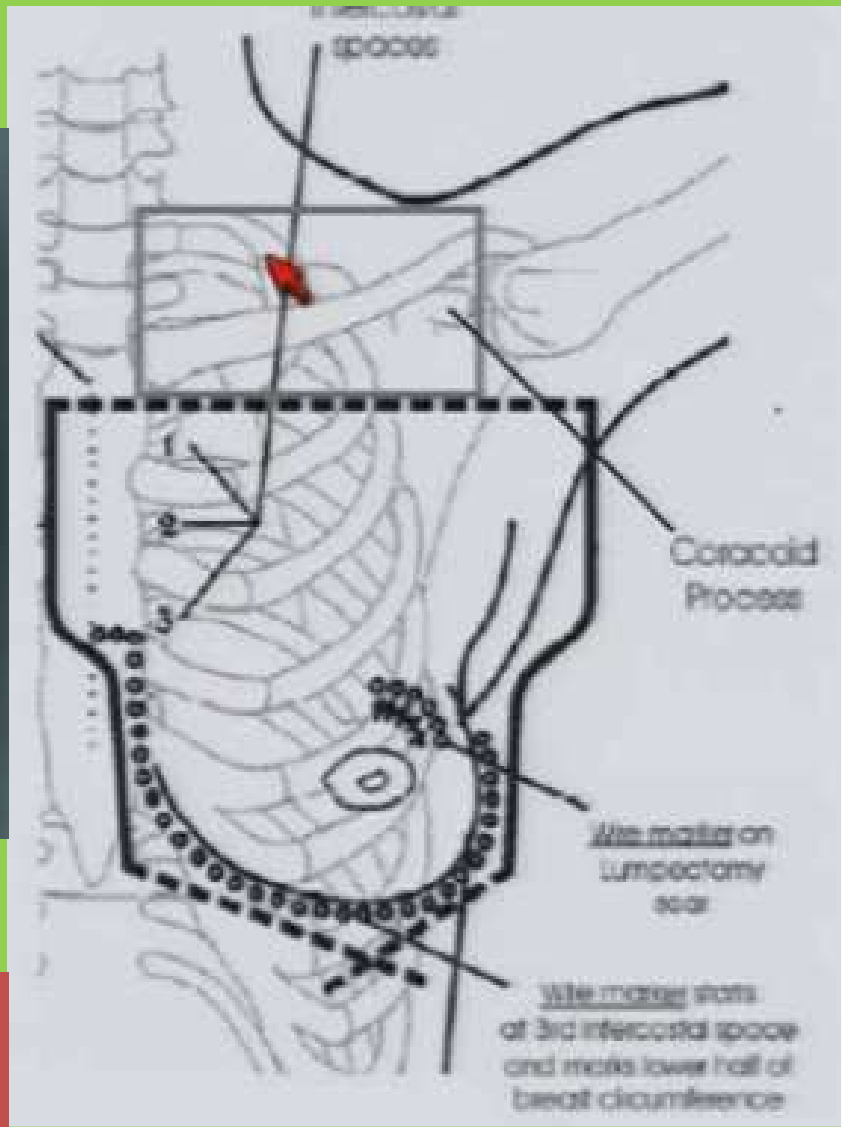
Post Mastectomy Radiotherapy (PMRT)

Evidence & Planning



Prof Manoj Gupta
IGMC, Shimla

ICRO Guwahati
6th November, 2016

Recurrence Risk

- **Positive Axillary Nodes**
  - ↑ with more LN involvement
  - 1-3 LN+: 5-15% at 10yrs
  - ≥4 LN+: 15-50%
  - Ratio of LN+ (>20%) = LRR >20%
- **Tumour Size**

  Increases with Size

Truong IJRBP. 68(1):59-65. 2007

Recurrence Risk

- **High Risk Features**
  - **Grade III Tumors**
  - **LVSI**
  - **TNBC**
  - **ER/PR Negative Tumours**

Where are the recurrences?

- >50% chest wall (mastectomy scar/skin)
- 20-40% supraclav or infraclavicular
- <5% post ALND (I/II)
- Internal mammary LN
  - 1/3 path involvement in high risk
  - Few clinical recurrences

Indication of PMRT

- **Definitive**
  - Tm size >5cm
  - 4 or >4 axillary nodes metastasis
  - Positive Surgical Margins
  - Pectoralis muscle involvement
- **Debatable**
  - 1to 3 axillary nodes metastasis
  - 2 to 5 cm primary tumor

↓

Early Breast Cancer

Evidences

- **Controlled Randomized Trials.**

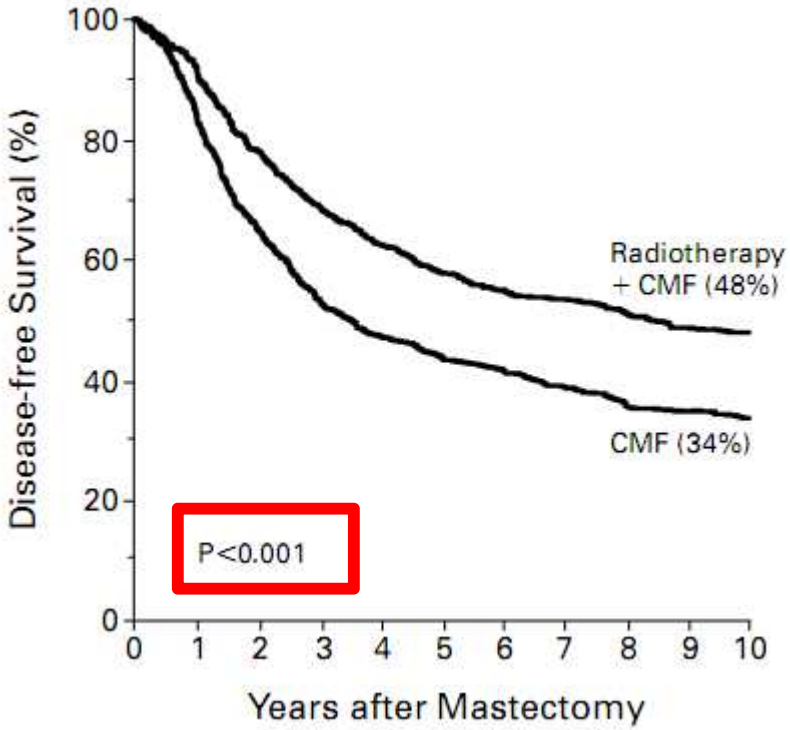
- **Meta analysis**

Danish 82b Trial

Pre menopausal Early Breast Cancer Majority T1 and T2(85%) pN +ve

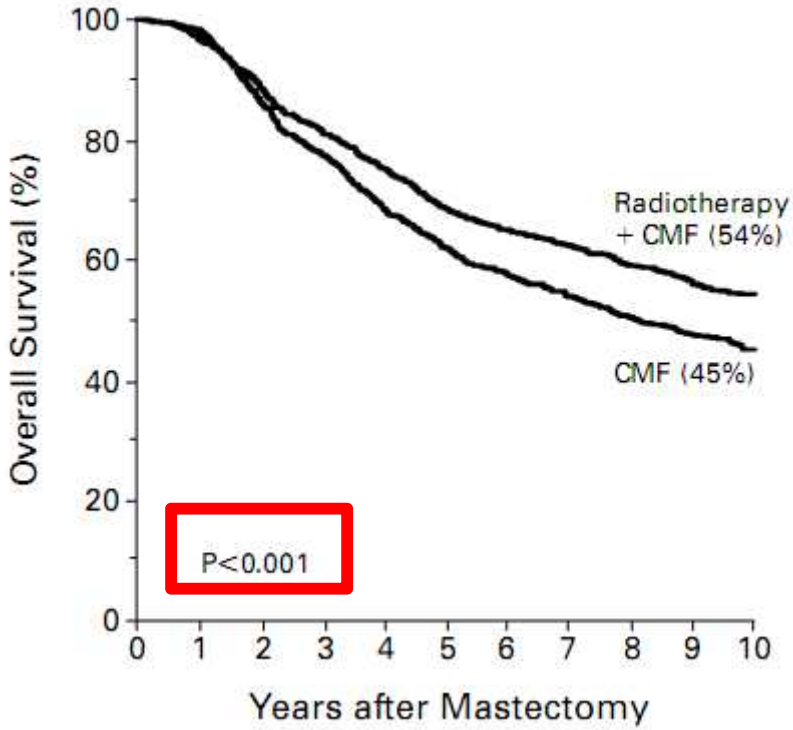
N=1708 (62% 1-3 nodes +)

CMF + PMRT



Disease Free Survival

CMF



Overall Survival

Median Follow Up 10Years

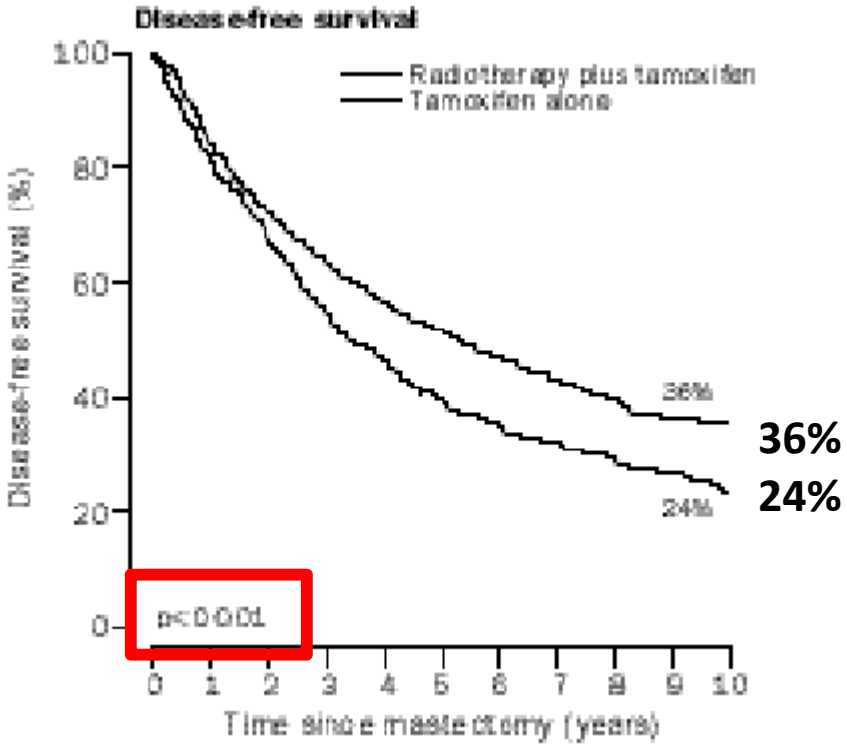
The New England Journal of Medicine Volume 337 Number 14 October 2, 1997

Danish 82c Trial

Post menopausal Early Breast Cancer Majority T1 and T2(87%) pN +ve

N=1375 (58% 1-3 Nodes +)

TMX + PMRT

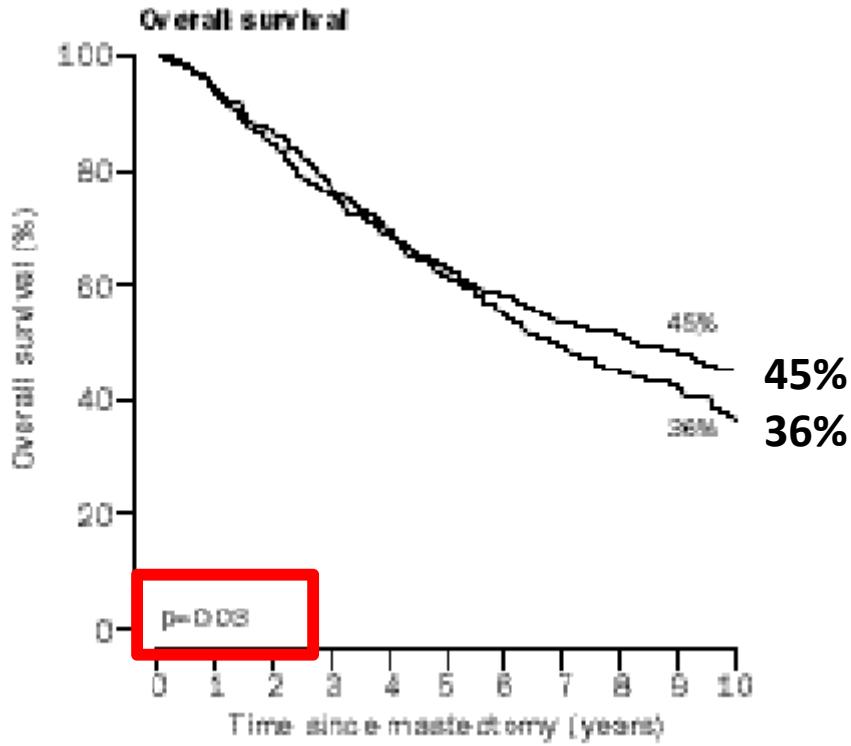


36%

24%

Disease Free Survival

TMX



45%

36%

Overall Survival

Median Follow Up 10 Years

THE LANCET • Vol 353 • May 15, 1999

British Columbia Trial

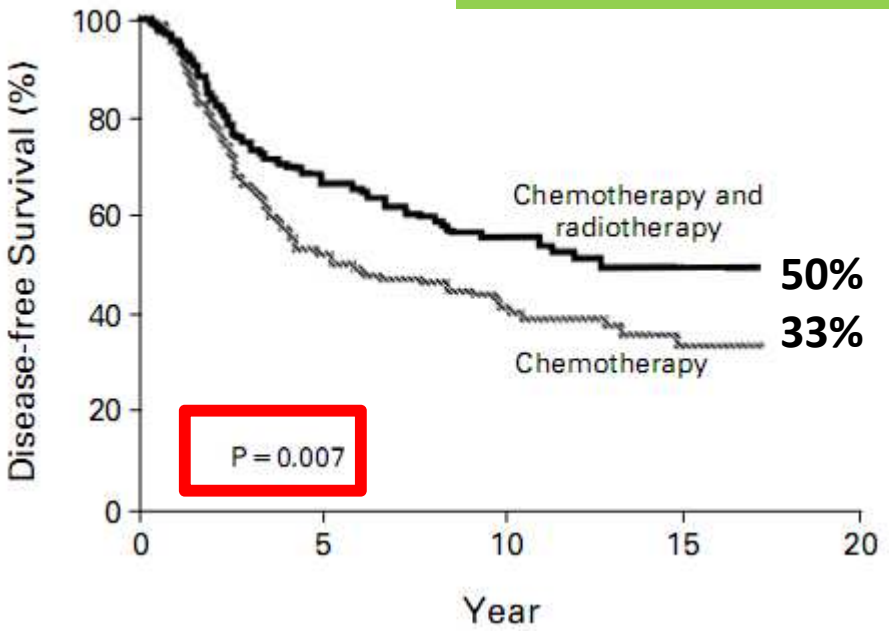
Pre menopausal Early Breast Cancer Majority T1 & T2 with pN+ve

N=318 (60% 1-3 nodes +)

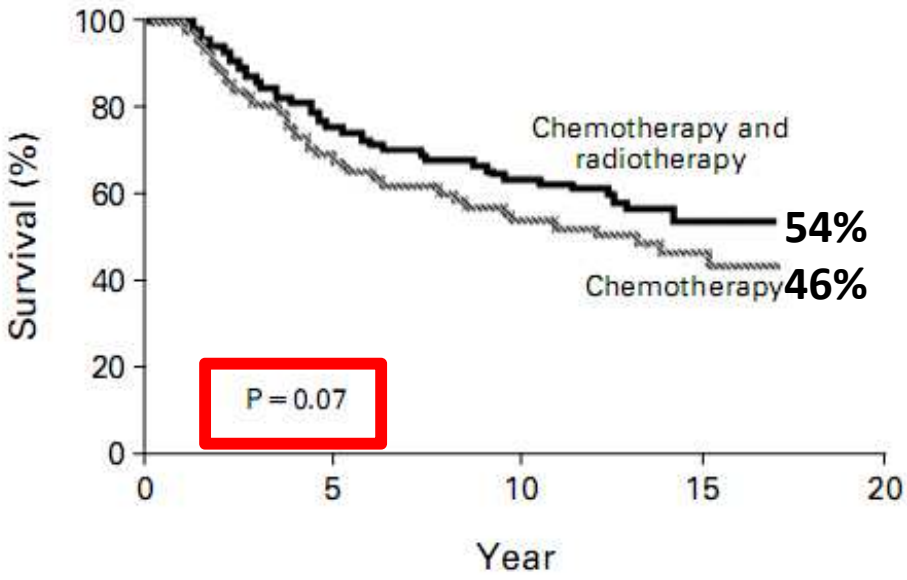
CMF + PMRT

CMF

Median Follow Up 15 Years



Disease Free Survival

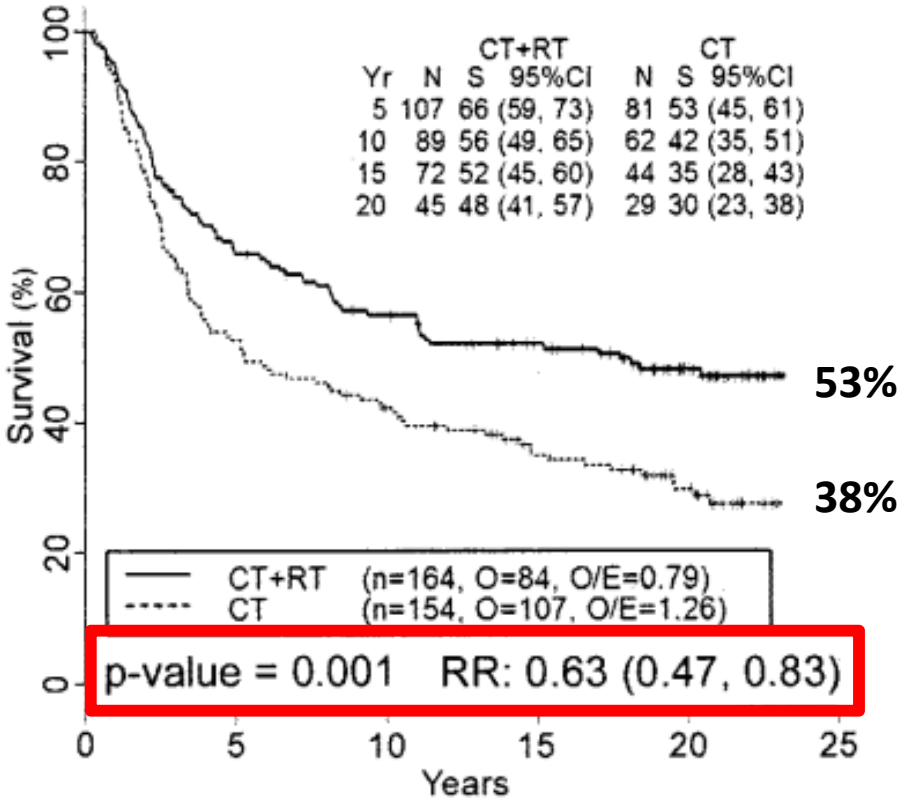


Overall Survival

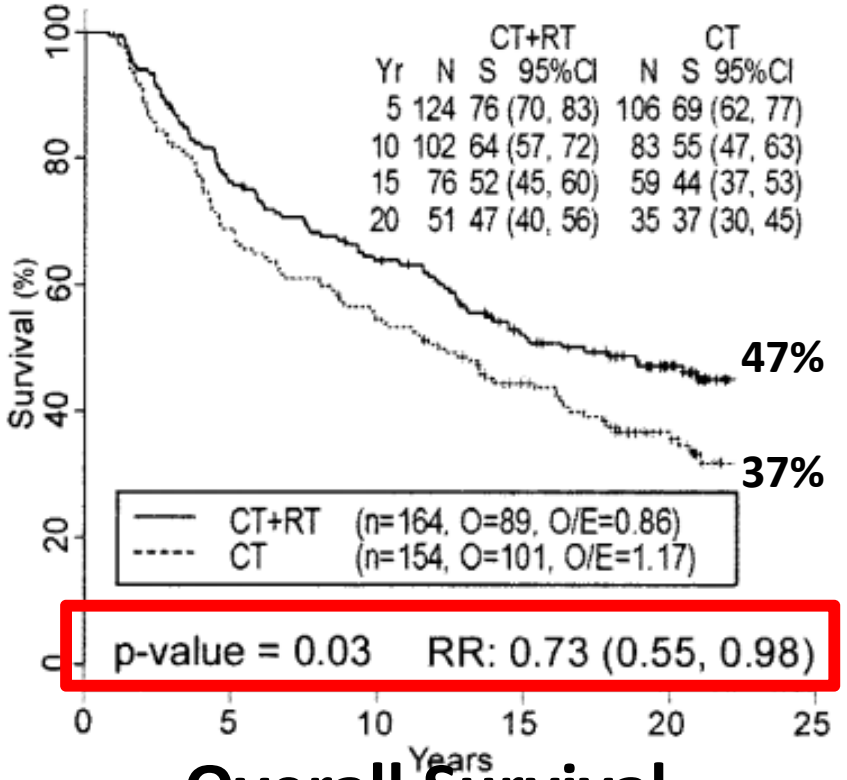
The New England Journal of Medicine Volume 337 Number 14 October 2, 1997

Updated Result of British Columbia

Median Follow Up 20 Years



Breast ca Specific Survival



Overall Survival

Journal of the National Cancer Institute, Vol. 97, No. 2, January 19, 2005

Limitation of these Results

ECOG: 10 Year Cumulative Incidence of Loco-Regional Failure without XRT

Tumor Size, No. of Nodes	No. of Patients	Isolated LRF %	Isolated LRF SE
T1, 1-3	407	9.1	1.5
T2, 1-3	576	7.0	1.1
T3, 1-3	35	22.9	7.2

Danish trial 82b[6]	30
Danish trial 82c[7]	31
Canadian[8*]	33

Recht et al, JCO, 1999

Limitation of these Results

NSABP

	1-3 LN+		
	≤ 2	2.1-5	> 5
No. of patients	1,045	1,489	229
Isolated LF, %	4.3	7.2	5.2
Isolated RF, %	2.4	3.5	2.3
Isolated LRF, %	6.0	9.7	7.5
LRF with or without DF, %	10.6	15.3	11.4
DF, %	24.6	35.7	40.5

NOTE. Subcolumn headings indicate tumor size (in centimeters).
Abbreviations: LN+, positive lymph nodes; LF, local failure; RF, regional failu

Taghian et al, JCO, 2004

Limitation of these Results

Multi-Institutional Studies with no XRT

Table 6. Ten-Year Cumulative Rates of Locoregional Failure With or Without Distant Failure According to Number of Positive Lymph Nodes (LN+)

Number LN+	1-3 LN+ (%)	≥ 4 LN+ (%)	Median No. of LN Dissected	Chemotherapy Used
Danish trial 82b[6]	30	42	7	CMF
Danish trial 82c[7]	31	46	7	CMF
Canadian[8]*	33	46	11	CMF
ECOG[9]†	13	29	15	CMF
MDA[10]‡	14	25-34‖	17	Doxorubicin based
IBCSG,[11]† premenopausal	19.7	30-38%‖	~15¶	CMF**
IBCSG,[11]† postmenopausal	16§	29-35%‖	~15¶	CMF or tamoxifen††
NSABP†	13	24-32‖	16	Doxorubicin/CMF‡‡

Taghian et al, JCO, 2004

Limitation of these Results

- **Surgery was not adequate specially the axillary dissection as compare to other trials.**
- **Median no of lymph nodes removed**
  - **Danish Trials 7**
  - **British Columbia 11**

Danish Trial 83b & 83c

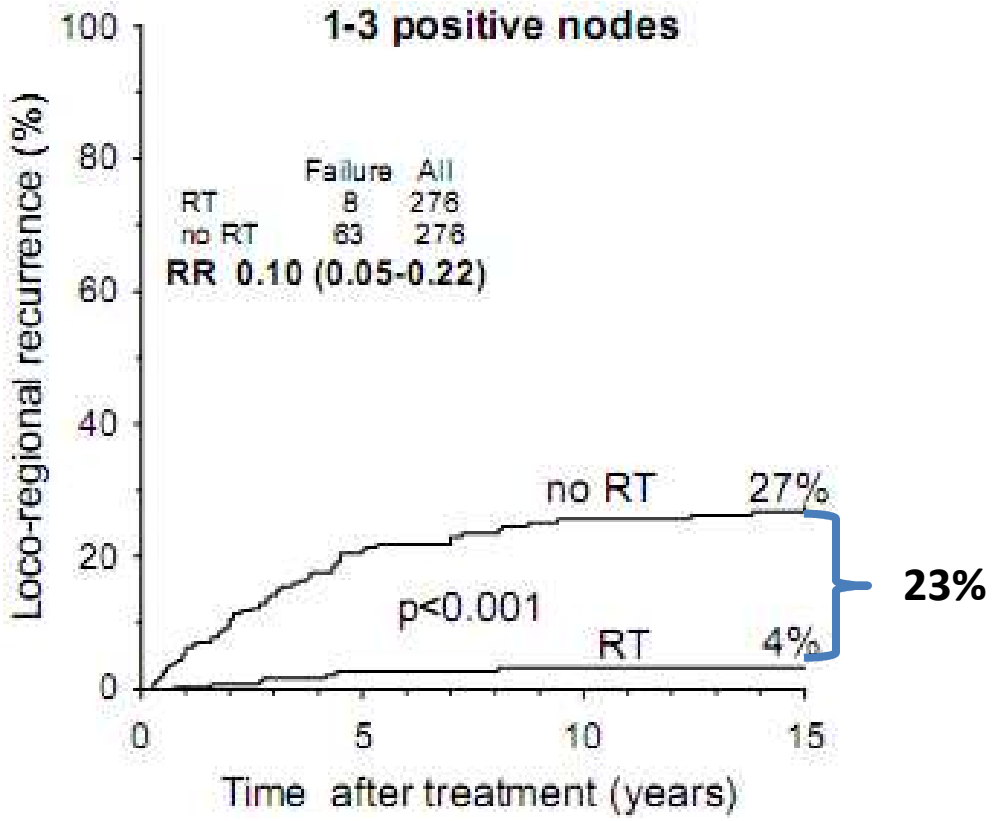
Sub-group Analysis

- **Only select patients with no of nodes removed 8 or more.**
- **Further grouped based on 1-3 nodes or ⩾ 4 nodes**
- **N=1152**

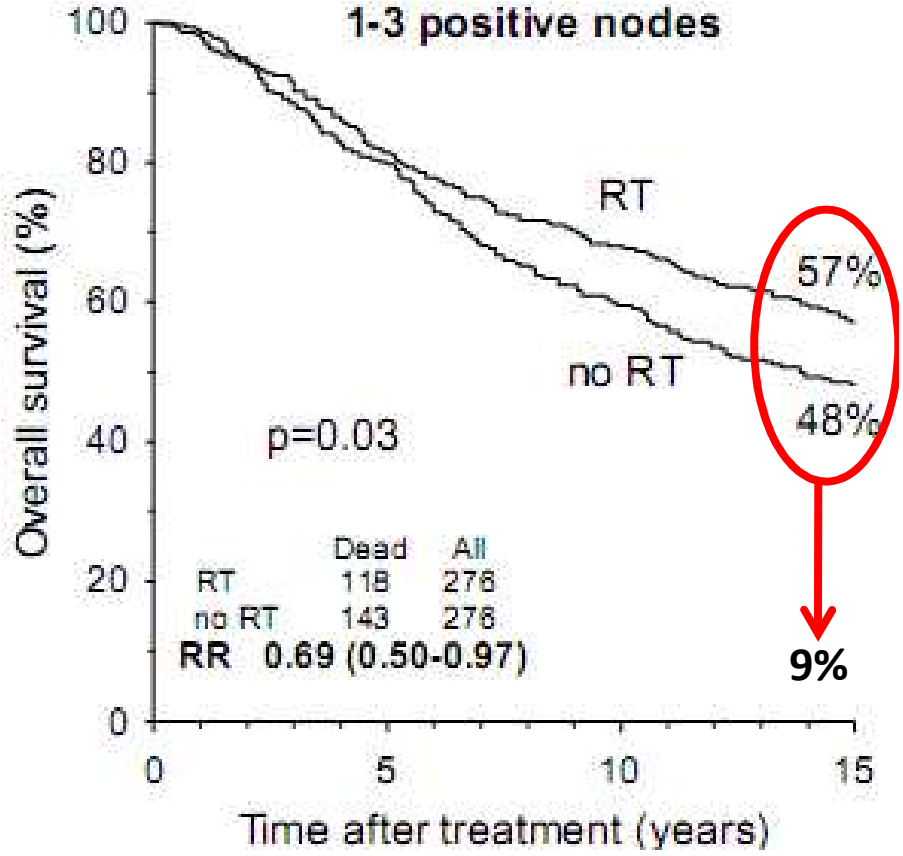
M. Overgaard et al. / Radiotherapy and Oncology 82 (2007) 247–253

Danish Trial 83b & 83c
Sub-group Analysis

Loco regional Recurrence



Median Follow Up 15 Years



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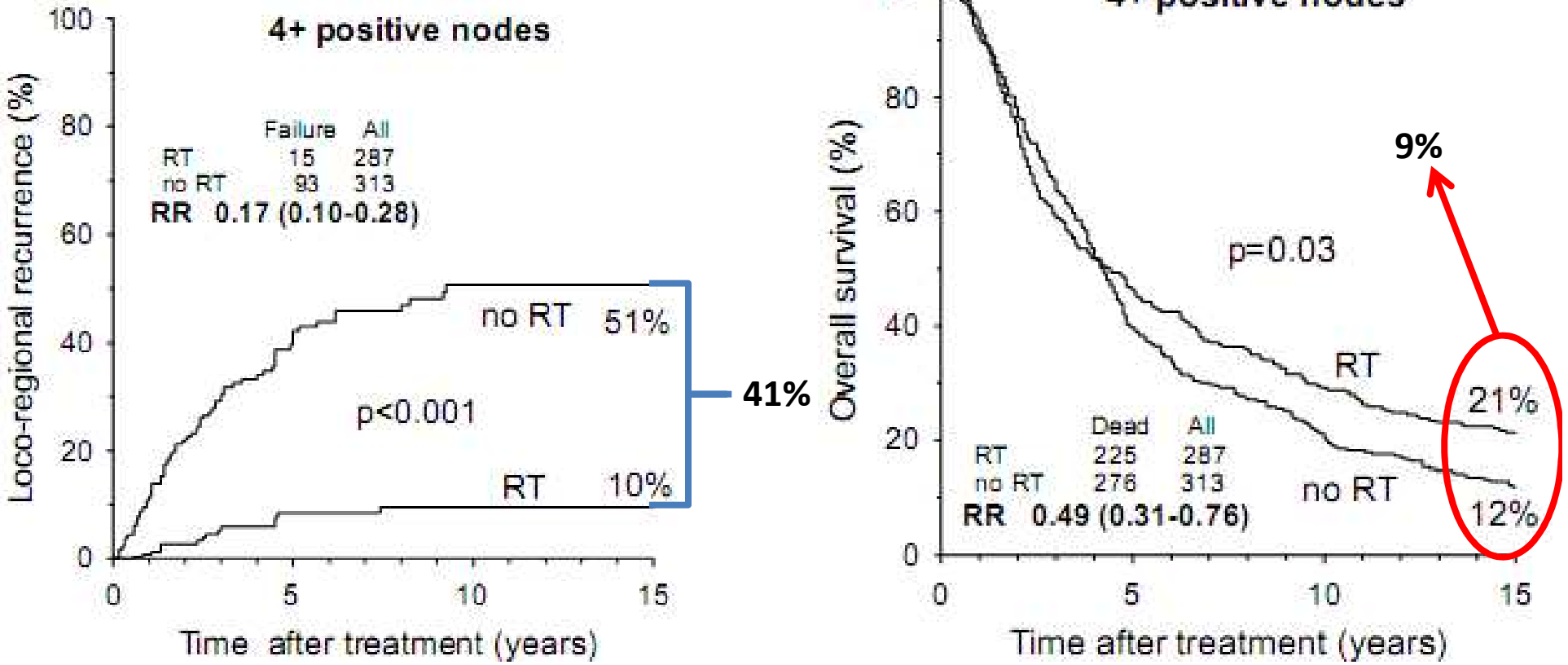
Danish Trial 83b & 83c
Sub-group Analysis

Loco regional Recurrence

Median Follow Up 15 Years



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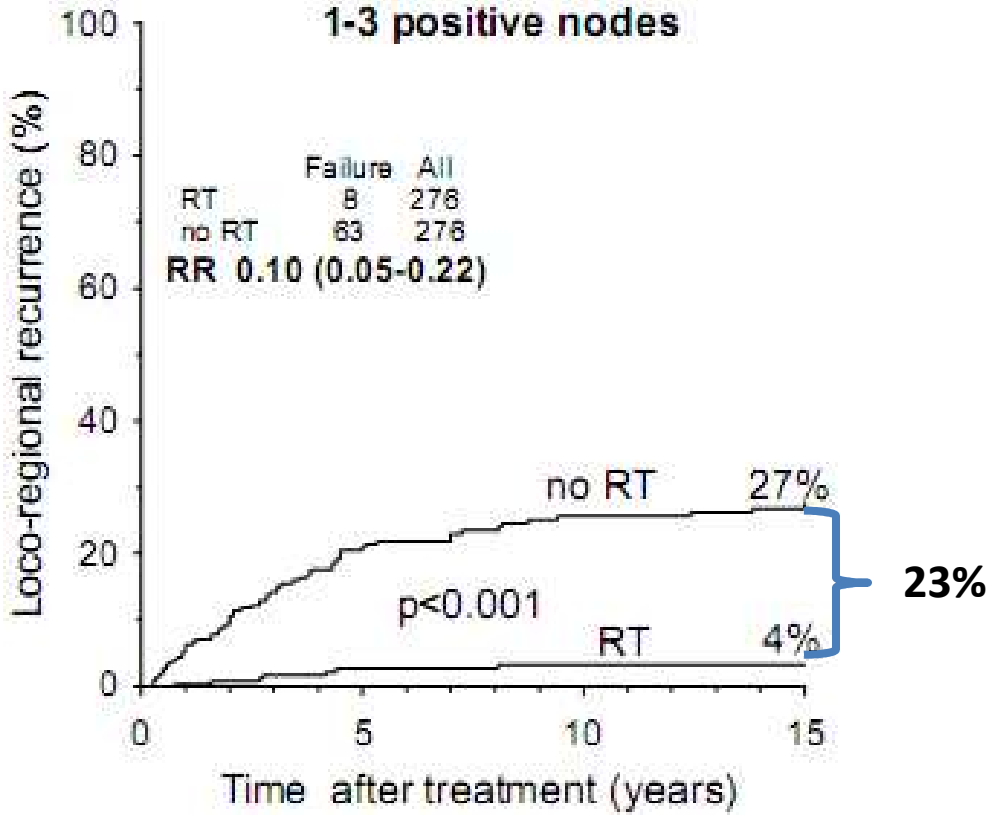
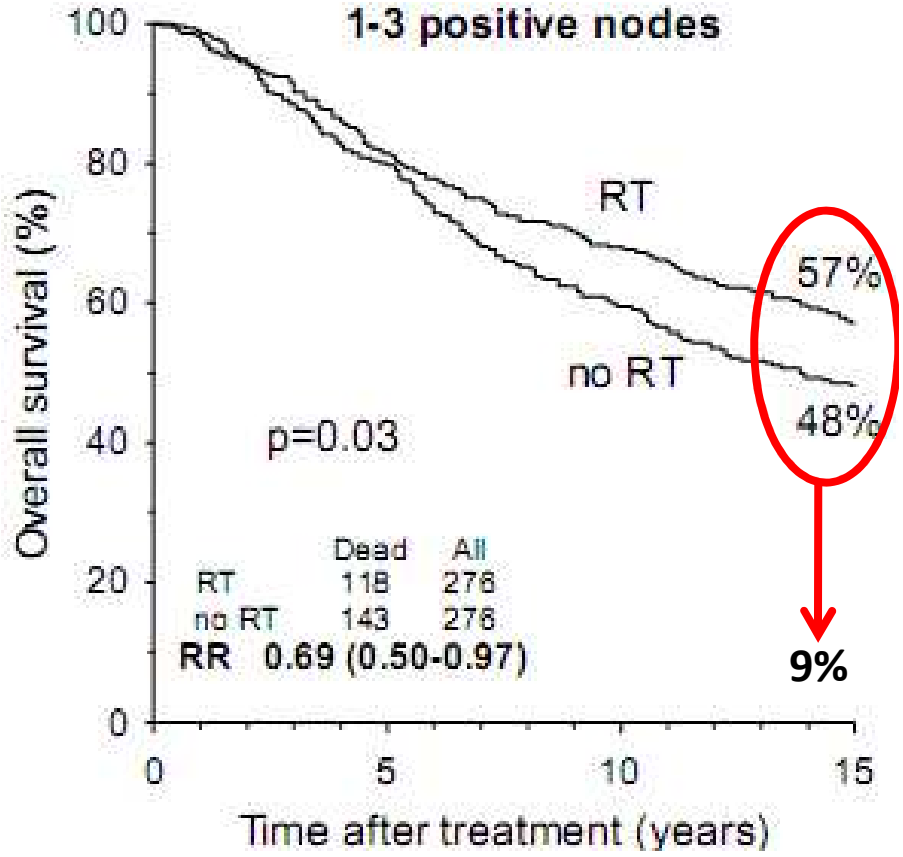
Danish Trial 83b & 83c
Sub-group Analysis

Loco regional Recurrence



Median Follow Up 15 Years

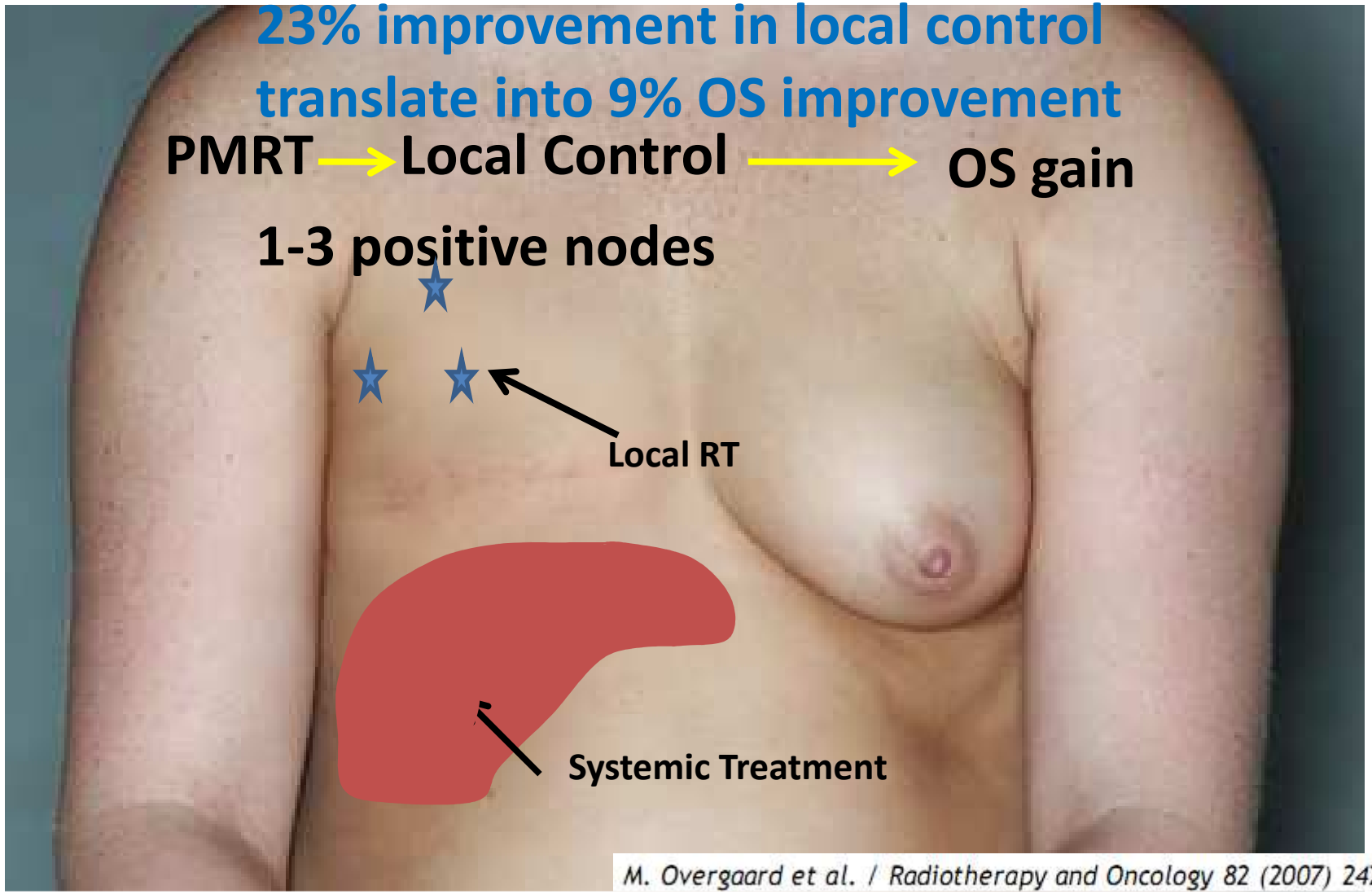


M. Overgaard et al. / Radiotherapy and Oncology 82 (2007) 247–253

Danish Trial 83b & 83c

Sub-group Analysis (Hypothesis)

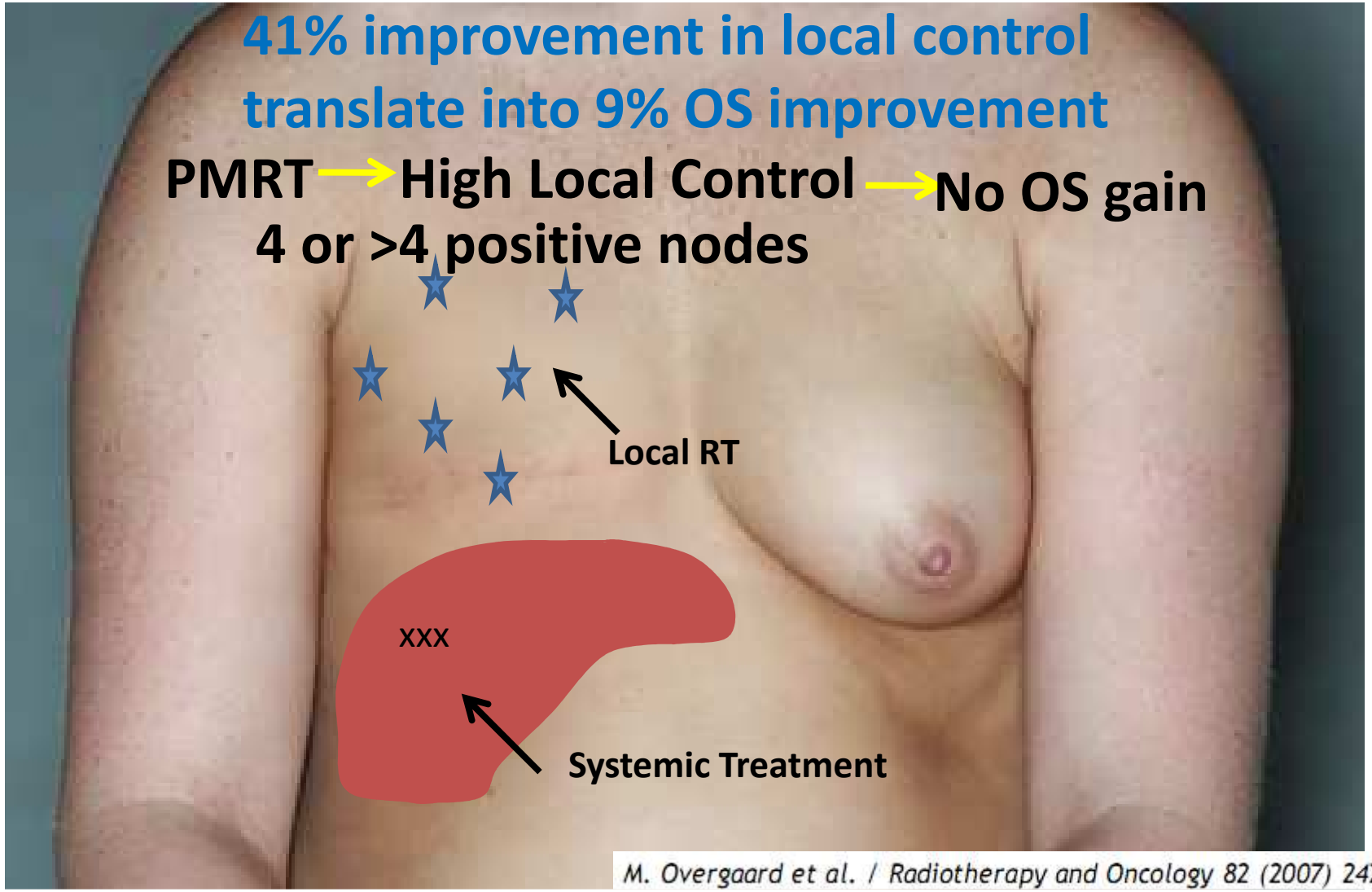
Larger Proportion of patients will have survival benefit



Danish Trial 83b & 83c

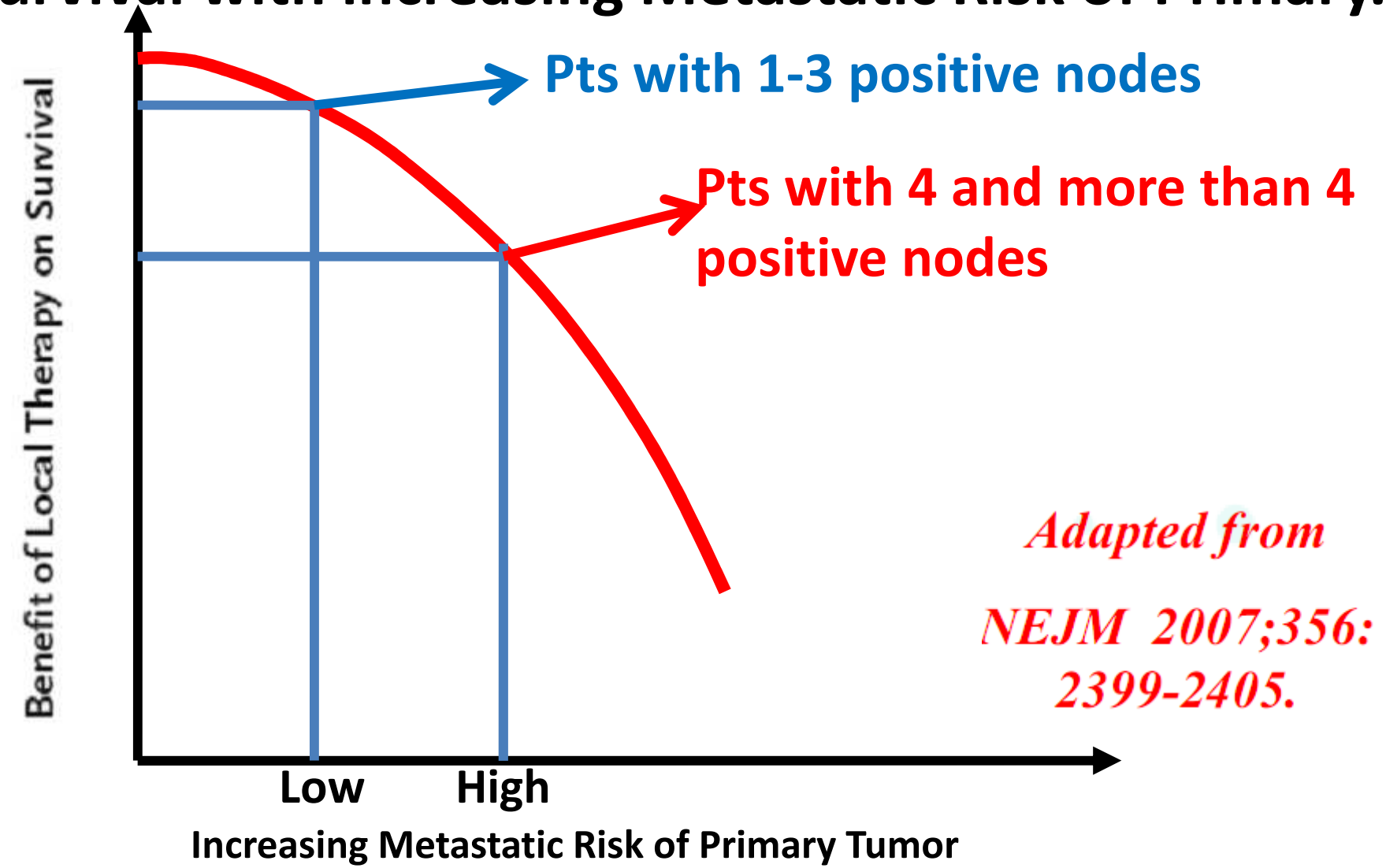
Sub-group Analysis

Limited Proportion of patients will have survival benefit



M. Overgaard et al. / Radiotherapy and Oncology 82 (2007) 247–253

Hypothetical benefit of Local Tumor Control on Survival with increasing Metastatic Risk of Primary.



Adapted from

NEJM 2007;356: 2399-2405.

Radiotherapy and Oncology 90 (2009) 74–79

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Postmastectomy irradiation

High local recurrence risk is not associated with large survival reduction after postmastectomy radiotherapy in high-risk breast cancer: A subgroup analysis of DBCG 82 b&c ☆

Marianne Kyndi [a,b,*], Marie Overgaard [c], Hanne M. Nielsen [a], Flemming B. Sørensen [b], Helle Knudsen [d], Jens Overgaard [a]

[a] Department of Experimental Clinical Oncology, Aarhus University Hospital, Denmark
[b] Department of Pathology, Aarhus University Hospital, Denmark
[c] Department of Oncology, Århus University Hospital, Denmark
[d] Department of Pathology, Herlev Hospital, Denmark

Danish Trial 83b & 83c Sub-group Analysis

- **Among patients in 82b and 82c randomized to no radiation, 3 risk groups were identified**
- **Good: 4 of 5 favorable features**
  - **≤3 nodes**
  - **Size <2 cm**
  - **Grade 1**
  - **ER or PR positive, her2 negative**

Intermediate risk = all others

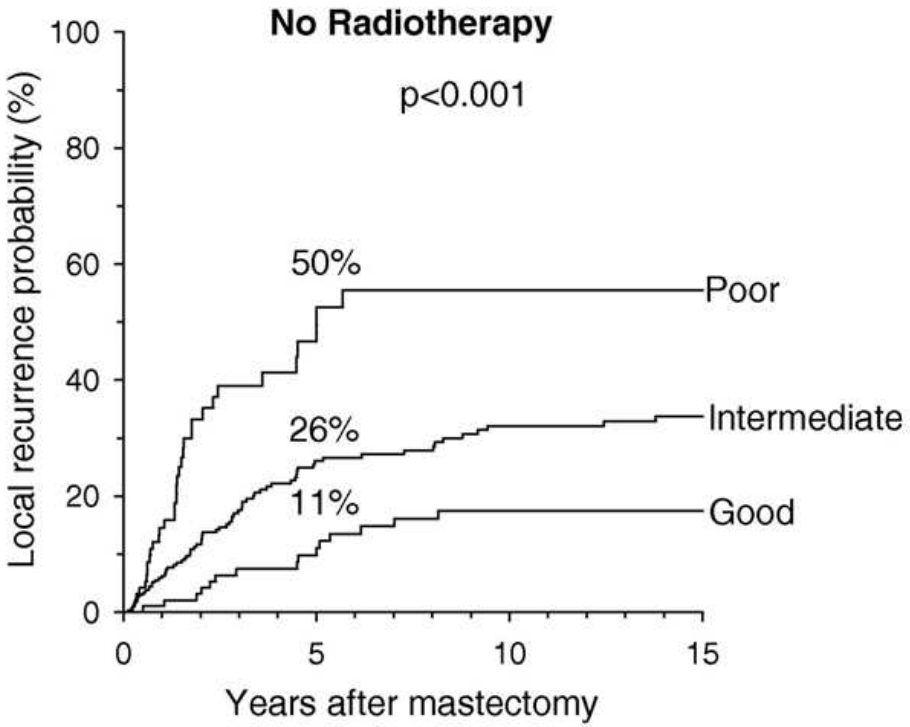
- **Poor: 2 of 3**
  - **Grade 3, >3 nodes, size >5 cm**

Radiother Oncol 2009 Jan;90(1):74-9

Danish Trial 83b & 83c

Sub-group Analysis

LRR by Risk Group



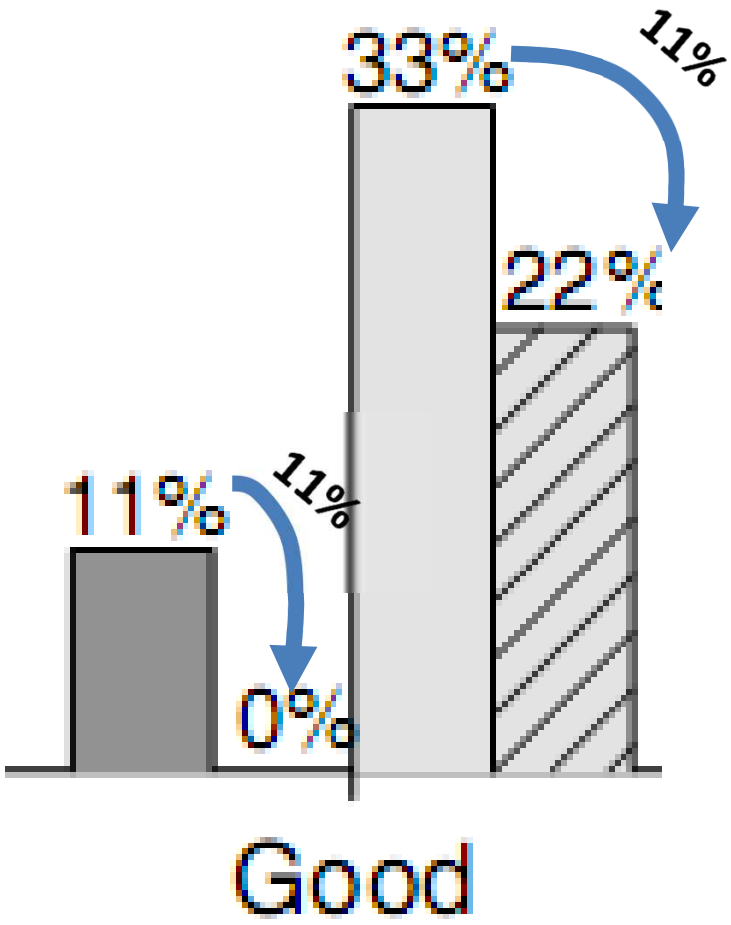
Good	101	74	57	46
Intermediate	303	132	93	69
Poor	107	19	10	8

Radiother Oncol 2009 Jan;90(1):74-9

Danish Trial 83b & 83c

Sub-group Analysis

5 year LRR & 15 year Breast Cancer Mortality by Risk Group



no RT Local rec. (5-year)

+ RT

no RT Breast cancer mortality

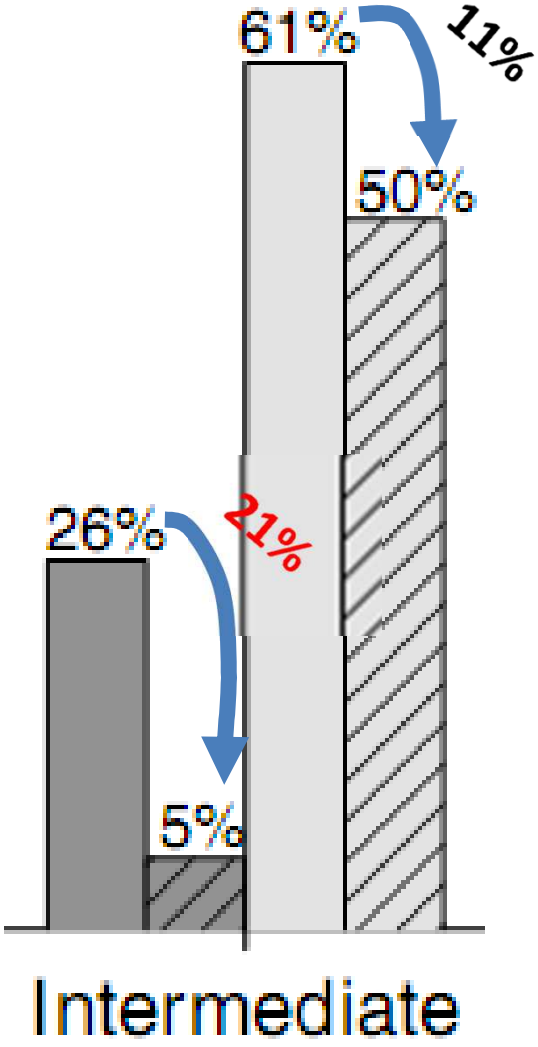
+ RT (15-year) 61%

Improvement in local control translate excellently into improvement in cancer specific survival

Radiother Oncol 2009 Jan;90(1):74-9

Danish Trial 83b & 83c
Sub-group Analysis

5 year LRR & 15 year Breast Cancer Mortality by Risk Group



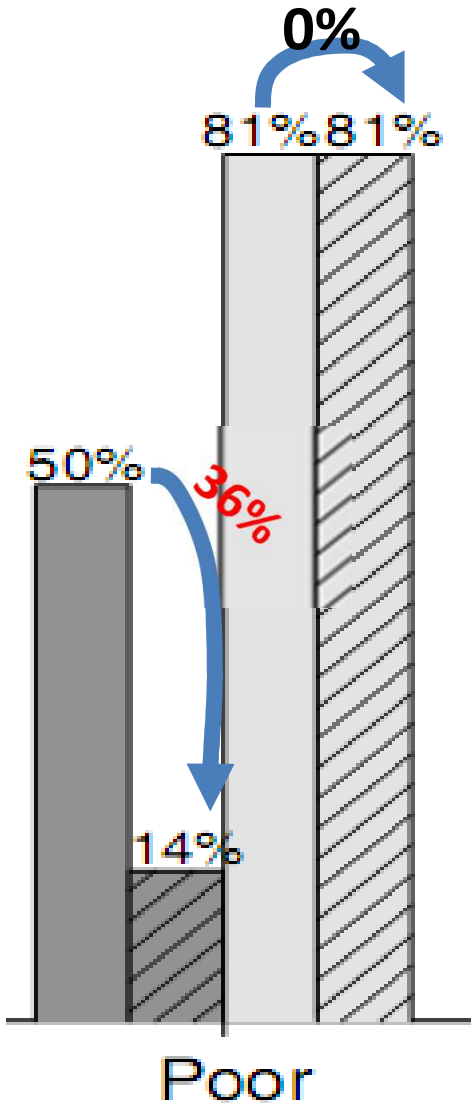
no RT Local rec. (5-year)
+ RT
no RT Breast cancer mortality
+ RT (15-year) 61%

Improvement in local control translate reasonable into improvement in cancer specific survival

Radiother Oncol 2009 Jan;90(1):74-9

Danish Trial 83b & 83c
Sub-group Analysis

5 year LRR & 15 year Breast Cancer Mortality by Risk Group



no RT Local rec. (5-year)

+ RT

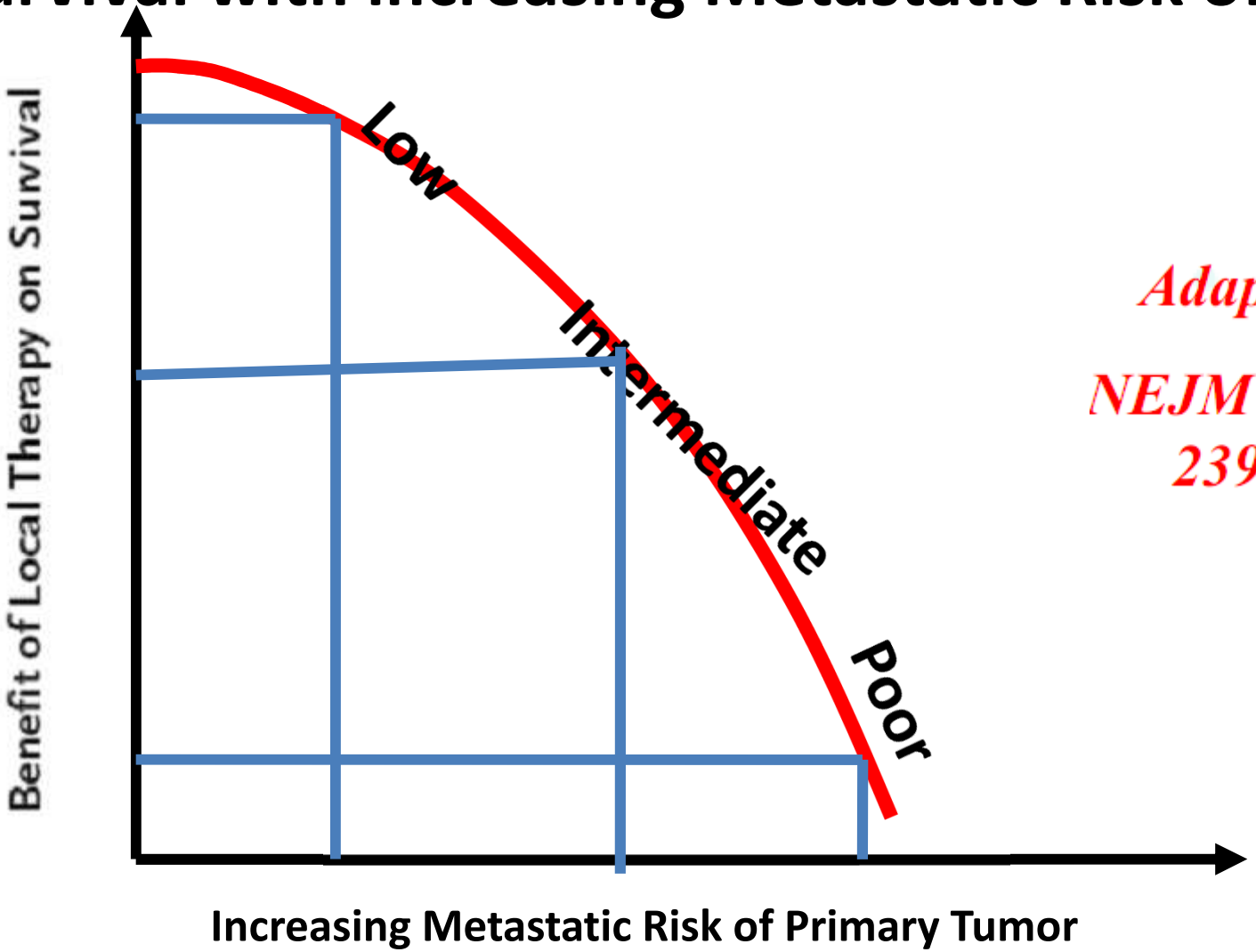
no RT Breast cancer mortality

+ RT (15-year) 61%

Improvement in local control does not translate into improvement in cancer specific survival

Radiother Oncol 2009 Jan;90(1):74-9

Hypothetical benefit of Local Tumor Control on Survival with increasing Metastatic Risk of Primary.



Adapted from

NEJM 2007;356: 2399-2405.

All reports related with Danish trial 83b & c make strong case of PMRT in patients with 1-3 positive axillary nodes

Evidences

- **Controlled Randomized Trials.**

- **Meta analysis**

Oxford 2005 Meta-analysis

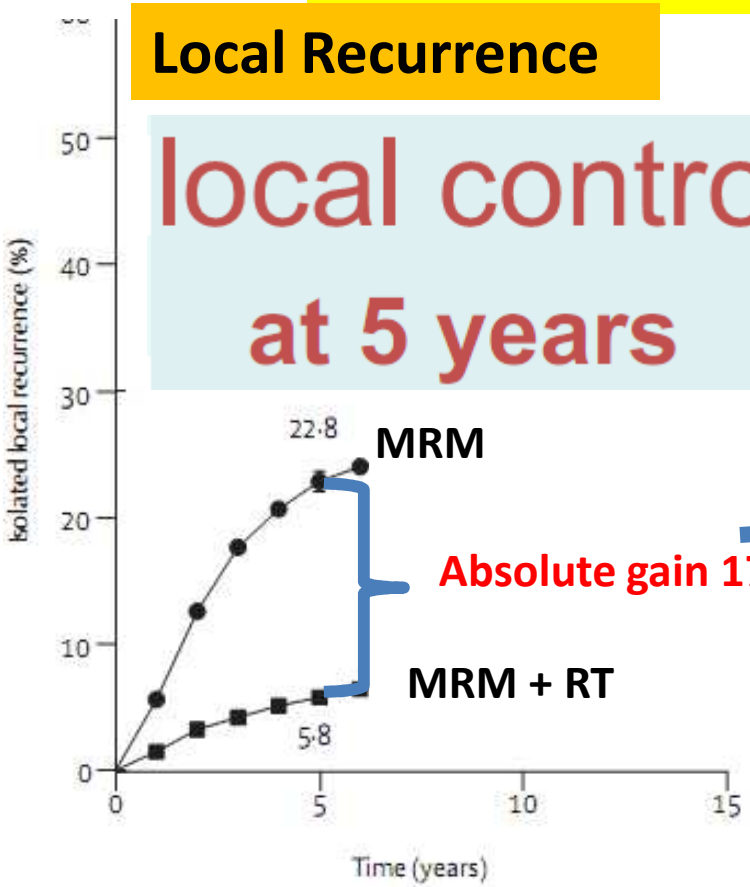
LN + patients → +/- Postmastectomy Radiation

Total No of Patients 8500

Local Recurrence

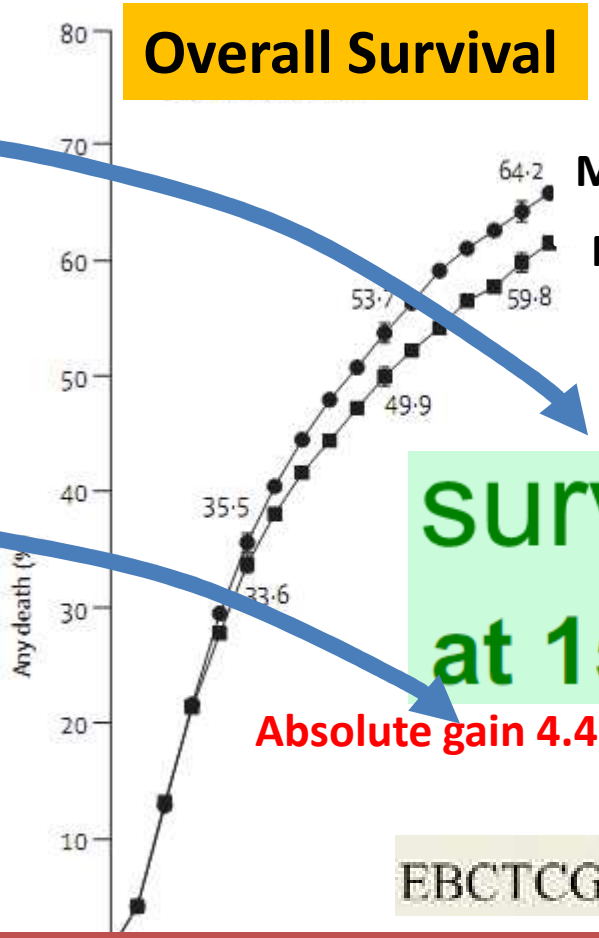
local control

at 5 years



Absolute gain 17%

Overall Survival



survival

at 15 years

Absolute gain 4.4%

EBCTCG, Lancet, 2005

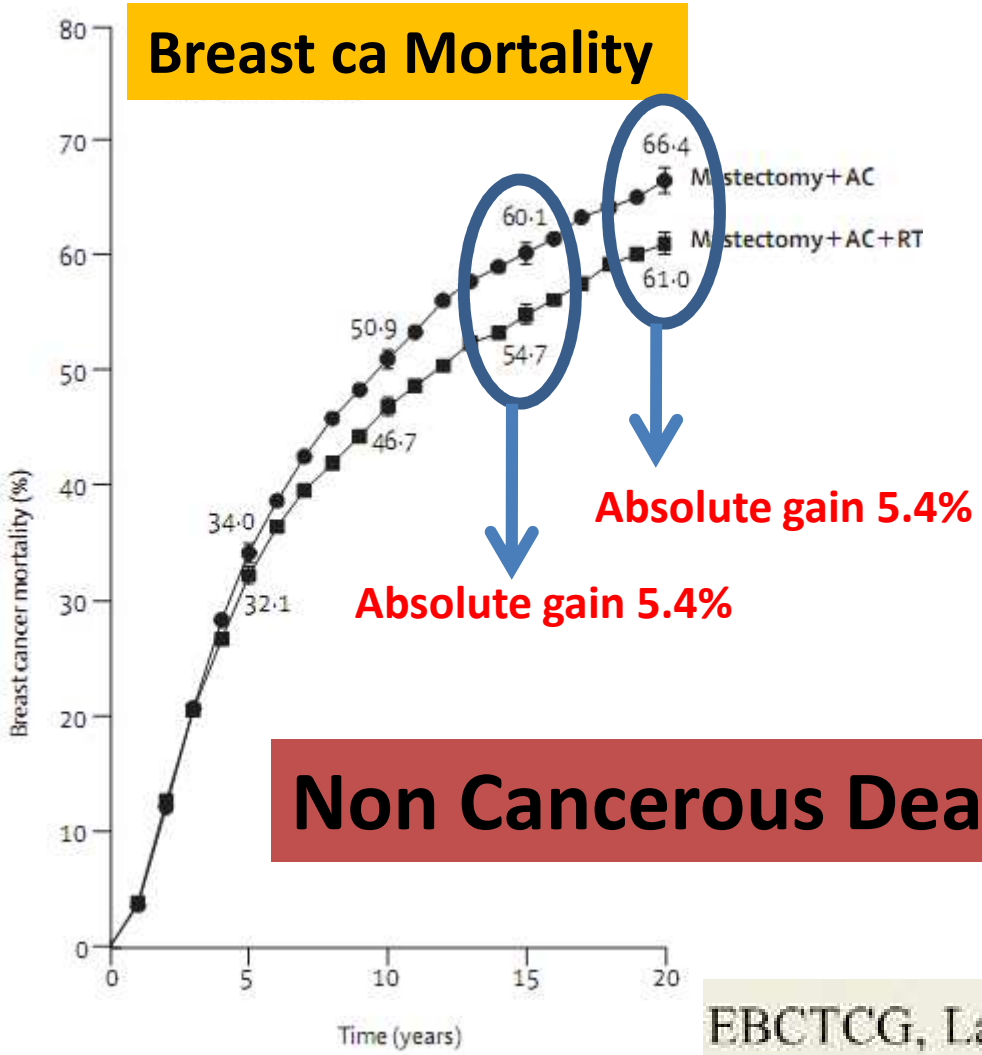
Every 4 LR avoided, 1 death is avoided over the following 15 years.

Oxford 2005 Meta-analysis

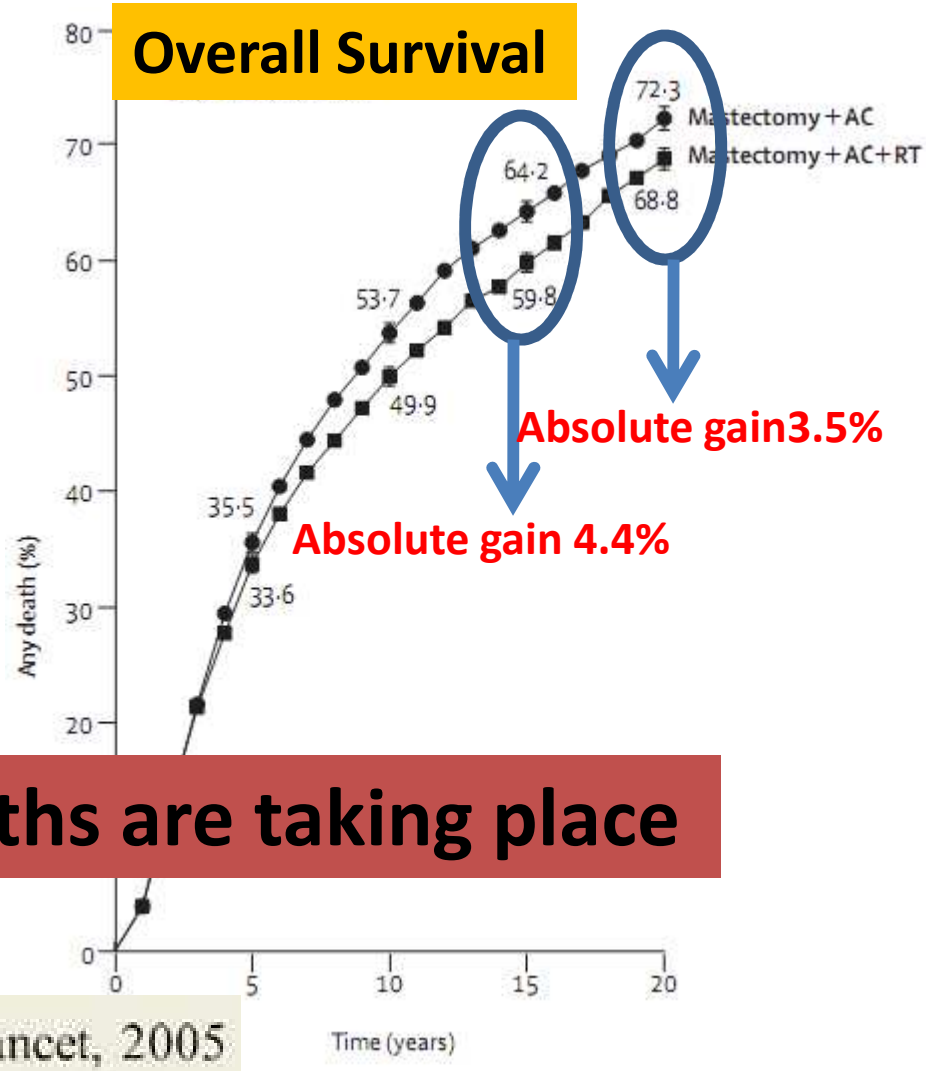
LN + patients → +/- Postmastectomy Radiation

Total No of Patients 8500

Breast ca Mortality



Overall Survival



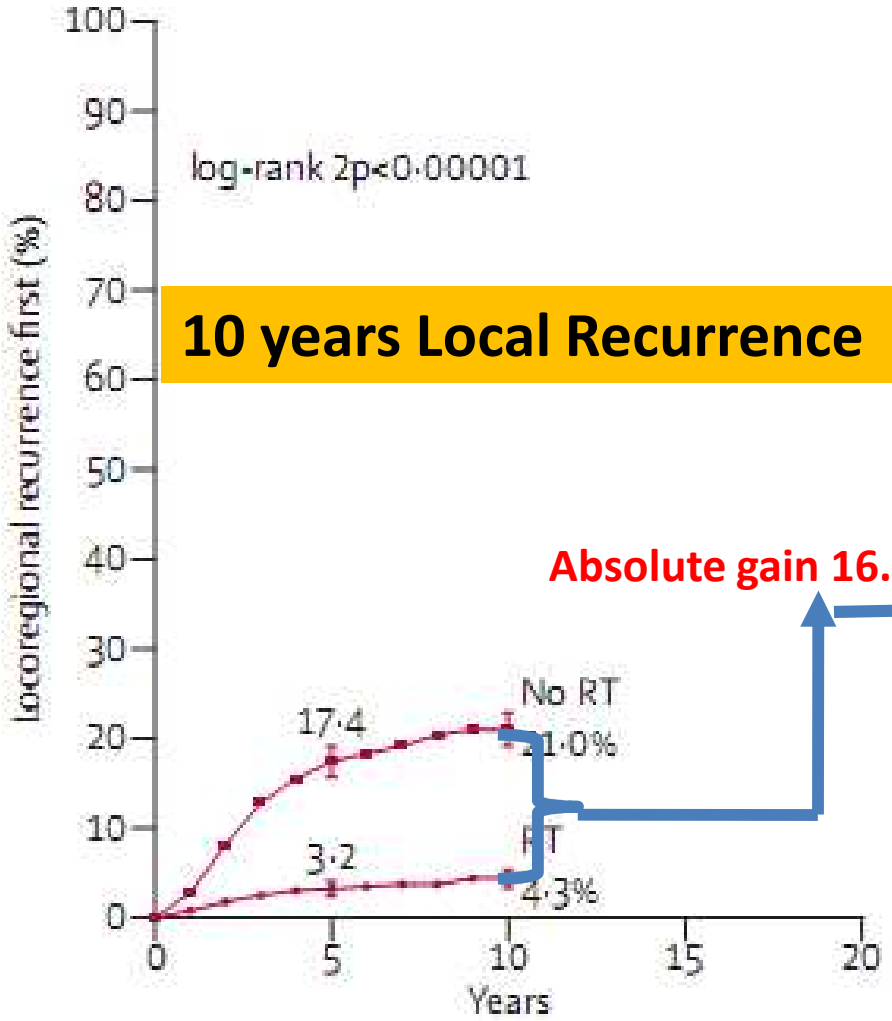
Non Cancerous Deaths are taking place

EBCTCG, Lancet, 2005

Oxford 2014 Meta-analysis

PMRT in 1-3 Positive Nodes

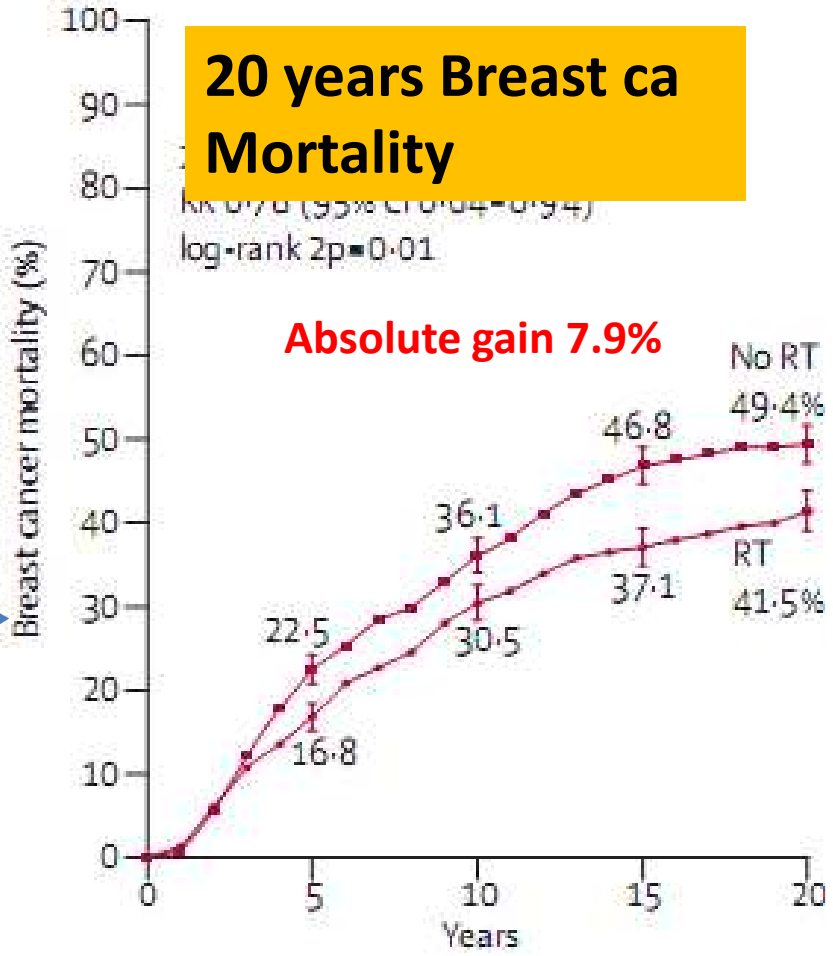
Total No of Patients 1133



10 years Local Recurrence

Absolute gain 16.7%

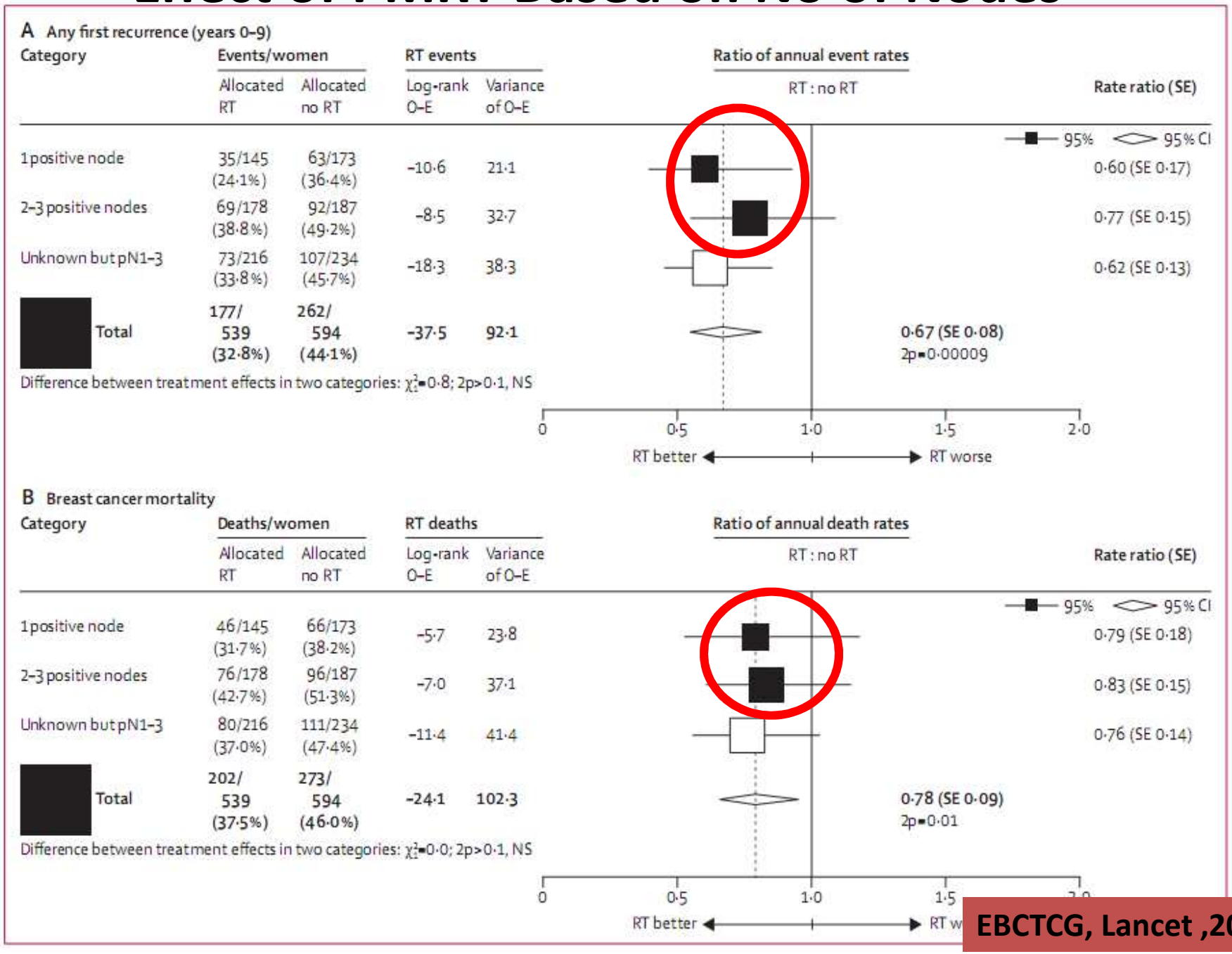
20 years Breast ca Mortality



Absolute gain 7.9%

EBCTCG, Lancet ,2014

Effect of PMRT Based on No of Nodes



EBCTCG, Lancet ,2014

Oxford Meta-analysis

- **This also support the use of PMRT in patients with early breast ca with 1-3 positive nodes**

Published Ahead of Print on September 19, 2016 as 10.1200/JCO.2016.69.1188
The latest version is at http://jco.ascopubs.org/cgi/doi/10.1200/JCO.2016.69.1188

JOURNAL OF CLINICAL ONCOLOGY

ASCO SPECIAL ARTICLE

Postmastectomy Radiotherapy: An American Society of Clinical Oncology, American Society for Radiation Oncology, and Society of Surgical Oncology Focused Guideline Update

Abram Recht, Elizabeth A. Comen, Richard E. Fine, Gini F. Fleming, Patricia H. Hardenbergh, Alice Y. Ho, Clifford A. Hudis, E. Shelley Hwang, Jeffrey J. Kirshner, Monica Morrow, Kilian E. Salerno, George W. Sledge Jr, Lawrence J. Solin, Patricia A. Spears, Timothy J. Whelan, Mark R. Somerfield, and Stephen B. Edge

Abram Recht, Beth Israel Deaconess Medical Center, Boston, MA; Elizabeth A. Comen, Alice Y. Ho, Clifford A. Hudis, Monica Morrow, Memorial Sloan Kettering Cancer Center; New York; Jeffrey J. Kirshner, Hematology Oncology Associates of Central New York East

Clinical Question 1

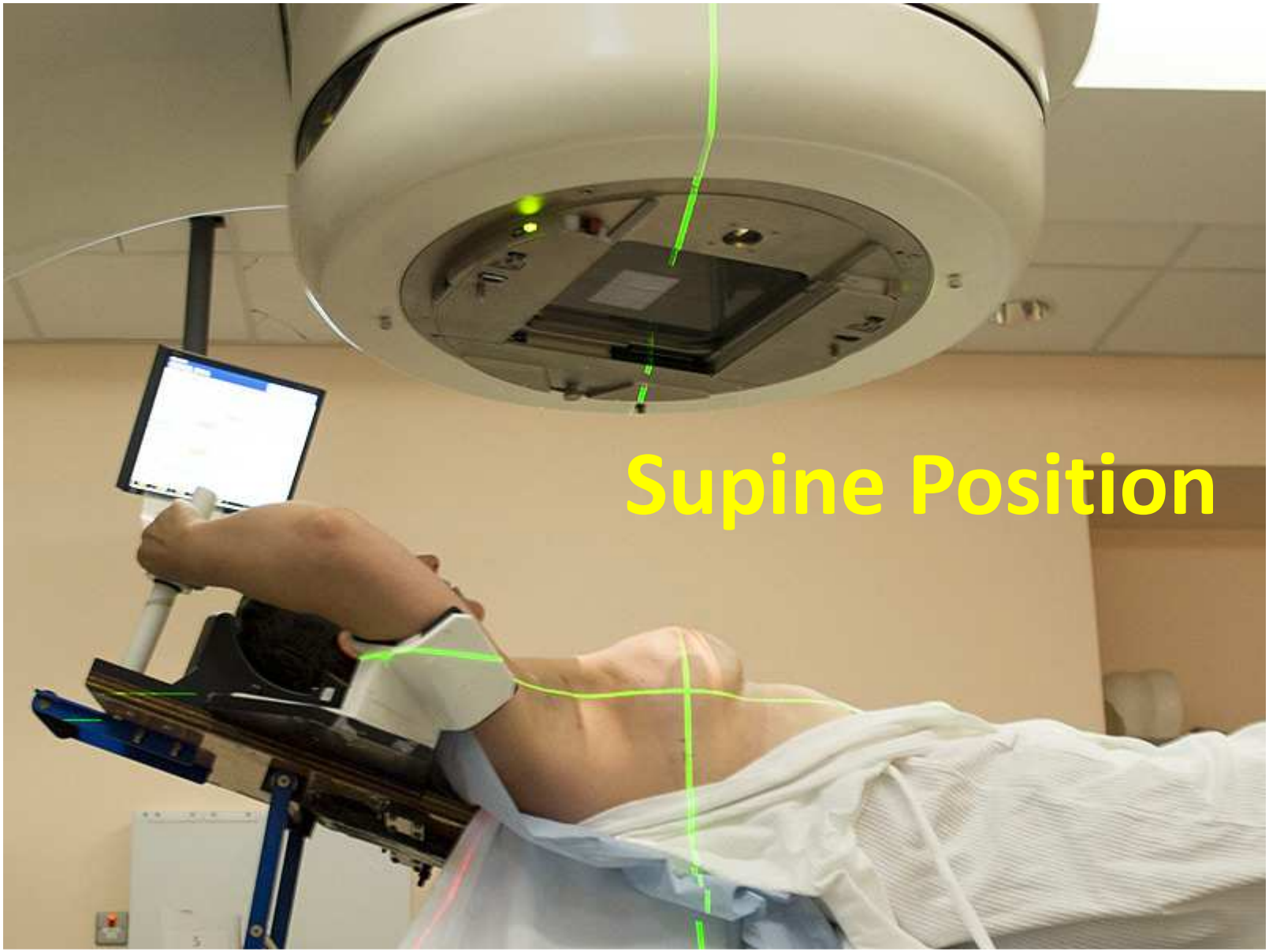
Is PMRT indicated in patients with T1-2 tumors with one to three positive axillary lymph nodes who undergo ALND?

Recommendations

Recommendation 1a. The panel unanimously agreed that the available evidence shows that PMRT reduces the risks of locoregional failure (LRF), any recurrence, and breast cancer mortality for patients with T1-2 breast cancer and one to three positive lymph nodes. 1

Radiotherapy Planning

Position of the Patient



Position of the Patient

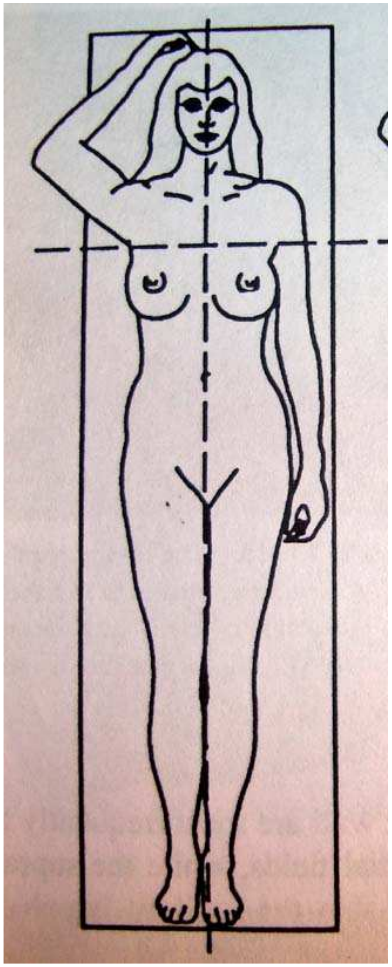
Symmetrical

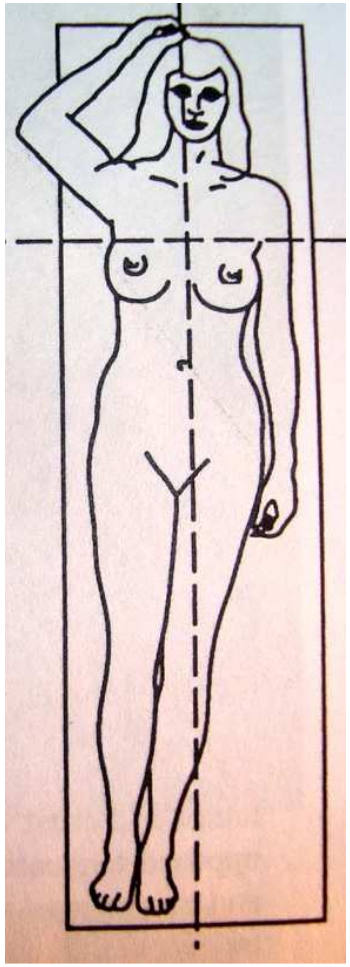
Position of the Patient
Asymmetrical

Arm on involved side elevated above the head and face turned away from involved side

Special Precautions & Difficulties

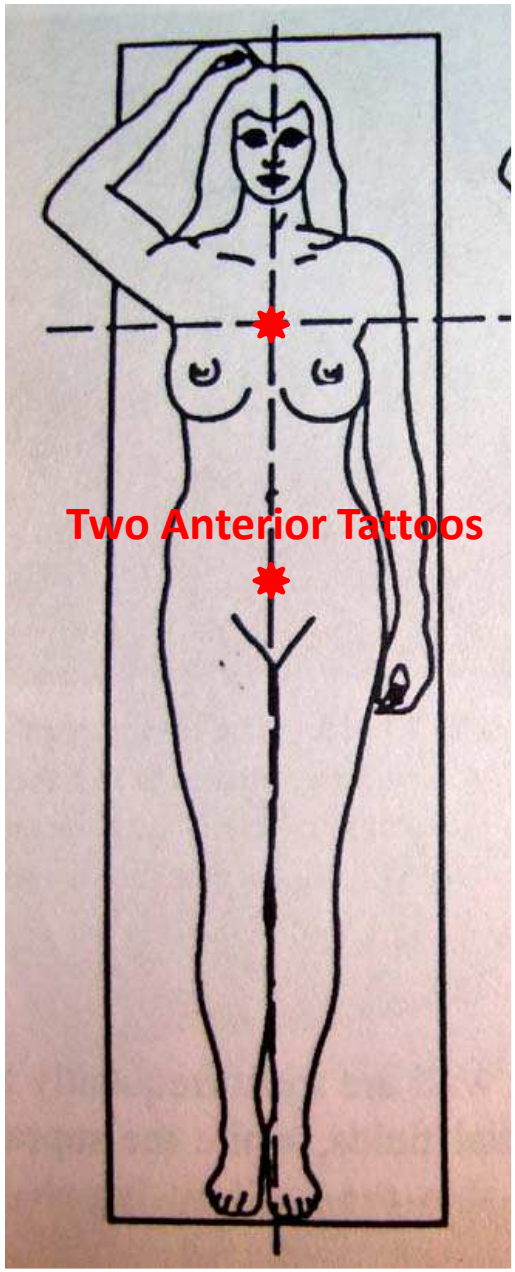
A small misalignment of the patient on the treatment couch will have the same effect as if the couch were angled.



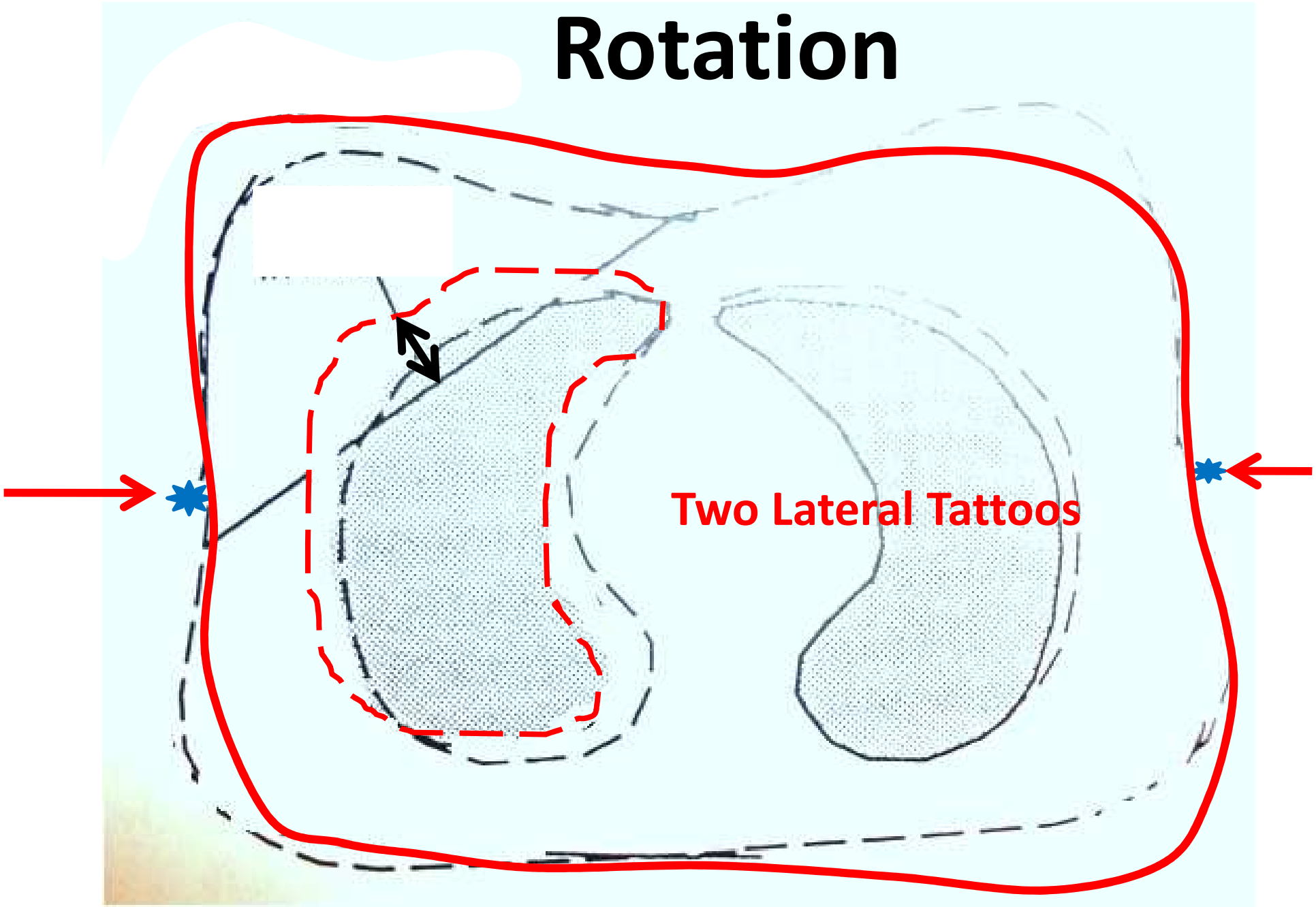


Tilt

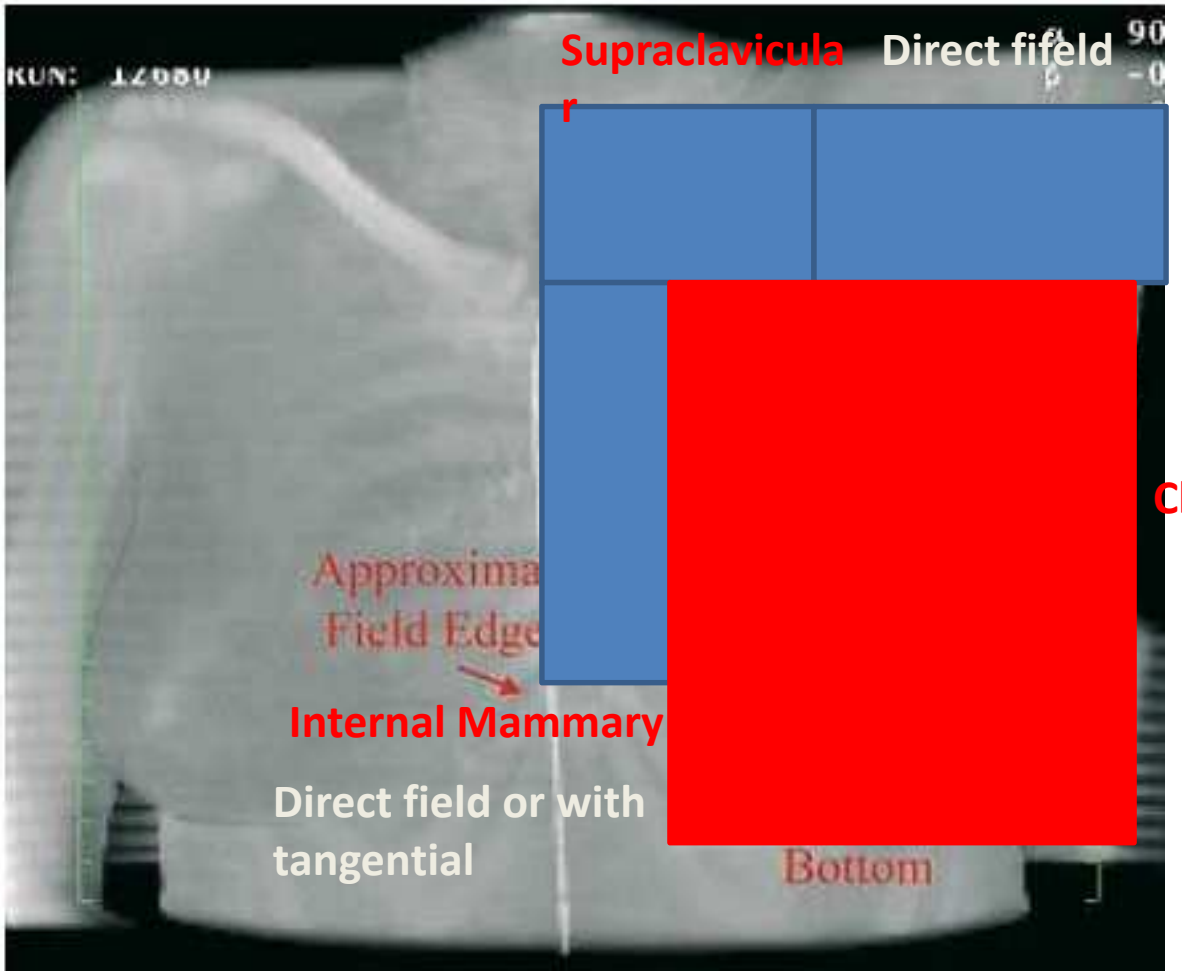
Tattoos are put over anterior surface so that patient remains straight throughout the treatment.



Rotation

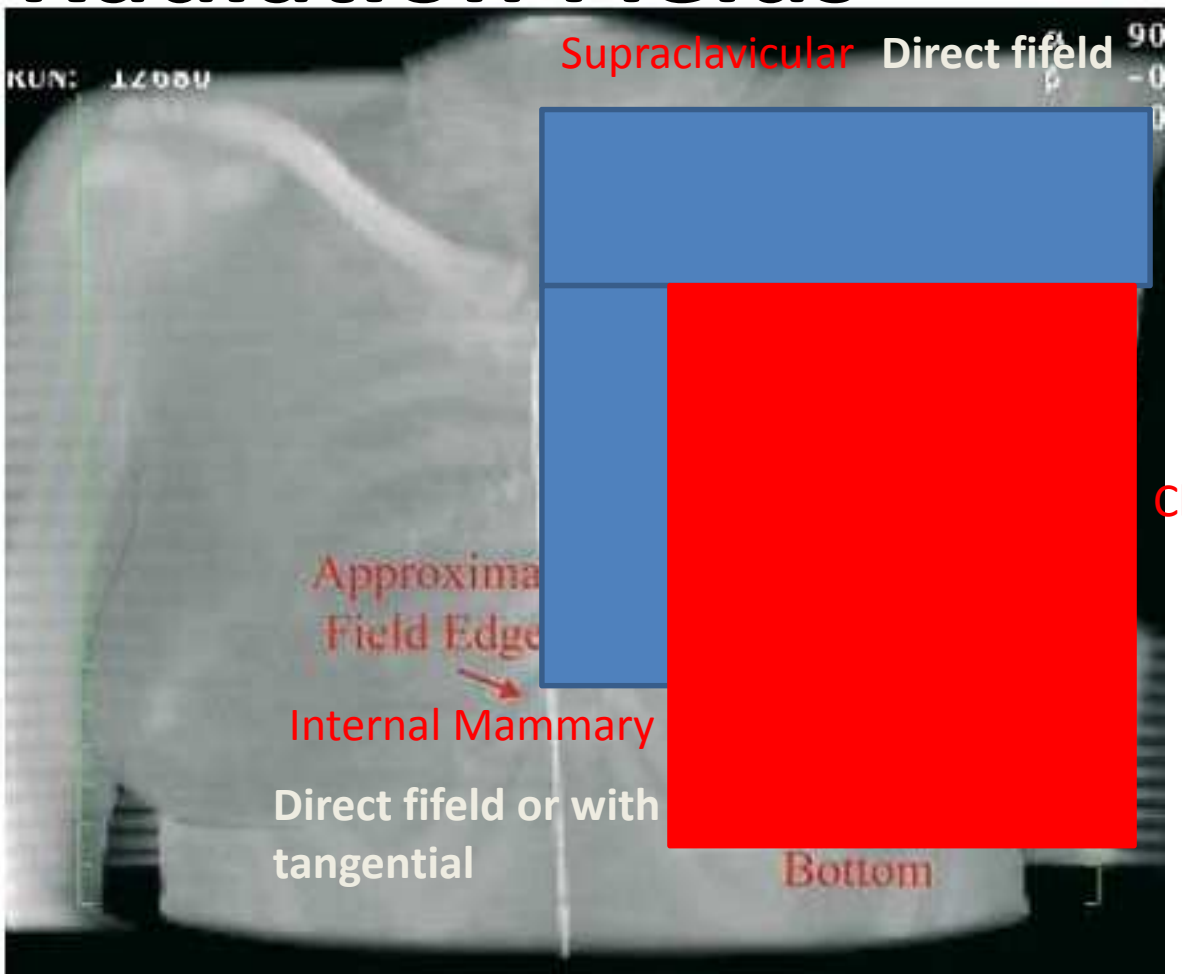


REGIONS TO BE TREATED AFTER MRM

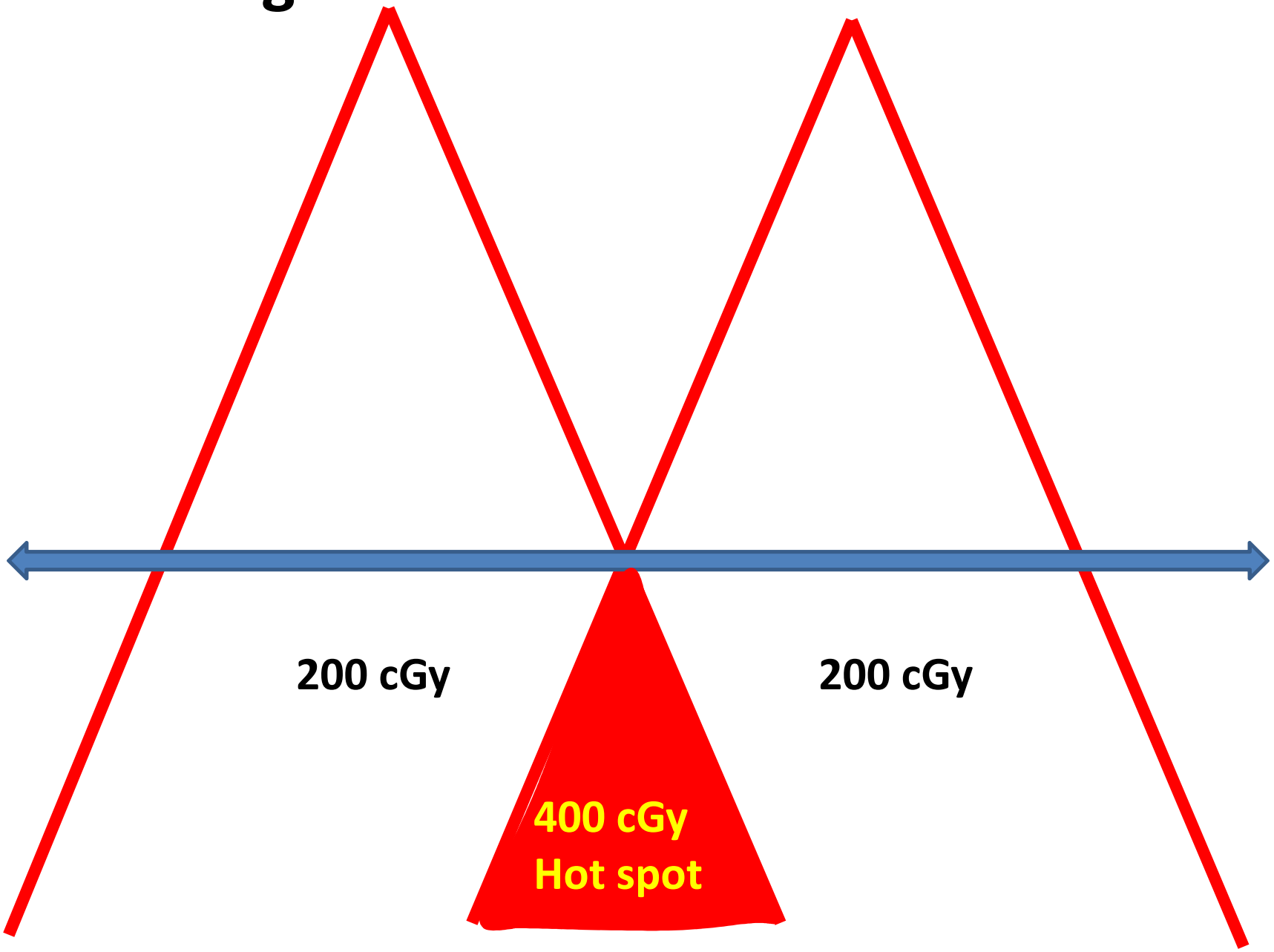


Difficulties in RT Delivery

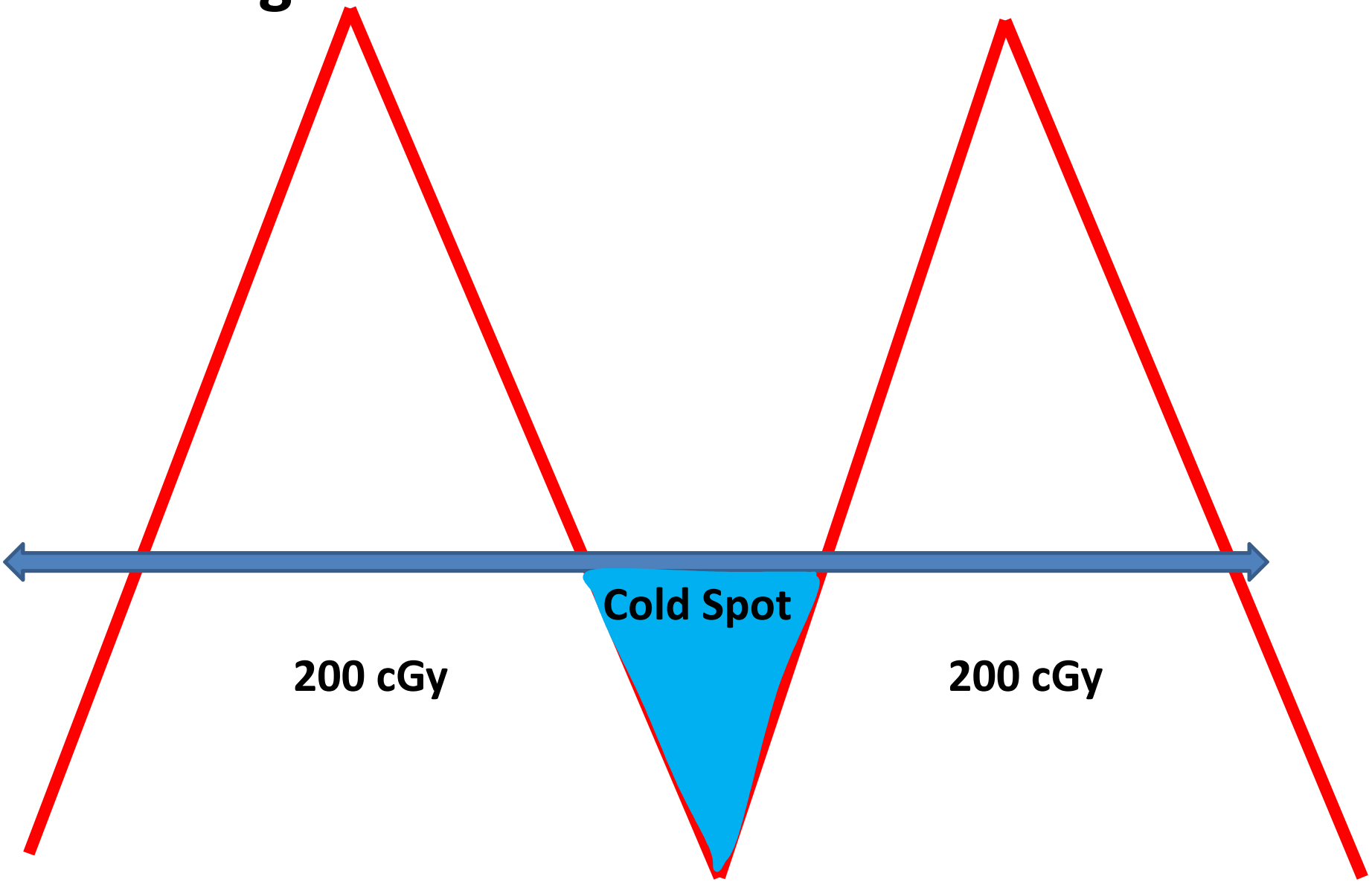
1.Matching of the adjacent Radiation Fields



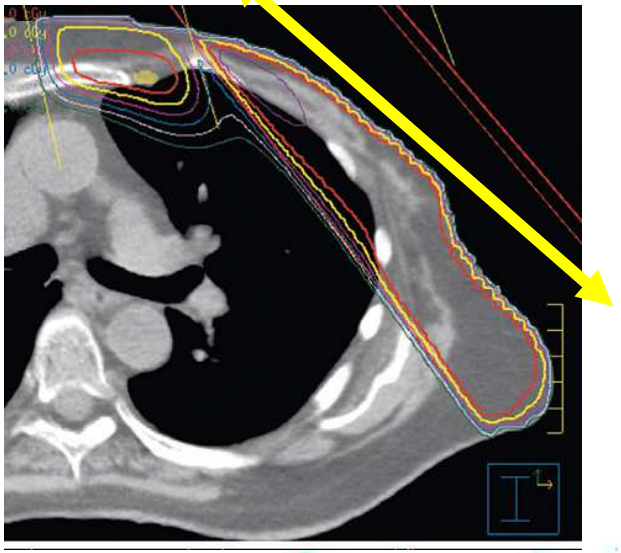
Divergent Nature of the Radiation Beam

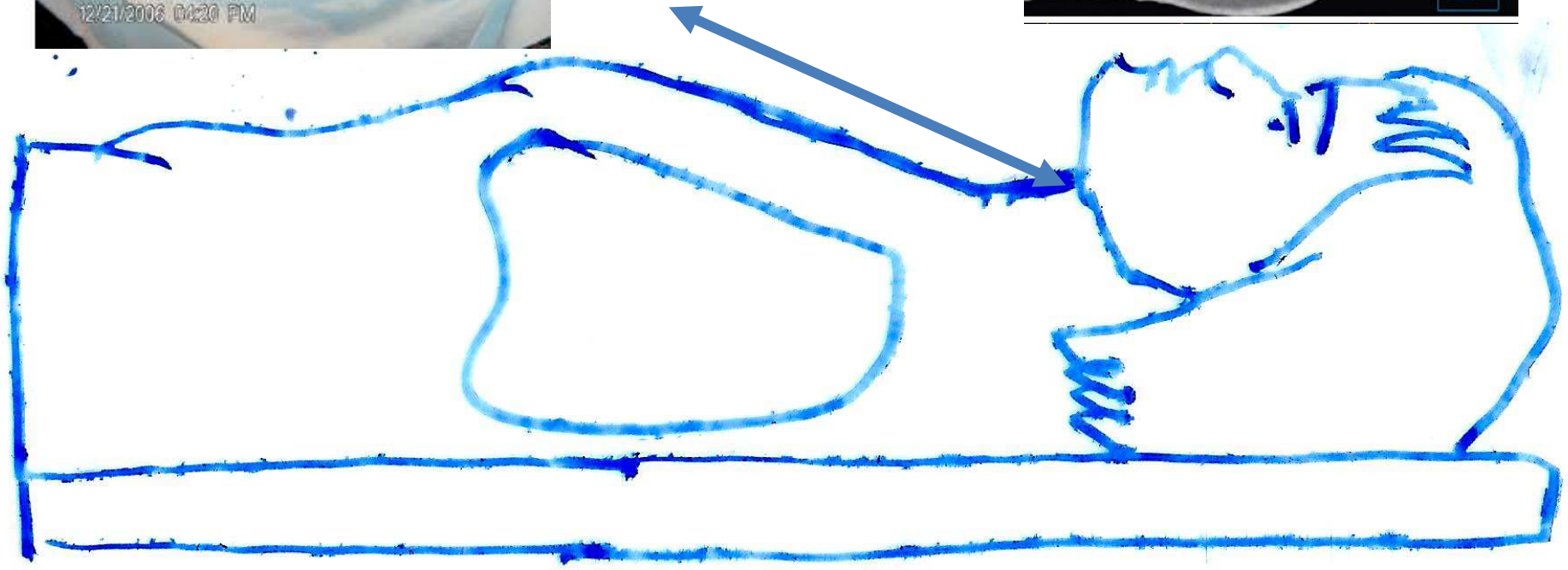


Divergent Nature of the Radiation Beam

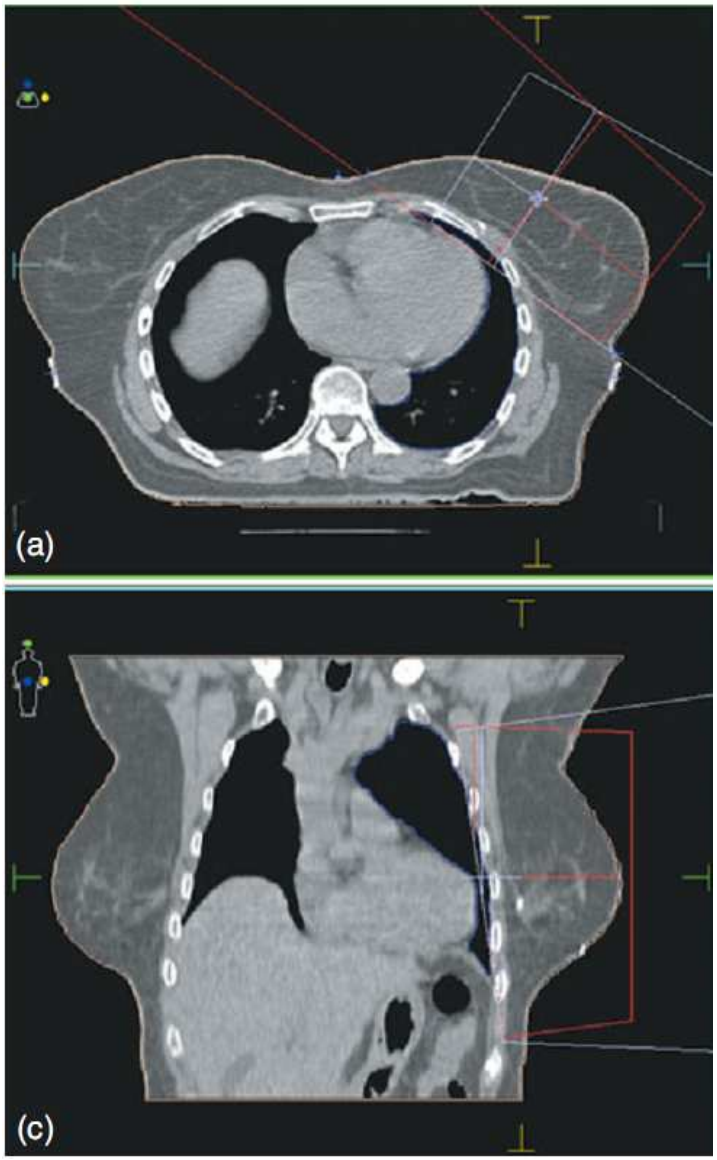


2. Sloping Chest Wall





3.Underlying Heart and Lung



Matching of the Adjacent radiation fields

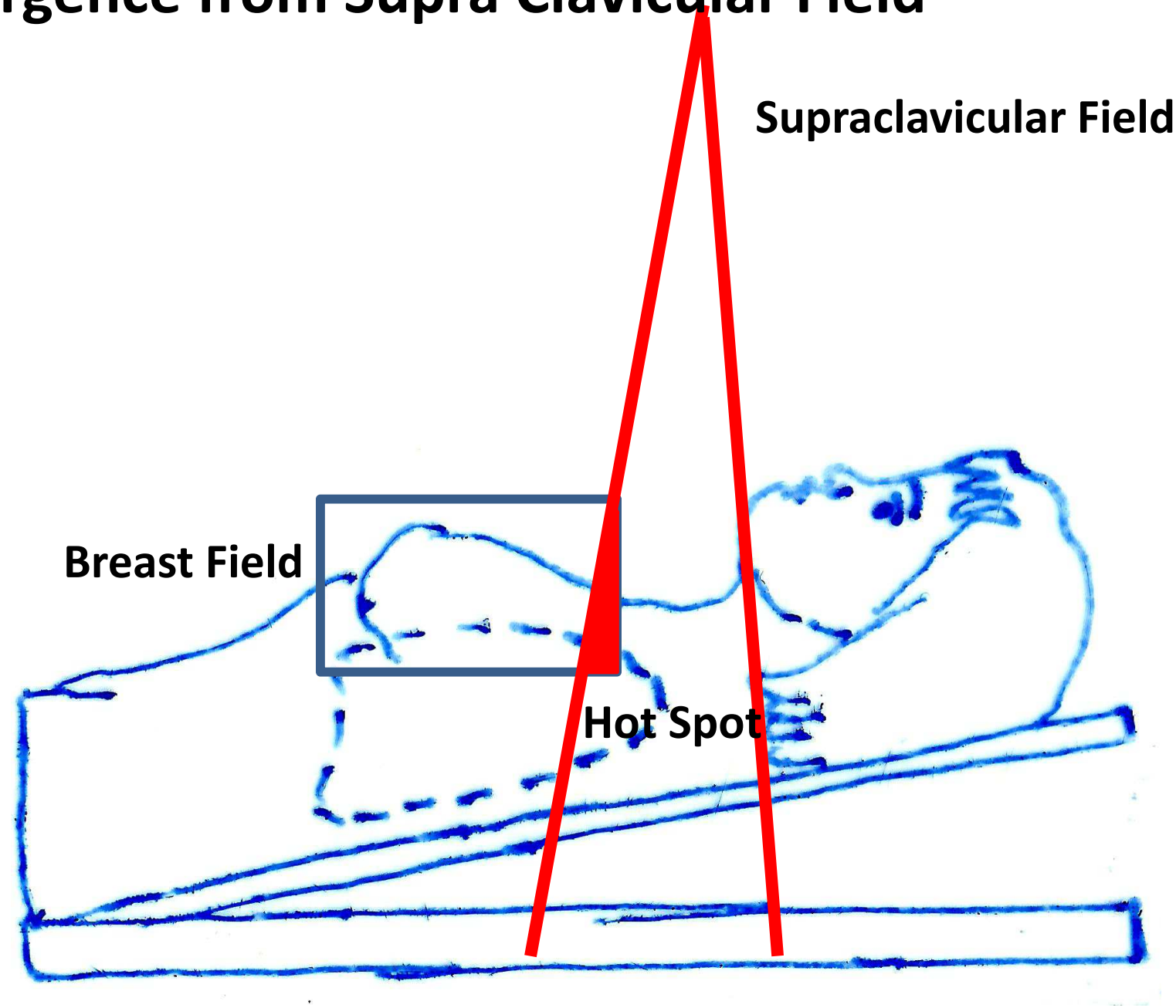
- **Matching of S/C and Tangent fields**

  Two Divergence

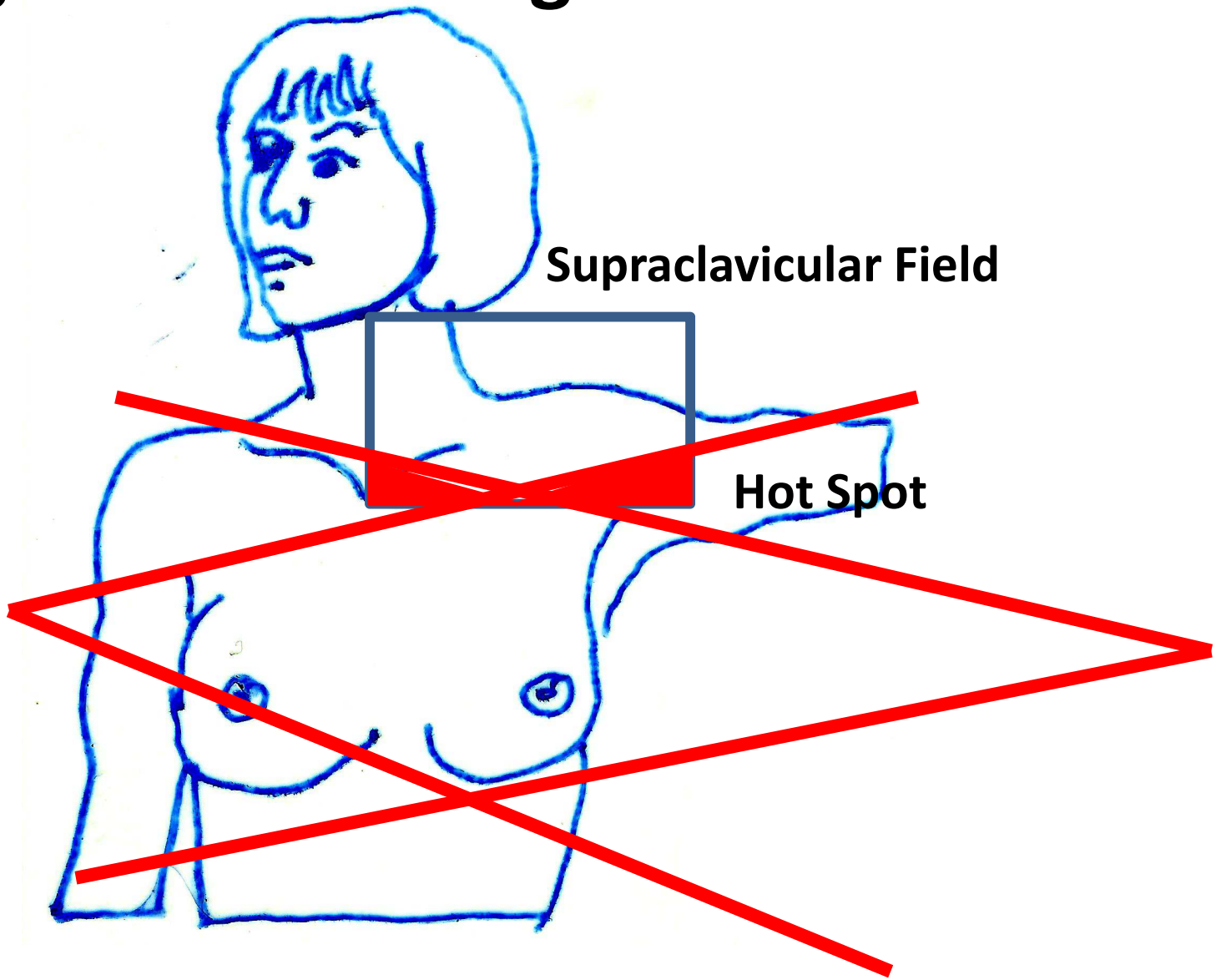
  1. **Divergence from Supra clavicular field**

  2. **Divergence from Tangential field**

Divergence from Supra Clavicular Field

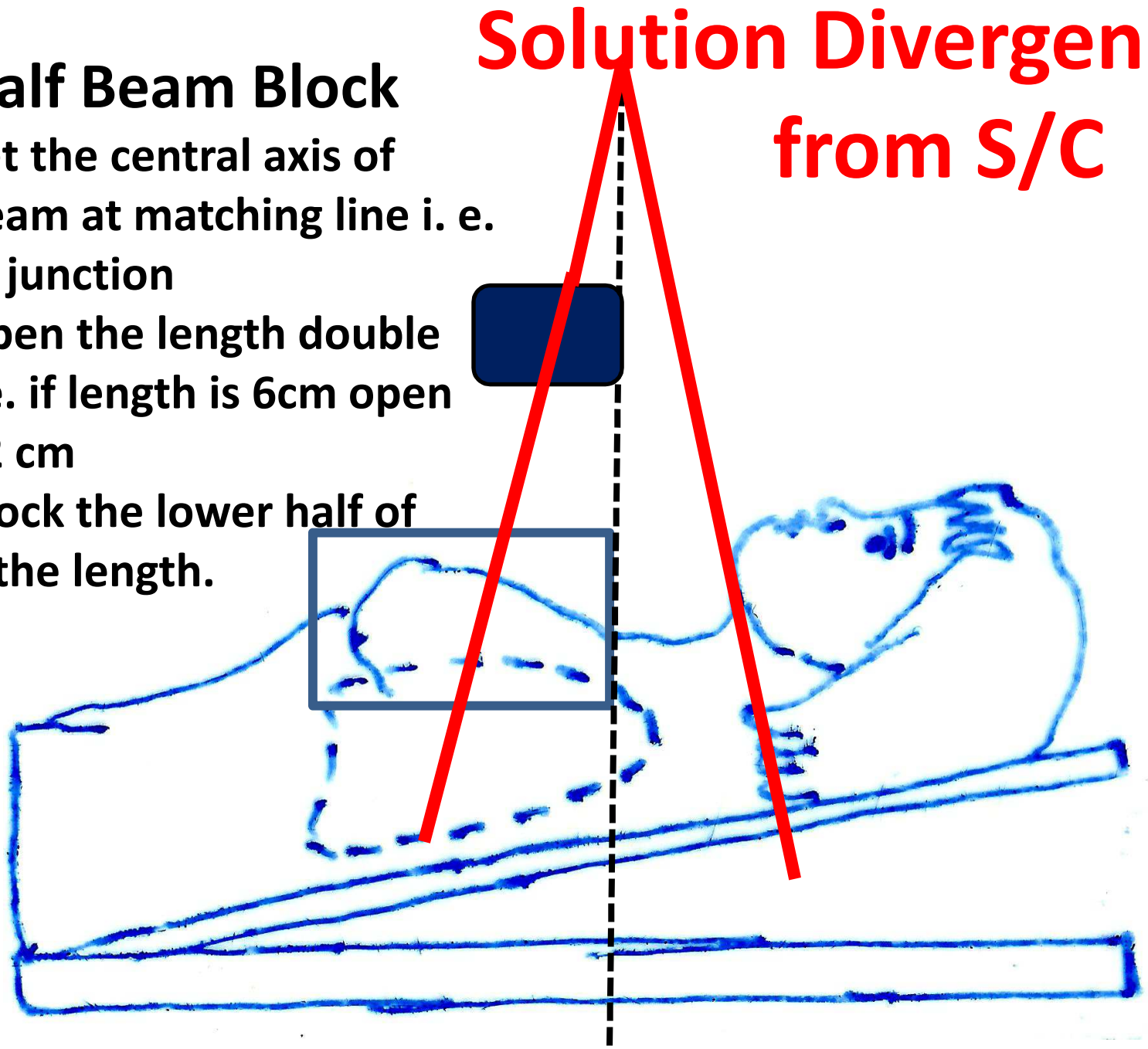


Divergence from Tangential



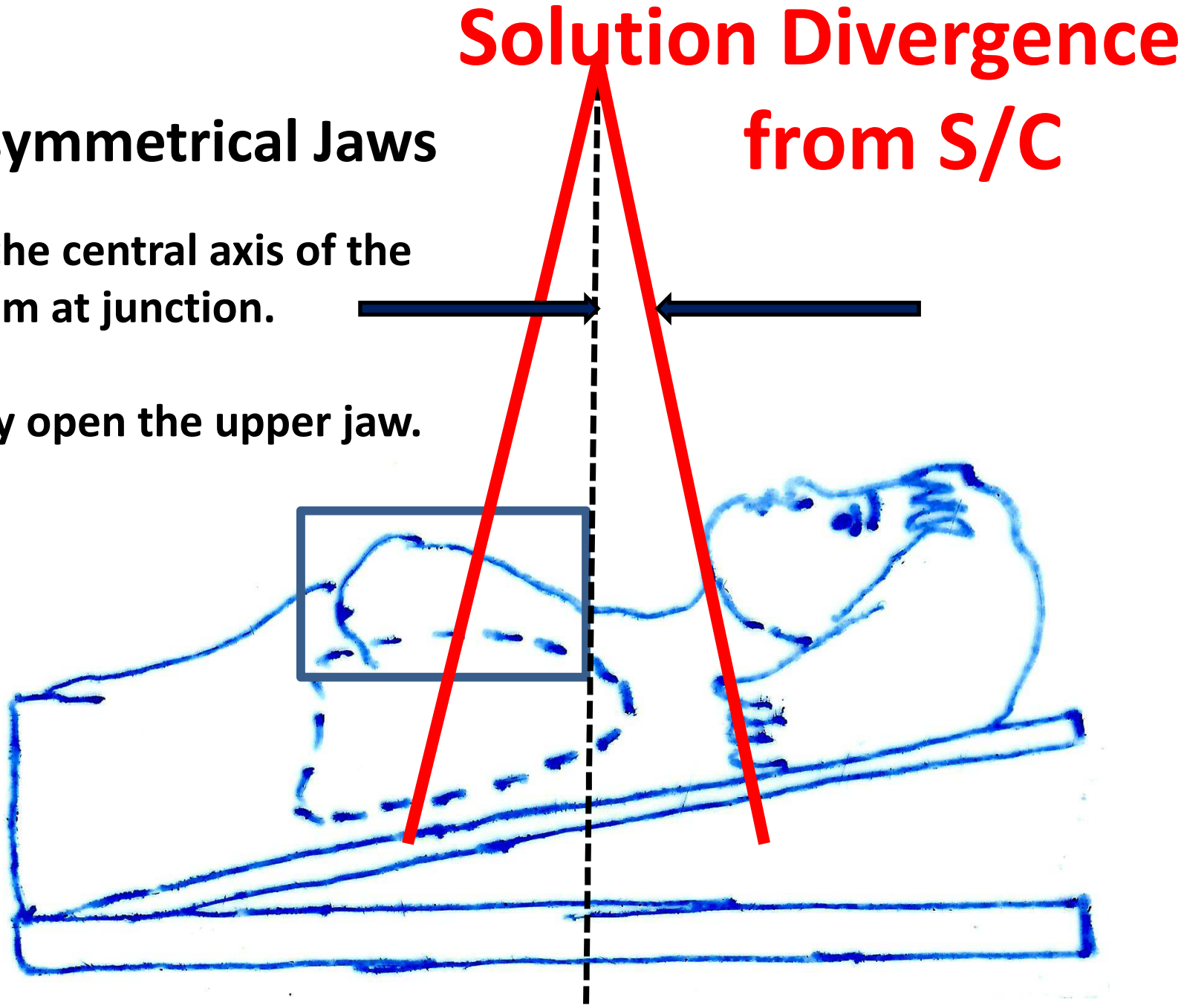
1. Half Beam Block

- Set the central axis of beam at matching line i. e. at junction
- Open the length double i.e. if length is 6cm open 12 cm
- Block the lower half of the length.



2. Asymmetrical Jaws

- Set the central axis of the beam at junction.
- Only open the upper jaw.



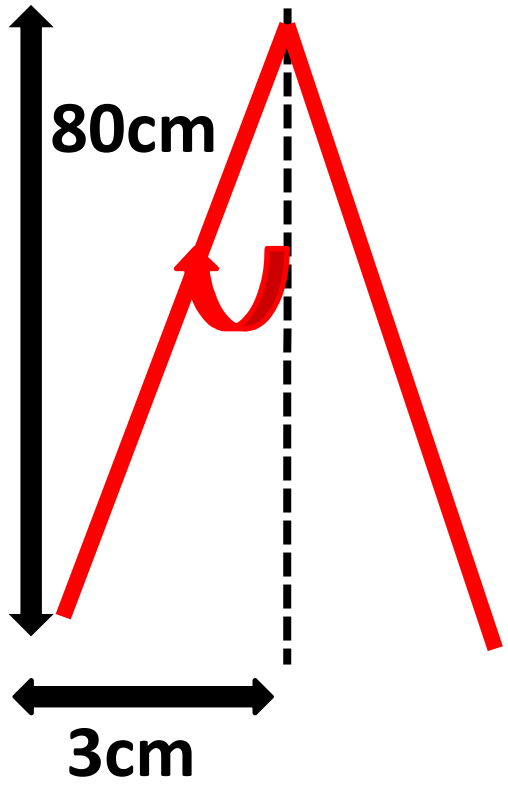
Solution Divergence from S/C

3. Gantry Rotation:

- First calculate the angle of divergence from s/c field

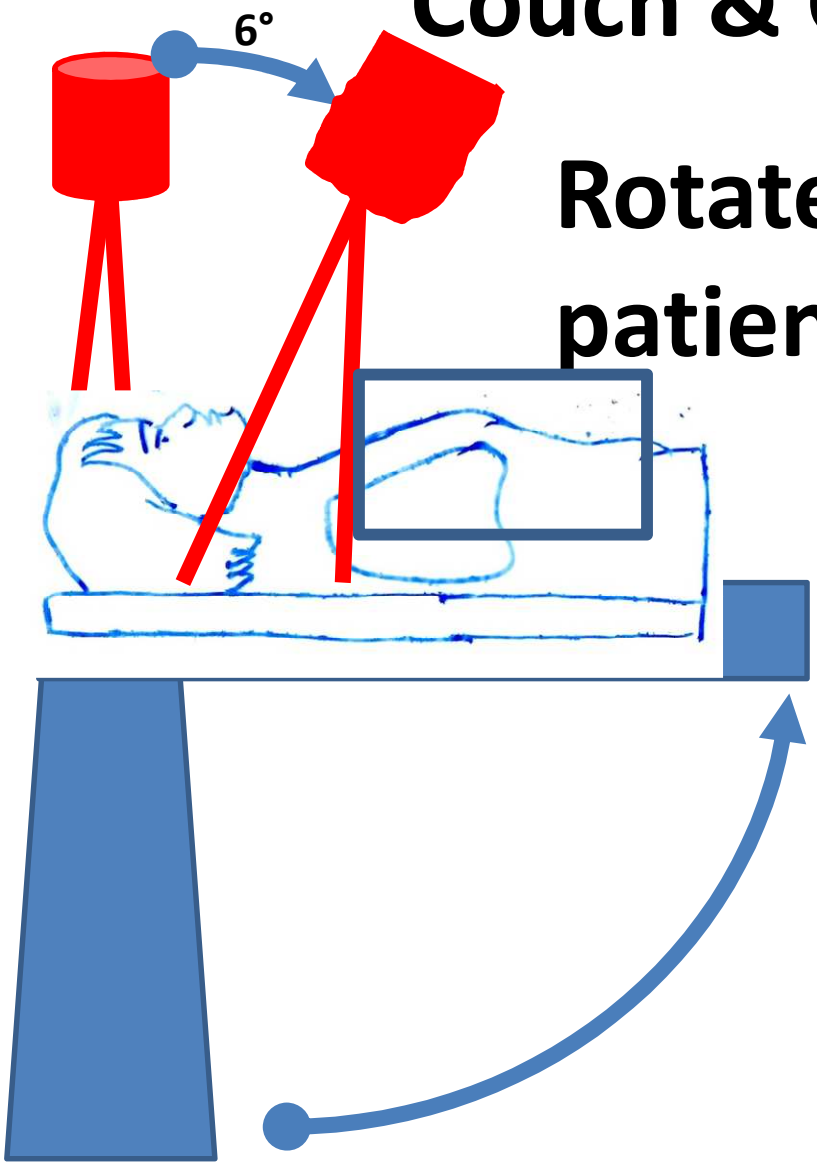
$$\text{Tan}\varnothing = \frac{\text{Half field length}}{\text{SSD}}$$

6^0



- Move couch 90°
- Rotate gantry 6° towards patient feet

Couch & Gantry Rotation



Rotate towards patient's feet


Equinox

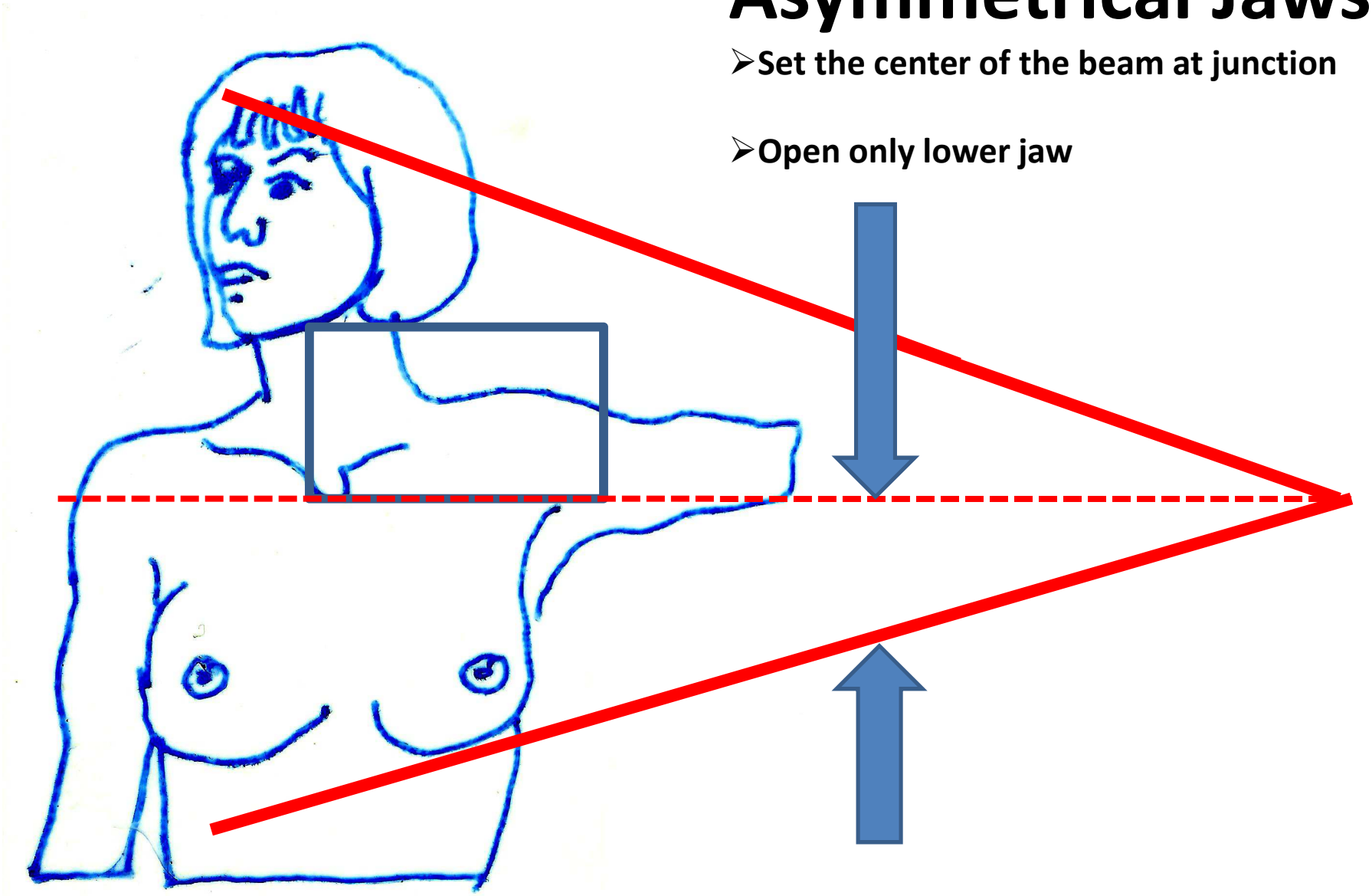

Equinox


Equinox

Solution Divergence from Tangent

Asymmetrical Jaws

- Set the center of the beam at junction
- Open only lower jaw



Solution Divergence from Tangent

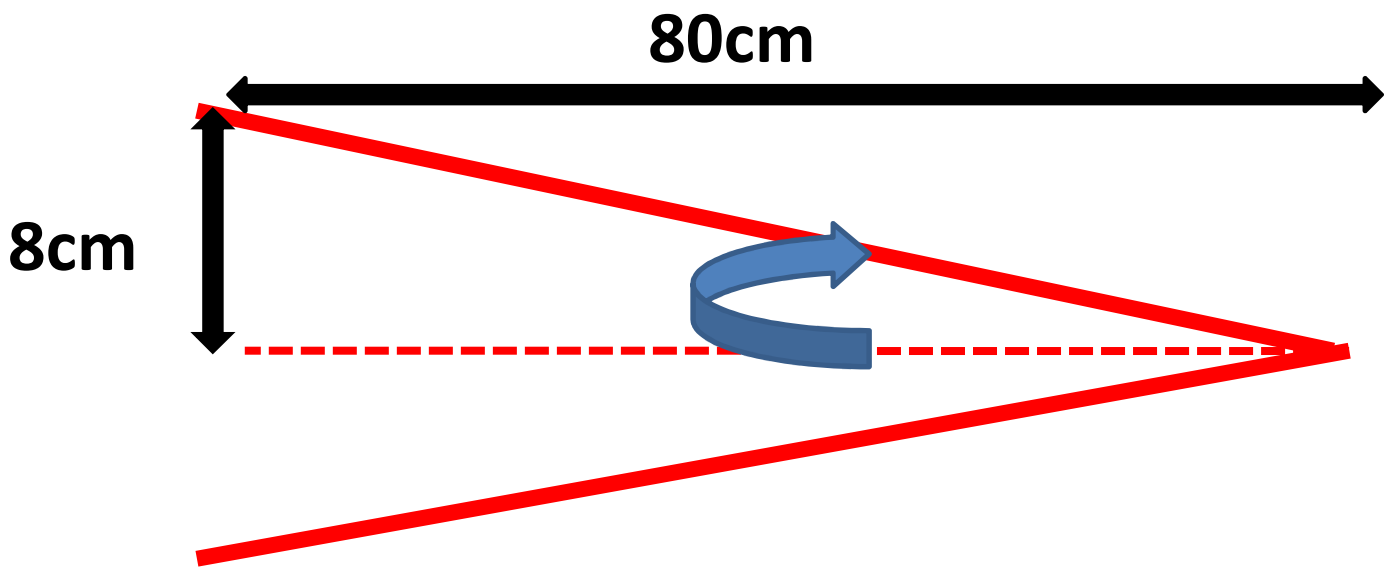
Couch Rotation

(a) Calculate the angle of divergence

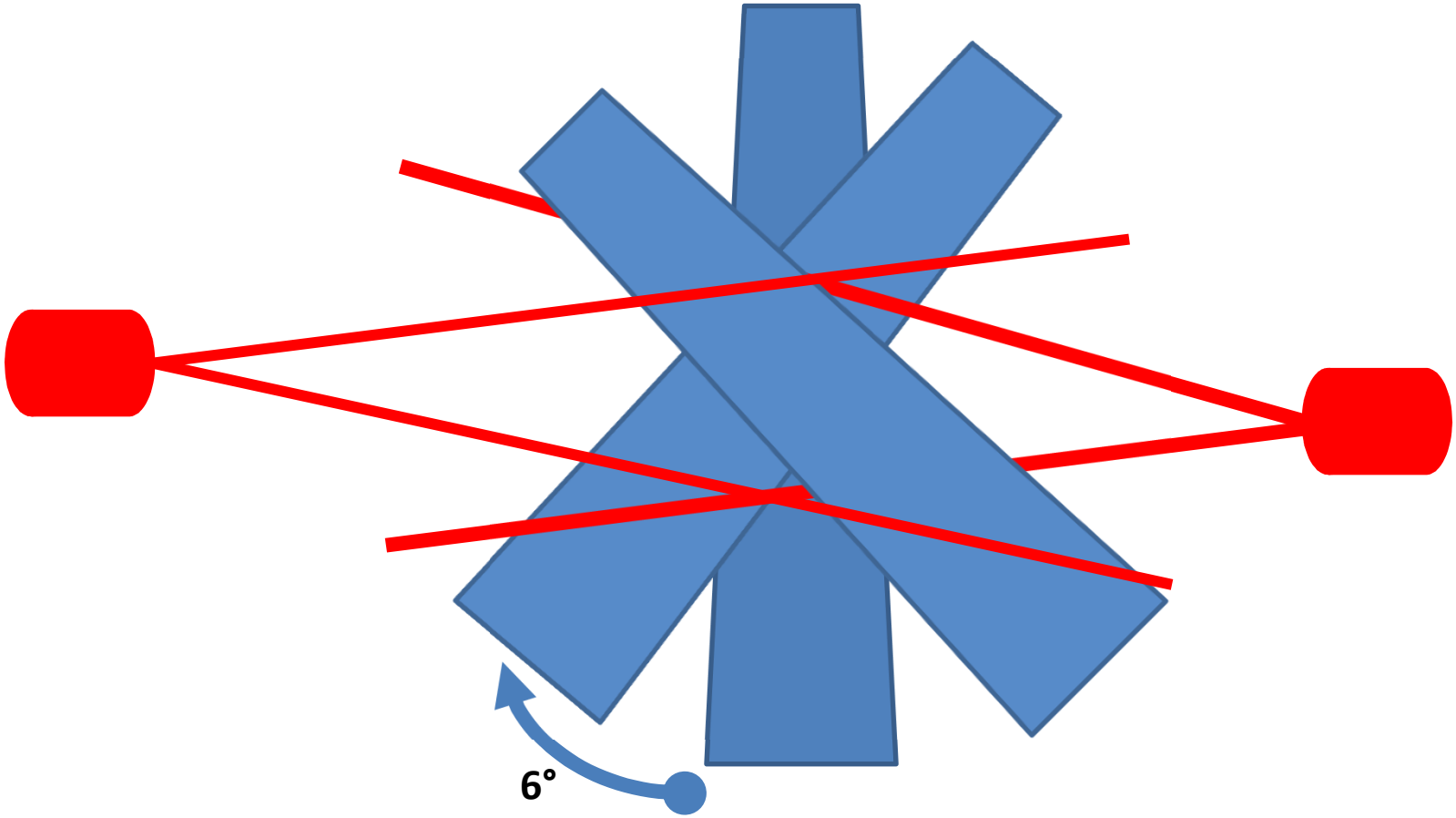
6°

(b) Set the tangential field as usual

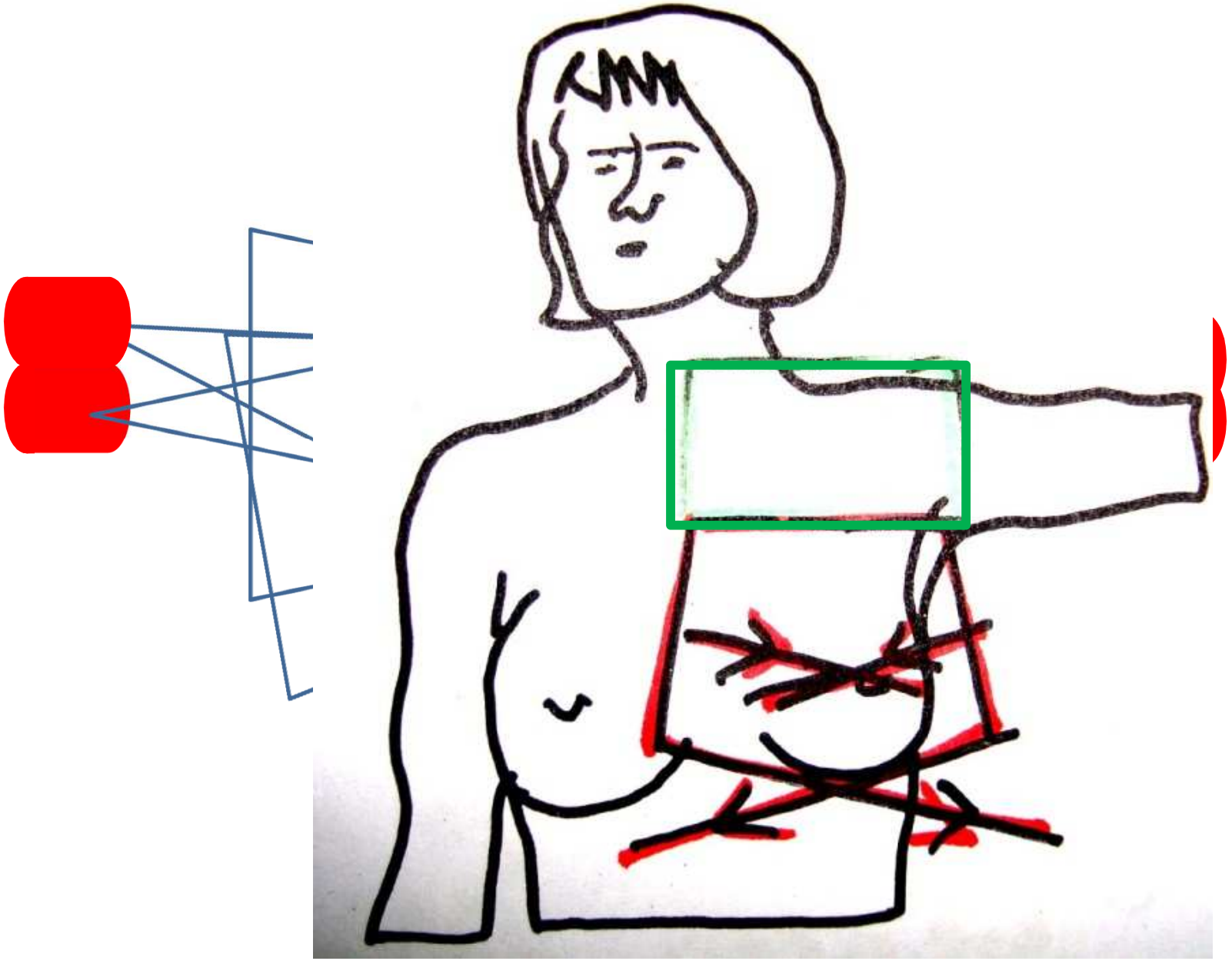
(b) Give couch twist 6° away from gantry in both MT and LT



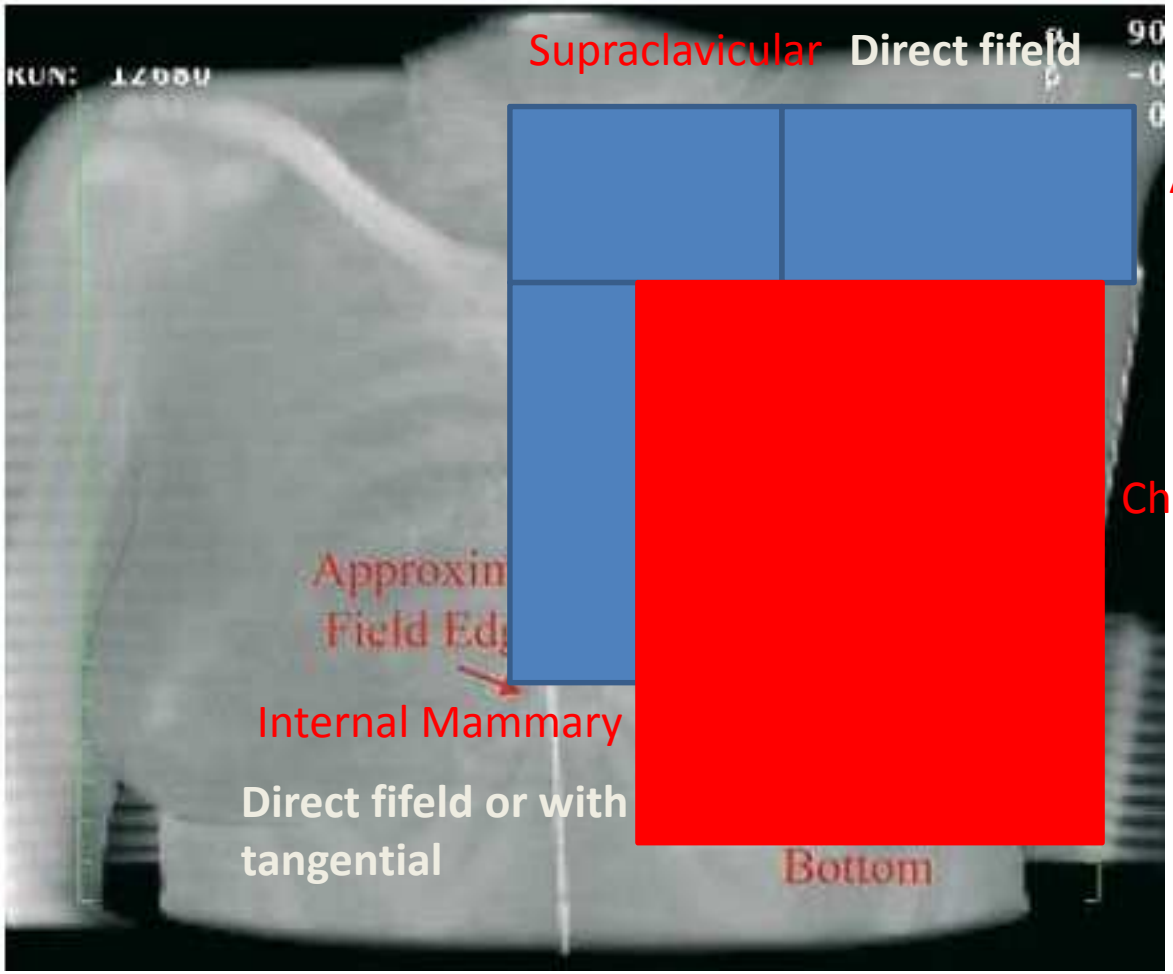
Couch Rotation: Away from the Gantry



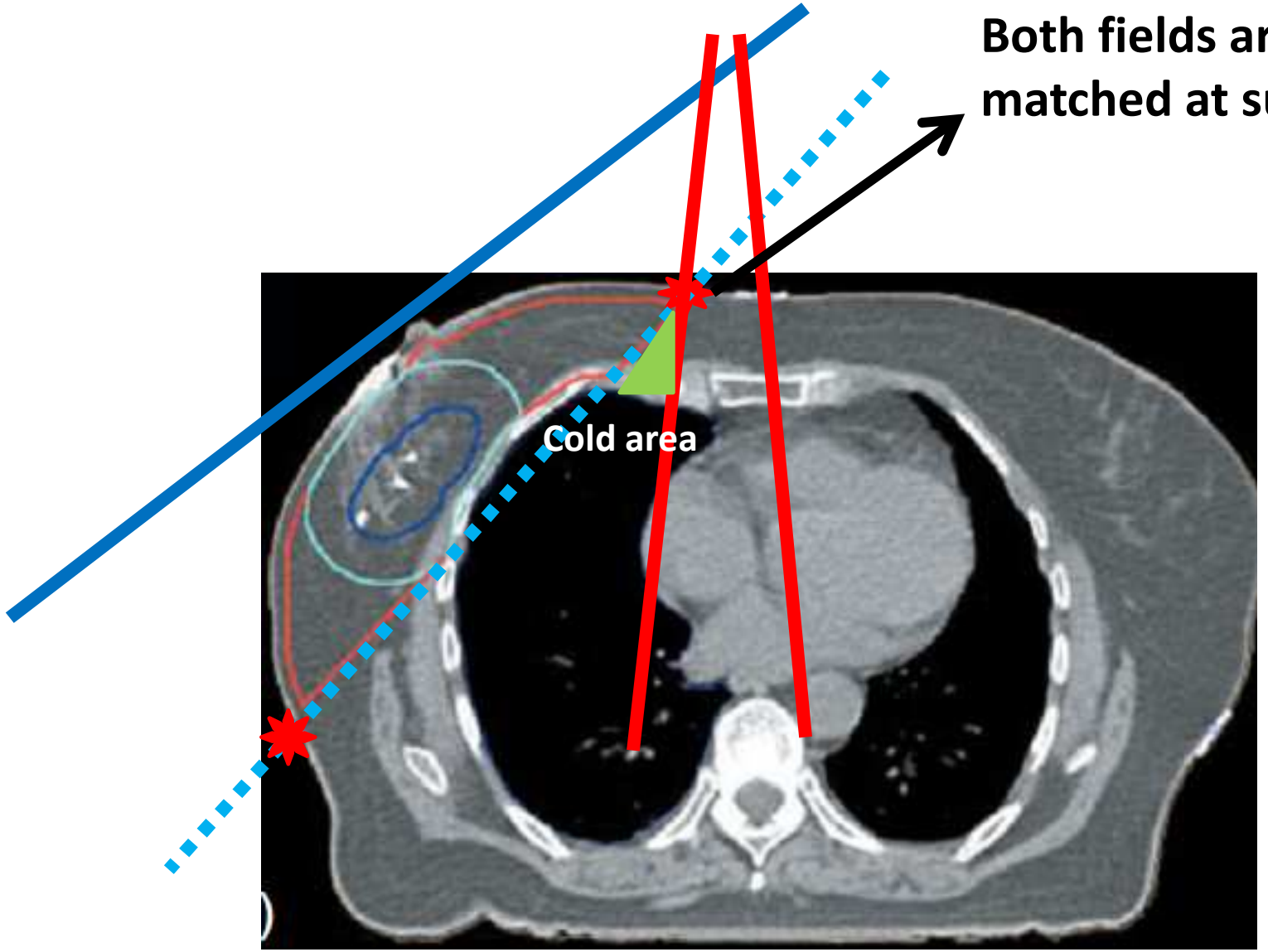
Couch Rotation: Away from the Gantry



Matching between Internal Mammary and Tangential fields



Both fields are matched at surface,.

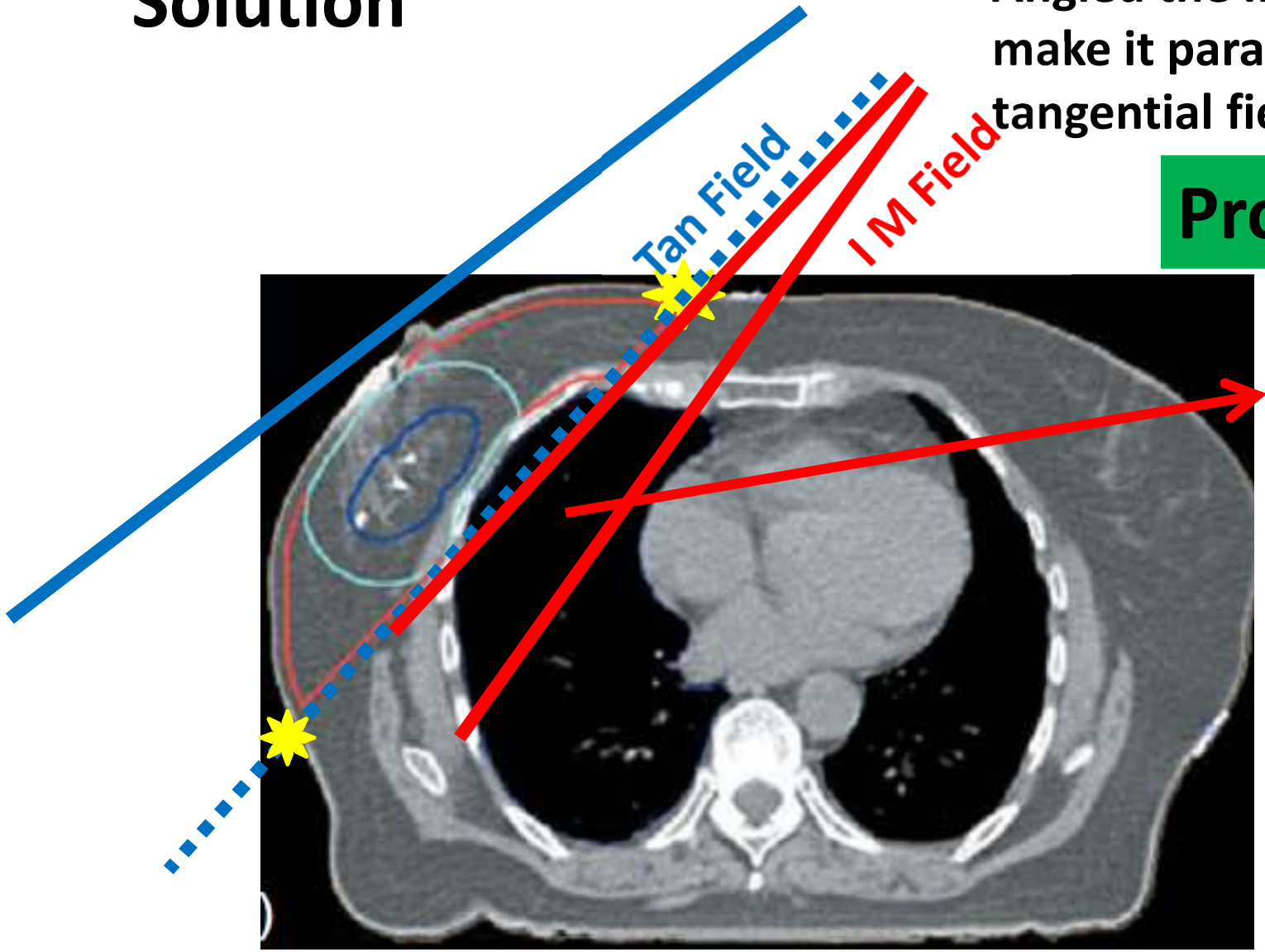


WHY?

Because both fields are angled in different direction

Solution

Angled the IM field to make it parallel to the tangential field



Problem

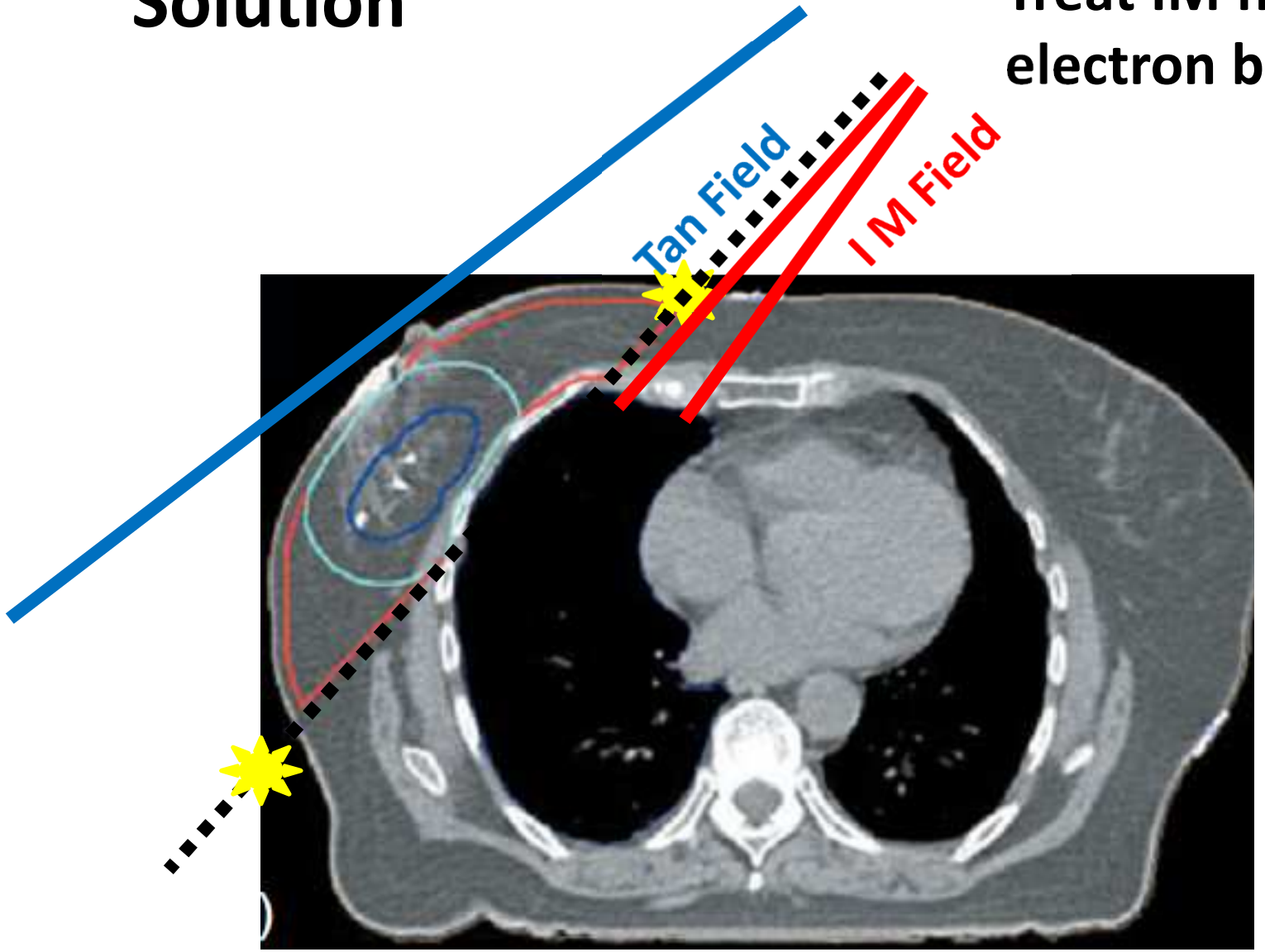
More lung will be irradiated by IM field.

Solution

Treat IM field with electron beam

Solution

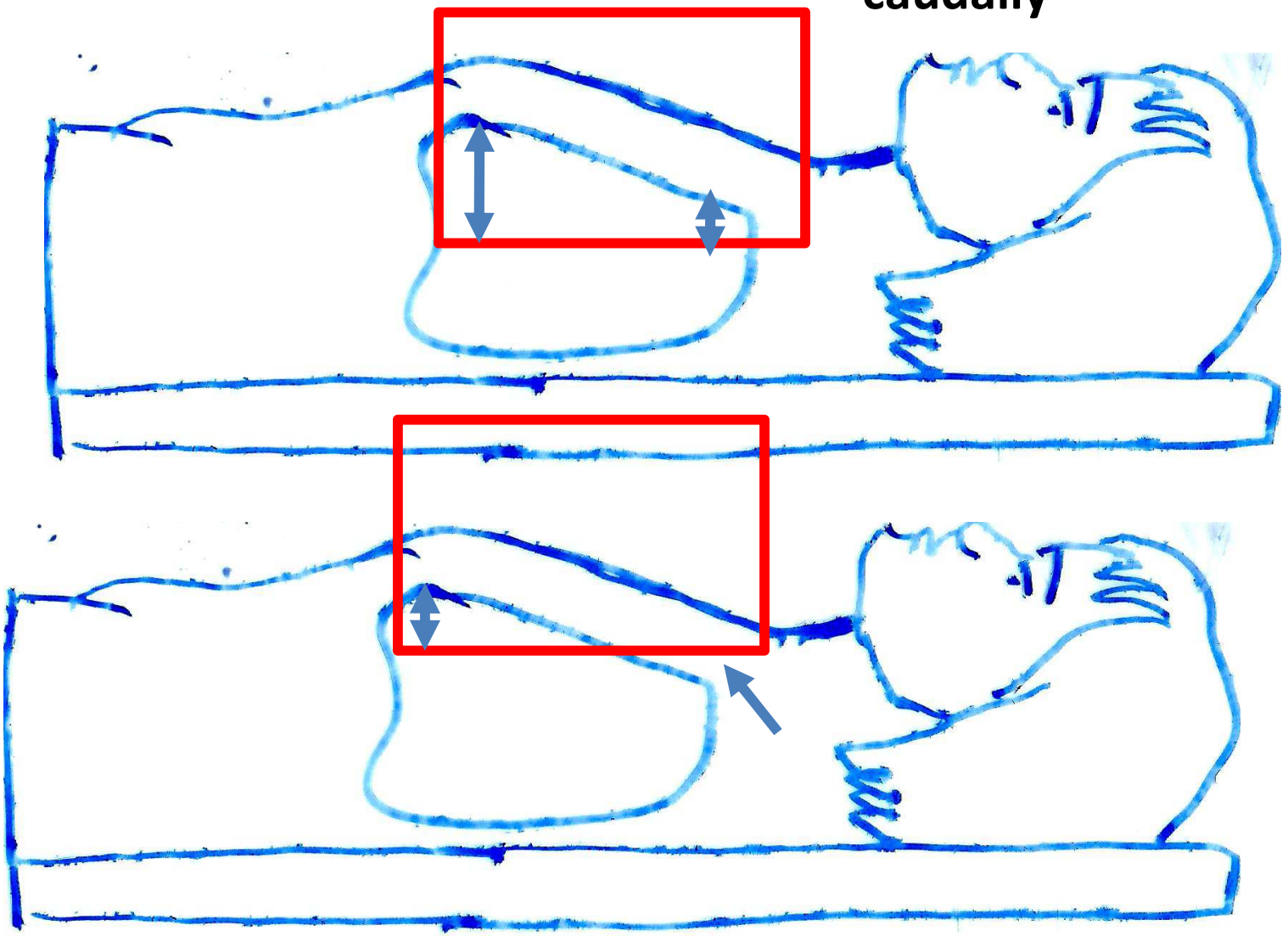
Treat IM field with electron beam



Sloping Chest Wall

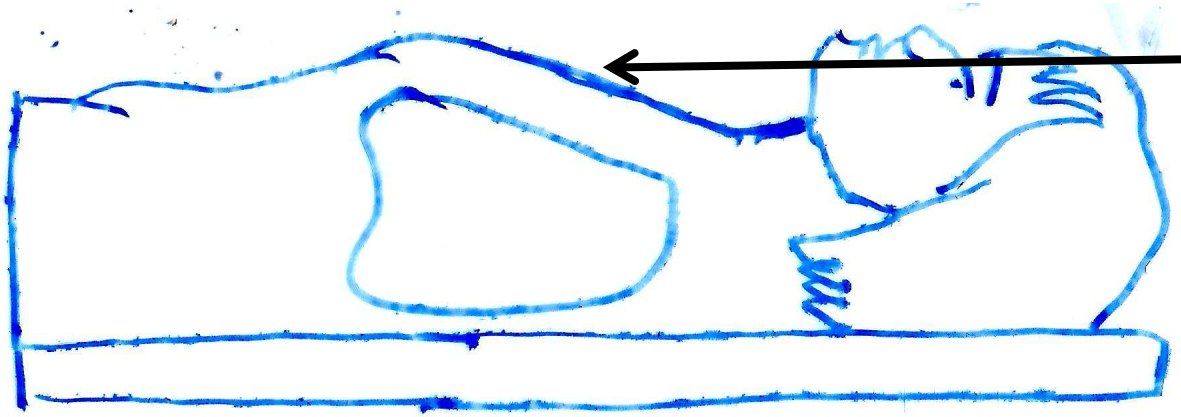
Problems

More lung comes in Tang field caudally

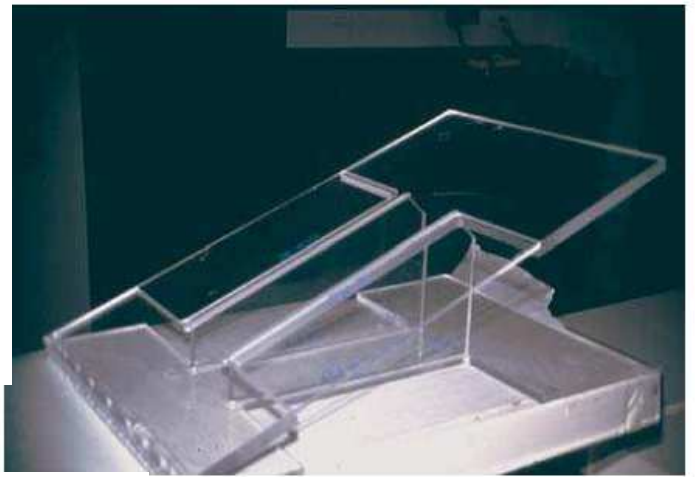


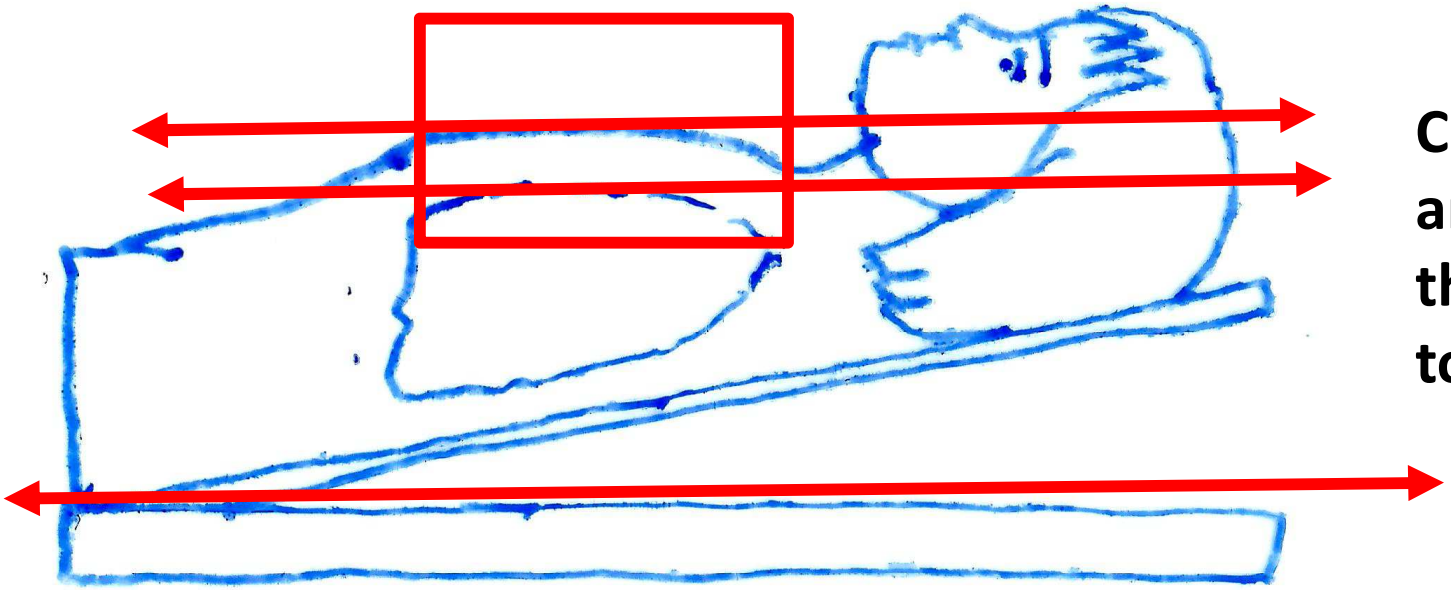
If field is set to reduce the lung caudally, then chest wall cranially will be missed

Solution 1



Sloping Chest wall



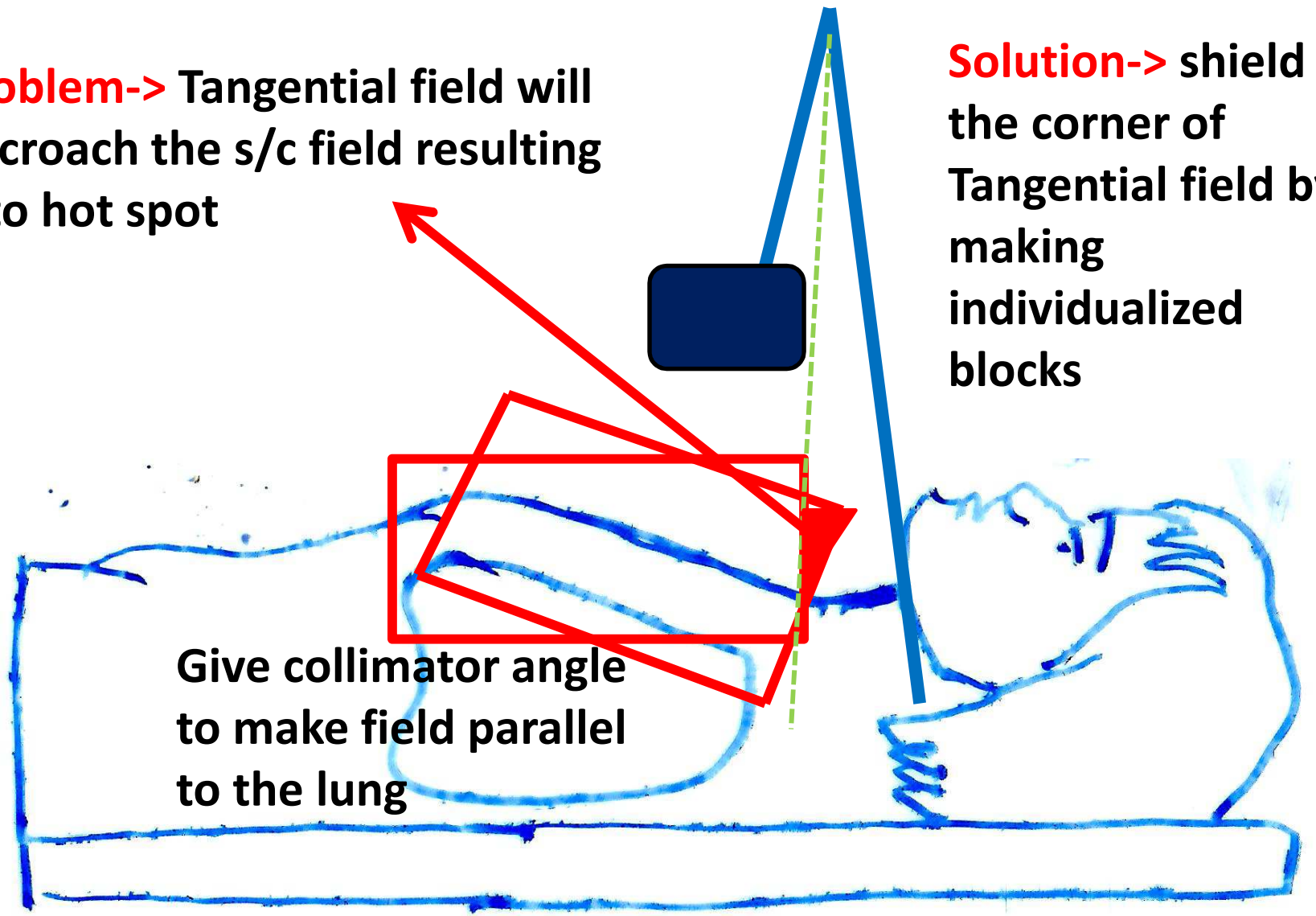


Chest wall and anterior border of the lung is parallel to the couch

Solution 2 → If Breast Board not available

Problem-> Tangential field will encroach the s/c field resulting into hot spot

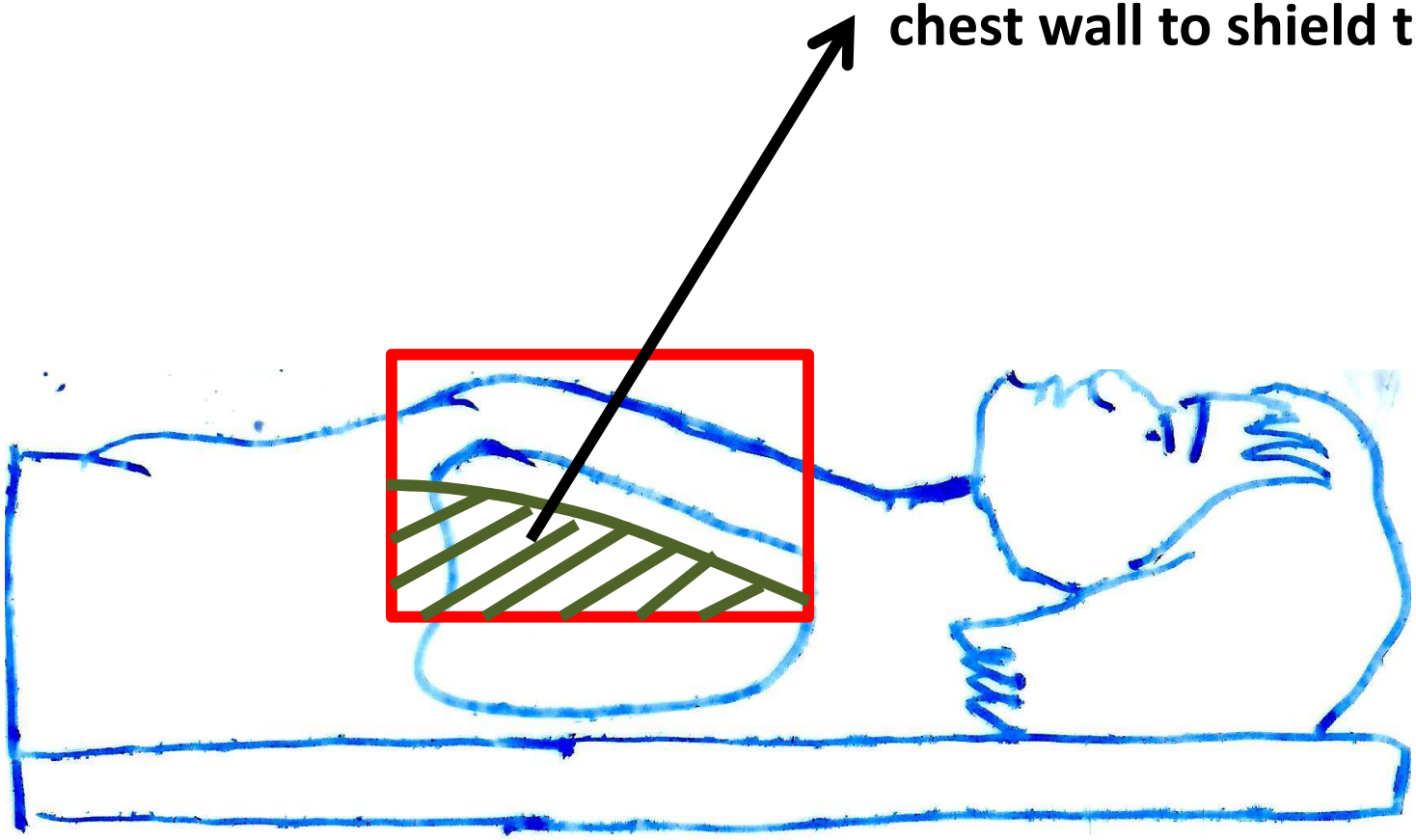
Solution-> shield the corner of Tangential field by making individualized blocks



Give collimator angle to make field parallel to the lung

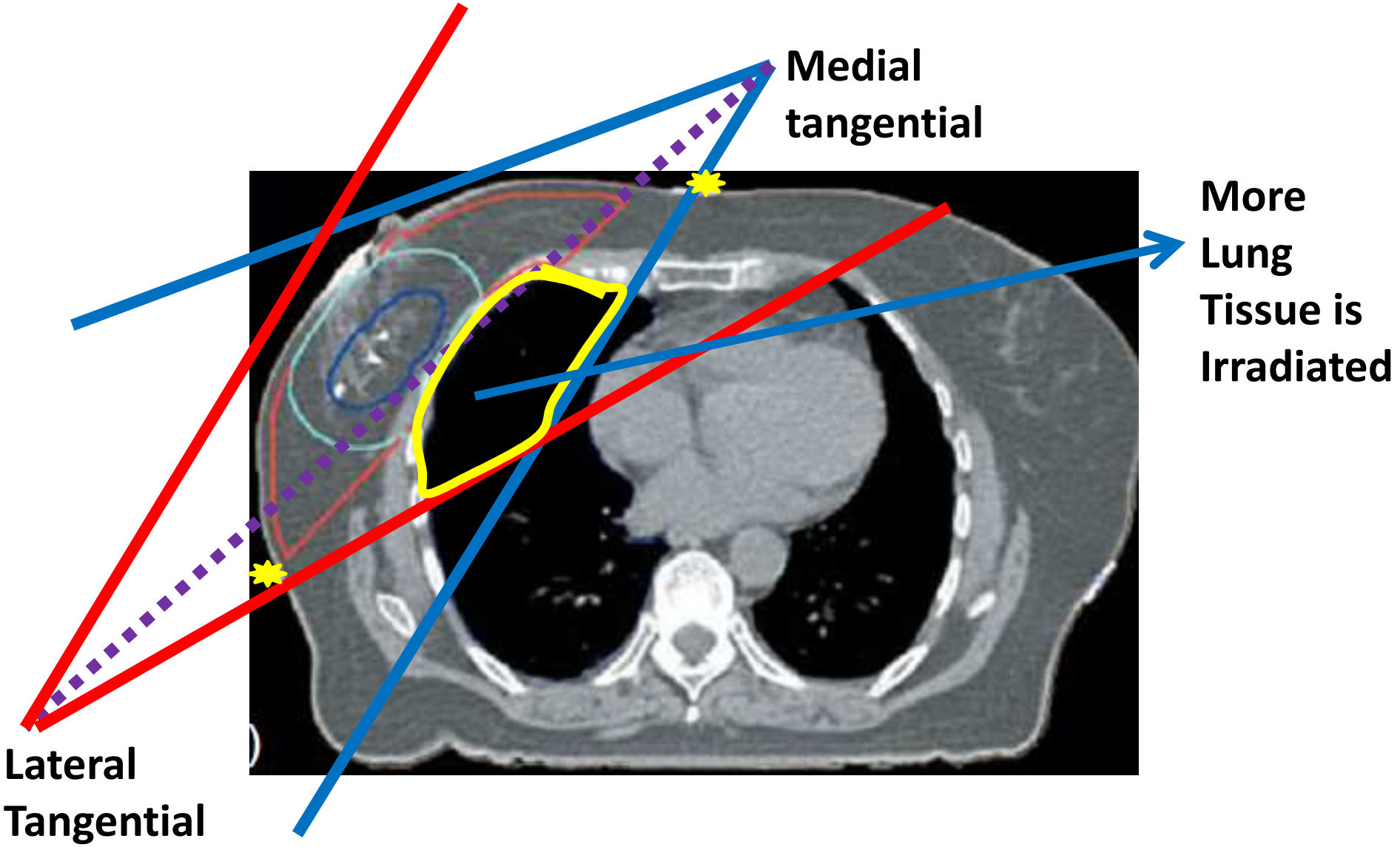
Solution 3 → If Breast Board not available

Shaped Blocks to be made individually parallel to the chest wall to shield the lung



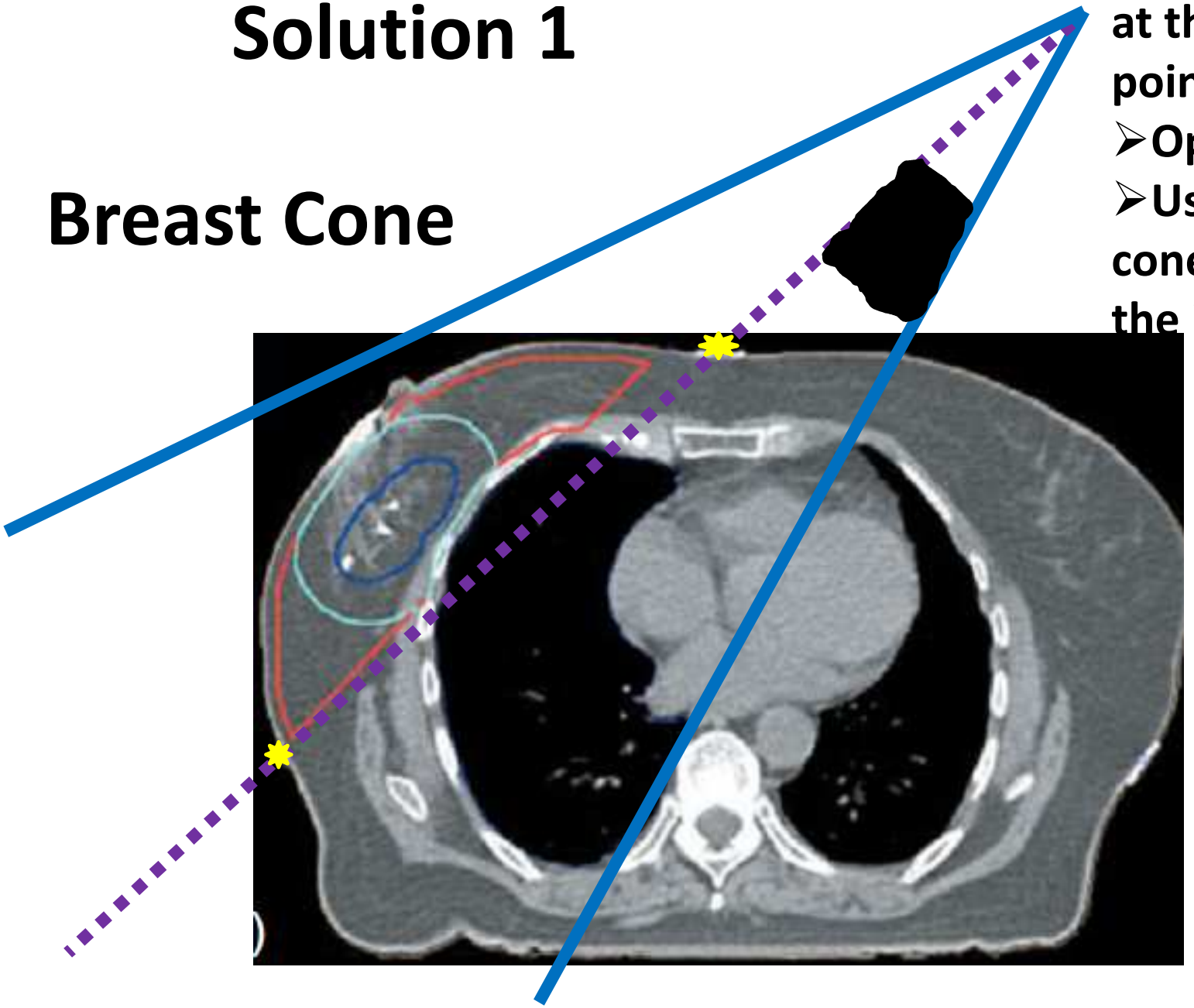
Underlying Heart and Lung

Divergence in Lung from Tangential field



Solution 1

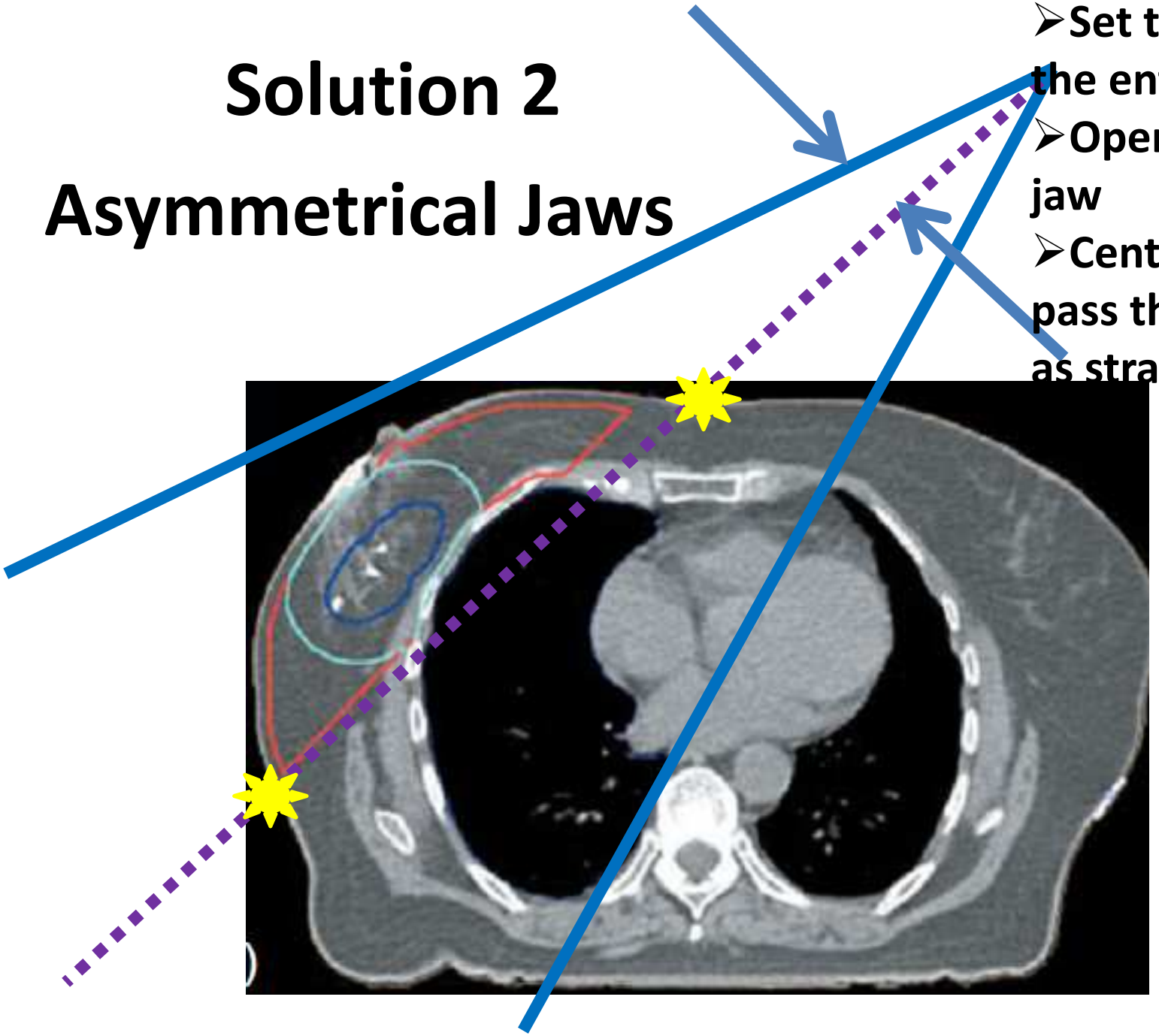
Breast Cone



- Set the center at the entry point
- Open the field
- Use breast cone to shield the inner half

Solution 2

Asymmetrical Jaws



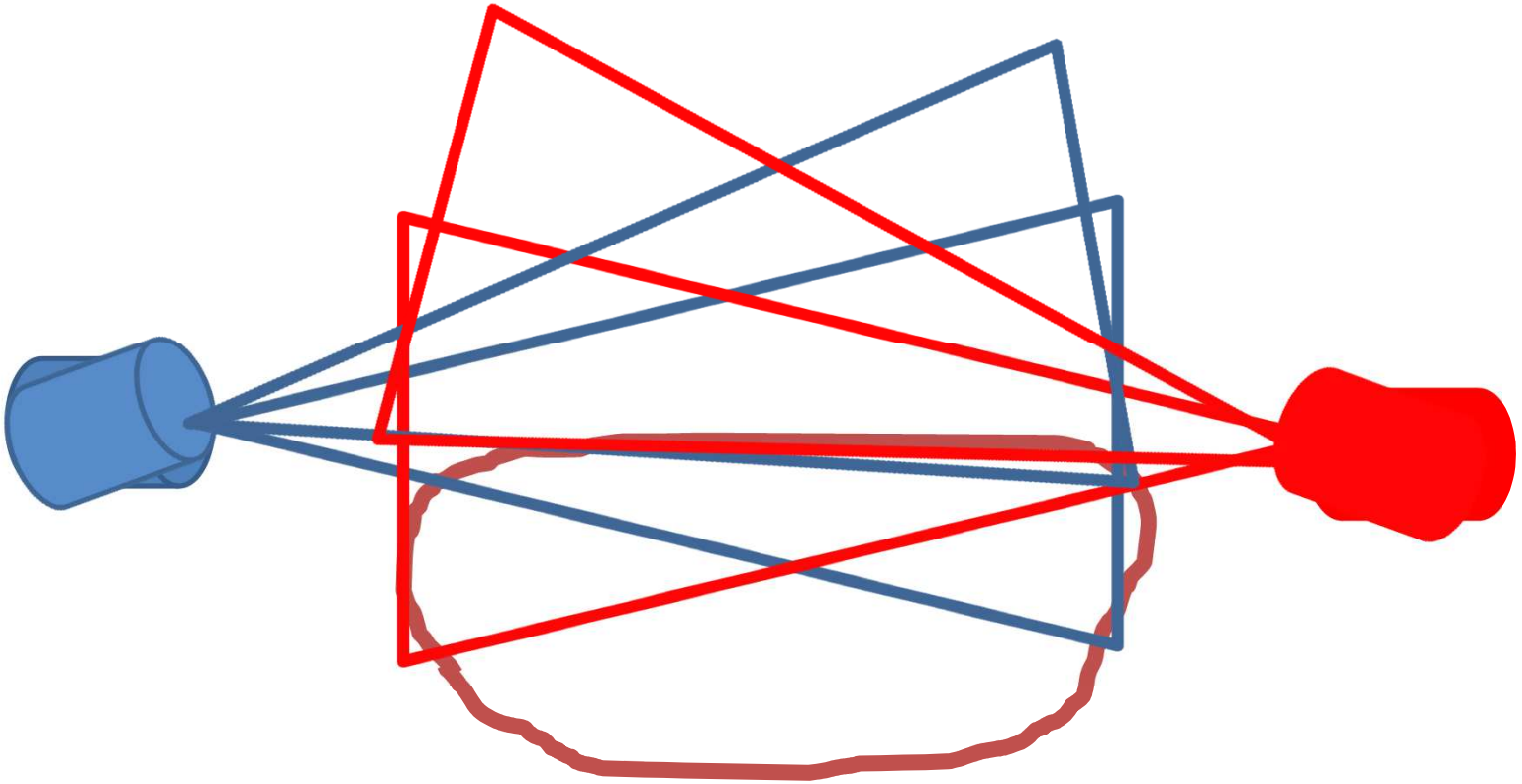
- Set the center at the entry point
- Open only one jaw
- Central axis will pass through lung as straight line

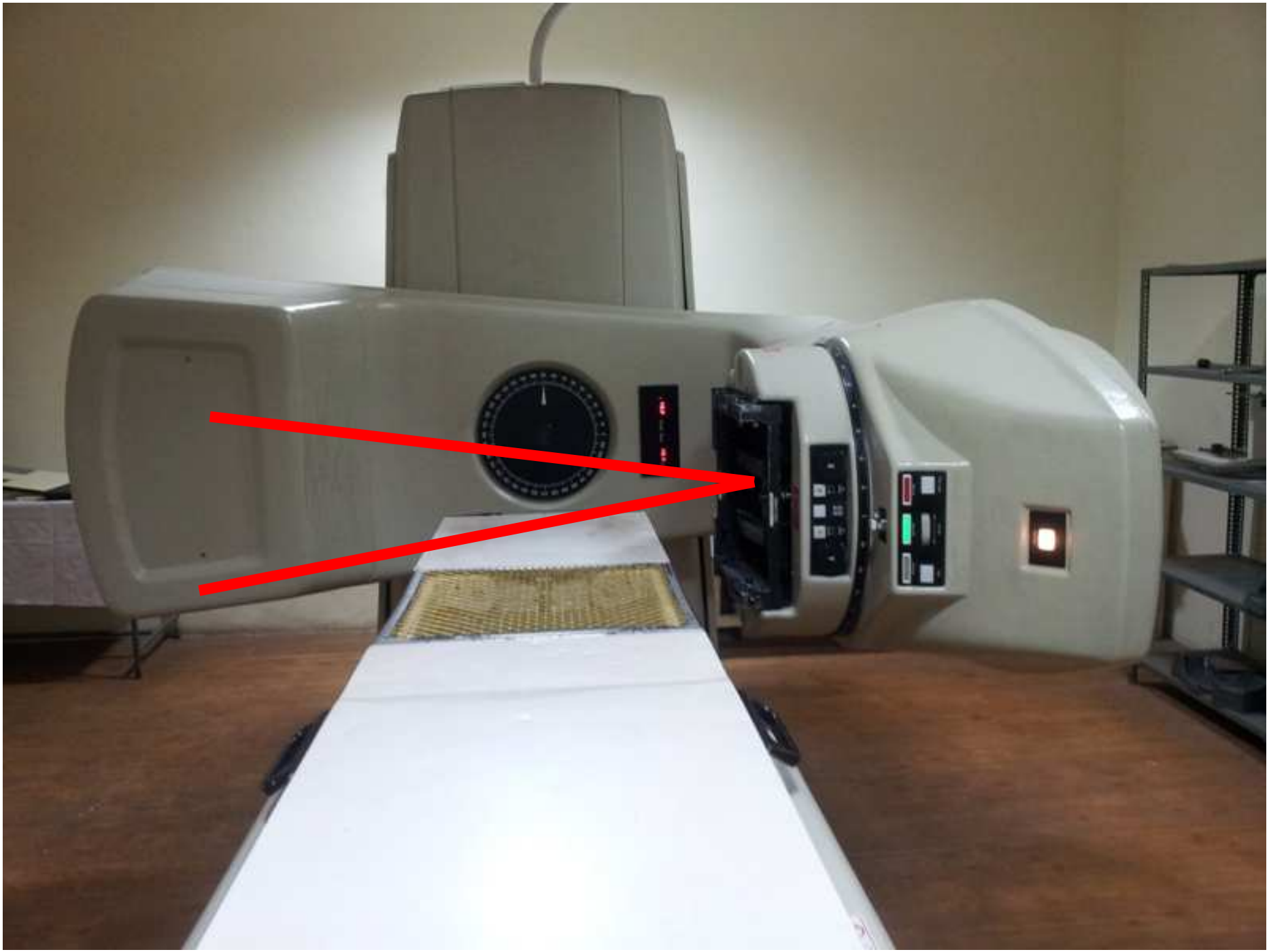
Solution 3

By Rotating gantry head upward

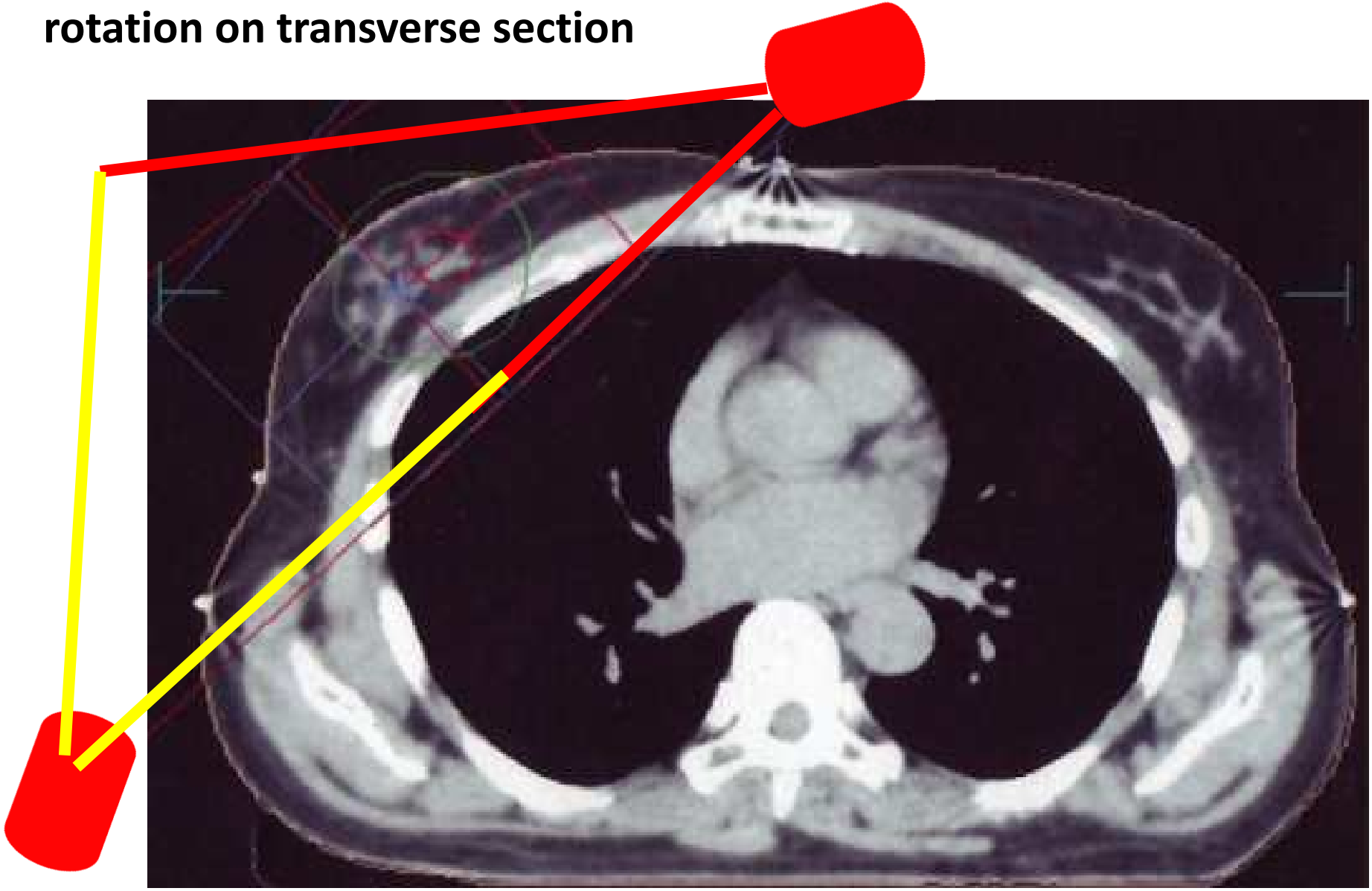
Calculate the angle of divergence by

$$\text{Tan}\varnothing = \frac{\text{Half field width}}{\text{SSD}}$$





Posterior edge of the beam becomes co-planer after gantry rotation on transverse section



Number of fields

- **If treating chest wall and all regional nodes then there are two techniques**
  - **Two fields Techniques**
  - **Three fields Techniques**

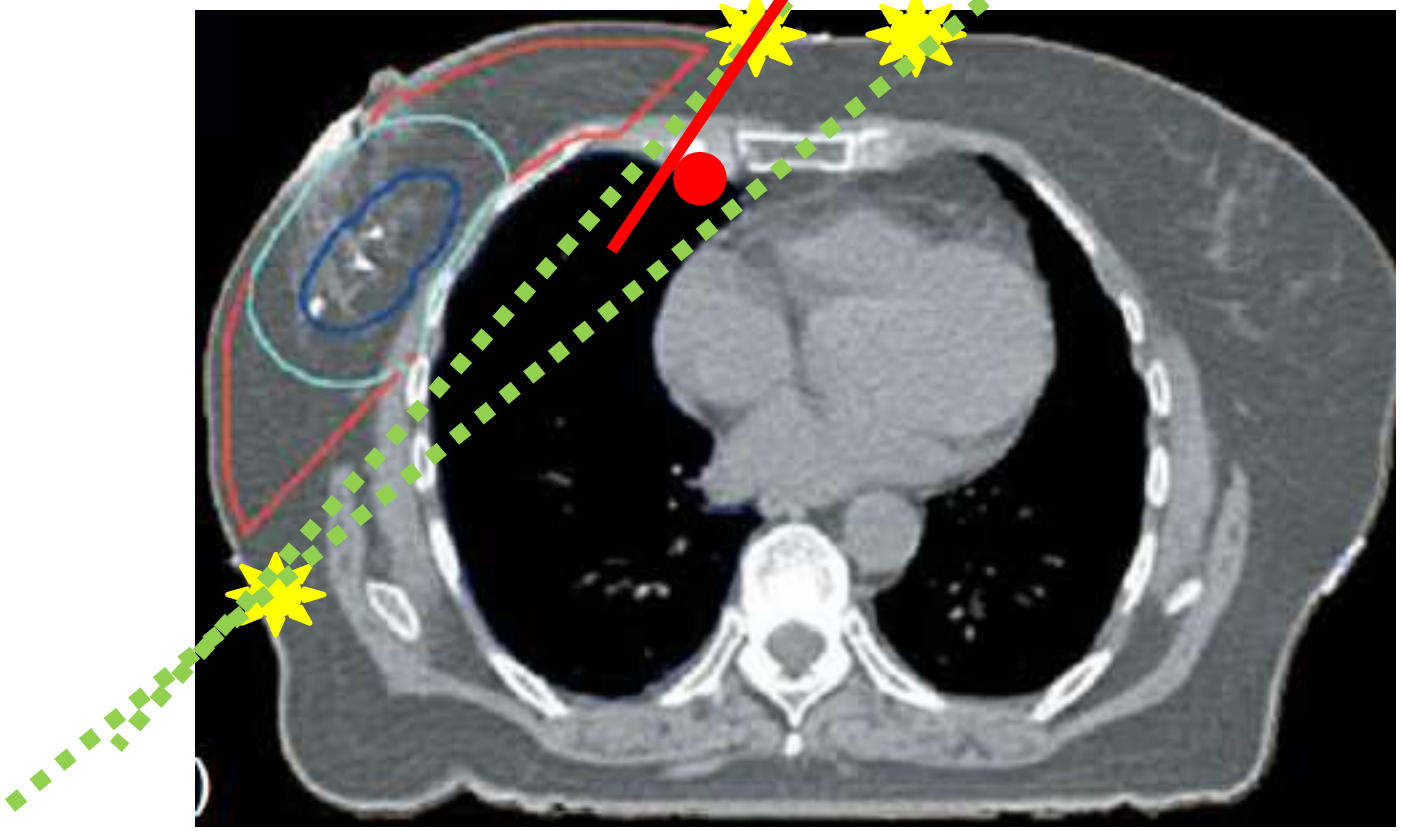
Two Field Technique

1. S/C and Axilla by single direct field
2. Internal mammary and chest wall together by tang field

Two Field Techniques

Drawbacks

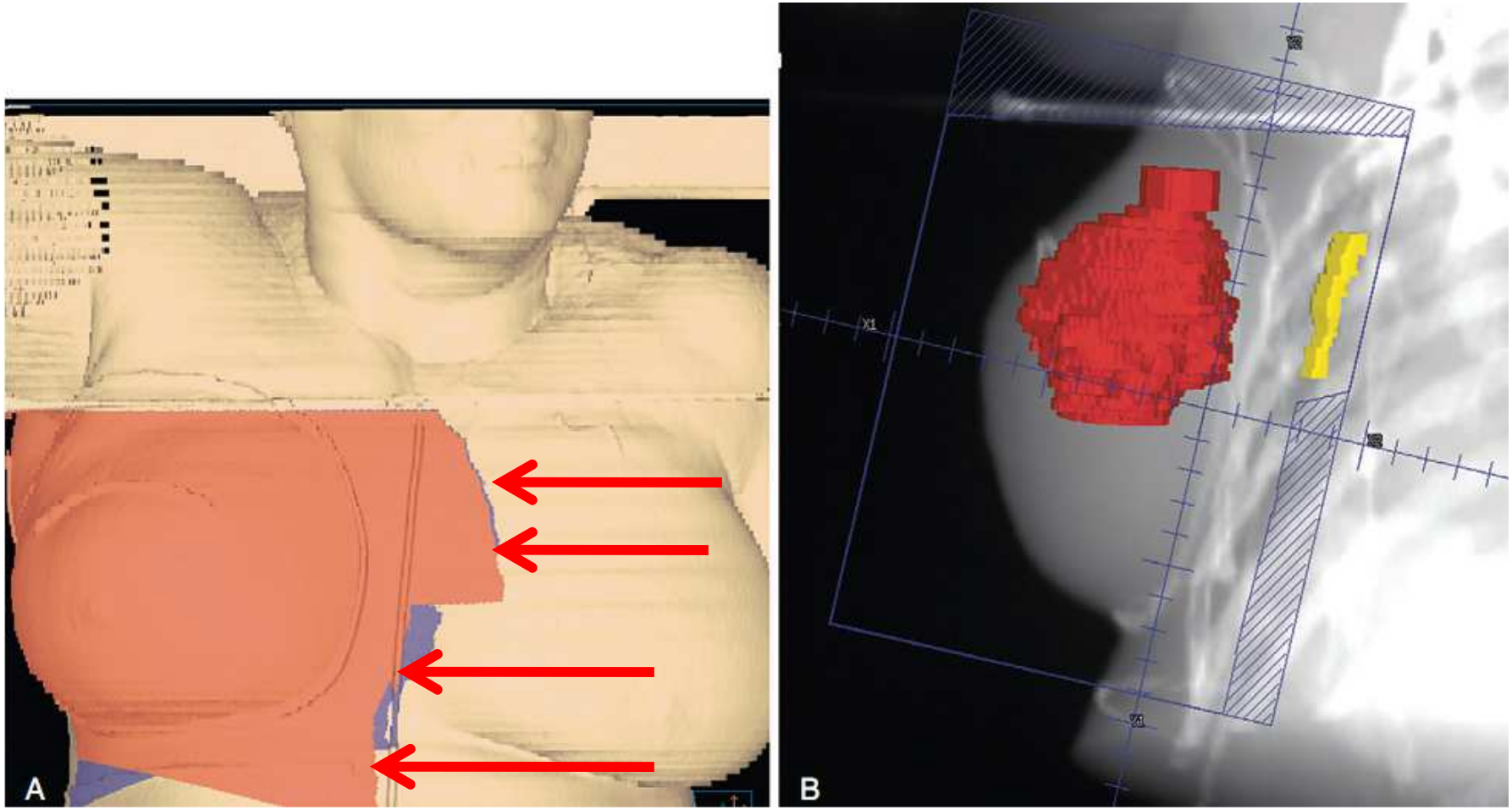
- More lung will be irradiated
- Opposite breast receive higher dose of radiation
- Portion of the heart will also be irradiated



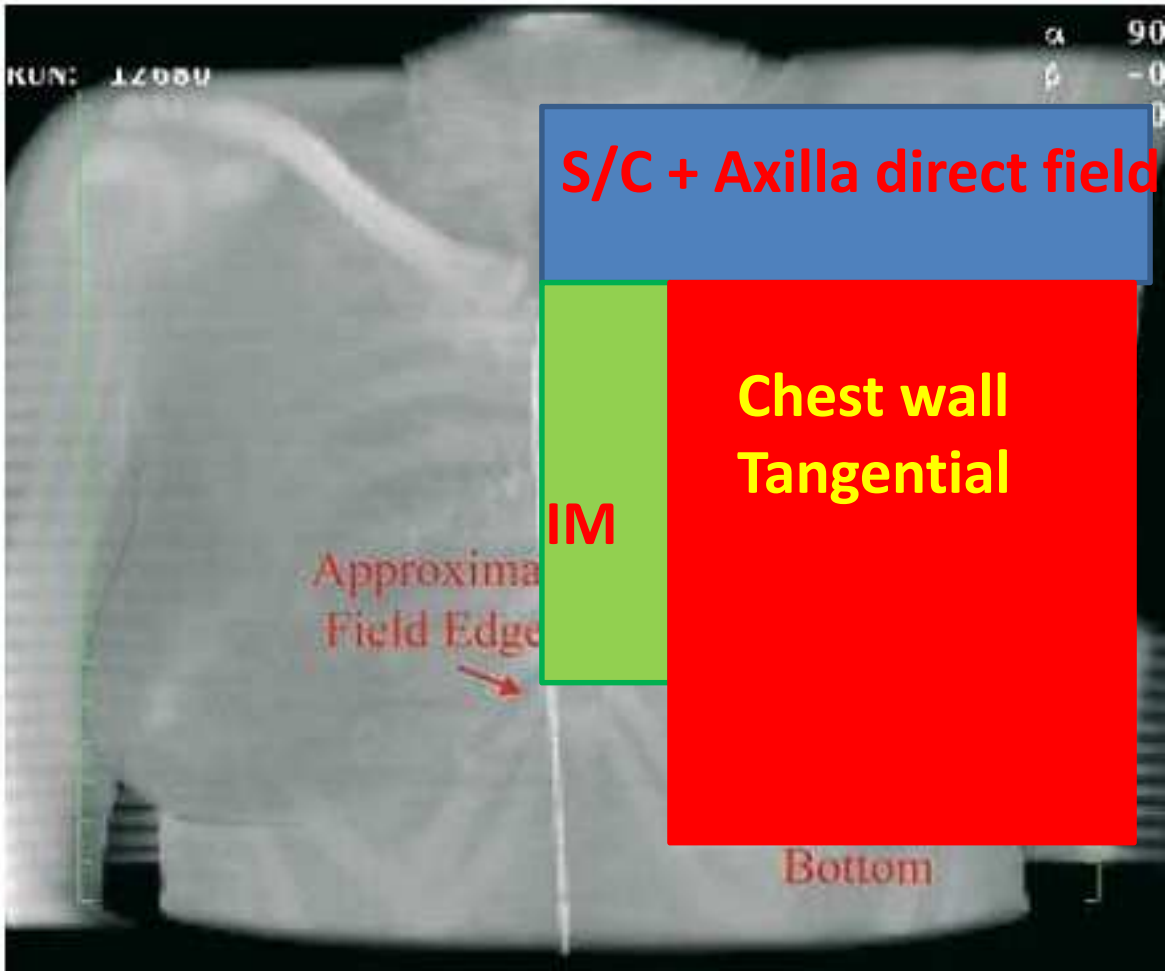
Deep Tangential or Extended Partial Tangential field

- Only LN of upper 3 intercostal space are involved

- The upper part of chest tangential field is extended medially to cover the internal mammary nodes of upper three intercostal space.



Three Fields Technique

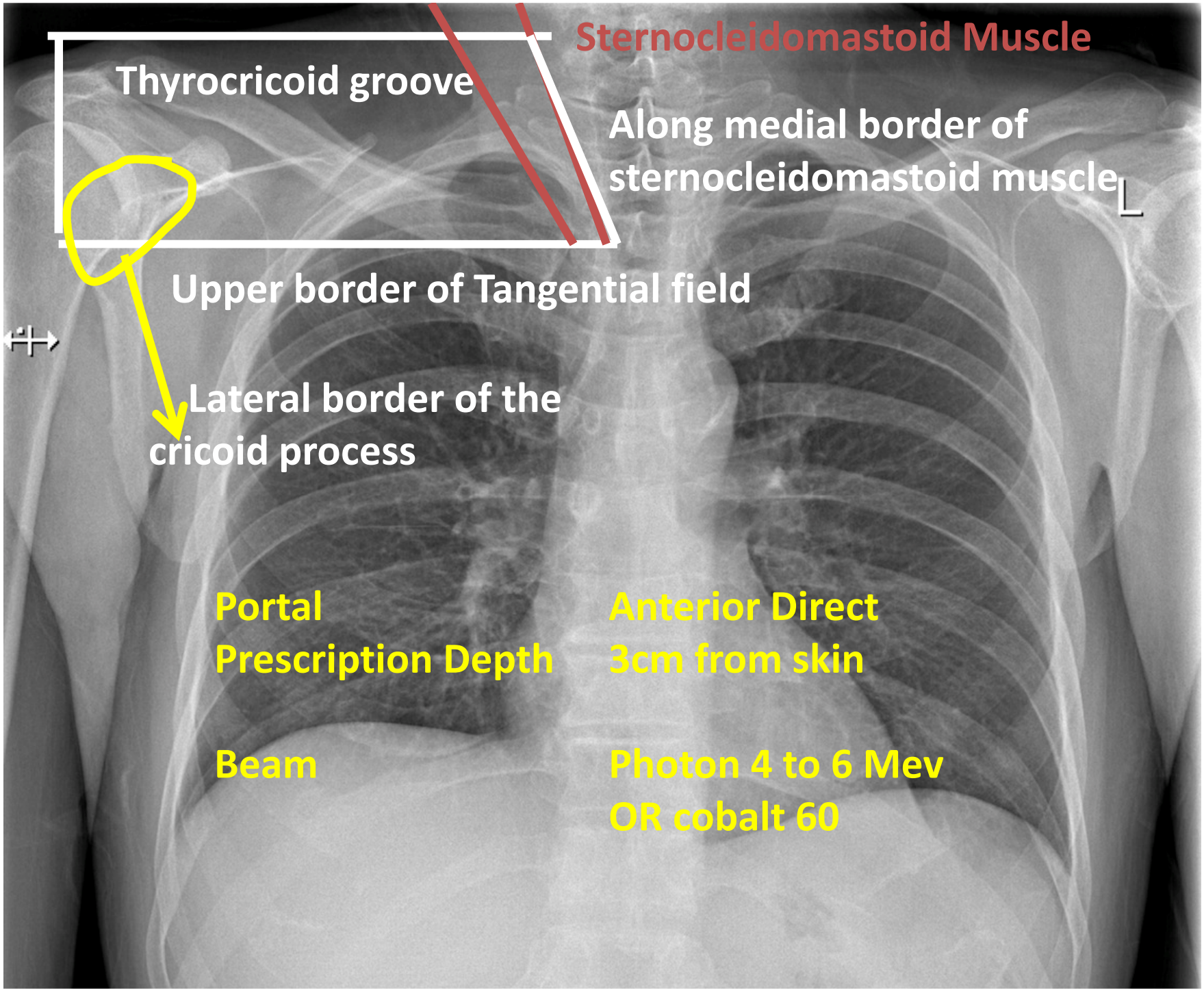


1. S/C + Axilla by direct field
2. IM by direct field
3. Chest wall by Tangential field

Field Boundaries

Supraclavicular RT

- **Indication:-**
  - **4 or > 4 axillary nodes positive**
  - **T3 or T4 tumors**
  - **Inadequate axillary dissection**
  - **No axillary dissection**

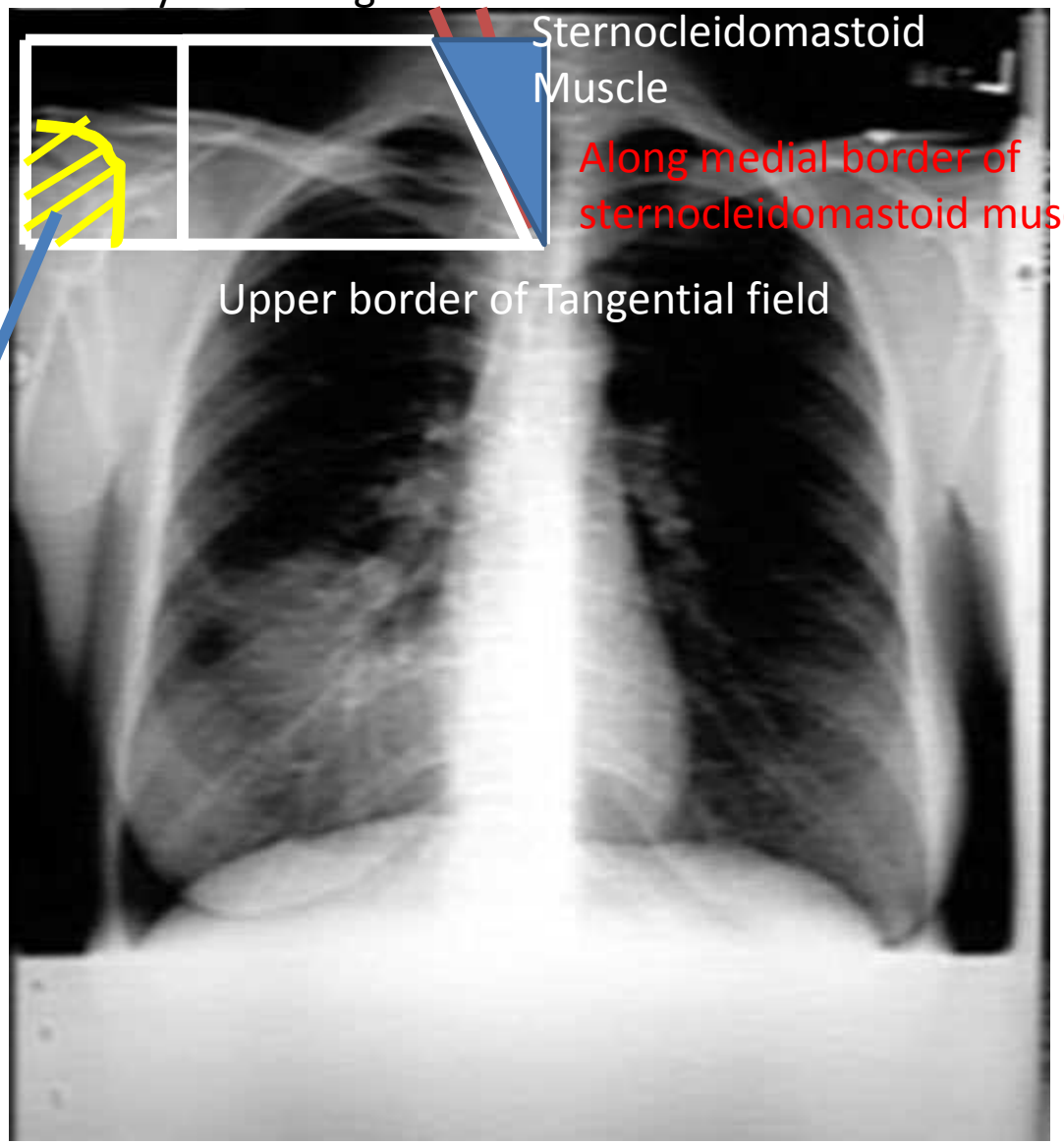

Sternocleidomastoid Muscle
Thyrocricoid groove
Along medial border of sternocleidomastoid muscle
L
Upper border of Tangential field
Lateral border of the cricoid process
Portal
Prescription Depth
Anterior Direct
3cm from skin
Beam
Photon 4 to 6 Mev
OR cobalt 60

RT to Axilla

- **Indication**
  - **Inadequate Axillary Dissection (< 10)**
  - **No axillary dissection in presence of positive sentinel node.**
  - **Extensive extra capsular extension**
  - **More than 75% nodes are positive (eg 15/20)**

Field Bounderies

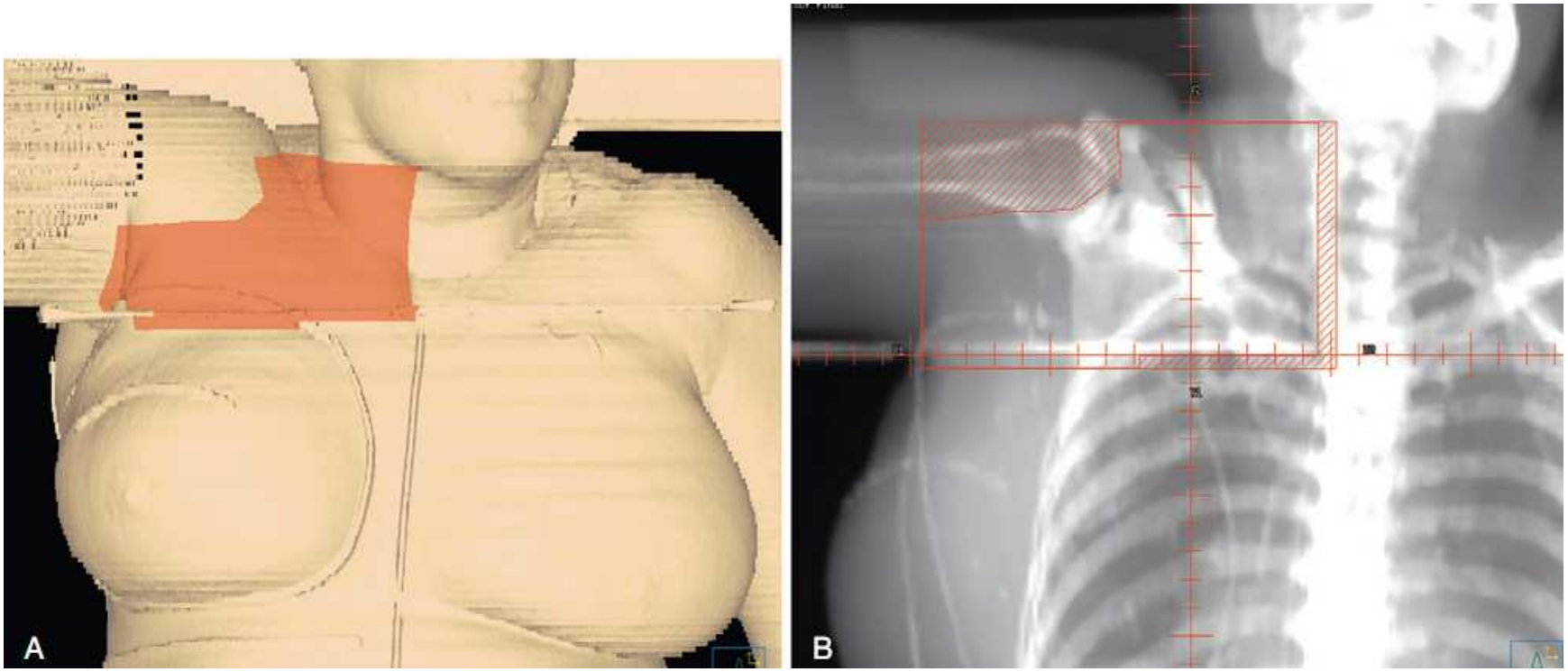
Lateral border is extended more laterally to include the axilla .



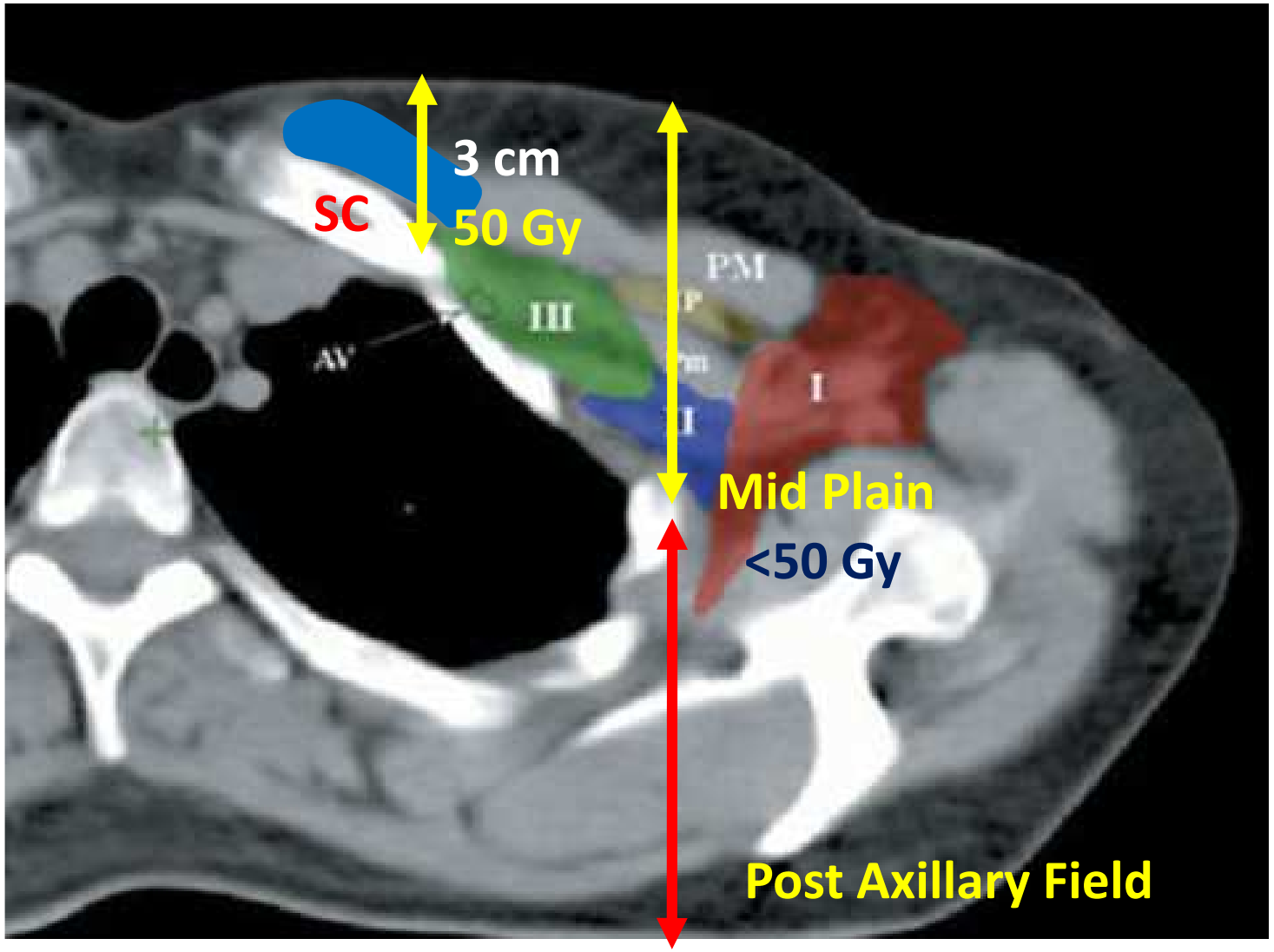
humeral head is shielded

Supraclavicular and Axilla

Beams eye view and projected field over skin

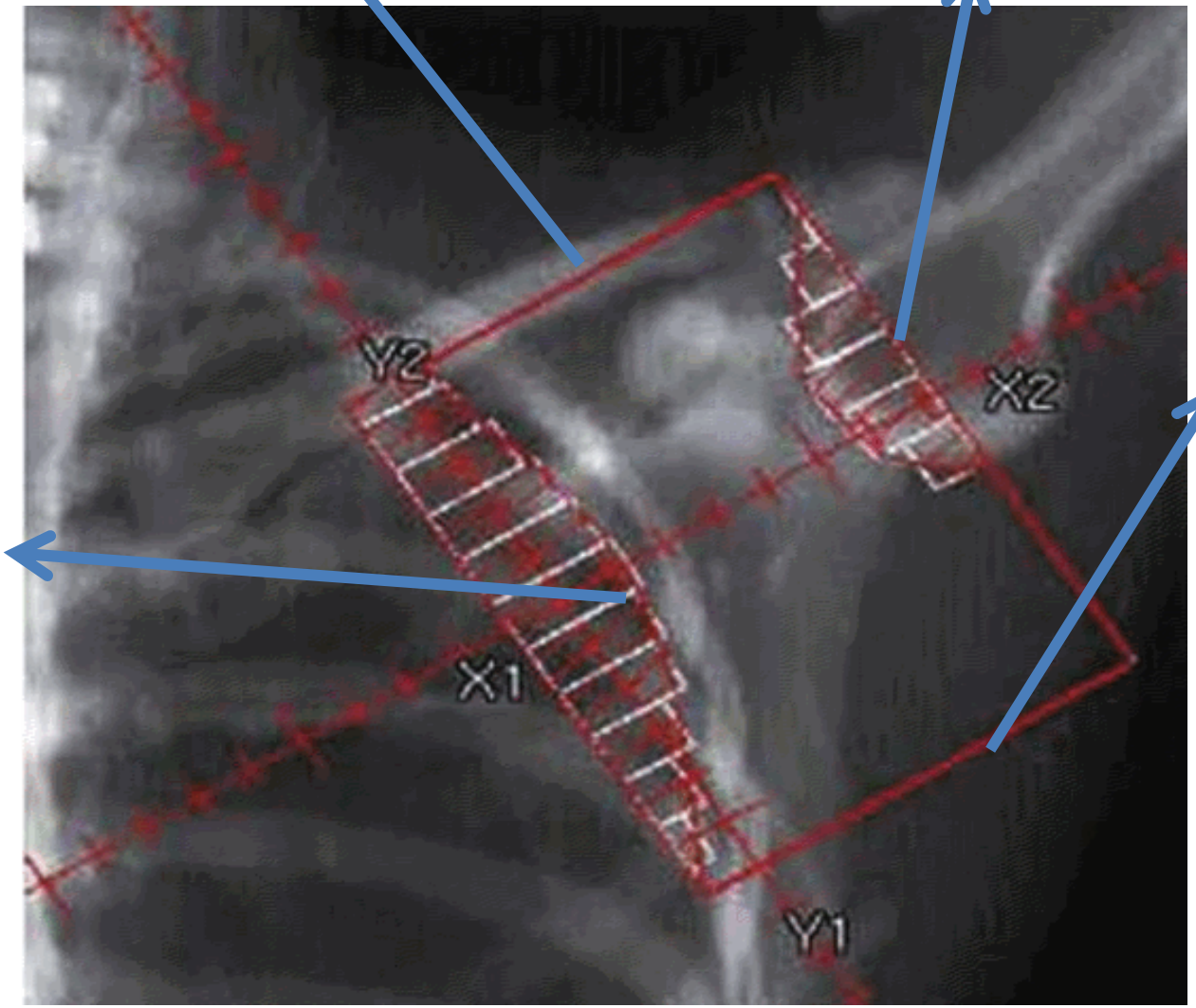


Posterior Axillary field



Upper Border along the spine of the scapula

Lateral border should match with lat border of ant axillary field with shielding of humeral head



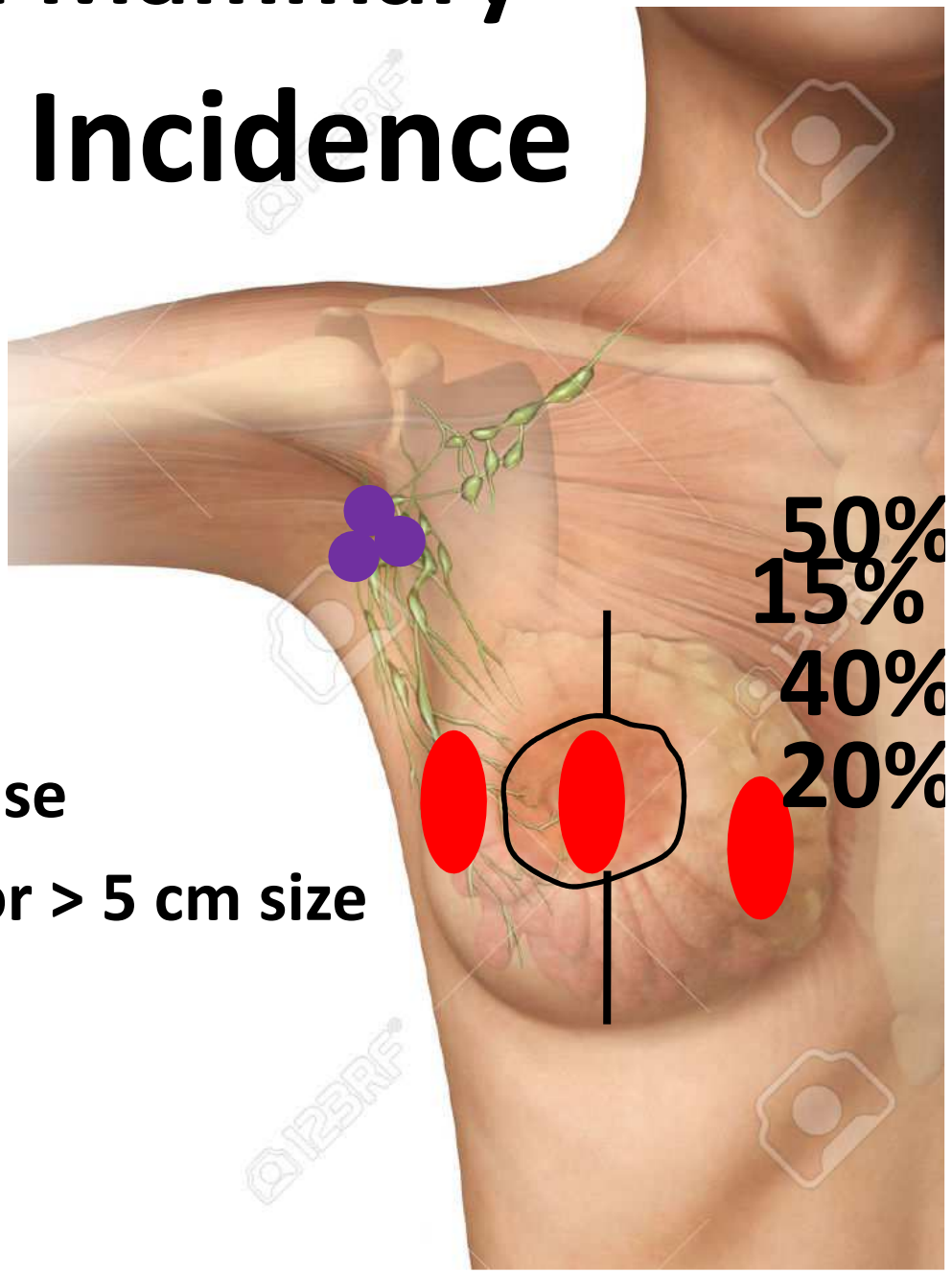
Medial border along the convex lateral wall of the bony thorax cage with 1 to 1.5 cm of lung

Inferior border should match the lower border of Ant axillary field

Dose from Posterior field

- **Calculate the contribution at mid plane by ant axillary + S/C fields**
- **Rest of the dose to be given from post field to make total dose 50Gy**
- **For example if the contribution from ant field is 35 Gy, give 15 Gy from post field.**

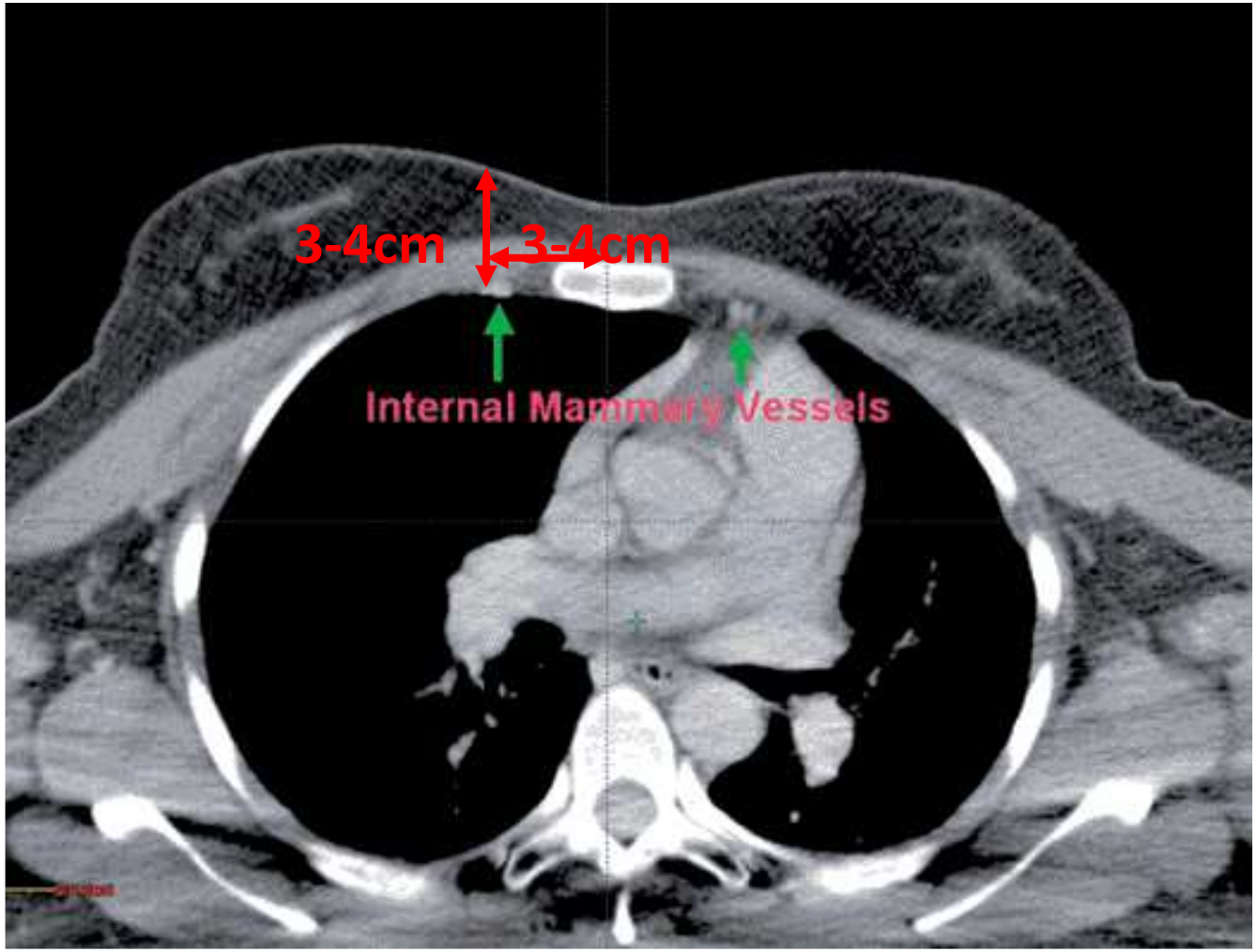
Internal Mammary Incidence



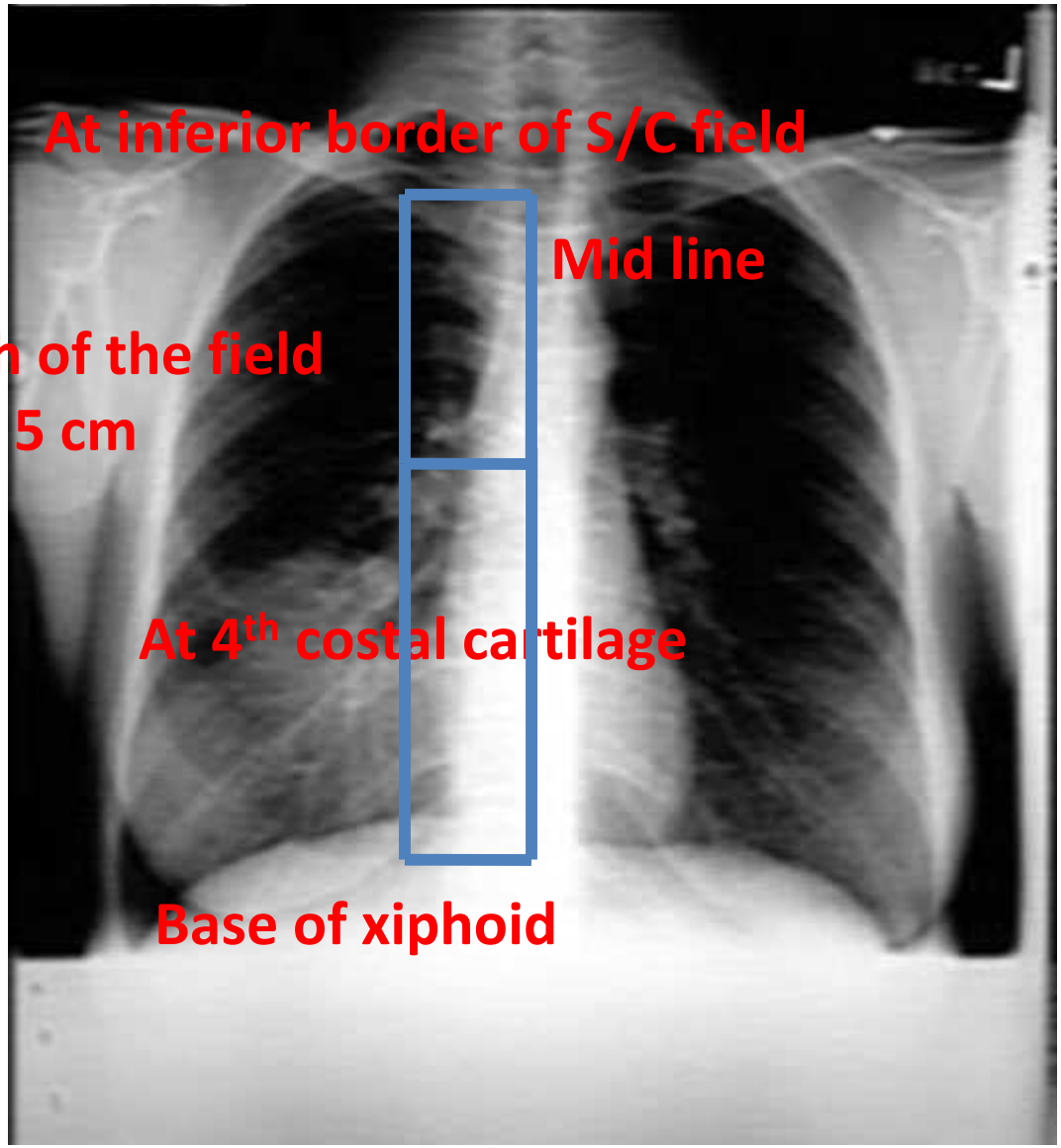
- **Indications:-**
  - **Extensive axillary disease**
  - **Central or medial tumor > 5 cm size**

Internal Mammary Nodes

Internal mammary nodes are in close proximity to the internal mammary vessels which are located approximately 3-4 cm lateral to mid line and 3-4 cm deep to the surface.



Field Bounderies



Prescription Depth

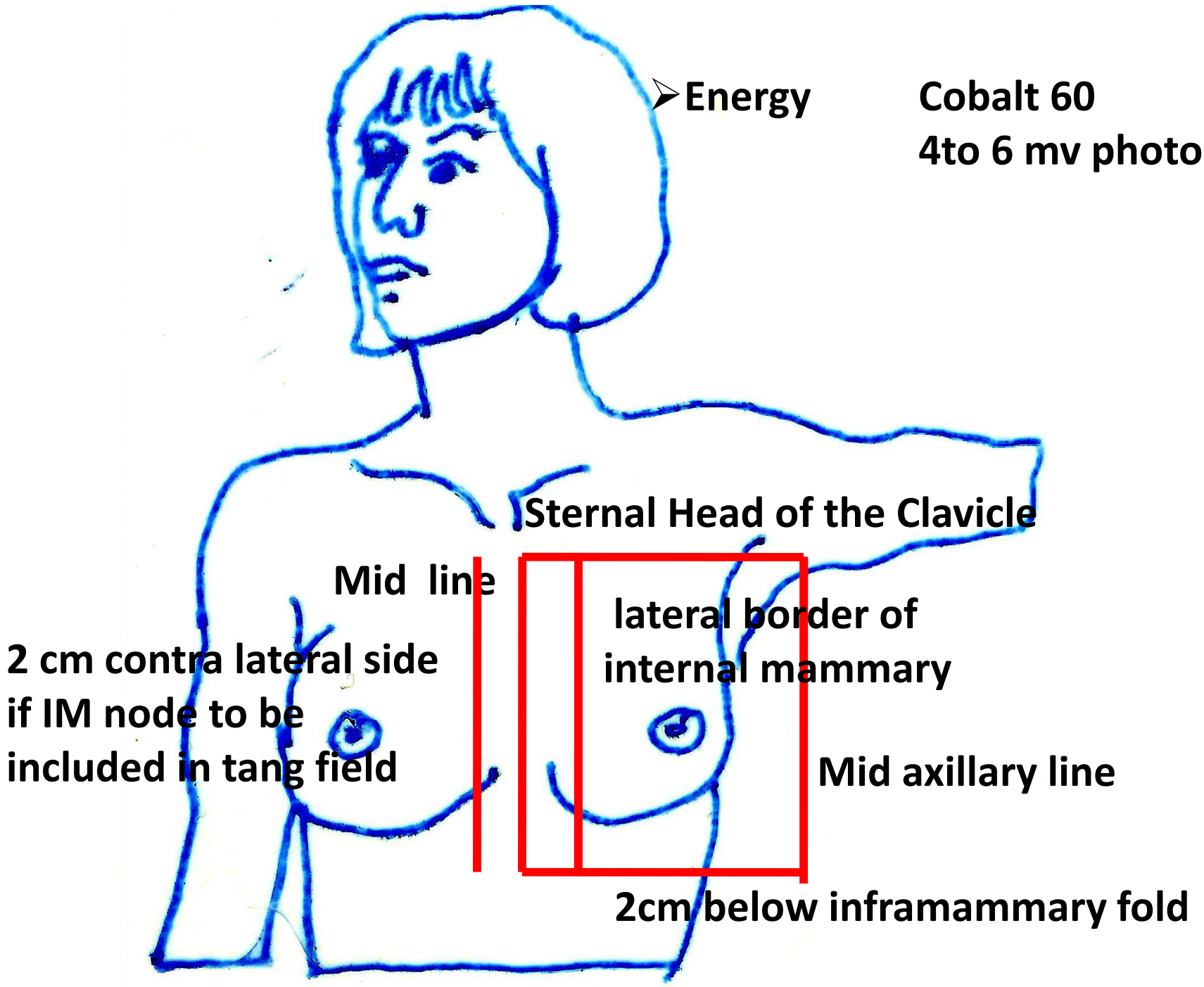
4 Cm

Radiation

Photon
OR
Electron

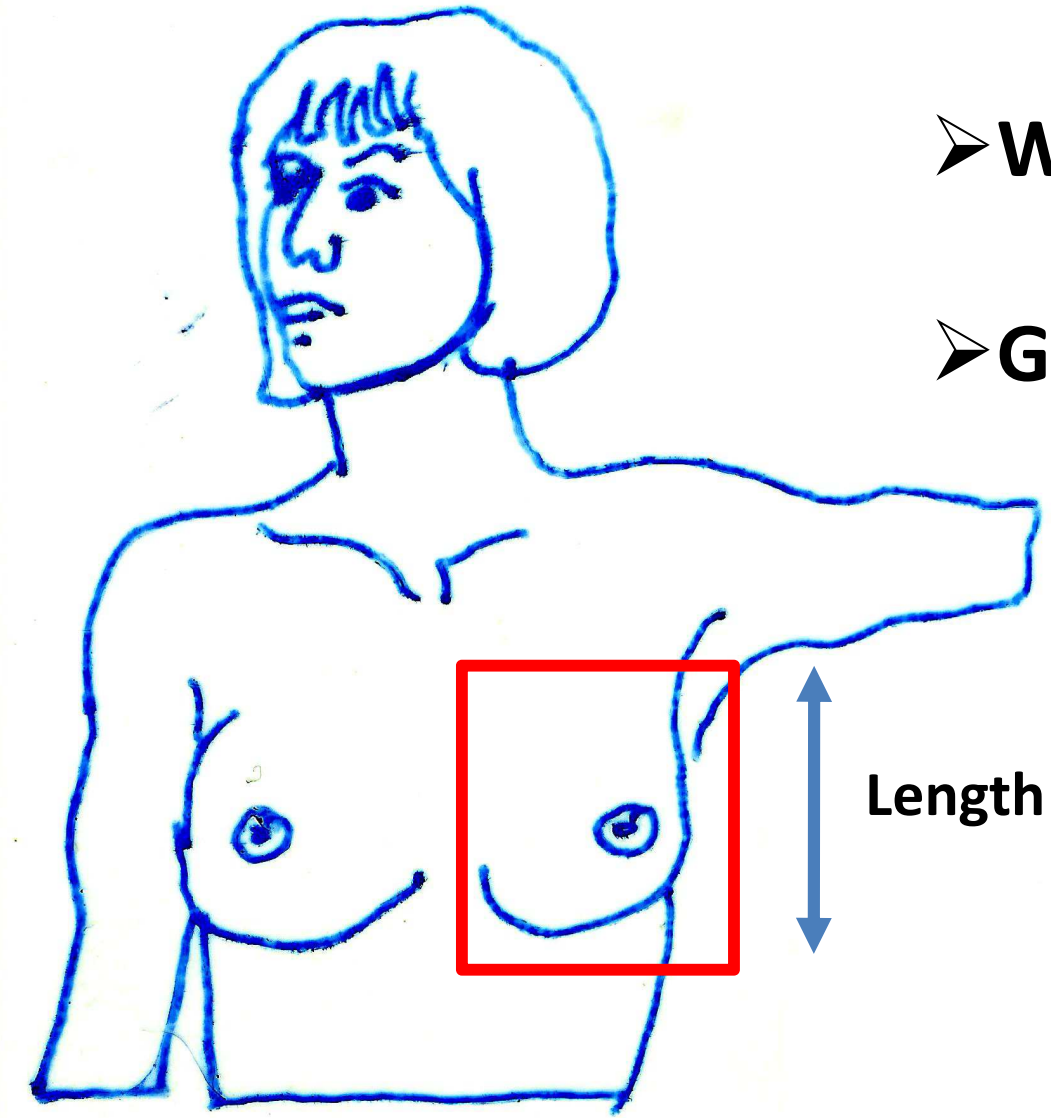
Chest wall Irradiation

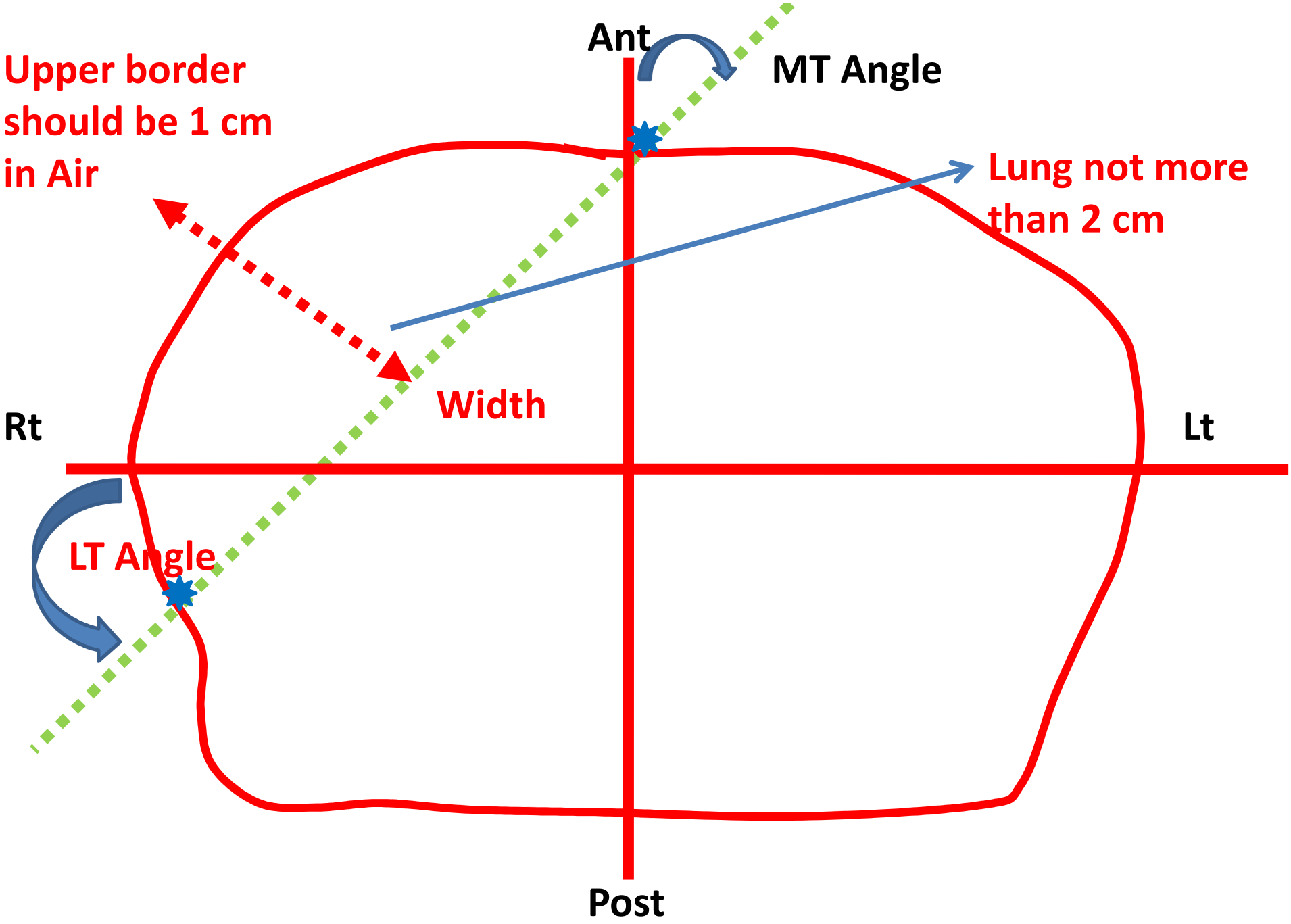
- **By two tangential fields**
  - **Medial Tangential**
  - **Lateral Tangential**


Energy
Cobalt 60
4to 6 mv photon
Sternal Head of the Clavicle
Mid line
lateral border of
internal mammary
2 cm contra lateral side
if IM node to be
included in tang field
Mid axillary line
2cm below inframammary fold

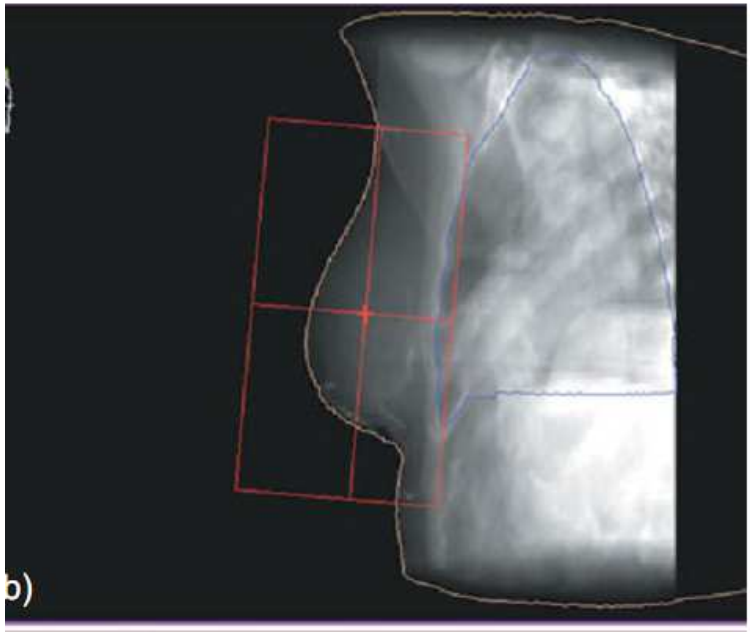
Parameter for Tangent Fields

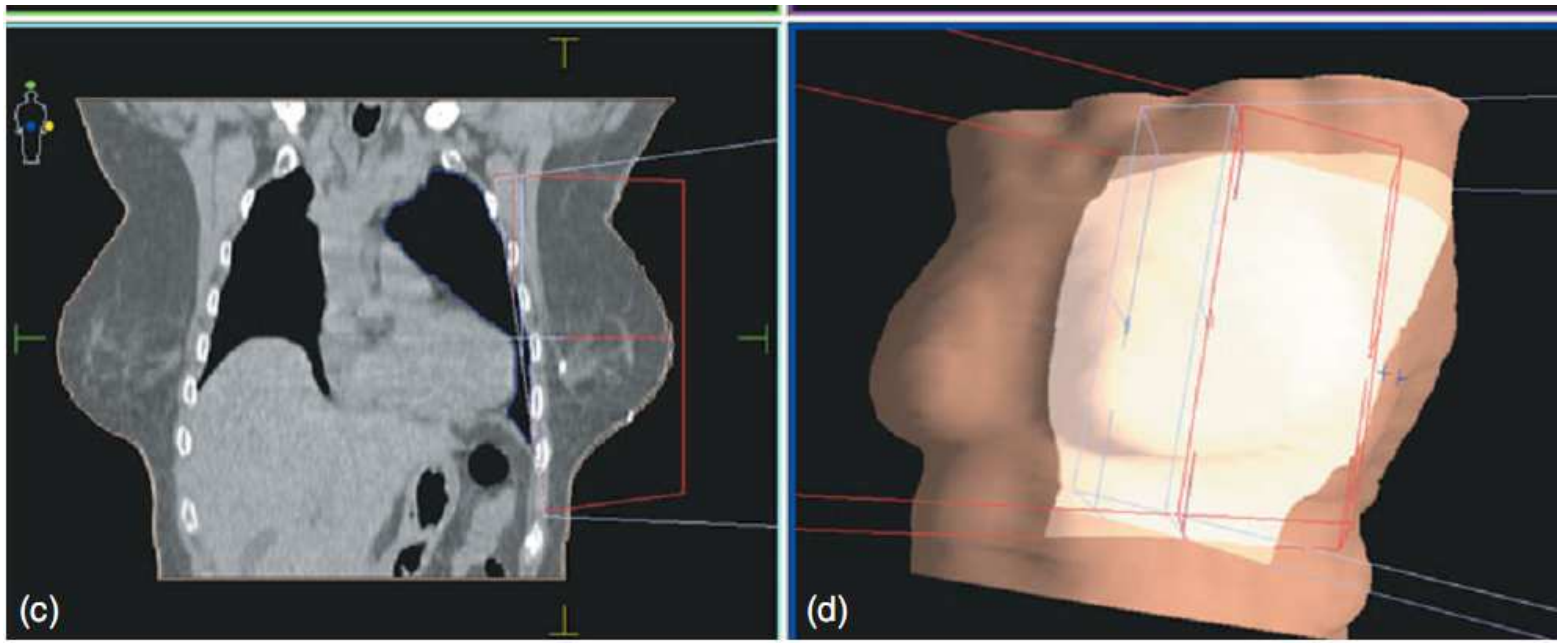
- Length
- Width
- Gantry Angle




Upper border
should be 1 cm
in Air
Ant
MT Angle
Lung not more
than 2 cm
Width
Rt
Lt
LT Angle
Post

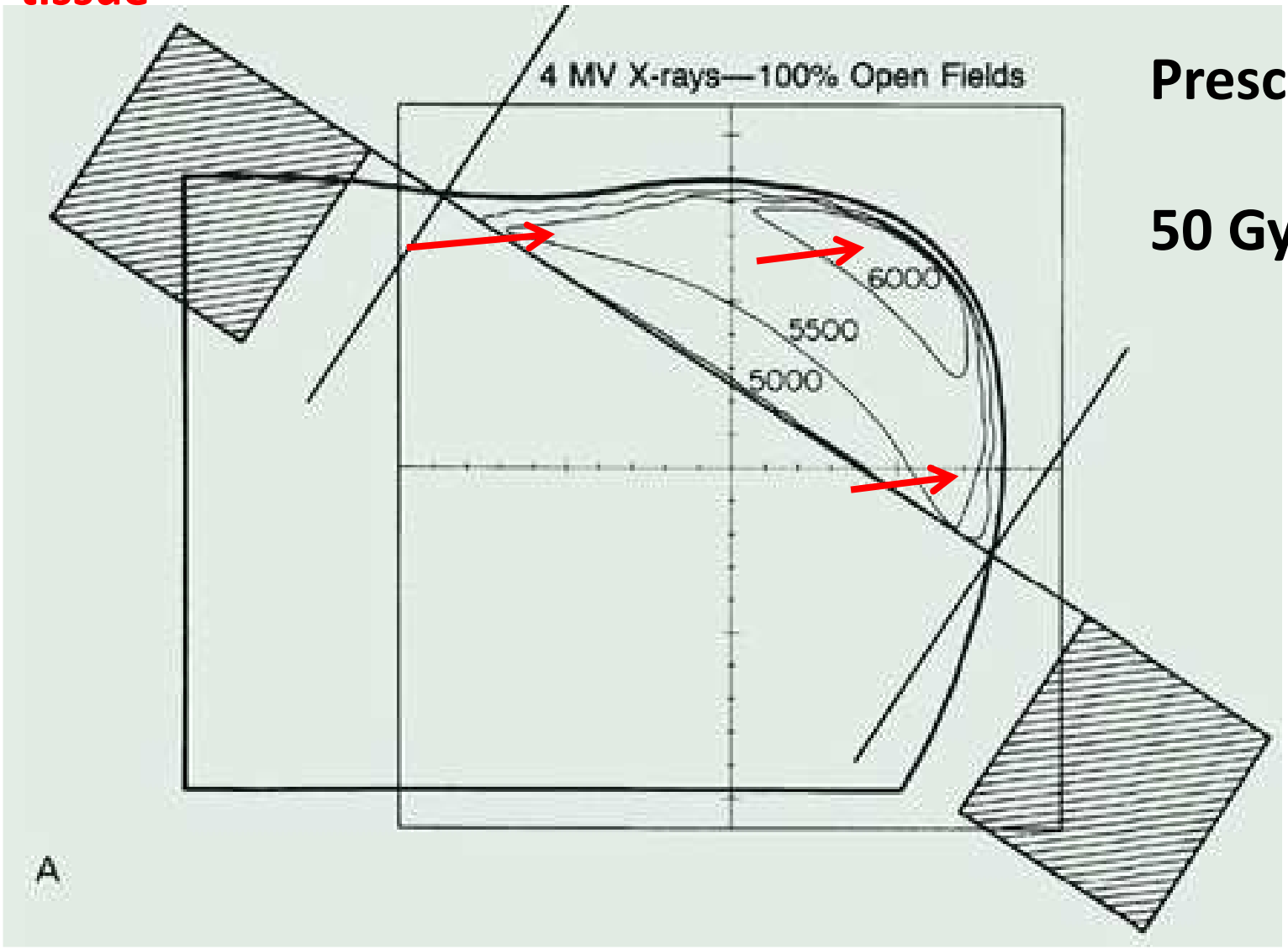
Tangent Portals





Dose distribution with two tangential fields

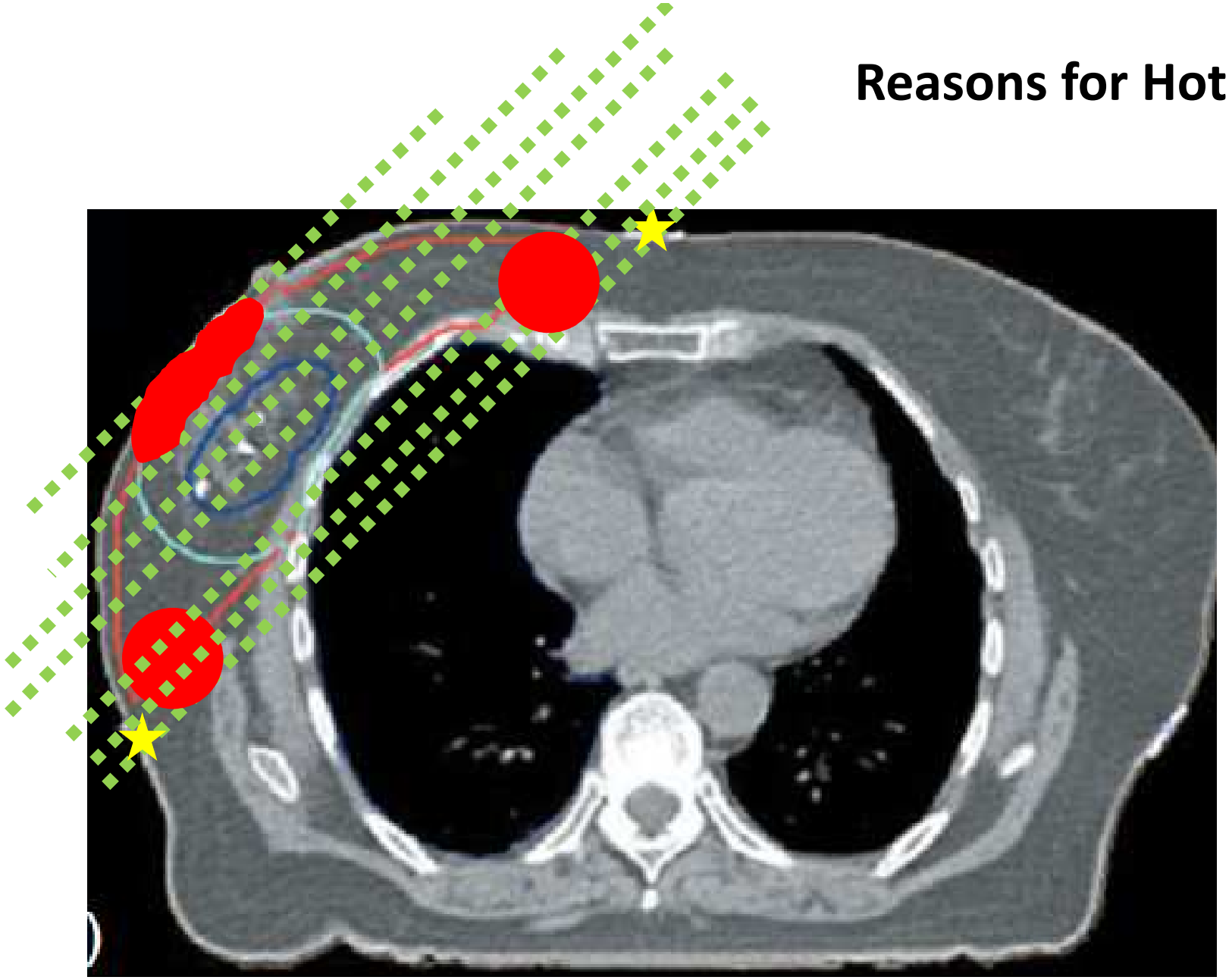
Note the higher doses at surface and medial and lateral deep breast tissue



Prescription

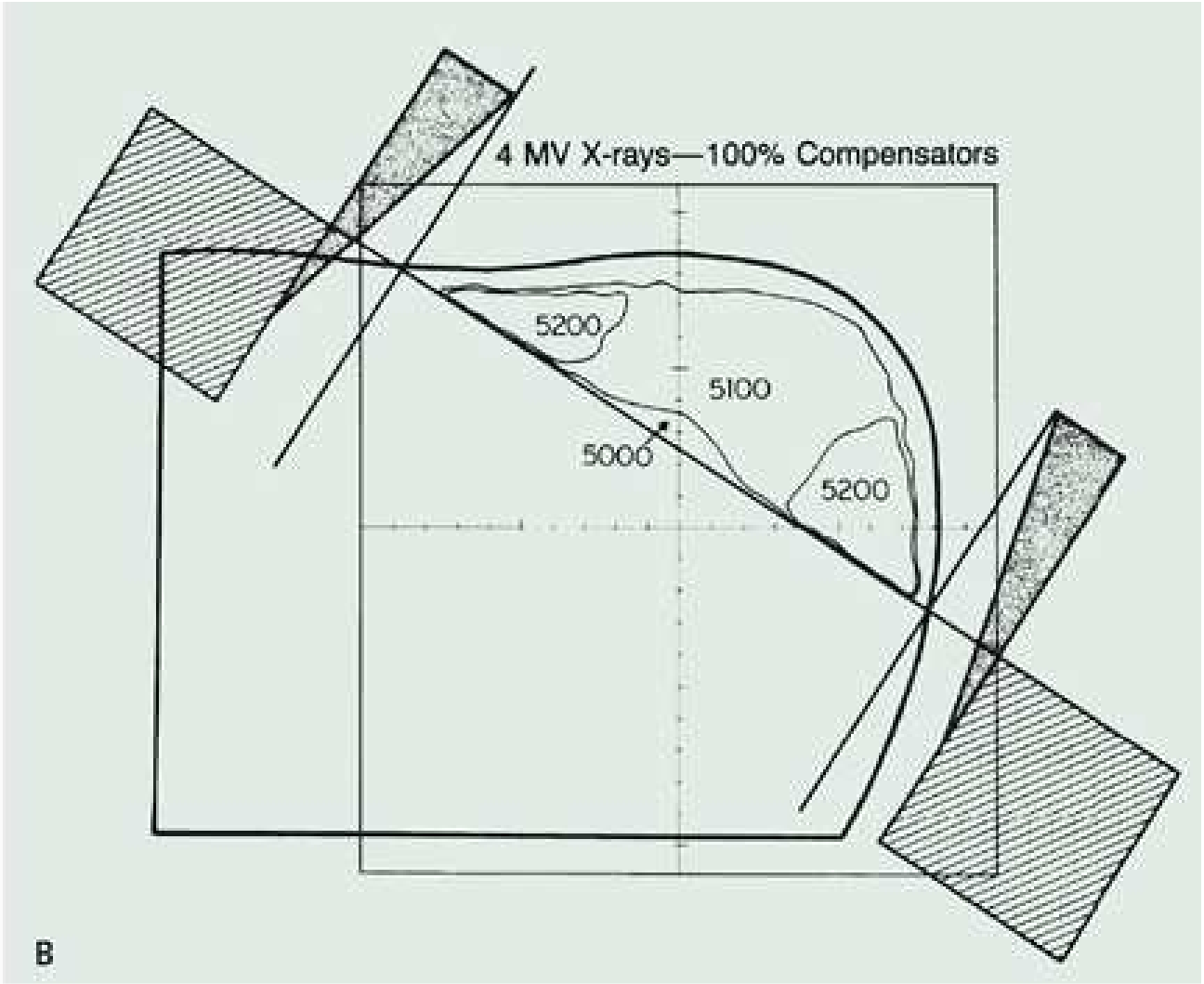
50 Gy/25 F/5W

Reasons for Hot spots



Solution:-

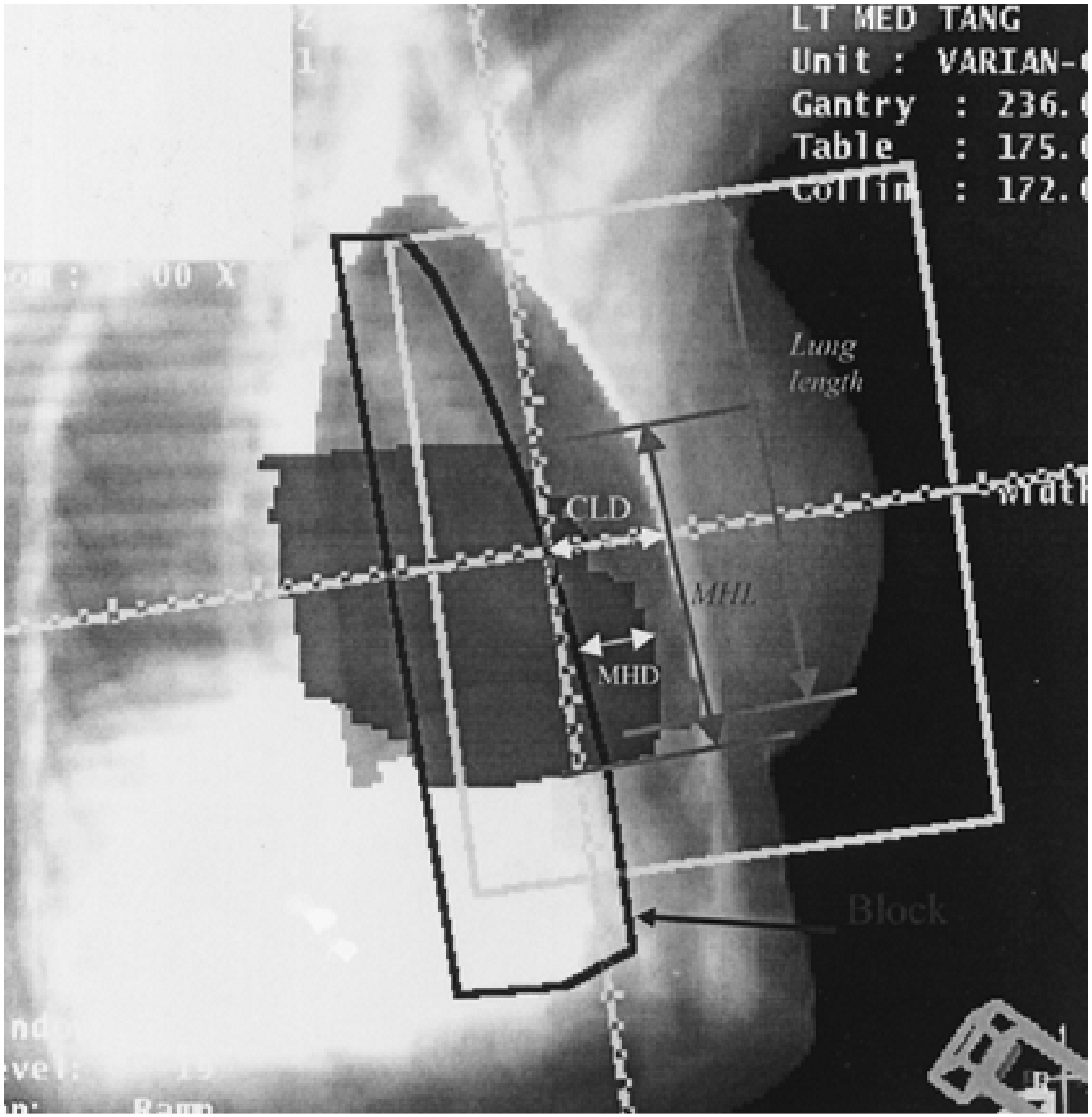
Use Wedge with thick end upward which act as compensator for missing tissues



It removes hot spots anteriorly.

The medial and lateral hot spots will still remain

Radiographic Parameter on Virtual simulation



Central Lung Distance(CLD) :- width of the lung at central axis

Lung Length:- Vertical lung distance included in the radiation portal.

Maximum Heart Distance (MHD):- maximum width of the heart in the tangent field.

Maximum Heart Length (MHL):- Maximum length of the heart in the tangent field.

Thanks

Greetings From Shimla