

**NOT TO BE MINISTERED UNTO BUT TO MINISTER**



# ***Every Gray counts- moving from IFRT to ISRT in Lymphoma***

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# Overview

Evolution of RT in lymphomas

Toxicity

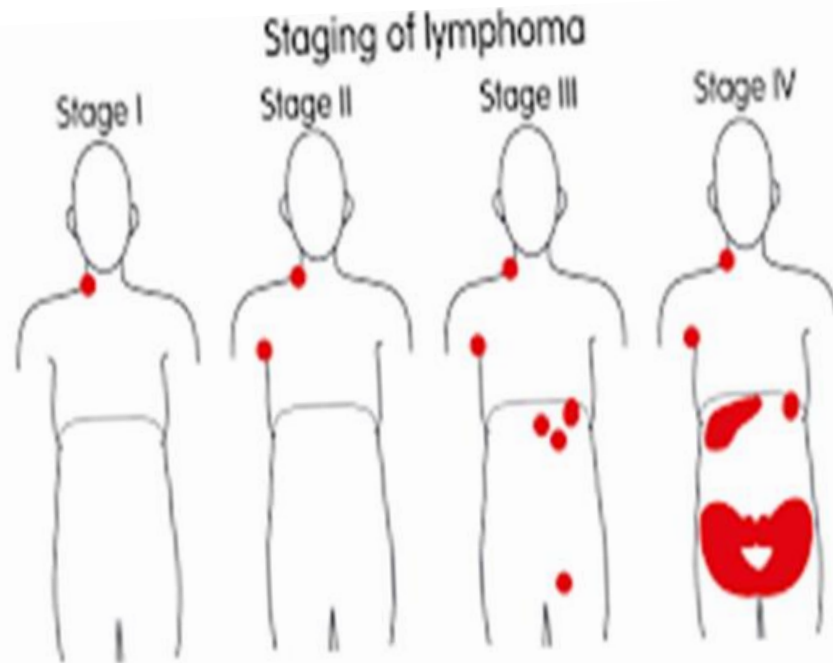
IFRT vs ISRT

Radiation dose reduction in lymphomas

How does every Gy count in RT in lymphomas?

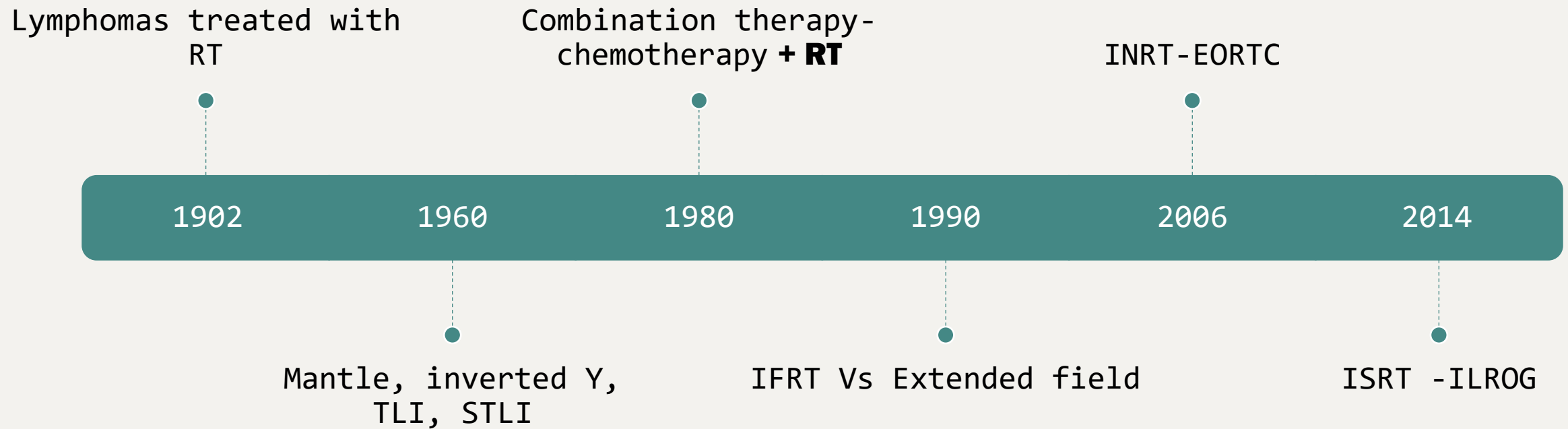


- Lymphoma is cancer of the lymphatic system (lymph glands)
- Lugano's classification (derived from Ann Arbor with Cotswolds)



A: absence of B symptoms B: fever, night sweats, weight loss

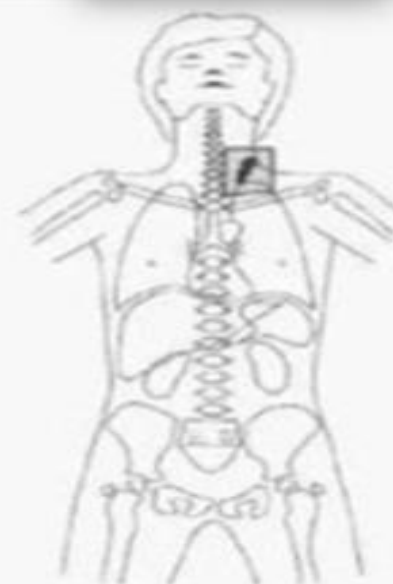
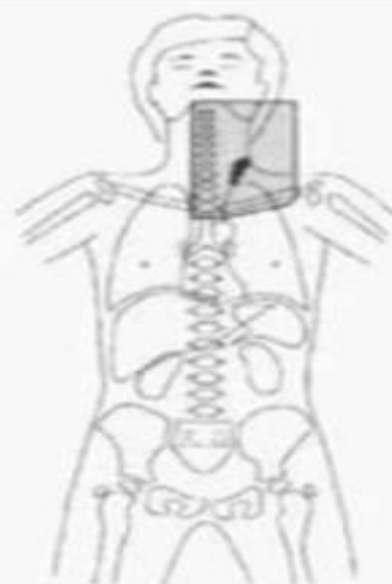
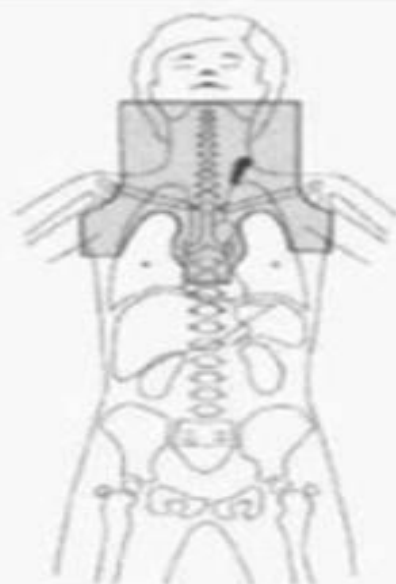
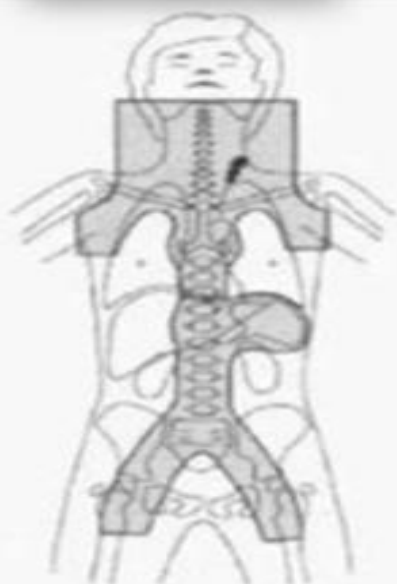
# ***Evolution of RT in lymphomas***





30-45 Gy

20-30 Gy



**Total nodal  
radiotherapy**

**Extended field  
radiotherapy**

**Involved field  
radiotherapy**

**Involved site  
radiotherapy**

All LN of both  
sides of  
diaphragm

Multiple involved  
& uninvolved LN  
groups of one side  
of diaphragm

Field is limited to  
site of clinically  
involved LN  
groups

Most limited  
radiation field,  
includes only  
involved LN.

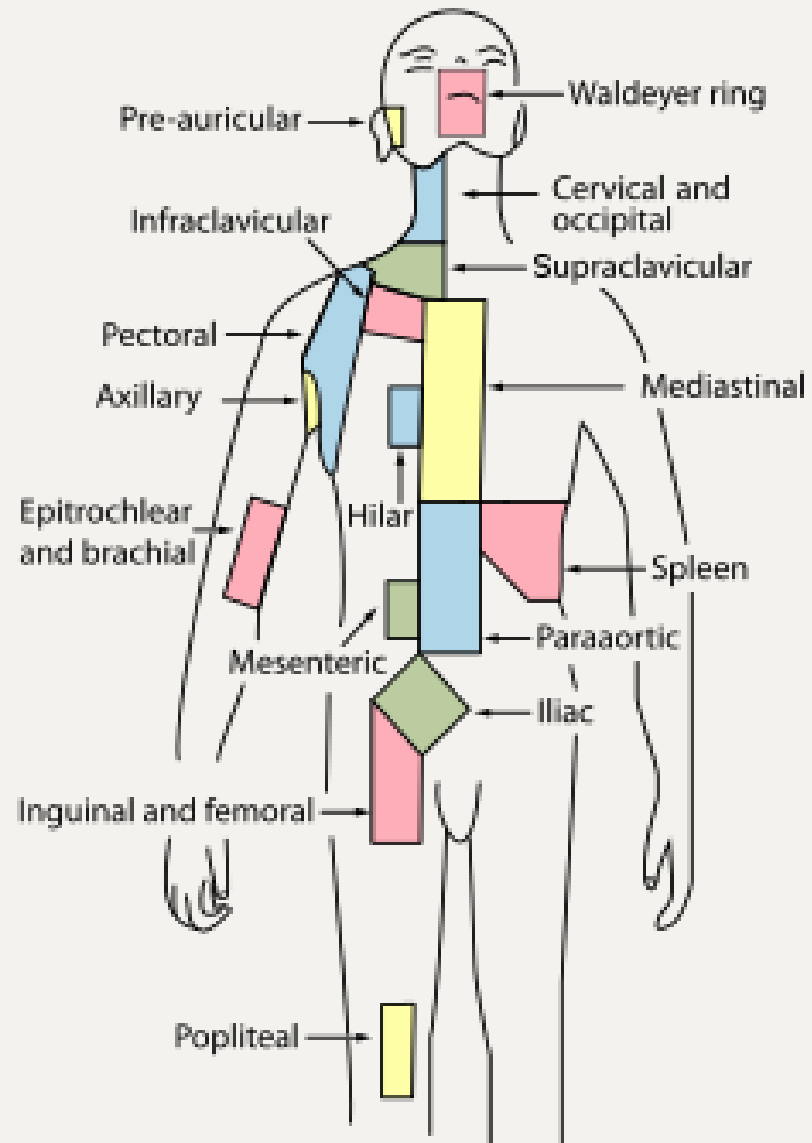
# ***Indications of RT in lymphomas***

## RT as curative

- Early-stage indolent non-Hodgkin lymphoma (NHL) and
  - Nodular lymphocyte-predominant HL (NLPHL)

## Consolidation RT

- ESHL and diffuse large B-cell lymphoma (DLBCL)
  - Primary extranodal lymphoma
- Advanced stage HL or aggressive NHL- residual and/or bulky site
  - Relapsed lymphoma

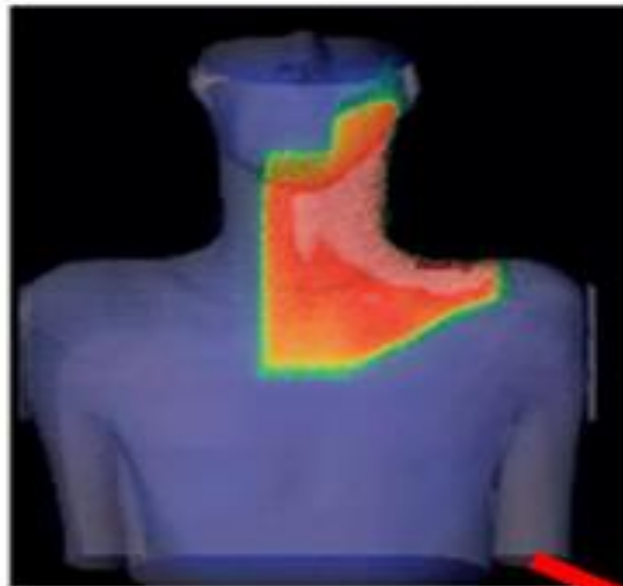
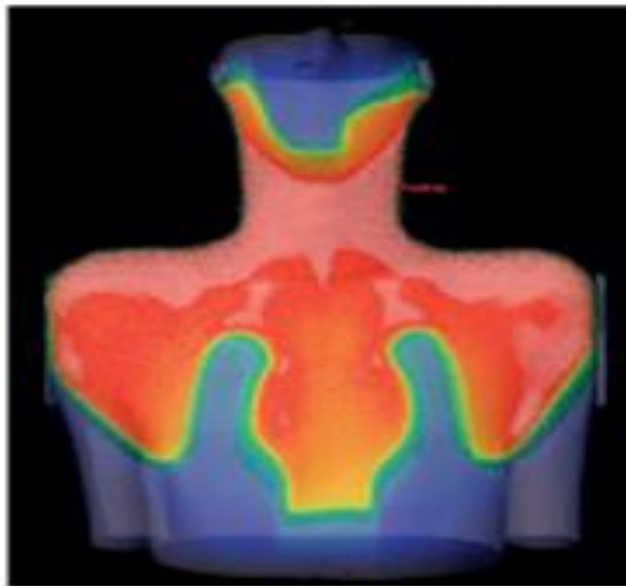


***Lymph node***

***groups***



## Mantle field (EFRT) or involved field (IFRT)



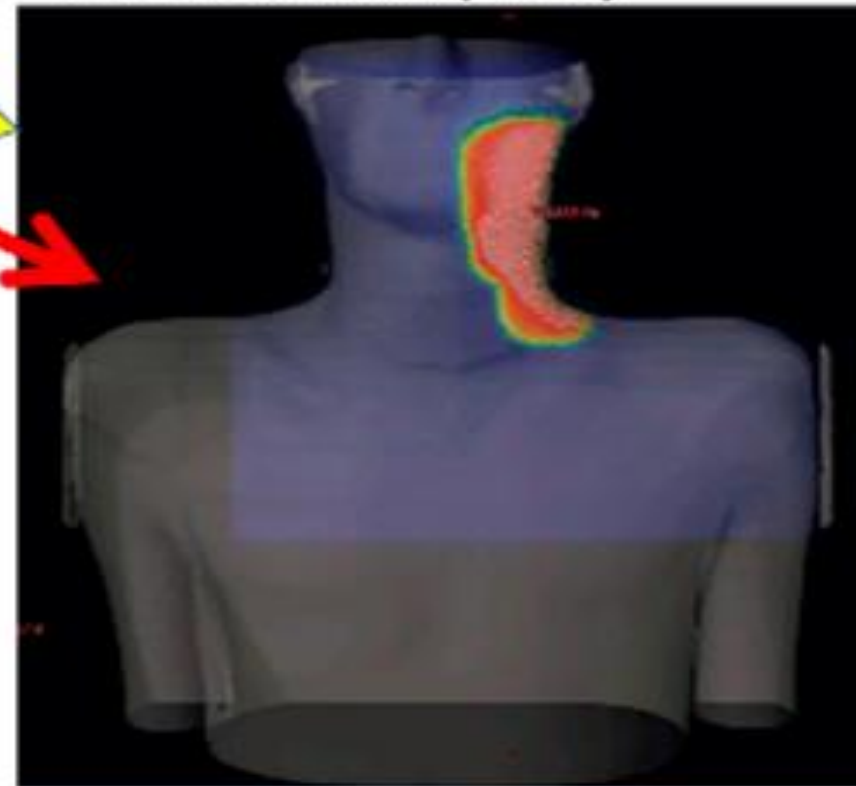
Based on:

- 2 D planning
- Regions
- Bony landmarks defining fields
- "Fixed" margins

Based on:

- 3 D planning
- Actual lymphoma involvement
- Contouring of volumes (GTV, CTV, PTV)
- Margins (GTV → CTV) based on clinical judgement and (CTV → PTV) based on internal and setup uncertainties

Involved site (ISRT) or  
involved node (INRT)





1960's

2000's

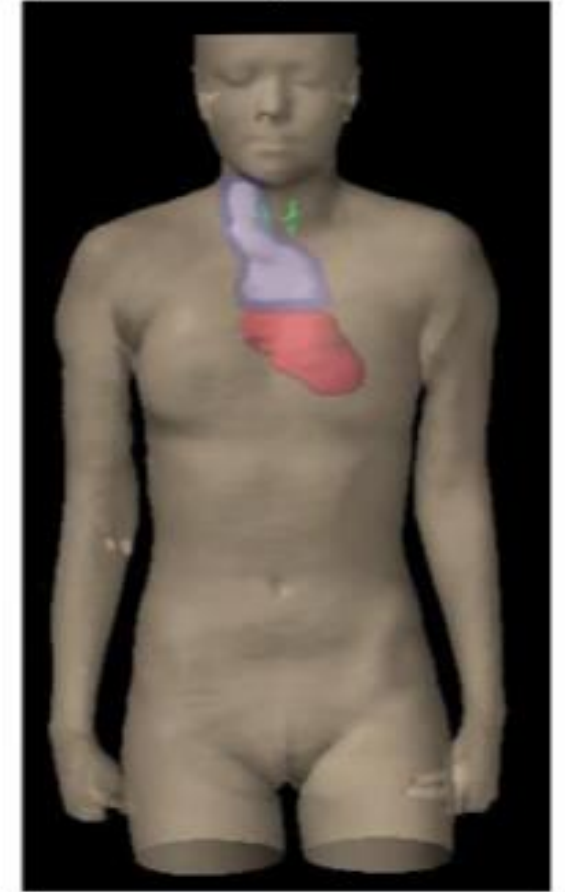
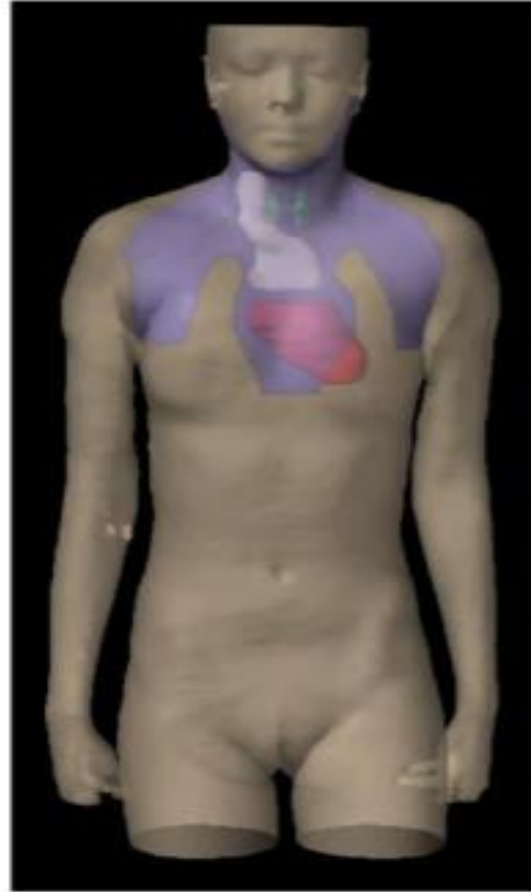
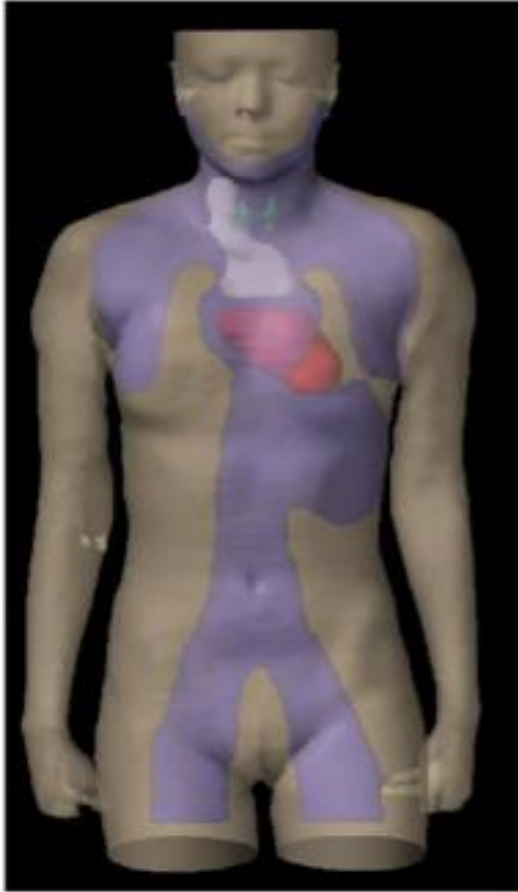


TLI

Mantle

IFRT

ISRT/INRT



2D

3D

IMRT, Proton Therapy,  
PET/CT-fusion, DIBH, IGRT

40-50 Gy

20-36 Gy



# ***Toxicity***

**Cardiopulmonary**

**Second malignant neoplasms**

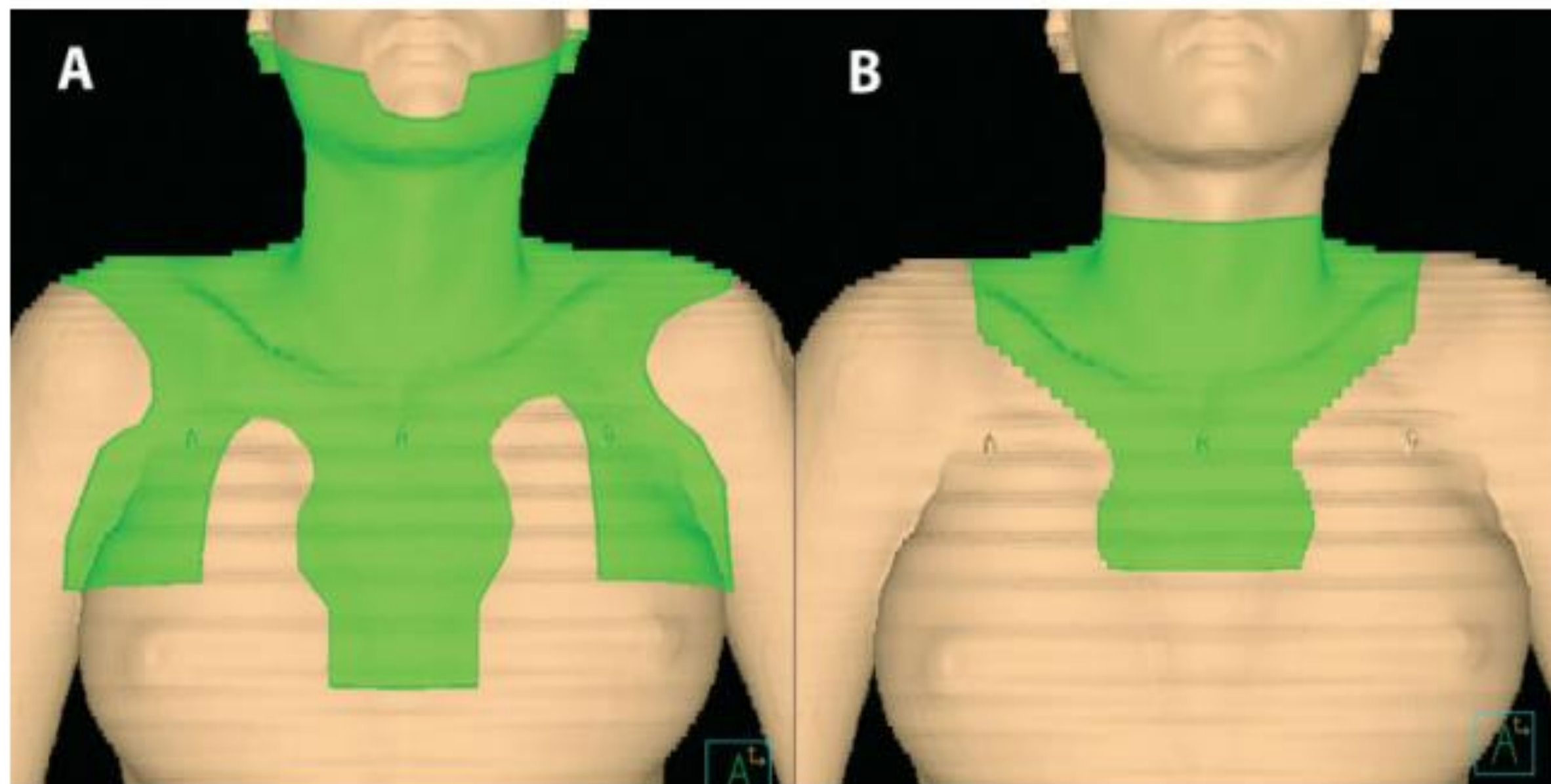
**Endocrinopathies-Hypothyroidism**



# Second malignancy in HL survivors

Study (year)	n	Median followup(years)	Dose (Gy)	Relative risk (95%CI)
Bhatia (1955-86)	1380	11	20-40	5.9 (1.2-30.3)
			>40	23.7 (3.7-152.3)
Castellino(1970-86)	2742	24	<30	1.9 (0.4-8.7)
			>30	7.4 (1.8-30.3)
Ng(1969-97)	1319	12	<u>Field</u>	
			Mantle	2.1 (0.8-4.6)
			STLI	4.2 (3.4-5.1)
			TLI	5.1 (2.8-8.5)
Conway(1961-2009)	734	18	Small field	0.87 (0.28-2.66)
			Mantle	2.9 (1.41-5.97)



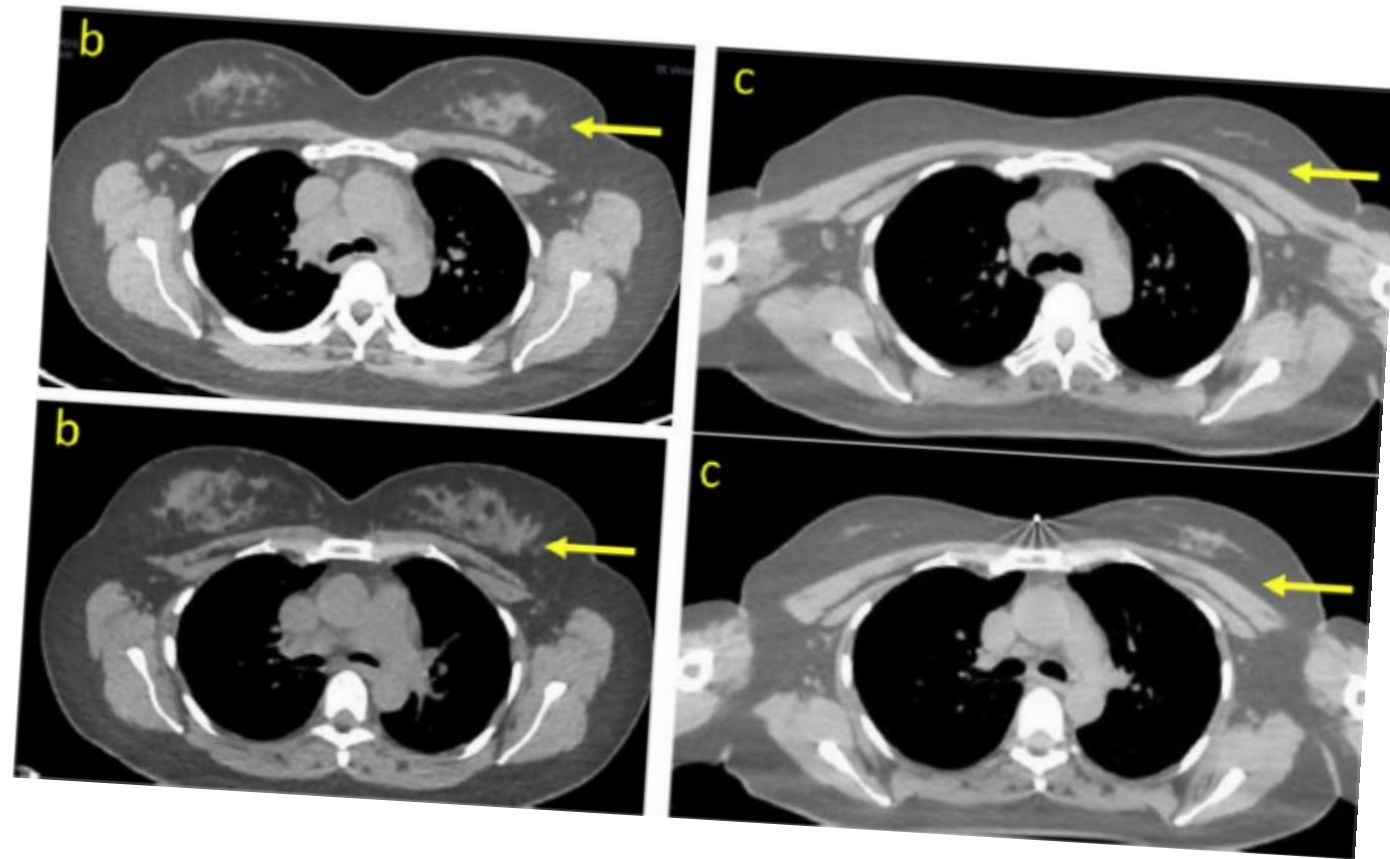




# **Arm position and volume of breasts**

B-arms above

C-arms by the sides

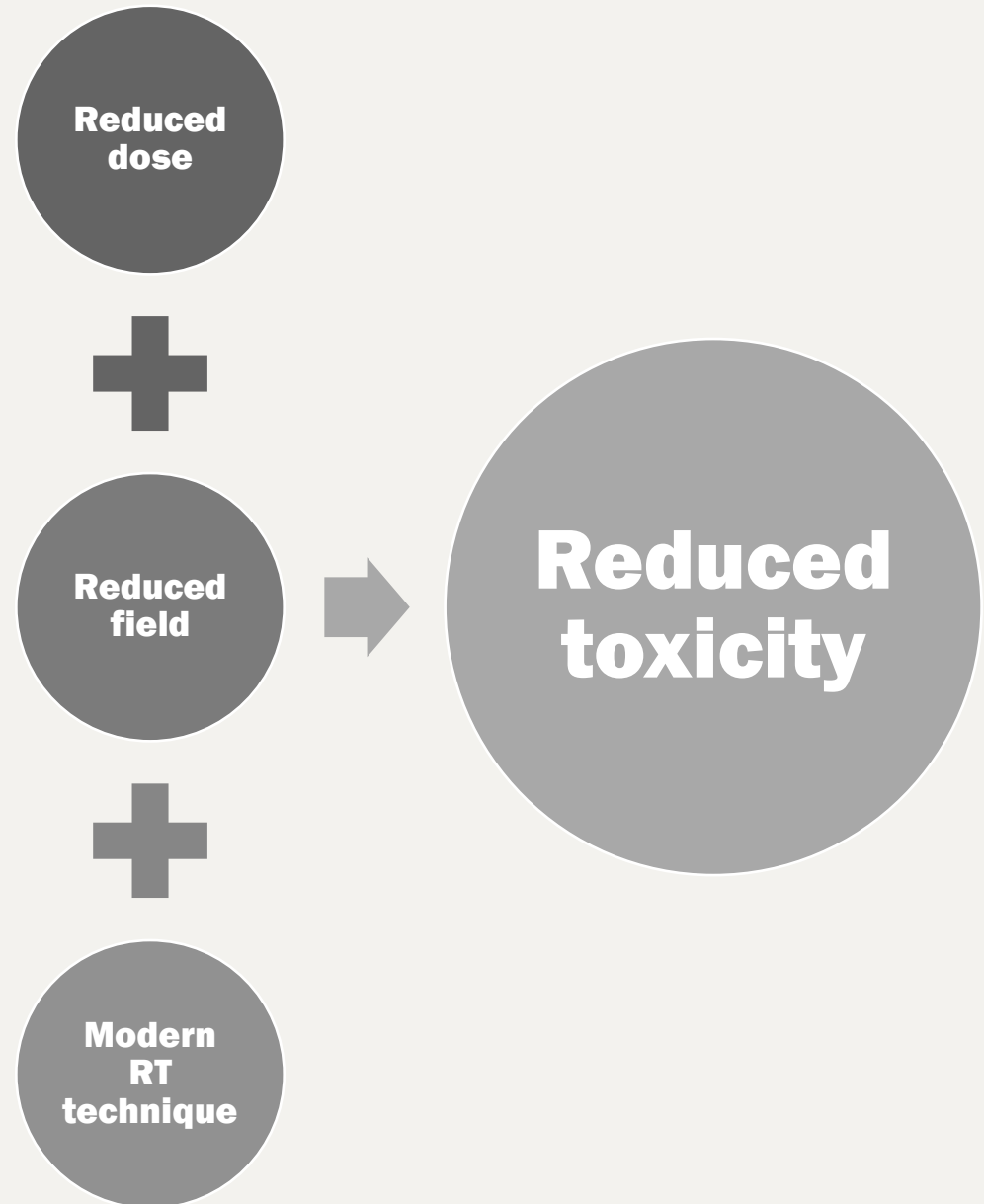


# Cardiac event in HL survivors

Study (year)	n	Median followup(years)	Mean dose to heart (Gy)	Rate ratio (95%CI)
Cutter(1965-95)	1852	19	0	1.0 (0.2-4.9)
			>0-30	1.5 (0.5-3.9)
			31-35	3.4 (1.9-6.0)
			36-40	5.5 (4.0-7.7)
			>40	12.1 (5.1-28.9)
van Nimwegen (1965-95)	2617	19	0	1.00 (0.6-1.67)
			1-5	1.14 (0.62-2.10)
			5-14	2.14 (1.28-3.58)
			15-19	2.76 (2.10-3.59)
			20-24	2.79 (2.23-3.49)
			25-34	3.21 (2.52-4.09)
			35-45	2.54 (0.96-6.69)



***Methods to  
reduce toxicity***



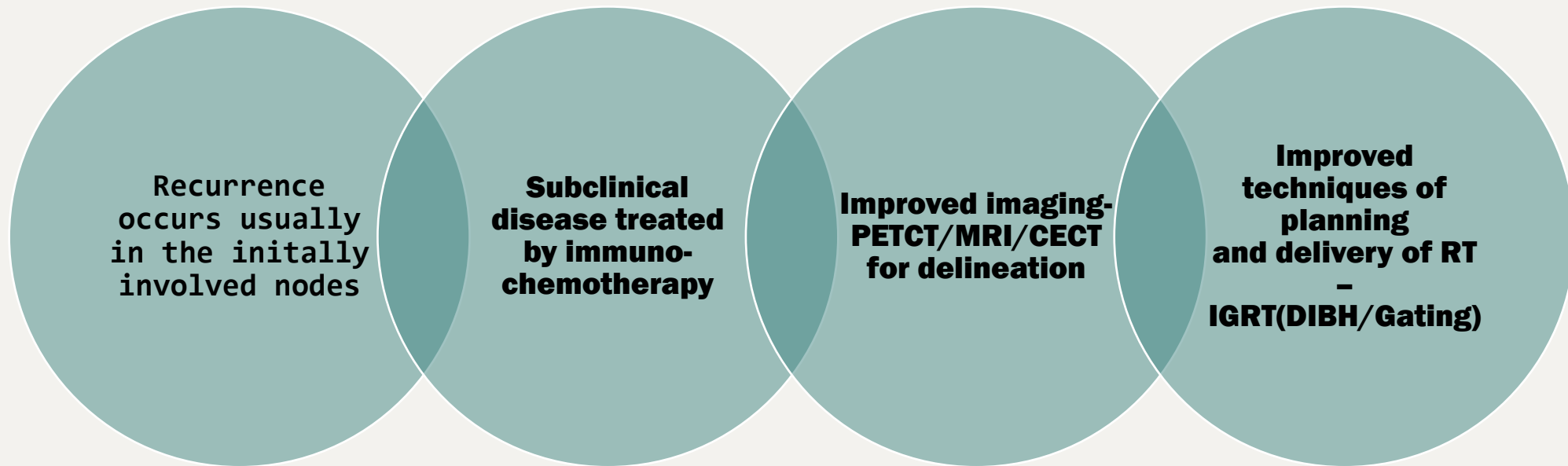
# **IFRT**

Region or organ	Field coverage
Supraclavicular	Unilateral or bilateral cervical/supraclavicular region
Mediastinum	Including bilateral medial supraclavicular LNs and lung hila
Axilla	Including the supraclavicular and infraclavicular LNs
Spleen	Spleen
Para-aortic LNs	Para-aortic LNs
Pelvis	Inguinal/femoral/external iliac regions





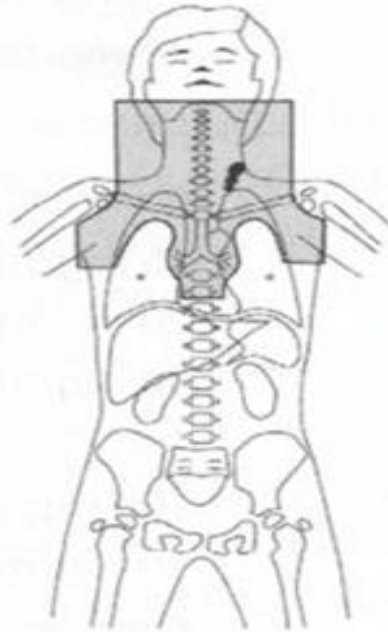
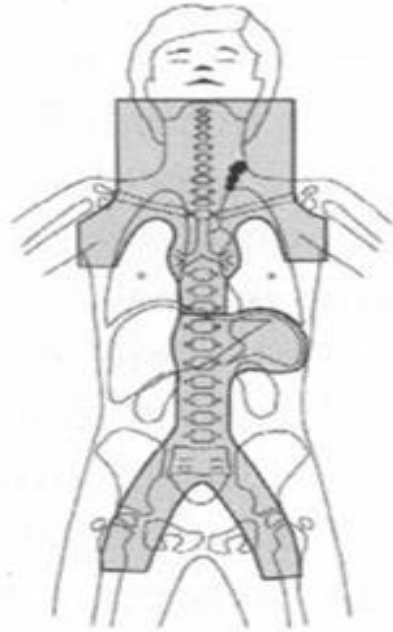
# ***Rationale of ISRT***



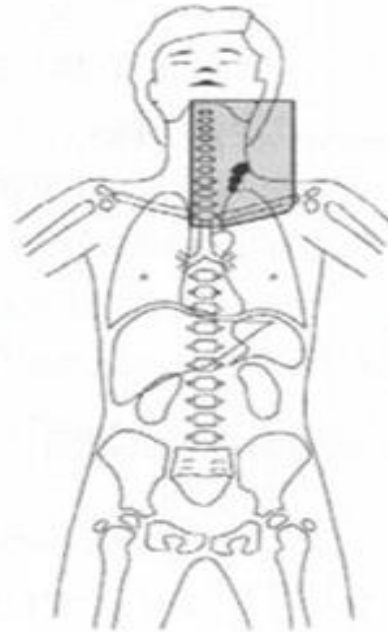
# Transformation of RT Volumes / Doses in HL

## ISRT – Specht L et al IJROBP 2014

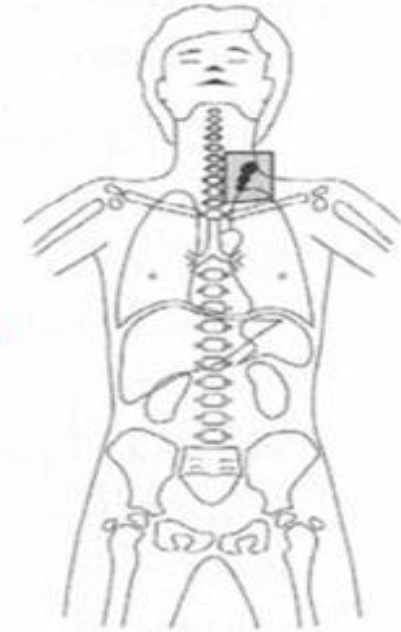
**1978**



**80 % reduction**



**2013**



**Total nodal**

**Regional nodal**

**Involved field**

**Involved site**

**Dose: 30-44 Gy**



**20-30 Gy**

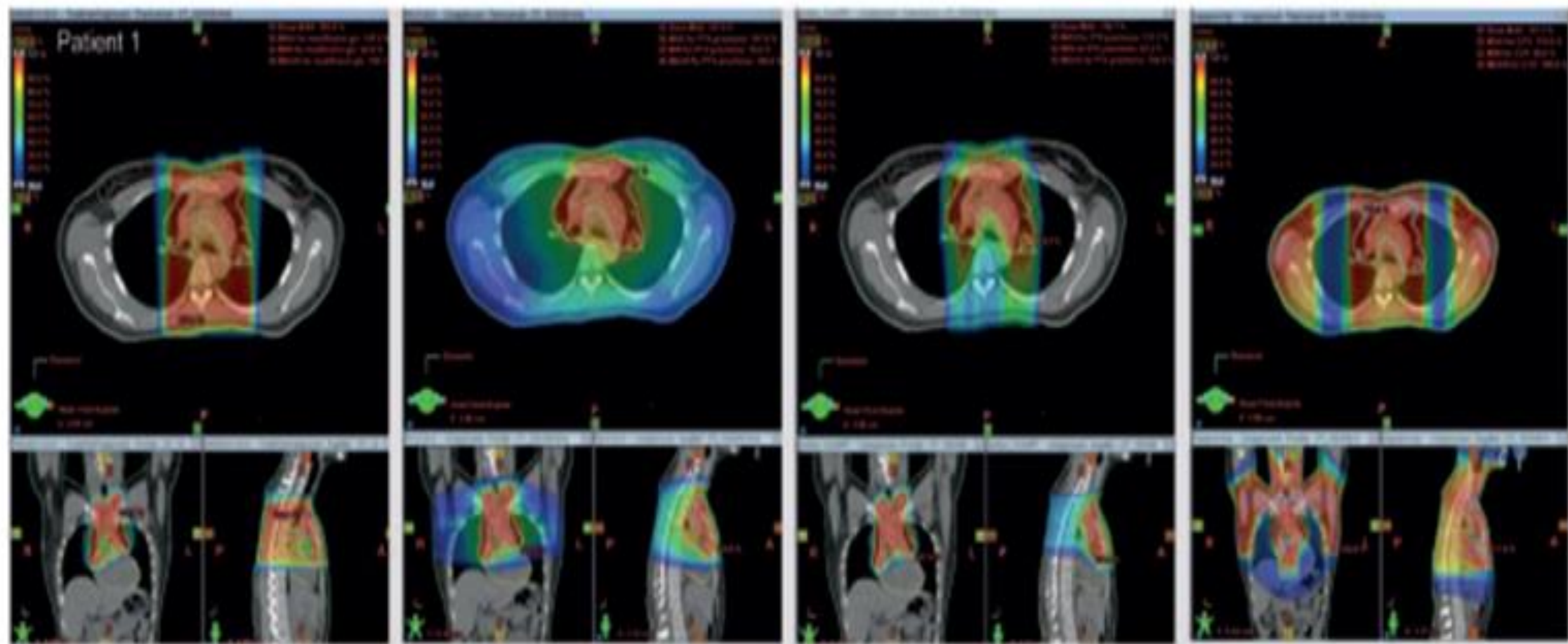
Two thirds of women with early-stage HD do not require radiation of the axillae  
Substantial reduction in breast, lung cancer risk, cardiac morbidity

AP-PA

IMRT

IMPT

Mantle field



Maraldo M et al. Ann Oncol 2013; 24: 2113-8

# **INRT Vs ISRT**

## **INRT**

- **EORTC-GELA**
- **Originally involved nodes**
- **PET in planning position prior to chemo and after**

## **ISRT**

- **ILROG**
- **Originally involved nodal site**
- **Larger CTV (accommodates uncertainty in delineation)**





## ***GTV: IFRT Vs ISRT***

**IFRT:** anatomical node **REGION** involved before chemotherapy, thus the involved field will include the entire neck including the supraclavicular fossa when a neck node was involved

**ISRT:** The GTV includes PET-positive **NODES** and should **be extended** to include nearby enlarged or **equivocal nodes**, particularly if disease demonstrates low FDG avidity

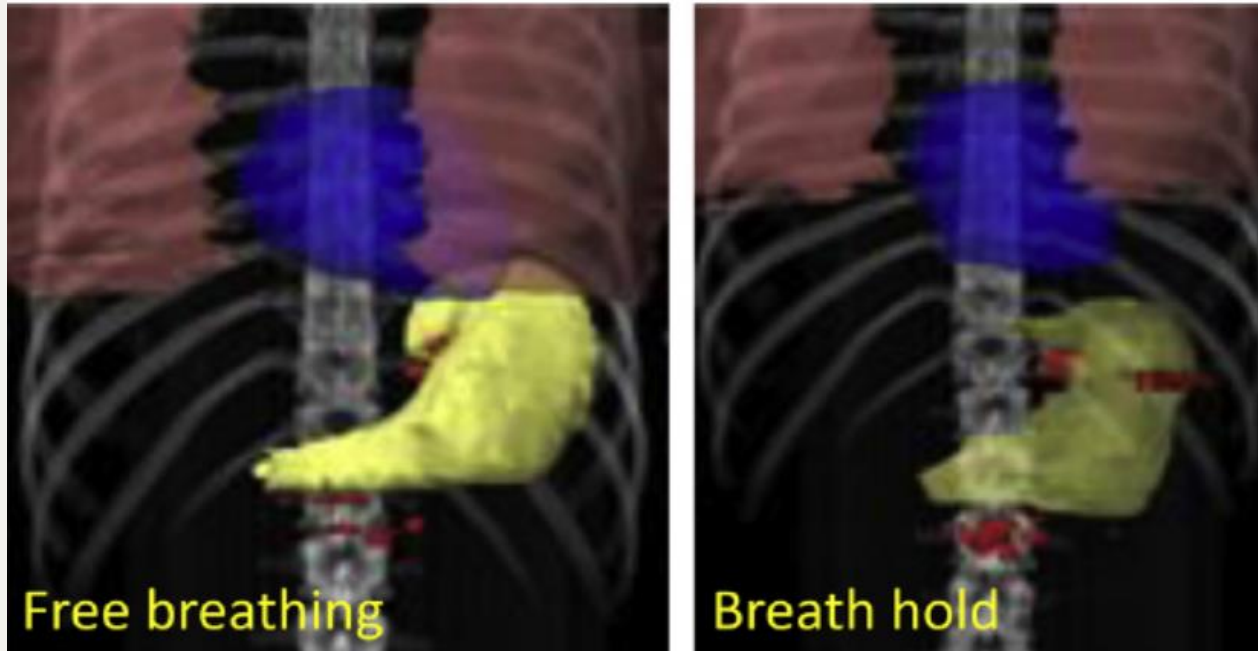


# CTV in ISRT

RT	CTV
<ul style="list-style-type: none"><li>• Early-stage indolent non-Hodgkin lymphoma (NHL) and<ul style="list-style-type: none"><li>• Nodular lymphocyte-predominant HL (NLPHL)</li></ul></li></ul>	evident sites plus an adequate volume to encompass potential adjacent subclinical disease
<ul style="list-style-type: none"><li>• ESHL and diffuse large B-cell lymphoma (DLBCL)</li></ul>	disease sites evident at diagnosis
<ul style="list-style-type: none"><li>• Primary extranodal lymphoma</li></ul>	entire involved organ because extranodal lymphomas often display an infiltrating or multifocal pattern
<ul style="list-style-type: none"><li>• Advanced stage HL or aggressive NHL- residual and/or bulky site</li></ul>	any residual GTV plus a subset of disease sites at elevated risk of harboring subclinical disease after systemic therapy
<ul style="list-style-type: none"><li>• Relapsed lymphoma</li></ul>	some or all relapse sites and selected sites of prior disease involvement

# Considerations in ISRT

- PET-CT + contrast CT +/- MRI



- DIBH for mediastinal and stomach locations

# **Evidence for reduced dose**

- Hodgkins: German Hodgkin Study Group HD1, HD5, HD10 and HD11 recommends 20 Gy for Early stage favourable and 30 Gy for unfavourable Hodgkins





# ISRT doses

Disease and stage	PET-CR post chemotherapy	PR post chemotherapy
Early stage indolent nodal or extranodal lymphoma	24-30 Gy (RT alone)	
Early stage HL	30 Gy	36-40 Gy
low-risk, limited-stage DLBCL	30-36 Gy	36-40 Gy
Advanced-Stage Aggressive NHL	30-36 Gy	36-50 Gy (PET positive residual)
Advanced-Stage Aggressive HL	30 Gy	36-45 Gy (PET positive residual)
Relapsed/Refractory Aggressive NHL	30-36 Gy	40-55 Gy (If RT is the sole salvage)
Relapsed/Refractory Aggressive HL	30 Gy	36-45 Gy (If RT is the sole salvage)



# Constraints

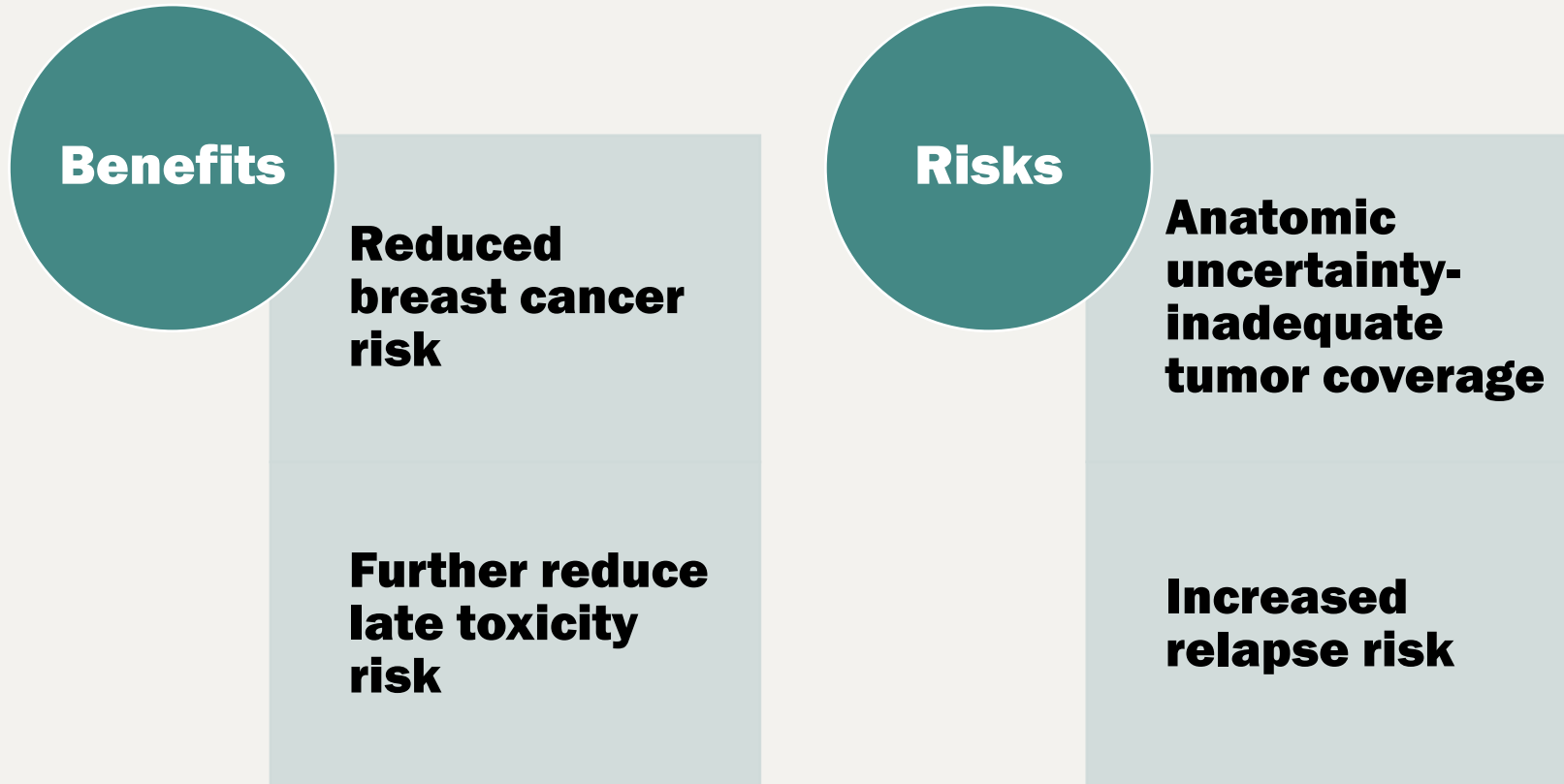
	Optimal*	Acceptable <sup>†</sup>	If necessary <sup>‡</sup>	Avoid
Heart (89, 145, 146)				
Mean (Gy)	<5	5-10	10-18	Coronary arteries and left ventricle
V15	<10%	10%-25%	25%-35%	
V30		<15%	15%-20%	
Lung (147)				
V5	<35%	35%-45%	45%-55%	
V20	<20%	20%-28%	28%-35%	
Mean (Gy)	<8	8-12	12-15	
Thyroid (148)				
V25	<62.5%			Whole thyroid
Breast				
Mean (Gy)	<4	4-15	>15	Glandular tissue
V4	<10%	10%-20%	>20%	
V10		<10%	>10%	

\* For favorable disease, small-volume early stage lymphoma.

<sup>†</sup> For bulky mediastinal disease.

<sup>‡</sup> Relapse/refractory disease setting. Adapted with permission from Dabaja et al.<sup>49</sup>

# ***Benefits/risks of ISRT***



## Favorable outcomes with de-escalated radiation therapy for limited-stage nodular lymphocyte-predominant Hodgkin lymphoma

Chelsea C. Pinnix,<sup>1</sup> Sarah A. Milgrom,<sup>1</sup> Chan Yoon Cheah,<sup>2-4</sup> Jillian R. Gunther,<sup>1</sup> Ethan B. Ludmir,<sup>1</sup> Christine F. Wogan,<sup>1</sup>

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### Key Points

- Short-term data suggest that stage I/II NLP HL can be treated with ISRT without a negative impact on disease-free survival.



**Involved site radiotherapy (ISRT) versus involved field radiotherapy (IFRT) in treating lymphoma: A single centre experience**

**Beshar Allos, Devinda Jayathilake, Anjali Zarkar, Andrea Stevens**

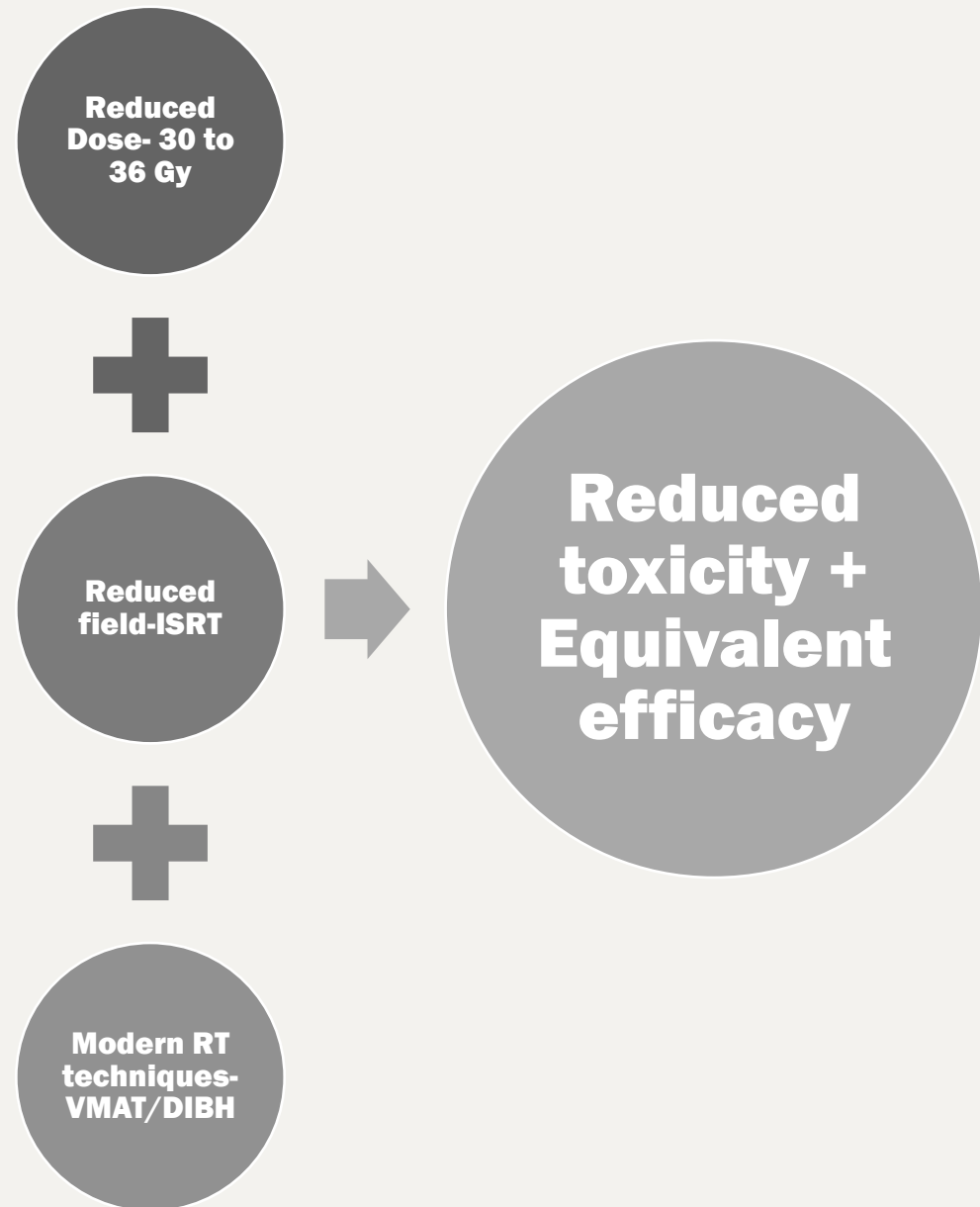
n	Relapse (%)	In field relapse (%)
IFRT-56	27.8	5.6
<b>ISRT -138</b>	11.6	6.2

**Conclusion:** Our retrospective analysis clearly shows no detriment to outcomes by switching to ISRT technique. In-field relapse rates are comparable between the two techniques thus validating the now common practice of ISRT in Lymphomas.





***In conclusion,  
every Gy counts***



# ***ISRT***

Highest cure rate  
with primary  
therapy



Fewest complications  
for optimal  
survivorship





Thank you!





