



Hodgkin Lymphoma: Radiation Volumes

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Università di Torino



The changing role of RT in the cure of HL

From

Maximal use as a single agent

To

Combination of chemotherapy and full dose-full volume radiotherapy

To

Combination of less chemotherapy and less radiotherapy

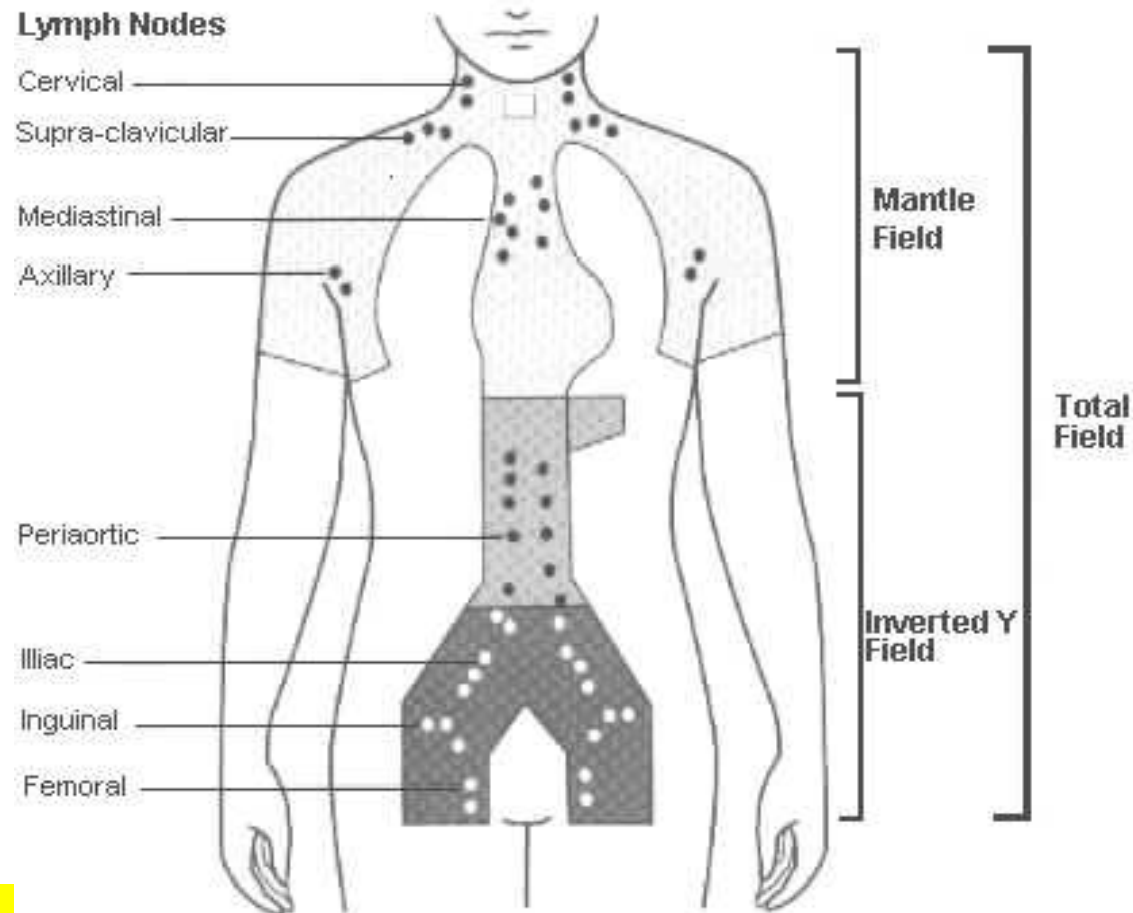
To

Questioning the need of radiotherapy

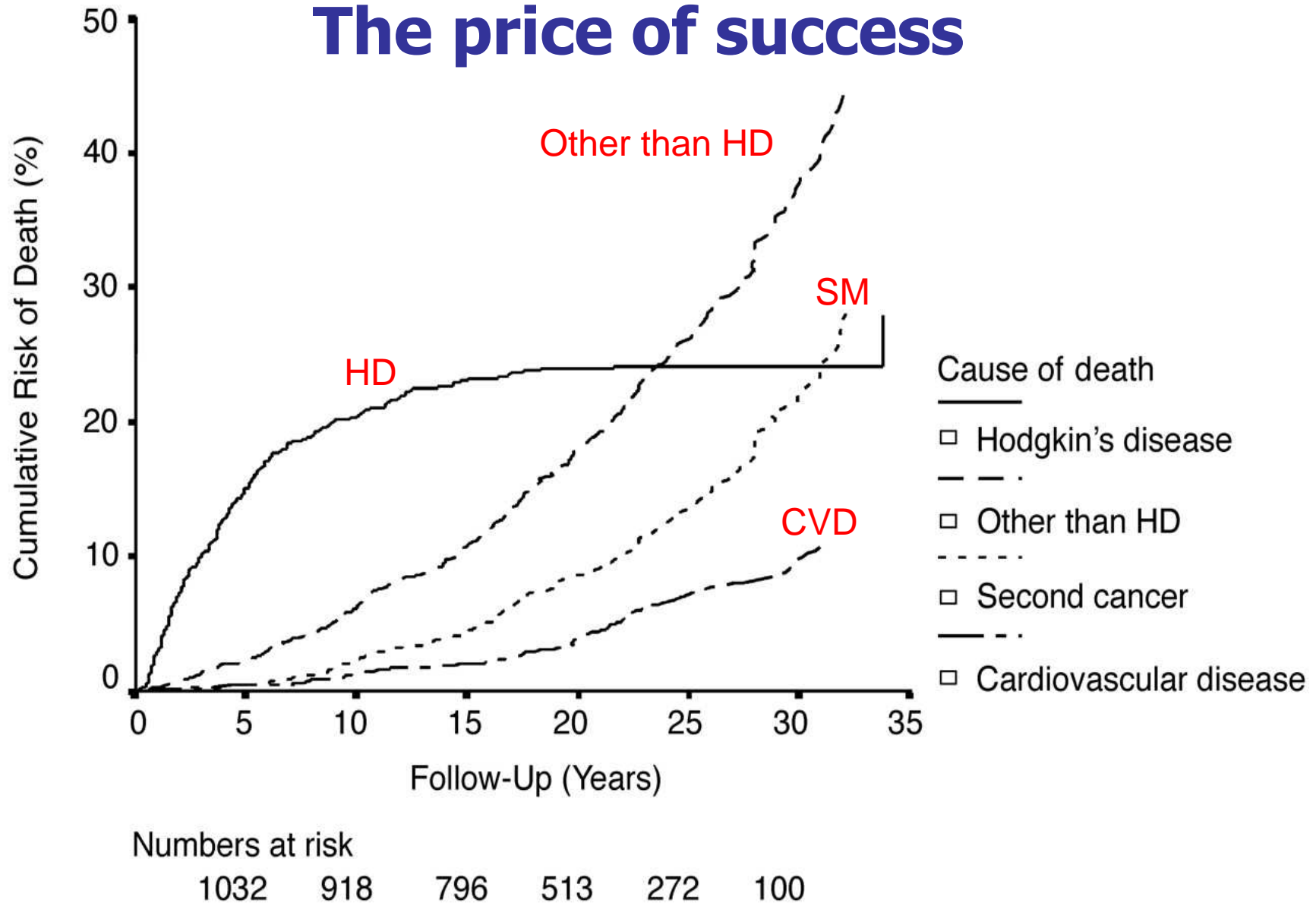


The Changing Role of Radiation Therapy in the Cure of Early Stage Hodgkin Lymphoma

- Radiation therapy alone with extended fields as standard (DFS @ 10 yrs: 80-90%)



The price of success

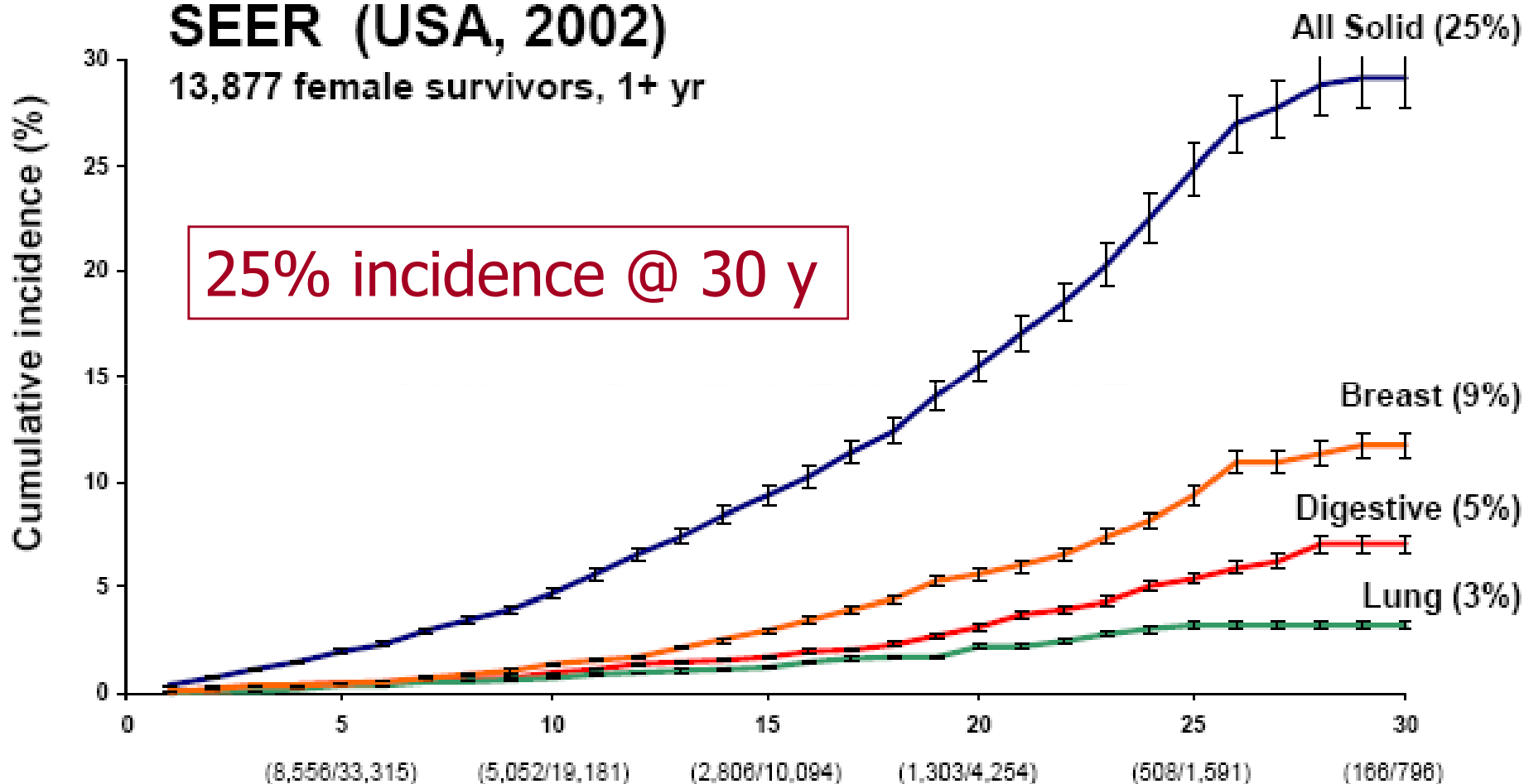


Aleman B., JCO 21; 18: 3431-3439, 2003

Second Cancer Risk After Hodgkin Lymphoma

SEER (USA, 2002)

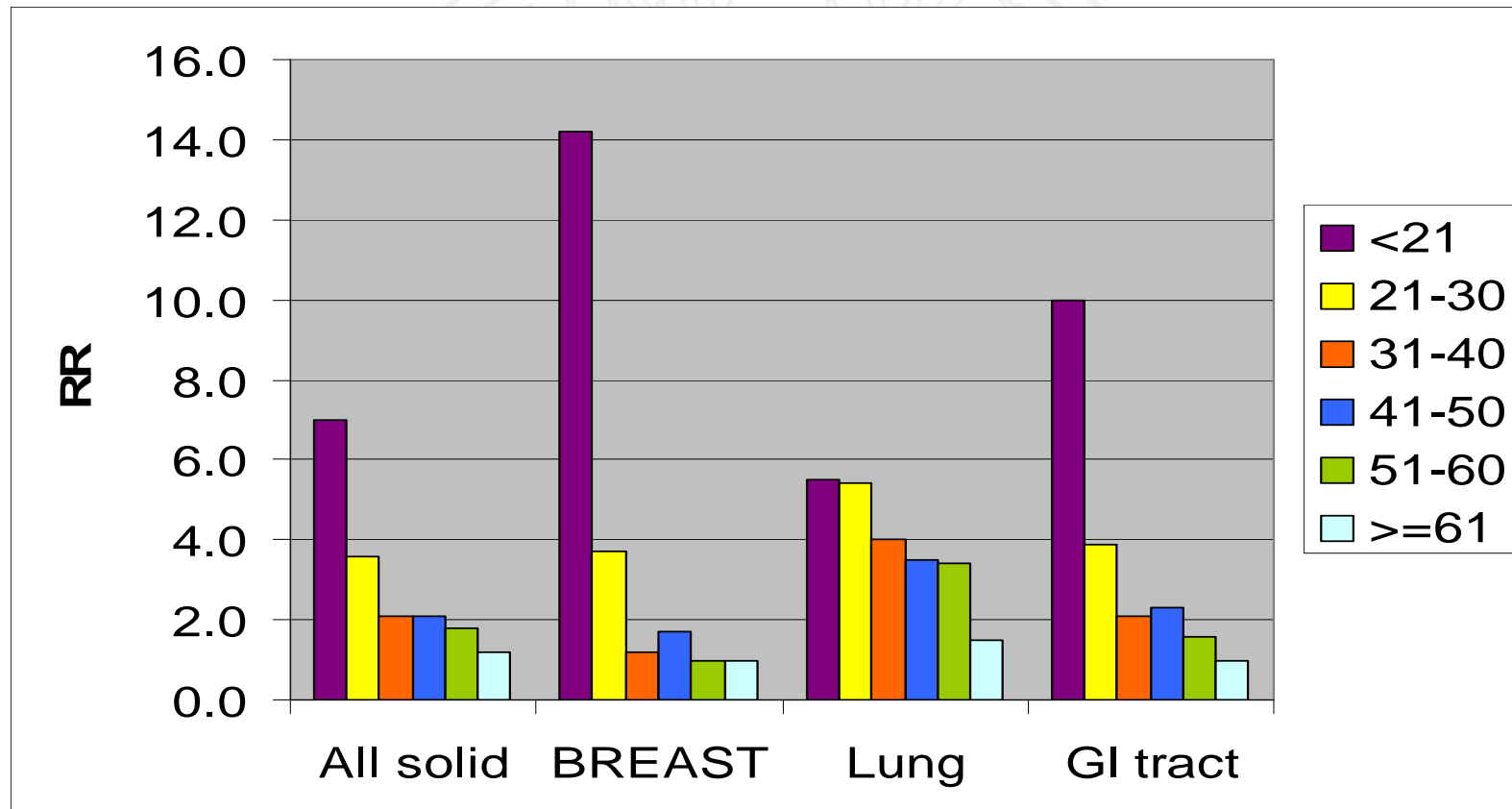
13,877 female survivors, 1+ yr



Dores et al JCO 20:3484, 2002

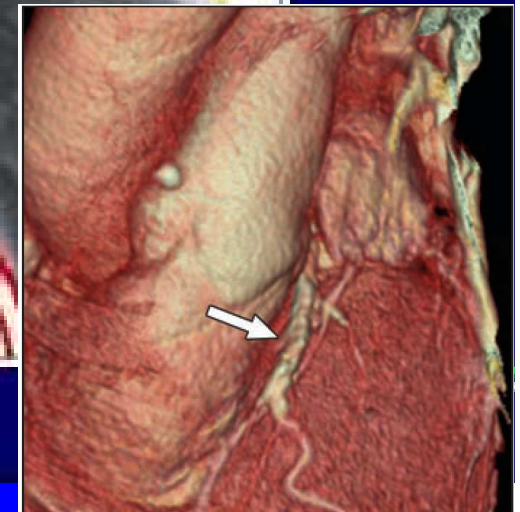
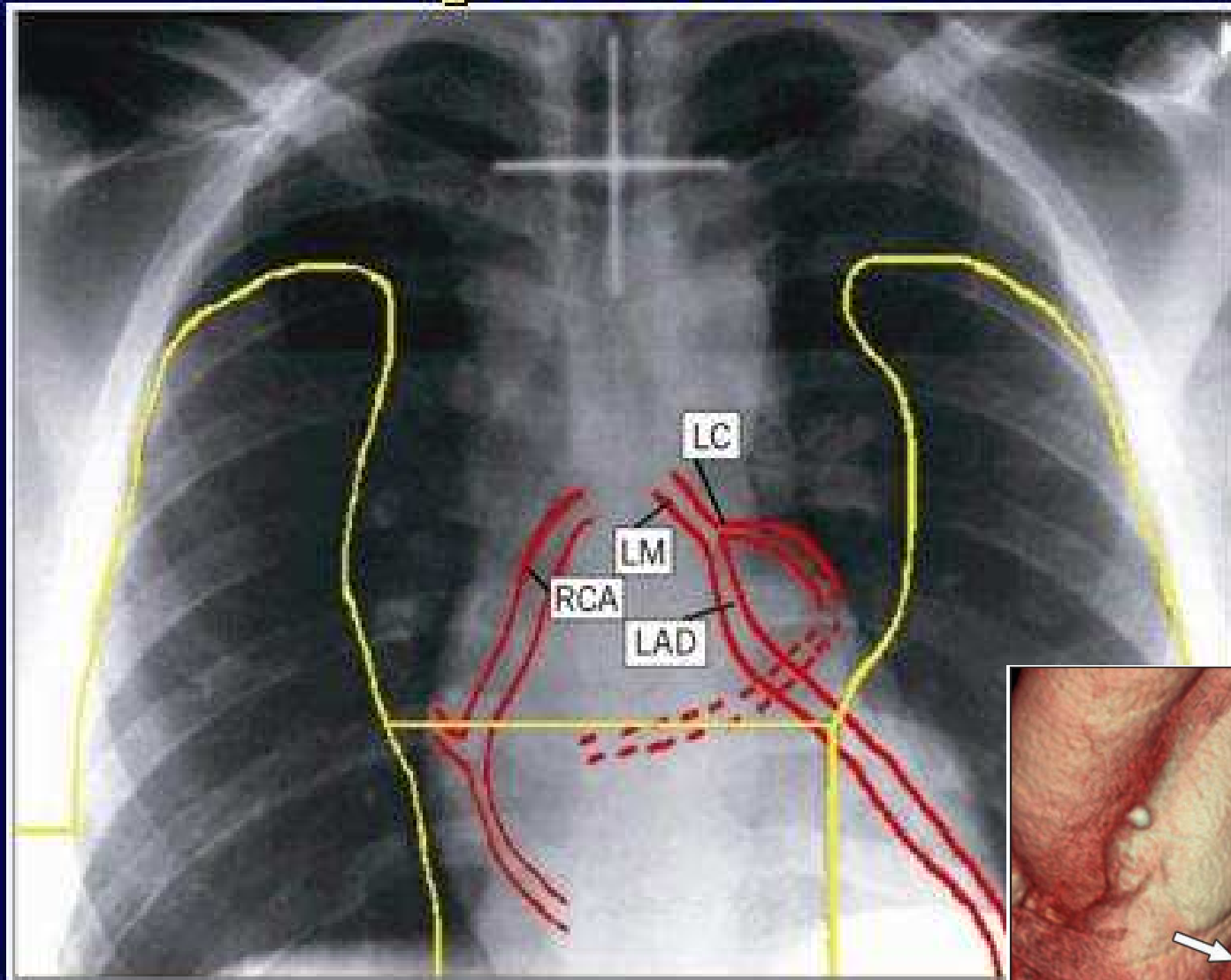
Relative risks of solid tumors by age at HL diagnosis

International cohort study: 32,591 HL patients
1,111 25-years survivors, population-based



Dores et al *JCO* 20:3484, 2002

Coronary Artery Disease



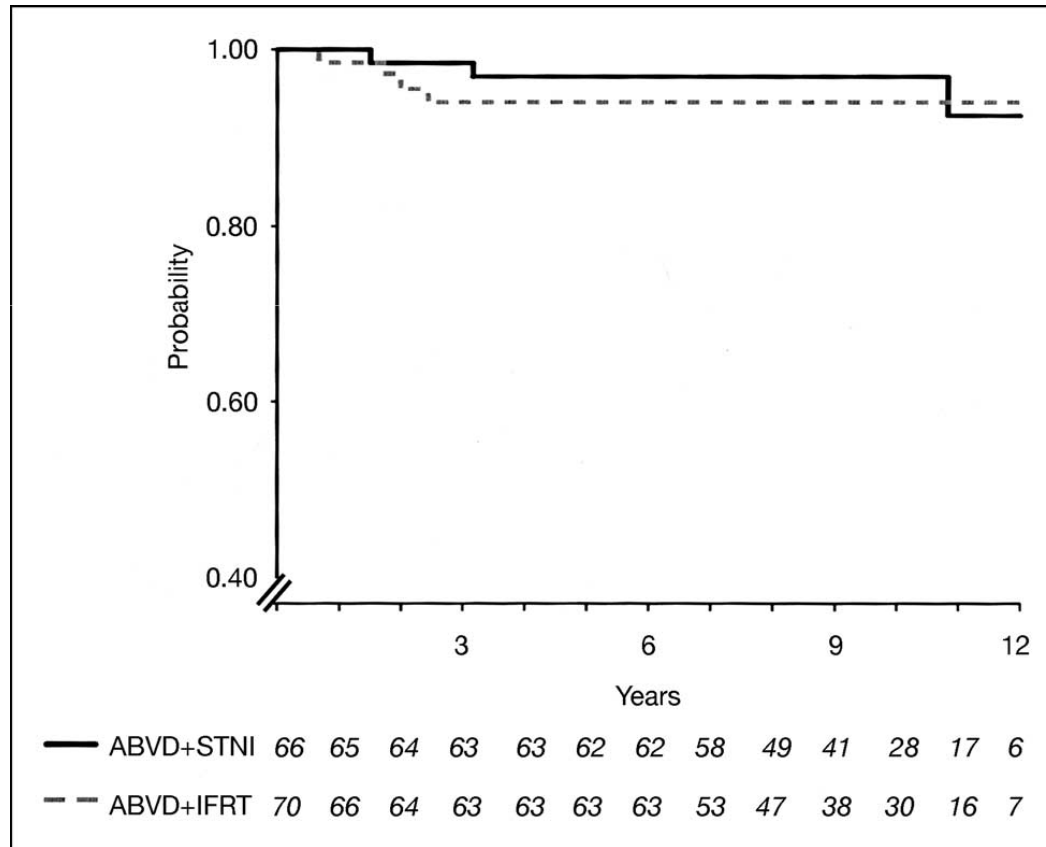
Current standard treatment in early stage cHL

- **Combined modality is the gold standard**
- **Short chemotherapy (3-4 cycles ABVD)**
- **36 Gy IFRT**



ABVD + STNI vs ABVD + IF-RT:

Bonadonna, JCO, 2004 [1+]



Other trials comparing
CMT with IF vs CMT
with EF:

Eich, IJROBP, 2005 [1+]

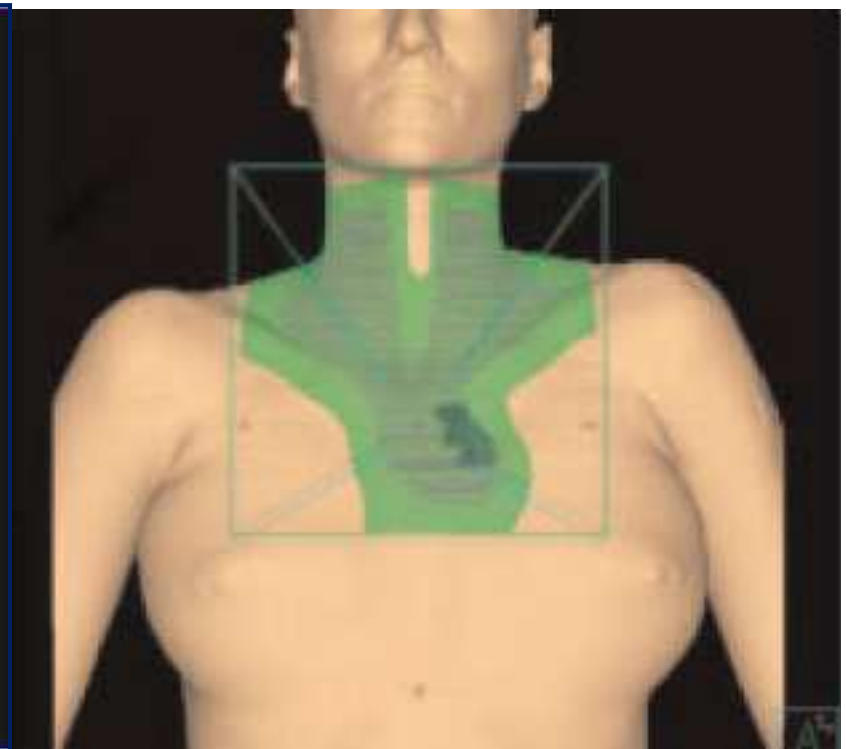
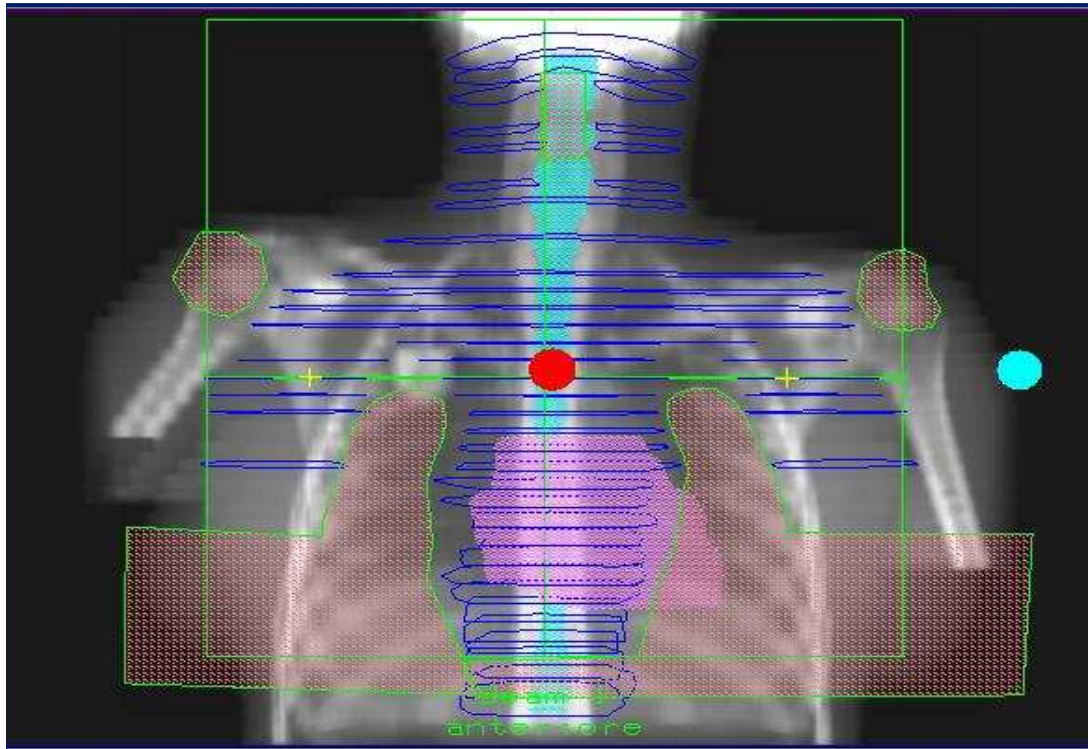
Gobbi, Cancer, 2003 [2]

The Involved Field Concept:

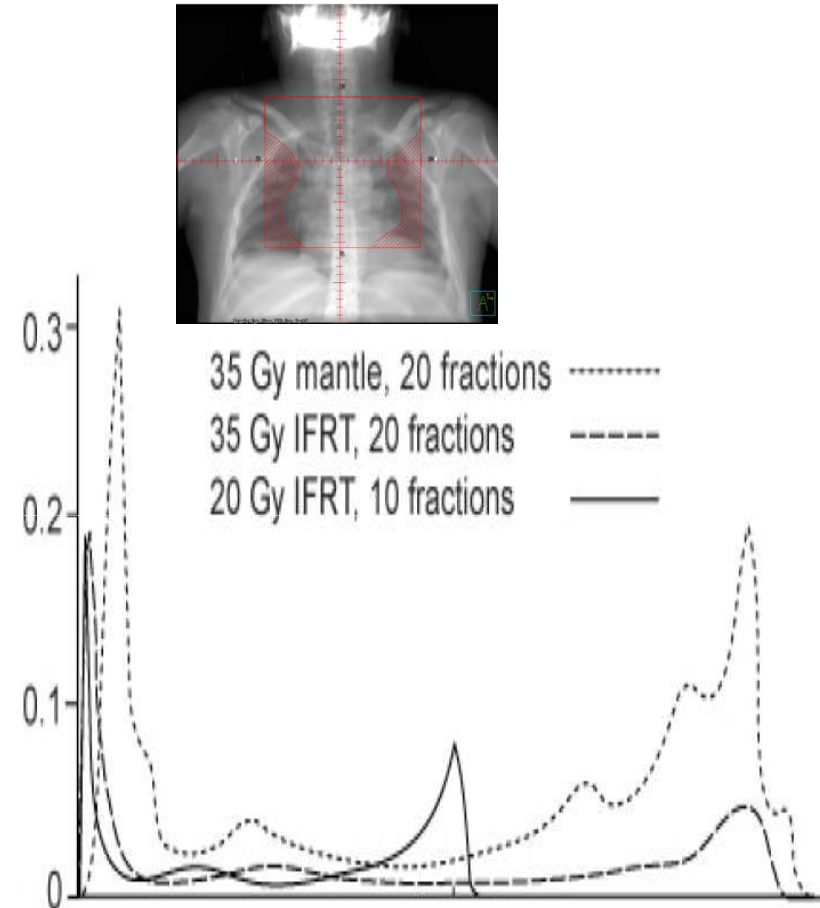
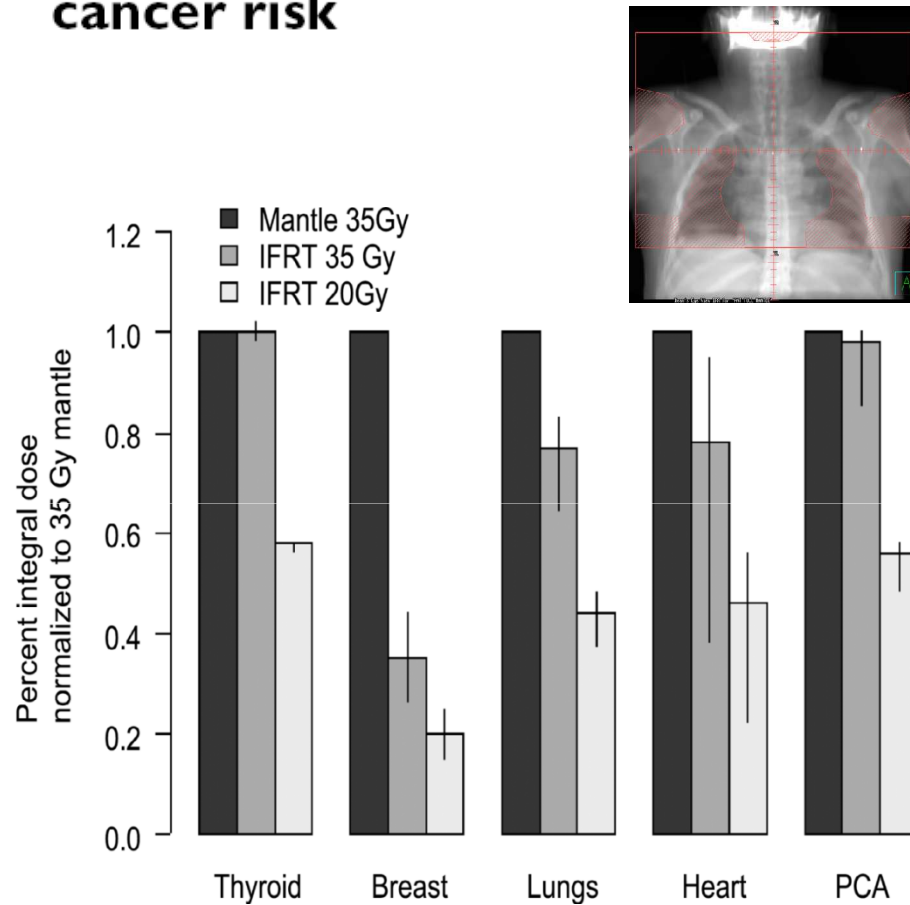
Yahalom J., *Annals of Oncology* 2002

- IF has become the standard field for irradiating patients after chemotherapy
- We treat a region, not an individual lymph node
- The main IF regions are: **neck** (unilateral, with supraclavicular), **mediastinum** (plus hilar regions), **axilla** (infra- and supraclavicular), **spleen**, **para-aortic**, **inguinal** (femoral and iliac)
- We use the initially involved prechemotherapy sites and volumes (exception: postchemo transverse diameter for mediastinal nodes)
- All borders are easy to outline (most are bony landmarks)

From EF-RT to IF-RT



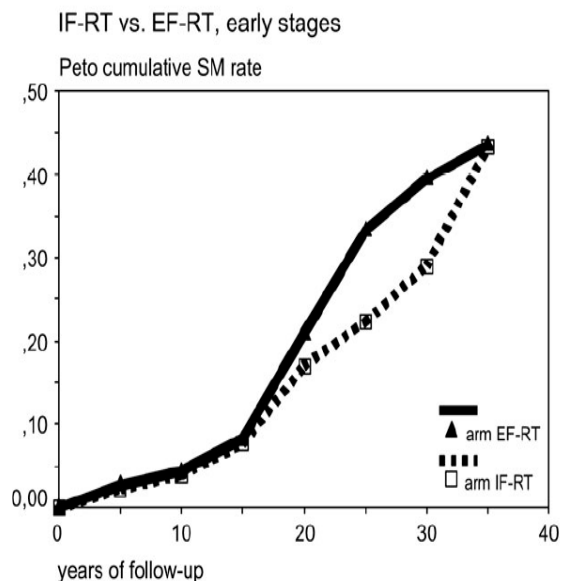
A comparison of mantle versus involved-field radiotherapy for Hodgkin's lymphoma: reduction in normal tissue dose and second cancer risk



The estimated ERR for radiation-induced breast cancer decreased by 64%. This is largely attributable to the smaller volume of breast tissue irradiated when axillary fields are omitted.

Second malignancy risk associated with treatment of Hodgkin's lymphoma: meta-analysis of the randomised trials

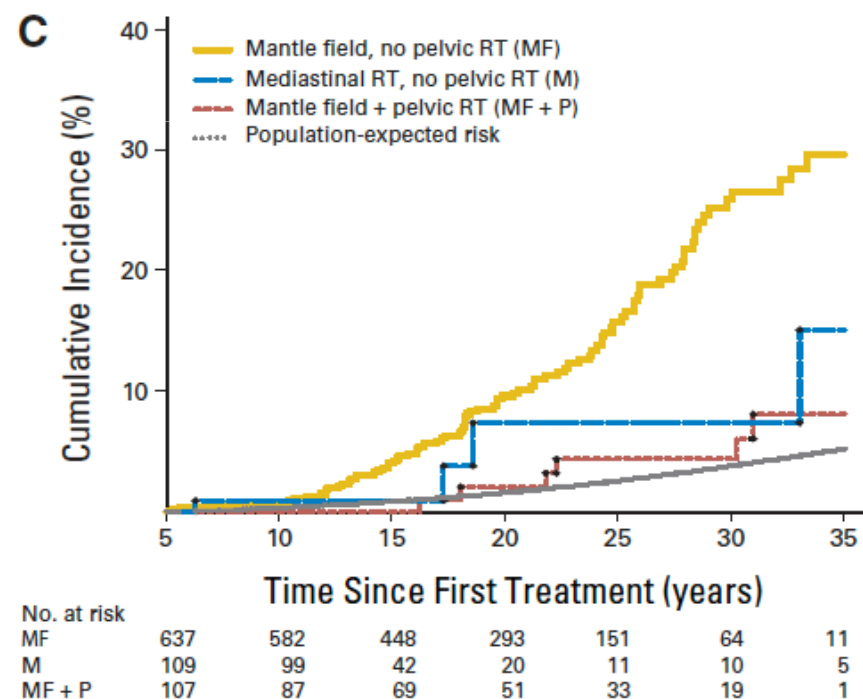
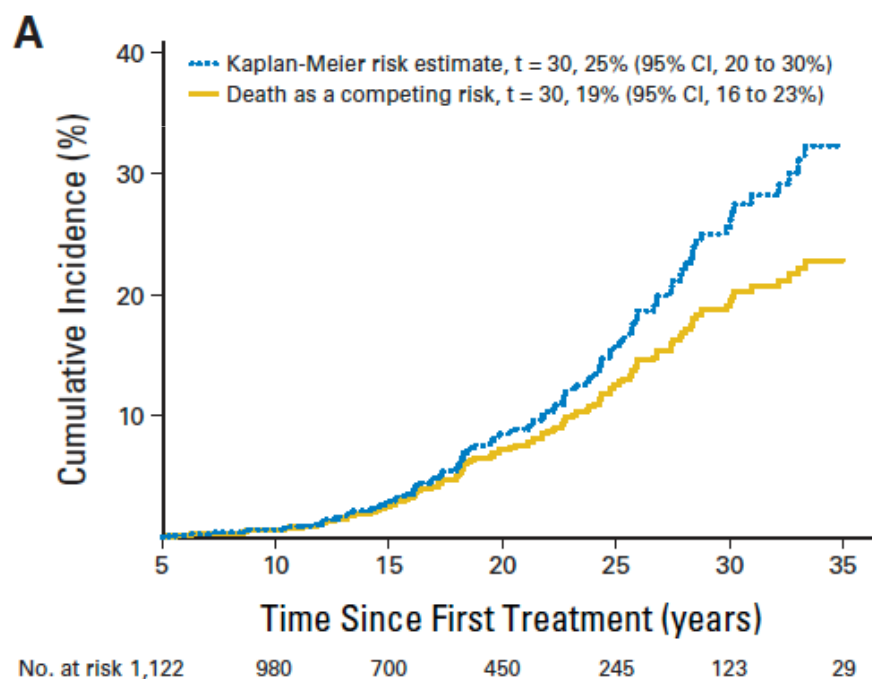
J. Franklin^{1*}, A. Pluetschow¹, M. Paus¹, L. Specht², A.-P. Anselmo³, A. Aviles⁴, G. Biti⁵, T. Bogatyreva⁶, G. Bonadonna⁷, C. Brillant¹, E. Cavalieri³, V. Diehl¹, H. Eghbali⁸, C. Fermé⁹, M. Henry-Amar¹⁰, R. Hoppe¹¹, S. Howard¹², R. Meyer¹³, D. Niedzwiecki¹⁴, S. Pavlovsky¹⁵, J. Radford¹⁶, J. Raemaekers¹⁷, D. Ryder¹⁶, P. Schiller¹, S. Shakhtarina⁶, P. Valagussa⁷, J. Wilimas¹² & J. Yahalom¹⁸



Breast cancer: significantly greater risk with EF-RT ($p = 0.04$, OR = 3.25) compared to IF-RT

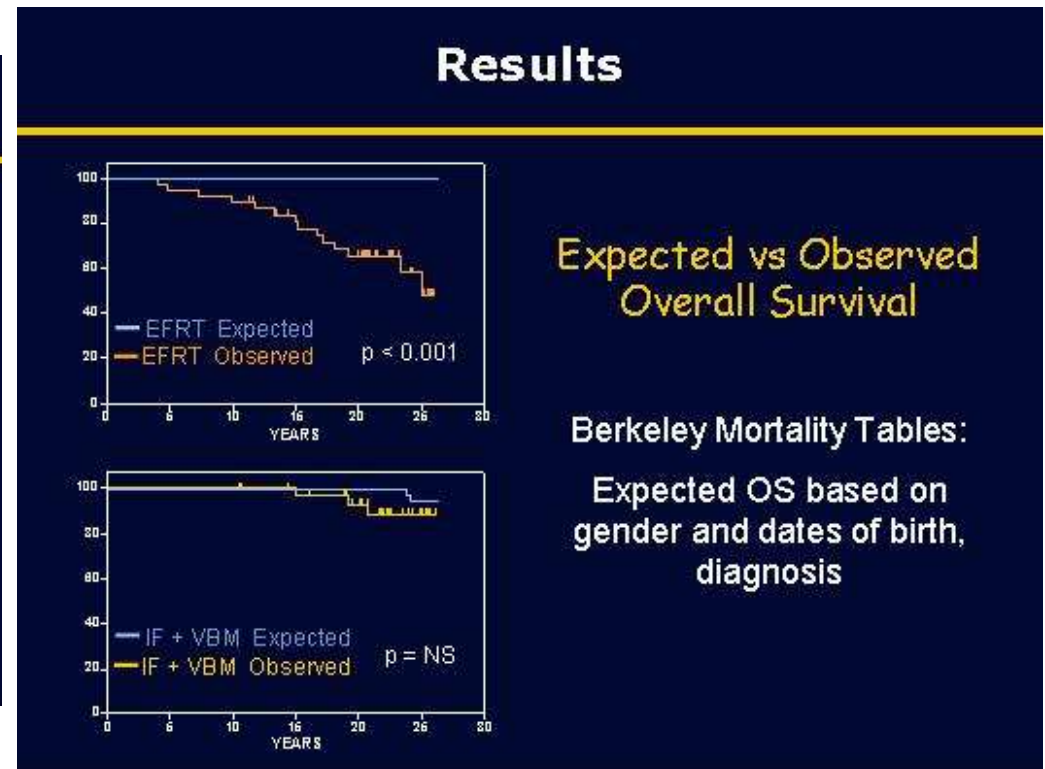
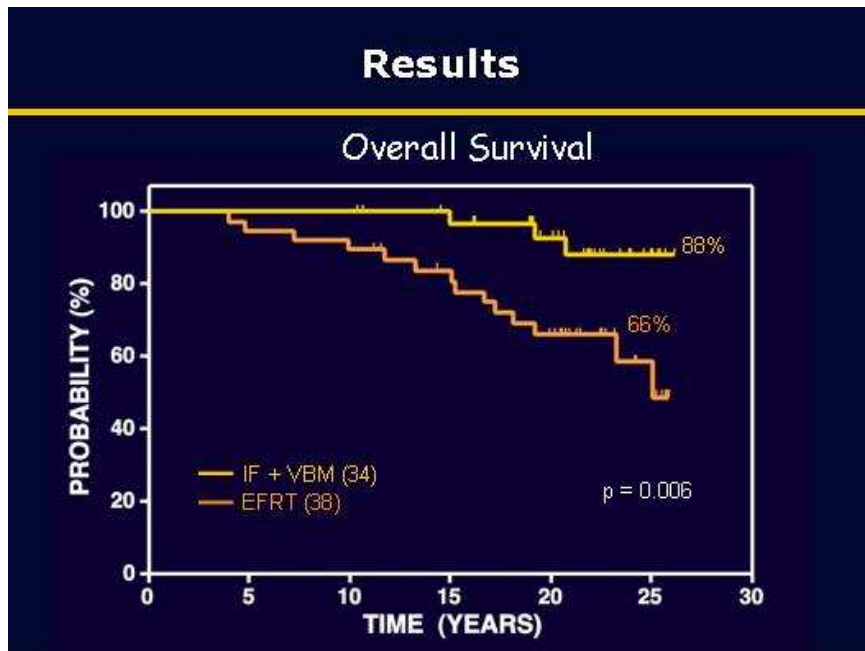
Breast Cancer Risk in Female Survivors of Hodgkin's Lymphoma: Lower Risk After Smaller Radiation Volumes

Marie L. De Bruin, Judith Sparidans, Mars B. van't Veer, Evert M. Noordijk, Marieke W.J. Louwman, José M. Zijlstra, Hendrik van den Berg, Nicola S. Russell, Annegien Broeks, Margreet H.A. Baaijens, Berthe M.P. Aleman, and Flora E. van Leeuwen



Long term outcome after IF-RT:

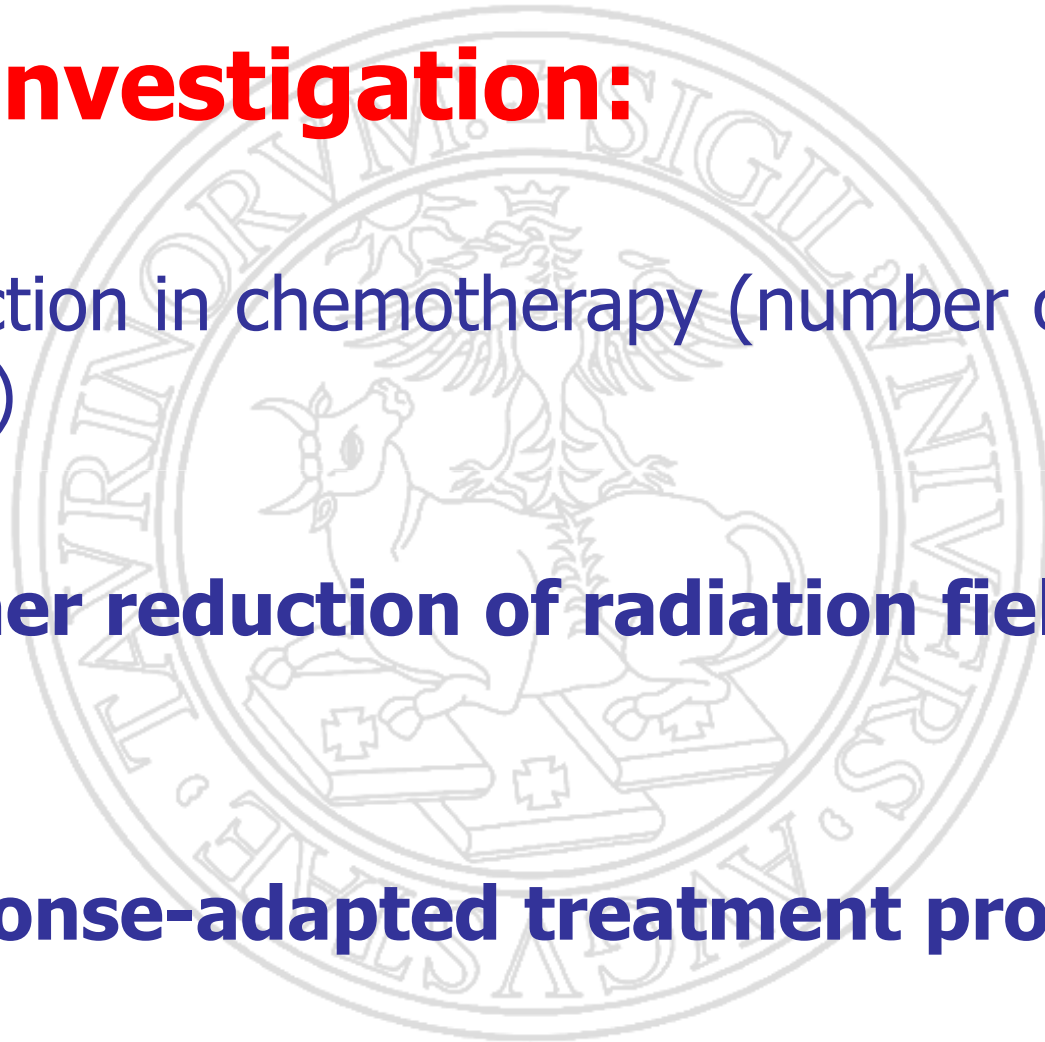
Extrapolation of late effects after EF-RT to current IF + chemotherapy regimens can be misleading (Horning, ASCO 2007)



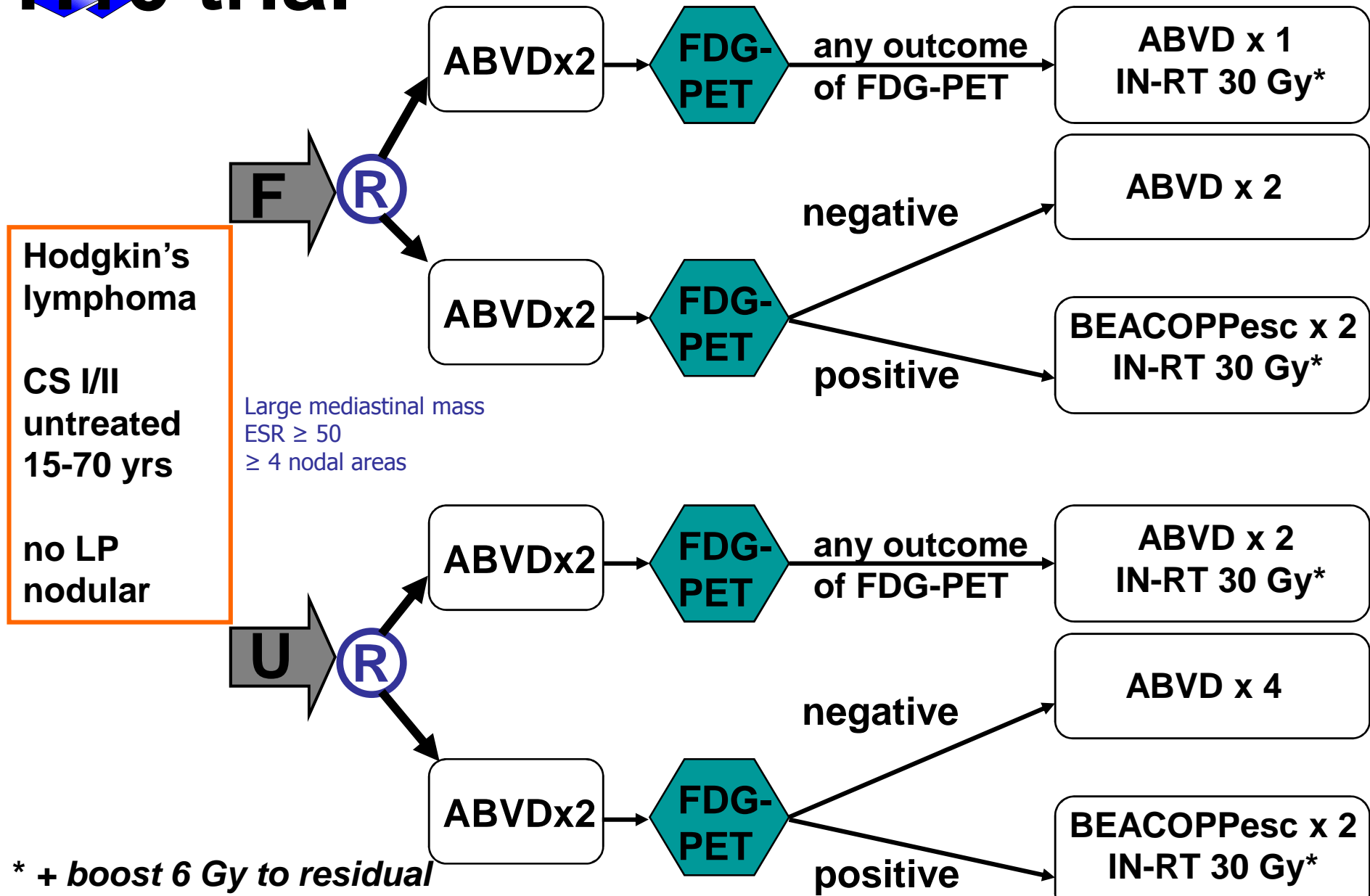
Long-term mortality of CMT (VBM + IFRT 36 Gy) does not overcome expected mortality: **impact of radiation volumes reduction in lowering long term mortality**

Under investigation:

- Reduction in chemotherapy (number of cycles, drugs)
- **Further reduction of radiation fields and doses**
- **Response-adapted treatment protocols**

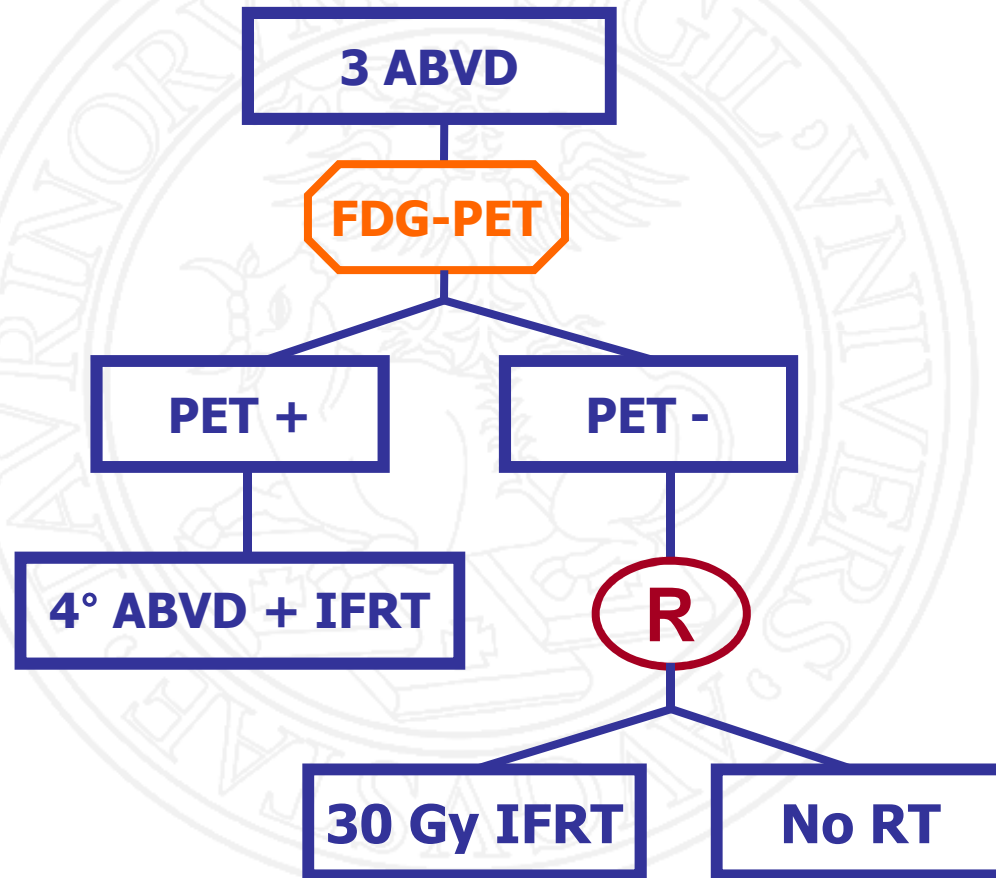


H10 trial

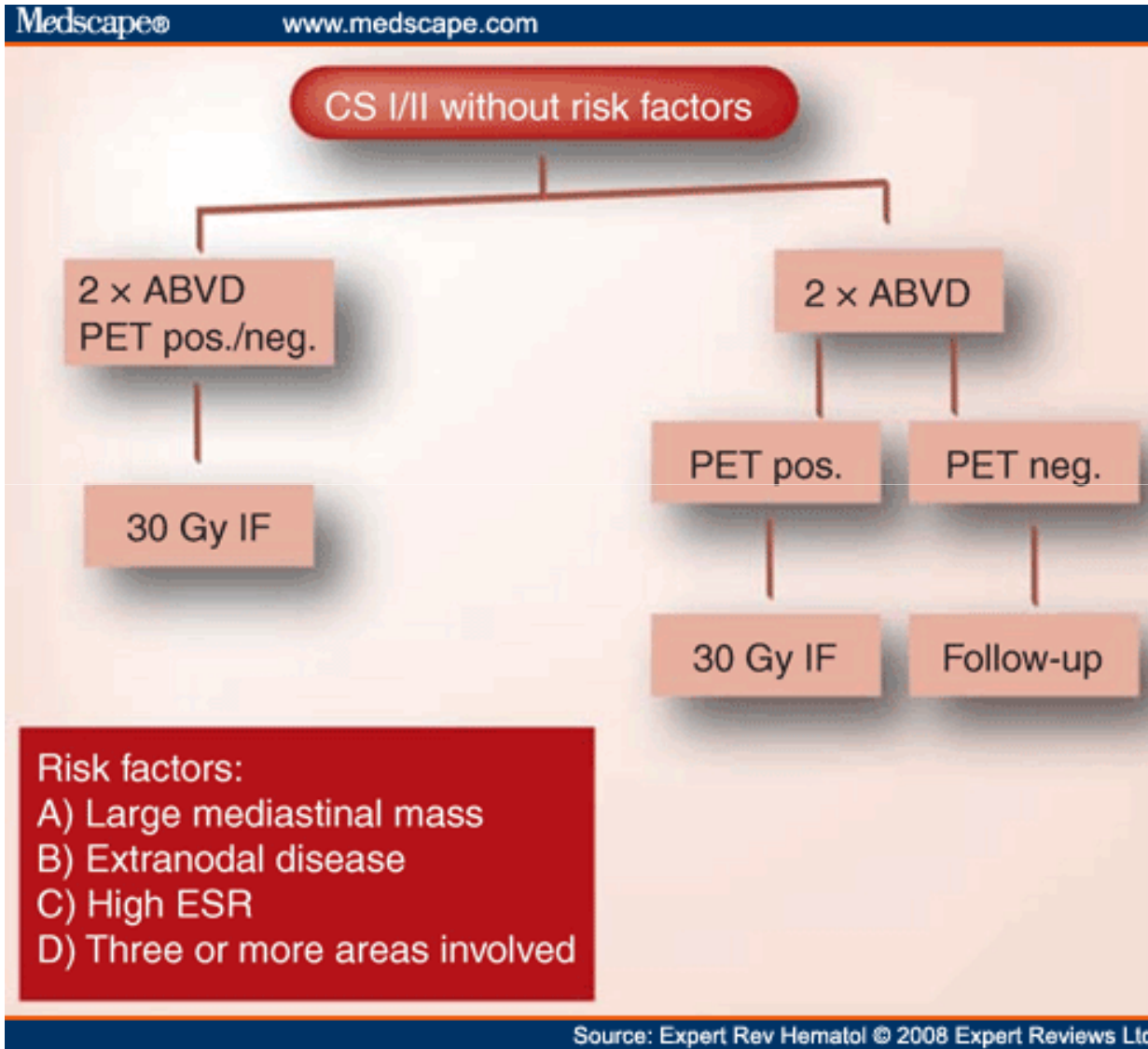


PET-response Adapted Therapy

The UK Trial: early stage



GHSG Study HD16



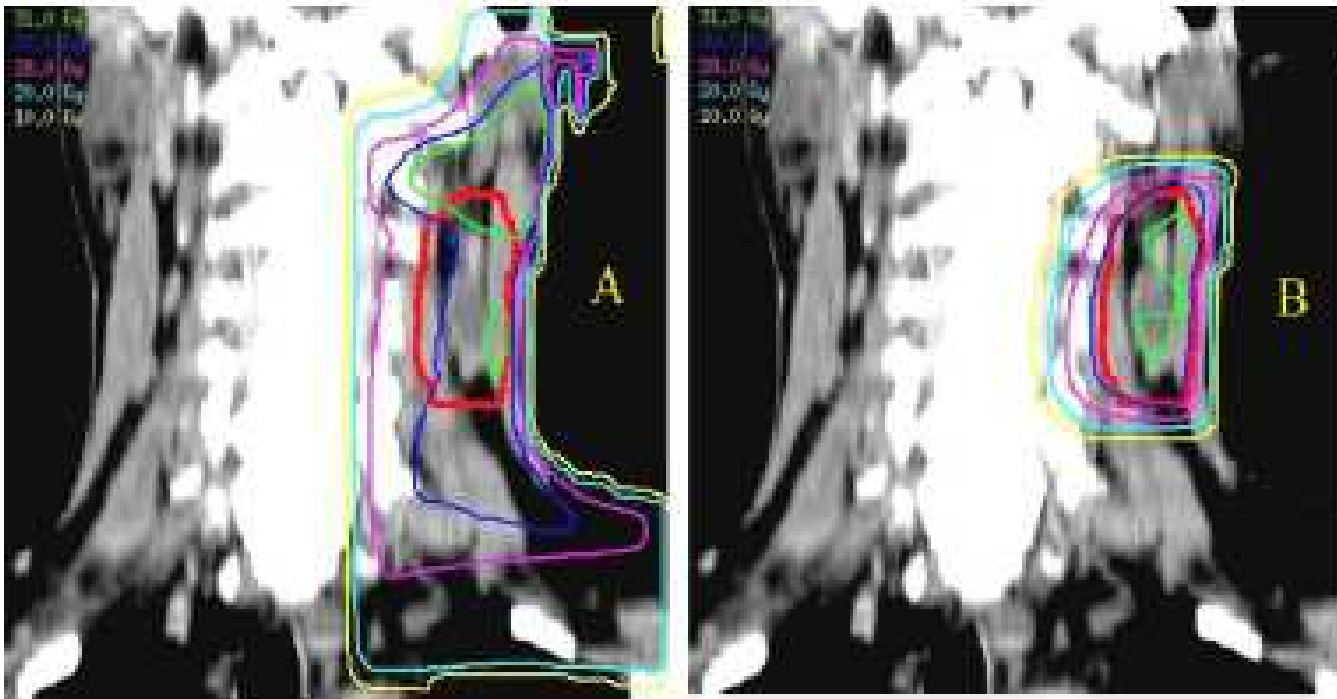
EORTC-GELA-IIL H10 study



- **Is chemotherapy alone as effective -but less toxic- as combined modality treatment in early stages HL who are PET-negative after two cycles of ABVD?**
 - **Response adapted treatment**
- **Can new RT fields further reduce toxicity?**
 - **From IFRT to INRT**



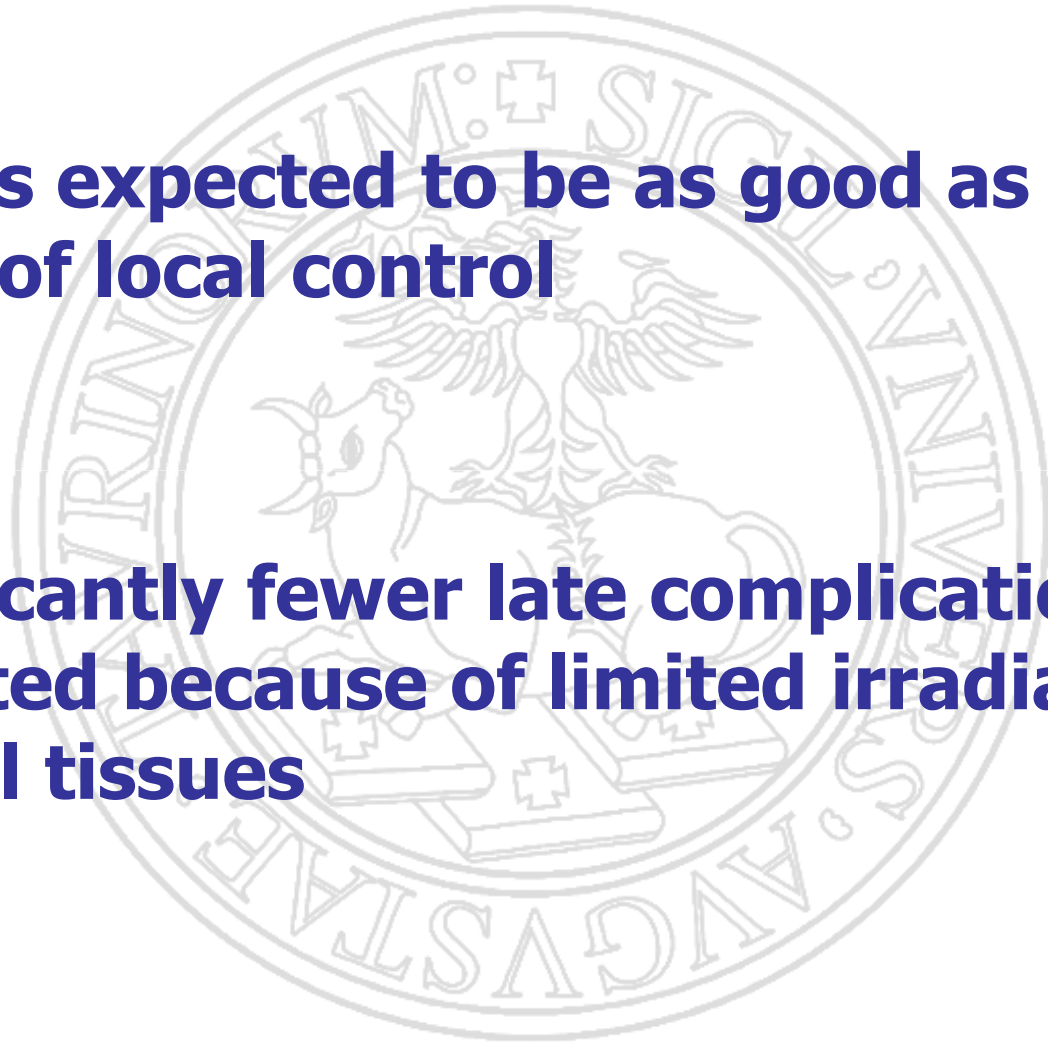
From IF-RT to IN-RT



- The concept of **IF-RT** which included the whole initially involved lymph node region can now be replaced by the concept of **involved-node RT**, which only includes the initially involved lymph node(s)

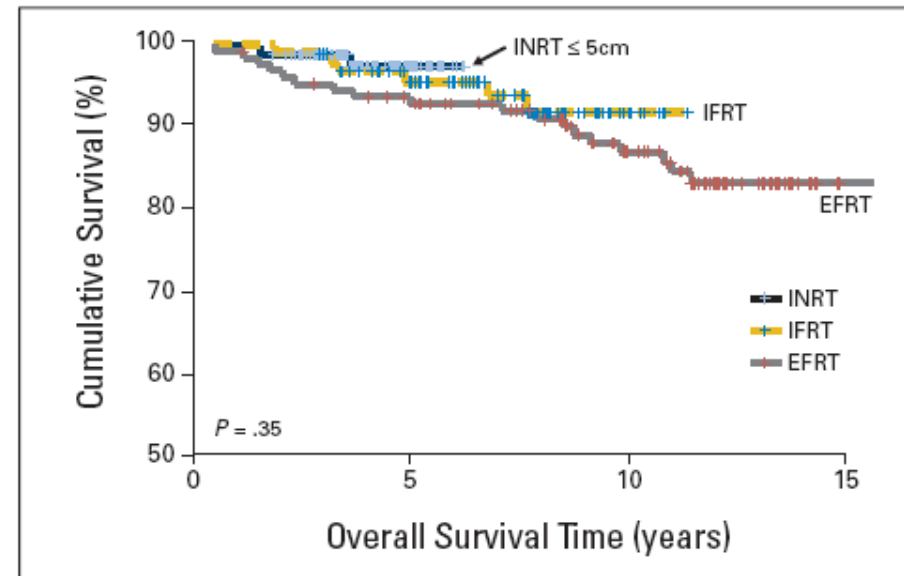
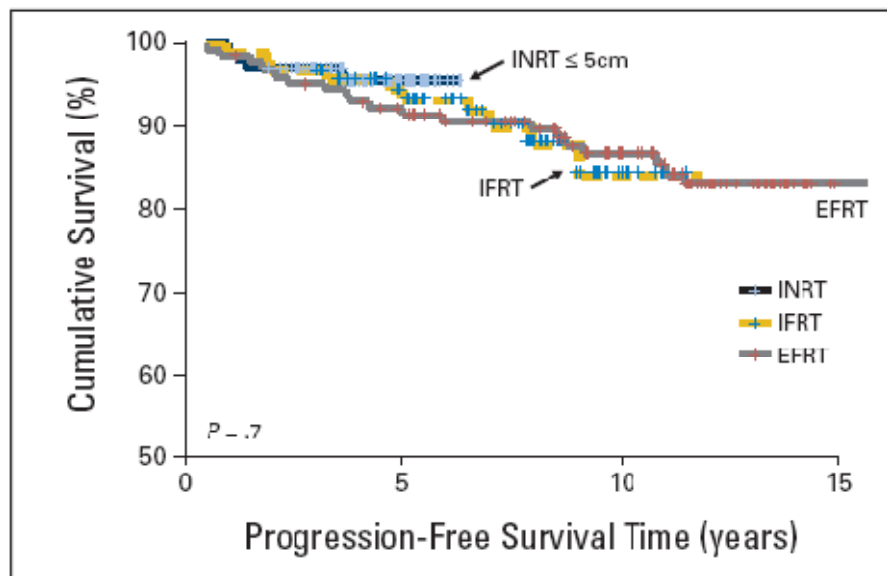
Reducing RT fields: from IFRT to INRT

- **INRT is expected to be as good as IFRT in terms of local control**
- **Significantly fewer late complications are expected because of limited irradiation of normal tissues**



Involved-Nodal Radiation Therapy As a Component of Combination Therapy for Limited-Stage Hodgkin's Lymphoma: A Question of Field Size

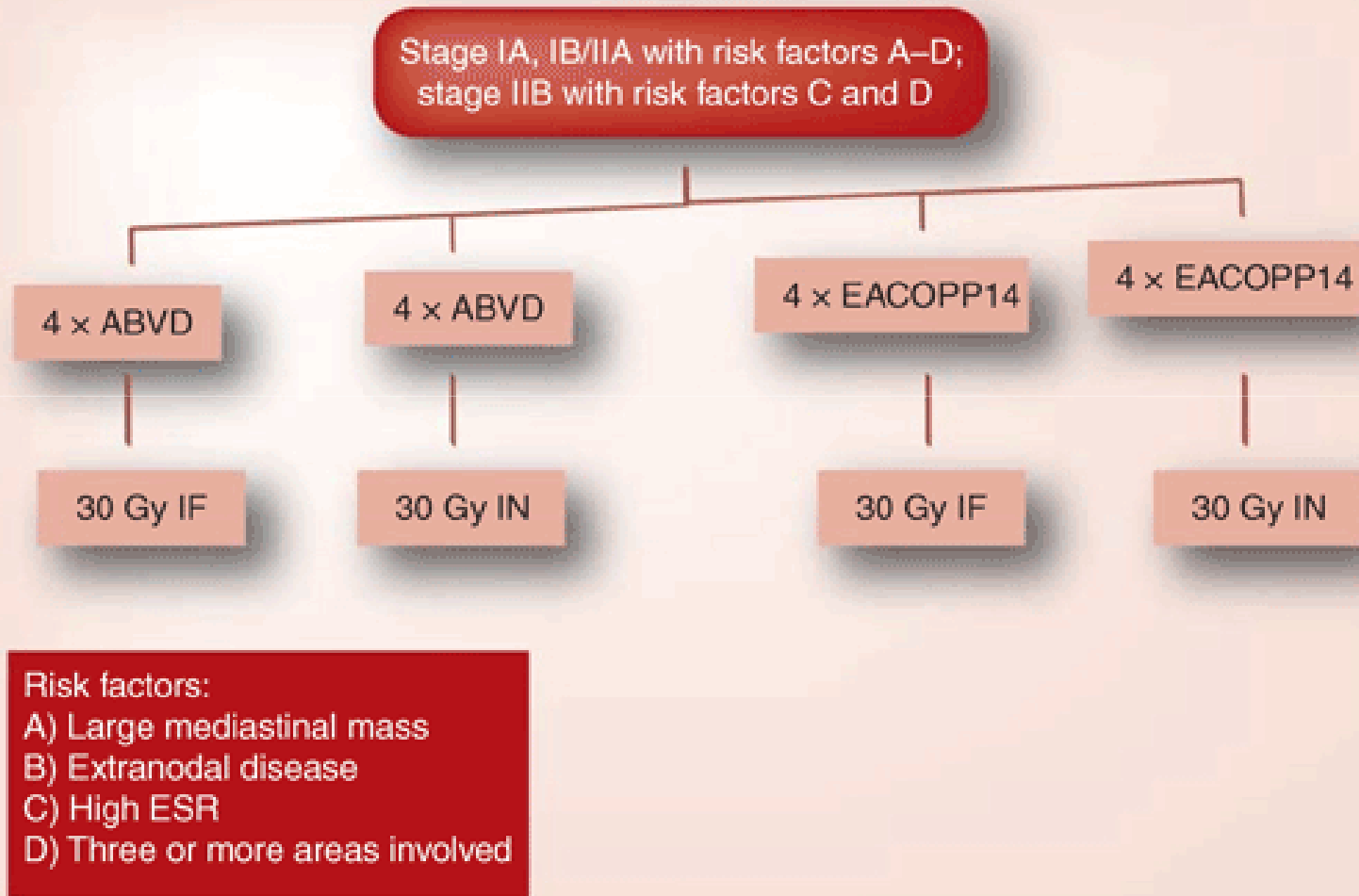
Belinda A. Campbell, Nick Voss, Tom Pickles, James Morris, Randy D. Gascoyne, Kerry J. Savage, and Joseph M. Connors



GHSB Study HD17

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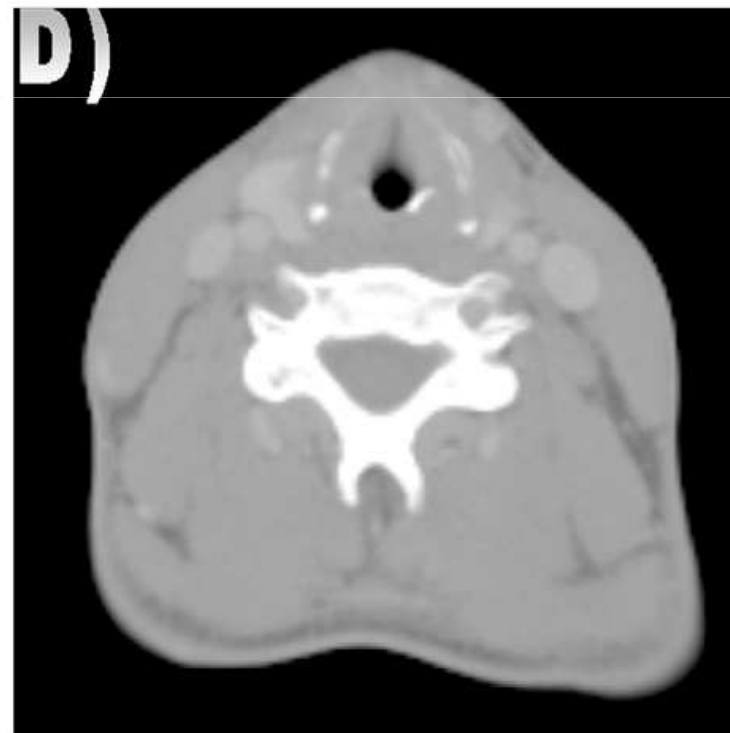
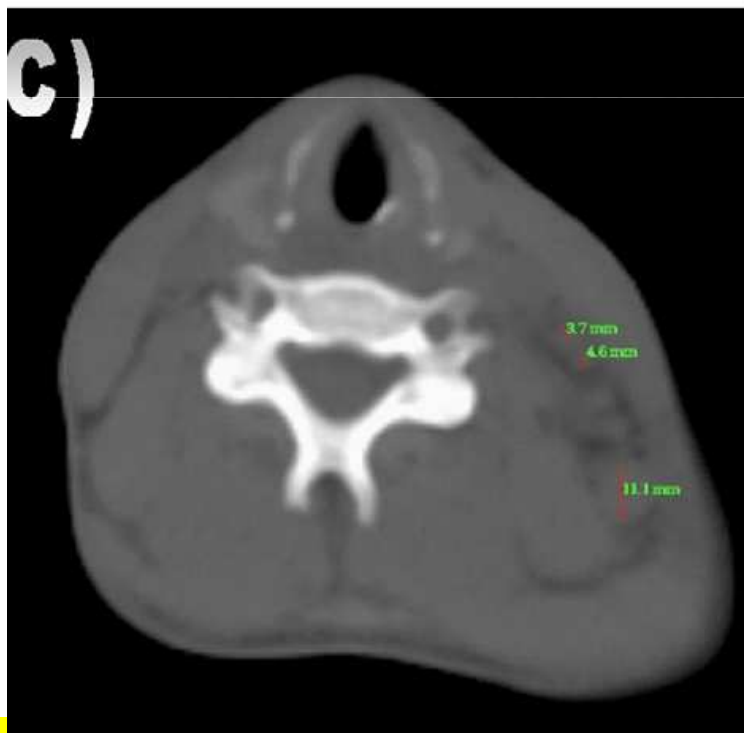
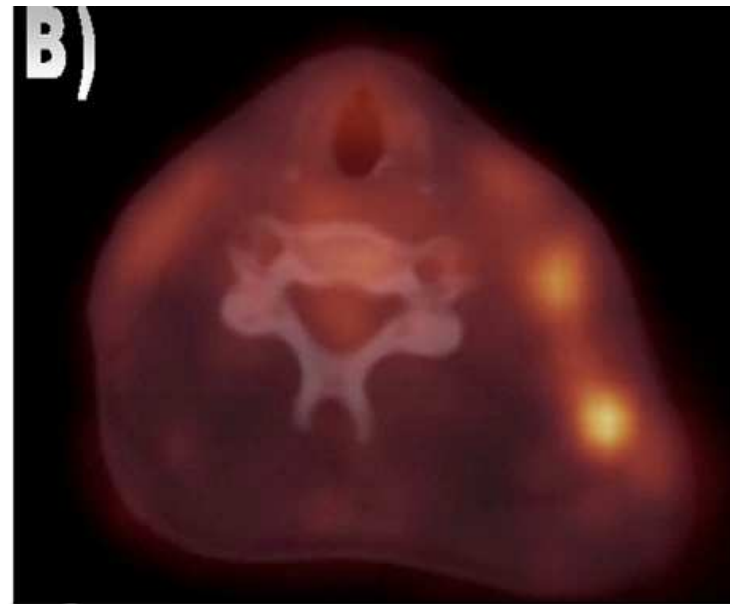
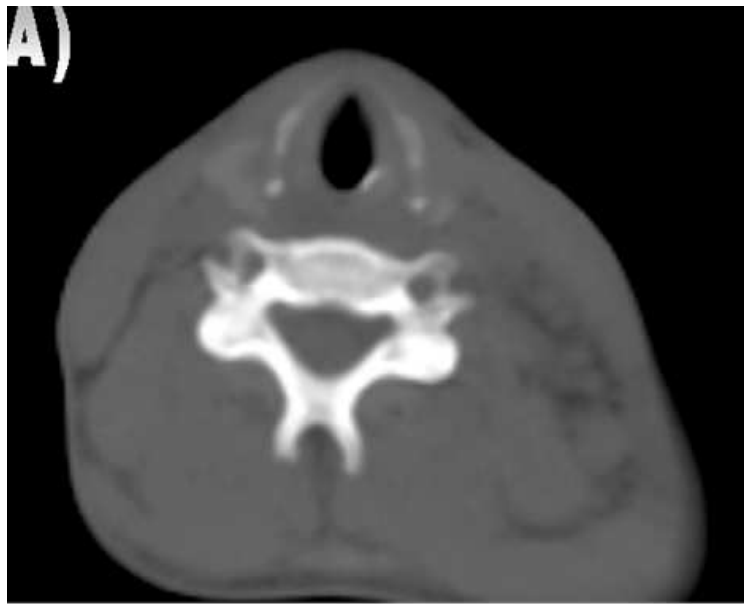
Reducing RT fields: from IFRT to INRT

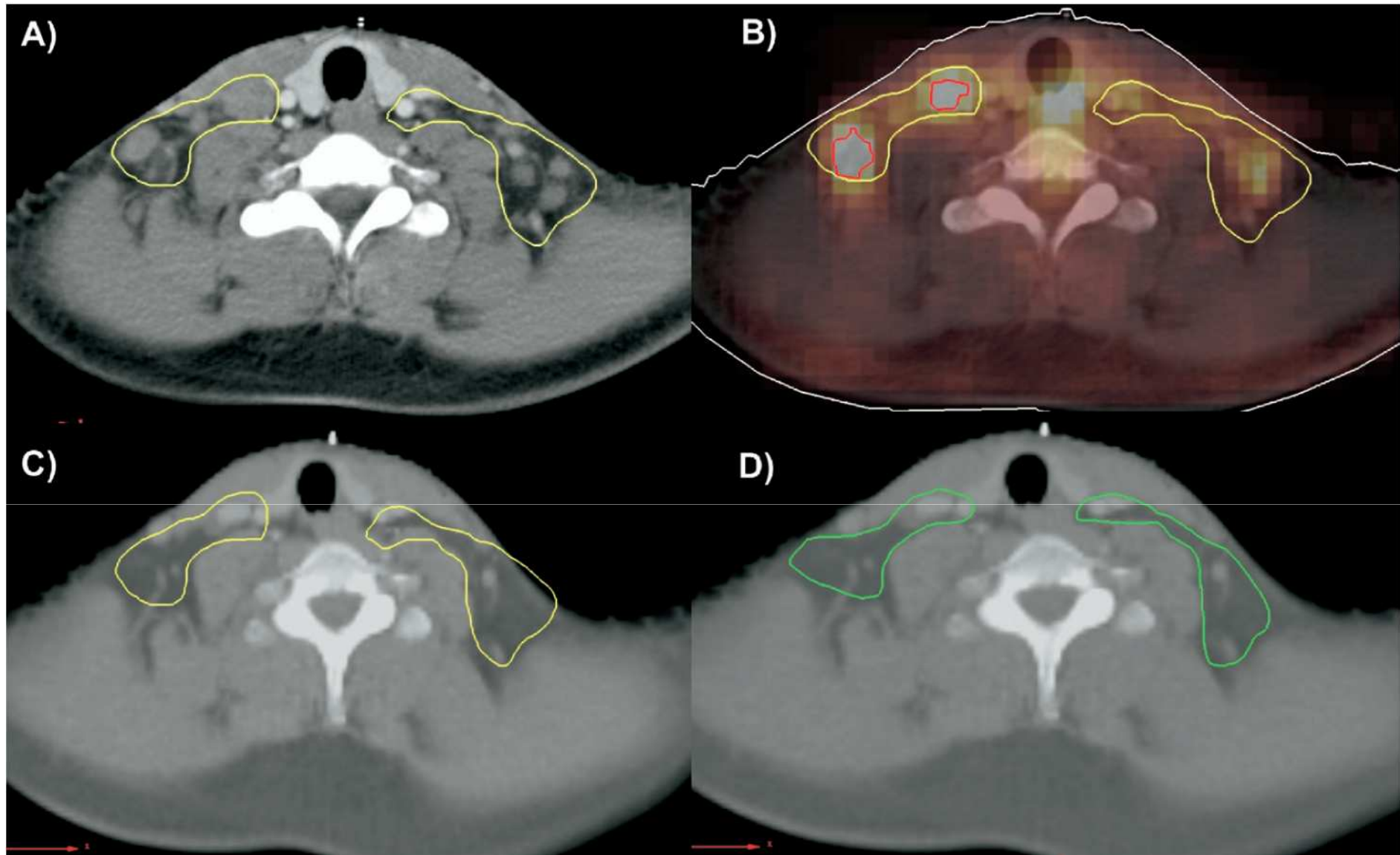
Involved-node radiotherapy (INRT) in patients with early Hodgkin lymphoma: Concepts and guidelines

Theodore Girinsky^{a,*}, Richard van der Maazen^b, Lena Specht^c, Berthe Aleman^d, Philip Poortmans^e, Yolande Lievens^f, Paul Meijnders^g, Mithra Ghalibafian^a, Jacobus Meerwaldt^h, Evert Noordijkⁱ, on behalf of the EORTC-GELA Lymphoma Group

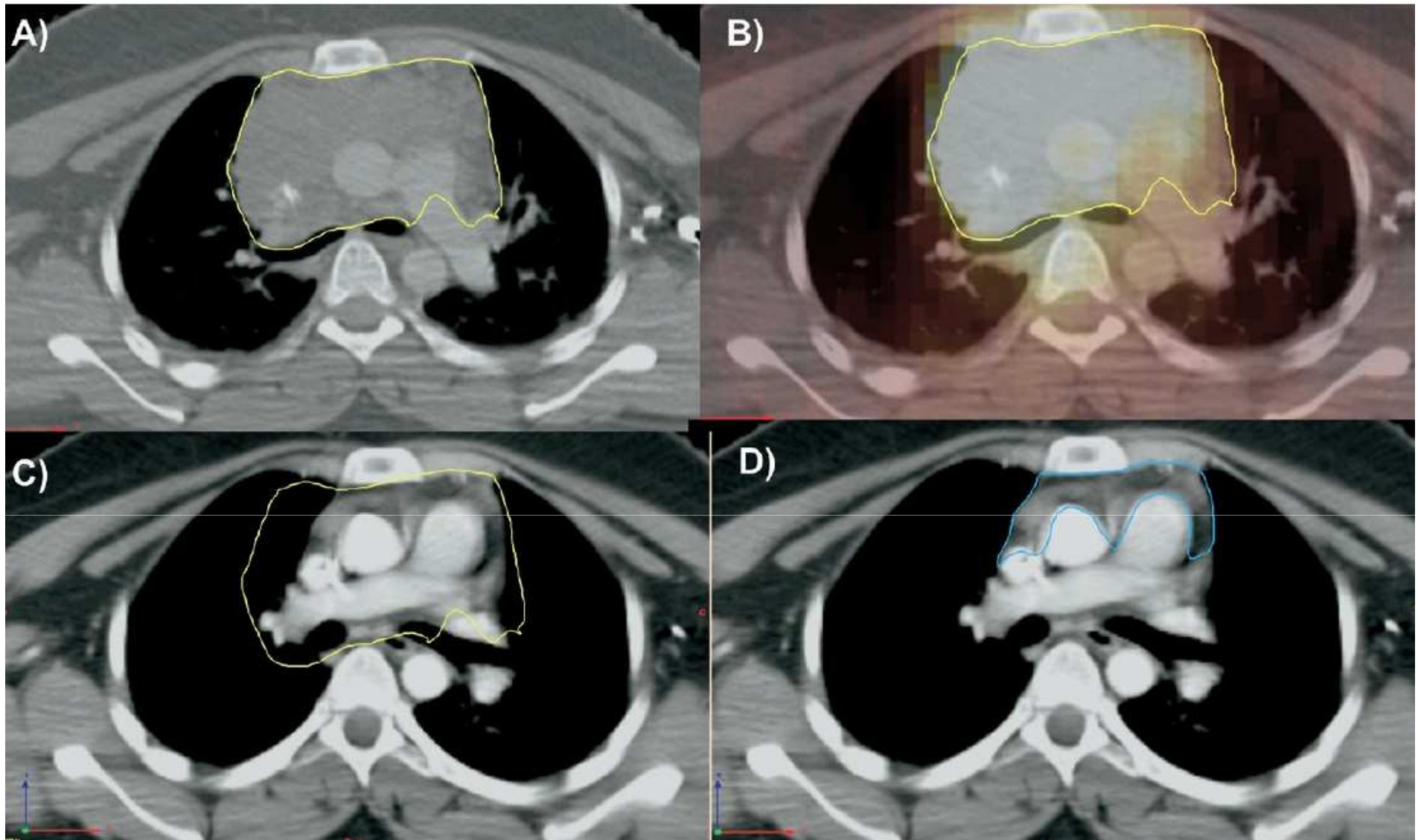
Assessment of initial lymph node involvement

- CT assessment can be extremely difficult
 - Usefulness of FDG-PET
 - Asymmetry on CT and/or FDG-PET
 - Comparison of pre- and post-chemotherapy CT scans (decrease in size or disappearance: surrogate proof of initial involvement)



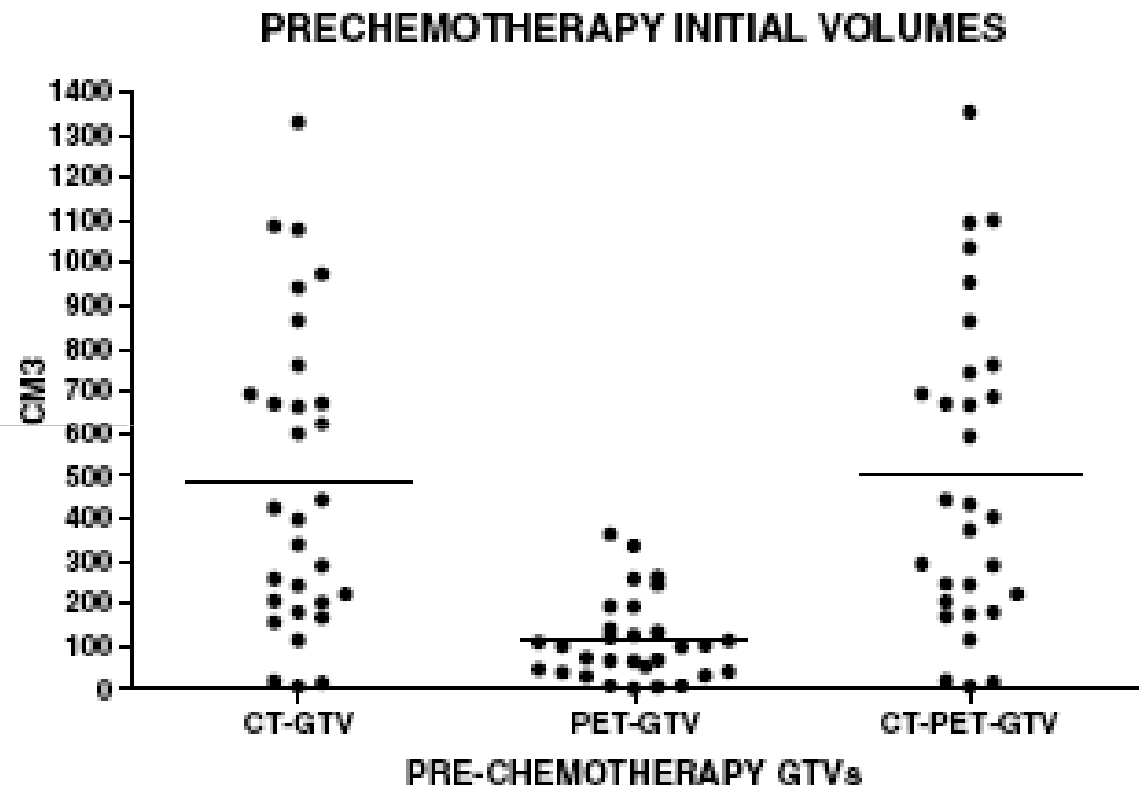
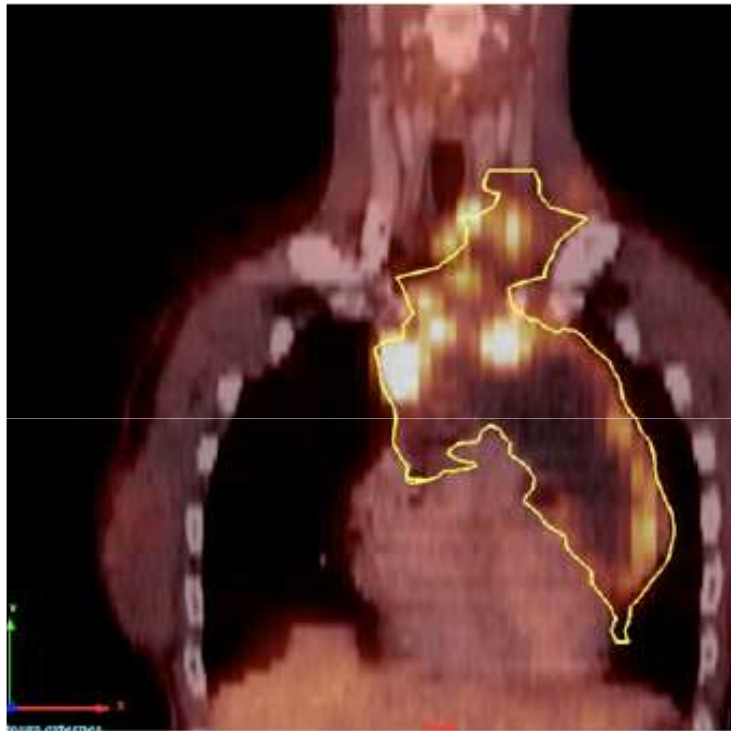


Adjustment of pre-chemotherapy CTV to post-chemotherapy CTV, to correct for shrinkage and replacement of normal structures

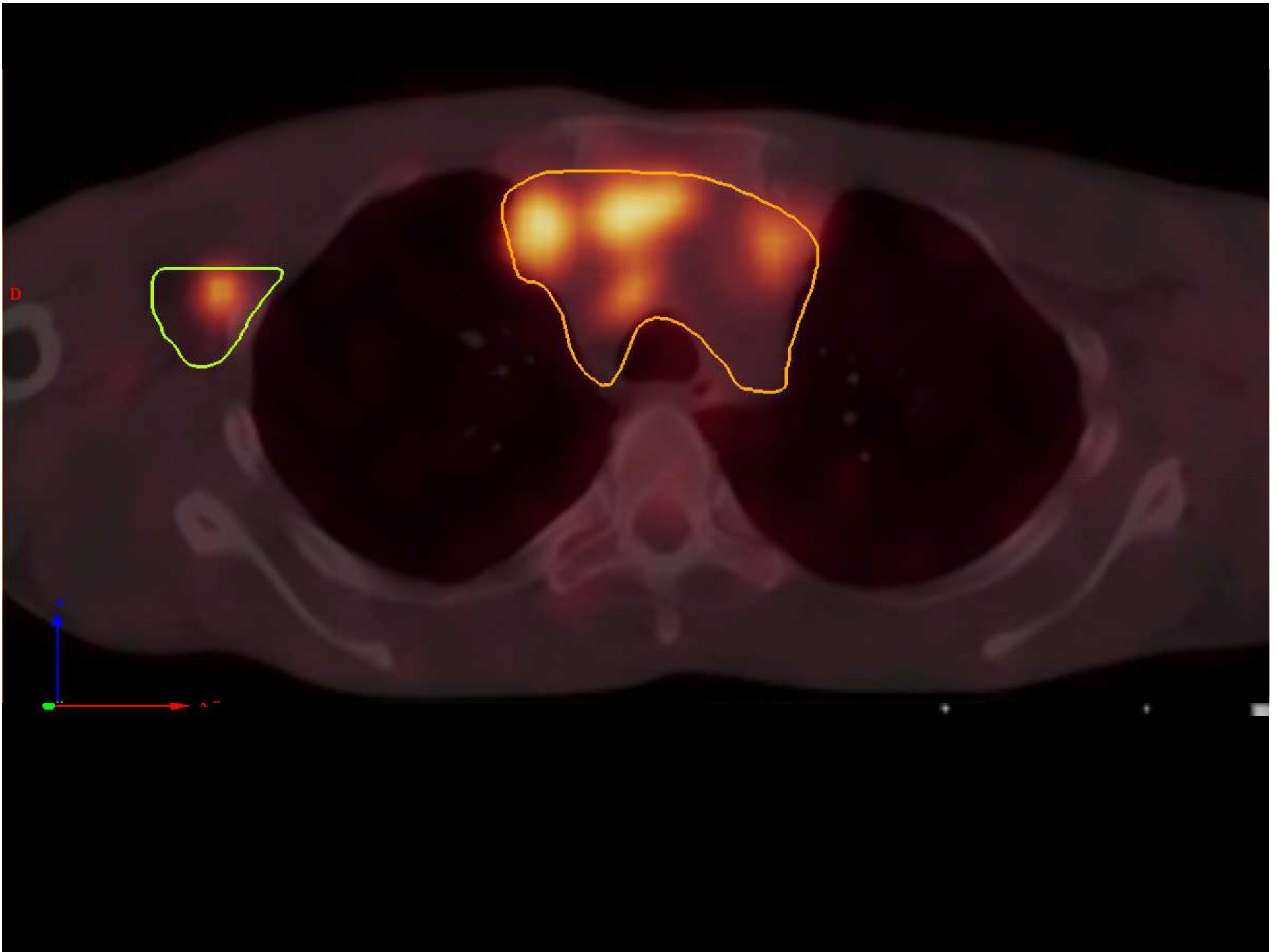


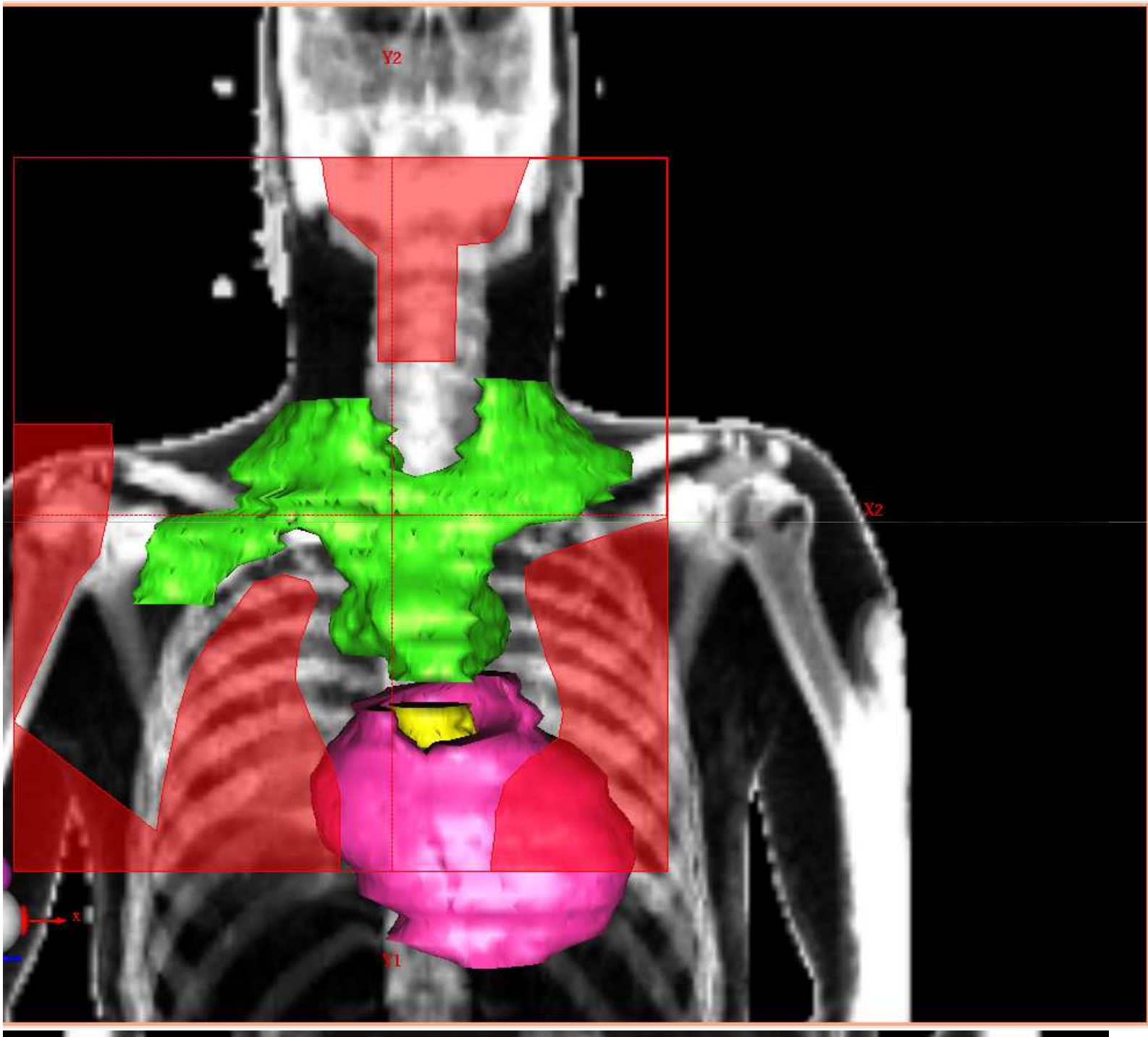
Adjustment of pre-chemotherapy GTV to post-chemotherapy GTV, to correct for shrinkage and replacement of normal structures

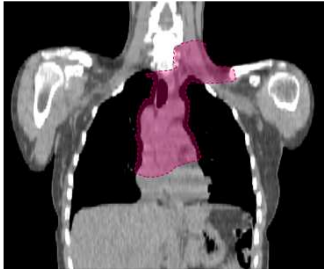
CT-PET not useful for radiation planning



FDG-PET avid areas represent a small part of the CT-GTV (approximately 25% of the total tumor mass seen on CT)







IFRT

Significant Reduction of Second Breast Cancer Risk in Patients Treated with Involved Nodes Radiation Therapy for Early Stage Hodgkin's Lymphoma



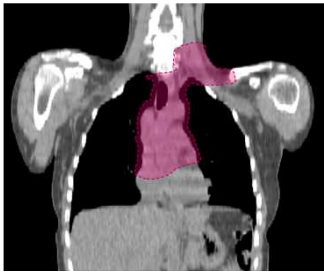
INRT

AIM

To evaluate if standard or low dose INRT can reduce second breast cancer risk in comparison with standard dose IFRT

PTS & METHODS

- 10 HL female patients under 30 yrs old with supra-diaphragmatic presentation
- 3 RT plans for comparison: IFRT 30 Gy, INRT 30 Gy and INRT 20 Gy
- Doses evaluation: mean bilateral breast dose and volumes receiving low (5 Gy= V5), intermediate (10 Gy=V10), high (20 Gy= V20) doses
- Second cancer risk model: cell initiation/inactivation/proliferation risk-model in order to estimate Excess Relative Risk (ERR) of radiation-induced BC at 20 years (1)



IFRT

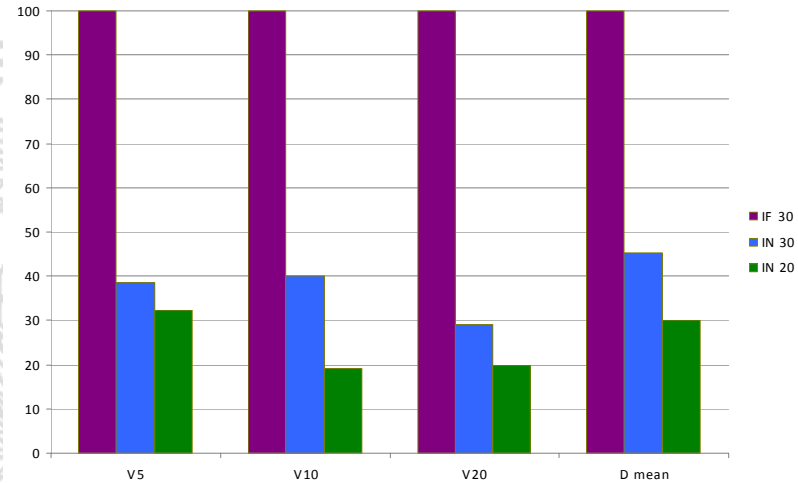
Significant Reduction of Second Breast Cancer Risk in Patients Treated with Involved Nodes Radiation Therapy for Early Stage Hodgkin's Lymphoma



INRT

RESULTS

Doses received by breast with **IFRT30**, **INRT30** and **INRT20**



Reduction in Breast Cancer Excess Relative Risk in comparison with IFRT 30 Gy:

INRT 30 Gy: 55 %

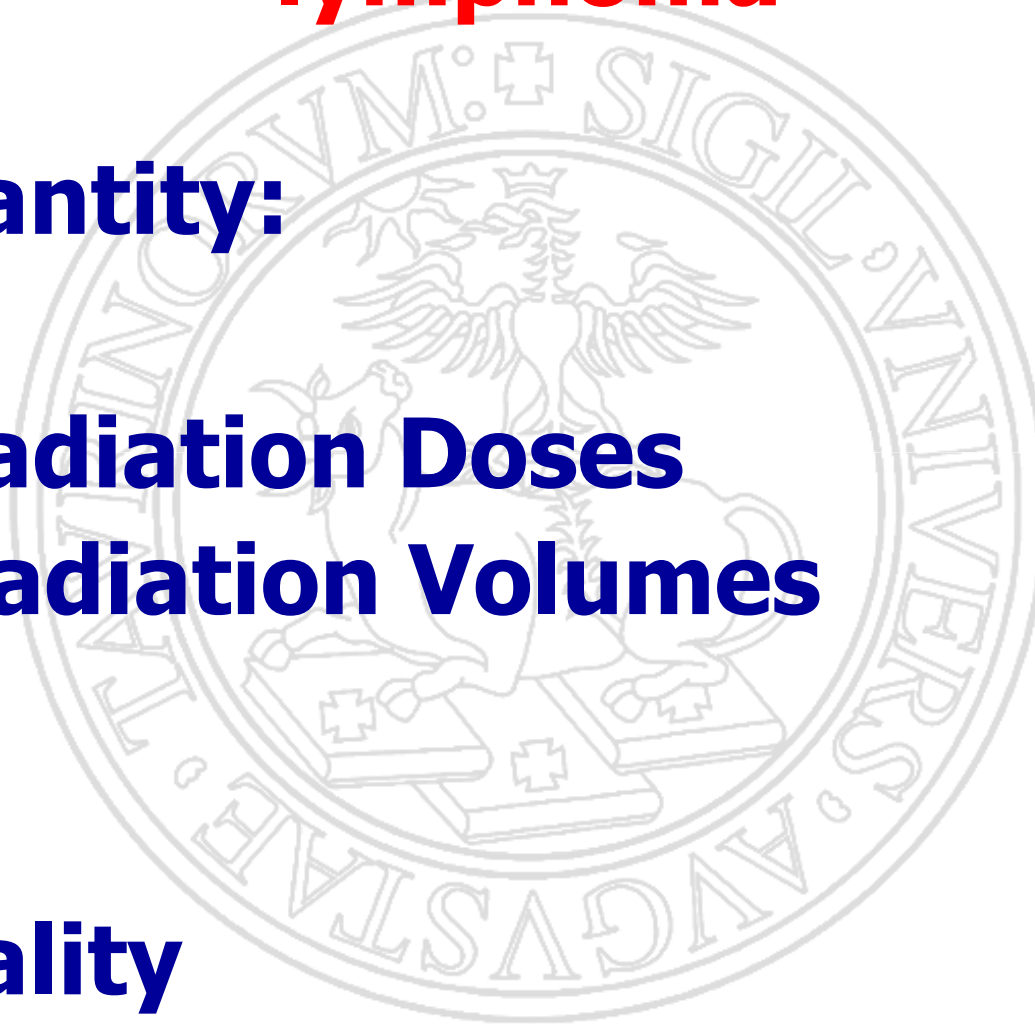
INRT20 Gy: 69 %

POSSIBLE ROLE FOR A MINI-RADIOTHERAPY APPROACH?



Evolution of Radiation Therapy in lymphoma

- **Quantity:**
 - **Radiation Doses**
 - **Radiation Volumes**
- **Quality**



How to improve radiotherapy results?

Treatment simulation:

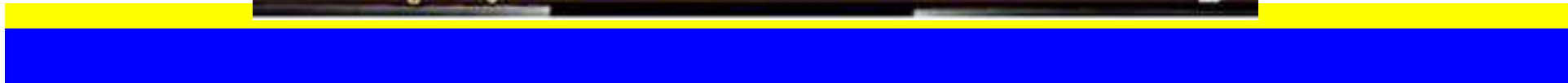
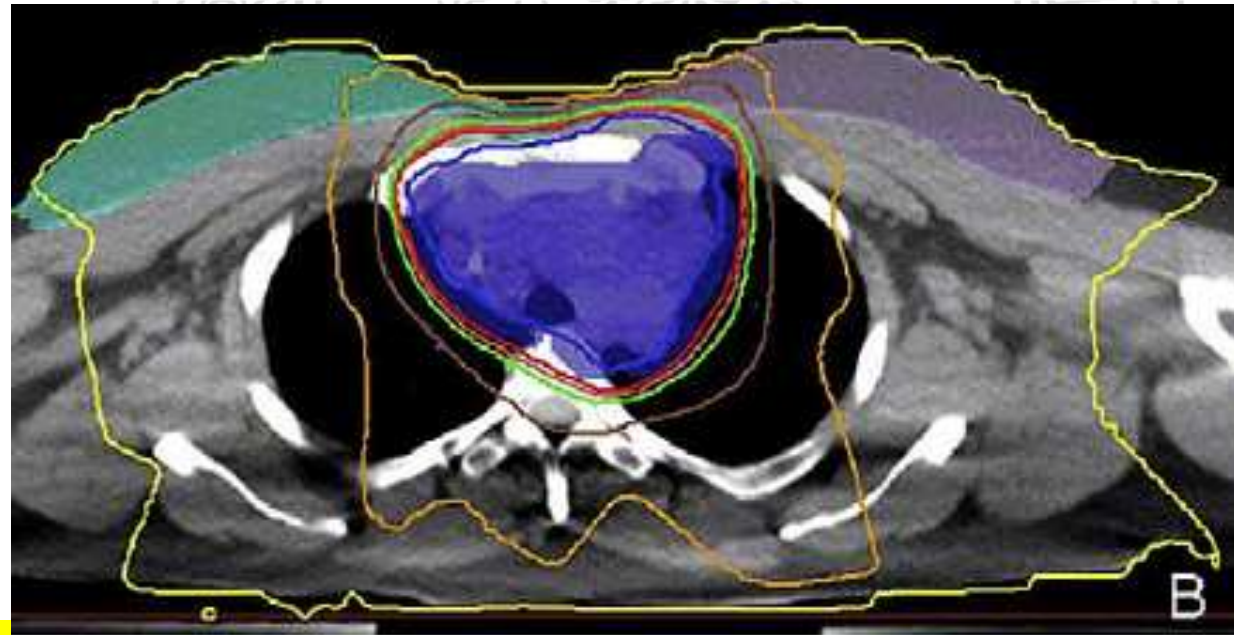
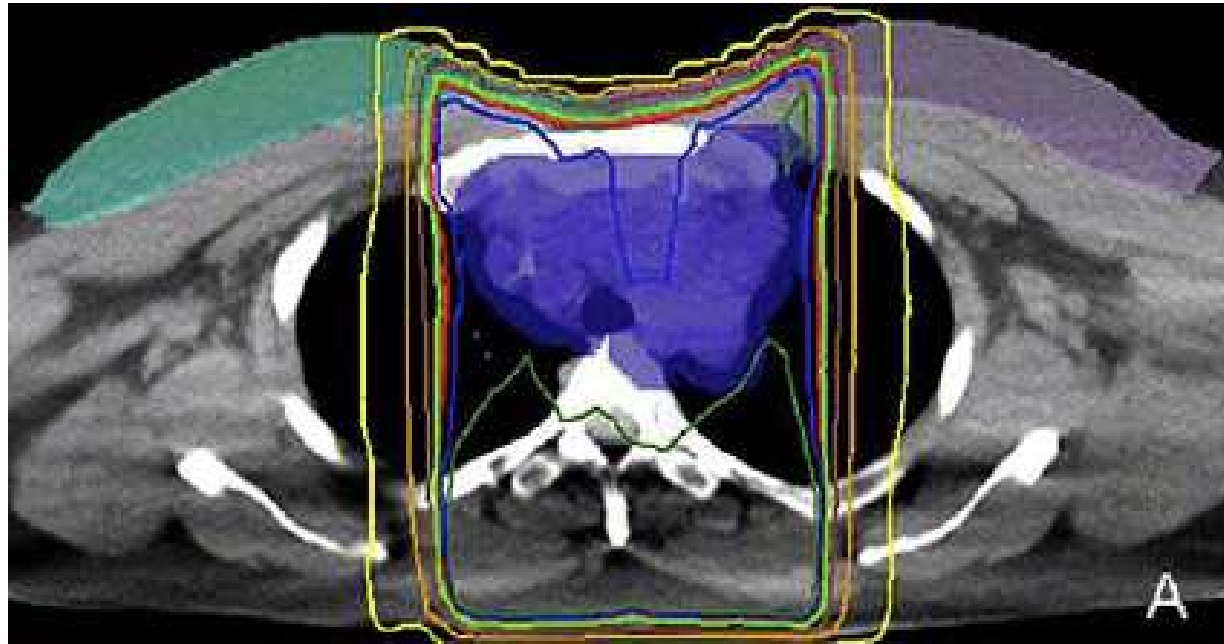
all relevant information on target definition is incorporated

Treatment planning:

involves selection of delivery technique and approach for optimizing target coverage and normal tissue avoidance

Radiation delivery and treatment verification





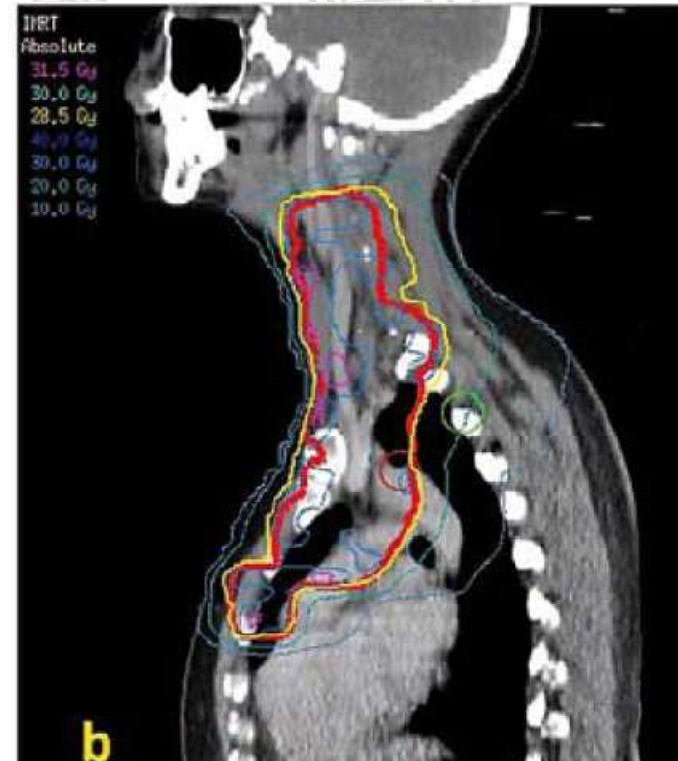
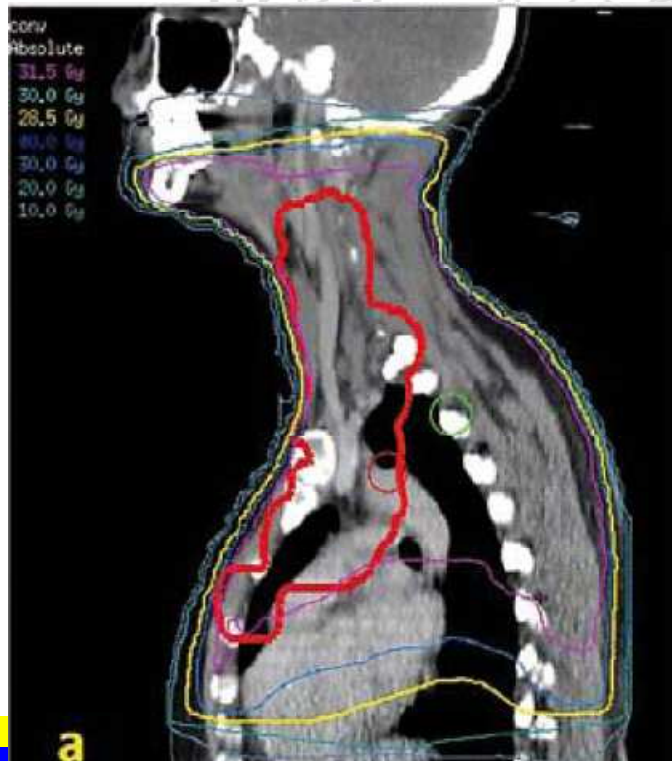
ASTRO Online CME

CLINICAL INVESTIGATION

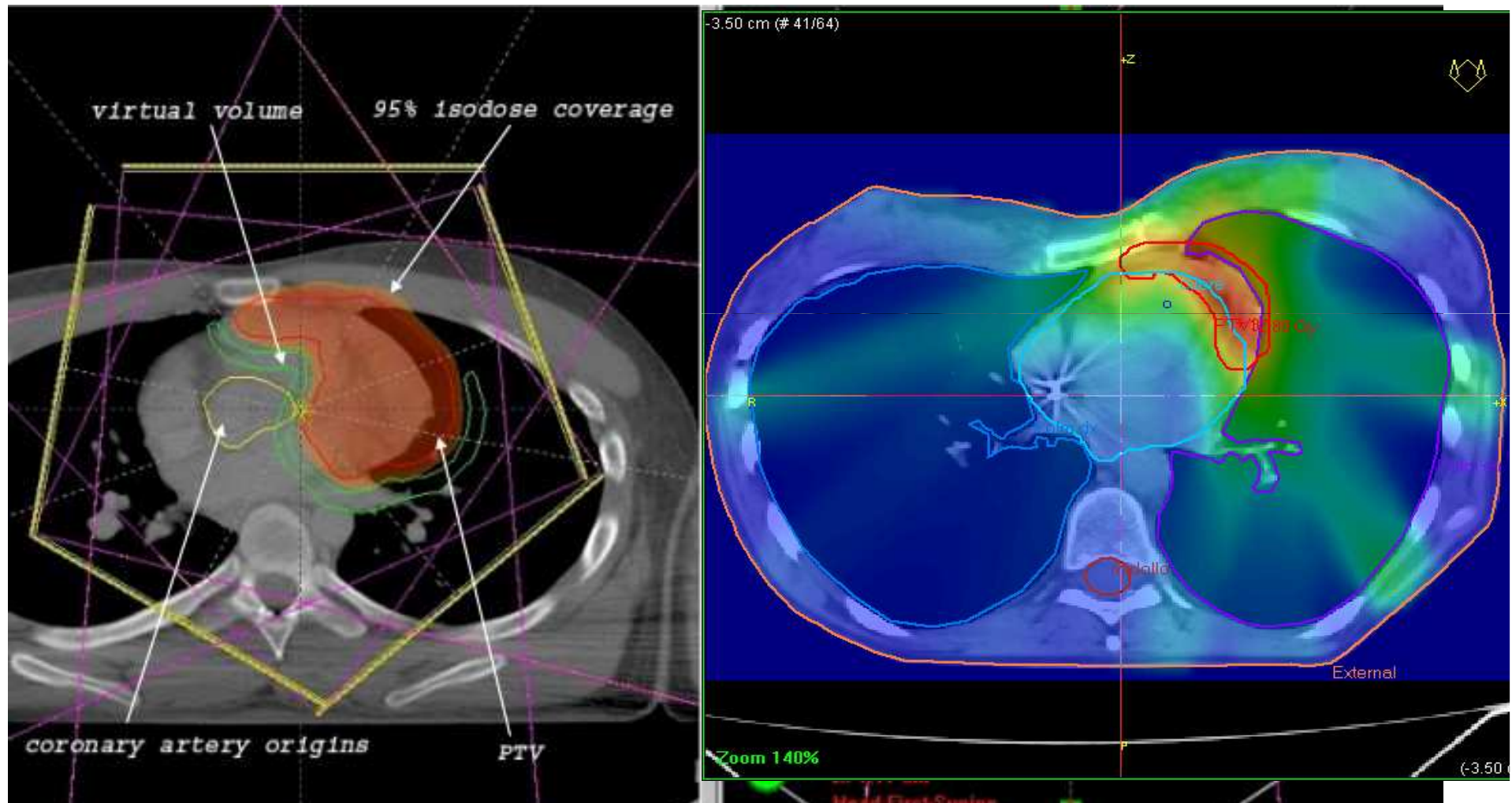
Hodgkin's Disease

IS INTENSITY-MODULATED RADIOTHERAPY BETTER THAN
CONVENTIONAL RADIATION TREATMENT AND THREE-DIMENSIONAL
CONFORMAL RADIOTHERAPY FOR MEDIASTINAL MASSES IN PATIENTS
WITH HODGKIN'S DISEASE, AND IS THERE A ROLE FOR BEAM
ORIENTATION OPTIMIZATION AND DOSE CONSTRAINTS ASSIGNED TO
VIRTUAL VOLUMES?

THEODORE GIRINSKY, M.D., CHARLOTTE PICHENOT, PH.D., ANNE BEAUDRE, PH.D.,
MITHRA GHALIBAFIAN, M.D., AND DIMITRI LEFKOPOULOS, PH.D.

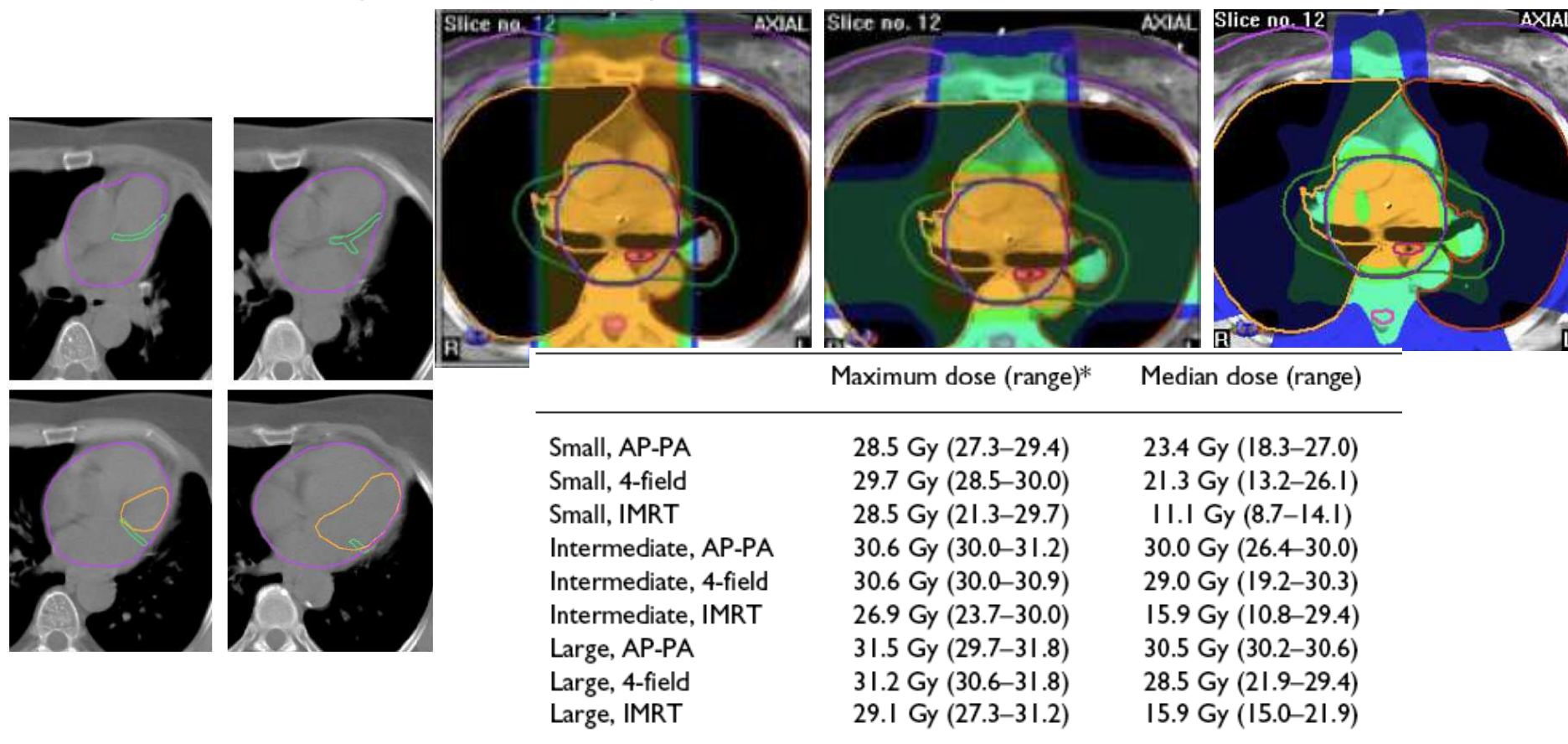


Combining field reduction with modern RT techniques



Influence of different treatment techniques on radiation dose to the LAD coronary artery

Carsten Nieder*¹, Sabine Schill², Peter Kneschaurek² and Michael Molls²



Conclusion: IMRT techniques are able to reduce the radiation dose to the heart. In addition to dose reduction to whole heart, individualised dose distributions can be created, which spare, e.g., one ventricle plus one of the coronary arteries. Certain patients with well-defined vessel pathology might profit from an approach of general heart sparing with further selective dose reduction, accounting for the individual aspects of pre-existing damage.

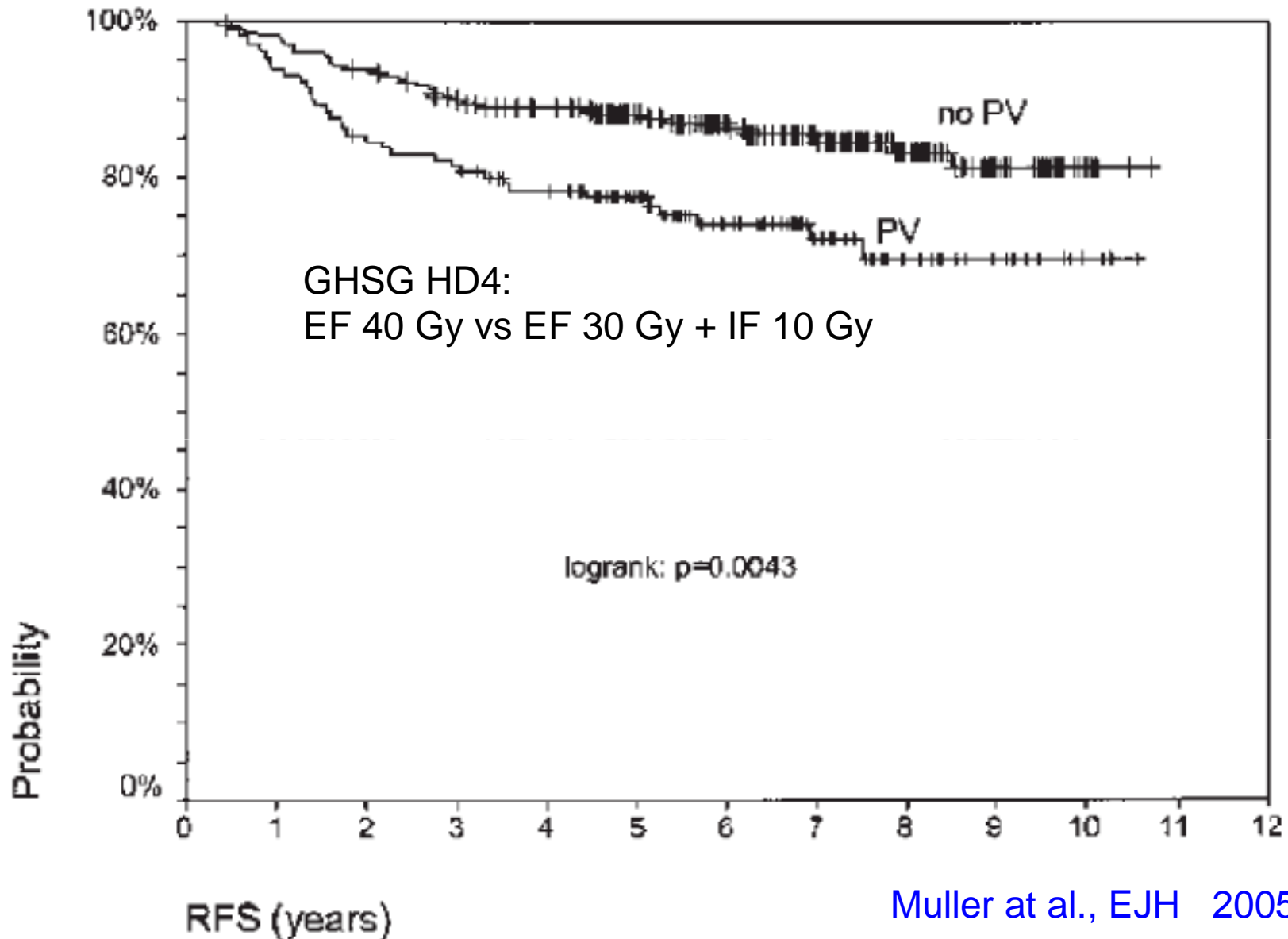
RT in lymphoma patients

- **Smaller fields**
- **Lower doses**
- **More sophisticated techniques**

Quality Assurance +++



GHSB HD4 trial: RFS relative to presence or absence of a relevant RT protocol violation (PV)

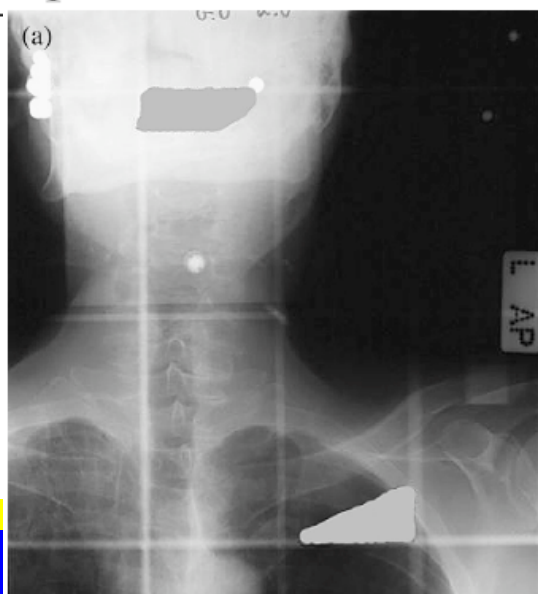


Muller et al., EJM 2005

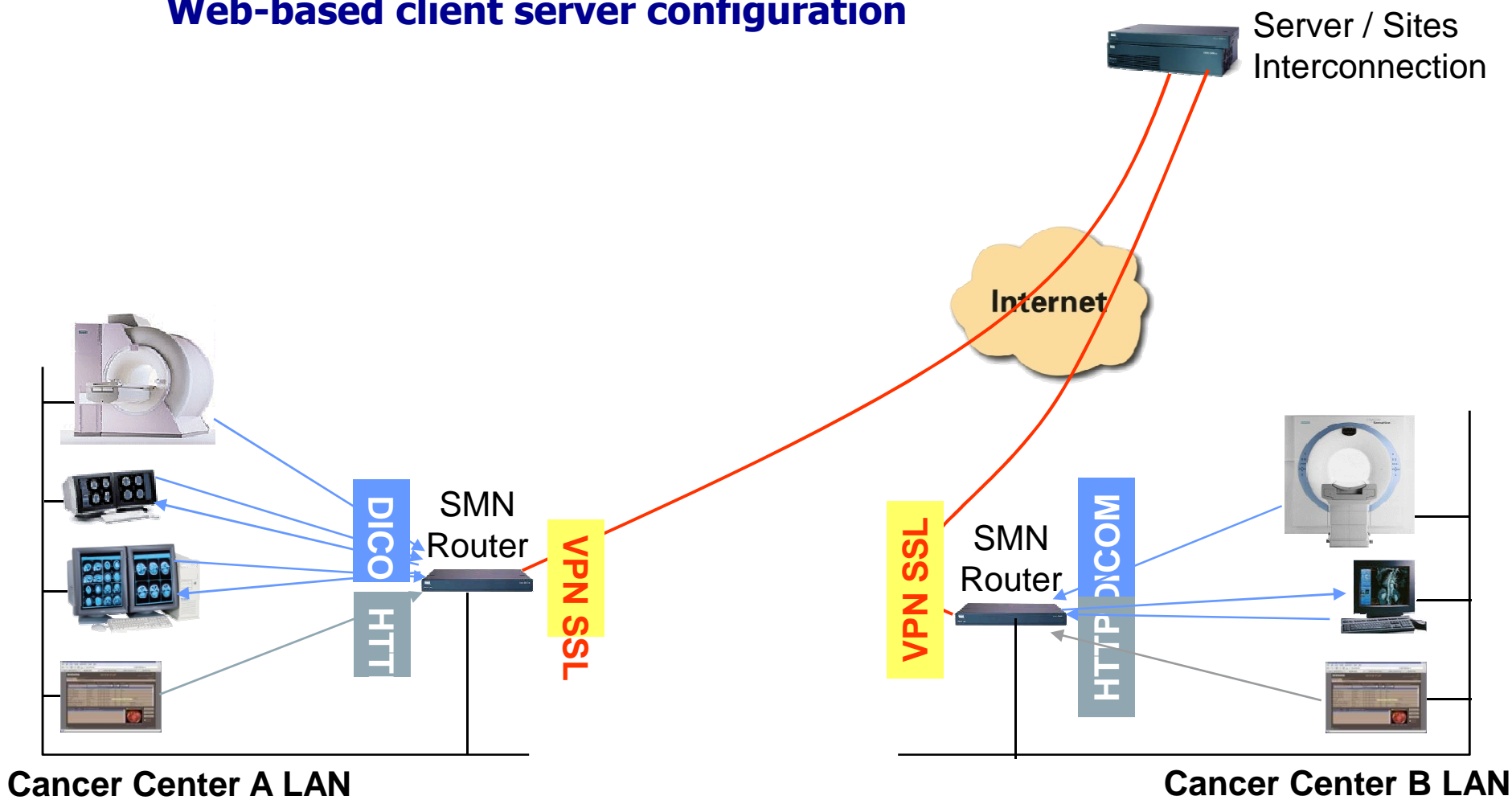
QUALITY CONTROL OF INVOLVED FIELD RADIOTHERAPY IN PATIENTS WITH EARLY-FAVORABLE (HD10) AND EARLY-UNFAVORABLE (HD11) HODGKIN'S LYMPHOMA: AN ANALYSIS OF THE GERMAN HODGKIN STUDY GROUP

Table 4. Evaluation of the performed involved field radiotherapy in general

Judgement	HD10 (%)	HD11 (%)
According to protocol	38.8	33.0
Acceptable	13.8	14.3
Not according to protocol	43.0	51.1
Judgement not possible	4.4	1.6



Web-based client server configuration



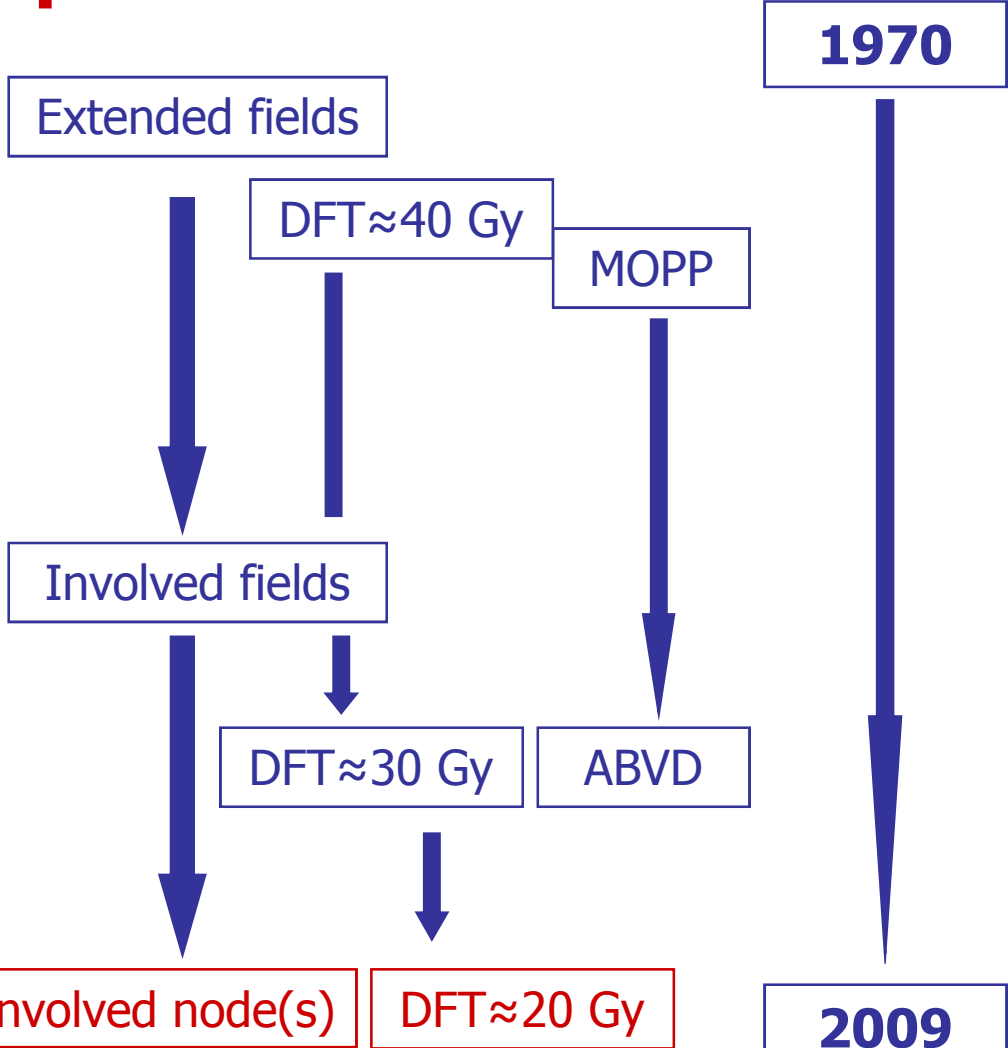
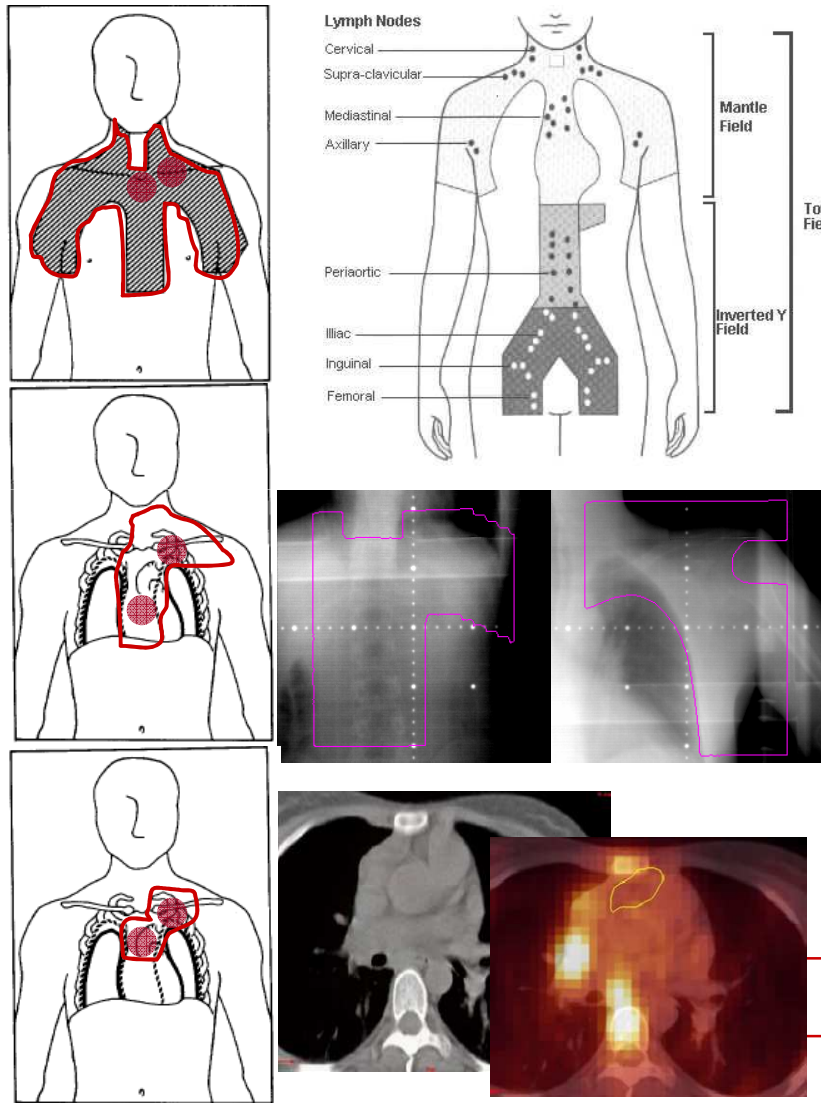
Diapositiva 44

TAG1

THE LOCAL CANCER CENTER SENDS ALL THE IMAGING DATA AND THE DESIGN OF THE RADIATION FIELDS FOR A REAL TIME QUALITY CONTROL

GIRINSKY theodore; 14/09/2008

Timeline of major changes in RT in Hodgkin's Lymphoma



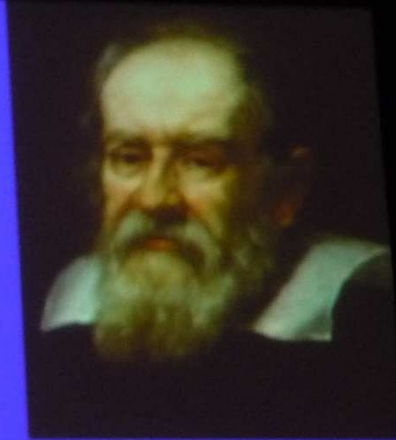
Mini-chemo; mini-RT

Optimal treatment of HL

Radiation oncologist vs hematologist



"Eppur si muove"
means
"and yet it moves"



Galileo Galilei 1633

*In a response to the Inquisition forcing him to deny
that the earth is not the center of the universe*

