

Cardiac Screening Among Hodgkin Lymphoma Survivors

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Case: 51 Year Old Male

- Had ABVD x 4 + 35Gy Mantle RT in 1993 at age 36.
- Noted to have consistently elevated blood pressure in 2003 (145/95 in clinic).
- Reported that GP found cholesterol to be “a little bit high”.
- Non-smoker, no diabetes.

Case: 51 Year Old Male

- 2004
 - BP elevated in clinic.
 - intended to reduce blood pressure and cholesterol through diet and exercise.

2005 – Myocardial Infarction



Cardiotoxic Exposures in HL Treatment

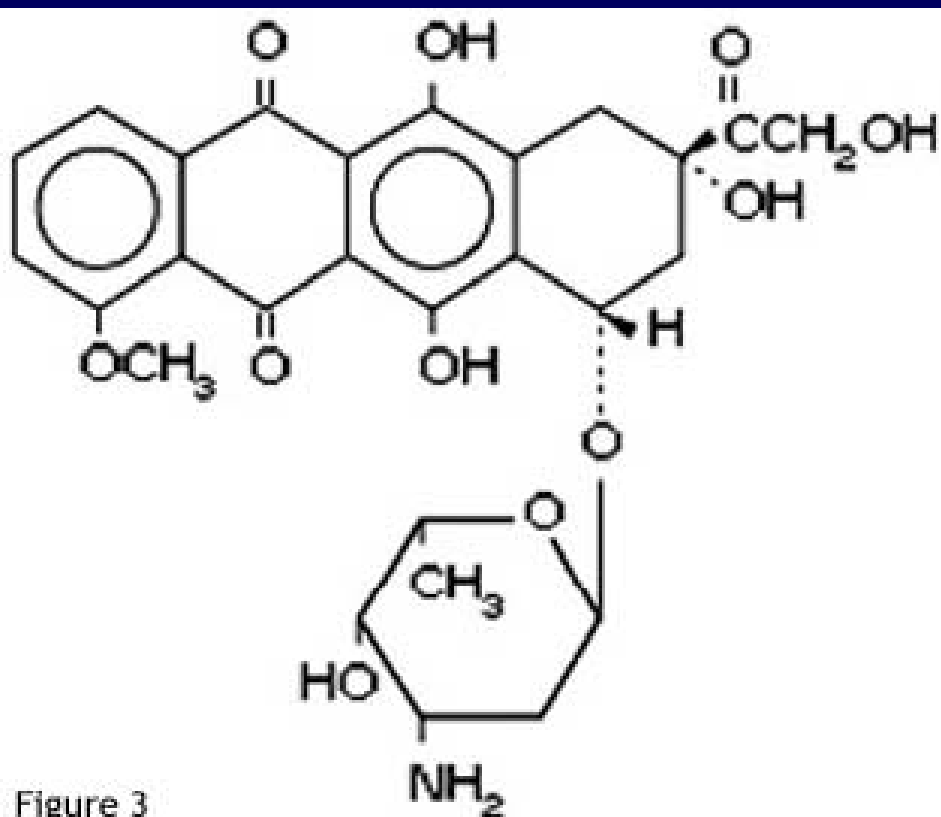
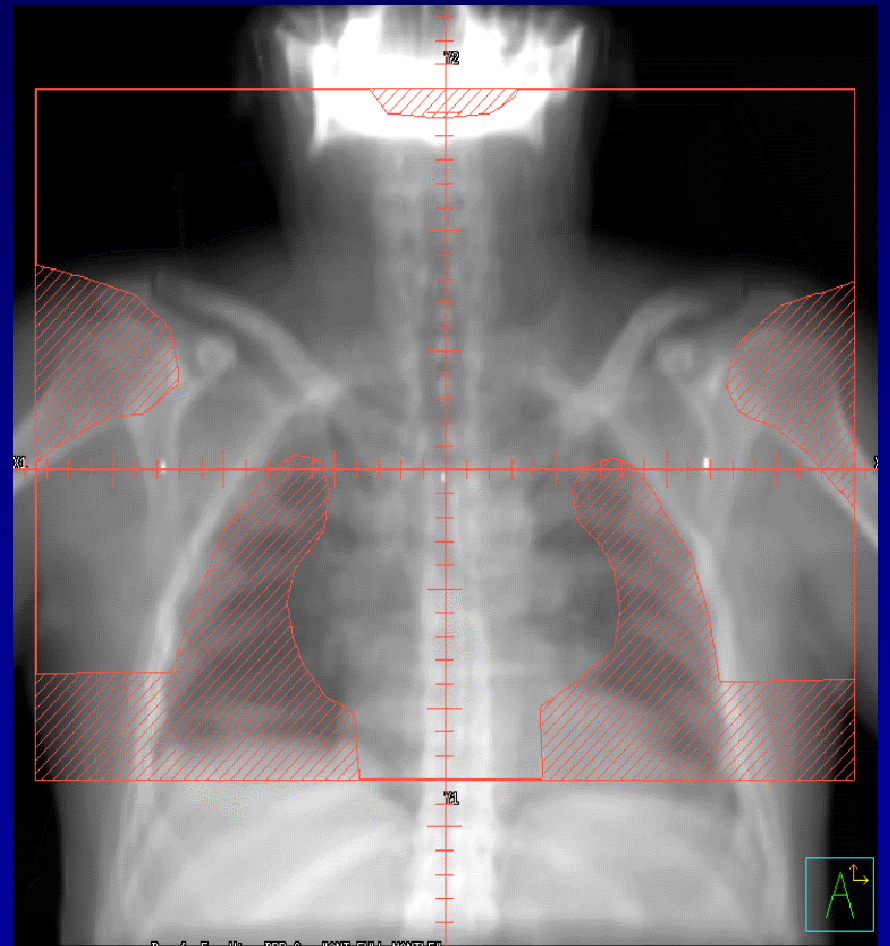
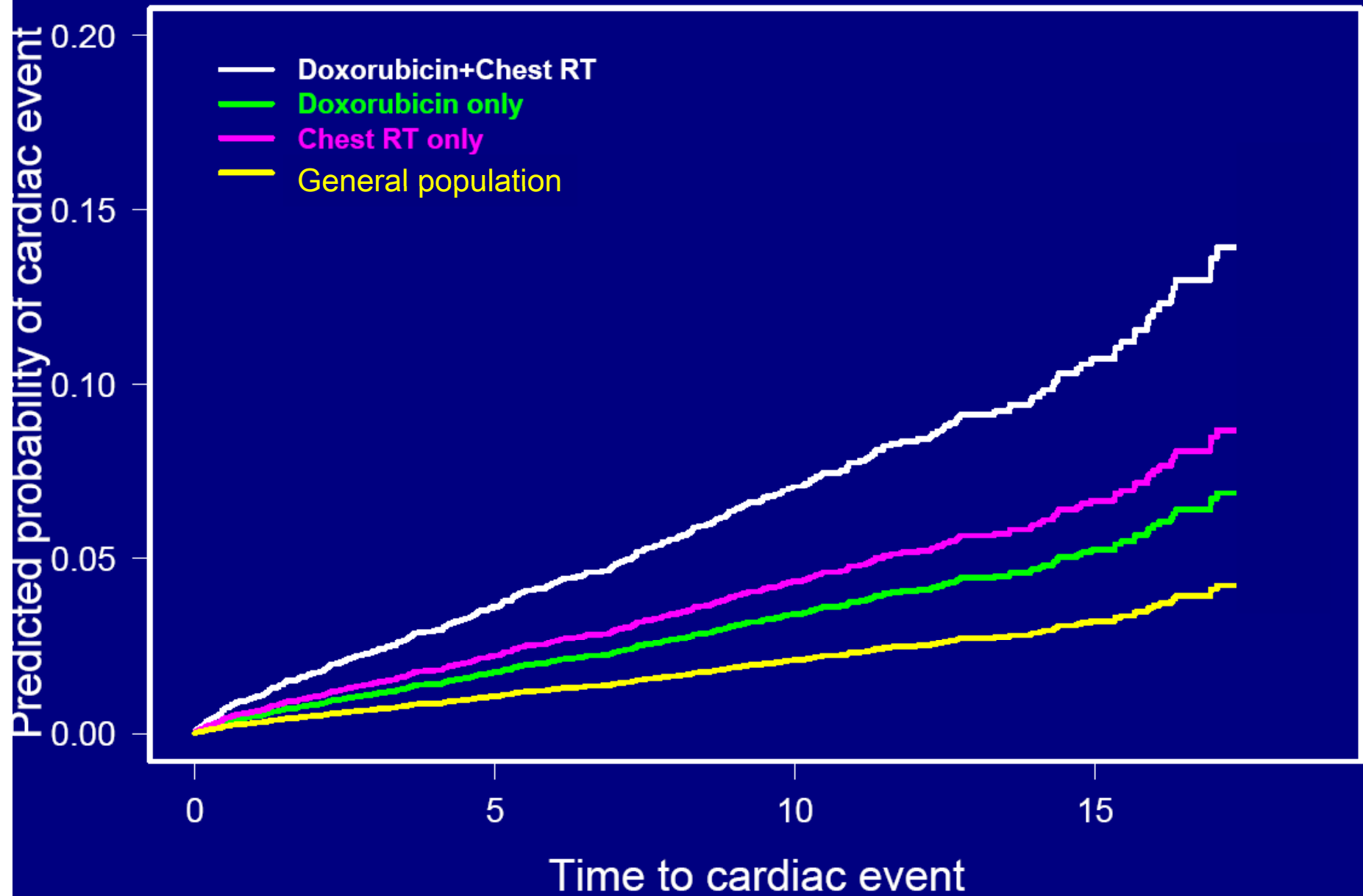


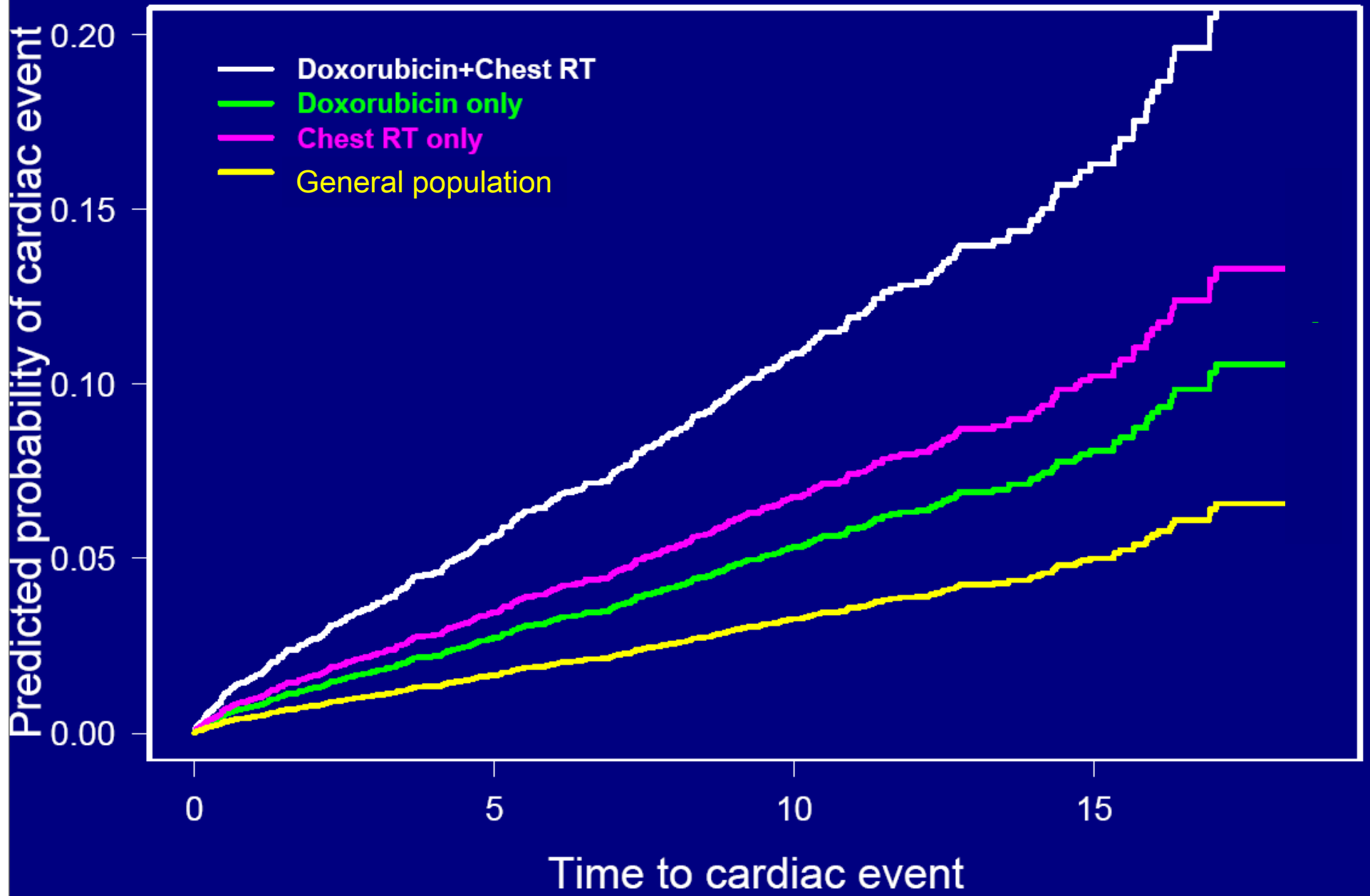
Figure 3
Doxorubicin, commonly called Adriamycin



HD Subcohort and matched controls 40 years old women, no diabetes



HD Subcohort and matched controls 40 years old men, no diabetes



The Significance of Traditional Cardiac Risk Factors in HL Survivors

- There is little information on the interaction between traditional risk factors and HL treatment .
- Glanzmann *et al.*, used the Framingham equation to estimate the risk of ischemic heart disease among 352 HL patients.
- Among survivors, the presence of cardiac risk factors conferred a 2.38 RR of ischemic heart disease compared to the expected rate among the general population with the same risk factors.

Cardiac Risk Factors in HL Survivors

- Traditional cardiac risk factors may be even more detrimental to the health of HL survivors than they are to members of the general population.

Hypertension in HL Survivors

- Most Clinical Practice Guidelines recommend intervention for blood pressure $>140/90$ measured on 5+ occasions.
 - Pharmacologic intervention if lifestyle modifications do not lower bp.

Lipid Management

US National Cholesterol Education Program

- For persons at increased risk because of the presence of multiple risk factors, the LDL-cholesterol goal should be <3.4 mmol/L.
- Drugs should be considered when LDL levels are high (>4.16 mmol/L).

Lipid Management

US National Cholesterol Education Program

- Multiple-risk-factor persons at highest risk (10-year risk >20 percent) need to attain even lower LDL cholesterol levels (LDL goal <2.6 mmol/L)
- Drug therapy should be considered simultaneously with therapeutic lifestyle changes when LDL-cholesterol levels are > 3.4 mmol/L.

15-Year Incidence of Cardiac Hospitalization by Treatment

Age at HL Dx	General Population (%)	Doxorubicin (%)	Chest RT (%)	Doxorubicin + Chest RT (%)
Males				
20	1.6	2.6	3.3	5.3
30	2.8	4.6	5.8	9.4
40	5.0	8.1	10.2	16.3
Females				
20	1.0	1.6	2.1	3.4
30	1.8	2.9	3.7	6.1
40	3.2	5.2	6.7	10.7

Conclusions

- HL survivors need their cardiac risk factors evaluated routinely.
 - Including those treated with doxorubicin without mediastinal RT, which is associated with persistent elevated risk.
- HL treatment, particularly ABVD + mantle RT could reasonably be considered a “risk factor” that places patients at intermediate risk (at least).
- Patients and primary care providers should be aware that their risk factors should be actively managed and controlled.

Screening Asymptomatic Patients

- Several studies have documented elevated rates of echocardiographic abnormalities in HL survivors.
- Among 294 HL survivors Heidenreich *et al.* found heart valve regurgitation in 29%.
- Left ventricular dysfunction was also more common among survivors than would be expected in the general population.

Screening Asymptomatic Patients (con't)

- Hequet *et al.* evaluated 141 lymphoma patients treated with anthracyclines, 30 of whom also received RT including the heart.
- 39 patients (28%) had asymptomatic cardiac dysfunction on echocardiography.
- The addition of RT to doxorubicin was significantly associated with an increased risk of asymptomatic ventricular dysfunction, compared to doxorubicin without RT.

Screening Asymptomatic Patients (con't)

- Adams *et al.*, found that 47/48 HL patients (98%) who were treated at age 6-28 had an abnormality on echocardiography, exercise stress testing, or resting or 24-hour ECG.
- Similar findings have been reported by others.

BUT: Uncertain Clinical Significance

- Adams *et al.*: all patients with cardiac test abnormalities described their health as “good or better”, and global health-related quality of life was poorly correlated with cardiac test results.
- Little evidence that starting ACE inhibitors for ventricular dysfunction provides clinically durable/meaningful effects.

Early Detection of Clinically Significant CAD

- Heidenreich et al. (Stanford)
- Enrolled 294 outpatients after mediastinal RT doses >35 Gy for Hodgkin's disease who had no known ischemic cardiac disease.
- 70% received RT doses 43-45Gy (vs. 35Gy common in Canada).
- 56% treated with chemotherapy (not described).
- Mean current age = 42 years
- Mean interval from RT = 15 years
- Patients underwent stress echocardiography and radionuclide perfusion imaging.

Results

Table 2. Stress Testing Results

Result	All Patients		Years After Irradiation						P
	No.	%	2-10		11-20		> 20		
	No.	%	No.	%	No.	%	No.	%	
Exercise time, Bruce protocol, minutes*									.05
Mean		9.9		10.4		9.8		9.4	
SD		2.5		2.5		2.5		2.5	
Duke Treadmill Score*									.03
Mean		9.3		10.2		9.0		9.0	
SD		3.2		3.0		3.2		3.1	
Resting wall motion abnormality	56 of 293	19	12 of 89	13	23 of 132	17	21 of 72	29	.04
Mild hypokinesia	39		8		18		13		
Moderate hypokinesia	12		4		4		4		
Severe hypokinesia/akinesia	5		0		1		4		
Fixed perfusion defect	17 of 274	6	4 of 83	5	6 of 122	5	7 of 69	10	.30
Stress induced wall motion abnormality	16 of 292	5	1 of 89	1	9 of 132	7	6 of 71	8	.05
Stress induced perfusion abnormality	32 of 274	12	4 of 83	5	14 of 122	11	14 of 69	20	.01
Stress induced ECG changes	20 of 282	8	3 of 85	5	12 of 128	10	5 of 69	7	.34
Coronary angiography performed†	40 of 294	14	5 of 89	6	19 of 132	14	16 of 73	22	.02

Abbreviation: SD, standard deviation.

*Sample size for exercise time and Duke Treadmill Score: years after irradiation, 2-10 (n = 62); 11-20 (n = 110); > 20 (n = 55).

†After stress testing but prior to a cardiac event. Includes one patient with acute myocardial infarction diagnosed at the time of angiography (coronary thrombus, with new Q waves on the electrocardiogram).

Author's Conclusions

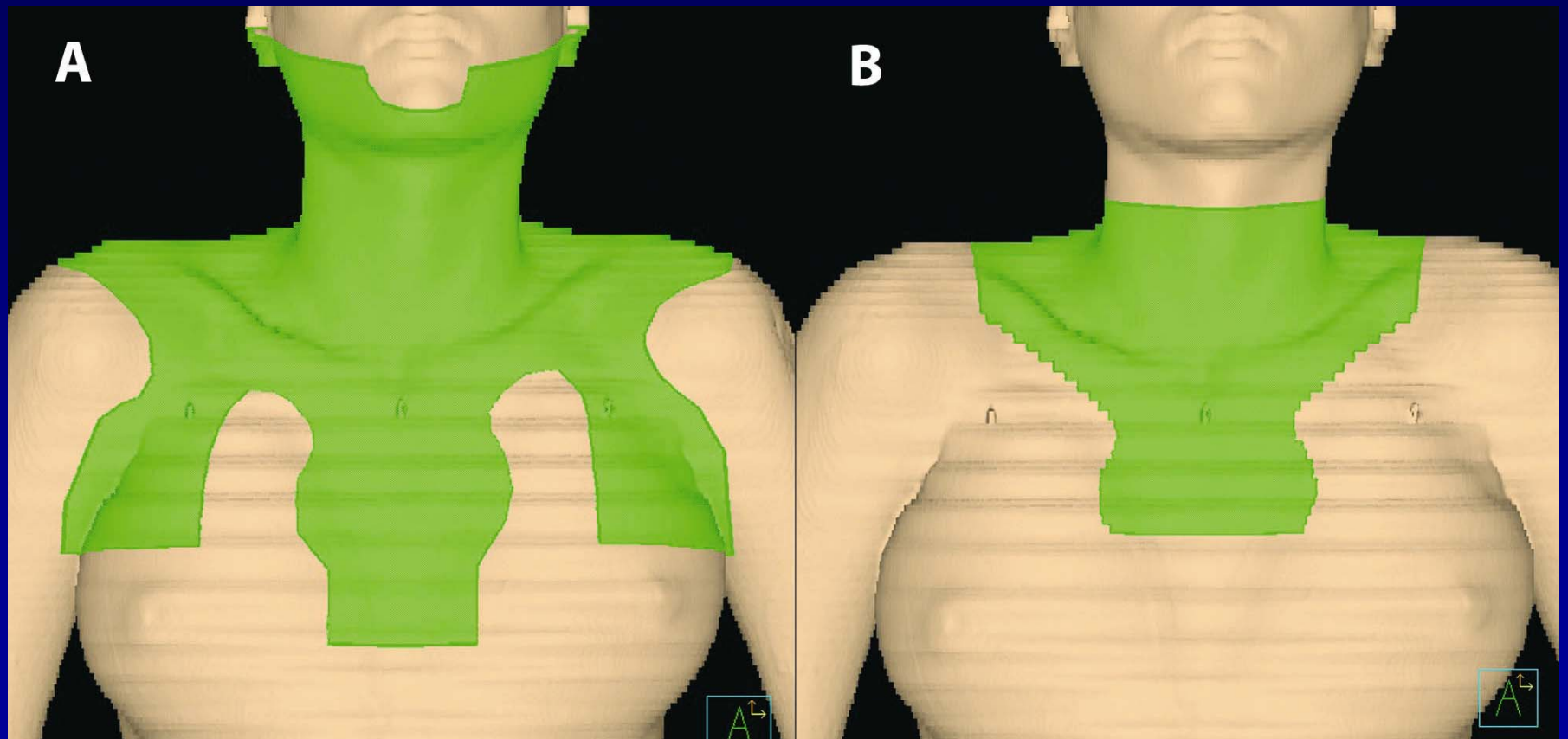
- Screening for coronary artery disease should be considered during follow-up care for asymptomatic patients who have received mediastinal irradiation to doses of 35Gy or more.
- Although the diagnostic yield will be greater for patients more than 10 years beyond RT, we recommend initiating screening 5 years after treatment.

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Conclusions

- Remains unclear if/when to screen asymptomatic patients.
- Reasonable to consider stress echo:
 - 10 years after mediastinal RT in all patients.
 - 5+ years after mediastinal RT in
 - men attained aged 45+ years
 - Patients receiving ABVD + mediastinal RT
 - Patients with other cardiac risk factors

Will Modern Treatment Reduce the Risk of Cardiac Toxicity?



Mantle RT

Involved-field RT

Reduction in Normal Tissue Dose With Transition From Mantle to IFRT

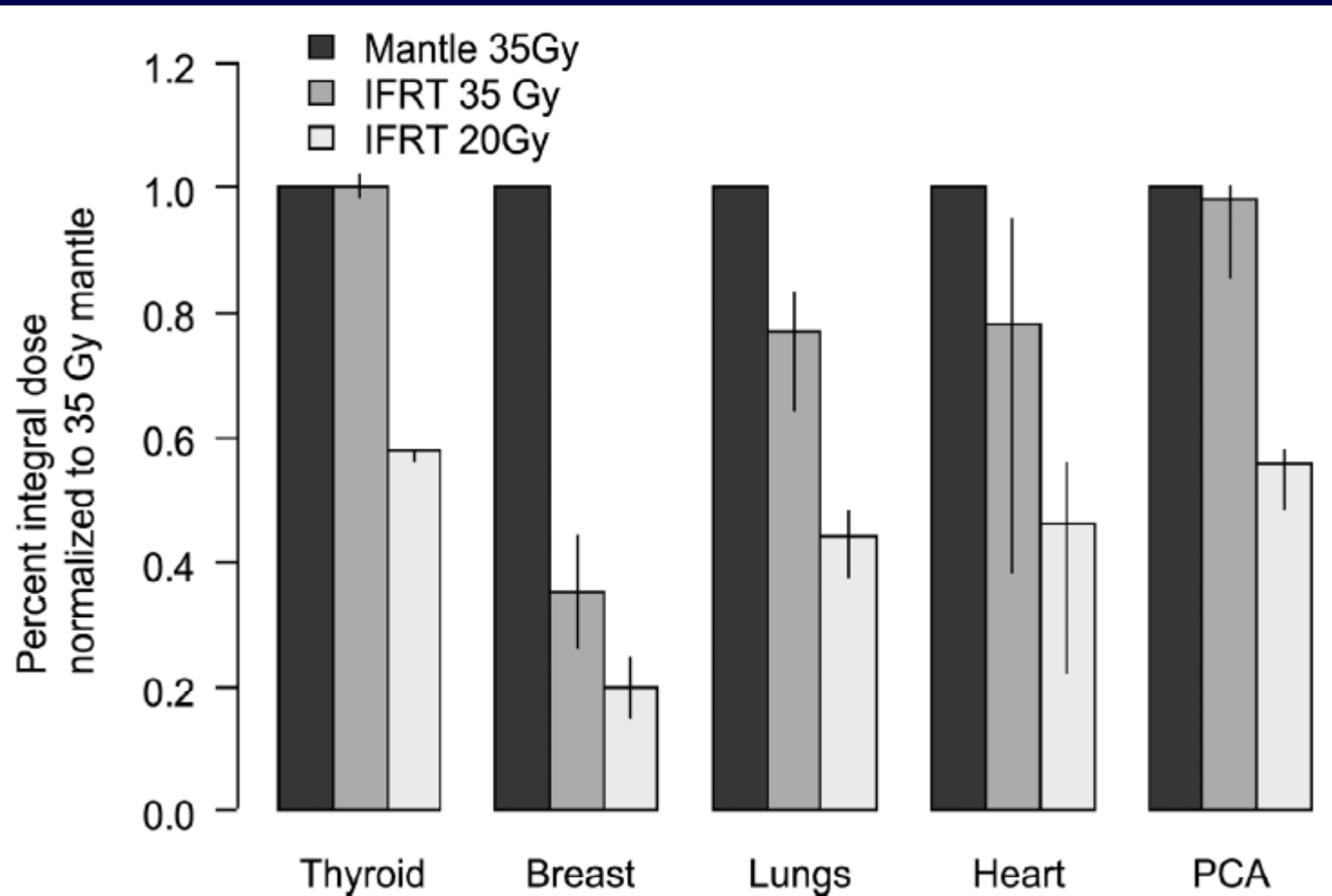
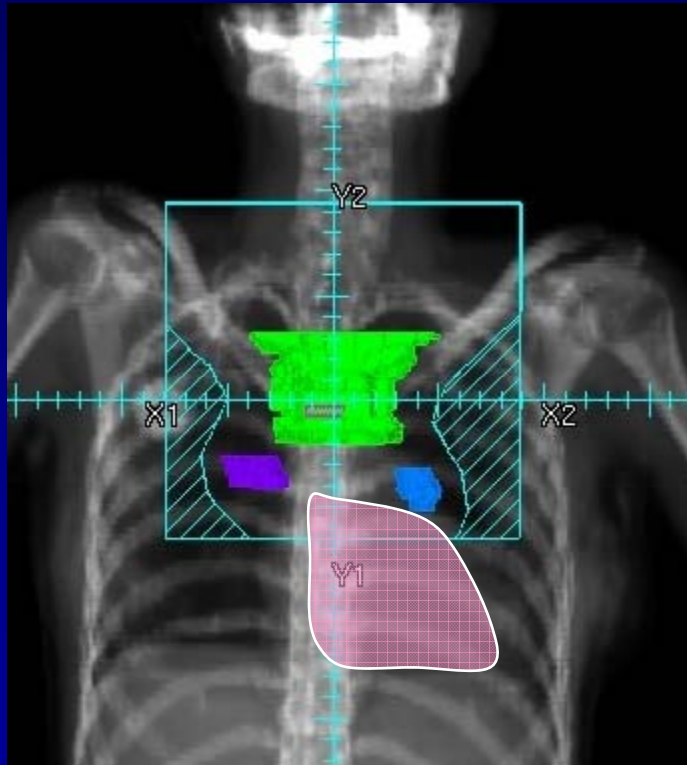


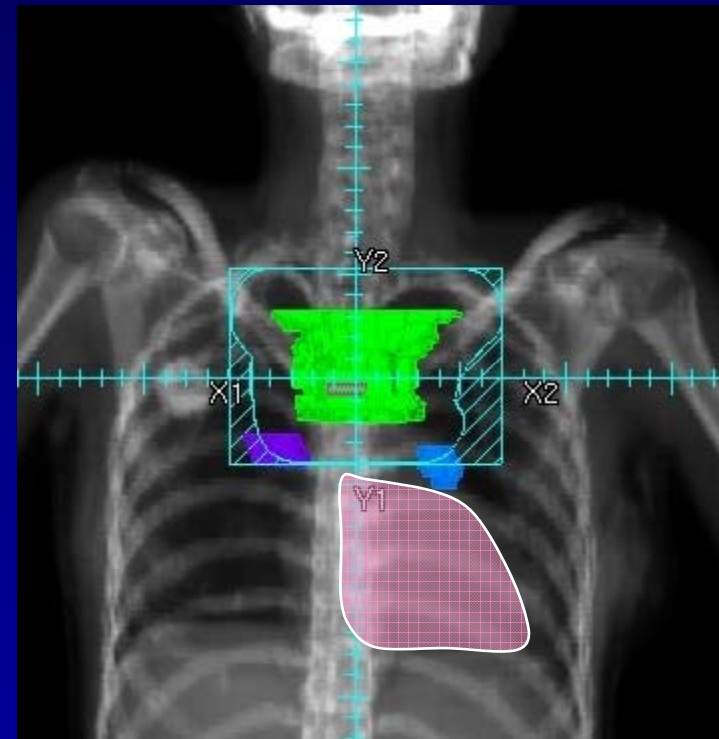
Figure 3
Proportional reduction in integral dose to normal tissues

Involved-node RT

Used in Ongoing EORTC & GHSB Trials



IFRT



Involved-node RT (INRT)

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