Terapie Oncologiche e Cardiotossicità

Torino, 21 settembre 2015

ñIl rischio di tossicità riguardo a: Trattamenti radiantiò

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Å HISTORICAL DATA

Å CURRENT OVERVIEW

Å FUTURE OPPORTUNITIES

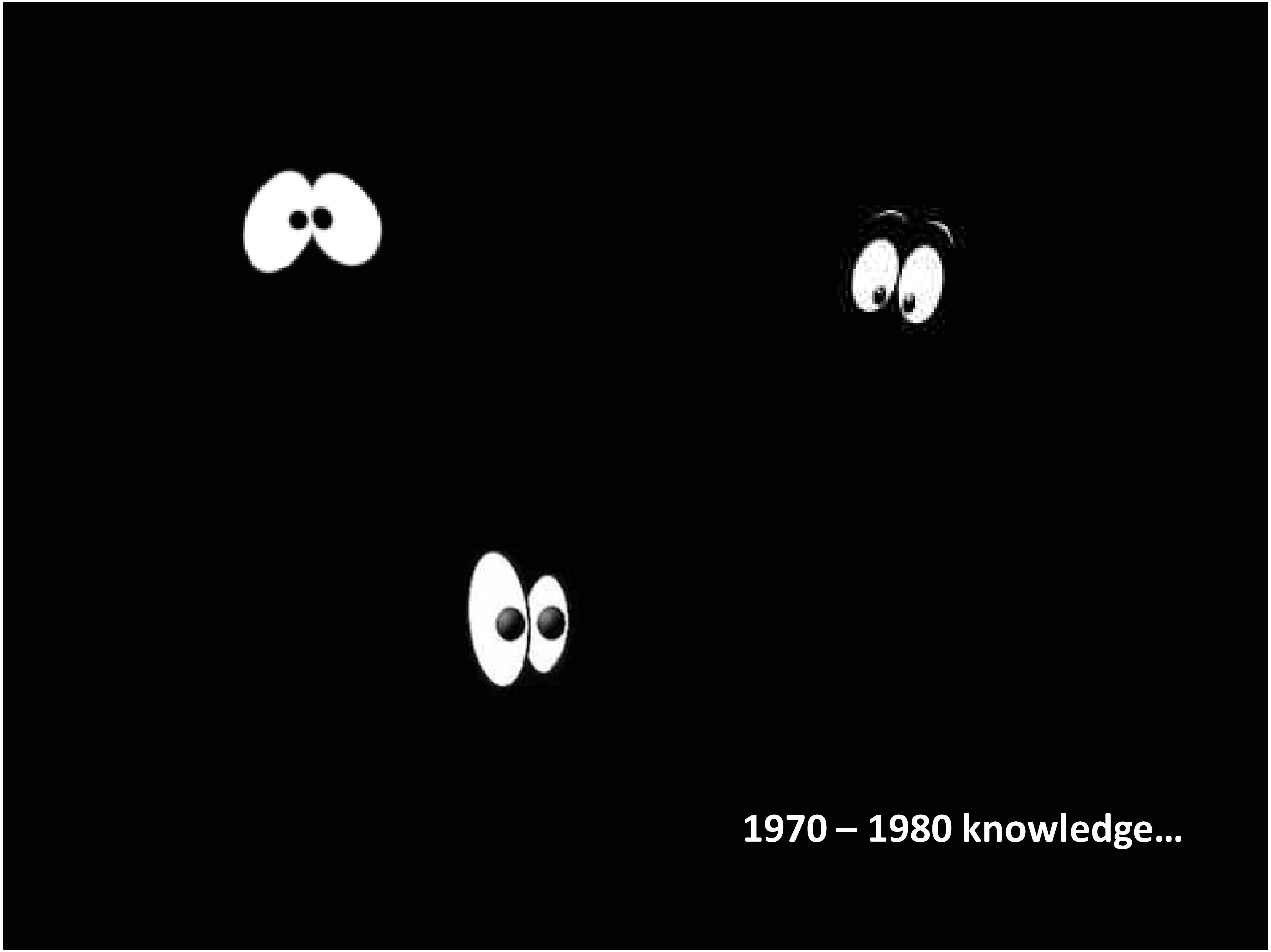
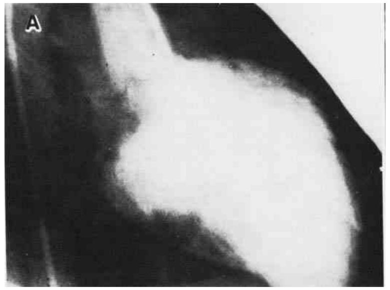

1970 – 1980 knowledge…

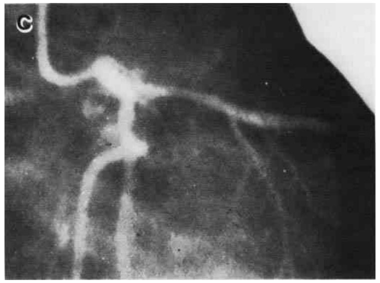
ımage has now been described and investigated e pathologic features of the damage have been ed with regard to all three layers of the heart.[6–9] ditis and pericardial effusion are the most com- ɔmplication of mediastinal radiotherapy involv- heart.[7] Only a few instances of cardiomyopathy) diffuse myocardial fibrosis have been de- [6,10,11]

demonstrated. We suggest a different mechanism myocardial infarction.

Case Report

In April 1978 a 17-year-old woman was found to hạ ular sclerosing Hodgkin's disease. The disease involvec cervical lymph nodes and the mediastinum and her pa





					arteries
13	Current case	19/F	4400	27	Normal coronary arteriogram

* At diagnosis or death.

LAD: left anterior descending artery.

demonstrated by coronary angiography (Fig. 3C). Furthermore, in our patient, the onset of the myocardial infarction was associated with pericarditis and pericardial effusion (Fig. 2) and later on, the course of her disease was complicated by "variant" angina pectoris which responded dramatically to treatment with corticosteroid hormones.

Pericarditis is the most common complication of irradiation of the heart.[7] In various series of patients treated with mantle radiotherapy for Hodgkin's disease, up to 30% of the patients had evidence of radiation induced pericarditis and pericardial effusion when the radiation doses exceed 3500 rad.[26,31] The actual rate of pericardial complications was shown to be proportional

coronary arteries, while the others have no detectable coronary occlusion when subsequently studied by coronary arteriography.[33,34] The main mechanism suggested for myocardial infarction with normal coronary arteries is coronary artery spasm.[35] This is also the pathophysiology suggested for the unusual type of angina named "variant" angina pectoris.[36] Vasospasm may result from various mechanical, nervous or pharmacologic stimuli acting on hypersensitive coronary vessels.[36] The case of our patient suggests that radiation-induced pericarditis may also serve as a trigger of coronary vasospasm. Lewis *et al.*[37] described a woman with "variant" angina pectoris, transient inferior leads ST segment elevation, transient complete heart block and selective right

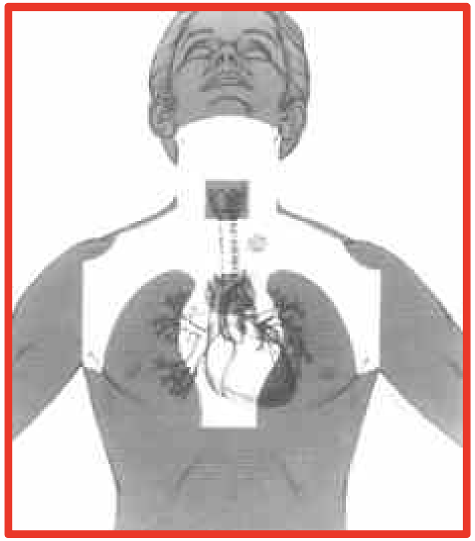
August 15, 1983 – *"Myocardial infarction due to coronary artery disease is a rare complication of radiotherapy involving the heart"*

Yahalom J et al. Cancer 1983; 53: 637-641

DISCOVERING RADIATION INDUCED HEART DISEASE…

DURING the past 30 years, Hodgkin's disease has become one of the most curable neoplasms; more than 75% of patients are expected to achieve long-term freedom from relapse with appropriate therapy.[1] However, overall survival has been affected by intercurrent or treatment-induced diseases. Among a group of patients treated for Hodgkin's disease at Stanford University, death caused by heart disease was exceeded only by death caused by Hodgkin's disease and other neoplasms.[2] A variety of radiation-induced or radiation-associated heart diseases have been characterized, including acute pericarditis during mediastinal irradiation, delayed acute pericarditis and pericardial effusions, peri-

tients have died from Hodg
and 290 from other causes.
The treatments given fo
disease and identified cases
heart disease are summari
1 and 2. Mantle irradiatio
encompassed cervical, sup
axillary, mediastinal, and p
lar lymph node regions w
1609 patients as part of to



- ✓ **2232 pts**
- ✓ **Enrollement: 1960-1991**

DOSE RELATED SIDE EFFECTS

bers of excess acute myocardial infarction deaths with increasing age at treatment, despite the decline in RR (P=.01).

The risk of acute myocardial infarction death also varied by latency period (Table 6). The RR of acute myocardial infarction death was already twice normal during the first 5 years after the initiation of Hodgkin's disease therapy and rose progressively with increasing observation to an RR of 5.6 at 20 or more years after initiation of therapy (χ for trend, P=.02). The AR rose progressively from 6.4 to 70.6 excess cases per 10 000 person-years of observation as the interval from initiation of therapy increased from less than 5 years to 20 or

under 30 years of age, 18.8 (8.2 to 37.2) for those 30 through 39 years, 7.0 (4.0 to 10.0) for those 40 through 49 years, 4.5 (2.4 to 7.5) for those 50 through 59 years, 2.2 (1.2 to 3.8) for those 60 through 69 years, and 1.6 (0.8 to 2.9) for those 60 years of age or older. The ARs rose progressively from 9.0 excess cases per 10 000 person-years of observation for those between 30 and 39 years of age to 52.7 for those 60 through 69 years of age. These data and the patterns of higher risks at shorter latency among those irradiated at younger ages suggest that there is no common age at which treatment-related increases in coronary artery disease risks are ex-

Hodgkin's disease patients, including 22.5% of females and 23.1% of males. Among white US adults, 25.5% currently smoke (95% CI, 24.9% to 26.0%), including 23.8% of females (95% CI, 23.1% to 24.5%) and 27.4% of males (95% CI, 26.5% to 28.2%). Among the 49 patients who died of myocardial infarction after mediastinal irradiation, 53% had a documented history of current or former cigarette smoking. The impact of other risk factors for coronary artery disease could not be adequately assessed in this population.

Risk for Death From Other Cardiac Diseases

Hancock SL et al. JAMA 1993; 270: 1949-1955

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Late cardiotoxicity after treatment for Hodgkin lymphoma

Berthe M. P. Aleman,[1] Alexandra W. van den Belt-Dusebout,[2] Marie L. De Bruin,[2] Mars B. van 't Veer,[3] Margreet H. A. Baaijens,[4] Jan Paul de Boer,[5] Augustinus A. M. Hart,[1] Willem J. Klokman,[2] Marianne A. Kuenen,[2] Gabey M. Ouwens,[2] Harry Bartelink,[1] and Flora E. van Leeuwen[2]

blood

- ✓ **1474 pts**
- ✓ **Enrollement: 1965-1995 (median follow-up 18,7 years)**
- ✓ **1241 mediastinal RT (87%)**
- ✓ **40 Gy/20 fr (RT) or 30-36 Gy (RT-CT)**

Treatment group	Time since diagnosis†					
	10 y, %	15 y, %	20 y, %	25 y, %	30 y, %	35 y, %
Actuarial risk according to the Kaplan-Meier method*						
No mediastinal RT	0.4	0.4	0.4	0.4	2.5	2.5
Mediastinal RT only	0.0	0.6	4.5	7.5	13.9	13.9
Mediastinal RT + CT, no anthracyclines	0.7	1.7	3.5	6.5	11.3	24.8
Mediastinal RT + anthracyclines	1.5	2.8	10.7	10.7	29.8	NA
All treatments	0.7	1.5	4.4	6.7	12.2	20.0
Cumulative incidence with death from any cause as competing risk*						
No mediastinal RT	0.4	0.4	0.4	0.4	2.0	2.0
Mediastinal RT only	0.0	0.6	4.2	6.8	11.7	11.7
Mediastinal RT + CT, no anthracyclines	0.6	1.5	2.8	4.9	7.6	14.3
Mediastinal RT + anthracyclines	1.4	2.5	7.9	7.9	15.7	NA
All treatments	0.6	1.3	3.7	5.4	8.9	13.1

Aleman B et al. Blood 2007;109(5):1878-1886

Cardiac Effects of Radiotherapy

Asymptomatic Cardiac Disease Following Mediastinal Irradiation

- ✓ 294 asymptomatic patients
- ✓ Previous RT for Hodgkin Lymphoma
- ✓ **RT dose ≥ 35 Gy**
- ✓ Each patient underwent TT Echocardiography

Echocardiographic Finding	All Patients n = 294	Years Following Irradiation: 2ï 10 n = 89	11ï 20 n = 132	> 20 n = 73	p Value*
Aortic regurgitation					
Trace (%)	27 (9)	9 (10)	13 (10)	5 (7)	0.71
Mild (%)	62 (21)	3 (3.4)	26 (20)	33 (45)	< 0.0001
Moderate or severe (%)	15 (5.1)	1 (1.1)	3 (2.3)	11 (15)	< 0.0001
Mitral regurgitation					
Trace (%)	87 (30)	27 (30)	44 (33)	16 (22)	0.21
Mild (%)	105 (36)	21 (24)	49 (37)	35 (48)	0.005
Moderate or severe (%)	10 (3.4)	2 (2.3)	5 (3.8)	3 (4.1)	0.71

Å ***Asymptomatic valve disease are more frequent in irradiated cohort than in the Framingham population.***

Å ***The latency period following irradiation is the most important risk factor for development of valvular abnormalities.***

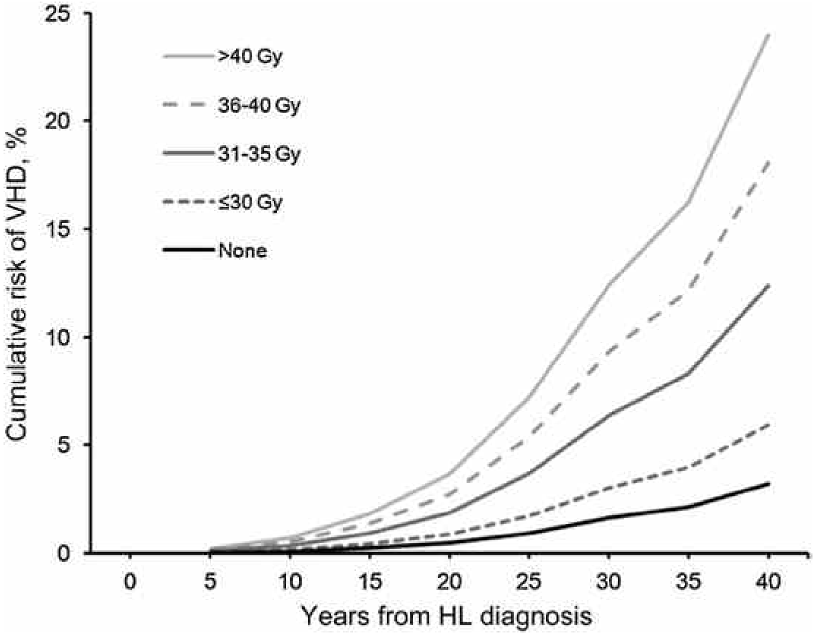
Å ***These findings suggest that echocardiography should be considered during follow-up care for asymptomatic patients who have received more than 35 Gy of mediastinal irradiation.***

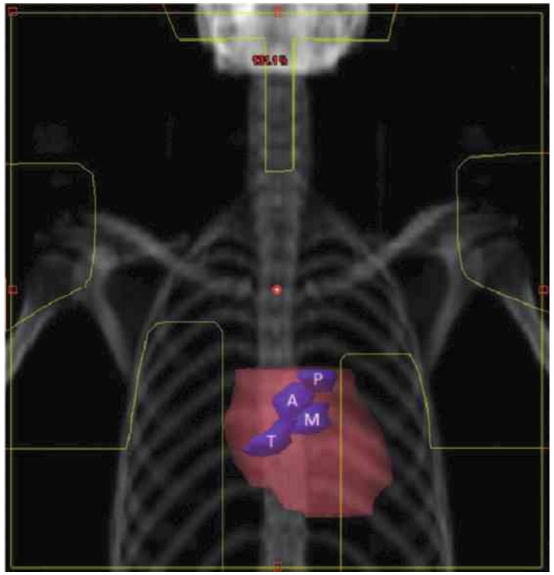
Heidenreich PA et al. JACC 2003;42(4):743-749

ARTICLE

Risk of Valvular Heart Disease After Treatment for Hodgkin Lymphoma

- ✓ *1852 patients*
- ✓ *Median follow up: 20 years*



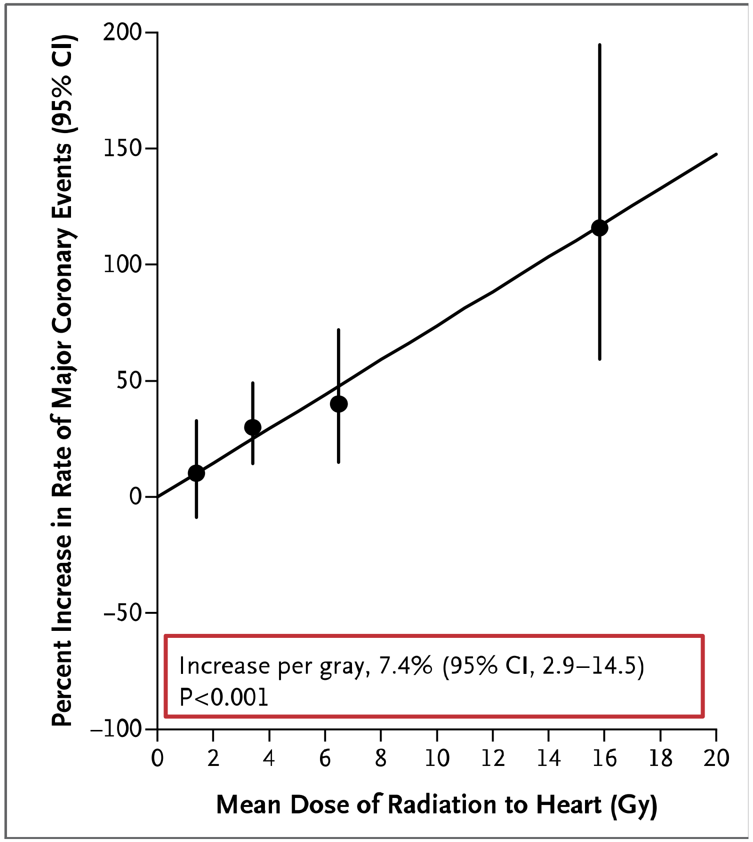


This study confirms that radiation dose to the heart valves is the main risk factor for the development of clinically significant VHD following treatment for HL.

Cutter et al JNCI 2015;107(4):djv008

Risk of Ischemic Heart Disease in Women after Radiotherapy for Breast Cancer

- ✓ Population-based case–control study of major coronary events
- ✓ 2168 women who underwent radiotherapy for breast cancer between 1958 and 2001
- ✓ 963 women with major coronary events and 1205 controls.



Darby SC et al. NEJM 2013;368(11): 987-998

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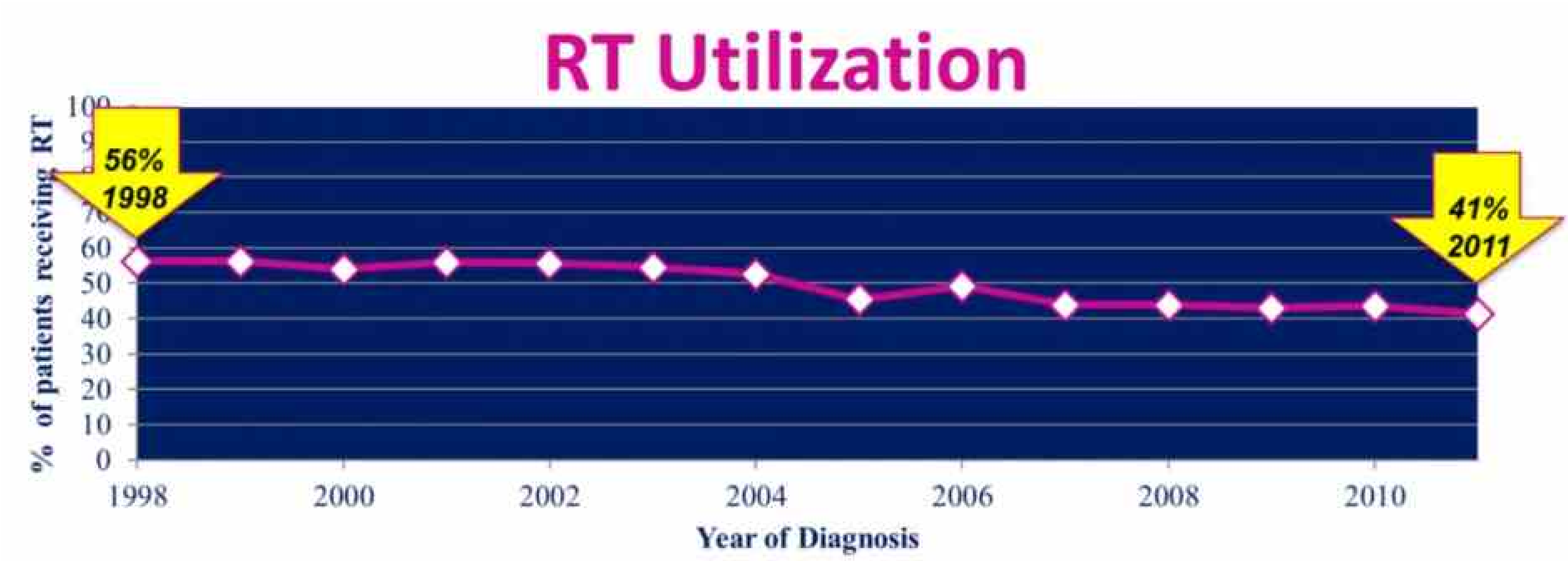
December 10, 2009 – *"Most of the late complications of treatment seen in HL survivors are related to RT."*

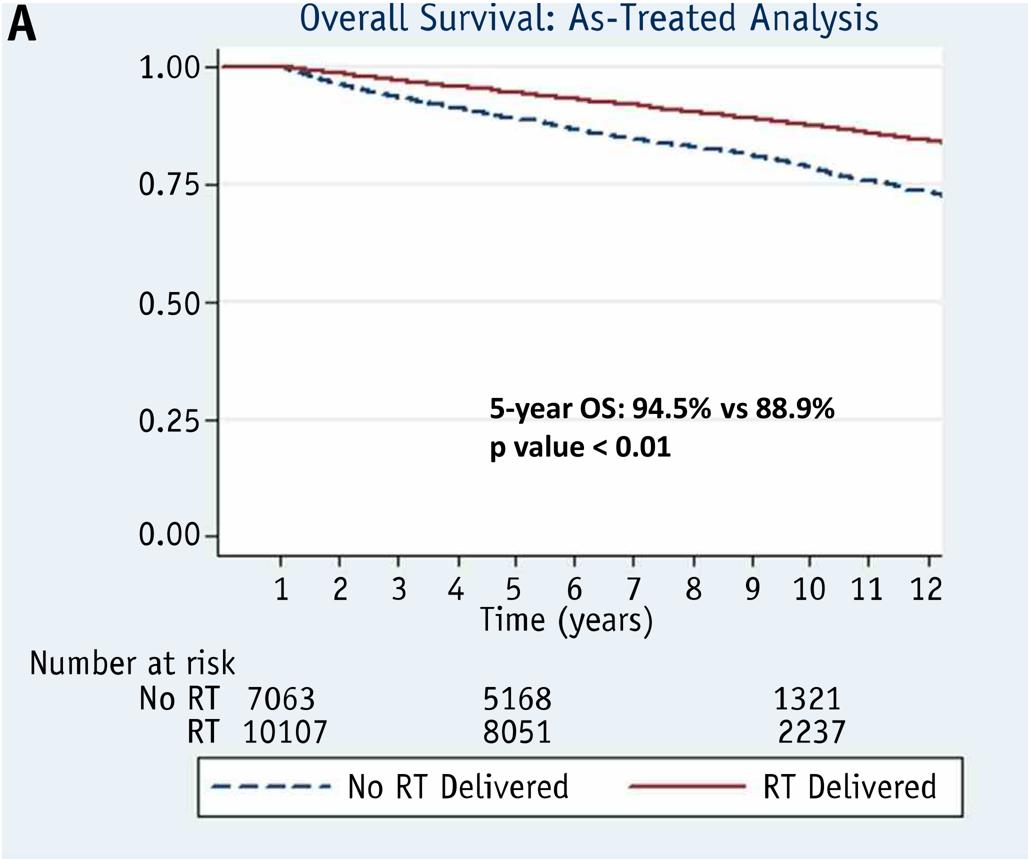
Straus D.J.

RT IN EARLY STAGE HODGKIN LYMPHOMA



Early-Stage Classic Hodgkin Lymphoma: The Utilization of Radiation Therapy and Its Impact on Overall Survival

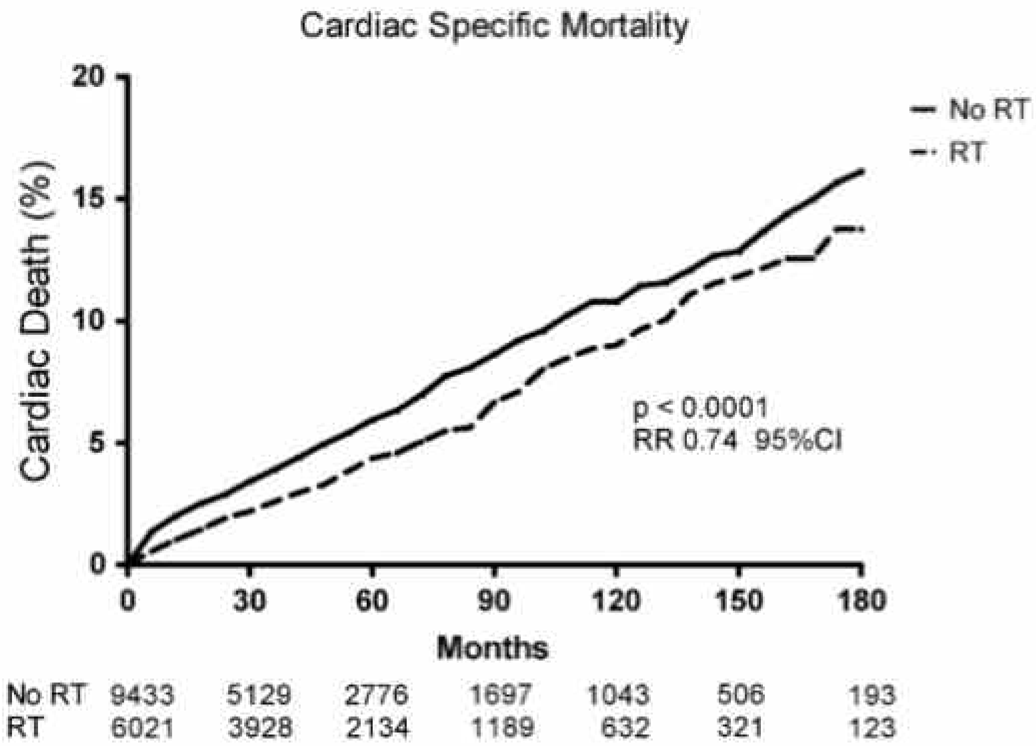
International Journal of Radiation Oncology biology • physics



Parikh et al. IJROBP 2015, in press

CARDIAC MORTALITY IN PATIENTS WITH STAGE I AND II DIFFUSE LARGE B-CELL LYMPHOMA TREATED WITH AND WITHOUT RADIATION: A SURVEILLANCE, EPIDEMIOLOGY, AND END-RESULTS ANALYSIS

- ✓ **> 15.000 pts**
- ✓ **Enrollement: 1988-2004**



Pugh TJ et al. IJROBP 2010; 76(3): 845-849

STRENGTHS AND WEAKNESSES

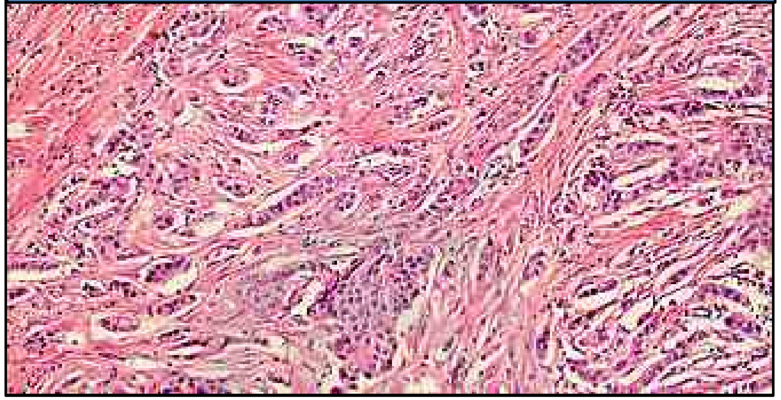
Å HISTORICAL DATA

Å CURRENT OVERVIEW

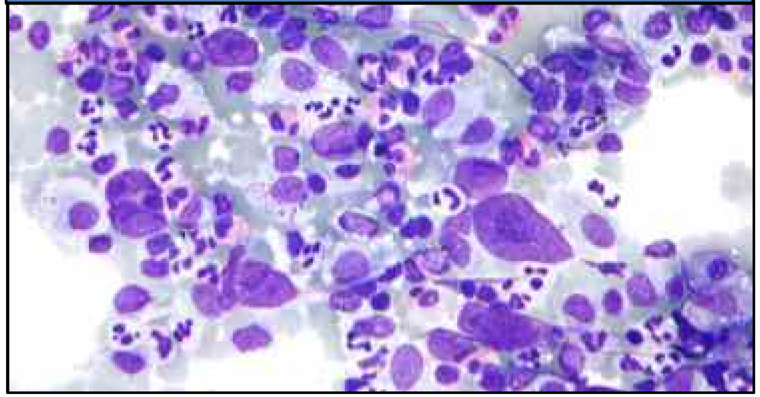
Å FUTURE OPPORTUNITIES

Radiation-associated cardiac disease is seen in patients treated for:

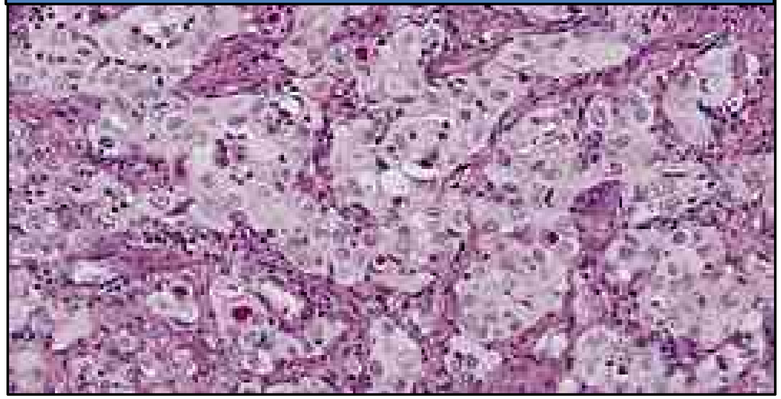
1) Breast cancer → **50 Gy/25 fractions**
(HYPO-RT 46 Gy/20 fr or 40Gy/15 fr)



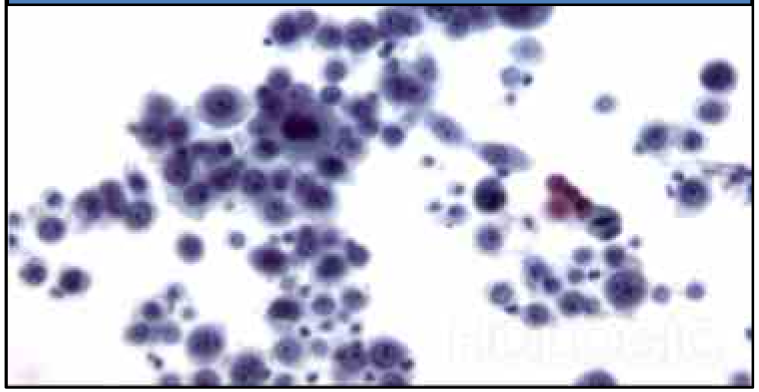
2) Lymphoma → **30–36 Gy/ 15–18 fractions**



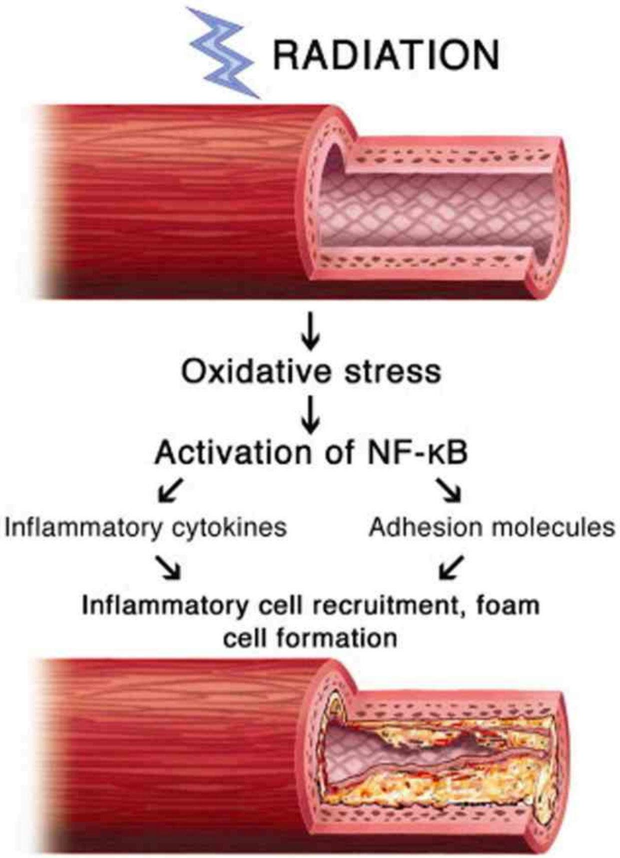
3) Lung cancer → **60–66 Gy/ 30–33 fractions**
(SBRT 54 Gy/3 fr or 55 Gy/5 fr or 60 Gy/8 fr)

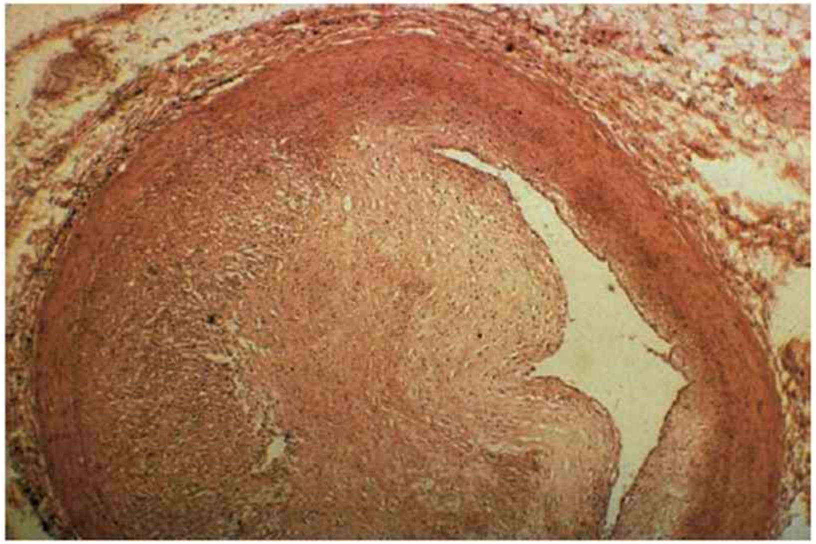


4) Esophageal cancer → **50 Gy/25 fractions**

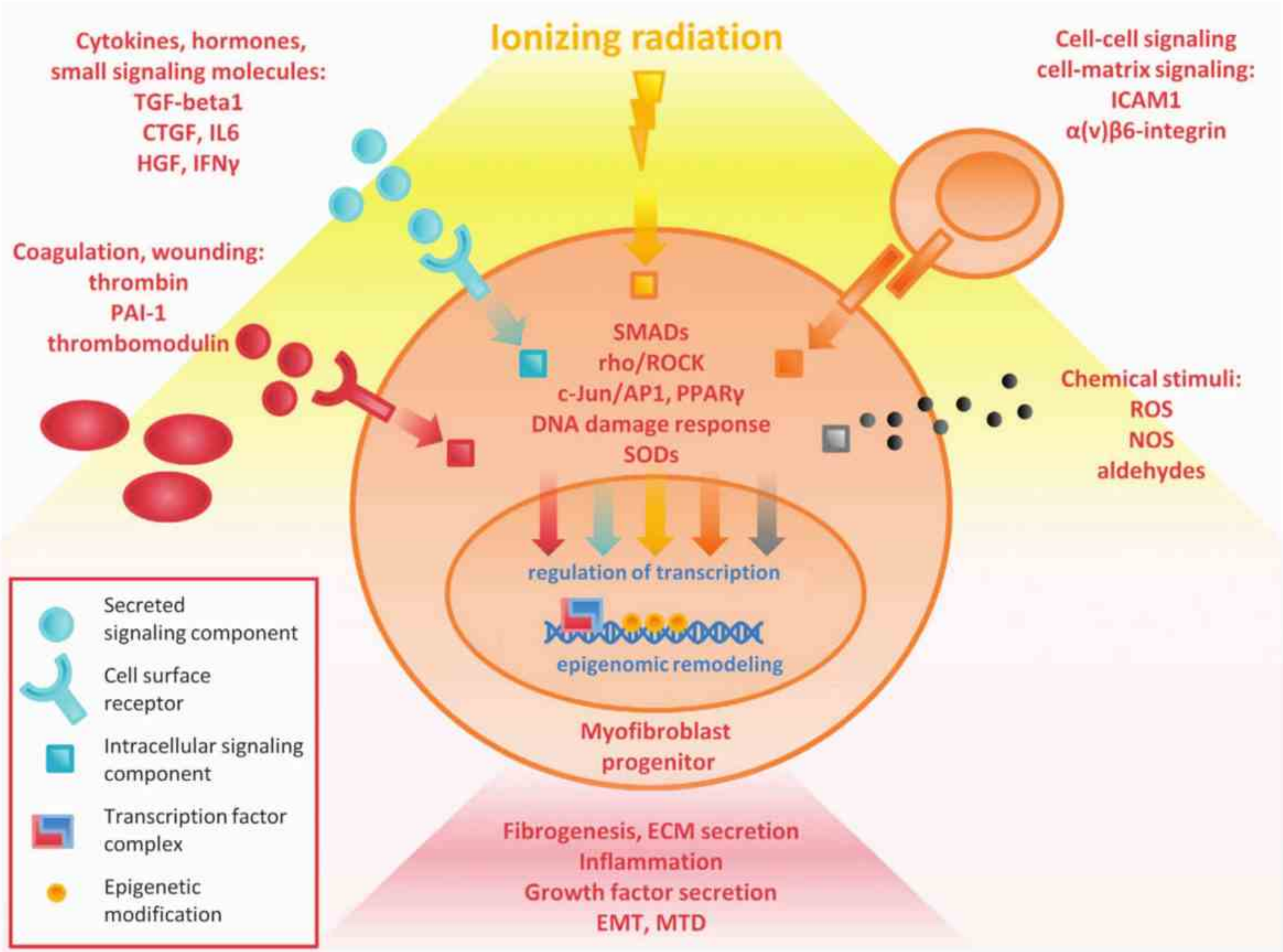


PATHOPHYSIOLOGY OF RADIATION INDUCED HEART DISEASE





Taunk NK et al. Front Oncol 2015;5:39


Ionizing radiation
Cytokines, hormones, small signaling molecules:
TGF-beta1
CTGF, IL6
HGF, IFNγ
Cell-cell signaling cell-matrix signaling:
ICAM1
α(v)β6-integrin
Coagulation, wounding:
thrombin
PAI-1
thrombomodulin
SMADs
rho/ROCK
c-Jun/AP1, PPARγ
DNA damage response
SODs
Chemical stimuli:
ROS
NOS
aldehydes
regulation of transcription
epigenomic remodeling
Myofibroblast progenitor
Fibrogenesis, ECM secretion
Inflammation
Growth factor secretion
EMT, MTD
Secreted signaling component
Cell surface receptor
Intracellular signaling component
Transcription factor complex
Epigenetic modification

Radiation-Induced Heart Disease

- Early toxicity (within 6 months)
  - Pericarditis
- Late toxicity (>5-10 yrs)
  - Functional valvular injury
  - Congestive heart failure
  - Cardiomyopathy
  - Coronary artery disease
  - Conduction defects

FACTORS AFFECTING RISK

Patients risk factors

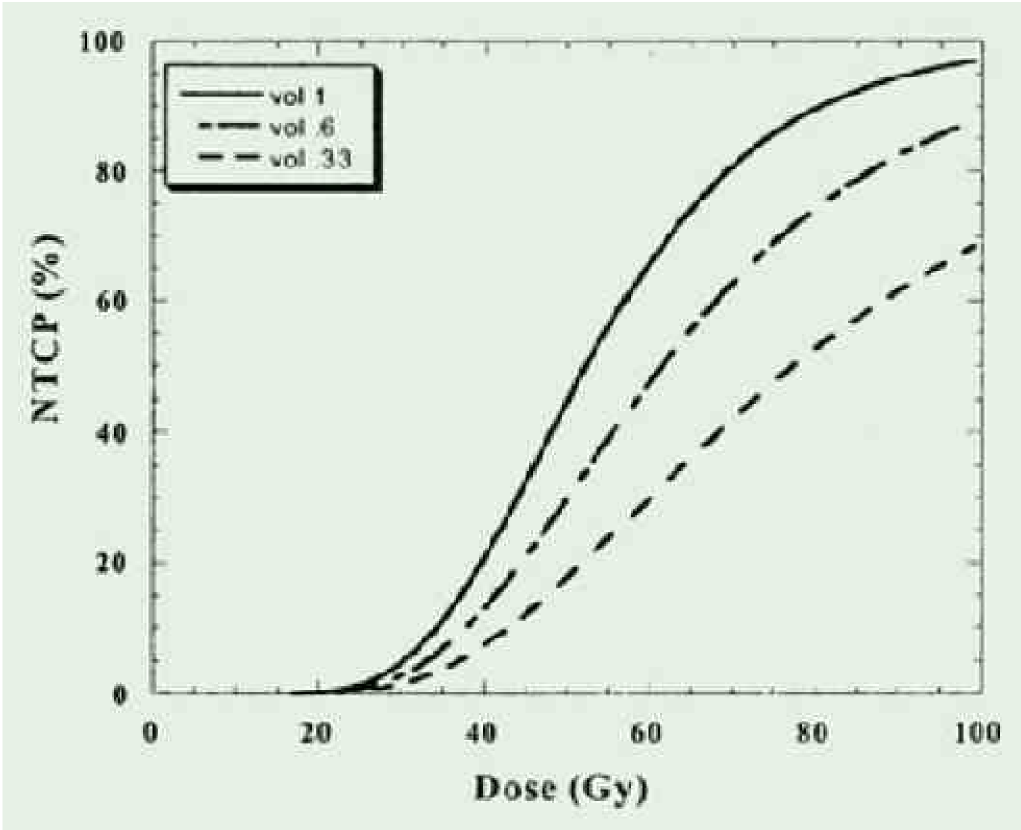
- AGE
- GENDER
- DIABETES MELLITUS
- HYPERTENSION
- ANEMIA
- SMOKING
- DYSLIPIDEMIA
- PARENTAL HISTORY OF CAD

Treatment risk factors

- ANTHRACYCLINE THERAPY
- PACLITAXEL (CHF in elderly)
- SYNERGISTIC CT-RT EFFECT
- MONOCLONAL ANTIBODIES
- 5-FLUOROURACIL

Gagliardi et al. Int J Rad Onc Biol Phys 2010

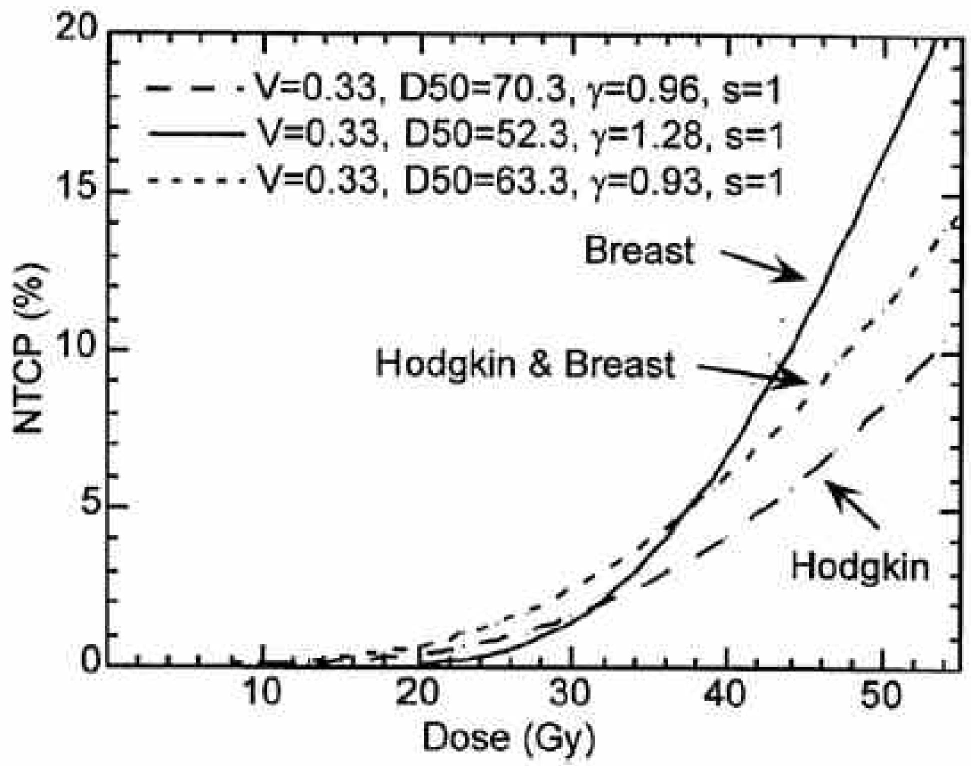
REVIEW OF DOSE/VOLUME FACTORS



Gagliardi G et al, 2001

CHALLENGES IN DEFINING VOLUMES

Heart region functionally most important for RT induced toxicity…?

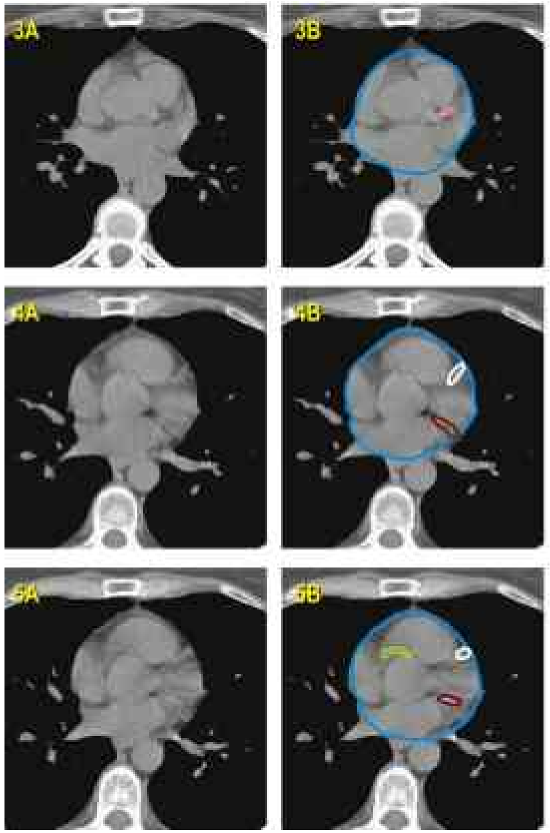


Gagliardi et al Int J Rad Onc Biol Phys 2010

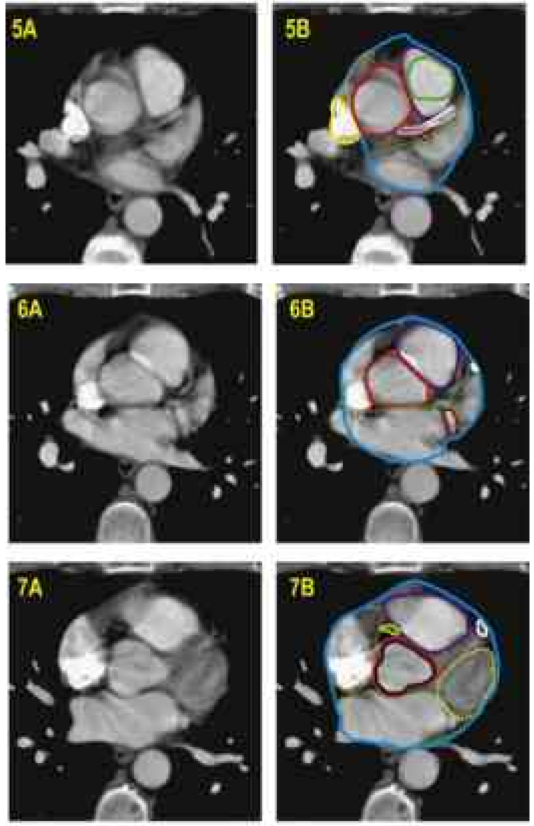
CLINICAL INVESTIGATION — Breast

DEVELOPMENT AND VALIDATION OF A HEART ATLAS TO STUDY CARDIAC EXPOSURE TO RADIATION FOLLOWING TREATMENT FOR BREAST CANCER

BASAL TC



IV CONTRAST MEDIA INFUSION



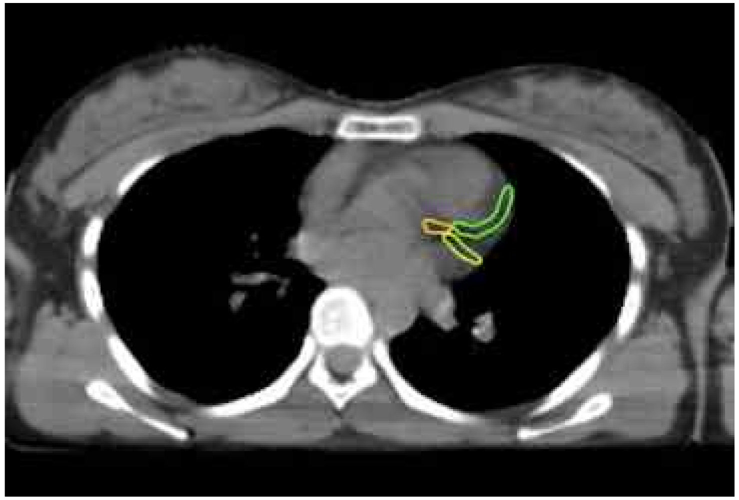
Feng M et al. IJROBP 2011; 79(1): 10-18

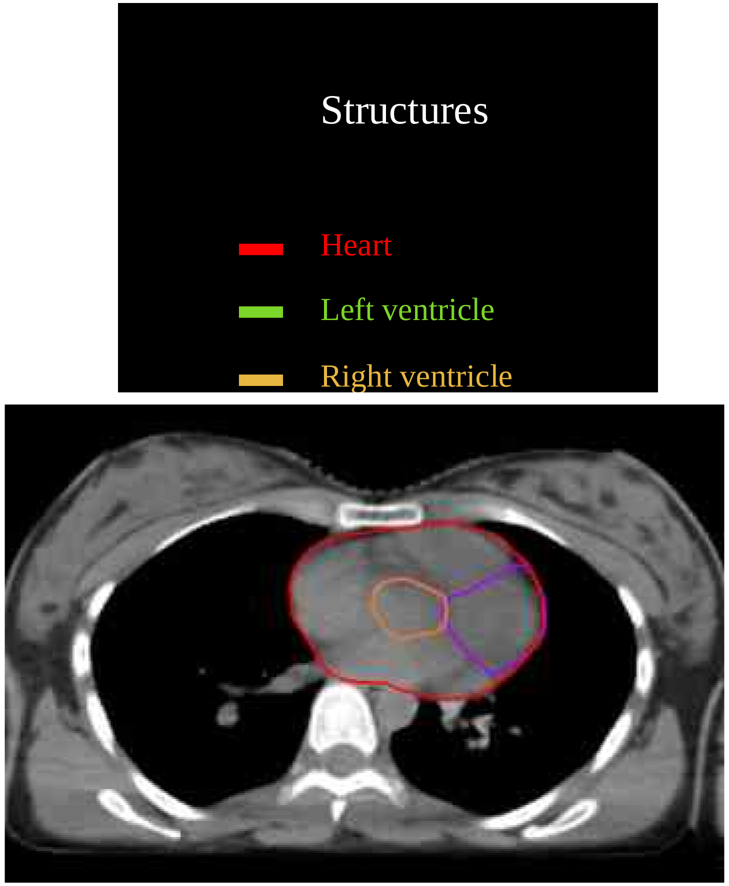
TREATMENT PLANNING

(Image fusion)

HEART STRUCTURES CONTOURING

CORONARIES DEFINITION





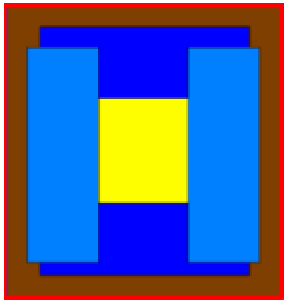
CHAMBERS AND VALVES DEFINITION

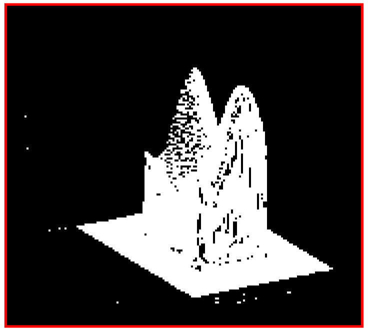
THE CONFORMALITY CONTINUUM

1980s	Late 1990s	2000s	2010s

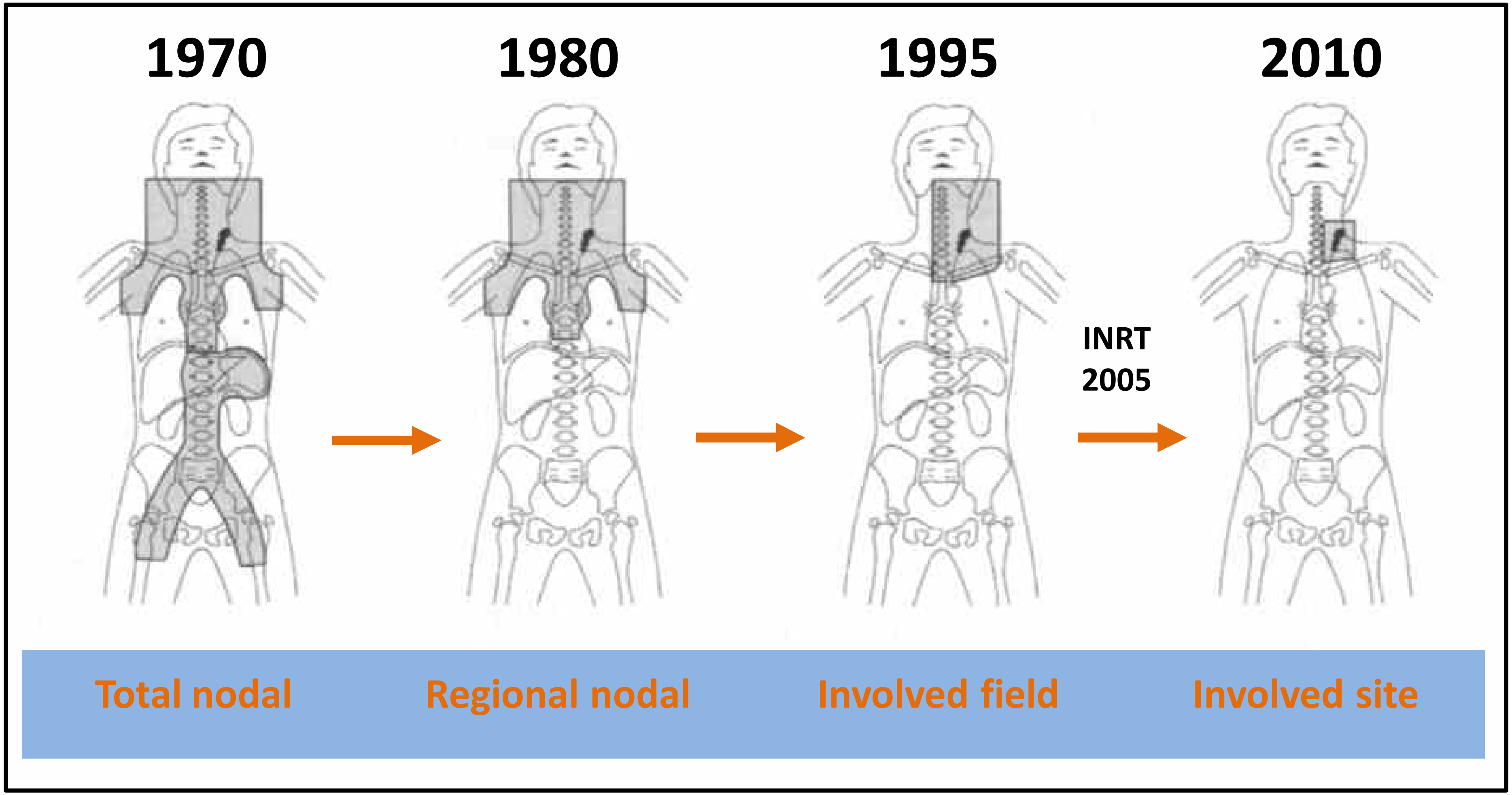
TREND – Improving Precision

2D	3D-CRT	IMRT/VMAT	IGRT





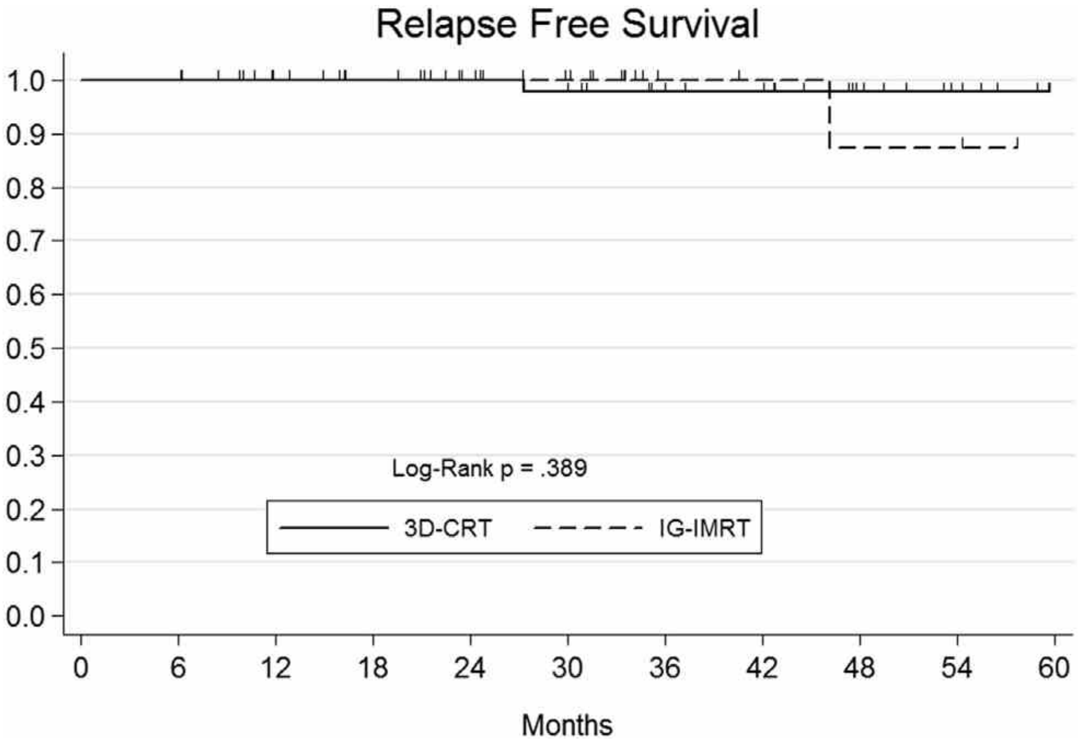
EVOLUTION OF RT VOLUME / DOSE IN LYMPHOMA



Dose: 36-44 Gy → 20-30 Gy

Involved-Site Image-Guided Intensity Modulated Versus 3D Conformal Radiation Therapy in Early Stage Supradiaphragmatic Hodgkin Lymphoma

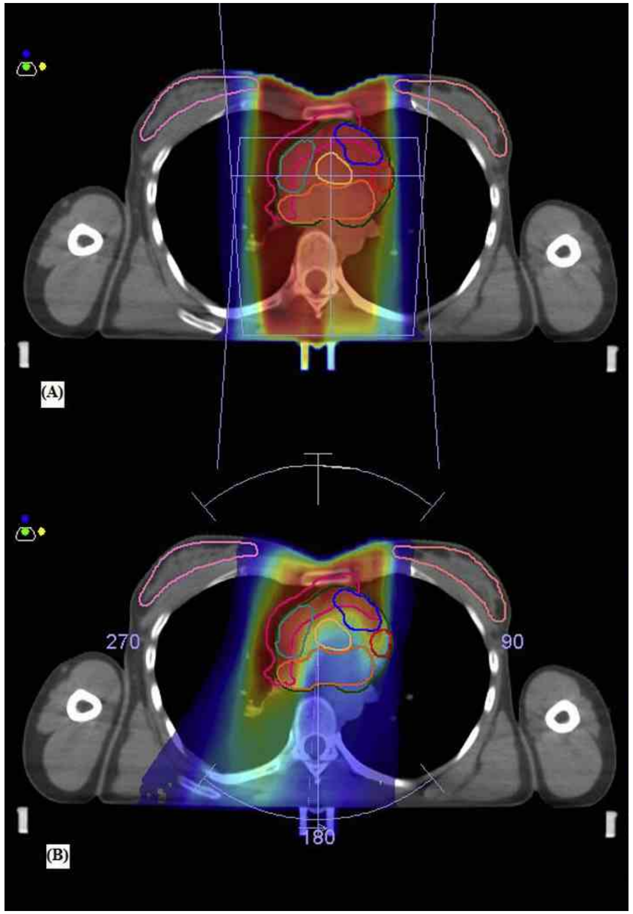
International Journal of Radiation Oncology biology • physics



Filippi AR et al. Int J Rad Onc Biol Phys 2014

Optimized Volumetric Modulated Arc Therapy Versus 3D-CRT for Early Stage Mediastinal Hodgkin Lymphoma Without Axillary Involvement: A Comparison of Second Cancers and Heart Disease Risk

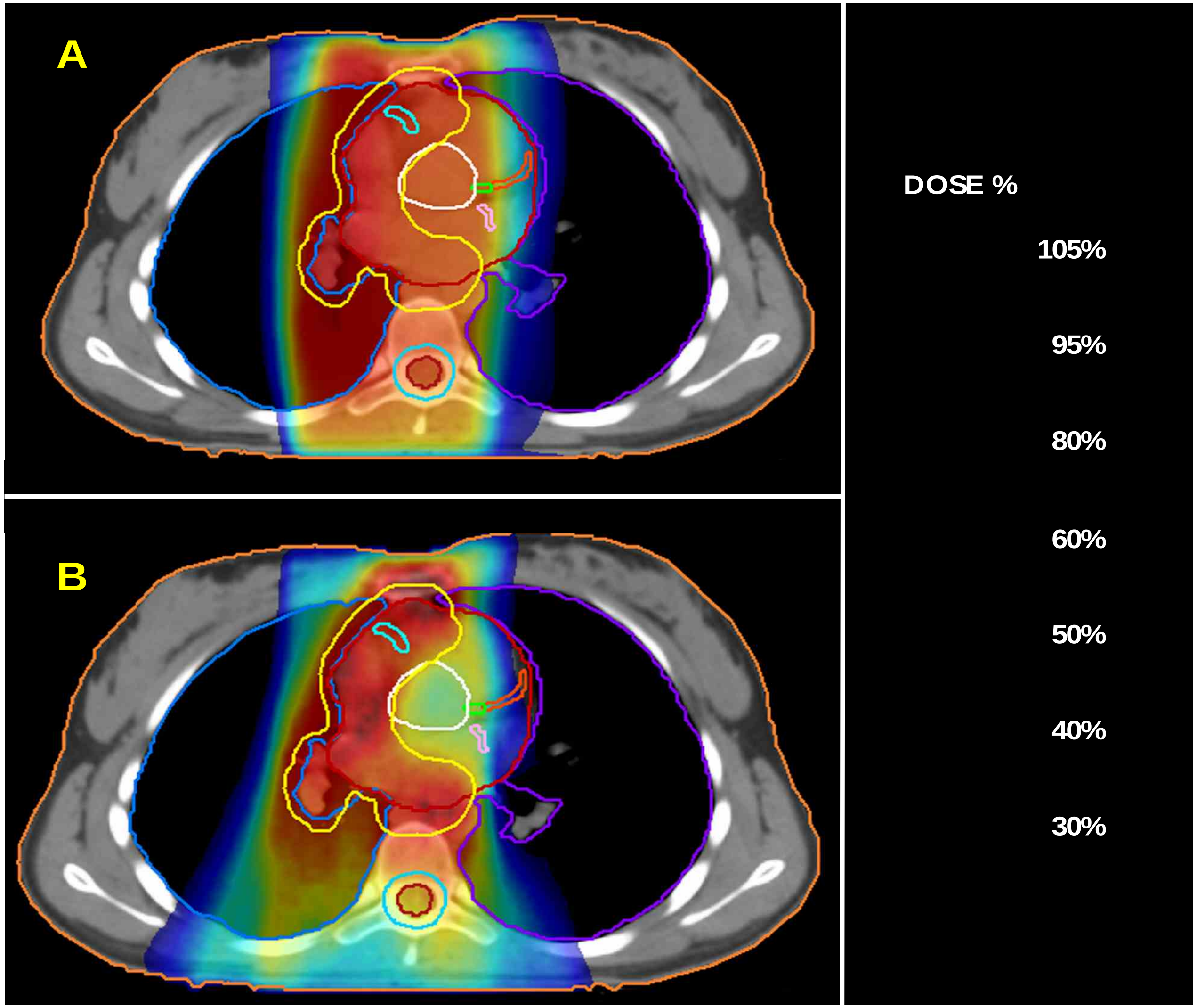
CrossMark



Site	Mean AER and SD		P value
	3D-CRT	VMAT	
Cardiac diseases	0.74 ± 1.50	0.37 ± 0.45	.038
Aortic valve	2.15 ± 2.27	0.26 ± 0.63	<.0001
Pulmonic valve	3.13 ± 3.24	1.36 ± 1.88	<.0001
Mitral valve	0.29 ± 1.10	0.003 ± 0.007	.12
Tricuspid valve	0.73 ± 2.11	0.07 ± 0.36	.045
All valves	1.57 ± 2.55	0.42 ± 1.14	<.0001

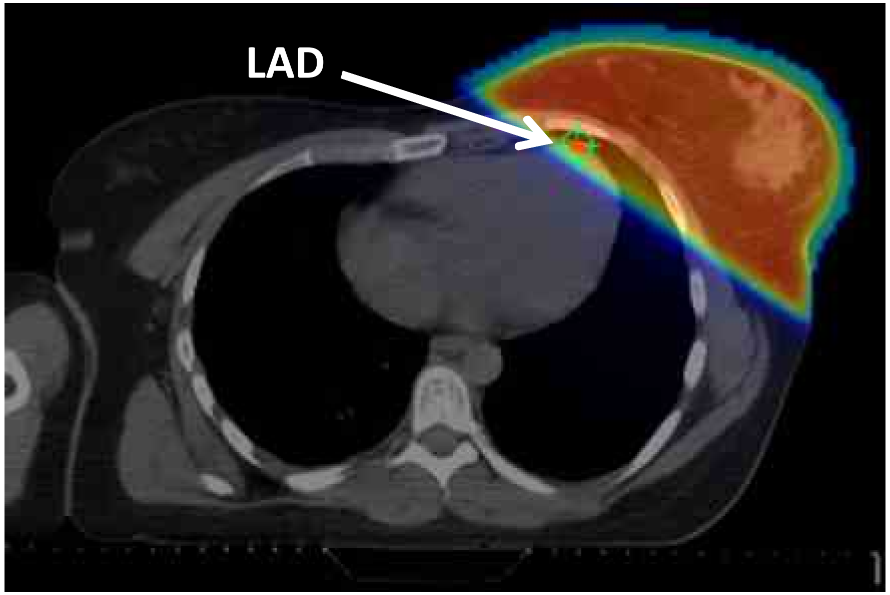
Filippi AR et al. IJROBP 2015;92(1):161-168

HODGKIN LYMPHOMA



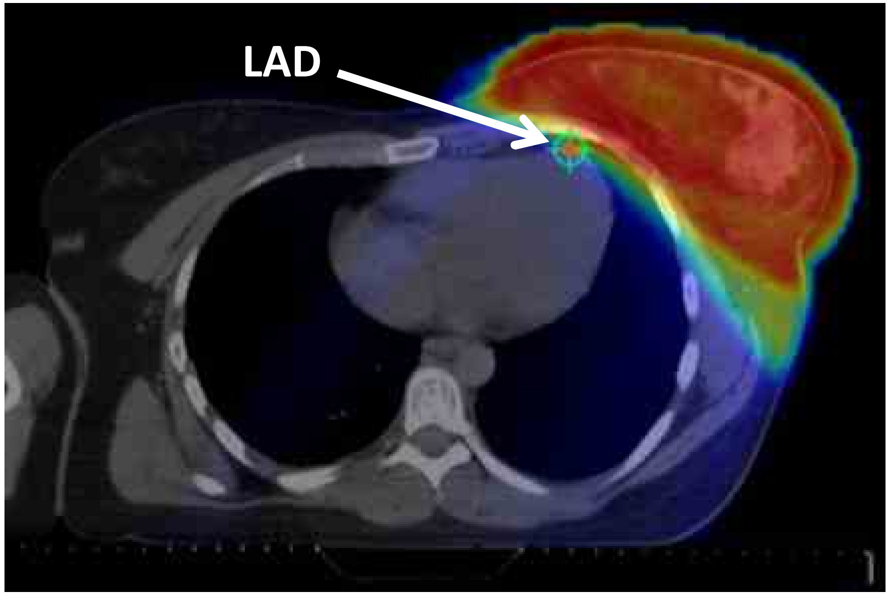
BREAST CANCER

TANGENTIAL FIELDS (3D-RT)



value: +38.8416
units: GY

IMRT



value: +18.5517
units: GY

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PHYSICS CONTRIBUTION

International Journal of
Radiation Oncology
biology ● physics

INFLUENCE OF RADIOTHERAPY ON THE LATEST GENERATION OF IMPLANTABLE CARDIOVERTER-DEFIBRILLATORS

Table 1. Results for all 11 ICDs

Device	Manufacturer	Model	Malfunction (not point of failure)	Dose at first malfunction (Gy)	Point of failure	Dose at point of failure (Gy)
1	Guidant	Ventak PRIZH VR HE 1852	Too-low shock energy of 22J	120	No shock	120
2	Guidant	Ventak PRIZH VR HE 1852		—	No shock	80
3	St. Jude Medical	Photon uDR model V-232	Sensing threshold 65% too low (Vmin)	90	No output	90
4	Medtronic	Marquis dr model 7274 VVE DDDR	Atrial sensing threshold 100% too high	10	Atrial sensing defect	120
			Battery charge time increase by 50%	120		
5	Medtronic	Marquis dr model 7274 VVE DDDR	Battery charge time increase by 40%	120	Complete sensing defect	120
6	Biotronik	Tupos LV/A+	Too-low shock energy of 18J	0.5	No shock and no output	1.5
7	Biotronik	Tupos LV/A+	Too-low shock energy of 21J	0.5	No shock and no output	2.5
8	Biotronik	Tupos LV/A+			No shock and no output	1.5
9	Biotronik	Tupos LV/A+	Too-low shock energy of 21J	10	No output and atrial sensing defect	120
			Sensing threshold 50% too low (Vmin)	20		
10	Biotronik	Tupos LV/A+		—	No shock and no output	0.5
11	St. Jude Medical	Photon uDR model V-232	Sensing threshold 65% too low (Vmin)	90	No output	90

Hurkmans C et al. Int J Rad Onc Biol Phys 2005;63(1):282-289

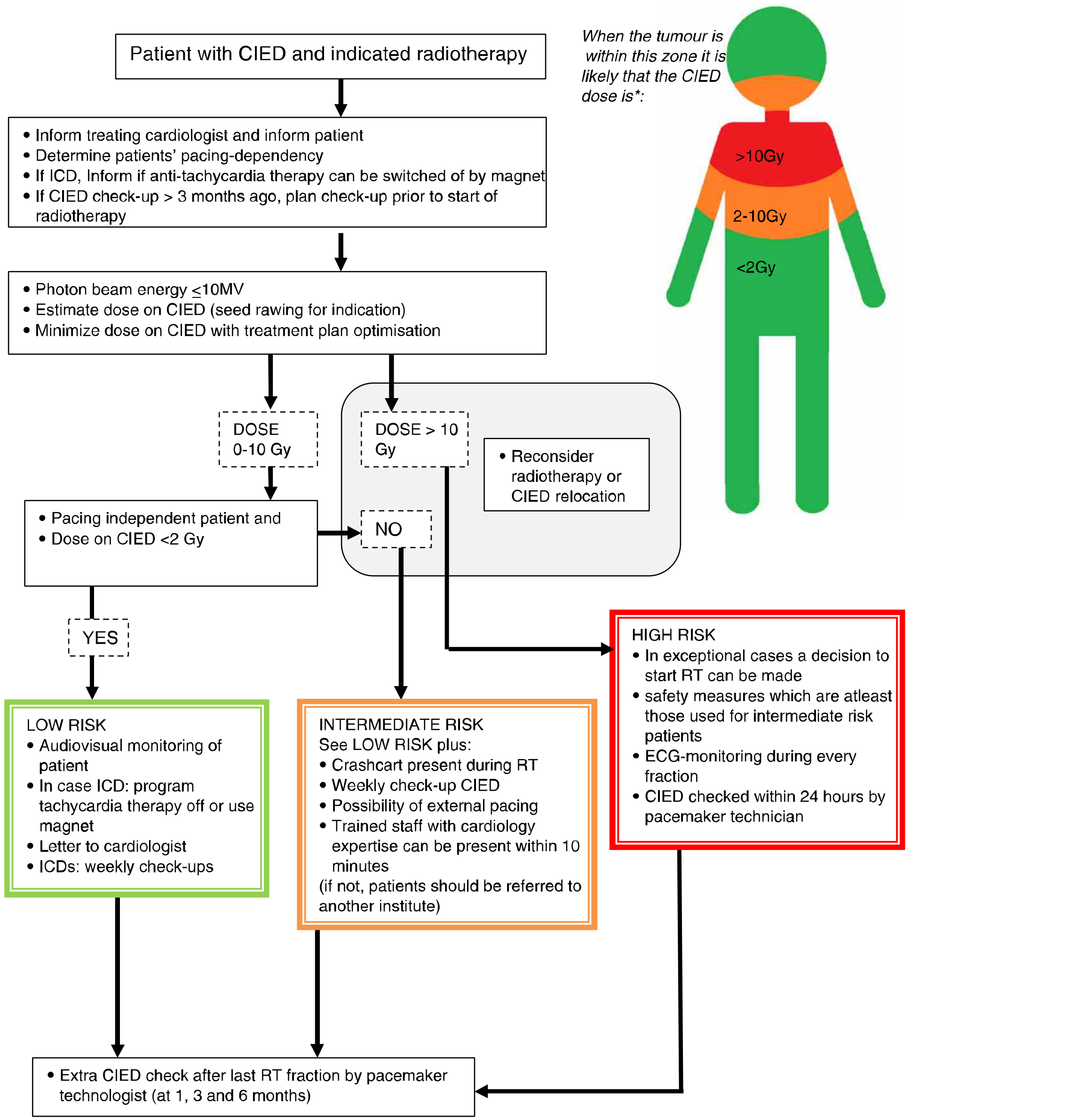


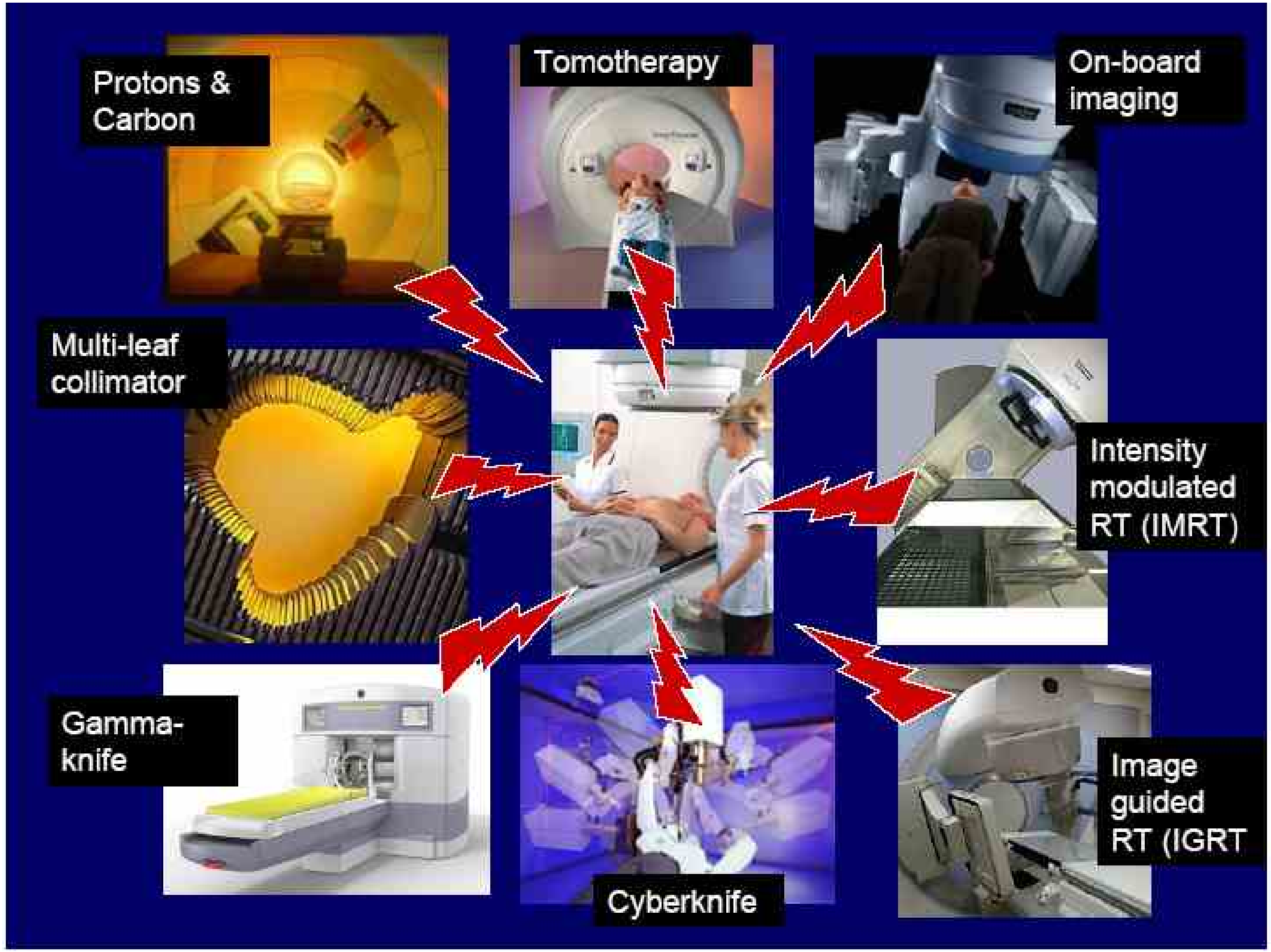
Figure 1 Flow diagram of Dutch guidelines. *Estimation of dose in case of a pectoral placed CIED.

- HISTORICAL DATA

- CURRENT OVERVIEW

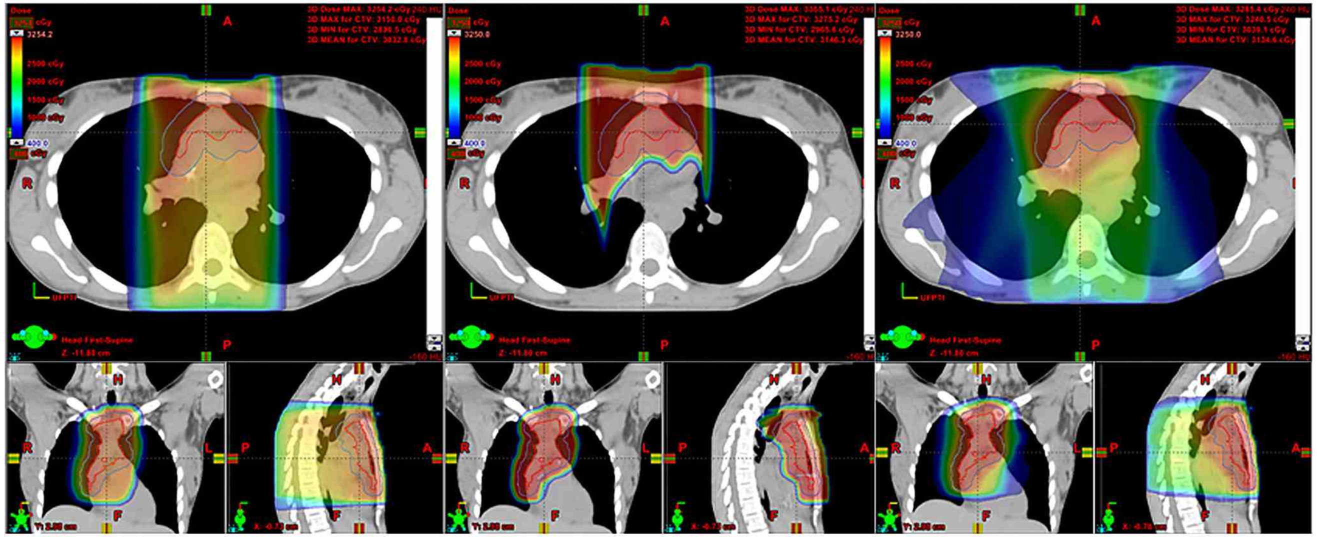
- FUTURE OPPORTUNITIES

TECHNICAL IMPROVEMENT



Involved-Node Proton Therapy in Combined Modality Therapy for Hodgkin Lymphoma: Results of a Phase 2 Study☆

International Journal of Radiation Oncology biology • physics
www.redjournal.org

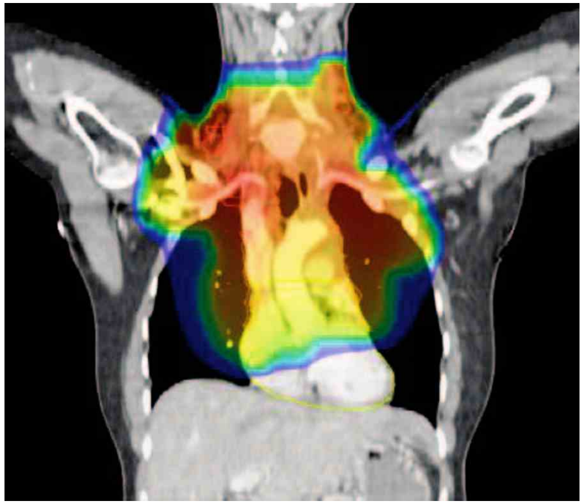


Structure	3DCRT Mean	3DCRT ±SD	IMRT Mean	IMRT ±SD	PT Mean	PT ±SD
Integral dose (joules)	122.9	62.3	103.8	48.6	53.6	32.0
Heart (Gy)	16.5	7.6	12.3	6.2	8.9	5.1
Lung (Gy)	11.6	3.7	9.8	2.8	7.1	2.5
Breast (Gy)	6.3	3.5	6.0	3.4	4.3	3.0
Thyroid (Gy)	19.3	10.1	17.7	9.3	15.8	9.7
Esophagus (Gy)	20.3	4.8	16.4	3.9	13.4	5.6

Hoppe BS et al, IJROBP 2014;89(5):1053-1059

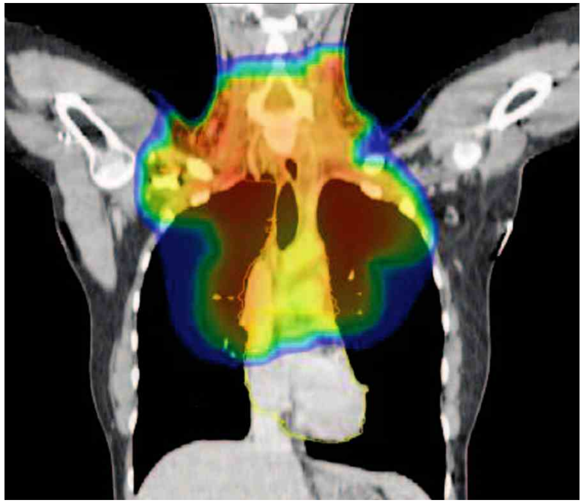
Prospective phase II trial of image-guided radiotherapy in Hodgkin lymphoma: Beneýt of deep inspiration breath-hold

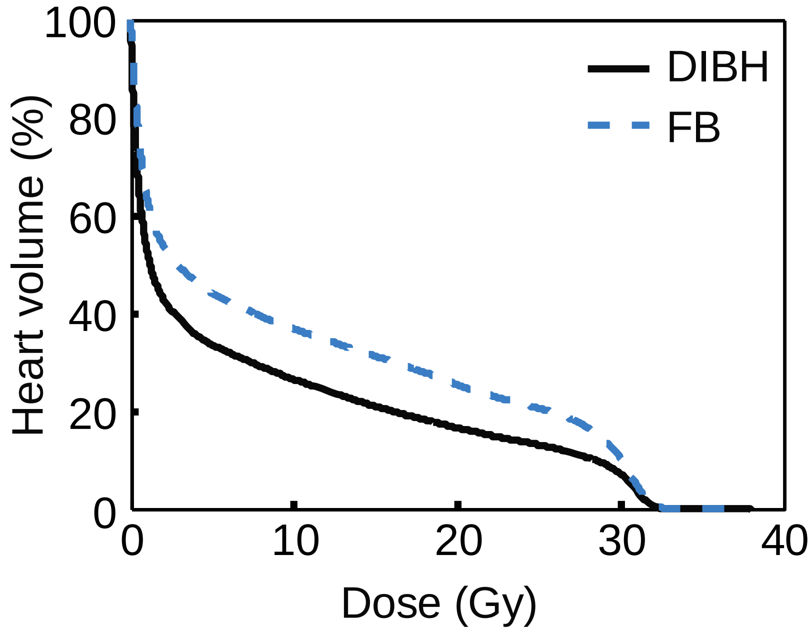
FREE BREATHING



DEEP INSPIRATION BREATH HOLD

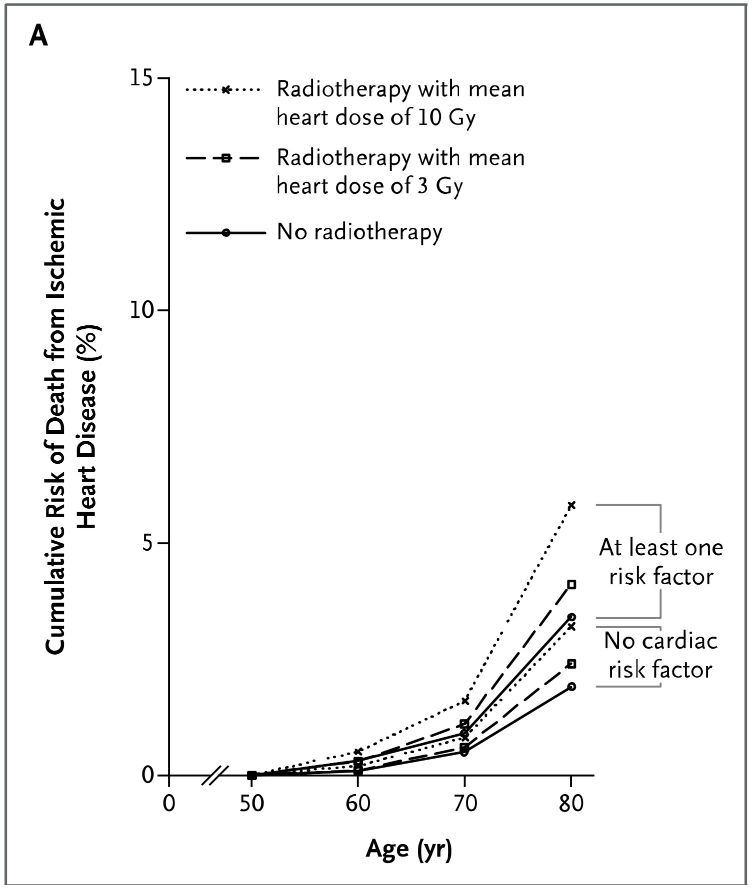
(DIBH)





Petersen PM et al. Acta Oncol. 2015;54:60-66

CARDIOVASCULAR RISK FACTORS



Darby SC et al. NEJM 2013;368(11): 987-998

SCORE

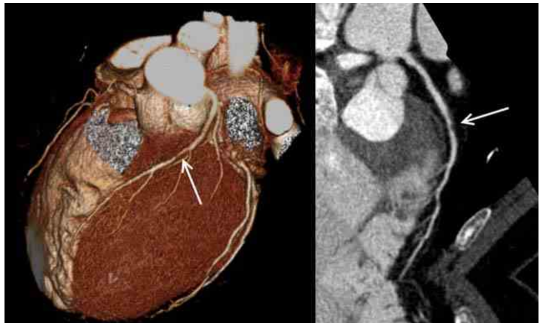
Age	Systolic blood pressure	Women Non-smoker 3	4	5	6	7	Women Smoker 3	4	5	6	7	Men Non-smoker 3	4	5	6	7	Men Smoker 3	4	5	6	7
65	180	4	5	6	7	8	8	9	11	13	15	7	8	10	12	15	13	16	19	23	28
	160	3	3	4	5	6	6	6	8	9	11	5	6	7	9	11	9	11	13	16	20
	140	2	2	3	3	4	4	5	5	6	8	4	4	5	6	8	7	8	10	12	14
	120	1	2	2	2	3	3	3	4	5	6	2	3	4	4	6	5	6	7	8	10
60	180	2	3	3	4	5	4	5	6	7	9	5	5	7	8	10	9	10	12	15	19
	160	2	2	2	3	3	3	4	4	5	6	3	4	5	6	7	6	7	9	11	13
	140	1	1	2	2	2	2	2	3	4	4	2	3	3	4	5	4	5	6	8	10
	120	1	1	1	1	2	1	2	2	3	3	2	2	2	3	4	3	4	4	5	7
55	180	1	1	2	2	2	2	3	3	4	5	3	3	4	5	6	5	6	8	10	12
	160	1	1	1	1	2	2	2	2	3	3	2	2	3	4	5	4	5	6	7	9
	140	1	1	1	1	1	1	1	2	2	2	1	2	2	3	3	3	3	4	5	6
	120	0	0	1	1	1	1	1	1	1	2	1	1	1	2	2	2	2	3	3	4
50	180	1	1	1	1	1	1	1	1	2	2	2	2	2	3	4	3	4	5	6	7
	160	0	0	1	1	1	1	1	1	1	2	1	1	2	2	3	2	3	3	4	5
	140	0	0	0	0	1	0	1	1	1	1	1	1	1	2	2	2	2	2	3	4
	120	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	2	2	3
40	180	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1	2	2
	160	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	1
	140	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	1	1
	120	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1

Total cholesterol:HDL cholesterol ratio

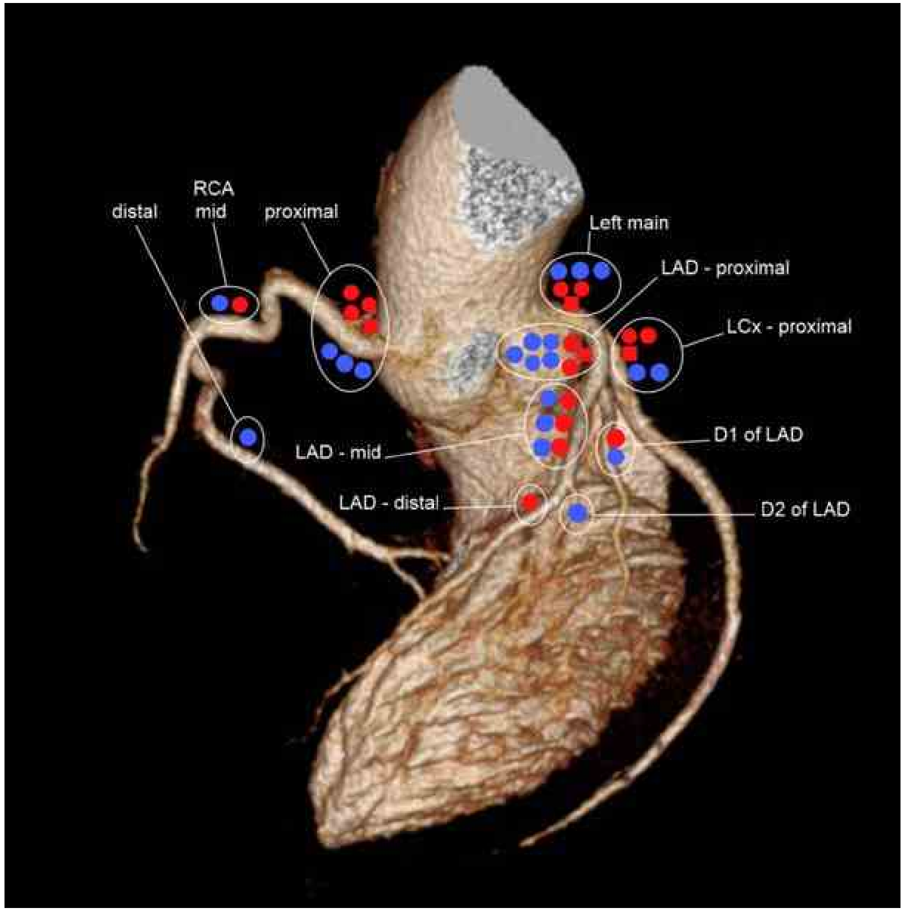
- 15% and over
- 10%–14%
- 5%–9%
- 3%–4%
- 2%
- 1%
- < 1%

10-year risk of fatal CVD in populations at **low CVD risk**

Coronary Artery Disease Detected by Coronary Computed Tomography Angiography in Adult Survivors of Childhood Hodgkin Lymphoma



Location of Plaque	No. (%)
Left main artery	6 (15)
Left anterior descending artery	
Proximal	8 (21)
Middle	6 (15)
Distal	1 (3)
Diagonals	2 (5)
Left circumflex artery	
Proximal	5 (13)
Distal	0 (0)
Right coronary artery	
Proximal	7 (18)
Middle	2 (5)
Distal	2 (5)



CAD prevalence: 39% (normal population: 8.5-11%)

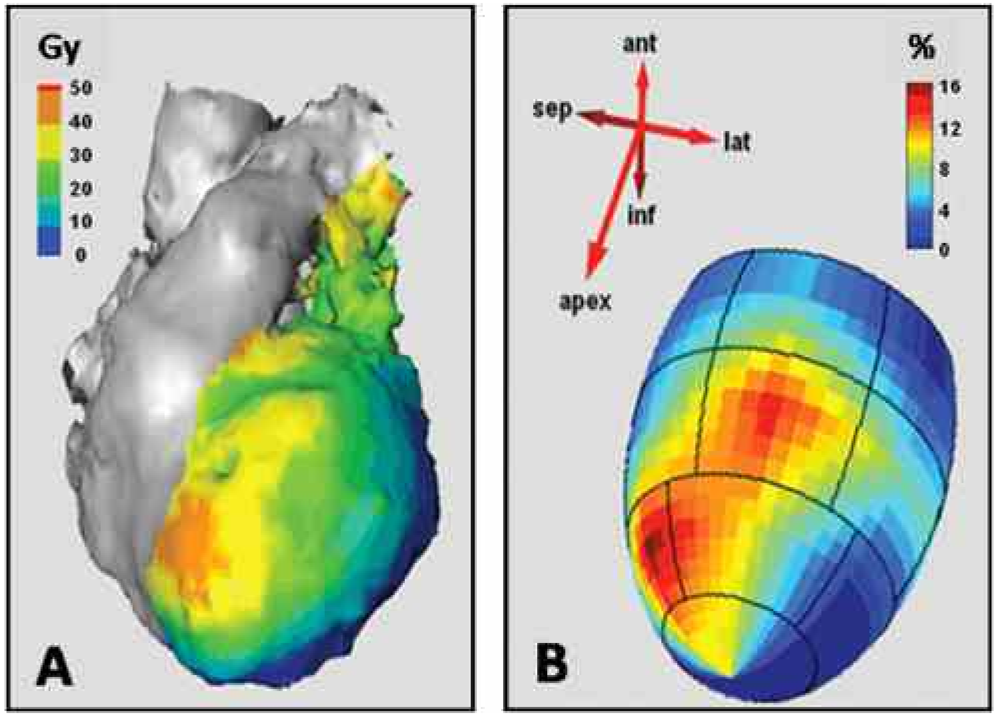
Mulrooney at al, Cancer; 2014

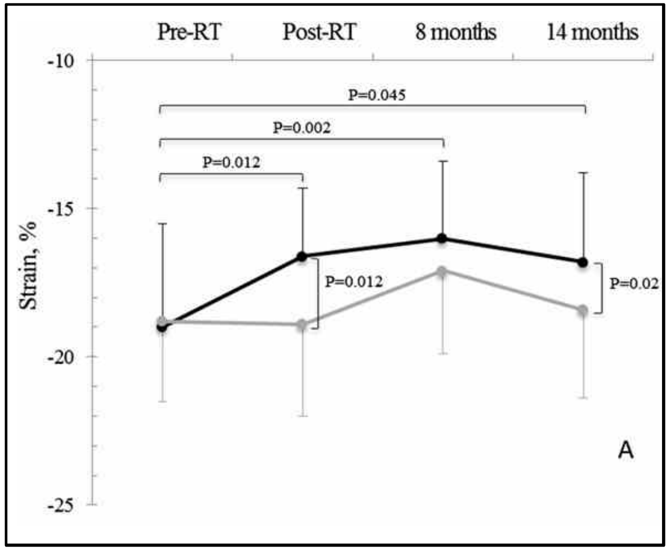
Department of Oncology, University of Turin

CLINICAL INVESTIGATION

ACUTE RADIATION EFFECTS ON CARDIAC FUNCTION DETECTED BY STRAIN RATE IMAGING IN BREAST CANCER PATIENTS

- ✓ *20 left sided and 10 right sided BC*
- ✓ *50 Gy/25 fr*
- ✓ *Mean dose LV: - apical 12.8 Gy*
  - mid 5.4 Gy
  - basal 4.5 Gy

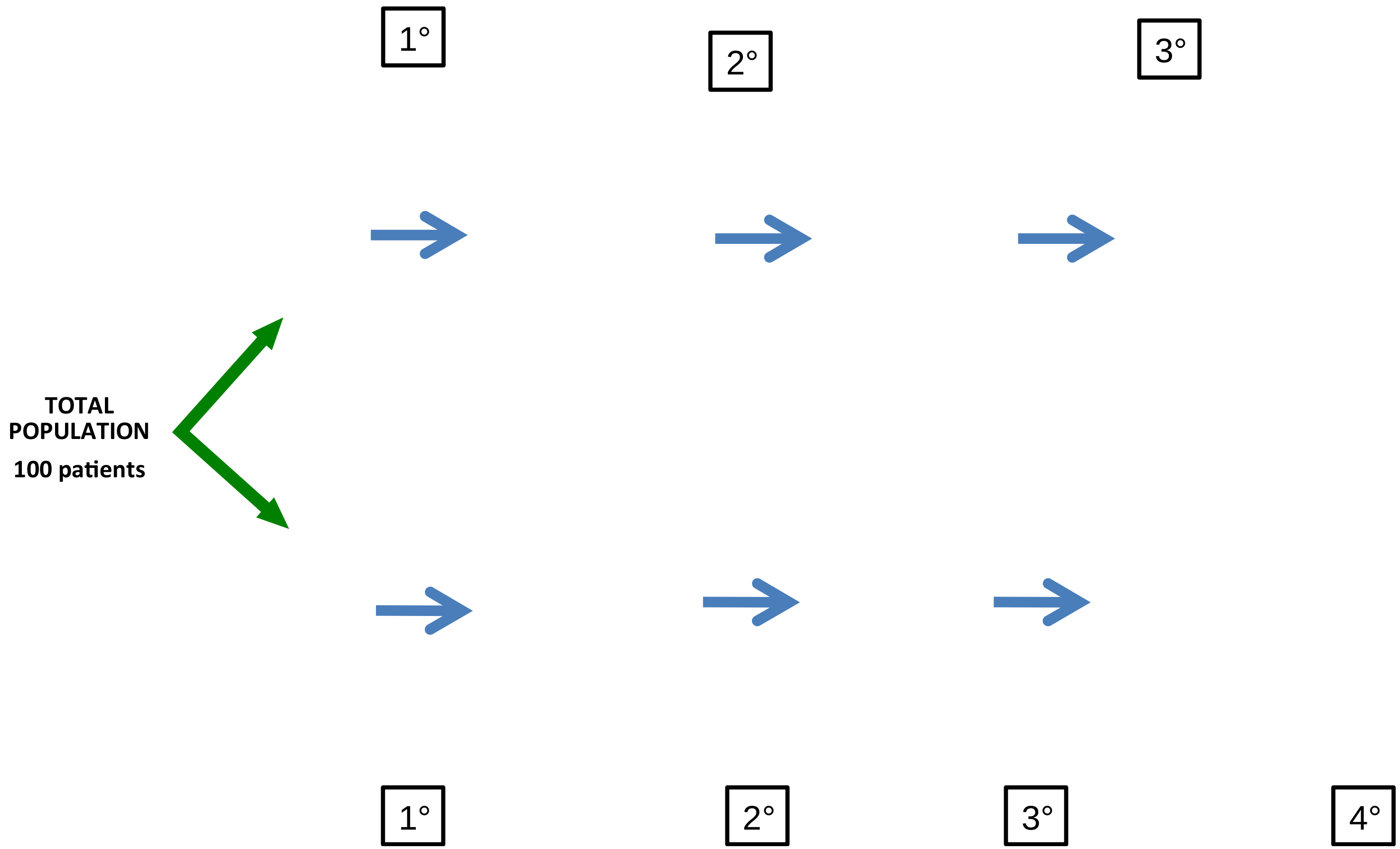




Erven et al. Int J Rad Onc Biol Phys 2010

CARDIOCARE

"SUBCLINICAL CARDIOTOXICITY DETECTED BY STRAIN RATE AFTER CHEMOTHERAPY AND MEDIASTINAL RADIATION THERAPY IN LYMPHOMA (HL – DLCL –PMBCL)"



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- *Giorgio Priolo*

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- *Mauro Giorgi*
- *Antonella Fava*
- *Elisa Pelloni*

FUTURE TOXICITY STUDIES

THE FOLLOWING POINTS SHOULD BE KEPT IN MIND:

a) Additional work is needed to better evaluate whether the ***modern radiotherapy treatment*** approaches for patients with cancer of the thoracic district ***are associated with significant cardiac toxicity.***

b) Additional study is needed to ***relate doses to subvolumes of the heart*** (e.g., coronary arteries) ***to clinical outcomes***.

c) Future studies should ***incorporate baseline cardiovascular risk factors***, such as the Framingham. This will allow consideration of potential interactive effects between RT and traditional cardiac risk factors.

a) *A* ***deeper understanding*** of the global physiological effects of thoracic RT is needed

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PIEMONTE | VALLE D'AOSTA
si prende cura di te

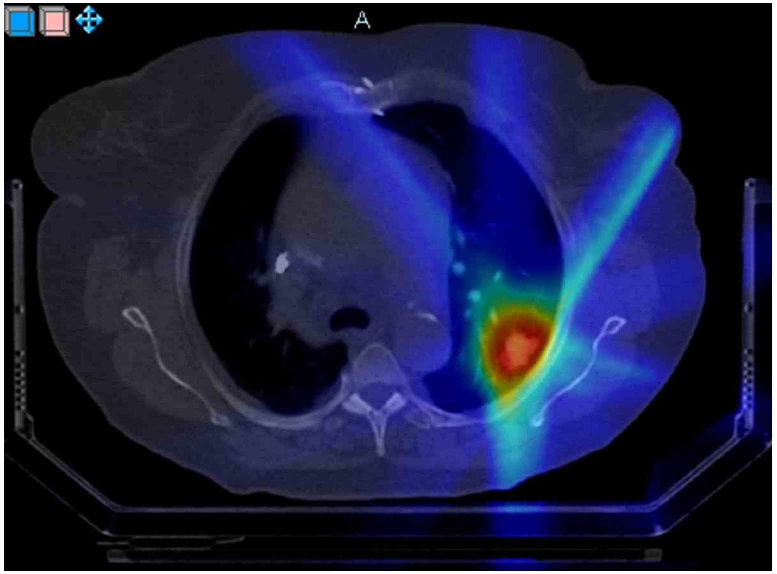
Protect Your HEART
You Only Have One

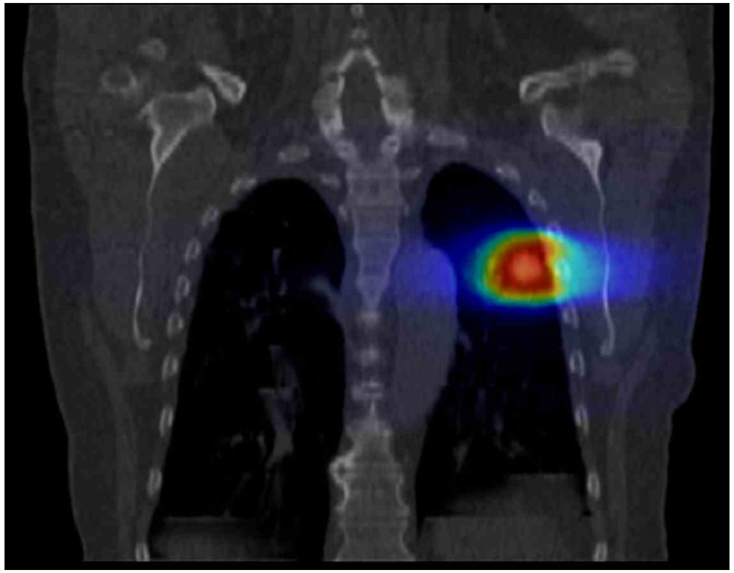
Thank you for your attention!

CLINICAL CASE)

P.L. female, 75 y.o.
January 2011: Nodular lesion at the apex of the left lung (cT1N0M0)
Clinical proof of malignancy (SUVmax 3.6; dimensional increase at CT exam)

Cardiovascular Hystory:
1990: Acute miocardial infarction (CABG + left ventricular aneurismectomy)
2004: Chronic Heart Disfunction (implanted ICD + biventricular PM)
2009: Last episode of VT, correctly treated by ICD
Ex smoker – Chronic Kidney Disease – Hypertension – TIA – NIDDM.

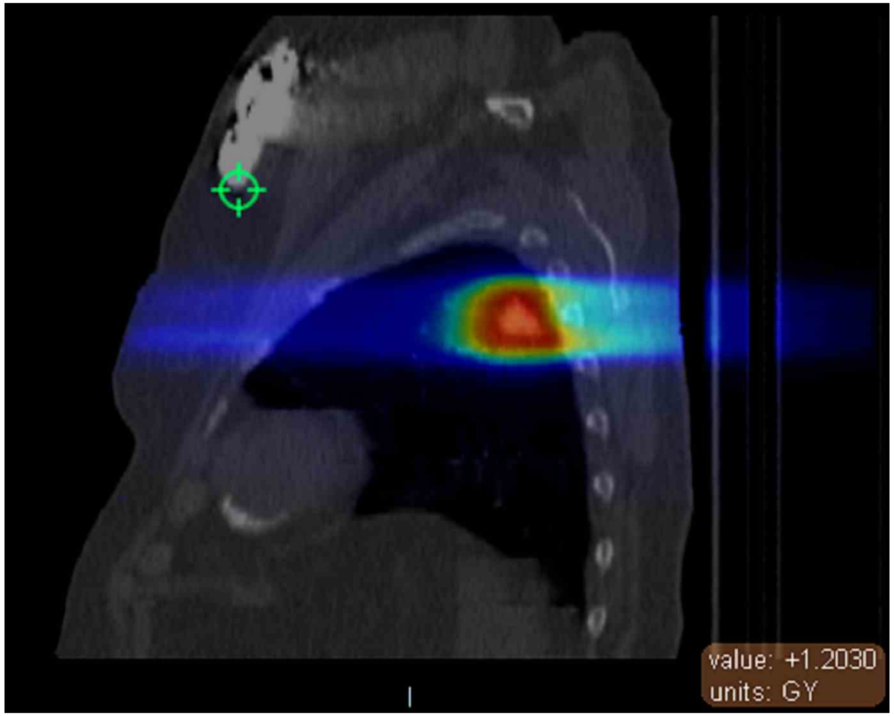




CLINICAL CASE
– March 2011 –

- **54 Gy/3 fractions**
- **Switch off tachycardia-therapy before every fraction**
- **Crashcart present during RT**
- **ICD check an reprogramming after every fraction**

Structure	Volume (cm³)	Plan Name	Min Dose Gy	Max Dose Gy	Mean Dose Gy
AORTA ASCENDE	63.344	1guscio	0.646	8.409	1.778
AORTA DISCEND	114.232	1guscio	0.000	15.291	2.117
COSTA	6.384	1guscio	13.286	41.708	27.002
CUORE	1242.776	1guscio	0.013	6.114	0.865
ESOFAGO	55.232	1guscio	0.000	5.704	1.534
External(Unsp.Tiss	22929.048	1guscio	0.000	50.189	1.207
ICD	99.640	1guscio	0.000	1.686	0.228
ITV	7.400	1guscio	46.054	52.595	49.753
PTV	18.416	1guscio	35.690	52.595	48.268
Polm dx	1519.496	1guscio	0.000	10.232	0.665
Polm sn	1461.240	1guscio	0.000	52.595	6.272
guscio	6381.736	1guscio	0.000	18.537	0.771



FOLLOW UP
- September 2015 -

- Stable disease

- RTOG Chronic radiological toxicity G1

- December 2011: major ventricular arrythmia, correctly recognised and cardioverted by ICD