La cardiotossicità in ambito di trattamenti radioterapici per neoplasie del distretto toracico

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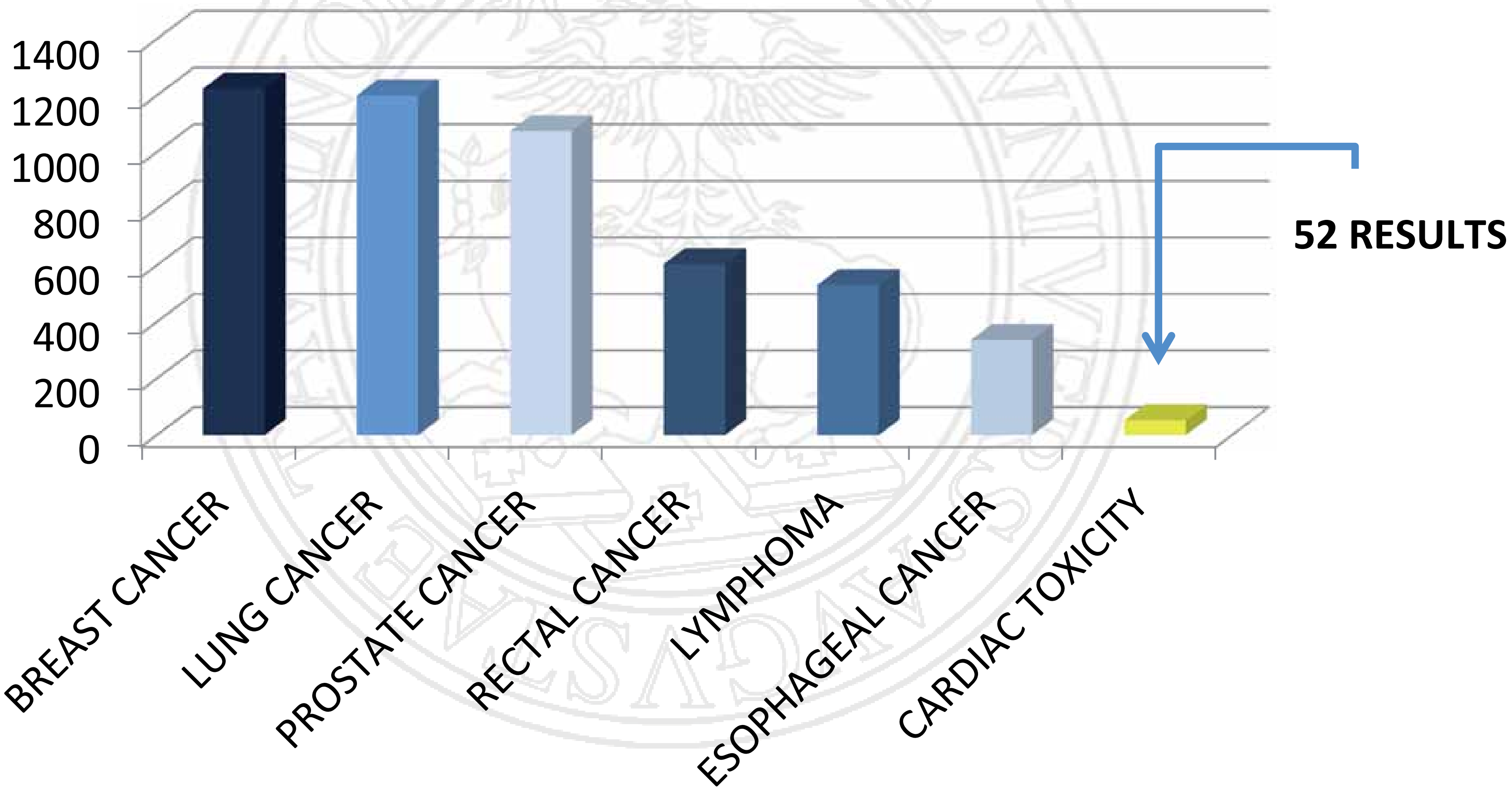
Torino, 7 Marzo 2013

RADIOTHERAPY 2012



INTRODUCTION

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

1) Breast cancer → **50 Gy/25 fractions** (hypofractionated RT 46 Gy/20 fractions)

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

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

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

INTRODUCTION

Radiation-Associated Cardiac Disease

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

Subclinical abnormalities are more common, and are noted in up to **50% of patients**, depending on the sensitivity of the endpoint considered and the associated comorbidities.

RADIATION DOSE–VOLUME EFFECTS IN THE HEART

Int. J. Radiation Oncology Biol. Phys., Vol. 76, No. 3, Supplement, pp. S77–S85, 2010

0360-3016/10/$–see front matter

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

BLOOD, 1 MARCH 2007 • VOLUME 109, NUMBER 5

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]

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- 1474 pts
- from1965 to1995
- median follow-up 18,7 years
- minimum follow-up 5 years
- **1241 mediastinal RT (87%)**
- 40 Gy/20 fr (RT)
- 30-36 Gy (RT-CT)

Risk factor	MI	AP	CHF*	Valvular disorders
Model 1, no. of events	102	129	82	159
Treatment, HR (95% CI)†				
Mediastinal RT (yes vs no)	2.42 (1.12-5.24)	4.85 (1.97-11.9)	7.37 (1.81-30.0)	7.01 (2.59-18.9)
Anthracycline-containing CT (yes vs no)	0.90 (0.50-1.62)	1.49 (0.89-2.49)	2.44 (1.37-4.33)	2.24 (1.40-3.59)
Cardiovascular risk factors, HR (95% CI)				
Recent smoking (yes vs no/unknown)	2.04 (1.29-3.23)	1.35 (0.85-2.16)	1.96 (1.16-3.30)	1.23 (0.80-1.88)
Hypertension (yes vs no/unknown)‡	0.52 (0.29-0.94)	0.90 (0.58-1.42)	1.07 (0.59-1.94)	1.28 (0.86-1.92)
Hypercholesterolemia (yes vs no/unknown)‡	4.12 (2.68-6.33)	4.55 (3.10-6.68)	1.48 (0.85-2.58)	1.65 (1.11-2.44)
Diabetes mellitus (yes vs no/unknown)‡	1.44 (0.73-2.83)	2.43 (1.45-4.09)	4.45 (2.54-7.81)	1.81 (1.07-3.04)
Model 2, no. of events	95	124	80	155
Treatment group, HR (95% CI)§				
Mediastinal RT only‖	1.00	1.00	1.00	1.00
Mediastinal RT + CT, no anthracyclines¶	1.17 (0.75-1.83)	0.78 (0.53-1.15)	1.33 (0.79-2.24)	0.85 (0.60-1.21)
Mediastinal RT + CT, anthracyclines#	1.00 (0.52-1.94)	1.32 (0.76-2.30)	2.81 (1.44-5.49)	2.10 (1.27-3.48)

BLOOD, 1 MARCH 2007 • VOLUME 109, NUMBER 5

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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

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Cardiac morbidity

A population-based case-cohort study of the risk of myocardial infarction following radiation therapy for breast cancer

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-**6686** patients from **1982 to 1988**

- All patients who receivet post-op RT for breast cancer in Ontario (Canada)

- Minimum follow up: **13.5 years**

-Variegated RT exposure (total dose- fractionation

- boost- internal mammary chain irradiation)

- No chemiotherapy

-***Detection of AMI***

Table 4
Adjusted (multivariable) case-cohort model of time to dAMI using Self-Prentice correction for underestimation of standard error of parameters

Variables	Adjusted hazard vAMI HR (95% CI)	Adjusted hazard vAMI <60 HR (95% CI)	Adjusted hazard vAMI ≥60 HR (95% CI)	Adjusted hazard dAMI HR (95% CI)
Age at RT	2.32 (1.51, 3.58)	N/A	N/A	7.11 (3.51, 14.42)
Smoking history prior to RT	1.71 (1.11, 2.64)	2.38 (1.21,4.70)	1.54 (0.85, 2.78)	0.77 (0.41, 1.44)
MI history prior to RT	2.01 (1.03, 3.90)	4.01 (1.26, 12.77)	1.67 (0.74, 3.78)	1.68 (0.82, 3.43)
Left breast	1.42 (0.92, 2.17)	0.86 (0.44, 1.68)	1.96 (1.09, 3.54)	1.07 (0.65, 1.72)
IMC RT	1.07 (0.60, 1.89)	1.62 (0.67, 3.90)	0.80 (0.37, 1.73)	1.90 (1.08, 3.35)
Daily dose >2.5 Gy	0.97 (0.50, 1.90)	0.48 (0.10, 2.35)	1.18 (0.55, 2.51)	1.37 (0.73, 2.56)

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Cardiac Effects of Radiotherapy

Asymptomatic Cardiac Disease Following Mediastinal Irradiation

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Carol S. Mariscal, RN,‡ Ingela Schnittger, MD, FACC†
Stanford, California

Table 2. Valvular Disease Following Irradiation

	Years Following Irradiation					General Population†	
Echocardiographic Finding	All Patients n = 294	2–10 n = 89	11–20 n = 132	>20 n = 73	p Value*	Prevalence (%)	Source
Aortic regurgitation							
Trace (%)	27 (9)	9 (10)	13 (10)	5 (7)	0.71	3.1	(14)
Mild (%)	62 (21)	3 (3.4)	26 (20)	33 (45)	< 0.0001	1.3	(14)
Moderate or severe (%)	15 (5.1)	1 (1.1)	3 (2.3)	11 (15)	< 0.0001	0.15	(14)
Mitral regurgitation							
Trace (%)	87 (30)	27 (30)	44 (33)	16 (22)	0.21	75	(14)
Mild (%)	105 (36)	21 (24)	49 (37)	35 (48)	0.005	13	(14)
Moderate or severe (%)	10 (3.4)	2 (2.3)	5 (3.8)	3 (4.1)	0.71	0.54	(14)
Tricuspid regurgitation							
Trace (%)	86 (29)	25 (28)	43 (33)	18 (25)	0.47	70	(14)
Mild (%)	43 (15)	8 (9)	19 (14)	16 (22)	0.07	13	(14)
Moderate or severe (%)	4 (1.4)	0 (0)	1 (0.8)	3 (4.1)	0.06	0.55	(14)
Pulmonic regurgitation‡							
Trace (%)	106 (36)	37 (42)	45 (34)	24 (33)	0.40	17	(32)
Mild (%)	20 (7)	2 (2)	9 (7)	9 (12)	0.04	< 0.5	(32)
Moderate or severe (%)	0 (0)	0 (0)	0 (0)	0 (0)	1.0	< 0.5	(32)
Aortic stenosis (%)	13 (4)	0 (0)	1 (1)	12 (16)	0.008	< 0.5	(33)

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doi:10.1016/j.ijrobp.2007.10.056

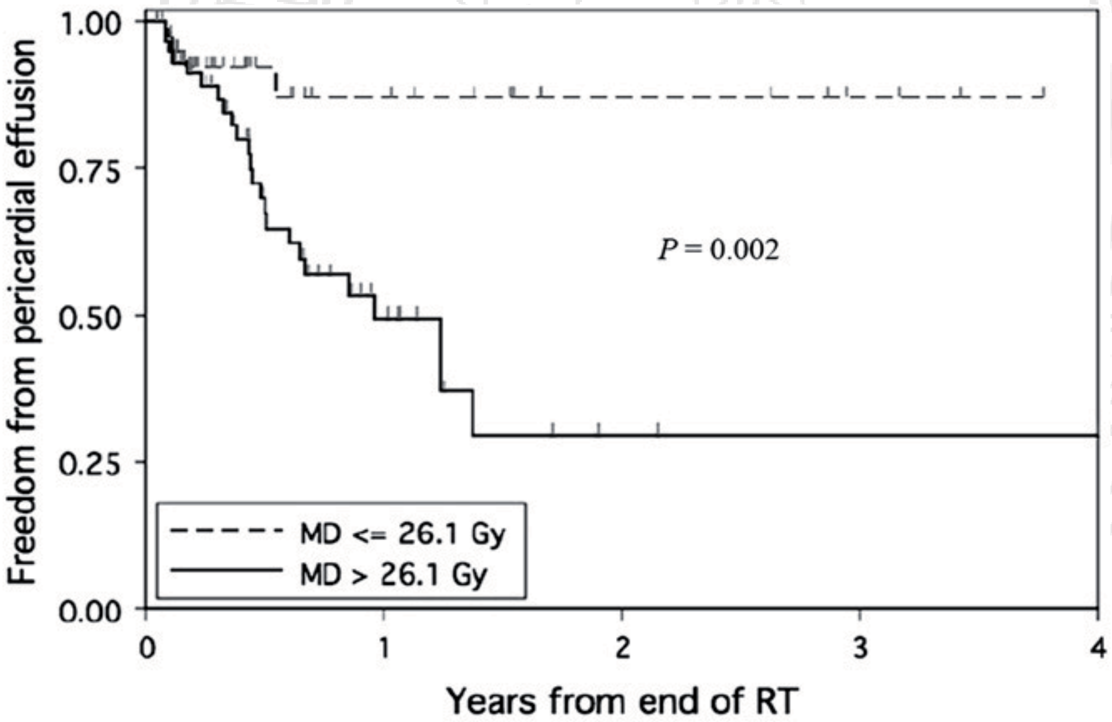
CLINICAL INVESTIGATION **Esophagus**

RISK FACTORS FOR PERICARDIAL EFFUSION IN INOPERABLE ESOPHAGEAL CANCER PATIENTS TREATED WITH DEFINITIVE CHEMORADIATION THERAPY

Xiong Wei, M.D.,* H. Helen Liu, Ph.D.,* Susan L. Tucker, Ph.D.,[†] Shulian Wang, M.D.,[§] Radhe Mohan, Ph.D.,* James D. Cox, M.D.,[‡] Ritsuko Komaki, M.D.,[‡] and Zhongxing Liao, M.D.[‡]

Departments of *Radiation Physics; [†]Bioinformatics and Computational Biology, and [‡]Radiation Oncology, The University of Texas M.D. Anderson Cancer Center, Houston, TX; and [§]Cancer Hospital, Peking Union Medical College and Chinese Academy of Medical Sciences, Beijing, China

- -101 patients from 2000 and 2003
- - Inoperable esophageal cancer
- - 3DCRT and concurrent CT
- - median RT dose: 50.4 Gy
- - median follow up: 8 months
- - PCE incidence: 27.7% (28/101)
- - ***The manually contoured heart served as the inner boundary of pericardium, which was extended 3D outward by 0.5 cm in thickness***

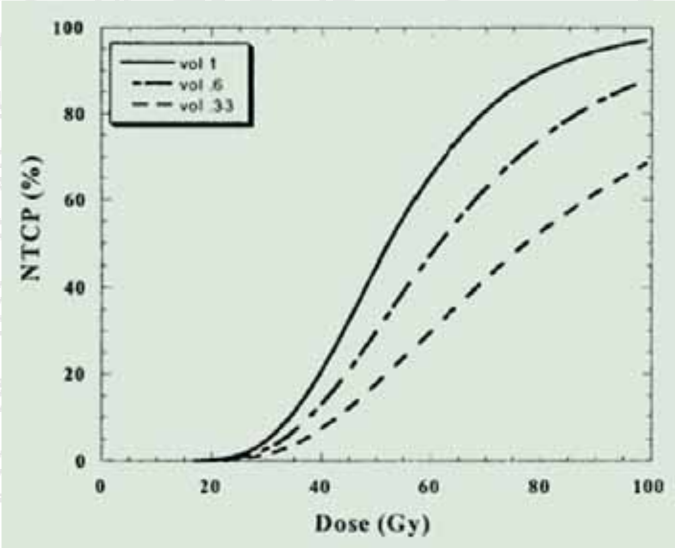


RADIATION DOSE–VOLUME EFFECTS IN THE HEART
Int. J. Radiation Oncology Biol. Phys., Vol. 76, No. 3, Supplement, pp. S77–S85, 2010

0360-3016/10/$–see front matter

REVIEW OF DOSE/VOLUME FACTORS

THE RISK OF CARDIAC EVENTS IS PROBABLY RELATED TO BOTH DOSE & IRRADIATED VOLUME



Gagliardi G et al, 2001

VOLUME RELATED:

- RR of **cardiac death** decreased with use of **subcarinal blocking** il HL patients (from 5.4 to 1.4). Hancock et al. (***JAMA 1993)***

- Higher **valvular** dysfunction in patients affected by **breast cancer** and receiving IMN-RT (HR 3.17) Hooning et al ***(JCI 2007)***

DOSE RELATED:

- Excess of **deaths** from heart disease in **children and adolescents** with HL receiving **42-45 Gy** Hancock et al (***JCO 1993)***
- Increase of aortic and mitral stenosis and regurgitation with RT dose >30 Gy in HL patients. Adams et al. ***(JCO 2004)***

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RECOMMENDED DOSE/VOLUME LIMITS

1) BREAST CANCER:

- ***minimize irradiated heart volume*** to the greatest possible degree without compromising the target coverage.
- NTCP value > 5% could jeopardise the beneficial effects of RT on survival.
- ***V25Gy < 10%*** (in 2 Gy per fraction) will be associated with a ***<1%*** probability of cardiac mortality 15 years after RT.

2) HODGKIN LYMPHOMA:

- Historically, ***whole heart doses up to 30 Gy*** were reasonably well tolerated (without chemotherapy)
- It seems prudent to ***limit whole heart doses to 15 Gy***, with field reductions, as appropriate in the given clinical situation, to areas of persistent (post-chemotherapy) residual tumor or to areas of previous bulky involvement.

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0360-3016/10/$–see front matter

RECOMMENDED DOSE/VOLUME LIMITS

3) PERICARDIUM:

- Mean pericardium dose ***<26 Gy***,

N.B: Care should be taken to differentiate between the DVHs for the heart vs. the pericardium.

4) PERFUSION DEFECTS:

-The ***irradiated volume of the left ventricle*** has been shown to be the most important predictor of a perfusion defect.

- Although currently there is no direct evidence that successful treatment of traditional cardiac risk factors will alter the natural history of radiation-associated cardiac disease, ***it is prudent to optimize patient cardiovascular risk profiles***

RADIATION DOSE–VOLUME EFFECTS IN THE HEART
Int. J. Radiation Oncology Biol. Phys., Vol. 76, No. 3, Supplement, pp. S77–S85, 2010

0360-3016/10/$–see front matter

CHALLENGES IN DEFINING VOLUMES

Critical delineation of heart subregions with CT:

- Difficult differentiation of inferior border from liver and diaphragm
- Heart motion during cardiac cycles
- Anatomic complexity (interaction of ventricles, valves, vasculature)

RADIATION DOSE–VOLUME EFFECTS IN THE HEART
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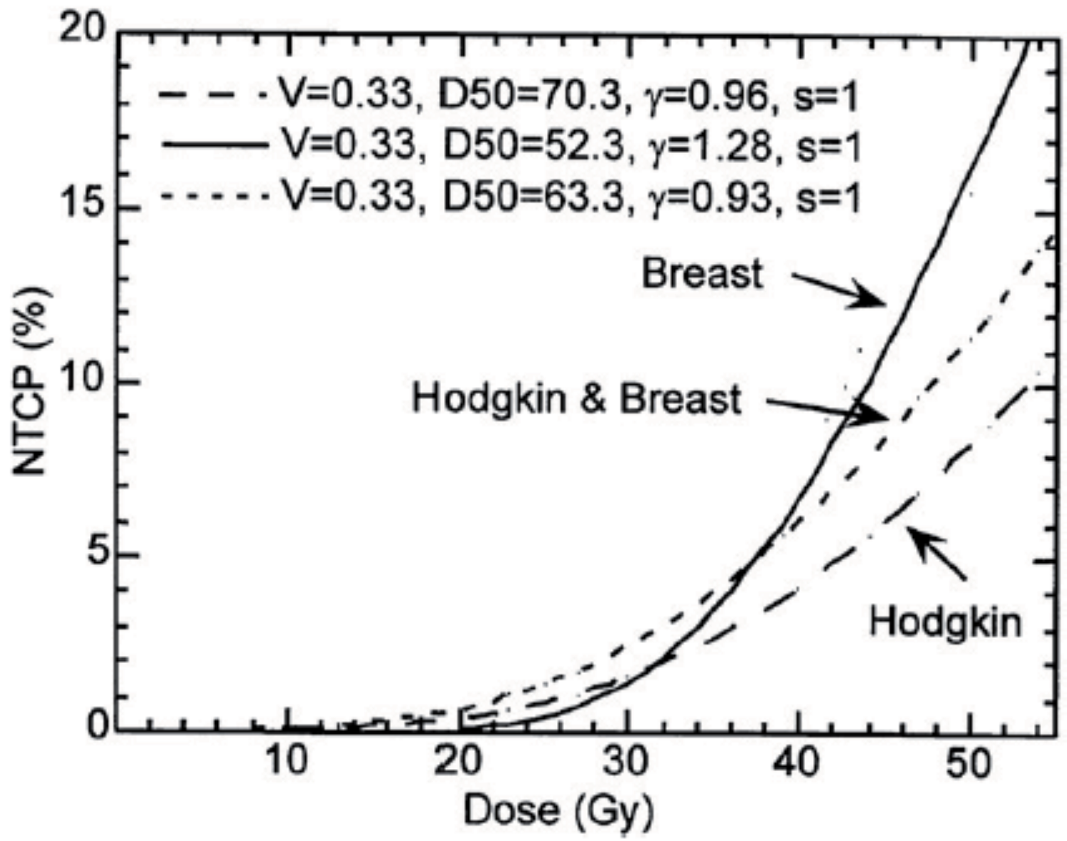
0360-3016/10/$–see front matter

CHALLENGES IN DEFINING VOLUMES

Heart region functionally most important for RT induced toxicity…?



Gagliardi et al Int J Rad Onc Biol Phys 2010

A detailed CT cardiac atlas was developed jointly by:

- **Cardiologist**
- **Cardiac radiologist**
- **Radiation oncologist**

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Int. J. Radiation Oncology Biol. Phys., Vol. 79, No. 1, pp. 10–18, 2011

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doi:10.1016/j.ijrobp.2009.10.058

CLINICAL INVESTIGATION **Breast**

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

Mary Feng, M.D.,* Jean M. Moran, Ph.D.,* Todd Koelling, M.D.,† Aamer Chughtai, M.D.,‡
June L. Chan, M.D.,* Laura Freedman, M.D.,* James A. Hayman, M.D.,*
Reshma Jagsi, M.D., D. Phil.,* Shruti Jolly, M.D.,* Janice Larouere, M.D.,*
Julie Soriano, M.D.,* Robin Marsh, C.M.D.,* and Lori J. Pierce, M.D.*

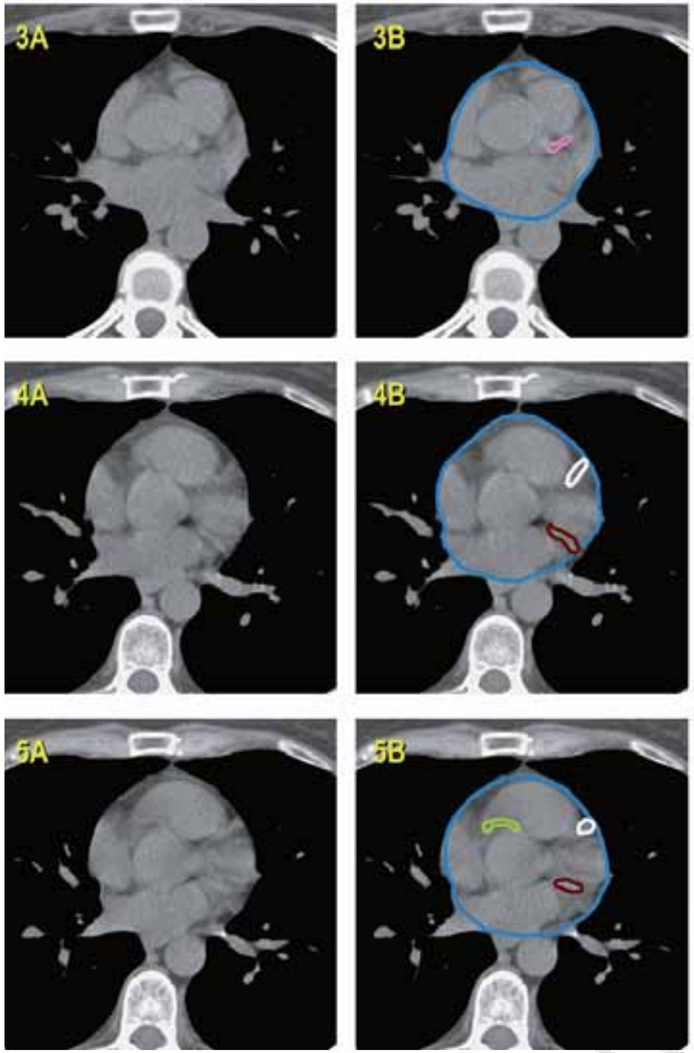
Department of *Radiation Oncology; Internal Medicine, Division of †Cardiology and; ‡Radiology, University of Michigan Medical Center, Ann Arbor, Michigan

Images were obtained with respiratory gating with and without intravenous contrast.

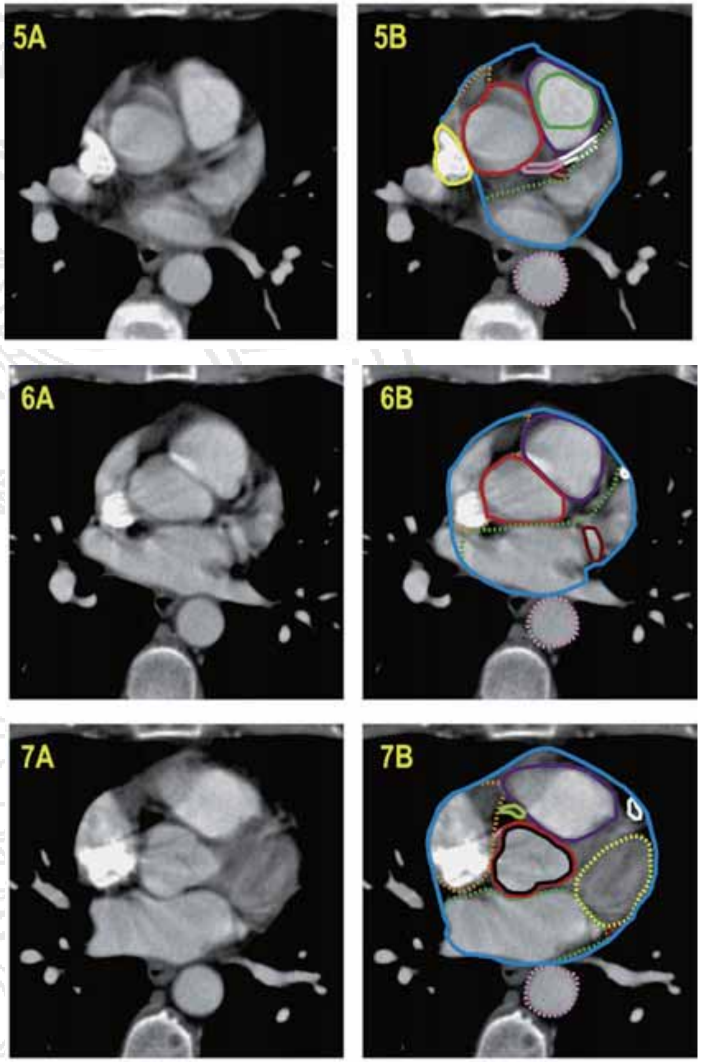
The **whole heart** was delineated, along with **substructures** including the chambers, great vessels, cardiac valves, the conduction system, and major coronary vessels.

The **contours** were agreed upon by all three investigators and **were considered to be the gold standard volumes for future reference**. Written guidelines for consistent delineation, as noted below, were also jointly developed

BASAL TC



IV CONTRAST MEDIA INFUSION



Future implications…

?

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0360-3016/07/$-see front matter

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doi:10.1016/j.ijrobp.2007.05.054

CLINICAL INVESTIGATION **Esophagus**

TEMPORAL CHANGE IN BRAIN NATRIURETIC PEPTIDE AFTER RADIOTHERAPY FOR THORACIC ESOPHAGEAL CANCER

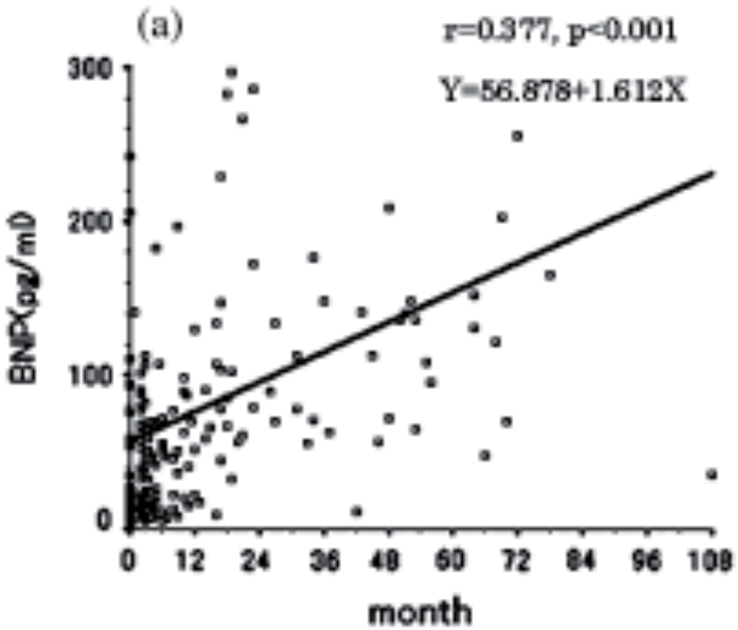
Keiichi Jingu, M.D.,* Kenji Nemoto, M.D.,† Tomohiro Kaneta, M.D.,‡ Minako Oikawa, M.D.,§ Yoshihiro Ogawa, M.D.,* Hisanori Ariga, M.D.,* Ken Takeda, M.D.,* Toru Sakayauchi, M.D.,* Keisuke Fujimoto, M.D.,* Kakutaro Narazaki, M.D.,* Yoshihiro Takai, M.D.,‖ Eiko Nakata, Ph.D.,‖ Hiroshi Fukuda, M.D.,¶ Shoki Takahashi, M.D.,‡ and Shogo Yamada, M.D.*

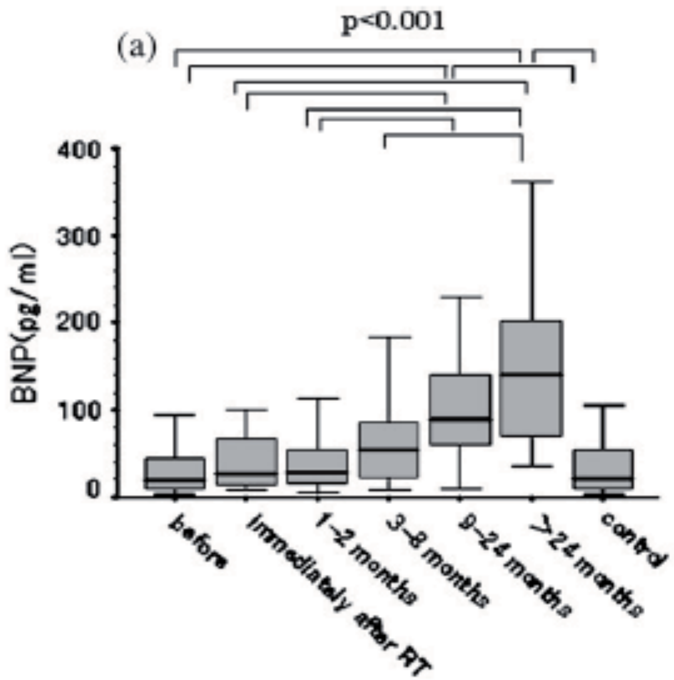
Departments of *Therapeutic Radiology, ‡Diagnostic Radiology, §Cardiovascular Internal Medicine, and ‖Radiological Technology, Course of Health Sciences, Tohoku University School of Medicine, Sendai, Japan; ¶Department of Nuclear Medicine and Radiology, Division of Brain Science, Institute of Development, Aging and Cancer, Tohoku University, Sendai, Japan; and †Department of Therapeutic Radiology, Yamagata University School of Medicine, Yamagata, Japan

- 197 pts treated for esophageal cancer.
- Plasma BNP was measured in all pts before and after RT
- 90 pts underwent FDG-PET (21.5± 17.8 months after RT)

- AP opposing fields until 40 Gy, then oblique opposing fields to avoid spinal cord.
- Total dose to GTV 60-70 Gy (median, 60Gy)
- Base of LV received 40 Gy in all pts by AP fields
- In middle-lower esophageal cancer pts received 20 Gy to posterior and inferior wall by oblique fields.

- ***BNP concentration has become a widely accepted index of heart failure or heart remodeling. BNP is released from the heart (LV) in response to volume expansion and pressure overload, and it is thought that BNP has a cardioprotective effect.***





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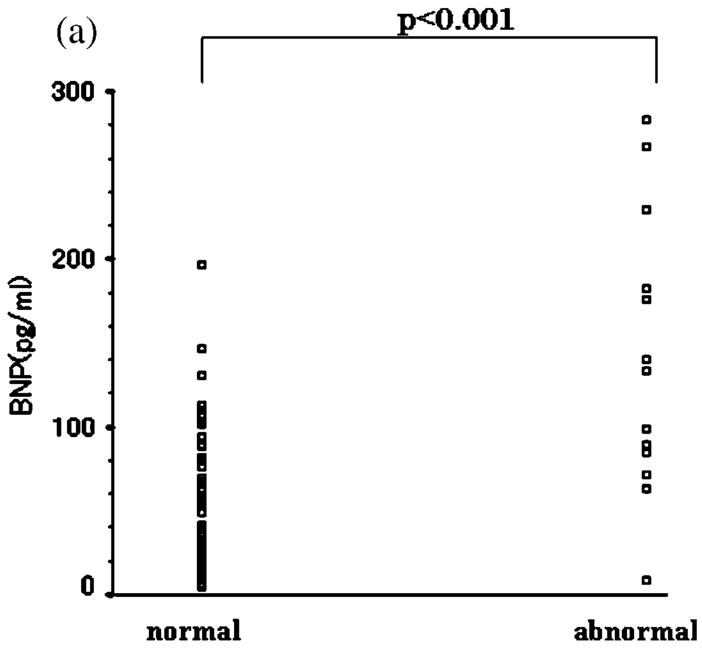

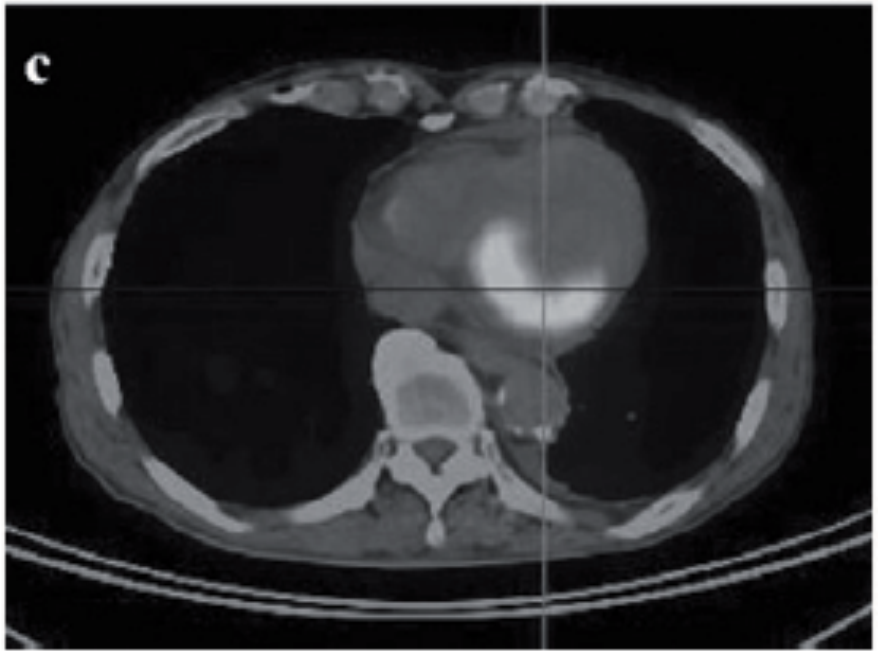

Lung Cancer (2008) 62, 351–355

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Cardiac blood biomarkers in patients receiving thoracic (chemo)radiation

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Table 1 Patient, disease and chemotherapy characteristics (N = 30)

Characteristic	Median or N	Range or %
Age	61	38–83
Male	17	57%
Female	13	43%
Diagnosis		
Non-small cell lung cancer	18	60%
Small cell lung cancer	4	13%
Esophagus cancer	5	17%
Gastroesophageal junction cancer	2	7%
Thymic carcinoma	1	3%

CONCLUSIONS

Our data demonstrate that elevations in TnT, CK-MB and NT-proBNP ***during thoracic (chemo)radiation*** should not routinely be attributed to treatment, and, if detected, require further clinical evaluation.

Table 5 Serum CK-MB and NT-proBNP levels

Biomarker	Baseline (mean ± S.E.)	Week 2 (mean ± S.E.)	P (vs. baseline)	Last day (mean ± S.E.)	P (vs. baseline)
CK-MB (ng/mL)	3.1 ± 0.4	3.2 ± 0.4	0.46	3.1 ± 0.4	0.74
NT-proBNP (pg/mL)	350 ± 90	580 ± 290	0.36	520 ± 160	0.23

P values determined using a two-tailed, paired t-test.

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CLINICAL INVESTIGATION

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

Katrien Erven, M.D.,* Ruxandra Jurcut, M.D., Ph.D.,[§] Caroline Weltens, M.D., Ph.D.,* Sorin Giusca, M.D.,[§] Joris Ector, M.D., Ph.D.,[†] Hans Wildiers, M.D., Ph.D.,[‡] Walter Van den Bogaert, M.D., Ph.D.,* and Jens-Uwe Voigt, M.D., Ph.D.[†]

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-20 left sided and 10 right sided BC

- 50 Gy/25 fr

- boost 16 Gy if breast- conserving surgery

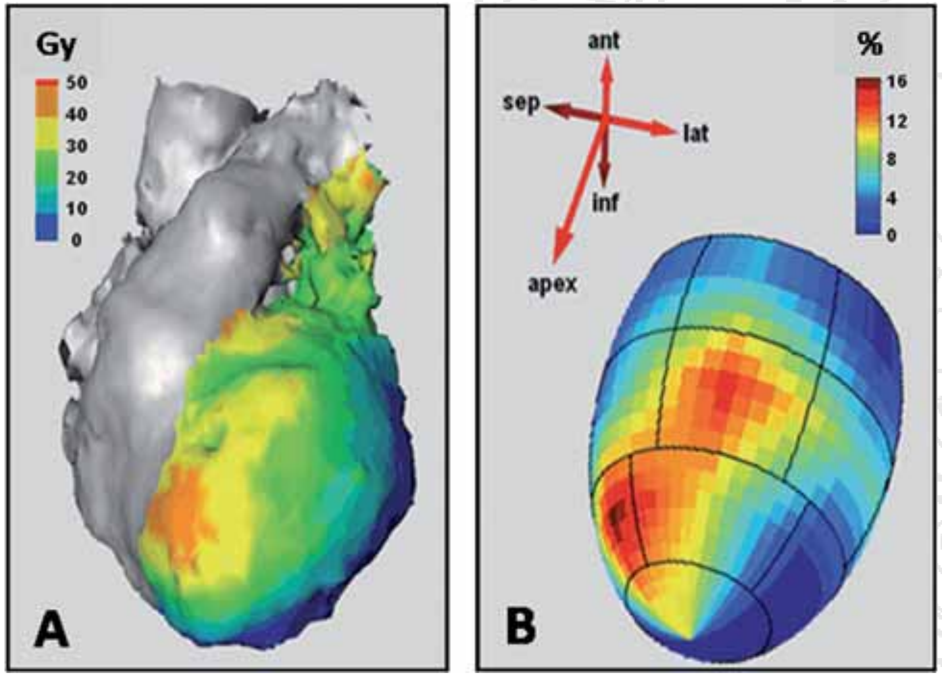
-Strain rate imaging (SRI) allows quantifying deformation properties of the myocardium, enabling evaluation of regional myocardial function

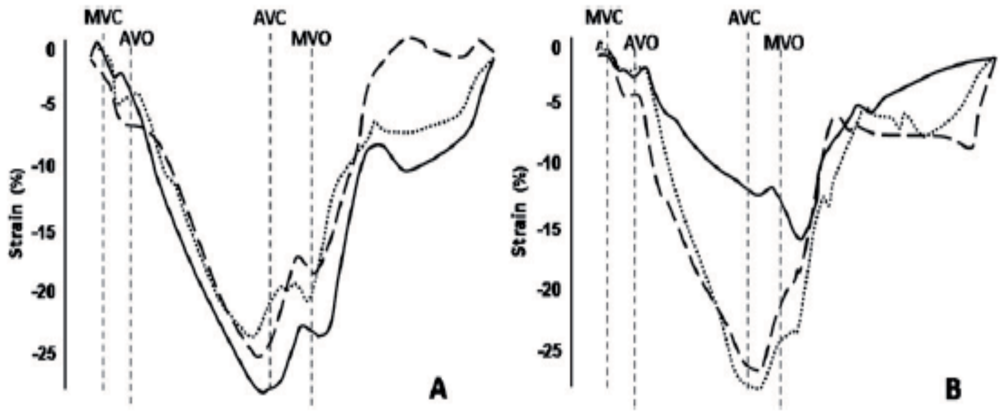
-Mean dose LV:

- apical 12.8 Gy

- mid 5.4 Gy

- basal 4.5 Gy





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- - 50 Gy/25 fr
- - boost 16 Gy if breast- conserving surgery
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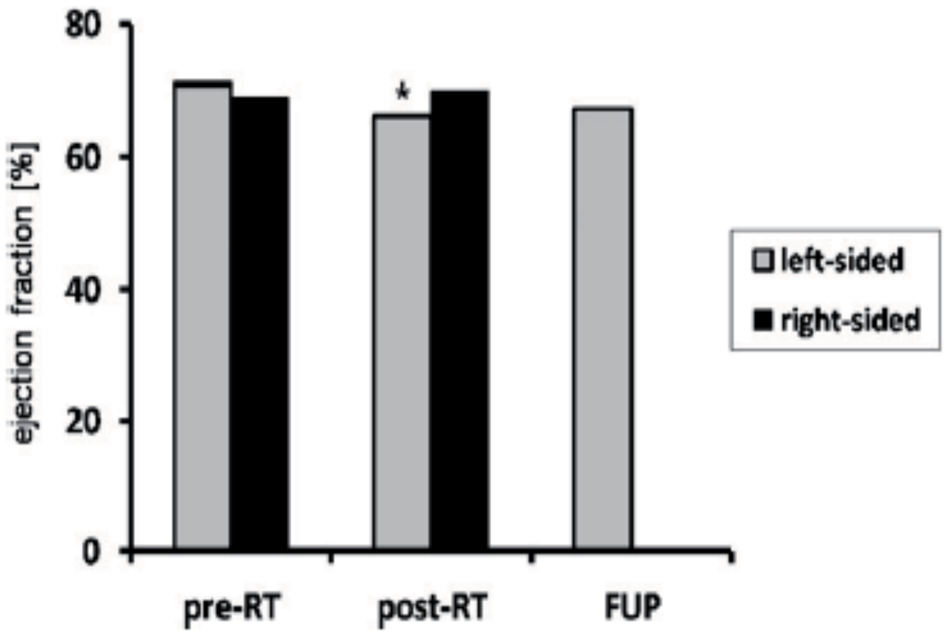

CONCLUSIONS

Echocardiographic Doppler-based SRI is a sensitive method to detect and quantify subtle regional changes in cardiac function early after RT. It might be a useful tool in the evaluation of modern RT techniques, with respect to cardiac toxicity.

The exact clinical significance of the early changes observed in deformation parameters is not clear, (later phase endothelial damage may lead to microvascular thrombosis, ischemia, and myocardial fibrosis. **Further studies are needed** to establish a relationship between the extent and the degree of regional dysfunction after RT and long- term outcome.

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CLINICAL INVESTIGATION

CARDIAC MAGNETIC RESONANCE IMAGING FINDINGS IN 20-YEAR SURVIVORS OF MEDIASTINAL RADIOTHERAPY FOR HODGKIN'S DISEASE

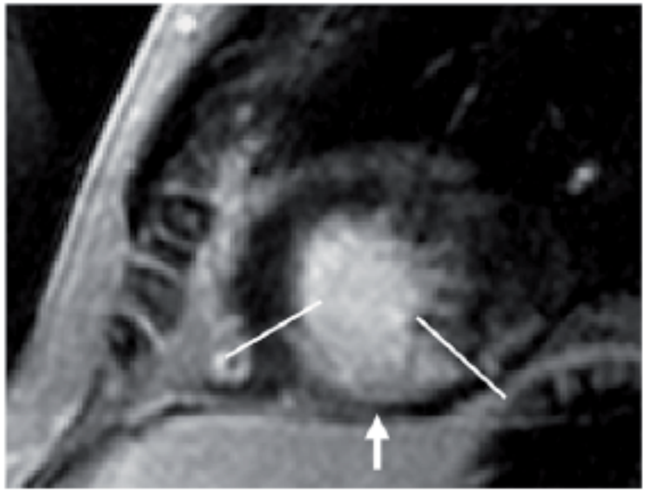
Wolfram Machann, M.D.,* Meinrad Beer, M.D.,* Margret Breunig, M.D.,[†] Stefan Störk, Ph.D.,[†] Christiane Angermann, M.D.,[†] Ines Seufert,[‡] Franz Schwab, Ph.D.,[‡] Oliver Kölbl, M.D.,[‡] Michael Flentje, M.D.,[‡] and Dirk Vordermark, M.D.[‡§]

Departments of *Radiology, [†]Cardiology, and [‡]Radiation Oncology, University of Würzburg, and [§]Department of Radiation Oncology, Martin Luther University Halle-Wittenberg, Germany

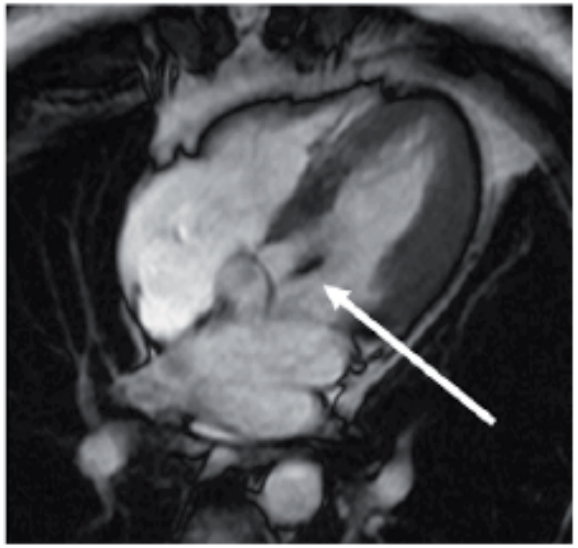
- 143 patients
- From 1978 to 1985
- All treated with mediastinal RT
- 40 Gy/20 fr (RT)
- 53 long term survivors (20-28 years)
- 31 patients undergone a 1.5-T MRI
- ***Cardiac magnetic resonance imaging (MRI) has recently been introduced as a sensitive and specific imaging method to detect and quantify abnormal cardiac function***

(a)

(b)



(c)



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Condition or factor	n (%)
Diabetes	0/31 (0)
Hyperlipoproteinemia	8/31 (26)
Hypertension	3/31 (10)
Current smokers	5/31 (16)
Previous smokers	2/31 (6)
Cerebrovascular disease	3/31 (10)
Coronary artery disease	3/31 (10)
Previous stent / PTCA	2/31 (6)
Family history of cardiac disease	15/31 (48)
Medication	
ACE inhibitor	3/31 (10)
AT1 antagonist	1/31 (3)
Beta blocker	6/31 (19)
Calcium antagonist	0/31 (0)
Antiarrhythmic	0/31 (0)
Nitrate	1/31 (3)
Acetylsalicylic acid	4/31 (13)
Anticoagulant	2/31 (6)
Diuretics	0/31 (0)
Statins	3/31 (10)

- 143 patients
- From 1978 to 1985
- All treated with mediastinal RT
- 40 Gy/20 fr (RT)
- 53 long term survivors (20-28 years)
- 31 patients undergone a 1.5-T MRI
- ***Cardiac magnetic resonance imaging (MRI) has recently been introduced as a sensitive and specific imaging method to detect and quantify abnormal cardiac function***

- ***7 pts*** *(23%) showed* ***reduced LVEF*** *(48 ± 3%)*

- ***13 pts*** *(42%) presented* ***hemodynamically relevant valvular dysfunctions*** *(8 aortic valves, 6 mitral valves, 1 tricuspid valve)*

- ***21 pts*** *(68%) had* ***any perfusion deficit*** *(at rest or at stress)*

- ***8 pts*** *(26%) had typically ischemic late enhancement in LV, ranging from small subendocardial to large transmural* ***infarctions***

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doi:10.1016/j.ijrobp.2008.07.018

ASTRO Online CME

CLINICAL INVESTIGATION **Breast**

POTENTIAL EFFECT OF ROBUST AND SIMPLE IMRT APPROACH FOR LEFT-SIDED BREAST CANCER ON CARDIAC MORTALITY

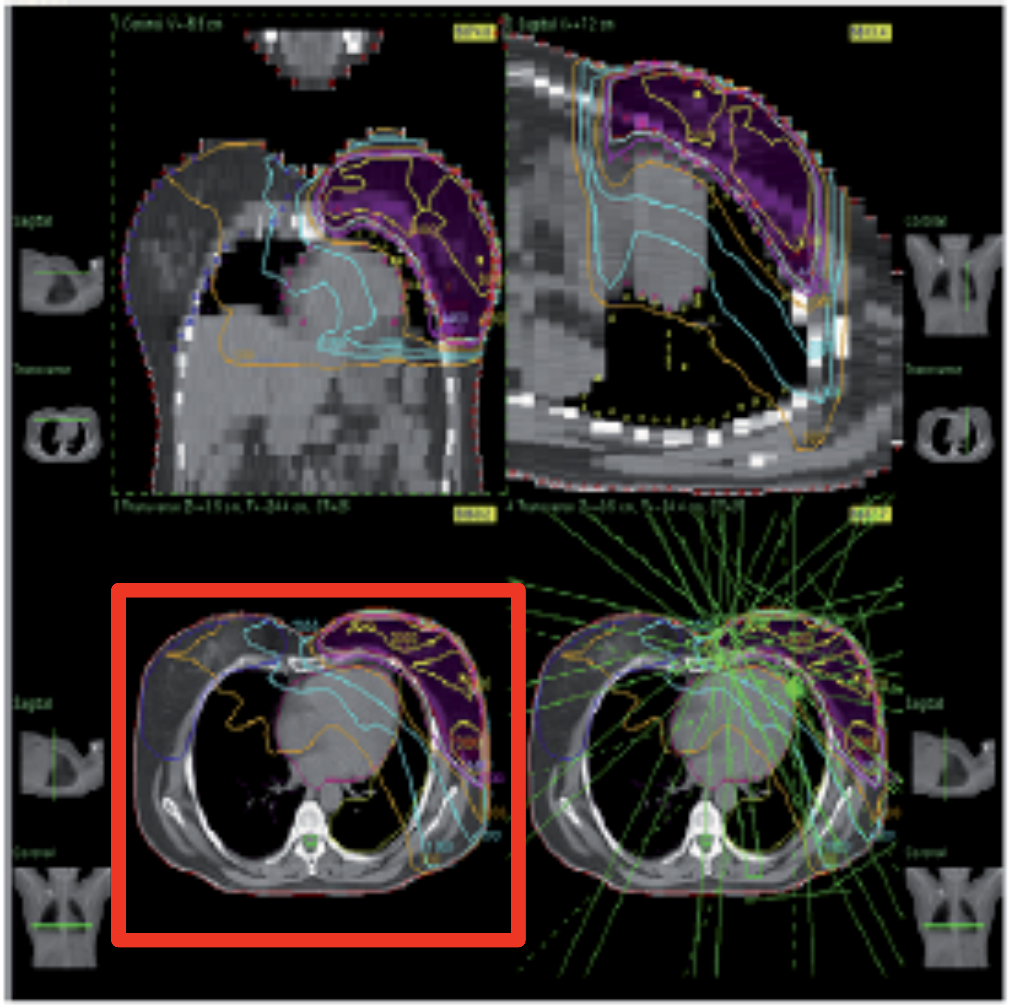
Frank Lohr, M.D.,* Mostafa El-Haddad, M.D., F.R.C.R.,*† Barbara Dobler, Ph.D.,*‡ Roland Grau, M.D.,* Hans-Joerg Wertz, M.Sc.,* Uta Kraus-Tiefenbacher, M.D.,* Volker Steil, M.Sc.,* Yasser Abo Madyan, M.D.,*† and Frederik Wenz, M.D.*

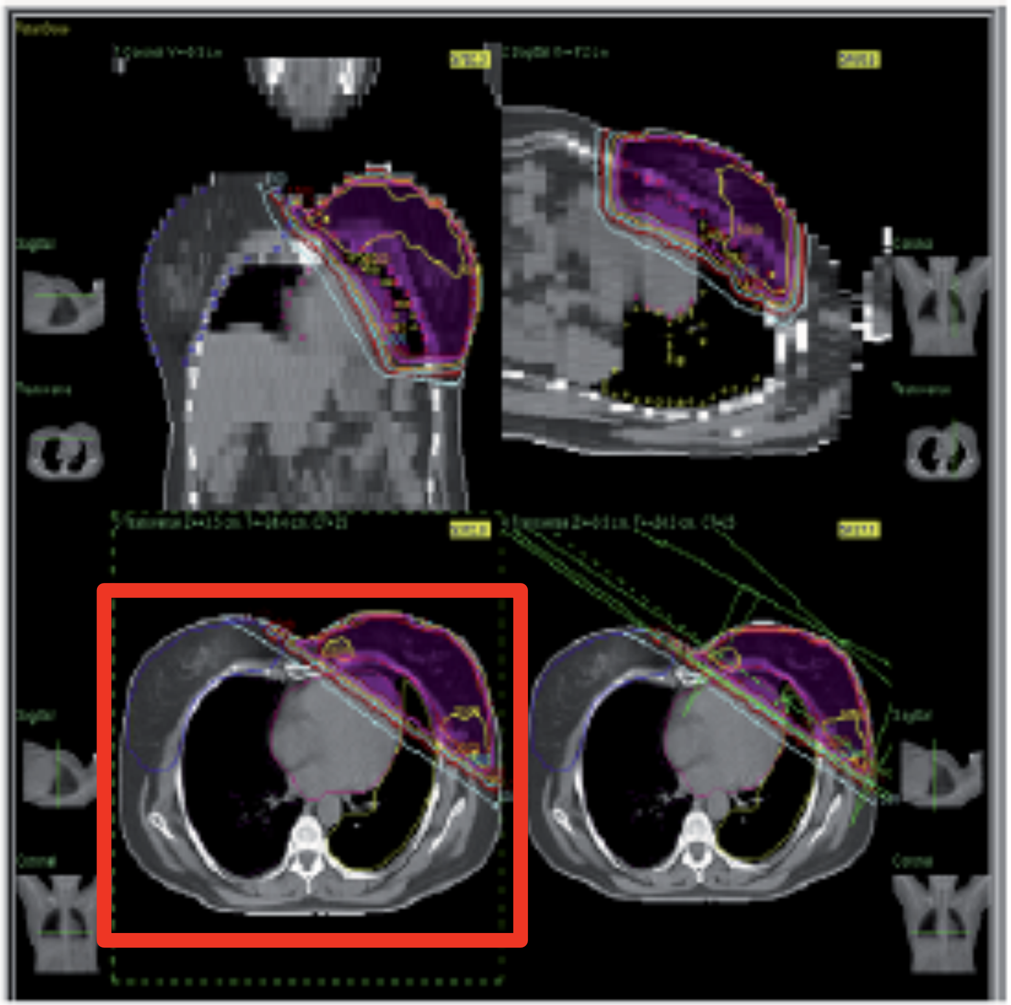
*Department of Radiation Oncology, Mannheim University Medical Center, University of Heidelberg, Mannheim, Germany; †Department of Oncology, Kasr-El-Einy Hospital, Cairo University, Cairo, Egypt; ‡Department of Radiotherapy, Regensburg University Medical Center, Regensburg, Germany

-14 patients

- Left-sided breast cancer

- Comparing of 3DCRT and IMRT plans





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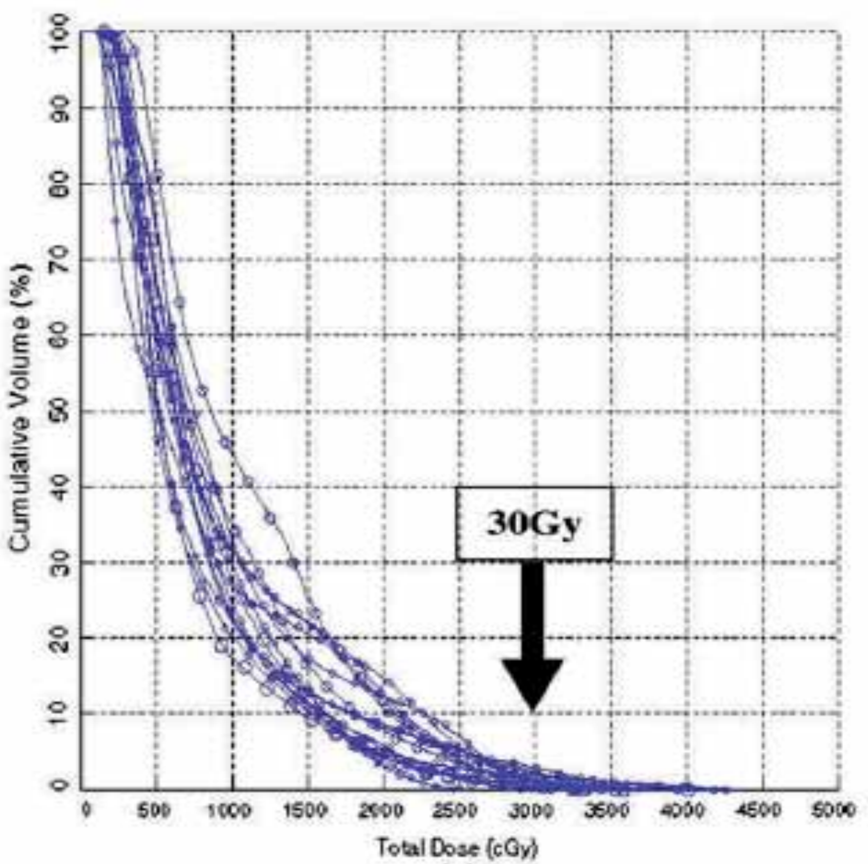
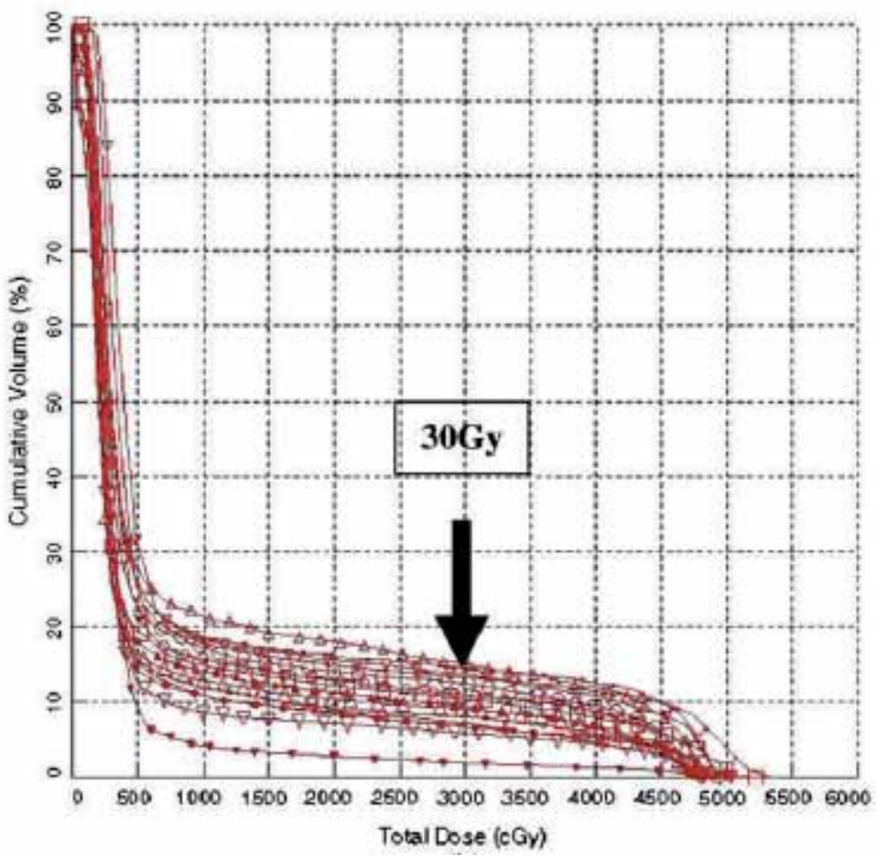
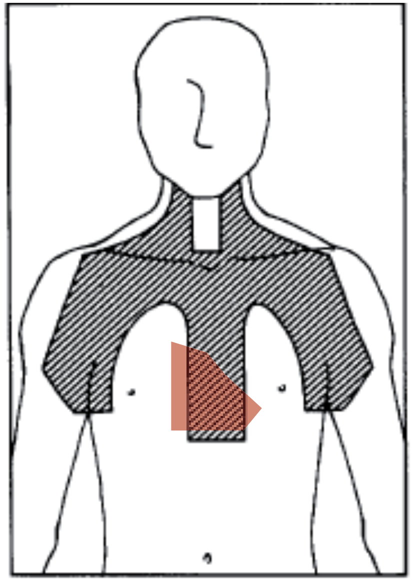
IMRT



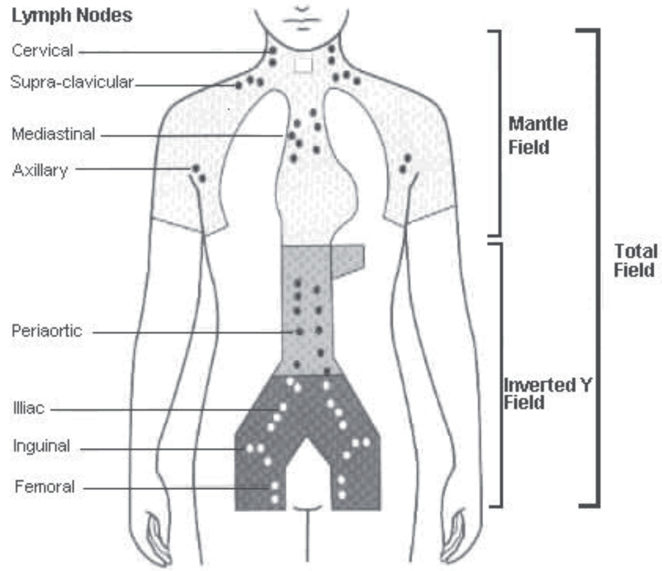
3DCRT

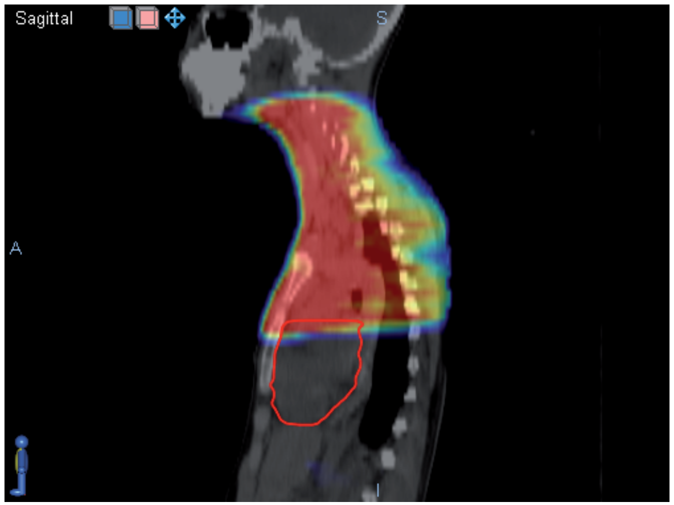


2DRT vs IMRT



‘70 – ‘90





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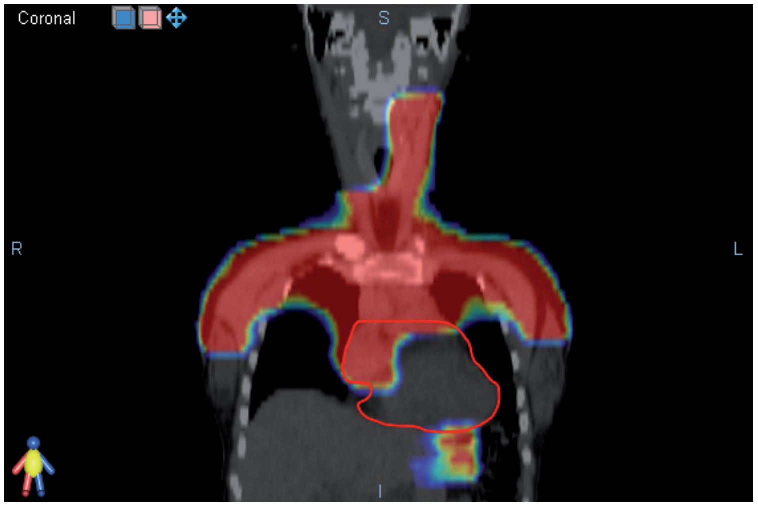

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PHYSICS CONTRIBUTION

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

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*Department of Radiotherapy, Catharina Hospital, Eindhoven, The Netherlands; †Department of Biomedical Engineering, Eindhoven University of Technology, Eindhoven, The Netherlands; ‡Department of Cardiology, Onze Lieve Vrouwe Gasthuis, Amsterdam, The Netherlands

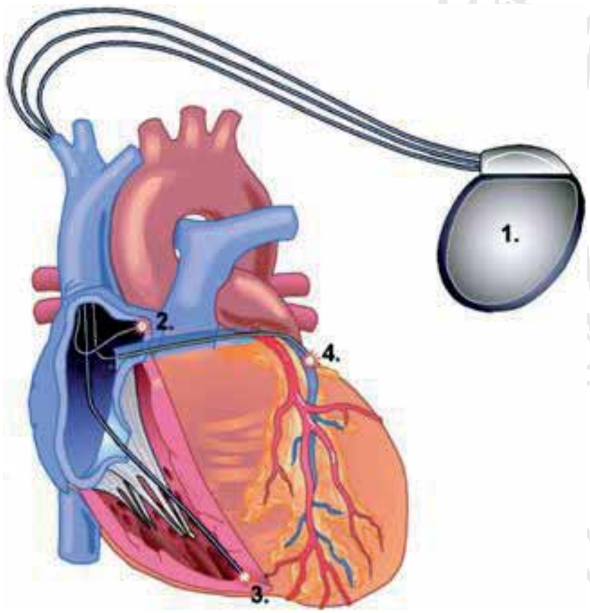

Table 1. Results for all 11 ICDs

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

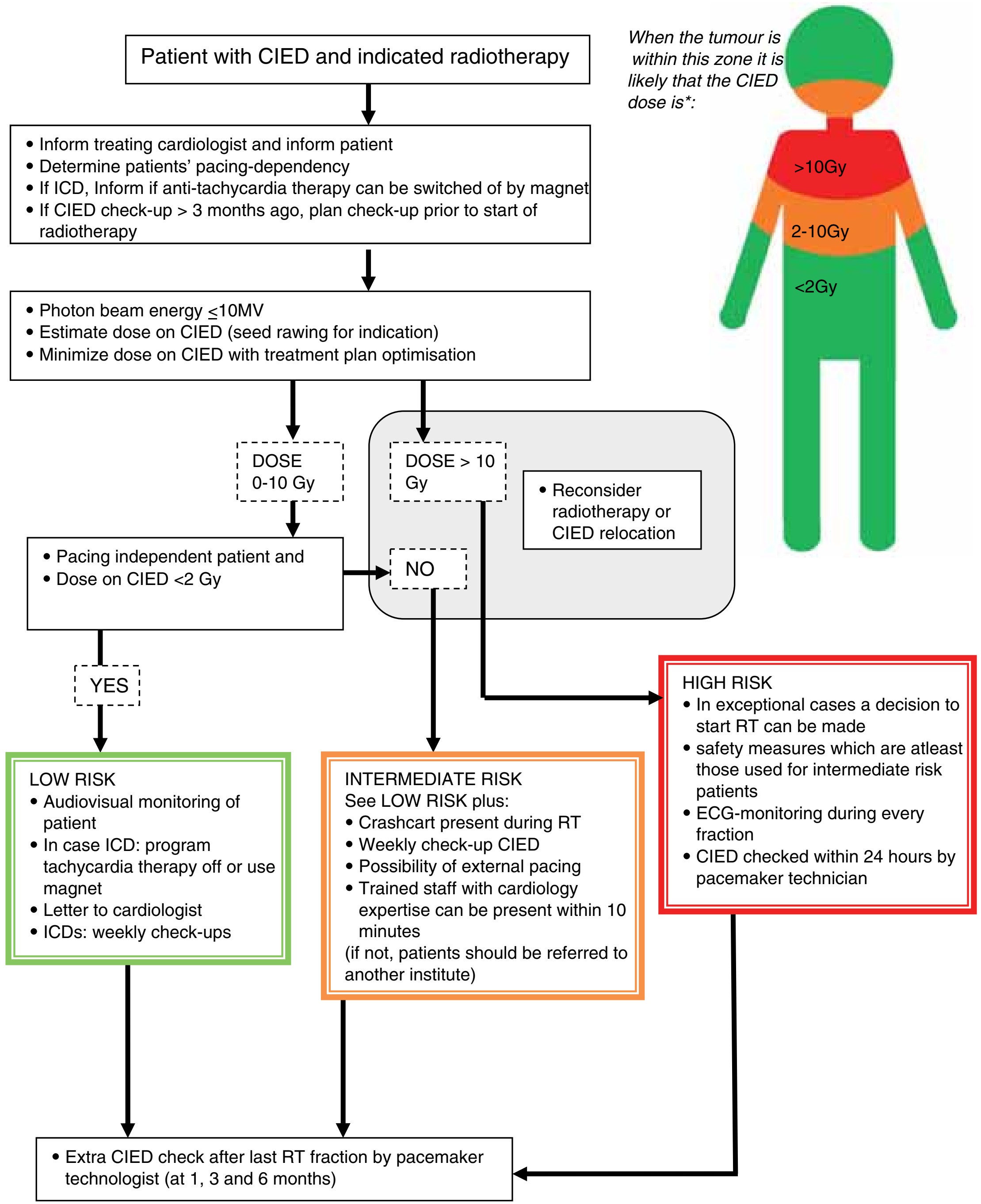

Figure 1 Flow diagram of Dutch guidelines. *Estimation of dose in case of a pectoral placed CIED.

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***. The clinical relevance of the ***perfusion abnormalities, observed despite modern techniques, needs clarification***.

b) Additional study is needed to ***relate doses to subvolumes of the heart*** (e.g., coronary arteries) ***to clinical outcomes***. Computed tomography contrast could be useful for defining the heart borders. Additional studies are indeed needed in radiation-treated patients with other thoracic tumors (e.g., lung cancer), in whom an increased rate of heart disease has been noted but dose–volume data are lacking.

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.

d) Additional work is needed to understand ***the impact of hypofractionated radiation regimens*** on the heart.

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

GRAZIE PER L'ATTENZIONE