of the coronary arteries was not an independent predictor of OS.
- However, inter-observer variation in localizing the root of the LCA and RCA was substantial, suggesting that manual identification of cardiac substructures on planning CT scans is challenging. Future work in our institution will include automatic voxel-based methods to identify the sensitive cardiac substructures in NSCLC patients to explain previous observations.

[1] McWilliam et al EJC 2017 [2] Stam et al R&O 2017

CONCLUSIONS:
- Even though dose to the base of the heart has been linked with survival, in this cohort, the dose to the roots of the coronary

## Dose to heart substructures is associated with non-cancer death after SBRT in stage I–II NSCLC patients

Barbara Stam [a], Heike Peulen [a], Matthias Guckenberger [b,c], Frederick Mantel [b], Andrew Hope [d], Maria Werner-Wasik [e], Jose Belderbos [a], Inga Grills [f], Nicolette O'Connell [g], Jan-Jakob Sonke [a,*]

MAASTRO CLINIC

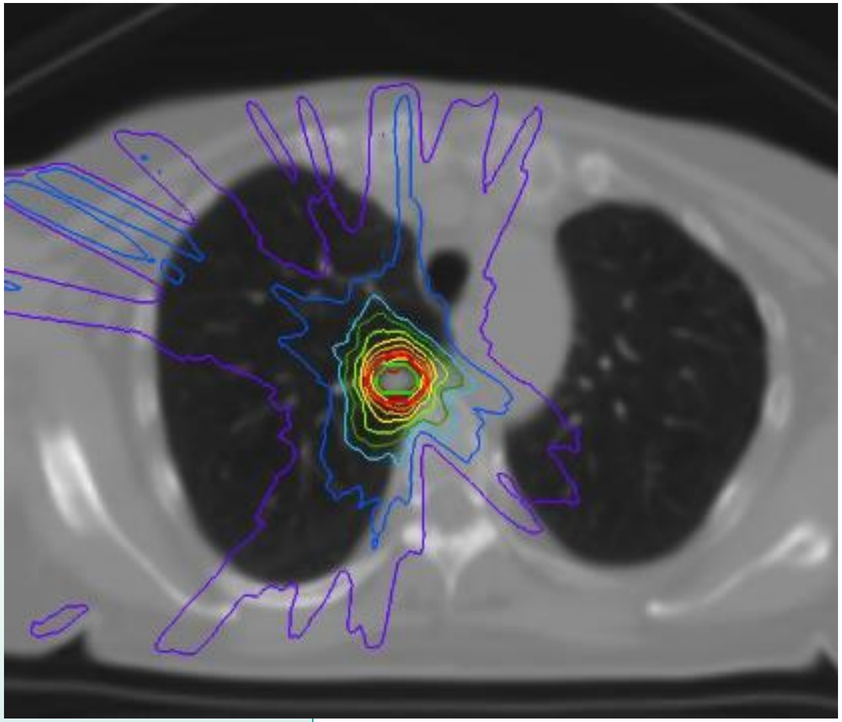
# Technical advances: MRI and Protons

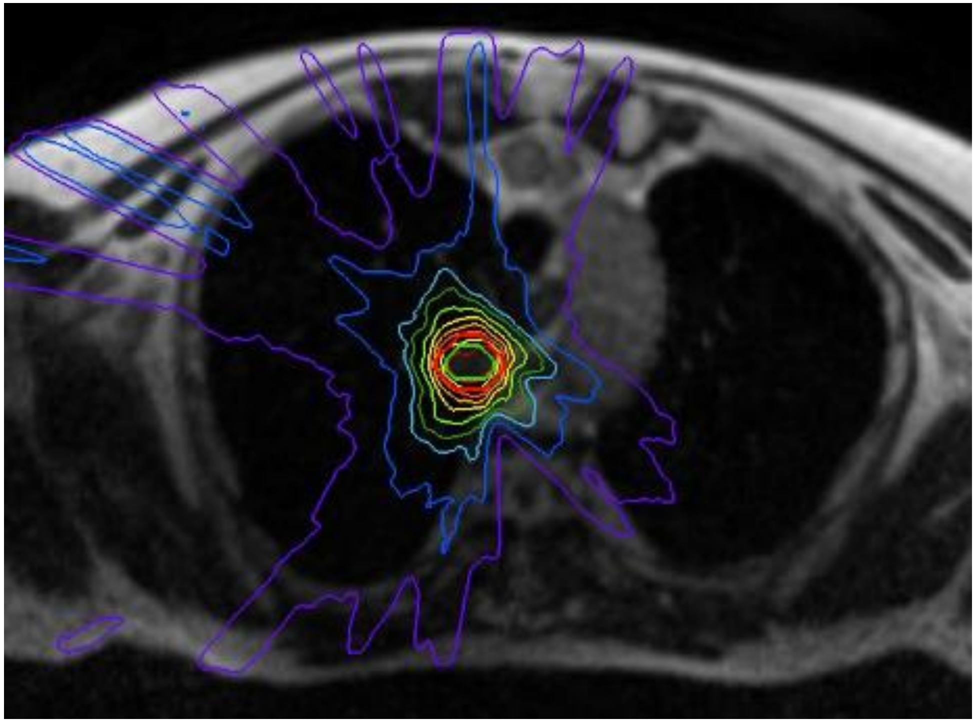
- Needed for all patients?

  *Peripheral:* SBRT with VMAT and CBCT

  *Central location/ Overlap thoracic wall*

# MRIdian (VUMC): reRT 8*7.5 Gy





2011 T3N0, lobectomy and adjuvant chemotherapy
2013 Nodal recurrence N7, 54 Gy + boost to 67.5 Gy
Visual dose recalculation prior RT

*Courtesy F. Spoelstra*

MAASTRO CLINIC

# Reirradiation with protons

- 3 large series (MD Anderson, Upenn/Chicago)
  - Majority passive scattered
  - Locoregional failure up to 40%
  - 2/3 series: Toxicity higher than reported with photons!

≥ grade 3 lung: 21% (vs 10%)

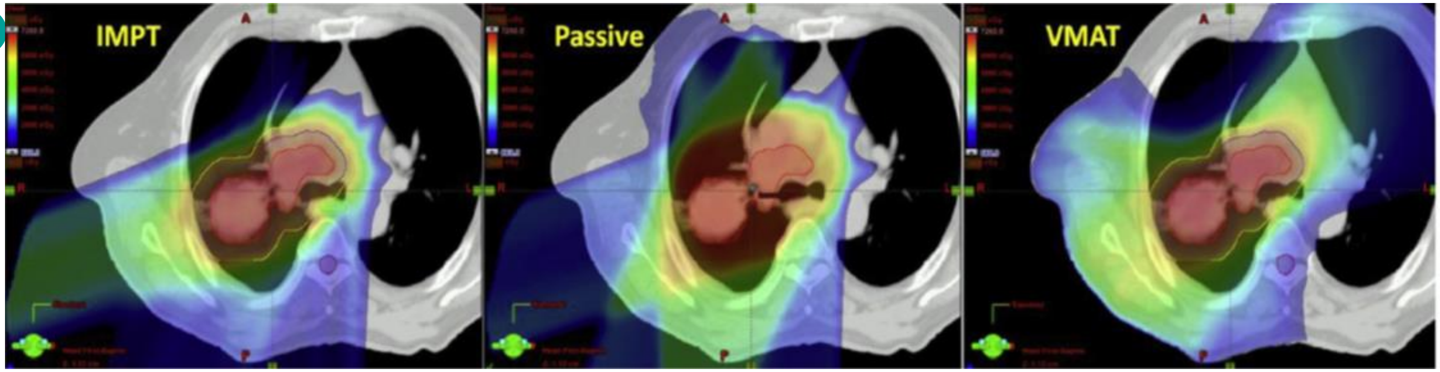
≥ grade 3 esophagus: 5-9% (vs 2%)

≥ grade 4: 6% (vs 0%)

*Mc Avoy, Radiother Oncol 2013*
*Mc Avoy, Int J Rad Oncol Biol Phys 2014*
*Chao, J Thorac Oncol 2017*

MAASTRO CLINIC

# Technique? Not entirely..




IMPT results in best sparing of all OARs

PSPT spares heart and contralateral lung, but not esophagus or ipsilateral lung compared to VMAT

*Chang et al. Int J Radiat Oncol Biol Phys 2016*

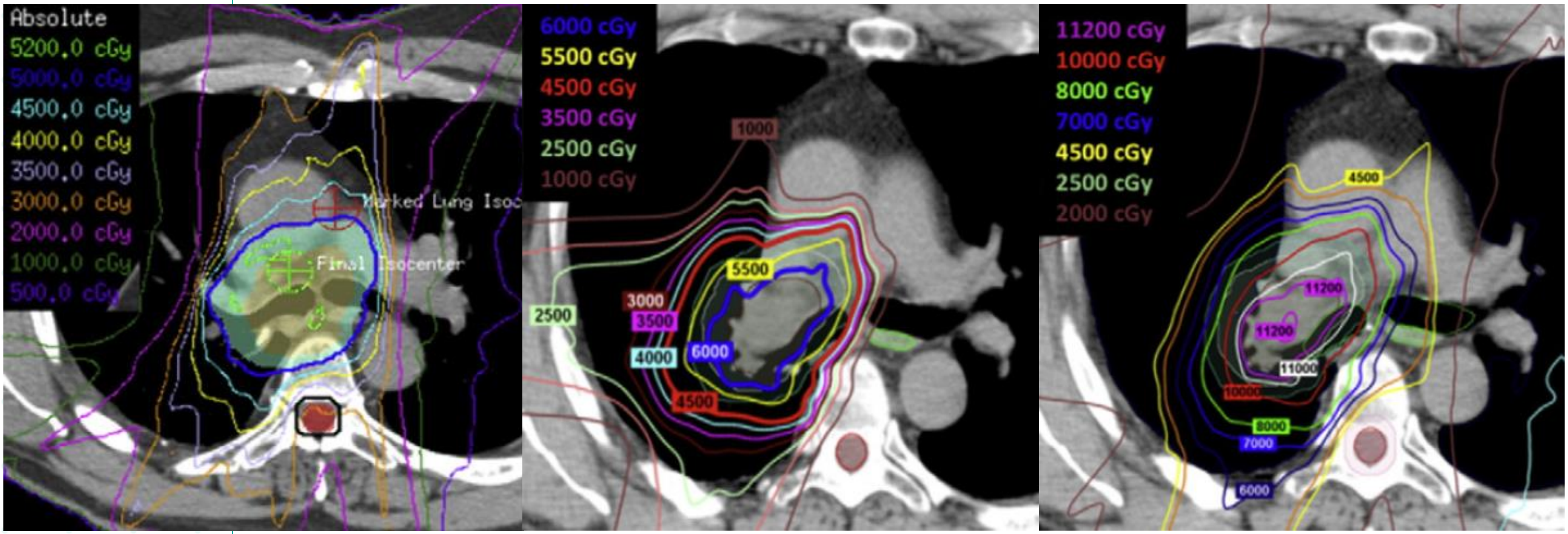
MAASTRO CLINIC

# Reirradiation of thoracic cancers with intensity modulated proton therapy

Jennifer C. Ho MD [a], Quynh-Nhu Nguyen MD [a], Heng Li PhD [a], Pamela K. Allen PhD [a], Xiaodong Zhang PhD [b], Zhongxing Liao MD [a], X. Ronald Zhu PhD [b], Daniel Gomez MD [a], Steven H. Lin MD, PhD [a], Michael Gillin PhD [b], Ritsuko Komaki MD [a], Stephen Hahn MD [a], Joe Y. Chang MD, PhD [a,*]

- Retrospective, N=27
  - 85% overlap 100% isodose
- Median time interval 29.5 months
- Median $EQD_2$ 66 Gy (range 43,2-84 Gy)
- Adaptation: CT weekly or once after 2-3 wks

*Ho, Pract Radiat Oncol 2018*




- Accumulated plans available: 22/27 pts
- 81% central
- 48% chemoRT
- Median EQD2sum: 124 Gy

*Ho, Pract Radiat Oncol 2018*

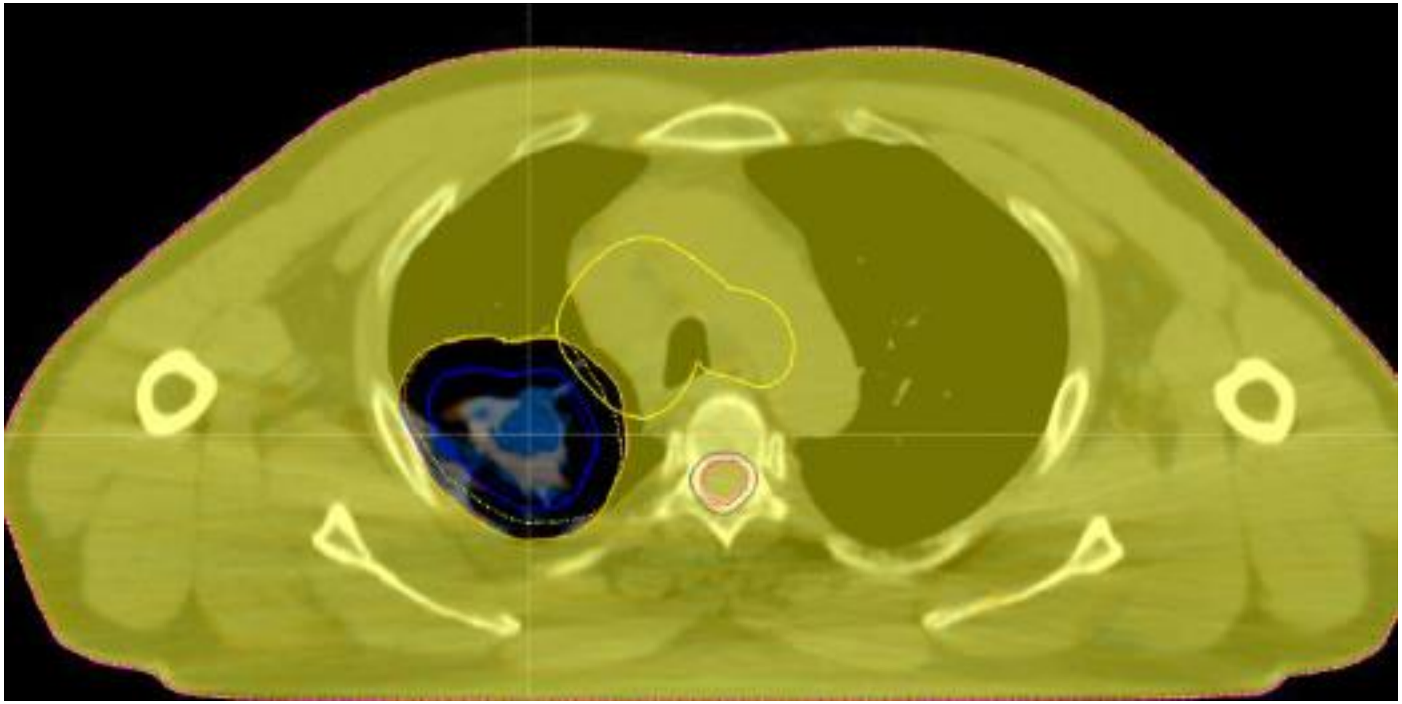
# Reirradiation of thoracic cancers with intensity modulated proton therapy

| Technique | 1 yr LC | med OS | Toxicity |
|---|---|---|---|
| IMPT | 78% | 18 mnths | No grade Gr 4/5<br>Gr 3 (lung) 7% |
| Conventional | 50-65% | 12 mnths | Central 20% grade 5 |
| SBRT | 70-90% | 20 mnths | Central 20% grade 5 |

*De Ruysscher et al; Lancet oncol 2014*
*Rulach et al; Clin Oncol 2018*
*Ho, Pract Radiat Oncol 2018*

MAASTRO CLINIC

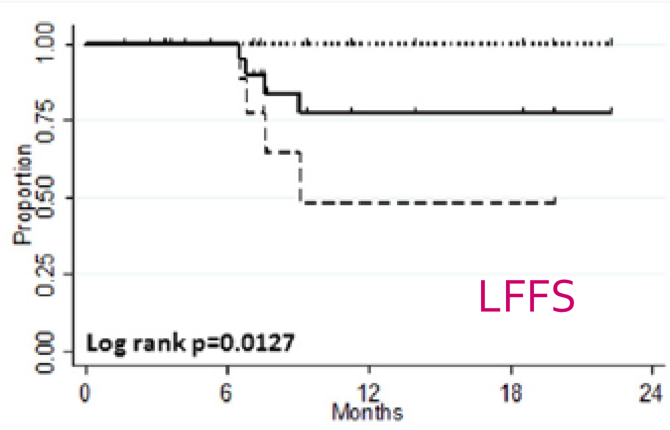
# Image guidance: CT-registration

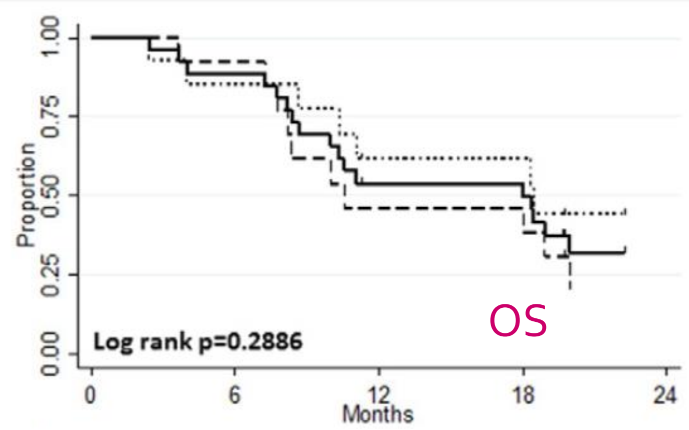


Combined deformable and non-deformable registration

# IMPT: Dose matters!

- ≥ 66 Gy vs ≤ 66 Gy
- LFFS
  - 1 yr: 100% vs 49%
- LRFFS
  - 1 yr: 84% vs 23%
- PFS
  - 1 yr: 76% vs 14%
- <u>But: not OS!</u>

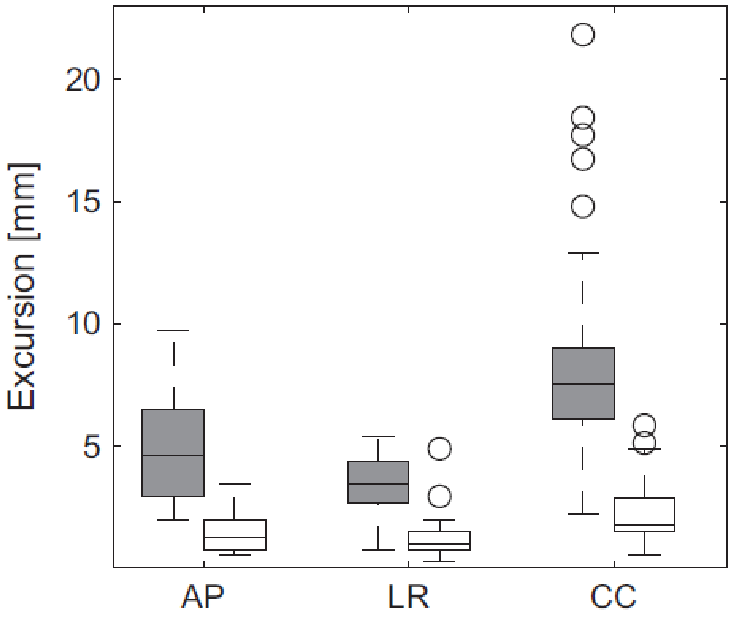



*Ho et al; Pract Radiat Oncol 2018*

MAASTRO CLINIC

# Motion management: Breathhold in NSCLC




Mean excursion (tumor+lnn)*

| mm | AP | LR | CC |
|---|---|---|---|
| FB | 4,7 | 3,3 | 8,5 |
| DIBH | 1,4 | 1,2 | 2,1 |

Reproducibility**

| mm | Intrafr | Interfr |
|---|---|---|
| Tumor position | 1,7 | 4,8 |
| Differential motion | 0,0 | 4,8 |

REGION H Rigshospitalet

Duration of breathhold: 20 sec

**Rydhog et al, Radiother Oncol 2017;*
***Josipovic et al, Radiother Oncol 2016;*

MAASTRO CLINIC

# Supported breath hold?: HFPV


*Lausanne, Multiple publiactions*

# Supported breath hold: Nasal high flow therapy?

Baseline
86 sec (1,5 min)

Flow 40L/min, 80% O2
270 sec (4,5 min)

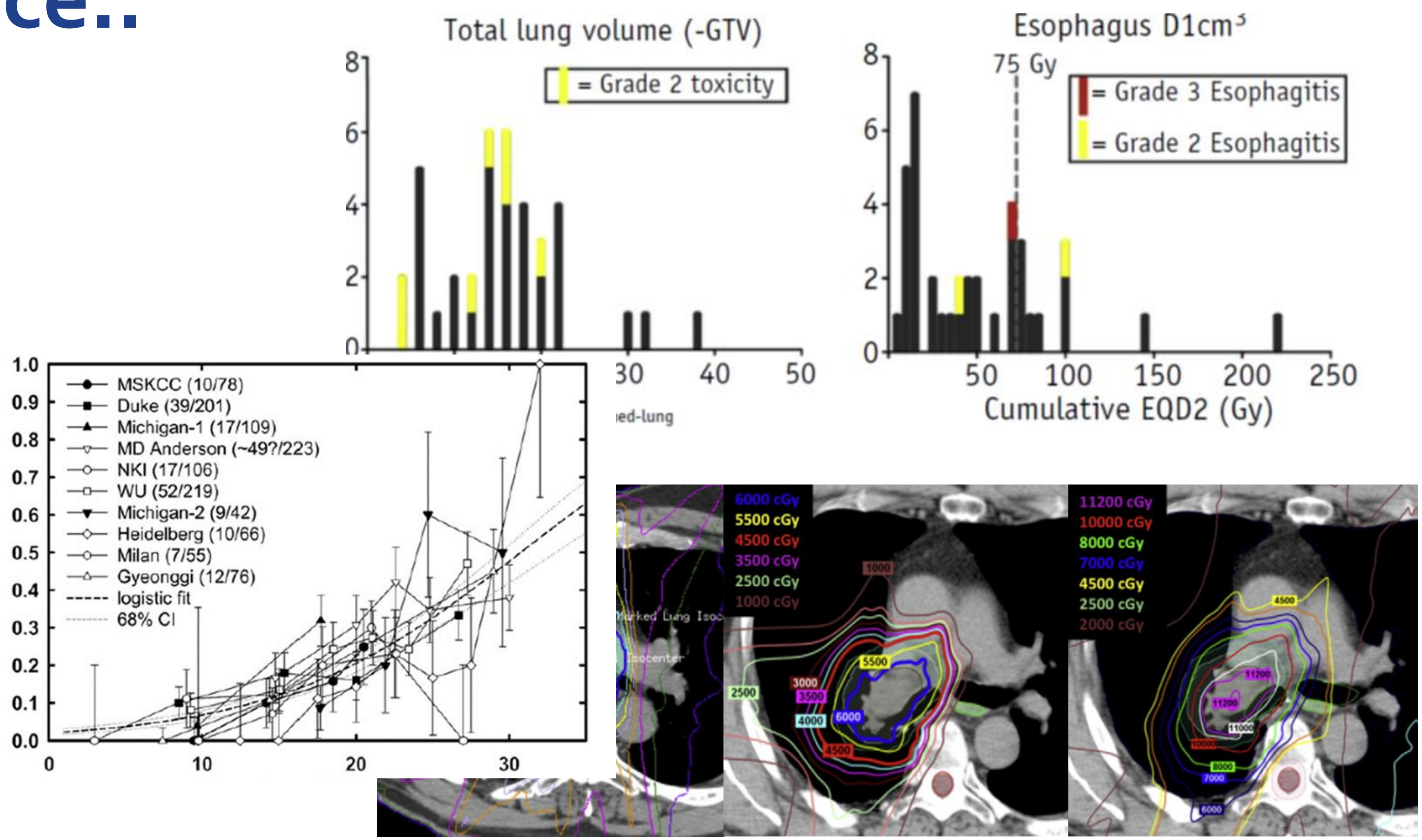

MAASTRO CLINIC

# High distant metastasis rate: role for adjuvant systemic therapy?

| IMPT | SBRT |
| --- | --- |
| LR: 15% | LR: 5% |
| RR: 30% | RR: 10% |
| M+: 33% | M+: 22% |

MAASTRO CLINIC

# Conclusions and Guidelines for clinical practice..



# General conclusions

- High-dose re-irradiation (cumulative EQD2 70-100 Gy) is feasible in selected patients
- Central location: added benefit of MRI/Protons
- No solid dose constraints
- Role of systemic therapy?
- Inform your patient about the uncertainties and risks

➔ Obvious need for prospective evidence

MAASTRO CLINIC

# Guidelines for clinical practice

- Patient selection
  - Performance status & Lung function
  - Full staging: PETCT + imaging brain
  - Tumor volume (< 3-4 cm)

- RT schedule
  - SBRT if possible
  - Overlap: consider
    - Hyperfractionation
    - (Induction) Chemotherapy
    - Advanced techniques in study

MAASTRO CLINIC

# Guidelines for clinical practice

- Dose accumulation
  - (First) RT dose reconstruction
  - Deformable/non-deformable registration?
  - If include repair: OAR constraints according to international guidelines for primary iriraditiation
    - maximum repair 30%
    - OARs: α/β =3 (spinal cord and brachial plexus: α/β =2)

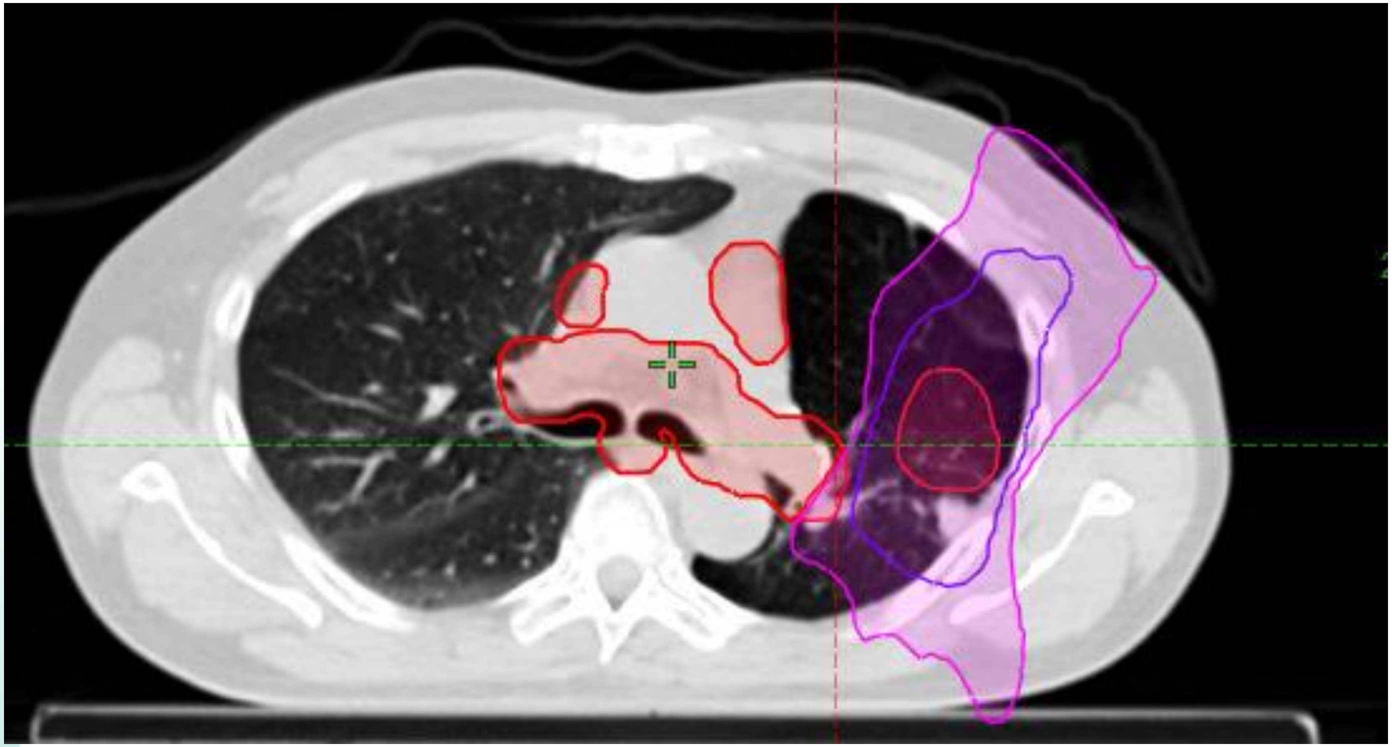
- Prospective outcome registration
  - Separate and accumulated dose
  - Systematic follow-up protocols including imaging

MAASTRO CLINIC

# RETHO-study

- Prospective, multicenter phase II
- $EQD_2$ re-RT ≥ 45 Gy
- Primary endpoint
  - Overall survival (goal> 12 mnths)
- Secondary endpoints/aims
  - LC, DFS
  - Toxicity ↔ cumulative dose OARs
- Including outcome registration

# Bottomline: talk with your patient!



MAASTRO CLINIC