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Radiation Therapy Contouring: Cardiac/Thoracic Anatomy

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Why is contouring important?

- **<u>Targets</u>:** Tumors and Nodal stations
- **<u>Normal tissues</u>:**
  - Reduce doses by blocking
  - Choosing beam angles with greatest separation between targets and OARs
  - Understanding dose-volume-toxicity relationships
  - Reducing toxicity

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Learning Objectives

1) Understand the need for consistency in normal tissue contouring in the thorax

2) Be able to access atlases developed by radiation oncologists to improve contour consistency

3) Use these atlases as a guide to standardize contours and improve normal tissue sparing

OARs highlighted today

- **Heart**
- **Brachial plexus**
- **Esophagus**

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Radiation can cause cardiac toxicity

The NEW ENGLAND JOURNAL of MEDICINE

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

Sarah C. Darby, Ph.D., Marianne Ewertz, D.M.Sc., Paul McGale, Ph.D., Anna M. Bennet, Ph.D., Ulla Blom-Goldman, M.D., Dorthe Brønnum, R.N., Candace Correa, M.D., David Cutter, F.R.C.R., Giovanna Gagliardi, Ph.D., Bruna Gigante, Ph.D., Maj-Britt Jensen, M.Sc., Andrew Nisbet, Ph.D., Richard Peto, F.R.S., Kazem Rahimi, D.M., Carolyn Taylor, D.Phil., and Per Hall, Ph.D.

(Reuters Health) - The radiation that might cure a breast cancer may also raise a woman's risk of having a heart attack or heart disease later in life, according a new study that looked back at the cases of 2,168 women in Sweden and Denmark

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Radiation can cause cardiac toxicity

METHODS

We conducted a population-based case–control study of major coronary events (i.e., myocardial infarction, coronary revascularization, or death from ischemic heart disease) in 2168 women who underwent radiotherapy for breast cancer between 1958 and 2001 in Sweden and Denmark; the study included 963 women with major coronary events and 1205 controls. Individual patient information was obtained from hospital records. For each woman, the mean radiation doses to the whole heart and to the left anterior descending coronary artery were estimated from her radiotherapy chart.

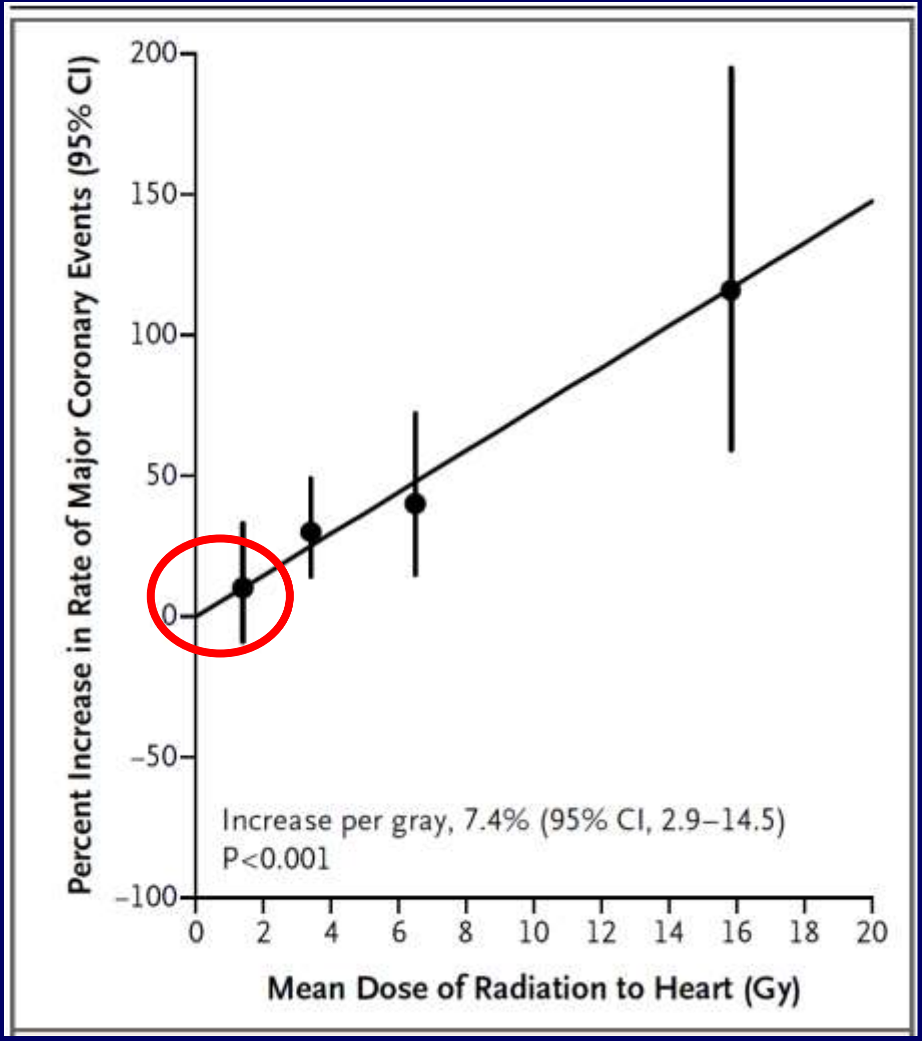
RESULTS

The overall average of the mean doses to the whole heart was 4.9 Gy (range, 0.03 to 27.72). Rates of major coronary events increased linearly with the mean dose to the heart by 7.4% per gray (95% confidence interval, 2.9 to 14.5; P<0.001), with no apparent threshold. The increase started within the first 5 years after radiotherapy and continued into the third decade after radiotherapy. The proportional increase in the rate of major coronary events per gray was similar in women with and women without cardiac risk factors at the time of radiotherapy.

Darby, et al, NEJM, 2013.

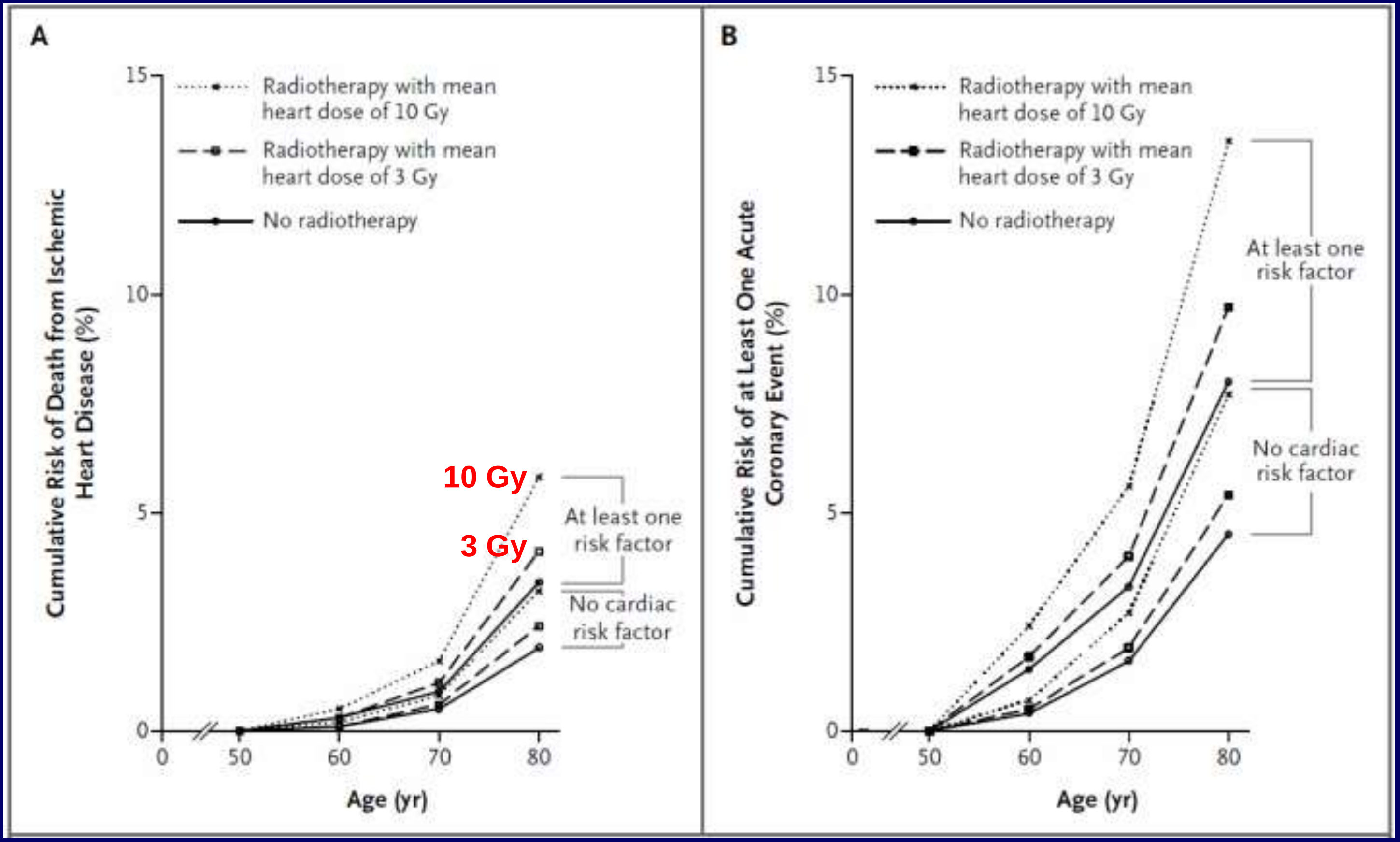
Dose effect on the heart

No threshold



Darby, et al, NEJM, 2013.

Dose effect on the heart



Darby, et al, NEJM, 2013.

How was dosimetry analyzed?

- Virtual simulation and planning based on CT or manual planning "were used to reconstruct each radiotherapy regimen on the CT scan of a woman with typical anatomy"
- (Virtual) Radiation doses to the structures of interest were then estimated
- In manual planning, the (virtual) doses were estimated on the basis of charts on which isodose curves had been drawn

Darby, et al, NEJM, 2013.

How was dosimetry analyzed?

- Dose-volume histograms for the whole heart and for the left anterior descending coronary artery were obtained
- Mean doses were calculated

Darby, et al, NEJM, 2013.

Are these results believable?

- In general? Probably
- Specifically? No
  - Reconstructed, hypothesized cardiac doses
  - Not based on reality

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What do we know about cardiac toxicity?

The time-course and extent of cardiac damage depends on dose

- In the past, Hodgkin's survivors were diagnosed with heart disease 1-2 years after radiotherapy (30 Gy+)
- Latency greater for lower doses of RT

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Cardiac toxicity after breast RT

SEER study of 300,000 women with breast cancer

Years since breast cancer diagnosis	No radiotherapy: No. of deaths left/right	No radiotherapy: Mortality ratio left versus right & 95% CI	Radiotherapy: No. of deaths left/right	Radiotherapy: Mortality ratio left versus right & 95% CI
Heart disease death				
< 5 years	2164/1972	1.03 (0.97-1.09)	700/633	1.04 (0.93-1.15)
5 - 9	1632/1479	1.05 (0.98-1.13)	521/442	1.10 (0.97-1.25)
10 - 14	806/758	1.01 (0.91-1.11)	281/197	1.37 (1.14-1.64)
15+	568/524	1.02 (0.91-1.15)	254/162	1.53 (1.25-1.86)
All other known causes				
< 5 years	14775/13522	1.04 (1.01-1.06)	6911/6516	1.01 (0.98-1.05)
5 - 9	8009/7863	0.97 (0.94-1.00)	3178/2990	1.01 (0.96-1.06)
10- 14	3472/3343	0.99 (0.94-1.04)	1165/1095	1.01 (0.93-1.10)
15+	2106/2040	0.98 (0.92-1.04)	611/560	1.04 (0.93-1.17)

0 0.5 1.0 1.5 2.0

Darby, et al. Lancet Oncology 2005

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Rationale for heart avoidance

VOLUME 25 · NUMBER 25 · SEPTEMBER 1 2007

JOURNAL OF CLINICAL ONCOLOGY — ASCO SPECIAL ARTICLE

American Society of Clinical Oncology Clinical Evidence Review on the Ongoing Care of Adult Cancer Survivors: Cardiac and Pulmonary Late Effects

Joseph R. Carver, Charles L. Shapiro, Andrea Ng, Linda Jacobs, Cindy Schwartz, Katherine S. Virgo, Karen L. Hagerty, Mark R. Somerfield, and David J. Vaughn for the ASCO Cancer Survivorship Expert Panel

Table 4. Spectrum of Radiation Damage to the Heart

Structure	Abnormality	Natural History	Pathology
Pericardium	Pericarditis	Chronic asymptomatic effusion and/or pericarditis with symptoms: hemodynamic compromise with either constriction or tamponade	Fibrous thickening and fluid production
Myocardium	Myocarditis	Progressive diastolic dysfunction and restrictive hemodynamics with symptoms: CHF	Diffuse interstitial fibrosis/microcirculatory damage leading to capillary obstruction/extensive fibrosis
Endocardium	Valvular damage	Over time, progressive stenosis and regurgitation	Cusp and/or leaflet fibrosis
Vascular System	Arteritis	Premature CAD/accelerated atherosclerosis	Ostial and proximal stenosis; LAD, RCA, and left main more than left circumflex
		Pulmonary hypertension	Pathology similar to atherosclerosis
Conduction System		All forms of heart block and conduction delay	Fibrosis of the conduction system
Autonomic Dysfunction		Supraventricular tachycardia; heart rate variability	

Abbreviations: CHF, congestive heart failure; CAD, coronary artery disease; LAD, left anterior descending [coronary artery]; RCA, right coronary artery.

Mechanisms of RT cardiac effects

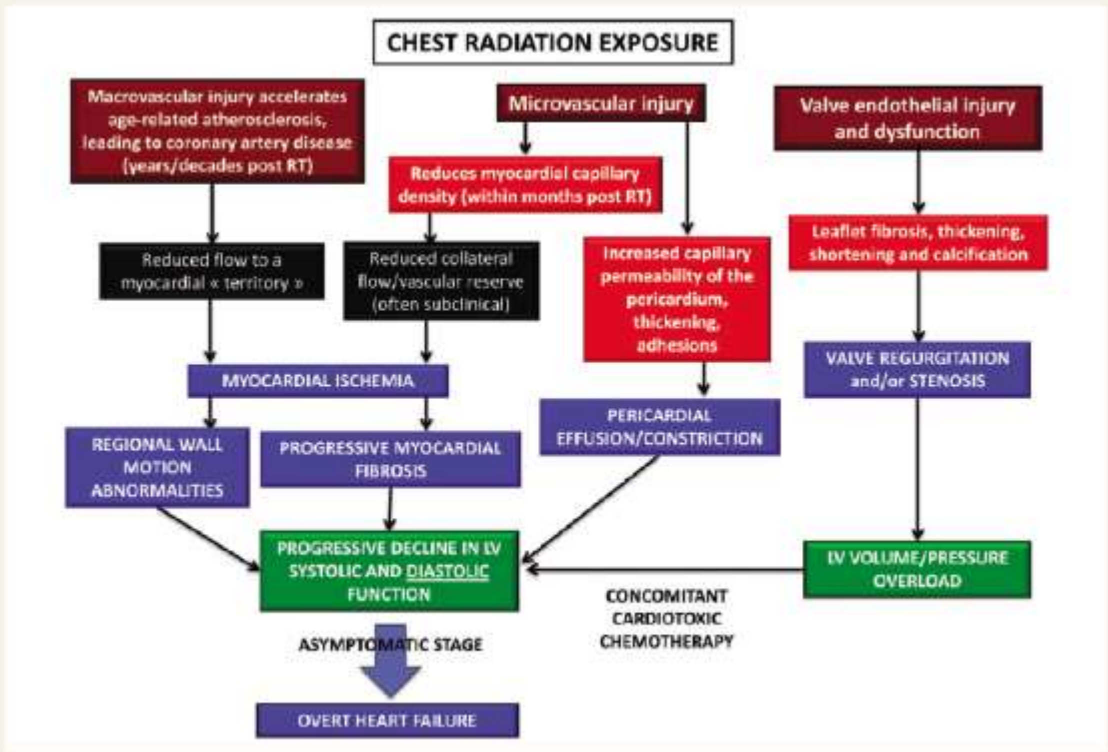

Figure 1 Pathophysiological manifestations of radiation-induced heart disease for different radiosensitive structures within the heart. LV: left ventricle; RT: radiotherapy.

Lancelloti, et al. Euro Heart J– Cardio Imaging, 2013.

Dose-volume-toxicity data in other organs

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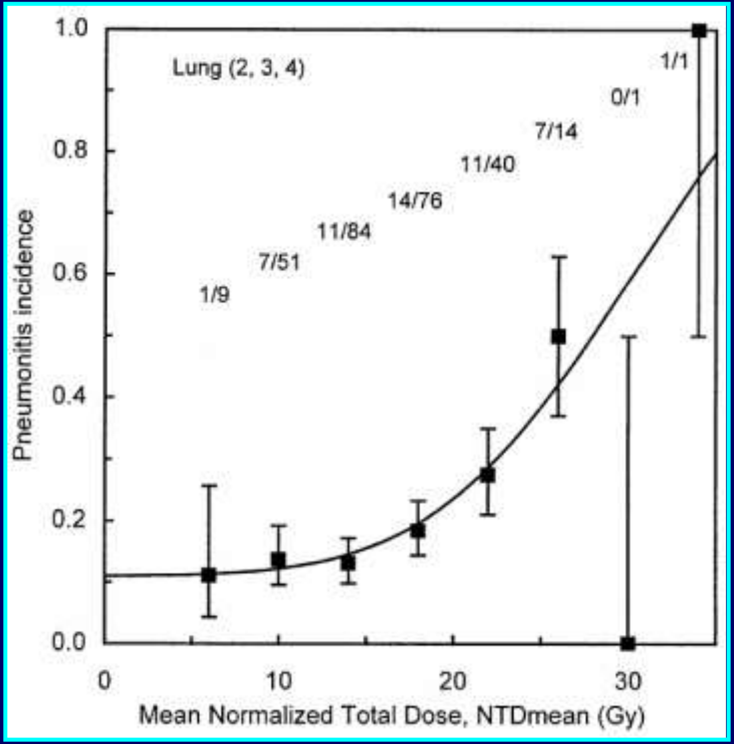
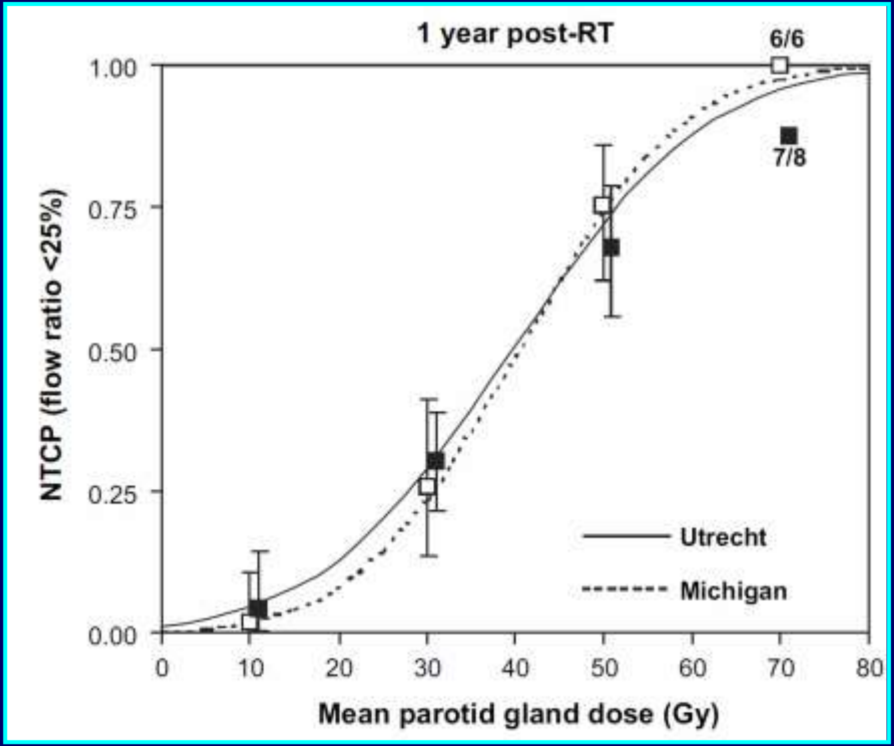
Pneumonitis



Kwa et al, IJROBP 1998

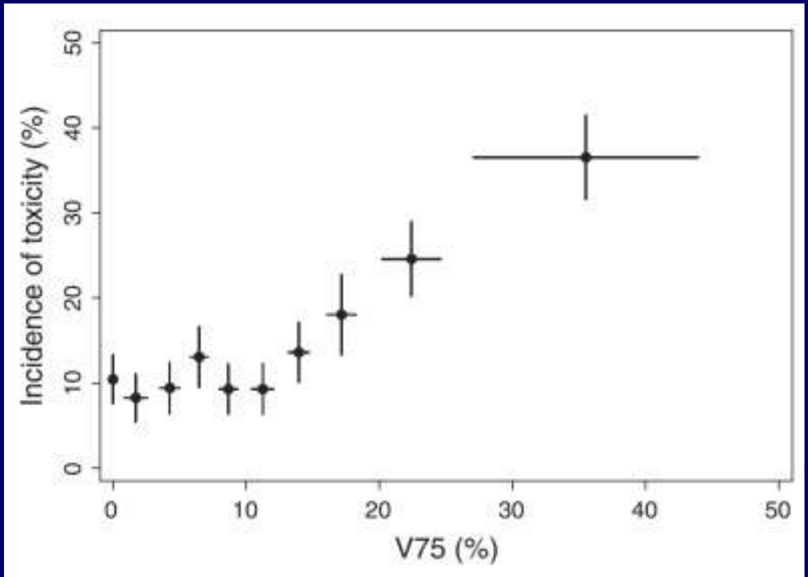
Xerostomia



Dijkema et al, IJROBP 2010

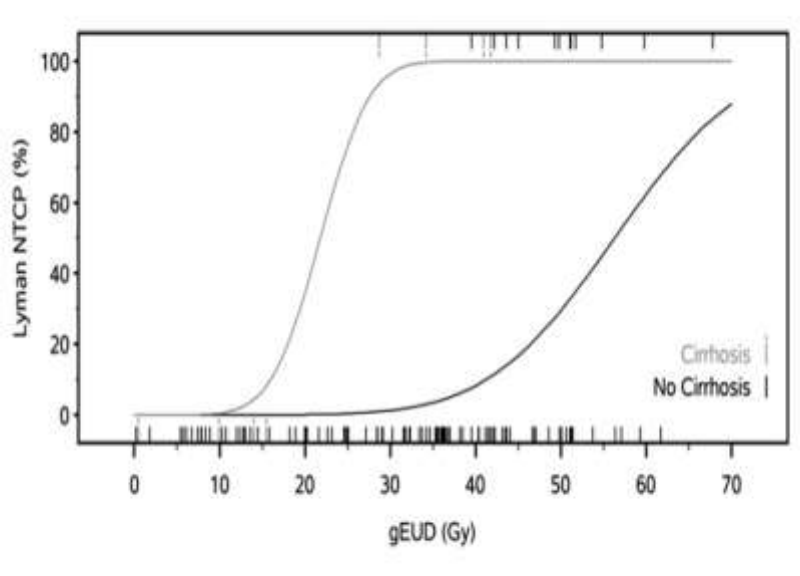
Dose-volume-toxicity data in other organs

Rectal Toxicity



Tucker, et al, IJROBP 2012

Gastric Bleed



Feng, et al, IJROBP 2012

Why haven't we had similar plots for cardiac damage?

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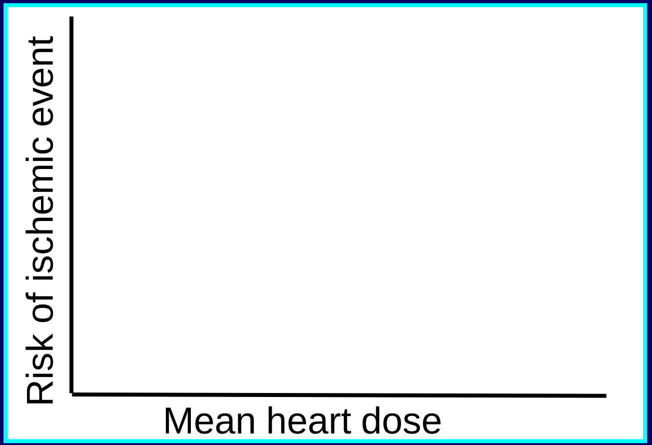
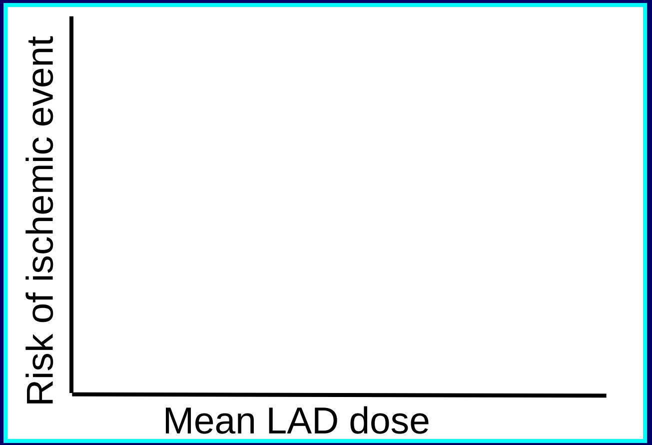
- In the pre-CT era, we could not accurately define the heart
- There is little agreement on how to define the heart
- Additionally, substructures of the heart may have specific importance





The data is hypothesized

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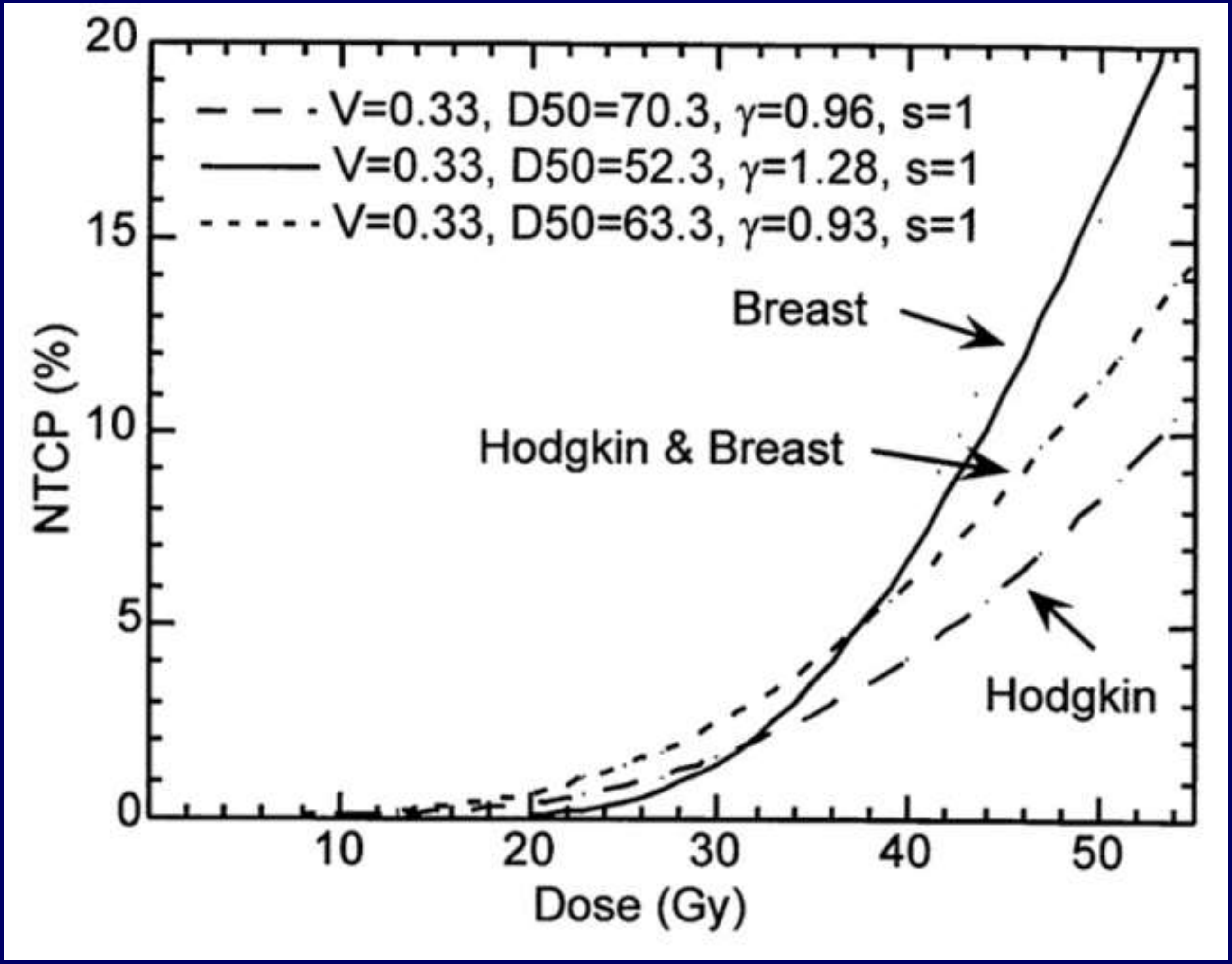
Table 3. Cardiac mortality from ischemic heart disease/myocardial infarction: Dose–volume predictors and NTCP parameters

Authors, Year, Reference	Diagnosis, No. of patients, Years of treatment	OAR	Dose data	Predictive parameters	NTCP parameters
Hancock *et al.* 1993 (17)	Hodgkin's 2232 patients 1960–1990	Heart	Dose up to 44 Gy Pre-3D dose data	$D_{mediastinum} > 30$ Gy	
Gagliardi *et al.* 1996 (25)	Breast 809 patients 1964–1976	Heart*	45–50 Gy[†] 1.8–2.5 Gy/fraction treatments reconstructed in 3D on average patients		RS[‡] (*CI 68%*) *D50* = 52.3 Gy (49;57) γ = 1.28 (1.04;1.64) *s* = 1 (0.63; at limit)
Eriksson *et al.* 2000[§] (51)	Hodgkin's 157 patients 1972–1985	Heart	~40 Gy[‖] 2 Gy/fraction Individual treatments reconstructed in 3D on phantom	$D_{35} > 38$ Gy	RS: Hodgkin's *D50* = 70.3 Gy γ = 0.96 *s* = 1 RS: Hodgkin's + breast *D50* = 63 Gy γ = 0.94 *s* = 1
Carr *et al.* 2005 (52)	Peptic ulcer, 1,859 patients, 1936–1965	Heart (Alderson Phantom)	1.5 Gy /fraction 250-kVp X-rays Treatment simulated on phantom	D_{mean} to 5% >12 Gy heart volume within the beam $D_{mean} > 2.5$ Gy whole heart volume	
Paszat *et al* 2007 (6)	Breast, 619 patients, 1982–1988	Heart	40–50 Gy 2–2.67 Gy/fraction to breast[¶] Pre-3D dose data	RT to Internal Mammary Chain	

Gagliardi, et al, QUANTEC, IJROBP 2010.

Hypothesized curves



Gagliardi, et al, QUANTEC, IJROBP 2010.

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How can we move forward?

- **We must first understand the relationship between dose and volume of heart (or cardiac substructures) and toxicity**
- **We can then incorporate these into treatment planning to minimize the risk of cardiac complications**

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Standardizing cardiac contours

Motivated by the lack of consistency in cardiac delineation, we

– Developed an atlas of cardiac substructure anatomy through a collaboration with cardiology and cardiac radiology

– Validated this atlas using a pre- and post-test study of 7 radiation oncologists

Cardiac atlas

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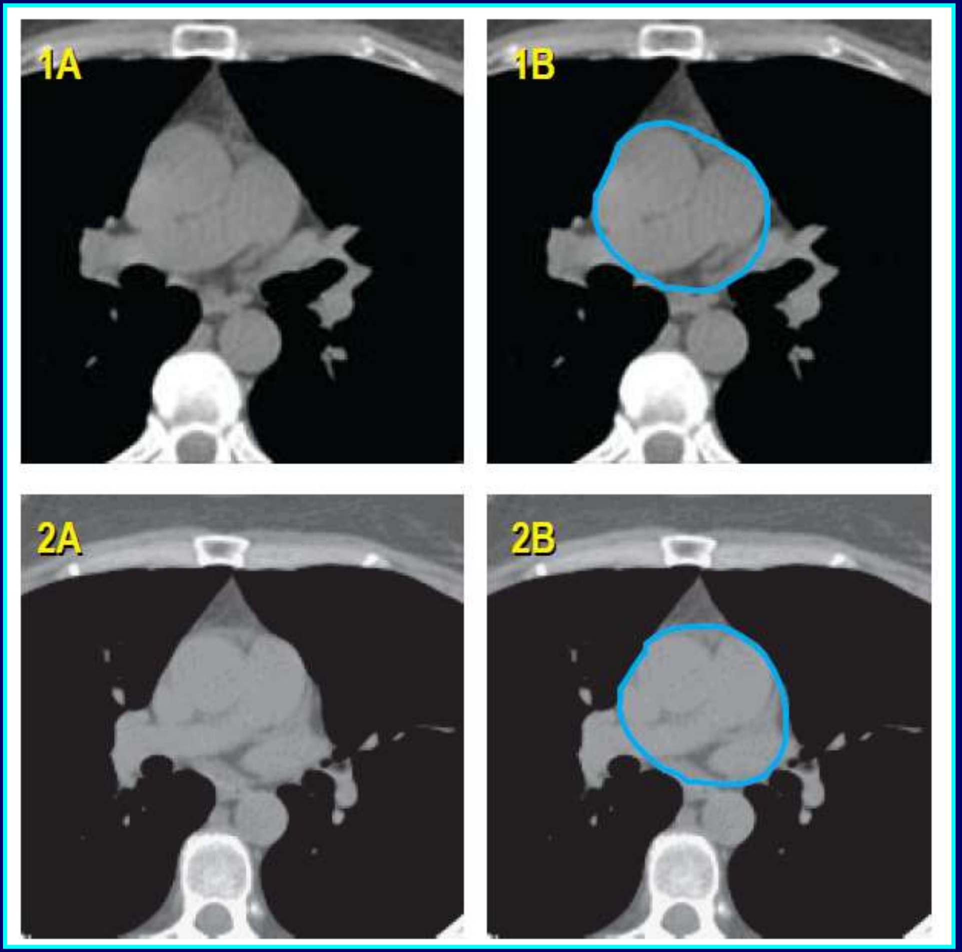
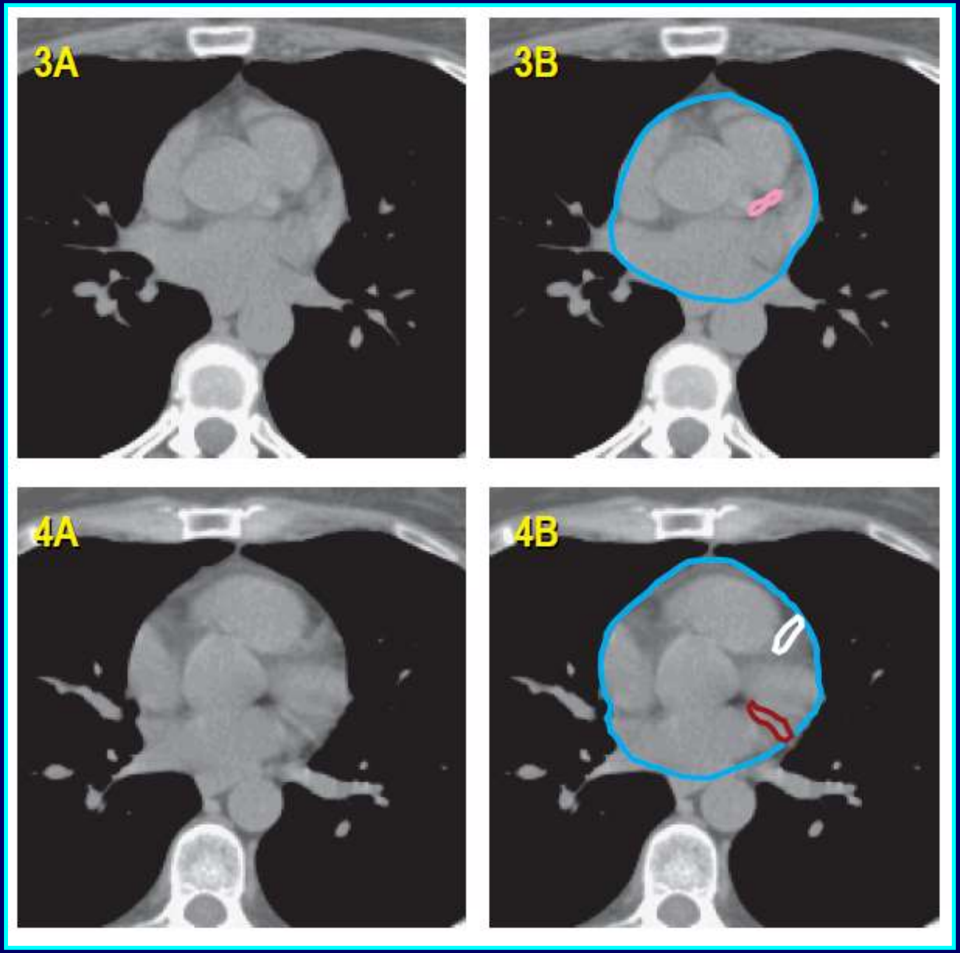
Heart begins just inferior to L pulmonary artery



Non-contrast CT

Feng, et al. IJROBP, 2011

Cardiac atlas



Non-contrast CT

Feng, et al. IJROBP, 2011

Cardiac atlas

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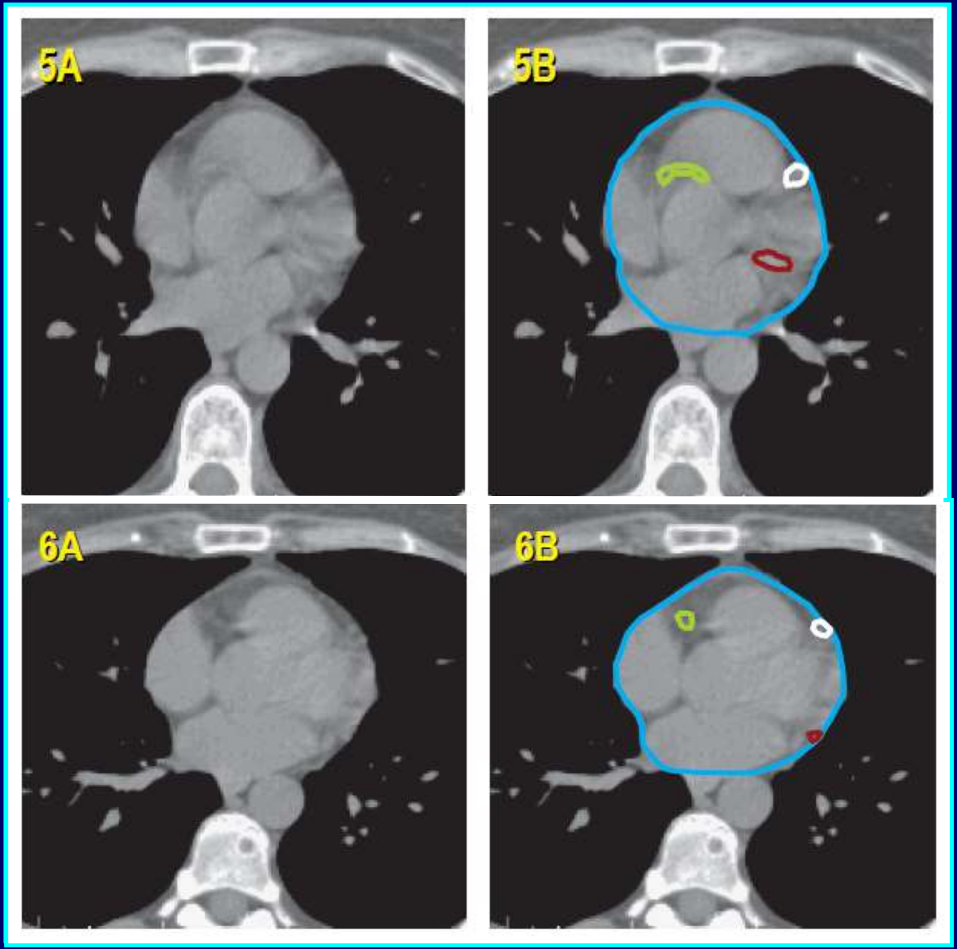
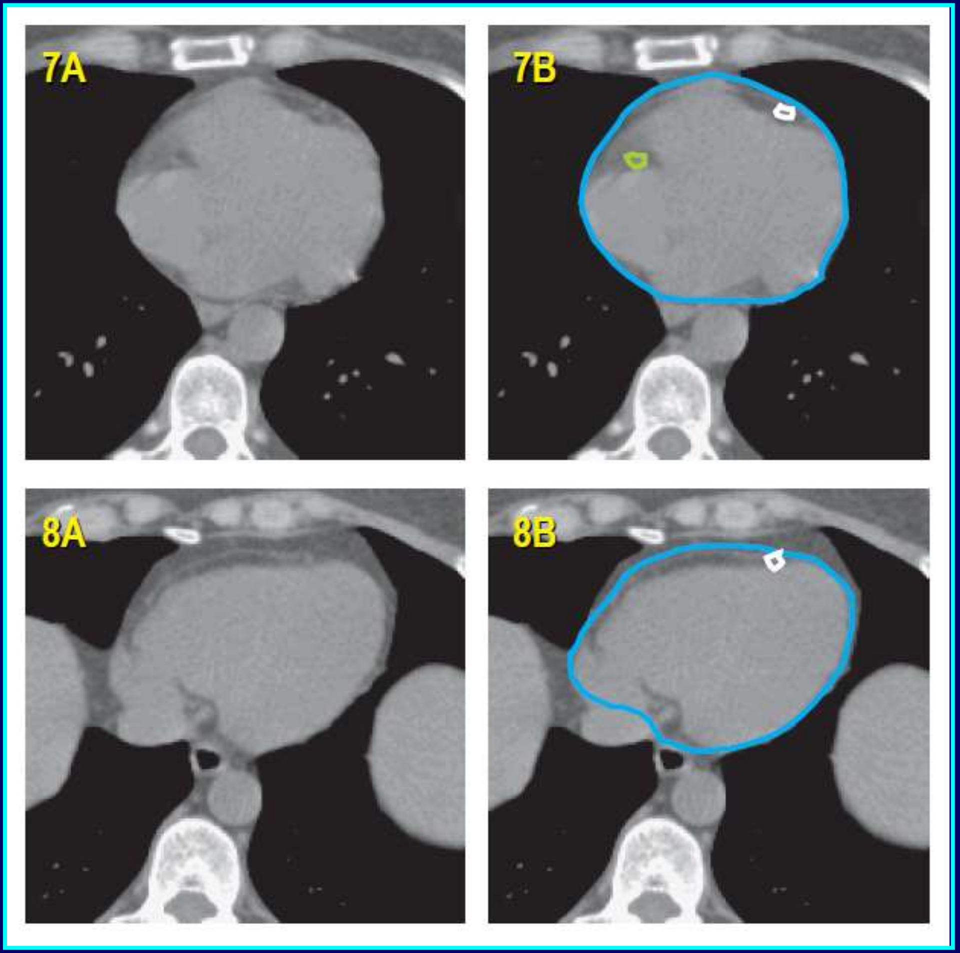


Non-contrast CT

Feng, et al. IJROBP, 2011

Cardiac atlas



Non-contrast CT

KEY

- Heart
- Right atrium
- Left atrium
- Right ventricle
- Left ventricle
- Pulmonary artery
- Superior vena cava
- Descending aorta
- Ascending aorta
- Aortic valve
- Pulmonic valve
- Mitral valve
- Tricuspid valve
- Left main coronary artery
- Left anterior descending artery
- Left circumflex
- Right coronary artery
- AV node

Feng, et al. IJROBP, 2011

Cardiac atlas

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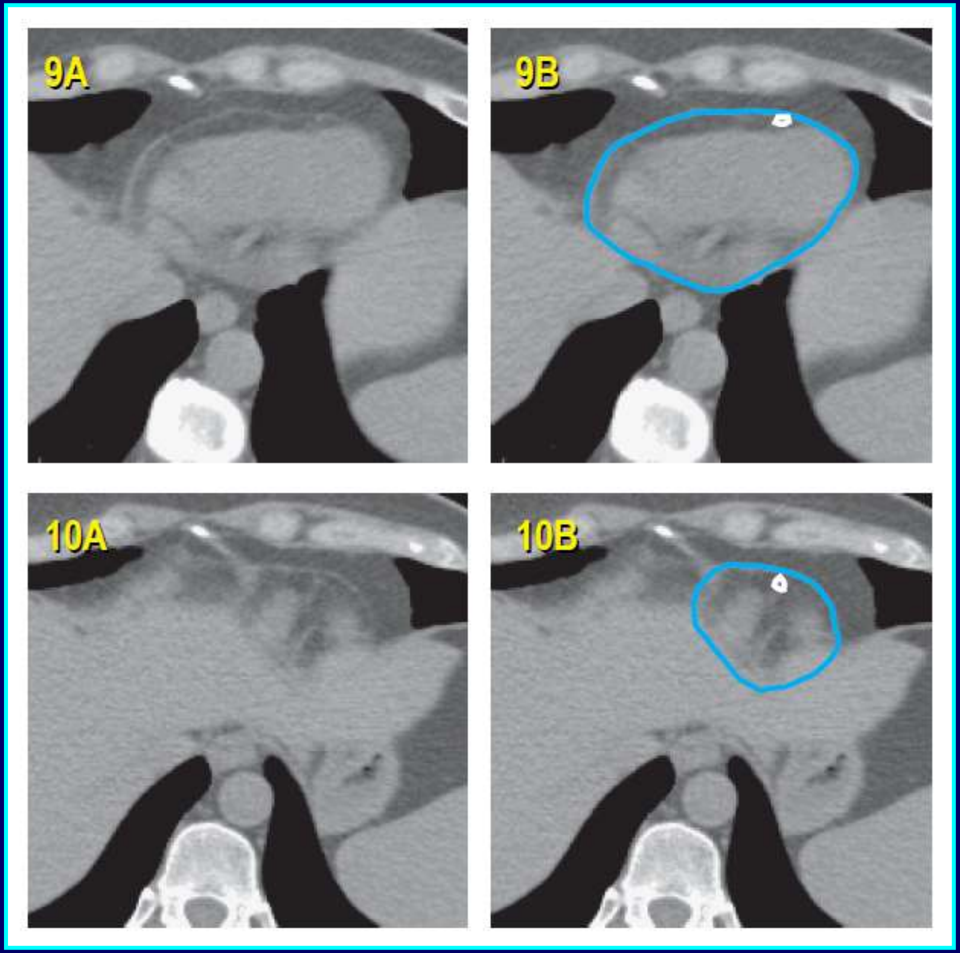

Non-contrast CT

Feng, et al. IJROBP, 2011

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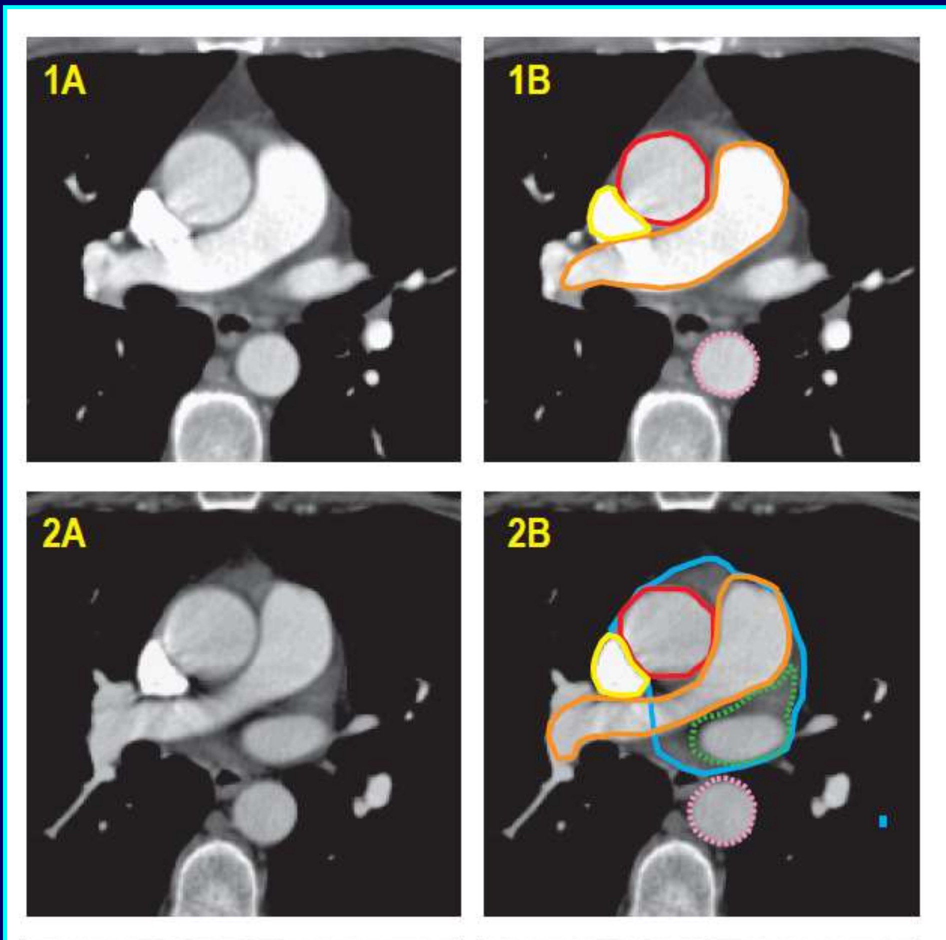
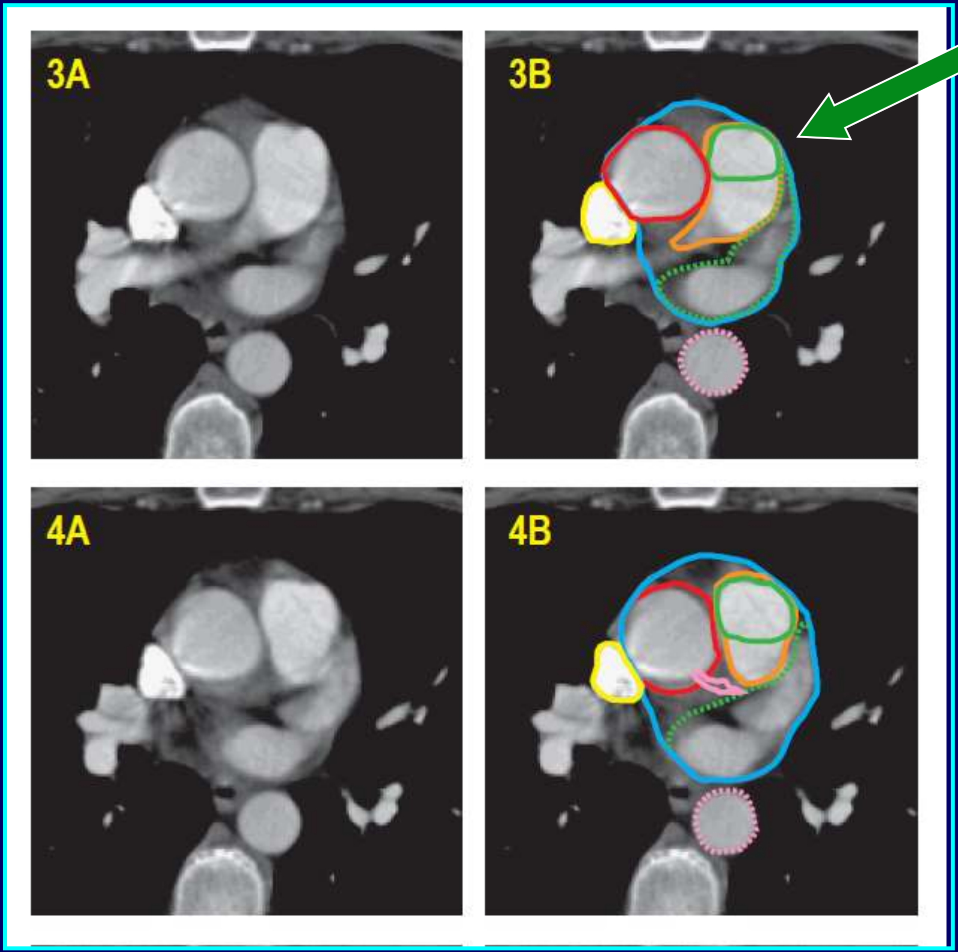
Cardiac atlas



Contrast CT

Feng, et al. IJROBP, 2011

Cardiac atlas

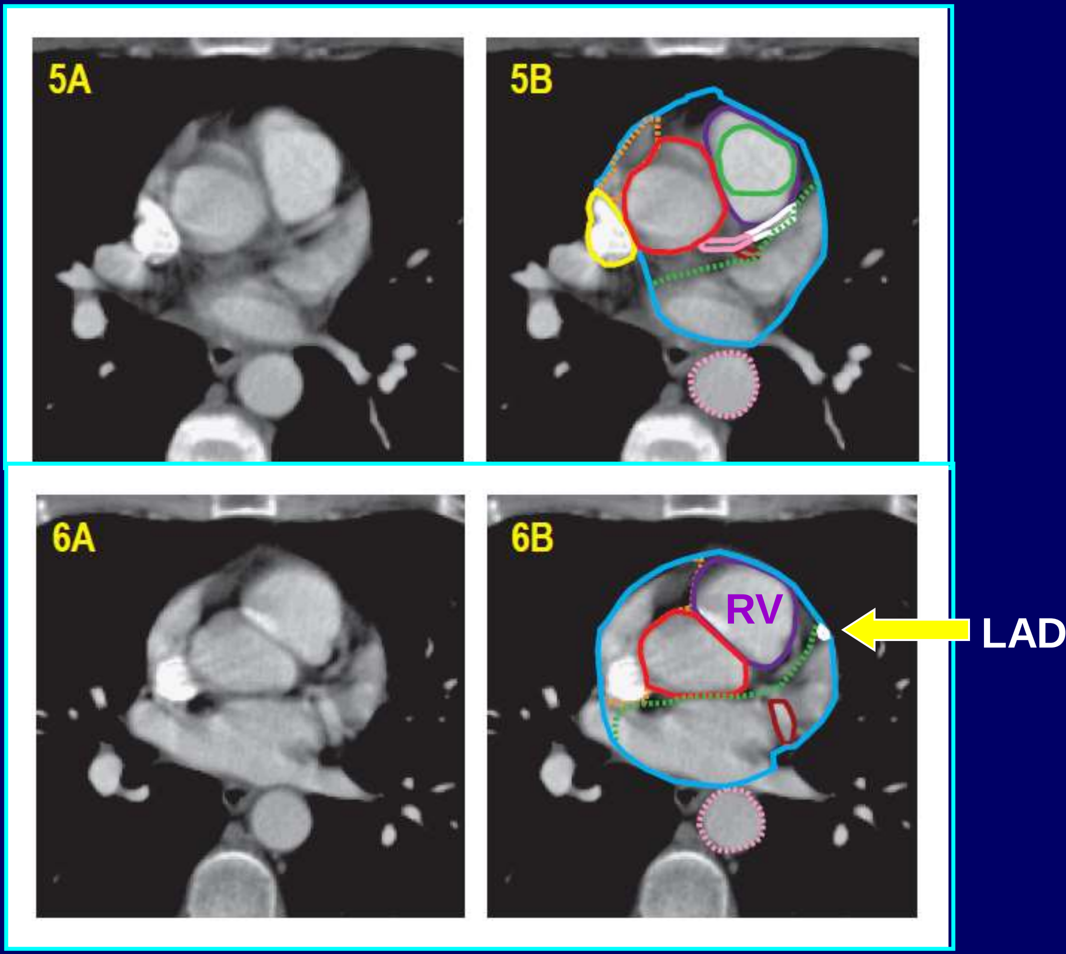


Pulmonic valve

Contrast CT

Feng, et al. IJROBP, 2011

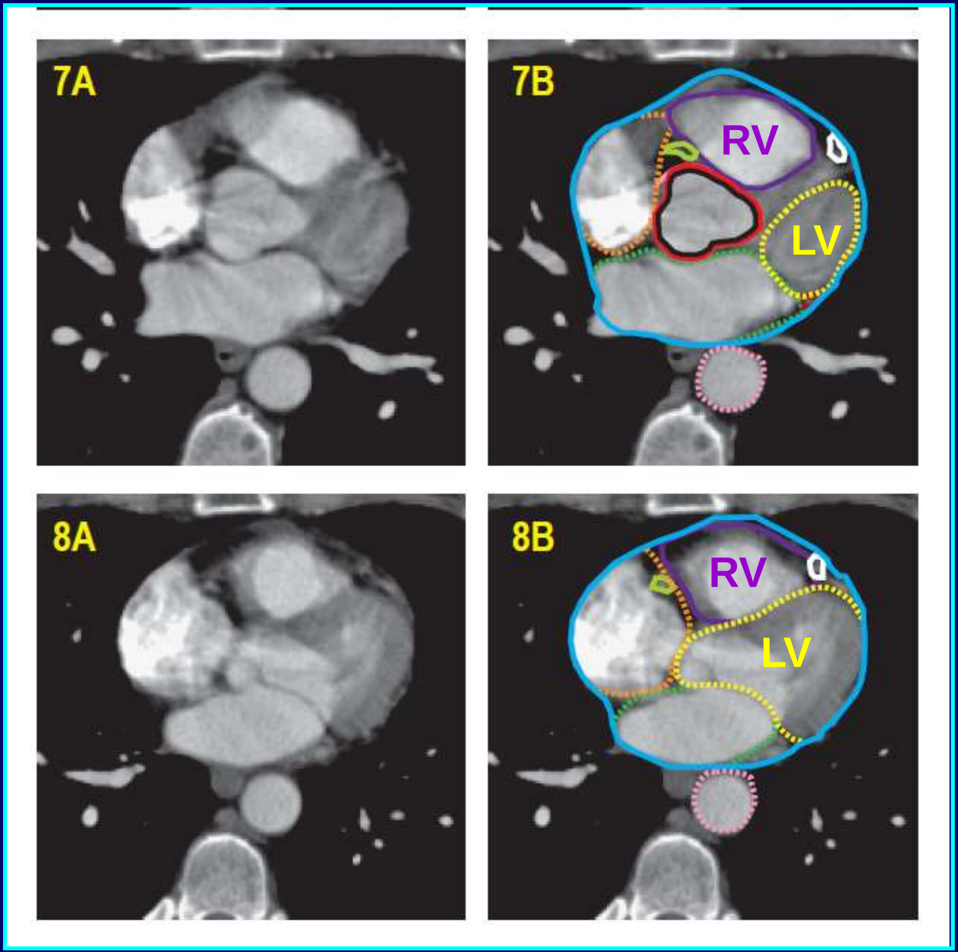
Cardiac atlas



Contrast CT

Feng, et al. IJROBP, 2011

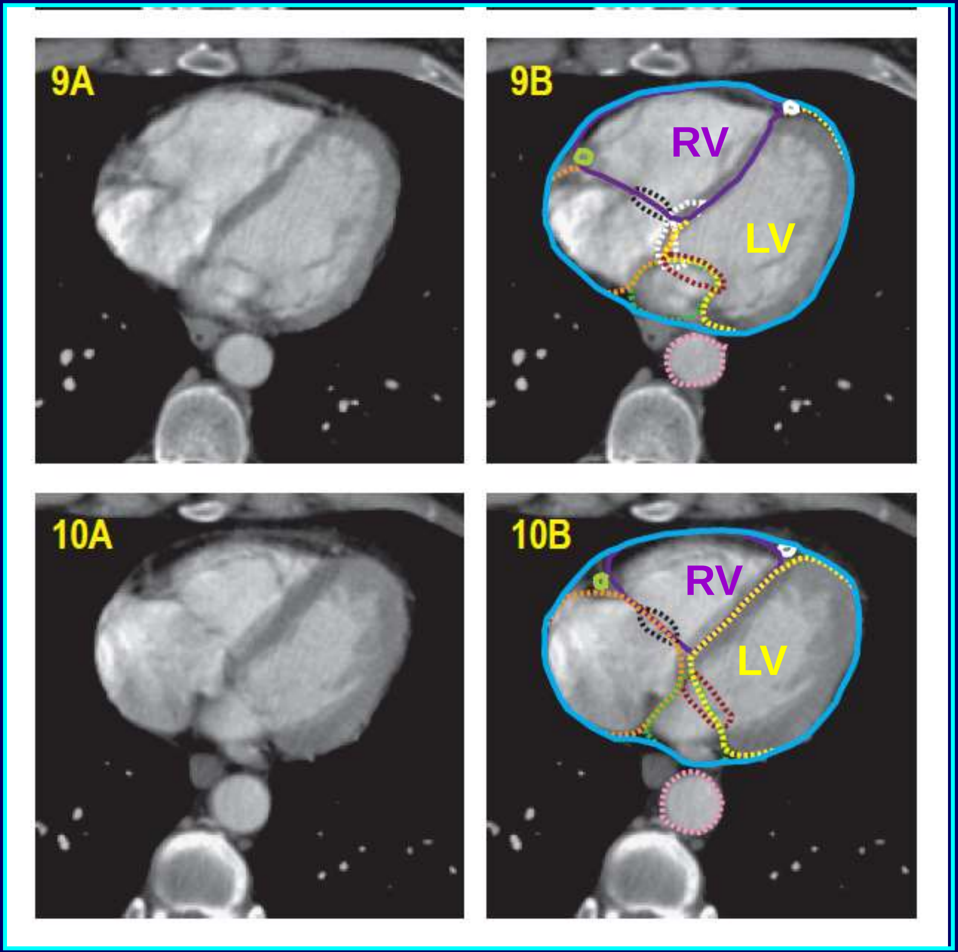
Cardiac atlas



Contrast CT

Feng, et al. IJROBP, 2011

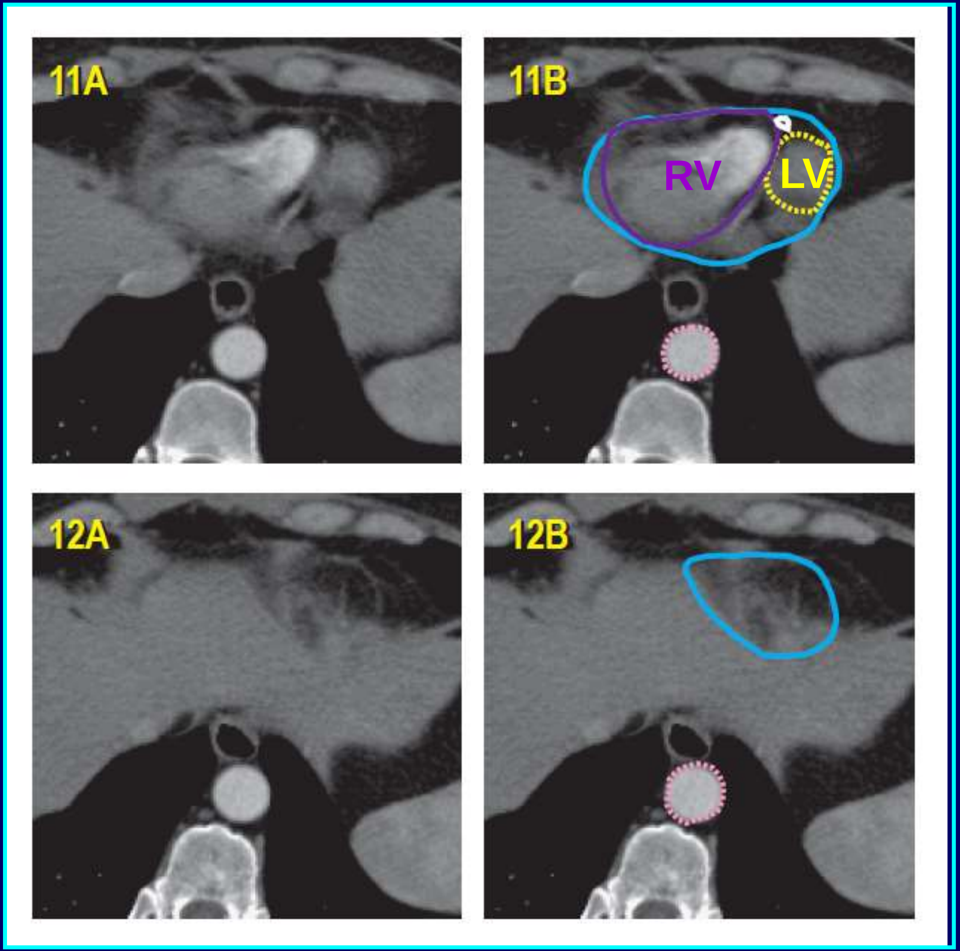
Cardiac atlas



Contrast CT

Feng, et al. IJROBP, 2011

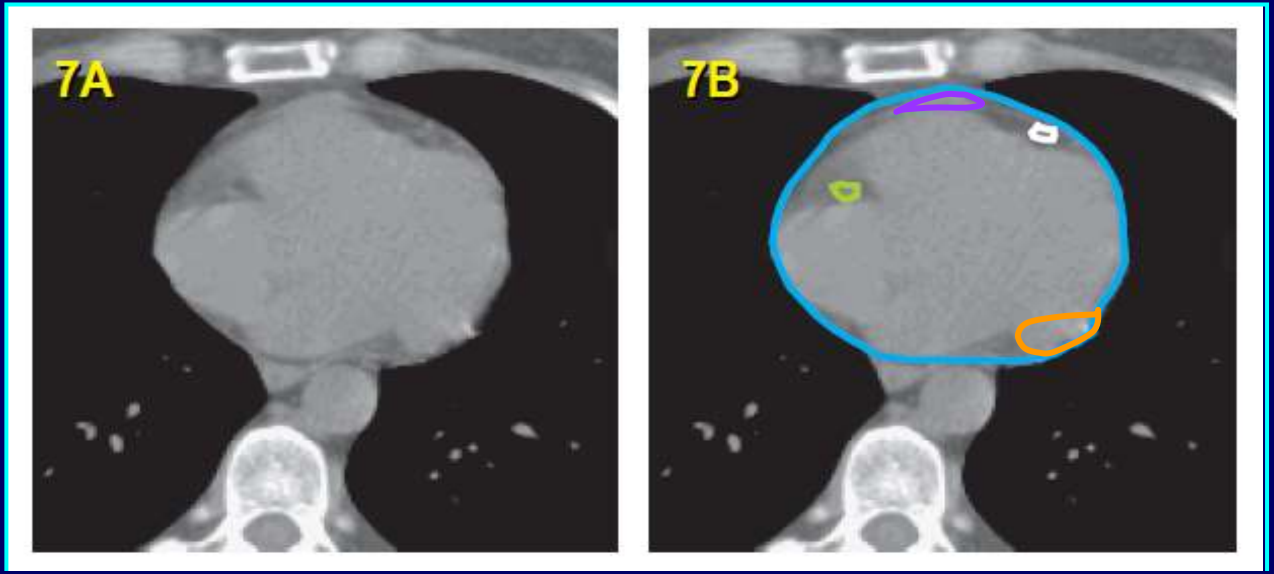
Cardiac atlas



Contrast CT

Feng, et al. IJROBP, 2011

Quiz

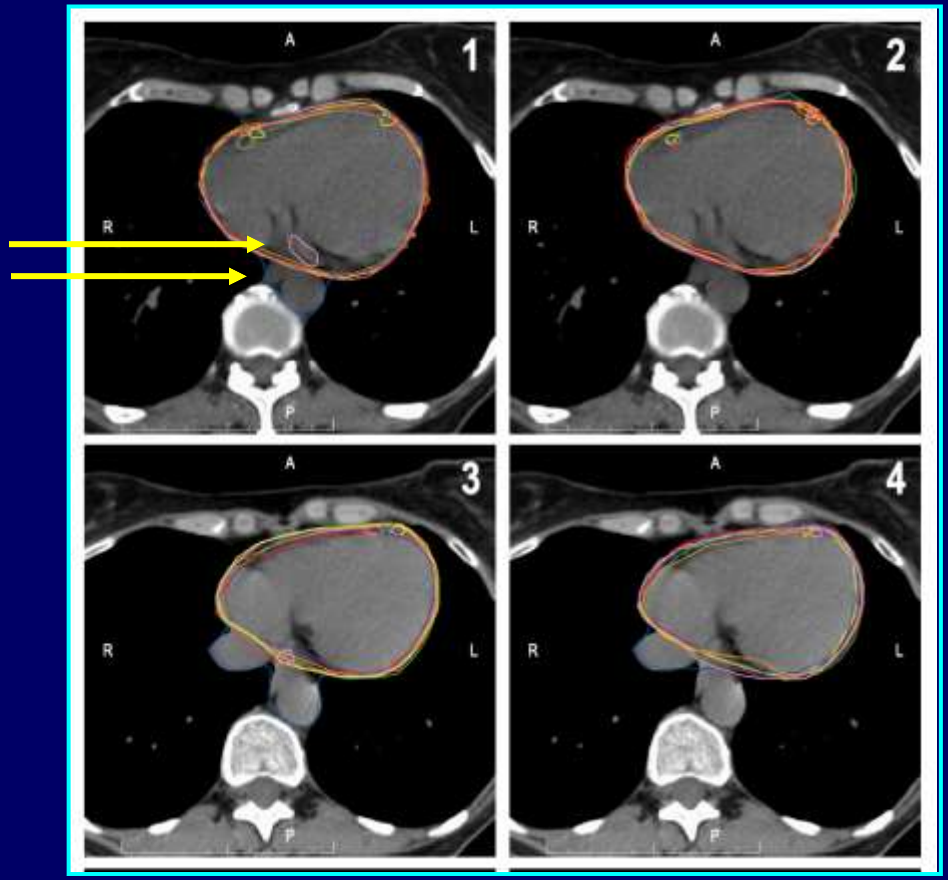


Which of these structures is the LAD?

A
B
C
D

Cardiac atlas

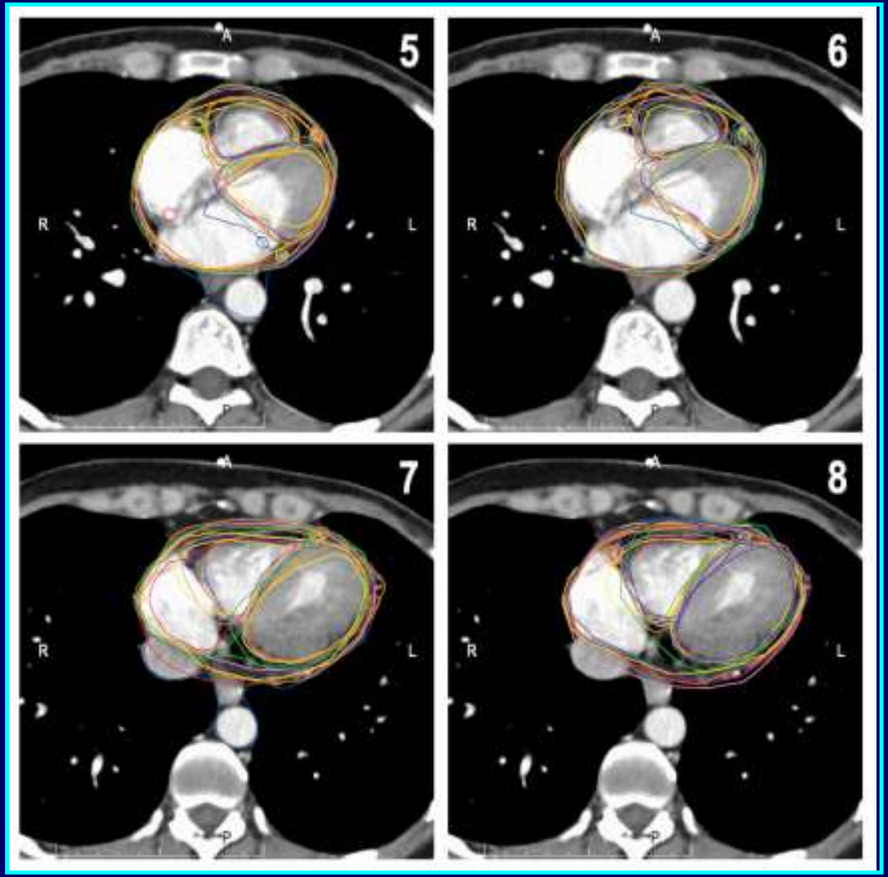
Multi-observer pre-test and post-test study



Pre-test **Post-test**

Feng, et al. IJROBP, 2011

Cardiac atlas



Pre-test **Post-test**

Feng, et al. IJROBP, 2011

Percent overlap of observer and gold standard contours

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Structure	Pre-atlas (mean ±SD)	Post-atlas (mean ±SD)	p-value
Heart	79 ± 13	91 ± 4	<0.001
L main	10 ± 22	22 ± 20	<0.001
LAD	35 ± 21	62 ± 16	<0.001
R coronary	11 ± 14	24 ± 18	0.002
Left ventricle	87 ± 11	92 ± 6	0.06
Right ventricle	65 ± 10	74 ± 8	0.003

Feng, et al. IJROBP, 2011

Concordance index

Structure	Pre-atlas (mean ±SD)	Post-atlas (mean ±SD)	p-value
Heart	0.76 ± 0.11	0.89 ± 0.03	<0.001
L main	0.05 ± 0.12	0.18 ± 0.16	<0.001
LAD	0.19 ± 0.11	0.34 ± 0.07	<0.001
R coronary	0.08 ± 0.10	0.18 ± 0.08	<0.001
Left ventricle	0.75 ± 0.06	0.79 ± 0.05	0.04
Right ventricle	0.55 ± 0.08	0.65 ± 0.08	<0.001

Feng, et al. IJROBP, 2011

Mean absolute value dose difference (Gy)

Structure	Pre-atlas (mean ±SD)	Post-atlas (mean ±SD)	p-value
Heart	0.88 ± 0.15	0.14 ± 0.14	<0.001
L main	1.68 ± 1.53	0.88 ± 1.56	0.005
LAD	3.90 ± 2.80	2.56 ± 3.31	<0.001
R coronary	1.15 ± 1.07	0.61 ± 0.39	0.001
Left ventricle	0.25 ± 0.20	0.15 ± 0.14	0.13
Right ventricle	1.06 ± 0.73	0.46 ± 0.37	0.008

Feng, et al. IJROBP, 2011

Cardiac summary

- Breast RT may increase the risk of cardiac death many years after treatment
- Unlike other structures such as the parotid gland, lung, and rectum, the heart's dose-volume-toxicity profile is not well-understood
- With a validated, detailed cardiac atlas, we can begin to collect information to elucidate the effect of RT on heart structures

OARs highlighted today

- **Heart**
- **Brachial plexus**
- **Esophagus**

OARs highlighted today

- **Heart**
- **Brachial plexus**
- **Esophagus**

Importance of the brachial plexus

- **Brachial plexus damage could lead to arm weakness or pain**
- **Commonly used dose limits range from 50 to 60 Gy**
- **Hot spots in treatment plans can be located in the brachial plexus if careful planning is not used**

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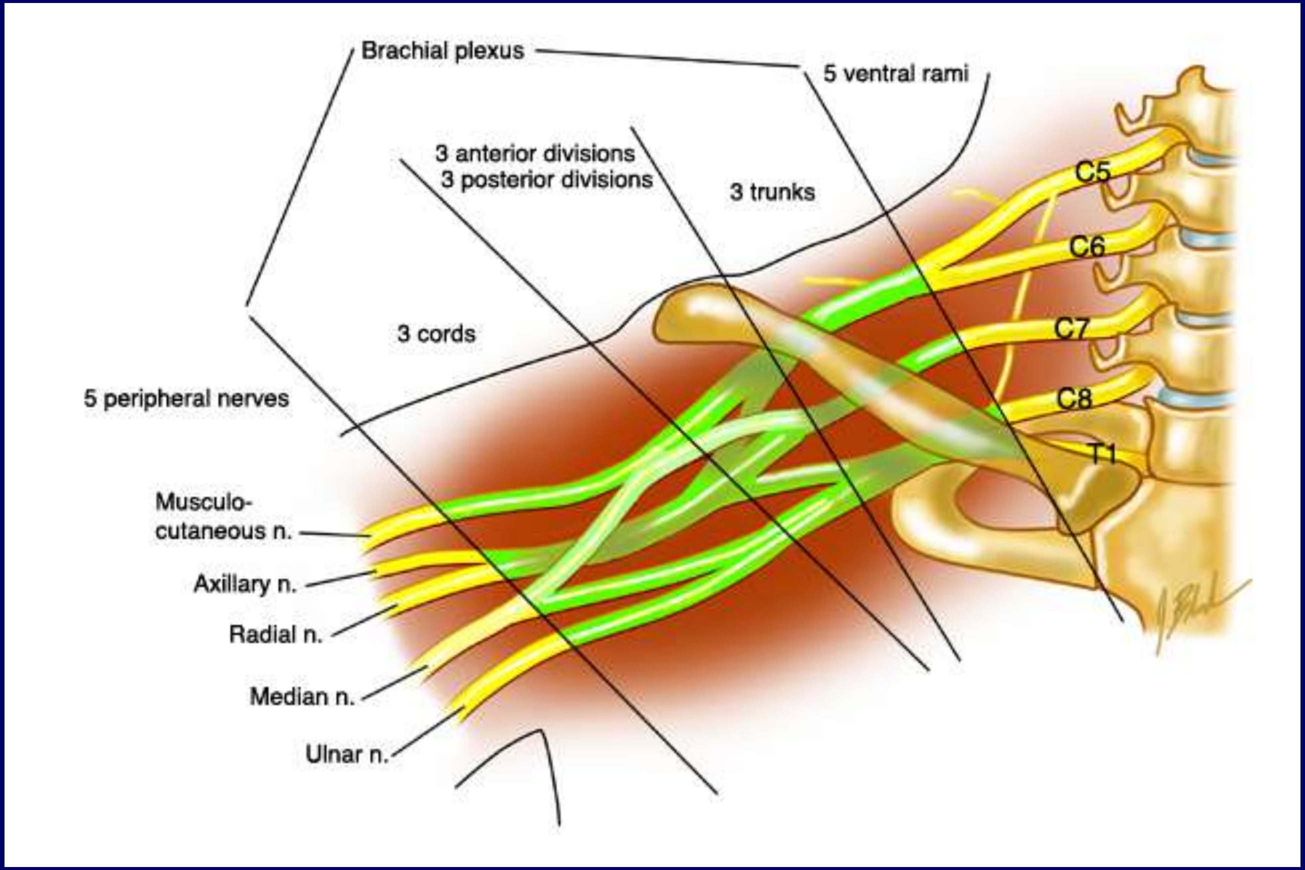
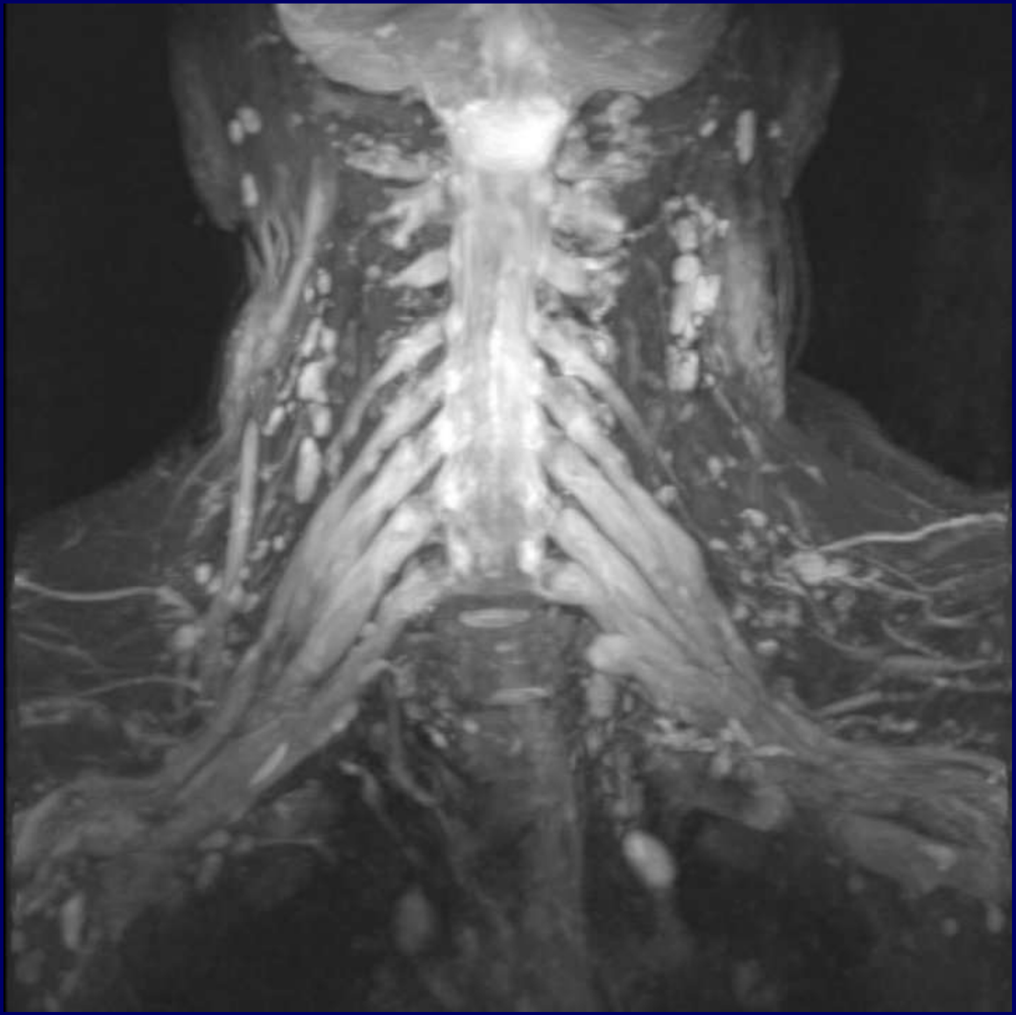
Brachial plexus anatomy



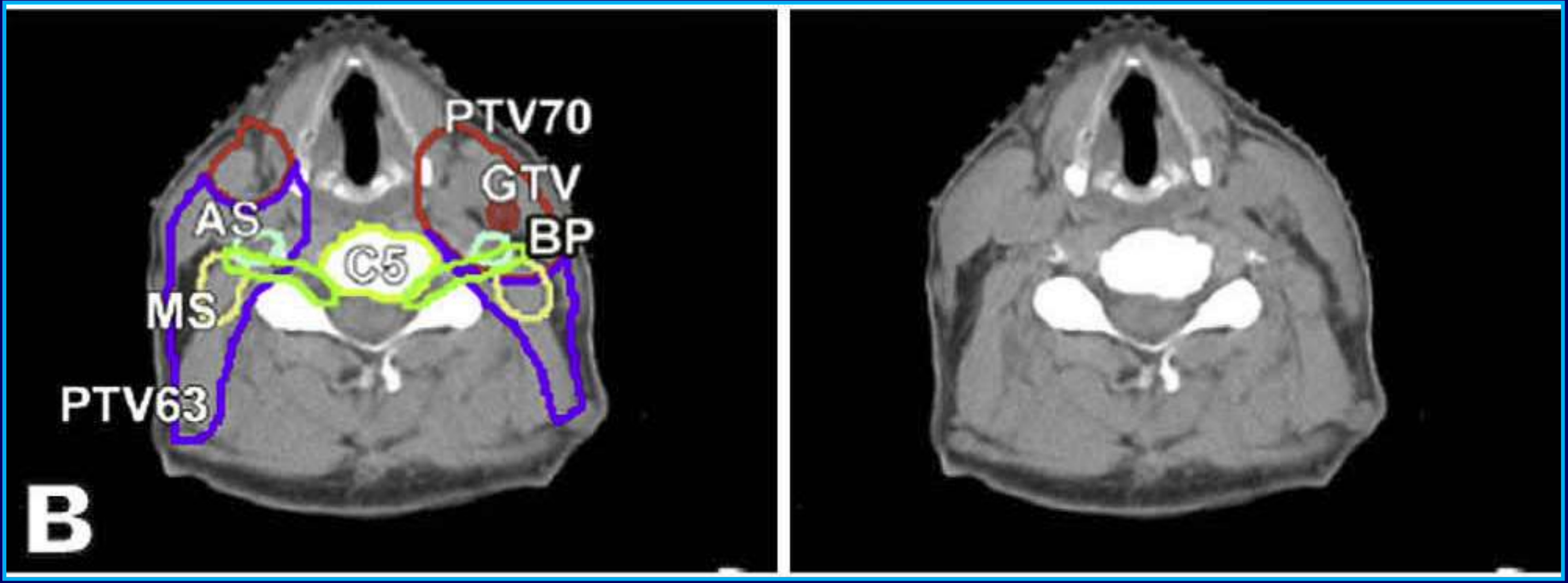
Brachial plexus on MRI



www.healthcare.siemens.com

Brachial plexus on CT

AS = anterior scalene MS = middle scalene BP = brachial plexus



Hall, et al. IJROBP 2008 and at http://www.rtog.org

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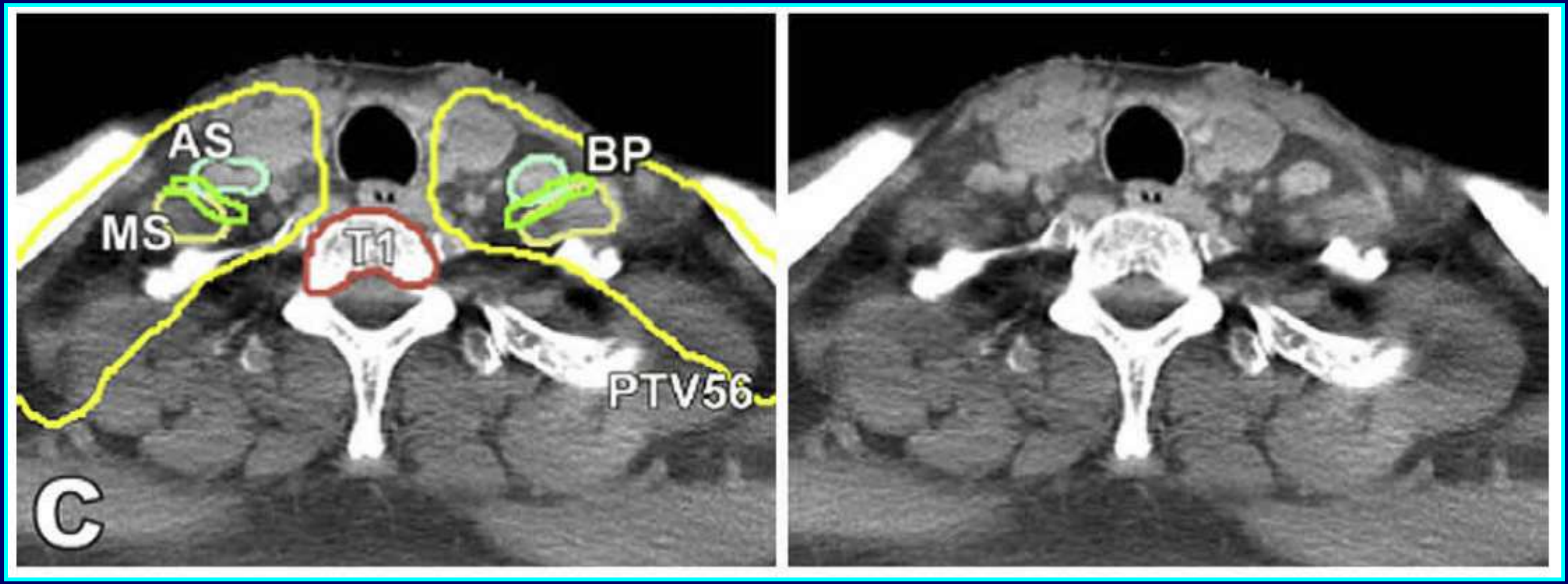

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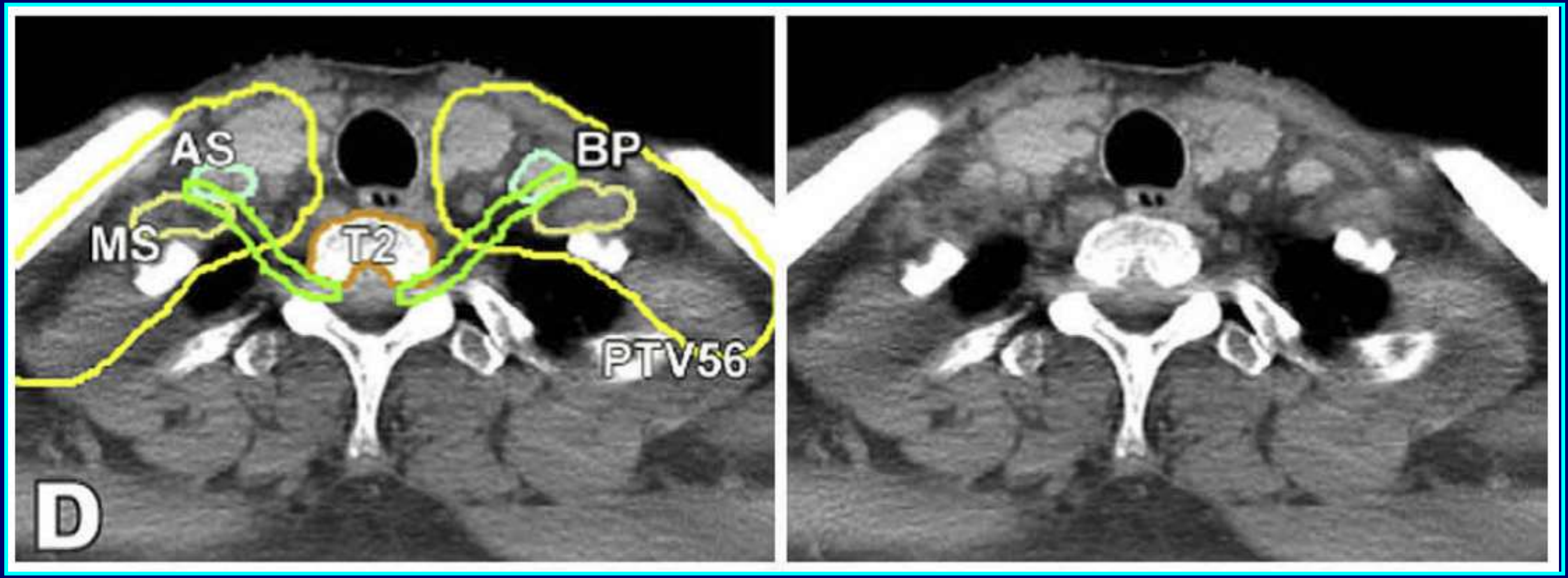

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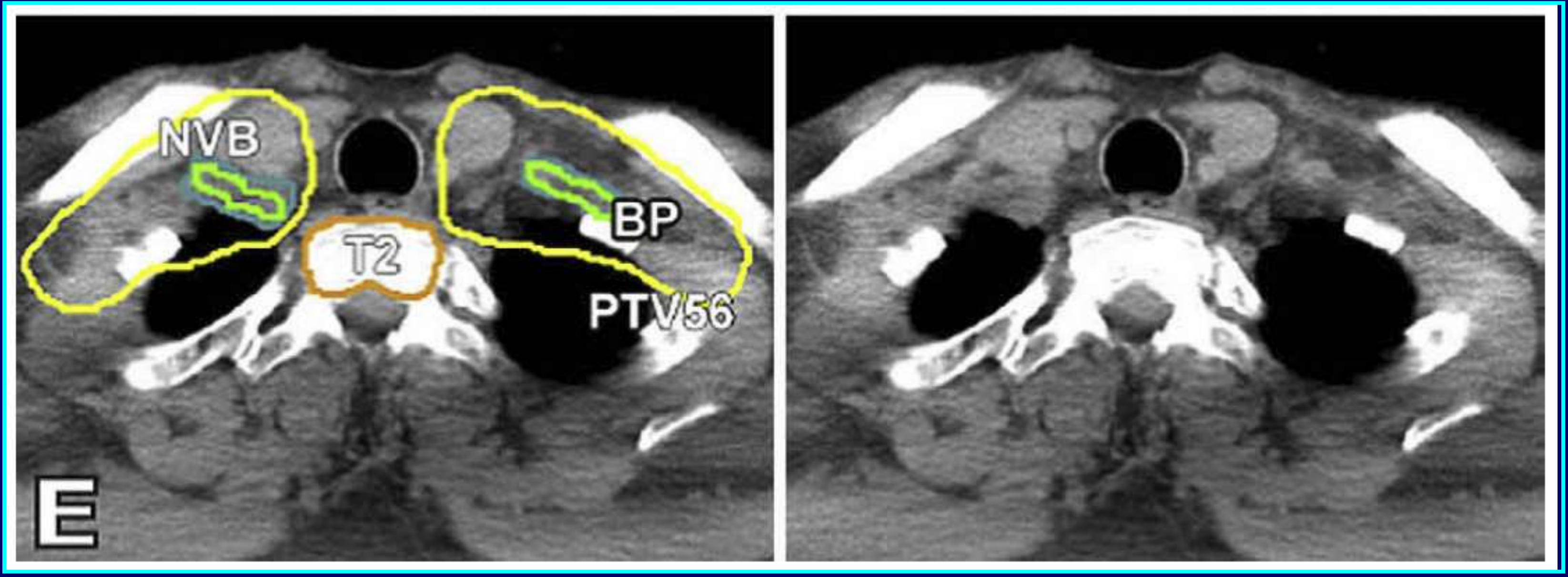

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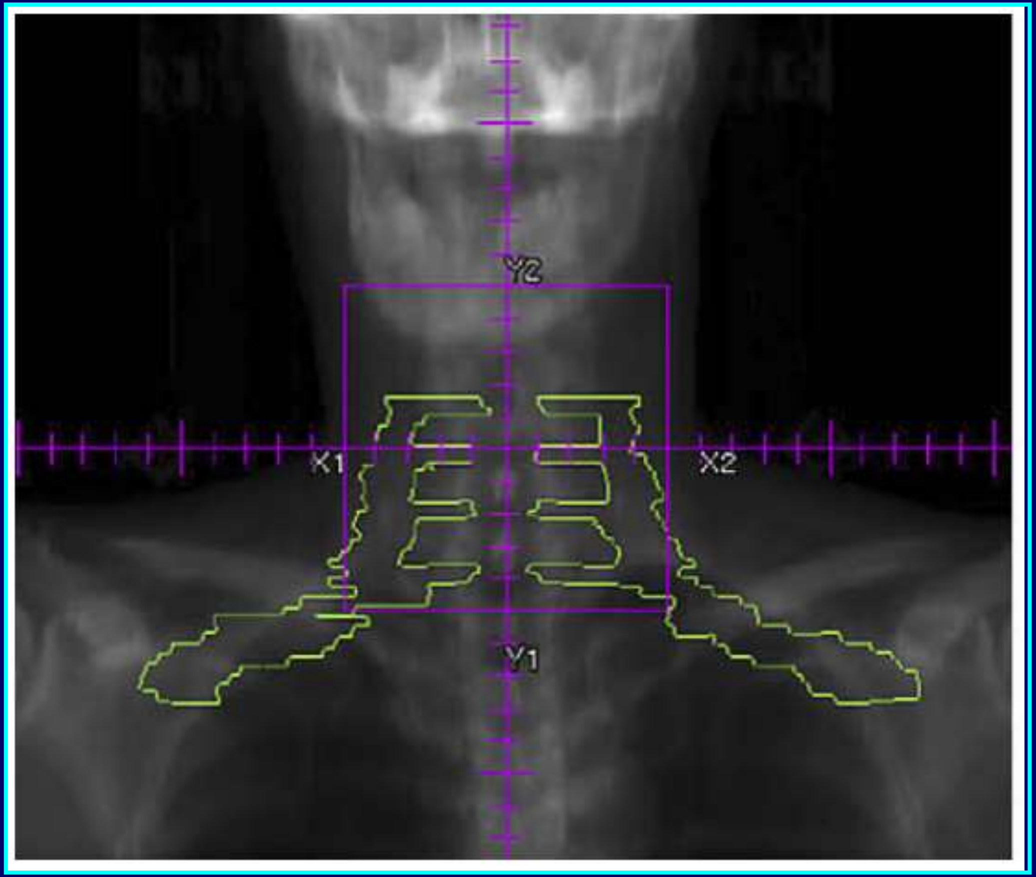
Brachial plexus

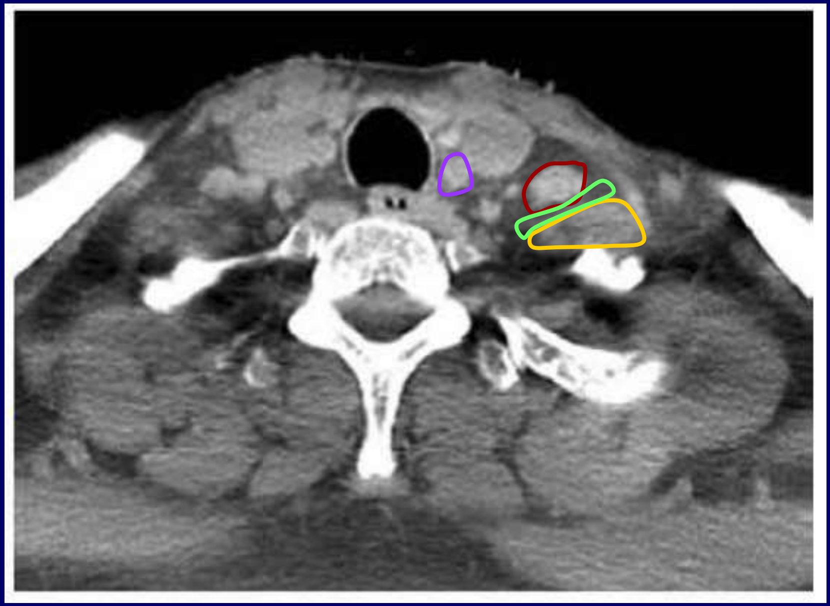


Hall, et al. IJROBP 2008 and at http://www.rtog.org

Quiz

Which of these structures Is the brachial plexus?

A
B
C
D



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Brachial plexopathy from RT

International Journal of
Radiation Oncology
biology • physics

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Clinical Investigation: Thoracic Cancer

Brachial Plexopathy in Apical Non-Small Cell Lung Cancer Treated With Definitive Radiation: Dosimetric Analysis and Clinical Implications

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Eblan, et al, IJROBP 2012

Brachial plexopathy from RT

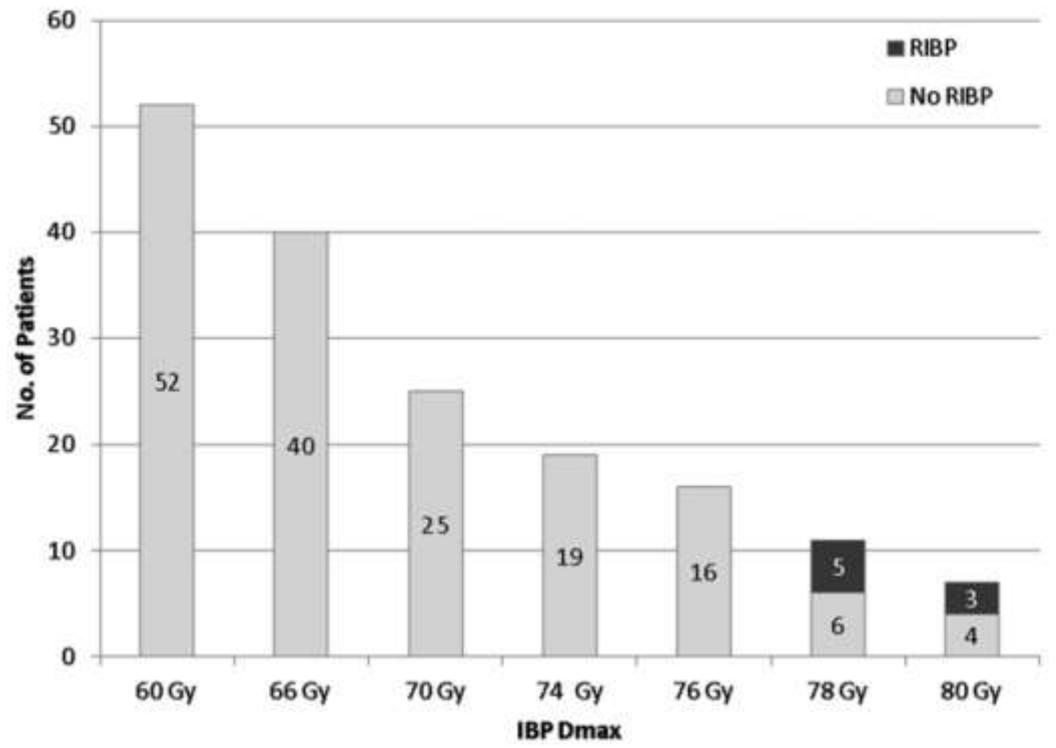


Fig. 2. Cumulative rate of RIBP as a function of maximal dose delivered to the IBP.

Eblan, et al, IJROBP 2012

OARs highlighted today

- **Heart**
- **Brachial plexus**
- **Esophagus**

University of Michigan Medical School

OARs highlighted today

- **Heart**
- **Brachial plexus**
- **Esophagus**

Esophagitis

- Can be a significant side effect of RT, especially if combined with chemotherapy for lung cancer
- Pain affects quality of life and causes patients to lose weight, which reduces the ability to tolerate treatment
- Multiple dose-volume limits have been proposed to minimize esophagitis

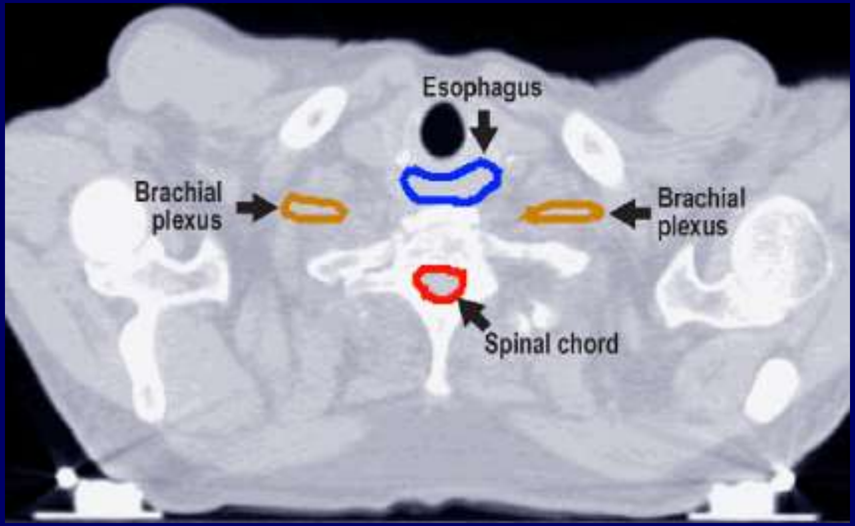
Esophageal contours

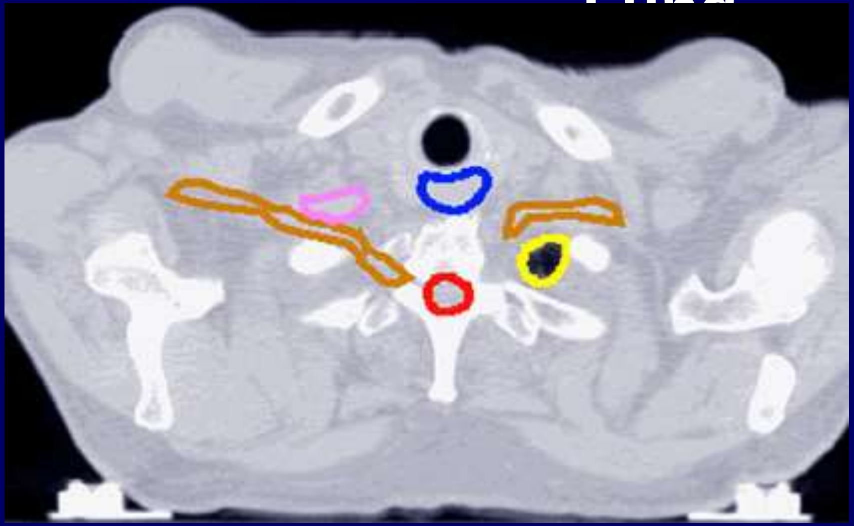
- **RTOG recommends contouring from the cricoid to the GE junction**
- **Esophageal diameter, shape, and position are variable**
- **Pay attention for accurate contours**

OAR Atlas for RTOG 1106

University of Michigan Medical School

The esophagus starts at the level of cricoid

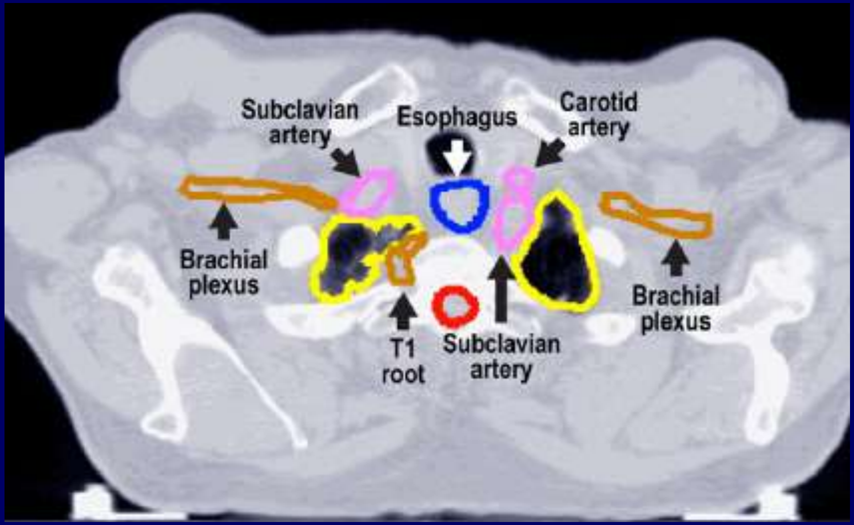


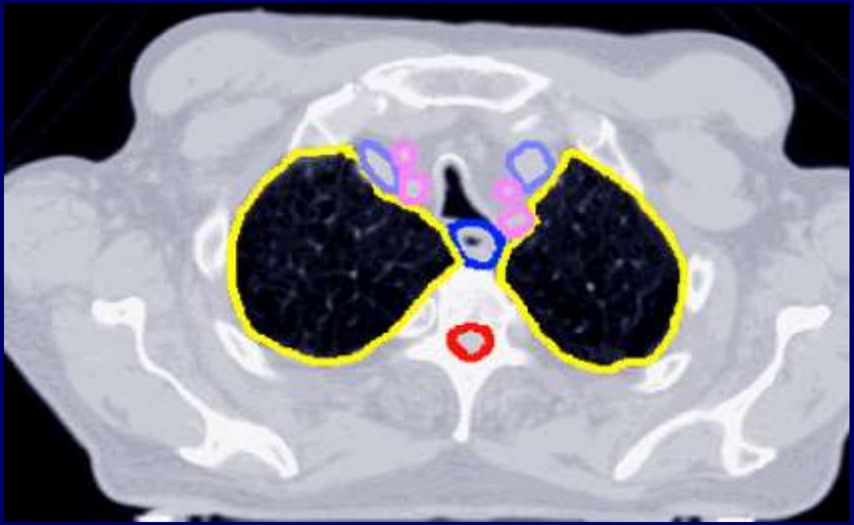


Kong, et al

Esophageal contours

Usually it quickly becomes round

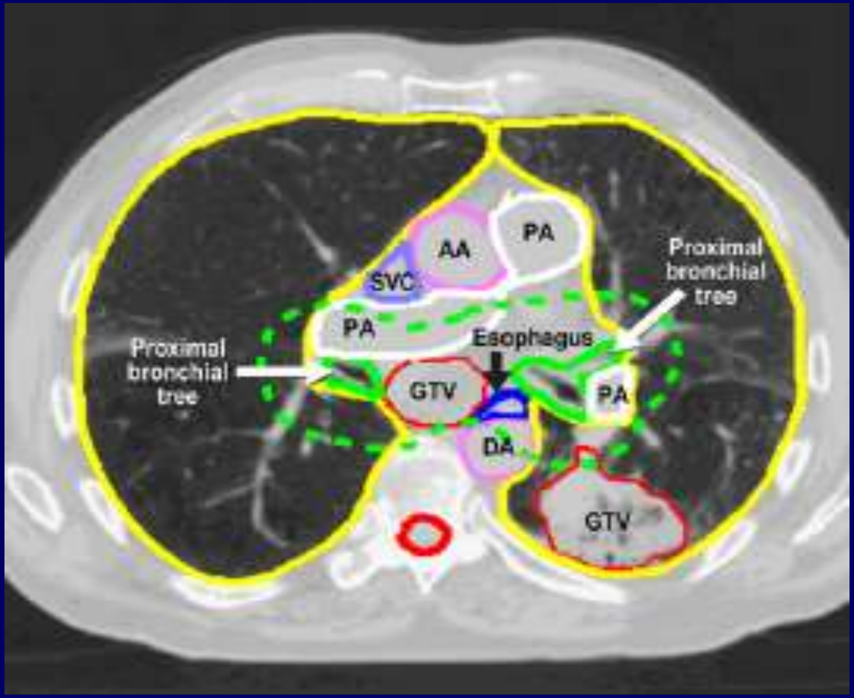


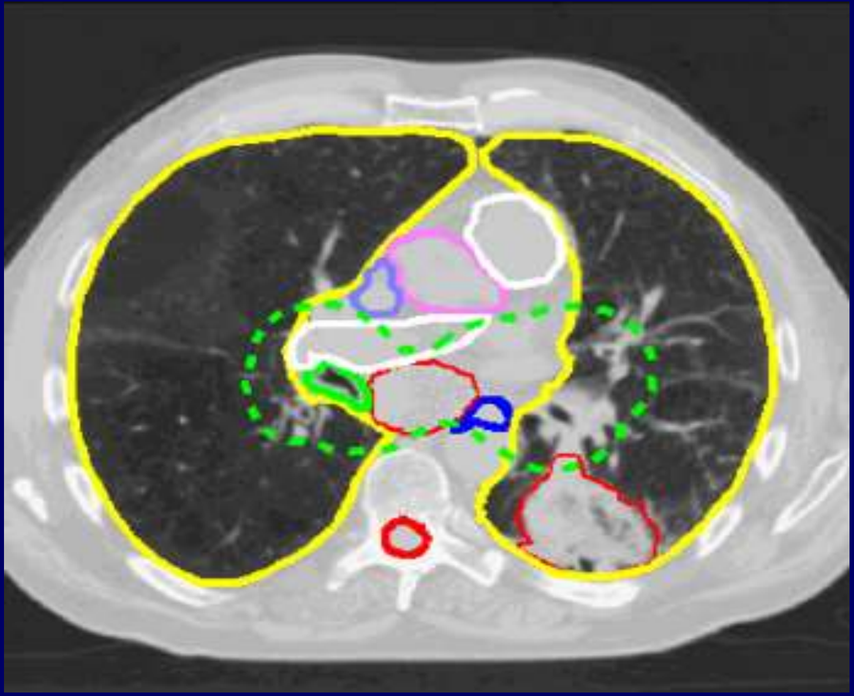


Kong, et al

Esophageal contours

Then it can take a turn to the side

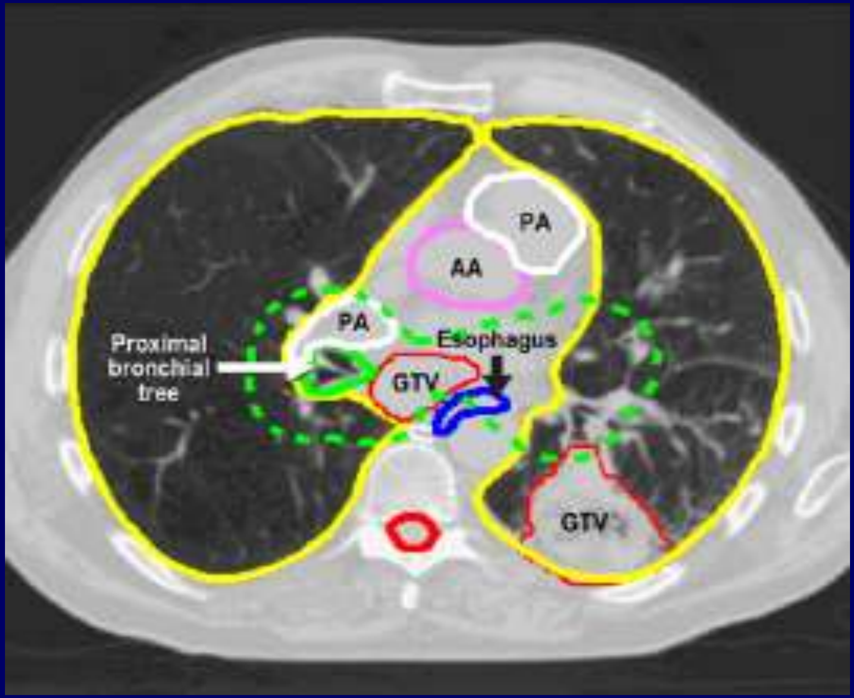


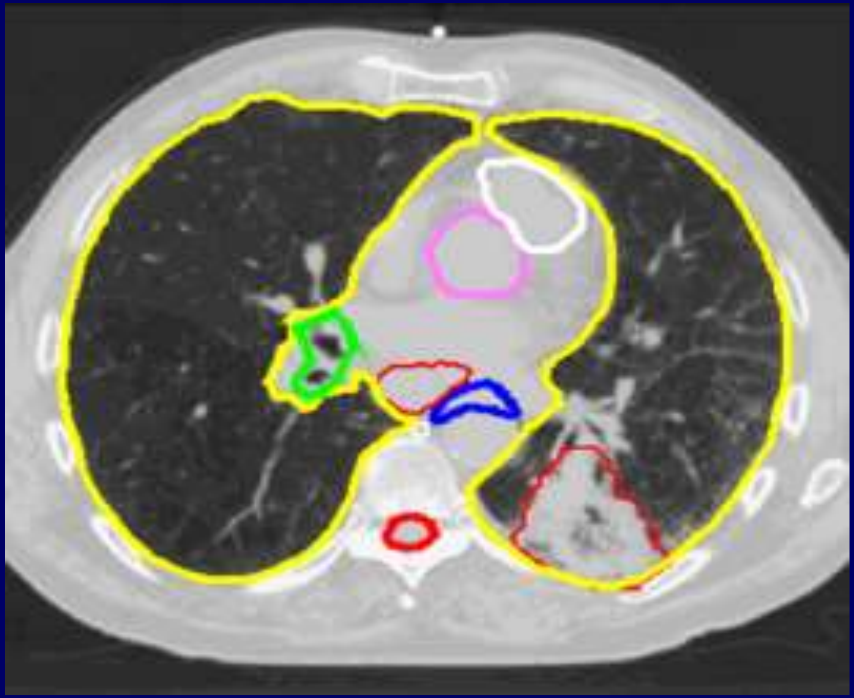


Kong, et al

Esophageal contours

…and flatten out more…

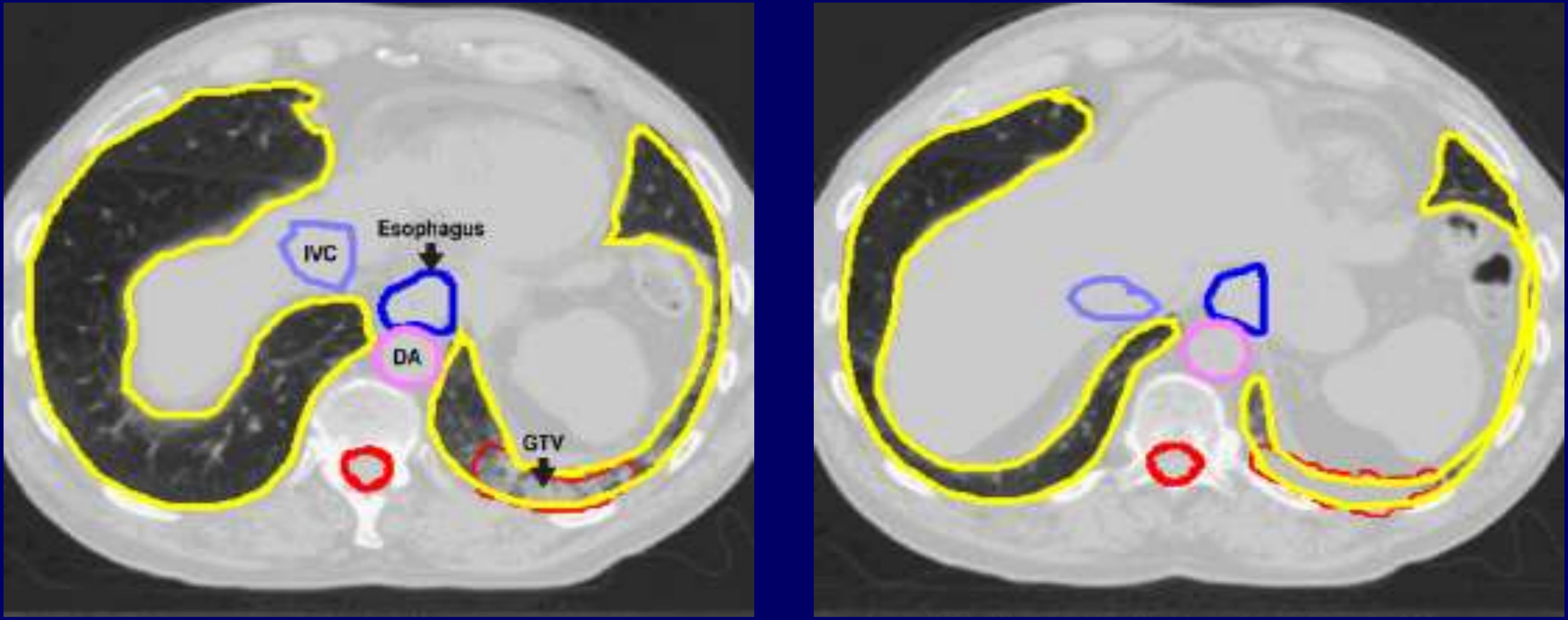




Kong, et al

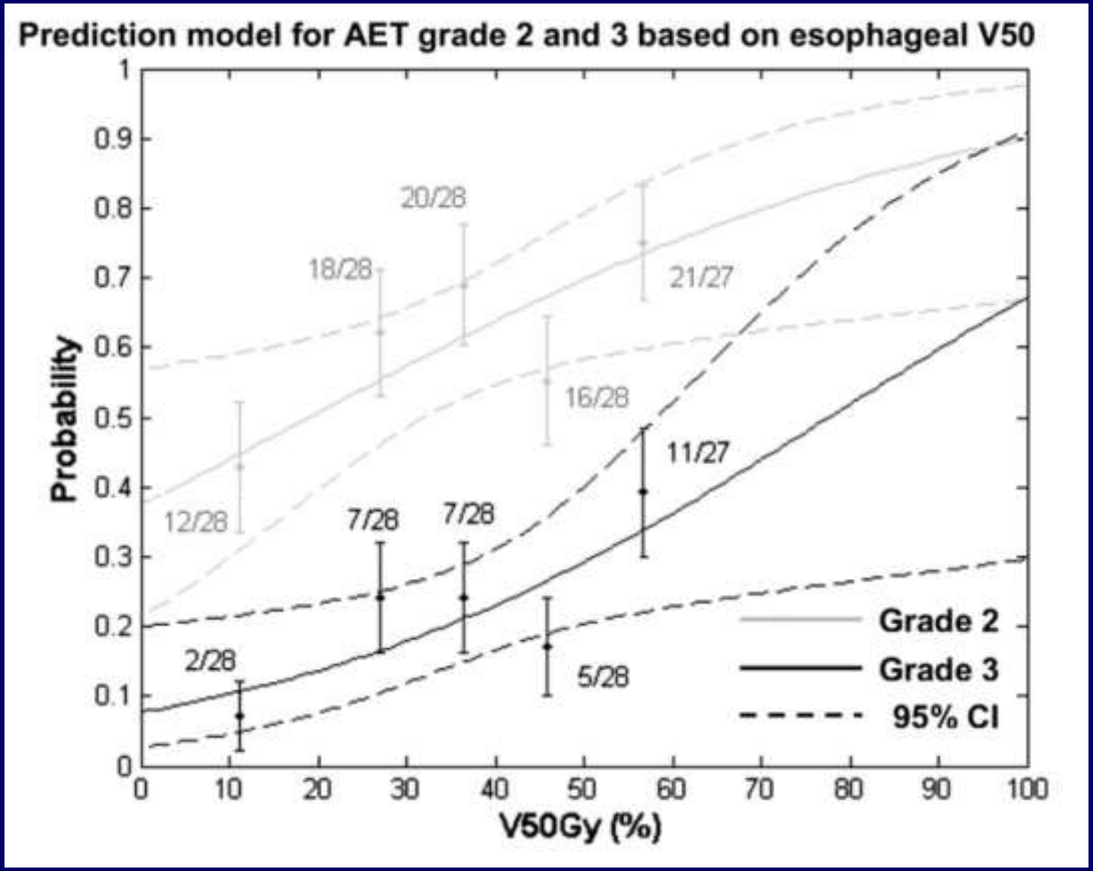
Esophageal contours

…before it rounds out again and joins the stomach.



Kong, et al

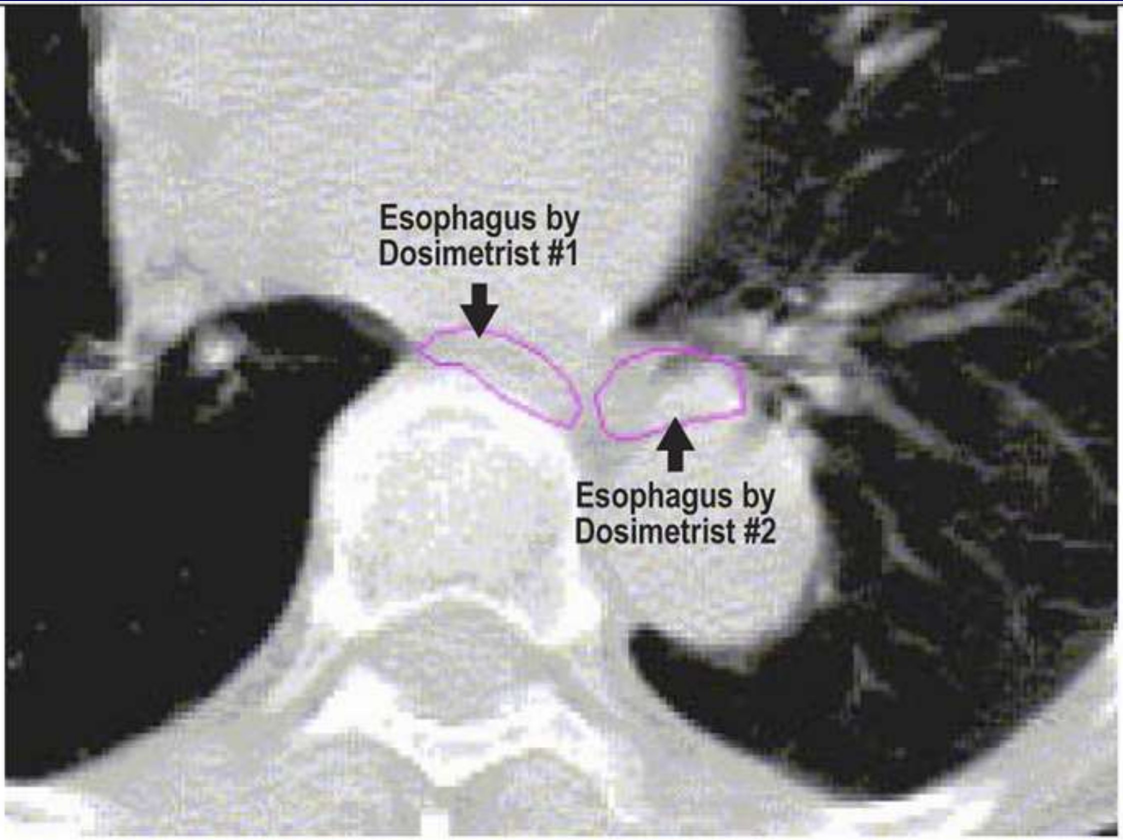
Esophagitis from RT



Kwint, et al, IJROBP 2012

Variability in esophageal contours

University of Michigan Medical School



A: Esophagus Contour Variants

Kong, et al, IJROBP 2011

Summary

- **Accurate OAR contouring is important for treatment planning**
- **Atlases have been created to improve consistency**
- **As centers create more uniform OAR contours, data can be compiled to build more realistic models to estimate and minimize toxicity risk**

Thanks for your attention