Management of Radiation Toxicities: Breast

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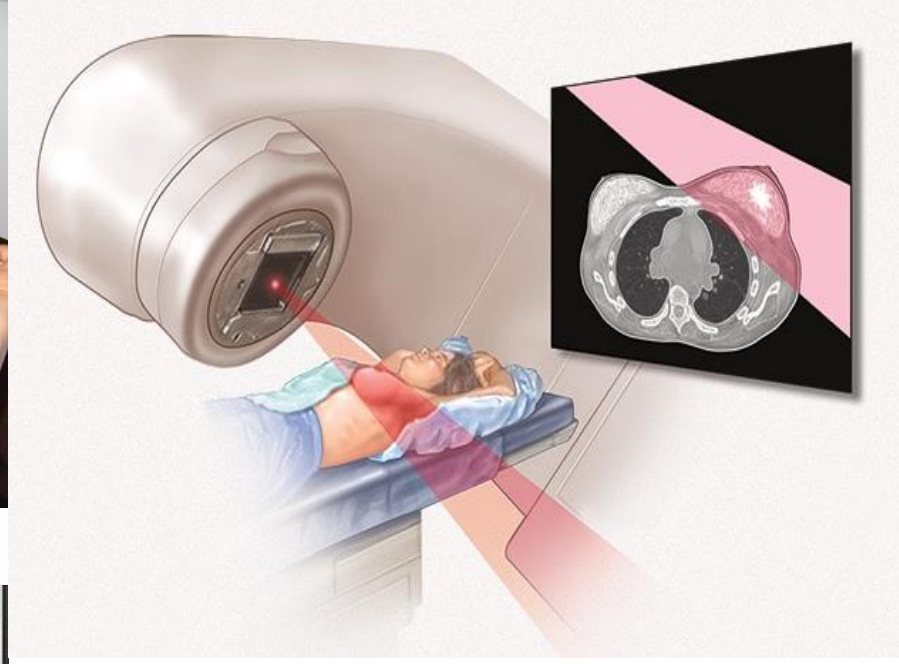
Why is it so important ???

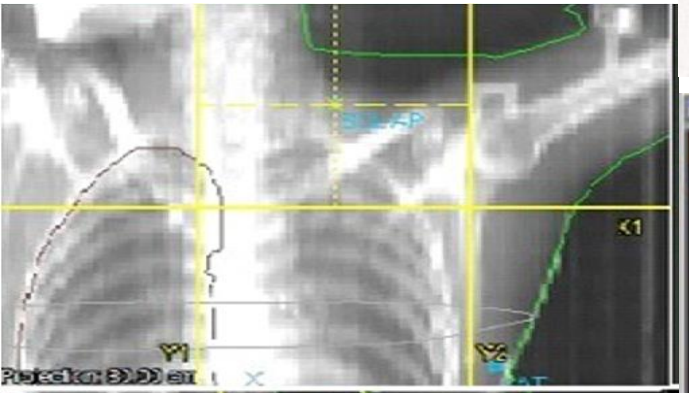
- Evolution / Revolution of
  - Diagnostic
  - Surgical intervention
  - Systemic therapy
  - Radiation: technique, dose

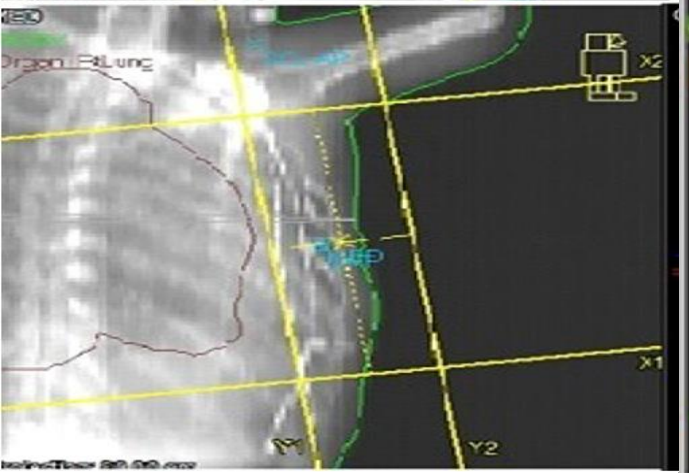
Survival improved dramatically

$\Rightarrow$Long-term survivors

$\Rightarrow$Quality of Life issues





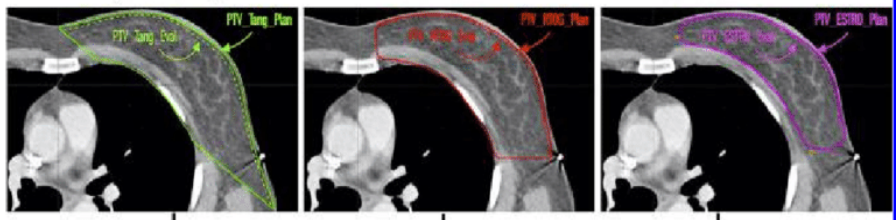


N = 10, Left Breast Cancer Patients

Target Delineation performed by 3 methods

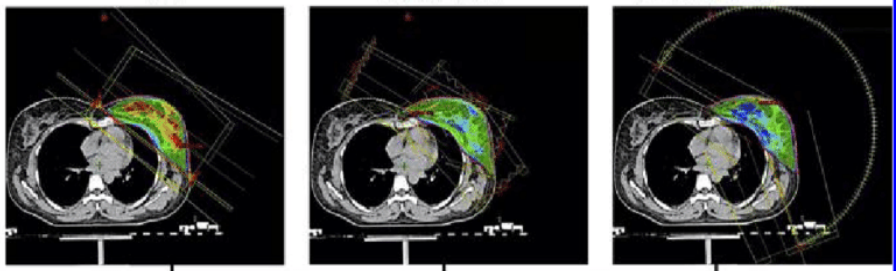
TANGENT (RTOG 0413)[5] | RTOG Consensus[3] | ESTRO Consensus[4]

All Delineations performed by single Radiation Oncologist; validated by study investigators



Each type of Target planned by 3 techniques

Field-in-Field (FiF)[7] | Inverse IMRT (IMRT)(5 Field)[7] | VMAT (2 continuous arc)[14]



All plans created by single Medical Physicist and met minimum acceptance criteria PQM scoring methodology communicated *a priori*

9 combinations of delineation & planning technique per patient

FiF - TANGENT	IMRT - TANGENT	VMAT - TANGENT
FiF - RTOG	IMRT - RTOG	VMAT - RTOG
FiF - ESTRO	IMRT - ESTRO	VMAT - ESTRO

Maximum permissible optimisation runs = 5 per combination
Maximum permissible planning time ≤ 2 days per combination
Plans generated for entire Cohort = 450

Plan Evaluation

PQM Scoring[11]

For each patient and each combination, plan with maximum PQM score selected for analysis
Total plans analysed = 90

Statistical Analysis

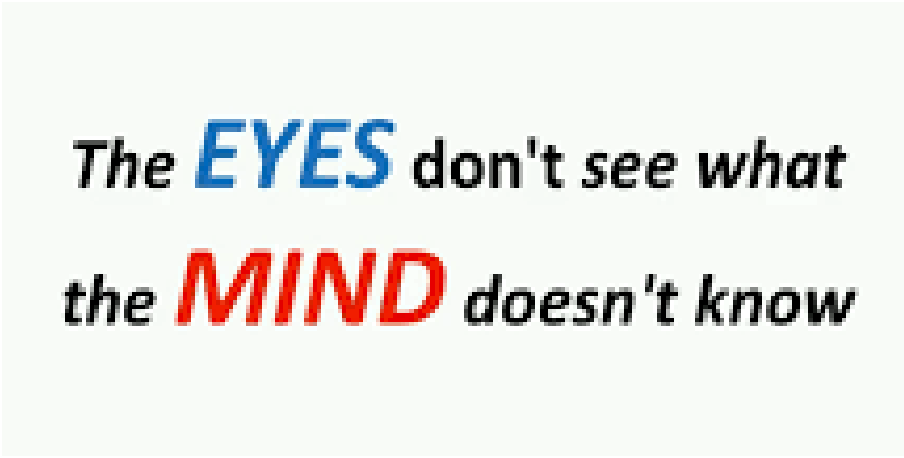
Research Question
For a given Target Delineation, which Planning Technique is optimal?

Sub-stratified by Cardiac Anatomy[9] | Sub-stratified by Breast Size[10]

Radiation effects

- **Skin and Breast tissue**
- Ribs / Chest wall
- Lungs
- **Heart**
- **Lymphedema**

- Second Malignancy: *Stochastic effects*



Breast Cancer Related Lymphedema

Breast Cancer Related Lymphedema (BCRL):

Myriad of symptoms:

- Sensation and function of the arm, hand, breast, or trunk,
- Psychological distress pertaining to body image
- Quality of Life

Lymphedema guidelines

- National Lymphedema Network (NLN)
- International Society of Lymphology (ISL)
- American Society of Breast Surgeons (ASBrS)
- National Comprehensive Cancer Network (NCCN)

- Screening for BCRL should be integrated as standard of care from the start of treatment for breast cancer.
- **Comprehensive BCRL diagnosis should incorporate**
  - ✓ **clinical examination**
  - ✓ **objective measurements**
  - ✓ **patient-reported symptoms**

However, standardized guidelines about how to incorporate subjective assessments have yet to be established.

Screening for BCRL

- Baseline Assessment before definitive surgery or radiation

  Specifically, volume of each upper extremity should be measured **at baseline and at regular intervals throughout and beyond treatment** for breast cancer

- Postoperative measurements *in relation to the preoperative baseline measurement*

  - to account for the pt's **natural asymmetry** between arms, which may be ≥5% for 28.3% of patients or ≥10% for 2.9% of patients

  - Failure to account for baseline asymmetry has been estimated to result in **over- or underdiagnosis** of BCRL in 40–50% of patients

Defining BCRL

Absolute Volume Difference：limb volume between the arm at risk for BCRL and the contralateral limb

- *Not accounting for Natural asymmetry*

Defining BCRL by Absolute Volume Change Relative to a Baseline：absolute volume increase of 200 ml or a circumferential increase of 2 cm in the affected arm

- may be significantly altered by weight fluctuations

Defining BCRL by Relative Volume Change: preferred definition

- volume changes in the affected limb relative to preoperative baseline measurements
- accounts for general body changes such as weight fluctuation

$$\mathrm{RVC} = \left((A2 \times U1) / (U2 \times A1)\right) - 1$$

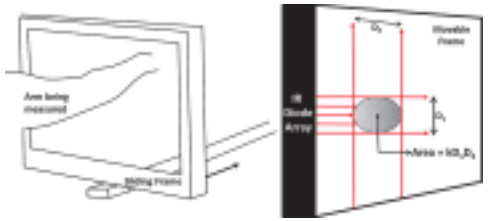
$A1$= volume of the affected limb at baseline
$A2$= volume of the affected limb at given time point
$U1$= volume of the unaffected limb at baseline
$U2$= volume of the unaffected limb at given time point

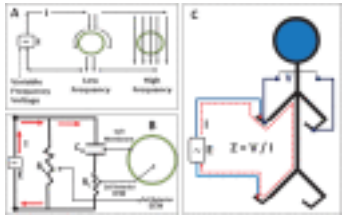
$$\mathrm{WAC} = \left((A2 \times W1) / (W2 \times A1)\right) - 1$$

$A1$=volume of the affected limb at baseline
$A2$=volume of the affected limb at given time point
$W1$=body weight at baseline
$W2$=body weight at given time point

Tests to quantify:

- **Water Volumetry**
- **Circumferential Tape Measurement**
- **Perometry**
- **Bioimpedance Spectroscopy (BIS)**
- **Lymphoscintigraphy**





Lymphedema stages

Staging	Method	Staging Features	Characteristics
International Society of Lymphology (ISL)	• Physical findings	• 0: latent/sub-clinical • I: spontaneously reversible • II: spontaneously irreversible • III: lymphostatic elephantiasis	• Widely accepted
Campisi	• Physical findings	• I: initial/irregular edema, • II: persistent LE • III: persistent LE with lymphangitis • IV: fibrolymphedema • V: elephantiasis	• Rely primarily on physical findings
Arm Dermal Backflow	• ICG lymphography	• 0: No dermal backflow • 1: Splash pattern around the axilla • 2: Stardust limited between olecranon and axilla lymphangitis • 3: Stardust distal to olecranon • 4: Stardust involving the hand • 5: Diffuse and stardust pattern involving the entire limb	• Safe • Information regarding the lymphatic flow for LVA planning
MD Anderson	• ICG lymphography	• 0: No dermal backflow • 1: Many patent lymphatics and minimal dermal backflow • 2: Moderate number of patent lymphatics and segmental dermal backflow • 3: Few patent lymphatics with extensive dermal backflow • 4: Dermal backflow involving the hand • 5: ICG does not move proximally to injection site	• Safe • Information regarding the lymphatic flow for LVA planning
Cheng's Lymphedema grading	• Circumferential difference and lymphoscintography	• 0: 0–9% • 1: 10–19% • 2: 20–29% • 3: 30–39% • 4: >40%	• Objective method
Taiwan Lymphoscintigraphy Staging	• Lymphoscintography	• L-0: Normal Lymphatic Drainage • P-1, P-2, P-3: Partial Obstruction • T-4, T-5, T-6: Total Obstruction	• Validated, Reliable

Risk Factors for BCRL

Treatment related

- Axillary L.N dissection
- Regional L.N Irradiation
- Lack of breast reconstruction
- *Chemotherapy (?) - fluid retention*

Non Treatment related

- High BMI
- Subclinical edema (post Sx)
- Local infection

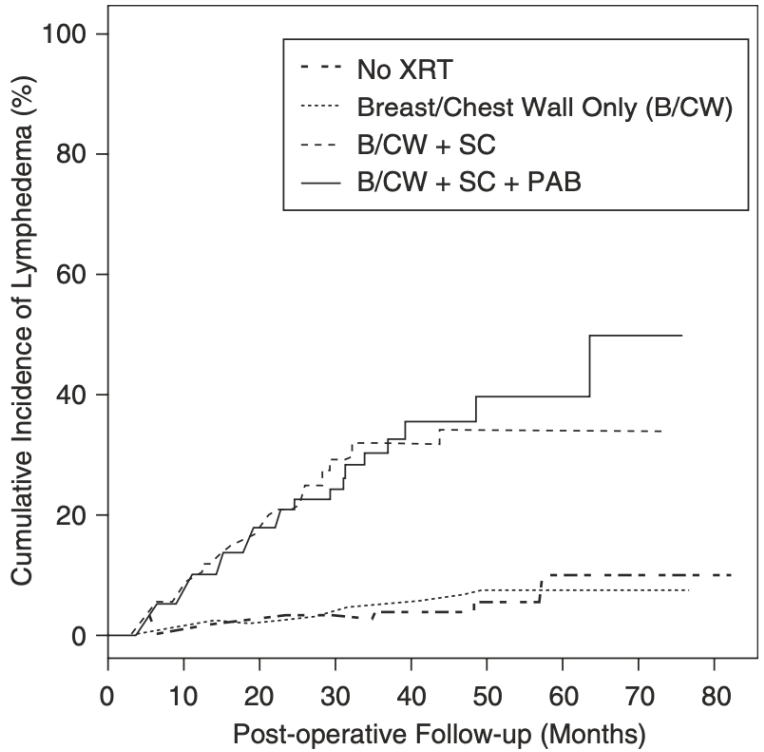


Fig. 5 BCRL incidence stratified by regimen of radiotherapy (*No XRT* no radiotherapy, *B/CW* breast/chest wall, *SC* supraclavicular irradiation, *PAB* posterior axillary boost). (Warren et al. 2014; Fig. 1) [48]

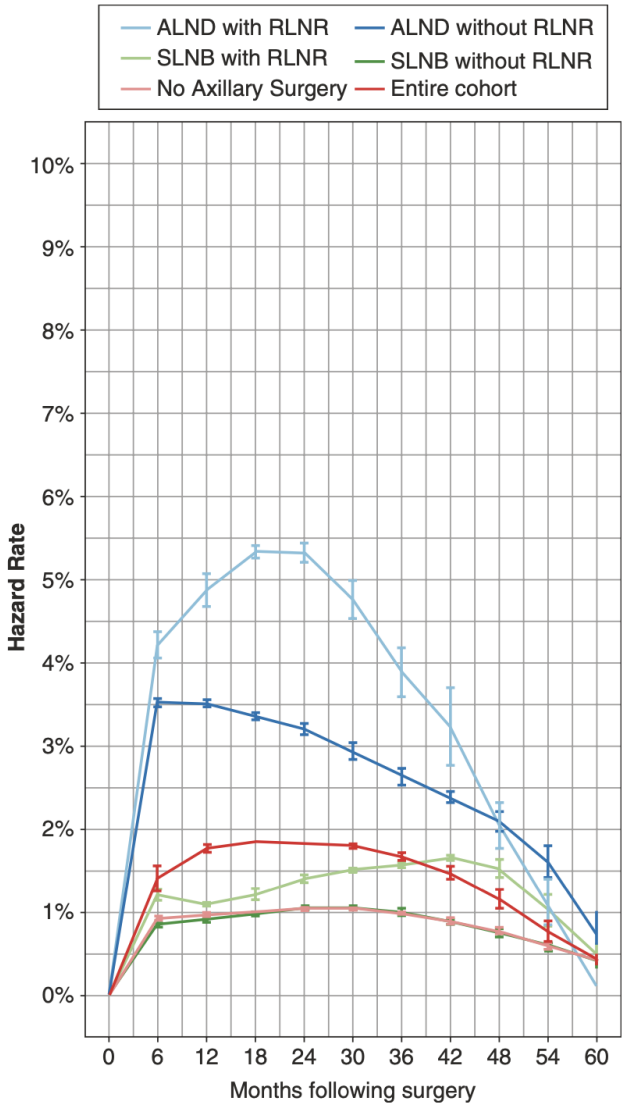


Fig. 6 Hazard rates for development of lymphedema following surgery with or without radiation (ALND axillary lymph node dissection, SLNB sentinel lymph node biopsy, RLNR regional lymph node radiation). (McDuff et al. 2018 (in press); Fig. 2) [75]

MA-20 trial: RLNR in pts

Either L.N +ve or L.N –ve with Gr III, ER/PR Neg, LVSI +

- decreasing local failure rates
- increasing disease-free survival (DFS)
- Increasing distant metastasis-free survival (DMFS)
- significant increase in lymphedema rates

EORTC AMAROS (After Mapping of the Axilla: Radiotherapy Or Surgery):

- 5-year cumulative incidence of clinically reported BCRL => RLNR (11%) vs 23% (ALND)
- 5-year cumulative incidence of BCRL, defined by an arm circumference increase of at least 10% *in the lower arm, the upper arm, or both*
  => RLNR (5%) vs ALND (13%)

Study	Two-year cumulative incidence of BCRL	Five-year cumulative incidence of BCRL
Warren et al. 2014[a] [48]		
No XRT	3.0%	
Breast/CW	3.1%	
Breast/CW with RLNR	21.9%	
ALND	24.3%	
No ALND	7.3%	
Breast/CW with RLNR + PAB	21.2%	
Chandra et al. 2015[a] [76]		
SC radiation only		
With PAB	20.98%	
Without PAB	22.27%	
<1/3 of SC lateral border radiated	19.50%	
1/3–2/3 of SC lateral border radiated	18.48%	
>2/3 of SC lateral border radiated	23.60%	
Gross et al. 2018[b] [77]		
Upper portion of the level I/II axilla	2.0%	7.7%
Majority of level I to III axilla	26.9%	37.1%
Entirety of anterior/posterior axilla	28.6%	36.7%
McDuff et al. 2018[a] [75]		
ALND		
Subsequent RLNR	19.0%	31.2%
No RLNR	12.7%	24.6%
SLNB		
Subsequent RLNR	4.3%	12.2%
No RLNR	3.7%	8.3%

[a]BCRL defined as an RVC or WAC of 10%, measured by a perometer, in the affected arm

[b]BCRL defined as an increase in arm circumference of at least 2.5 cm relative to a baseline obtained after surgery but before radiation therapy or an increase in arm circumference of at least 2 cm at 2 or more consecutive visits

Treatment for Lymphedema

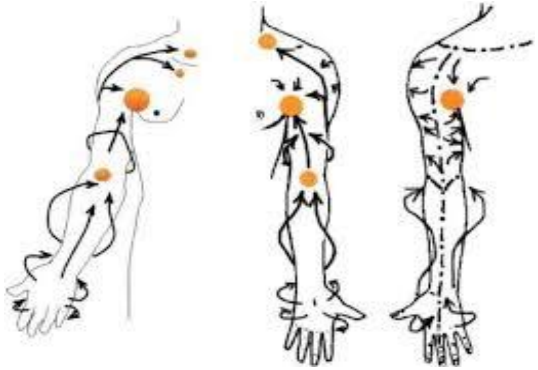
Complete Decongestive Therapy (CDT)

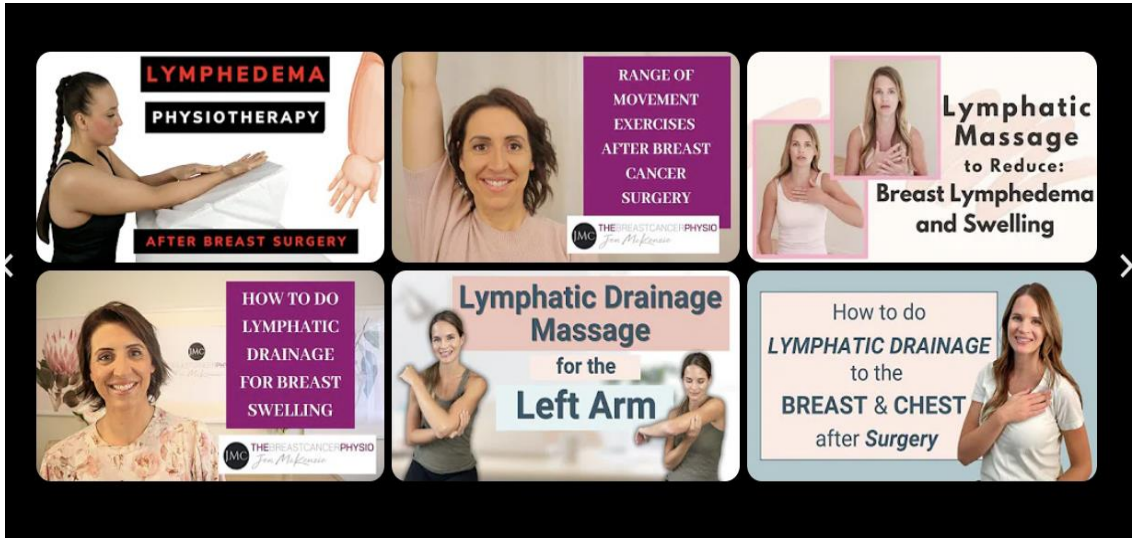
- **Reduction phase:** individualized reductive CDT in the clinic, which entails frequent appointments and typically lasts several weeks.

When limb volume stabilizes, the patient will enter the second phase

- **Maintenance:** focused on educating the patient about routine maintenance strategies,
  - Self Mannual Lymph Drainage (MLD)
  - Use of compression garments
  - Exercise
  - Skin care

- Treatment begins proximal, to “clear” proximal lymphotomes before moving to affected lymphotomes
- Massage is directed towards the cleared lymphotome
- Pressure is very light
- Strokes are rhythmic





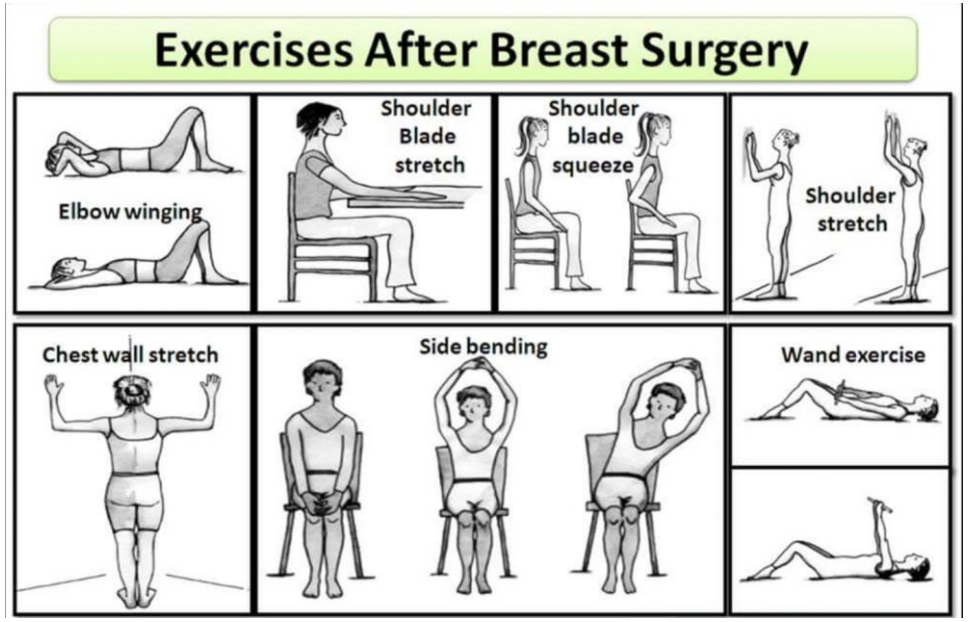
- Low stretch bandages
  - Provides low stretch when no contraction
  - Higher compression when muscles contract
- Prevent re-fill of lymphatics
- Work with muscle pumping
- Worn 23 hrs/ day (off only for bathing)
- Should re-wrap daily to prevent loosening
- Should have more compression (more layers) distally

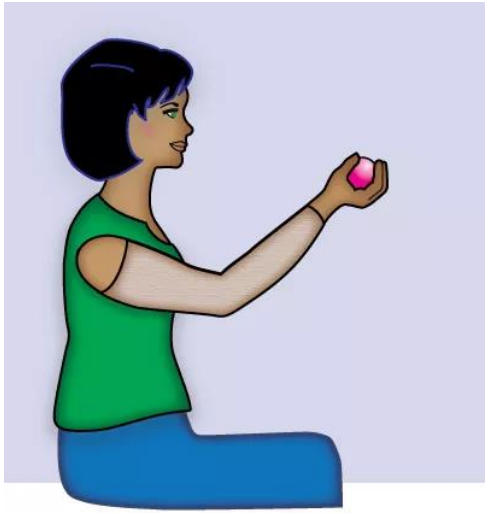
Exercise

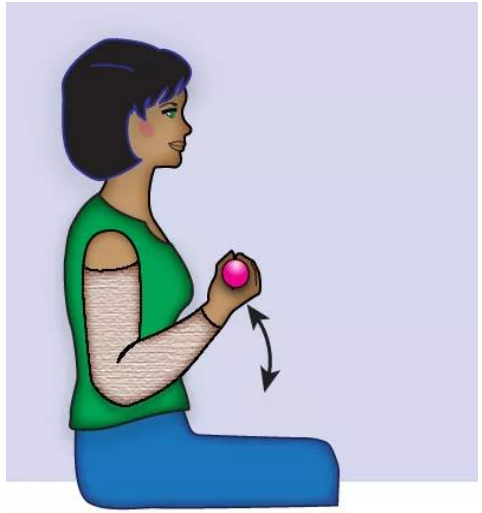
- For both as CDT and long-term management of lymphedema.

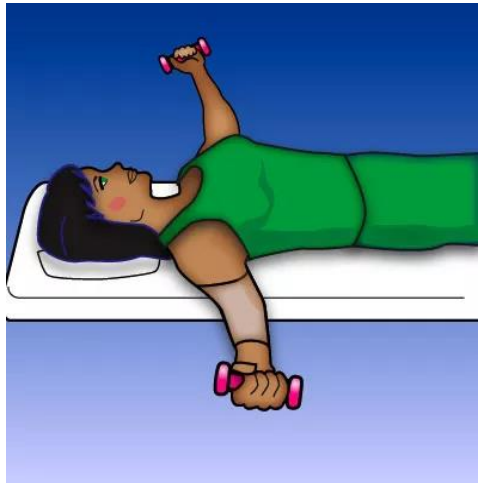
American College of Sports Medicine guideline

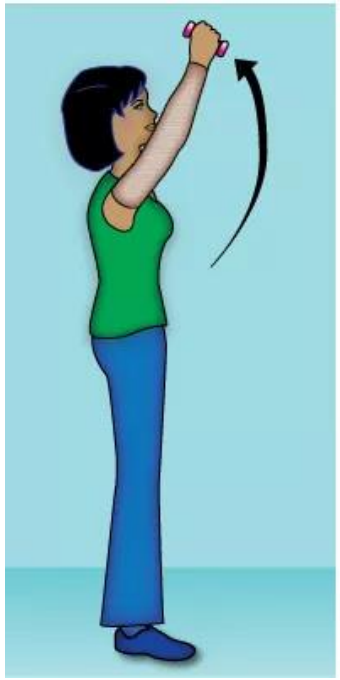
- 6–8 resistance exercises for the upper and lower extremities
- 75 min of vigorous aerobic activity per week or
- 150 min of moderate aerobic activity per week

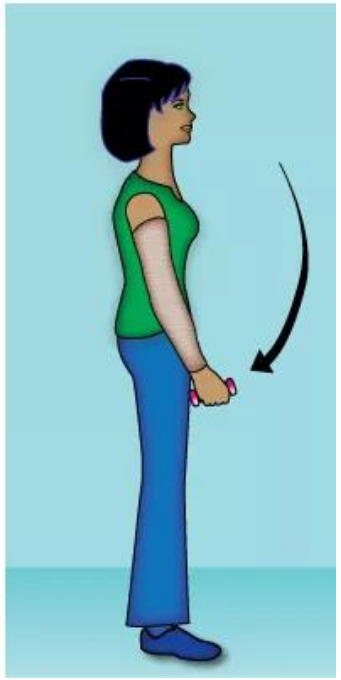

Exercises After Breast Surgery
Elbow winging
Shoulder Blade stretch
Shoulder blade squeeze
Shoulder stretch
Chest wall stretch
Side bending
Wand exercise

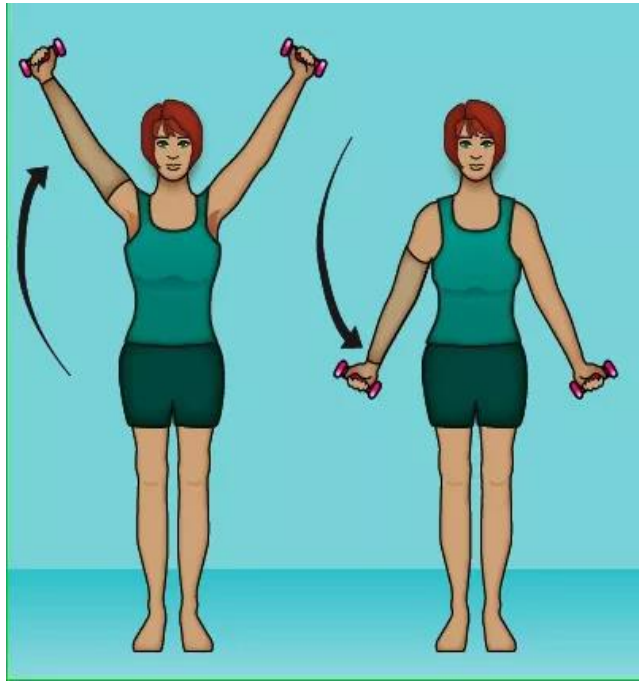












Intermittent Pneumatic Compression (IPC) devices

- Efficacy is not consistent in the literature.

- Research to elucidate the effects of IPC in patients with BCRL so that clinicians may better understand which patients will benefit most from IPC.

Surgical Intervention

- As second-line T/t
- As preventative step

  when performed **at the time of breast cancer surgery** for patients with high risk for developing BCRL.

Types:

- **Ablative procedures / Debulking procedures**
  - surgical removal of edematous or fibrotic tissue in pts with substantial volume of solid, non-pitting edema
- **Reroute lymphatic flow in the axilla** - for patients with pitting edema that is not yet fibrotic
  - lymphatic- venous anastomosis (LVA).
  - vascularized lymph node transfer (VLNT)

Precautionary Guidelines

- **Good skin care practices: Essential**
- **Use of a compression garment on the at-risk arm during air travel,**
- **Avoidance of venipuncture arm at risk for BCRL**
- **Avoid using of blood pressure cuffs on the arm at risk for BCRL**

Based on limited, low-level evidence

Breast Cancer Related Cardiotoxicity

Cardiac Toxicity: Breast Cancer

Meta-analysis:

- 4.3% increase in non-breast cancer-related death in pts, rcvd RT.

- Majority of non-breast cancer deaths were recorded as vascular deaths.

Questions:

- **What is the mechanism of radiation-induced heart disease?**
- **What dose of radiation to what part of the heart actually causes toxicity?**
- **Are there doses that are safe for the heart?**
- **What is the most meaningful parameter to guide treatment planning?**

Important findings

- Mean heart dose (MHD)
- Dose to the left anterior descending coronary artery (LAD)

Analysis revealed: cumulative relative risk of major coronary events increased **linearly with the MHD**

  - **7.4% per Gy beginning within the first few years after RT and continuing thereafter.**
  - increase in the rate of coronary events was highest in the first 9 years after RT (relative risk increasing approxi- mately 16% per Gy MHD).

- There was **no identifiable threshold dose** below which there was no association with cardiac events.

Table 4.4 Toxicity grading for radiation induced cardiovascular disease (RICVD)

CTCAE v5	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Pericarditis	Asymptomatic, ECG or physical findings (e.g., rub) consistent with pericarditis	Symptomatic pericarditis (e.g., chest pain)	Pericarditis with physiologic consequences (e.g., pericardial constriction)	Life-threatening consequences; urgentintervention indicated	Death
Valve disease	Asymptomatic valvular thickening with or without mild valvular regurgitation or stenosis by imaging	Asymptomatic; moderate regurgitation or stenosis by imaging	Symptomatic; severe regurgitation or stenosis by imaging; symptoms controlled with medical intervention	Life-threatening consequences; urgent intervention indicated (e.g., valve replacement, valvuloplasty)	Death
Restrictive cardiomyopathy	Imaging findings only	Symptomatic without signs of heart failure	Symptomatic heart failure or other cardiac symptoms, responsive to intervention; new onset of symptoms	Refractory heart failure or other poorly controlled cardiac symptoms	Death

Factors

Treatment related

- Treatment / Target volume
- Technique of RT
- Systemic therapy

Patient related

- Anatomy
- Age
- Pre existing comorbidities

Special attention in patients with

- unfavorable cardiac anatomy,
- nodal, particularly, IMN irradiation,
- pre-existing risk factors for cardiac disease,
- older patients
- receiving cardiotoxic systemic therapy

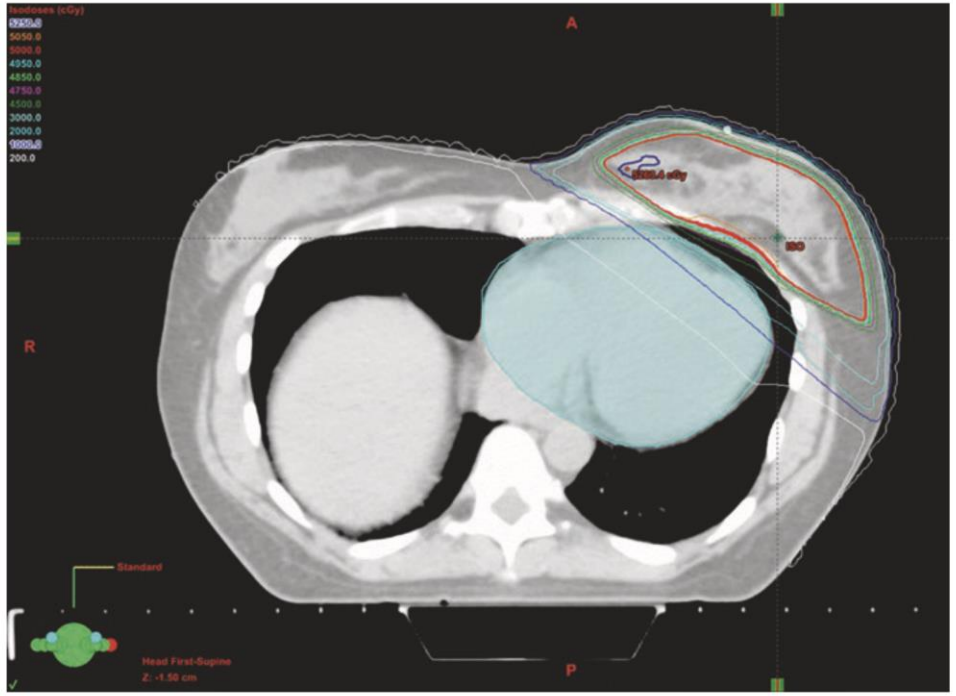
Cardiac sparing RT

- IMRT / VMAT
- DIBH
- Prone
- Proton
- Avoid RT in Elderly / high cardiac morbidity

Radioprotectants: No drug to have been approved for use in mitigating or preventing RICVD.

- Statins, ACE inhibitors, Amifostine, Melatonin are some of the drugs which have shown good results in animal testing.

IMRT and Arc Therapy



- Conform dose to the target
- Minimizing dose to critical structures.

Successfully limit the high-dose regions within the heart

<u>But at the expense of</u>

- increasing the low-dose region to the heart
- overall higher Mean Heart Dose

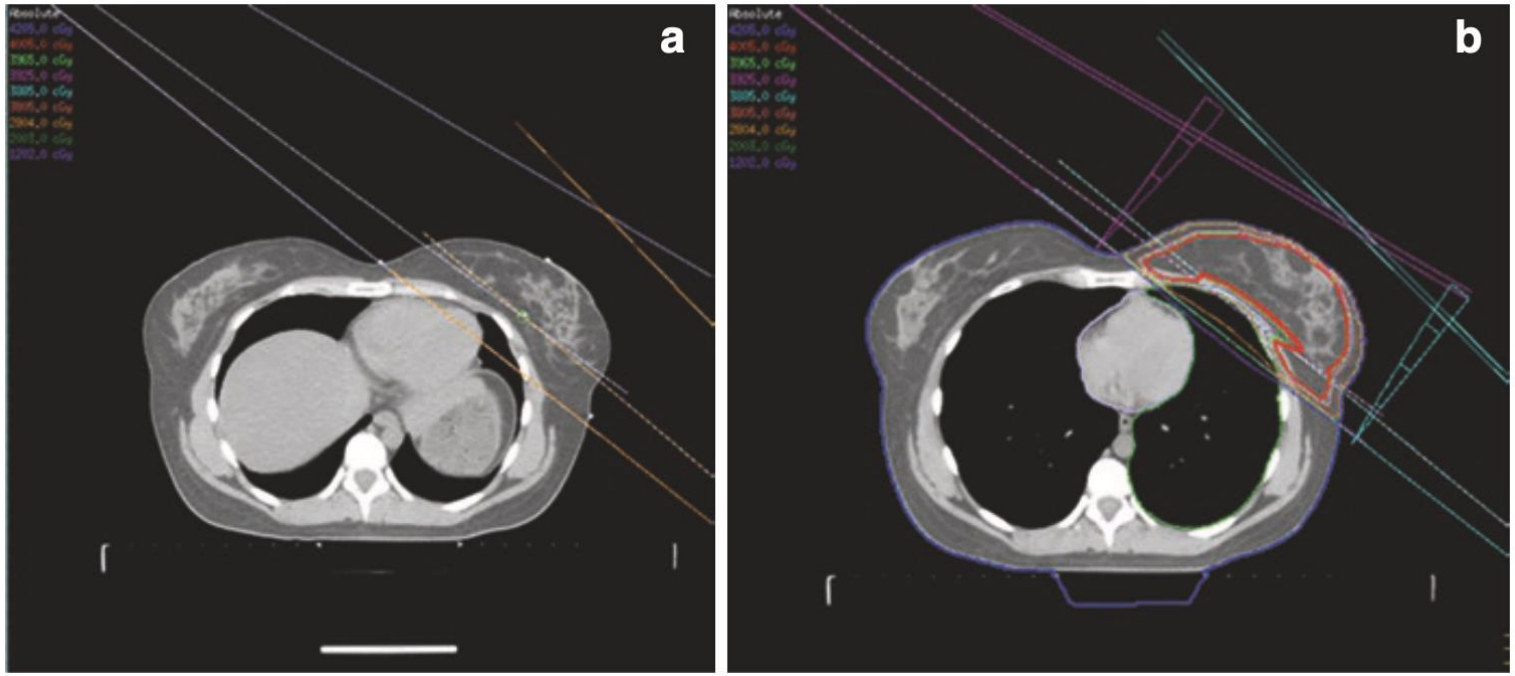
Deep Inspiration Breath Hold

- Deep inspiration displaces the heart inferiorly and posteriorly

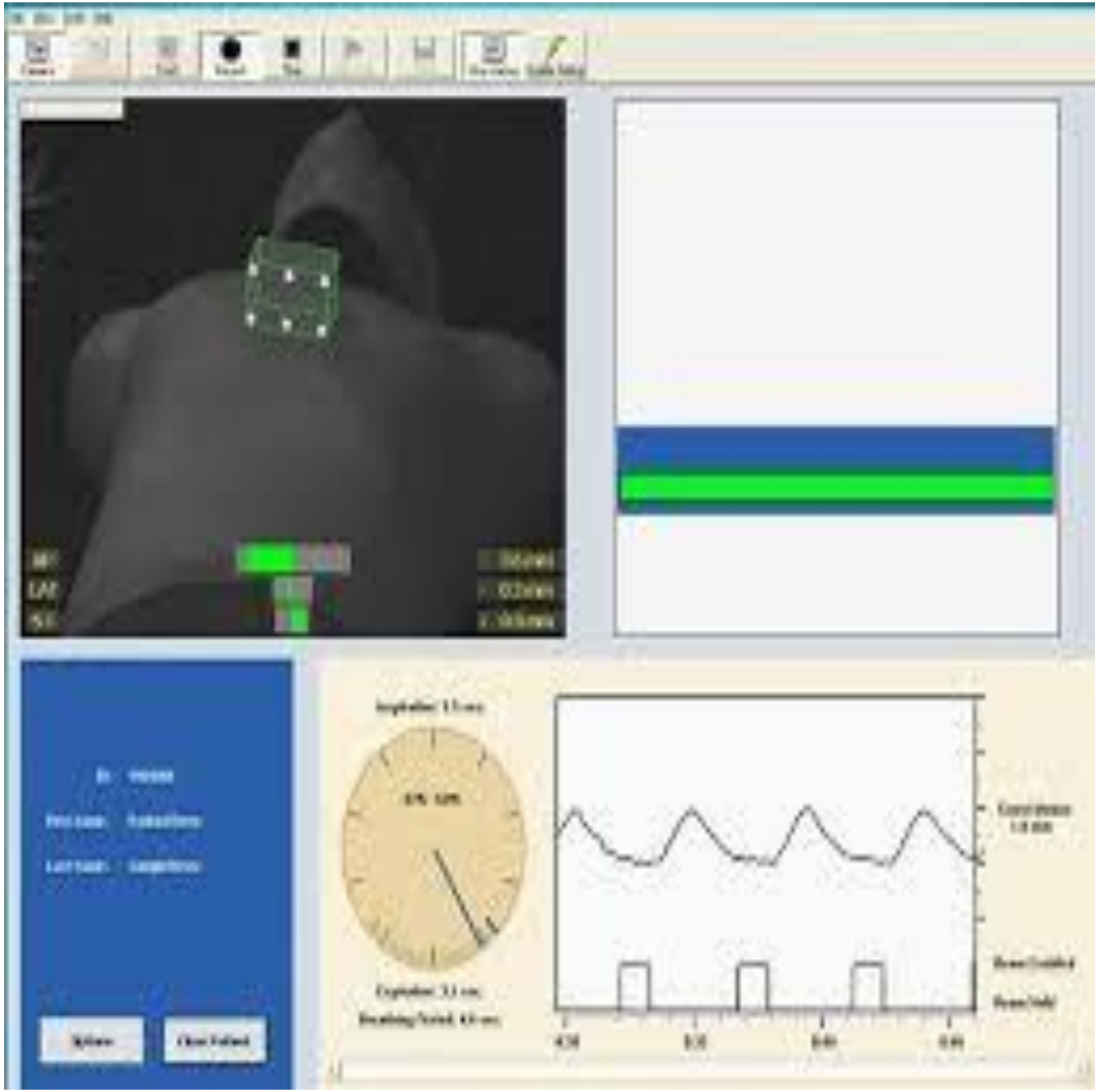
=> reducing the volume of irradiated heart

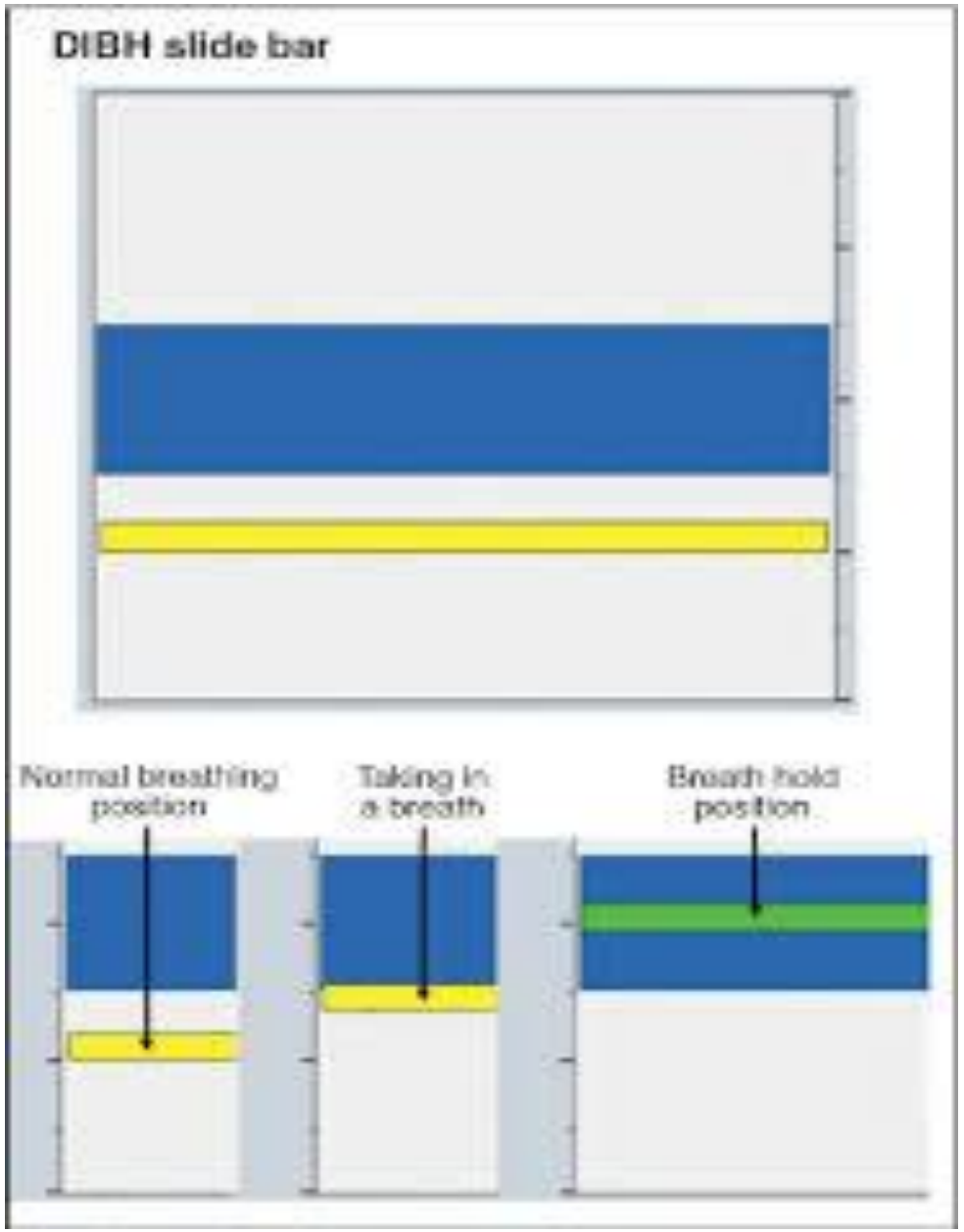
Significantly lower

- Mean heart dose,
- V20 Gy,
- V40 Gy

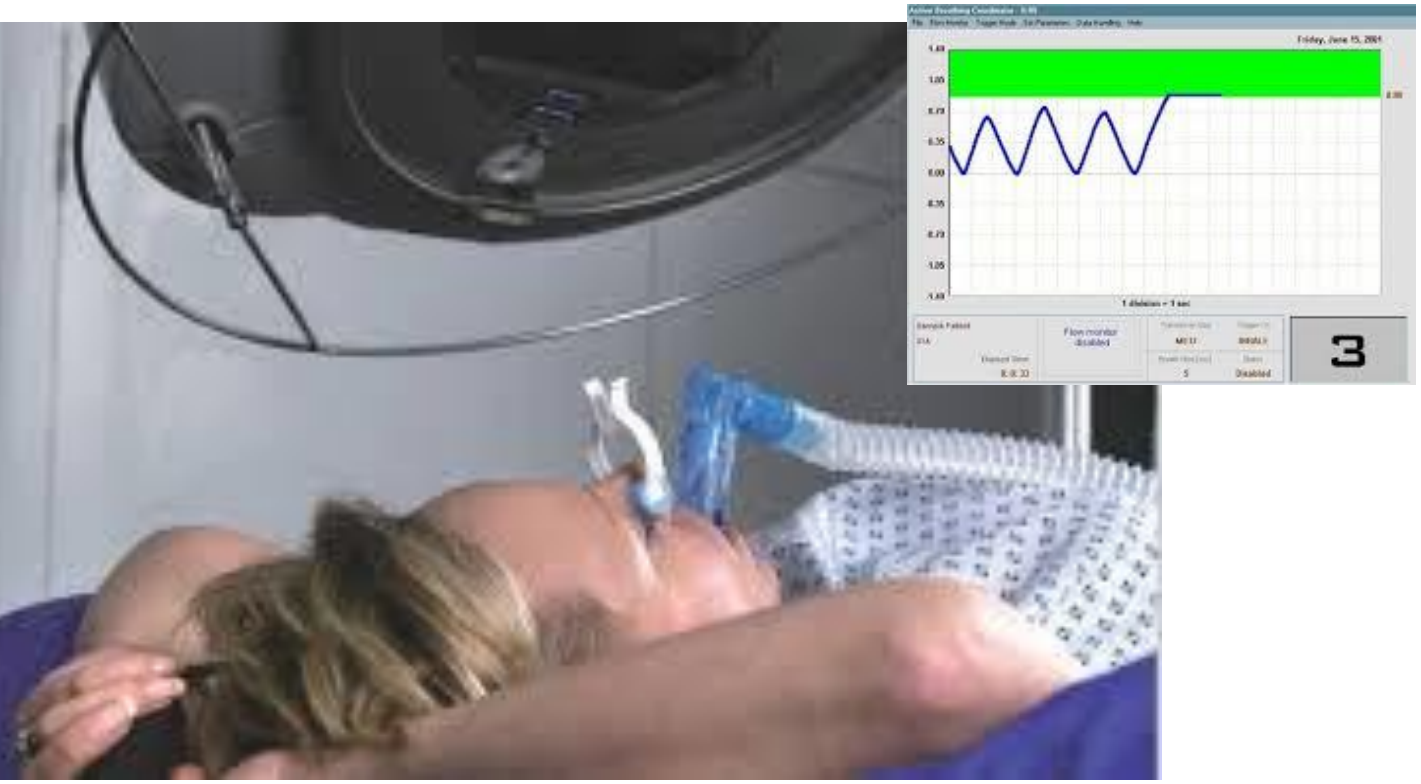


Varian RPM




DIBH slide bar
Normal breathing position
Taking in a breath
Breath hold position

Elekta ABC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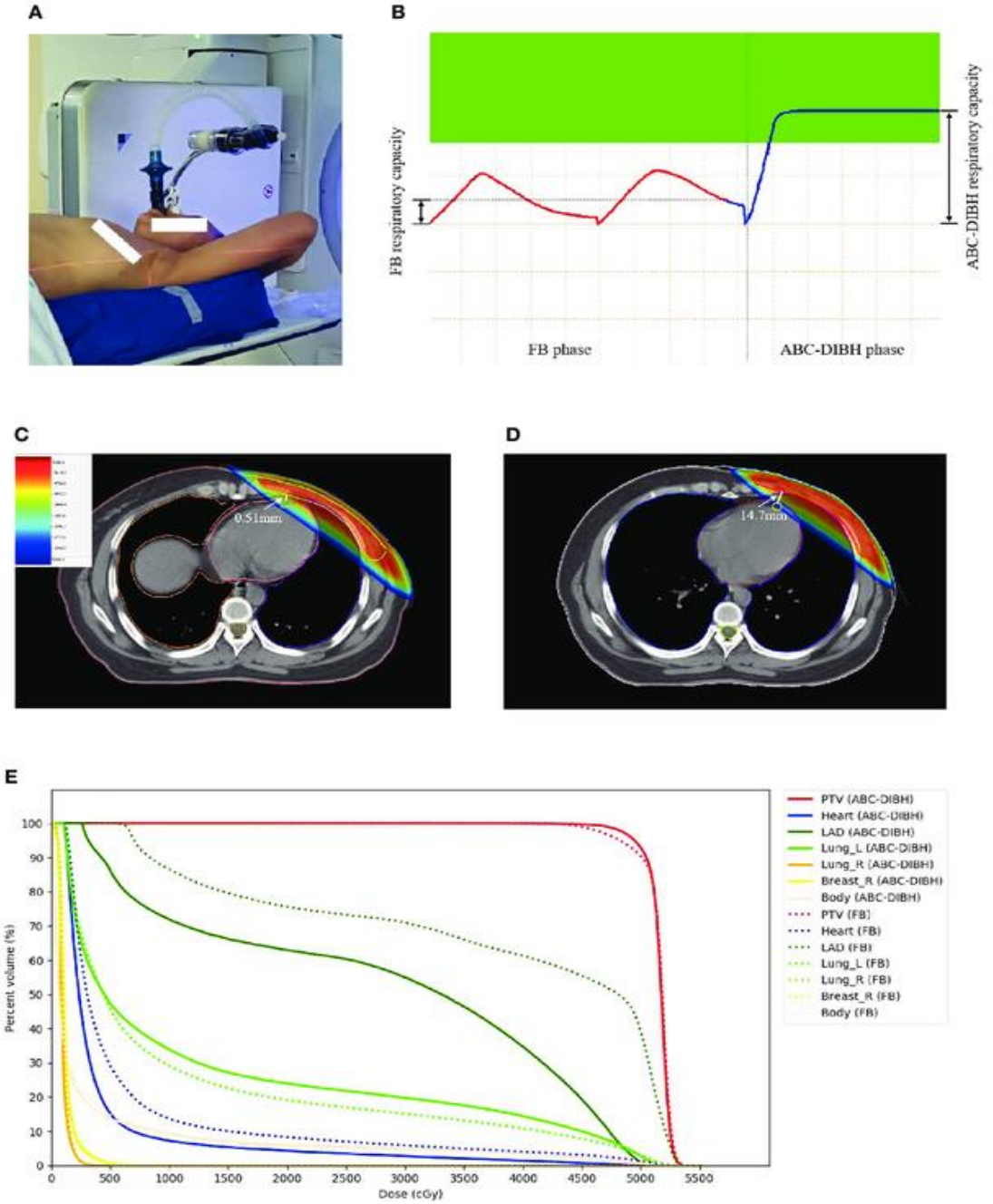
A
B
FB respiratory capacity
ABC-DIBH respiratory capacity
FB phase
ABC-DIBH phase
C
0.51mm
D
14.7mm
E
Percent volume (%)
Dose (cGy)
PTV (ABC-DIBH)
Heart (ABC-DIBH)
LAD (ABC-DIBH)
Lung_L (ABC-DIBH)
Lung_R (ABC-DIBH)
Breast_R (ABC-DIBH)
Body (ABC-DIBH)
PTV (FB)
Heart (FB)
LAD (FB)
Lung_L (FB)
Lung_R (FB)
Breast_R (FB)
Body (FB)

Align RT

A


alignrt®
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Default ROI
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VRT mm -17.1
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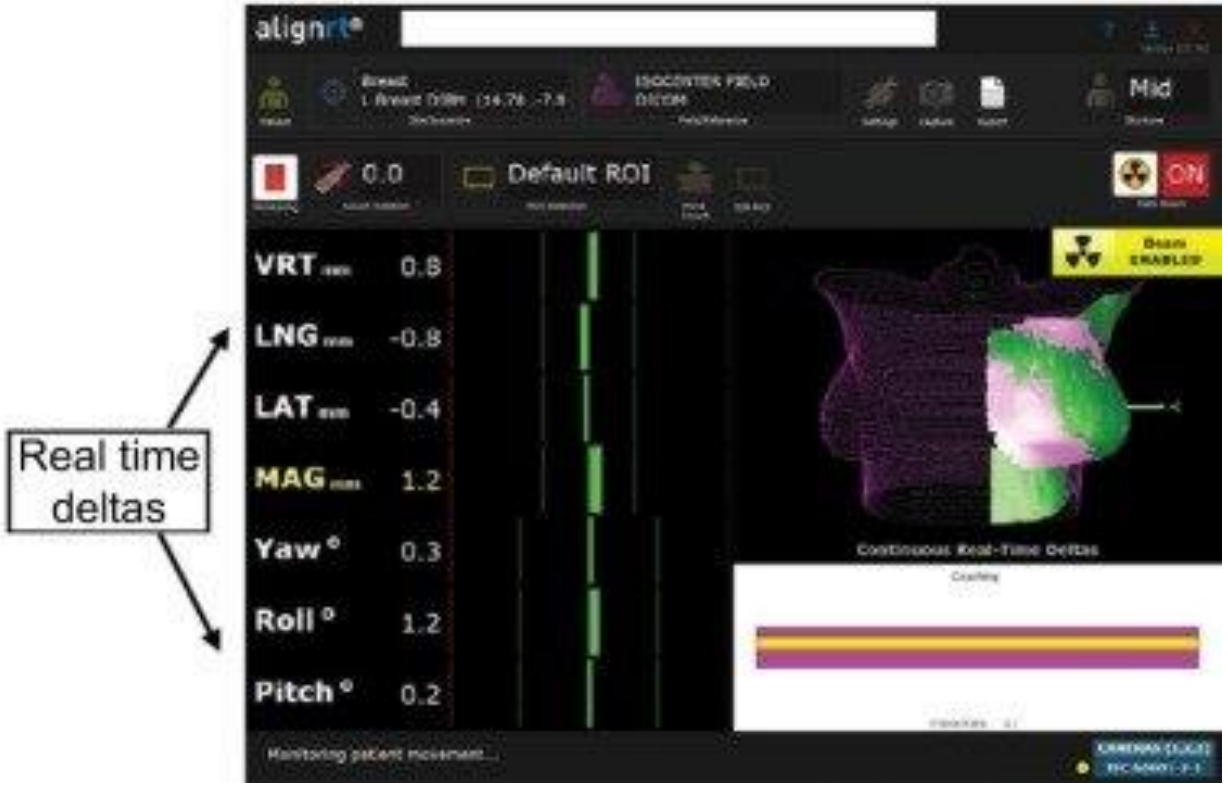
Continuous Real-Time Deltas
Real time deltas

B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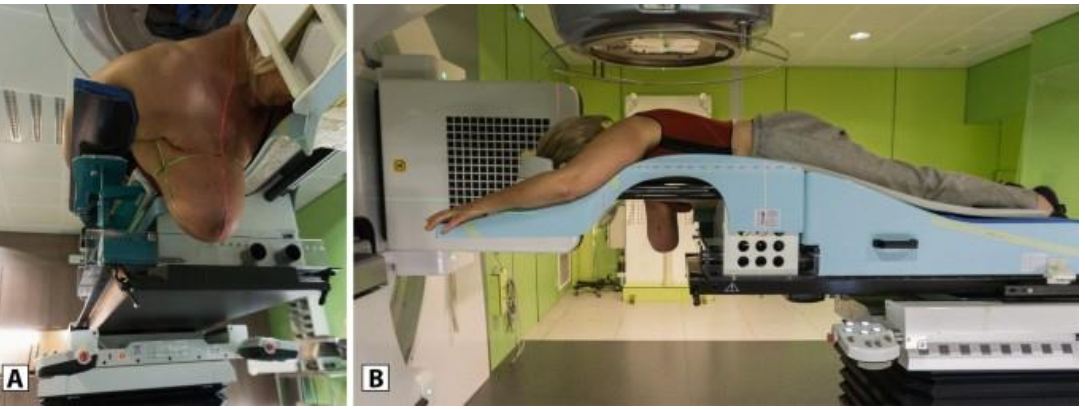
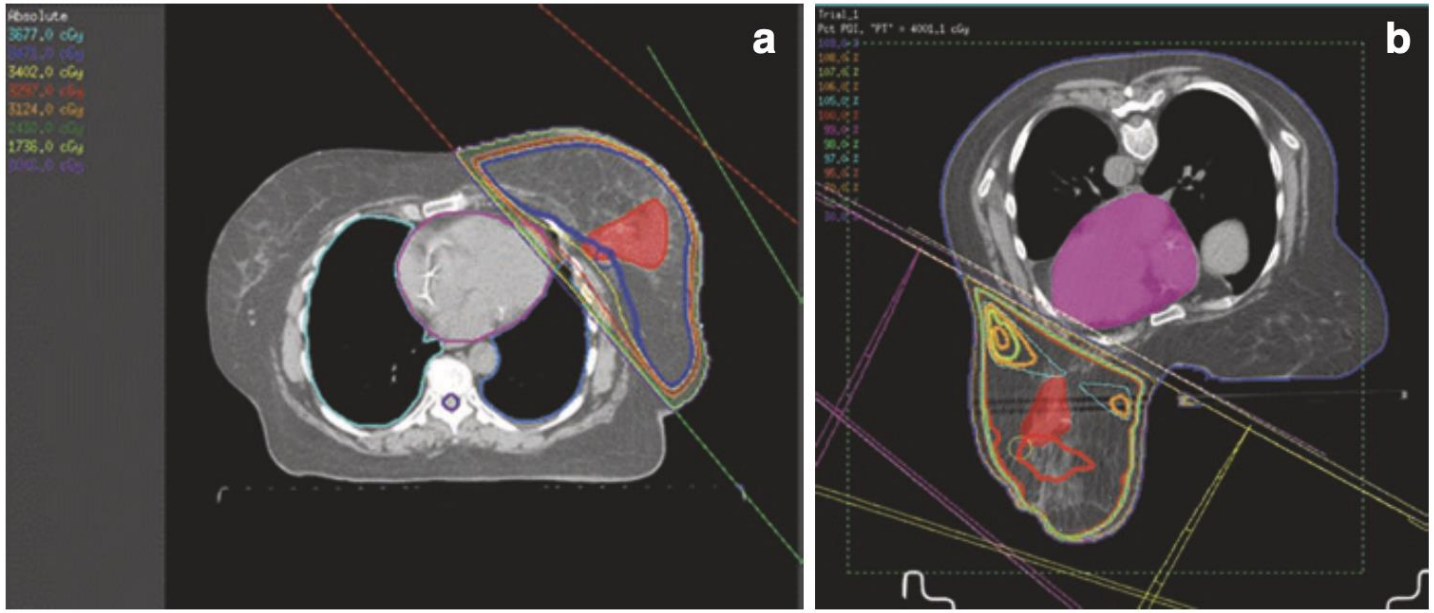
Yaw ° 0.3
Roll ° 1.2
Pitch ° 0.2
Continuous Real-Time Deltas
Real time deltas

Prone Positioning

- Decrease cardiac dose from tangential breast irradiation.
- Reduce skin toxicity in women with large, pendulous breasts
- Reduce lung dose.

- Not for N+ve





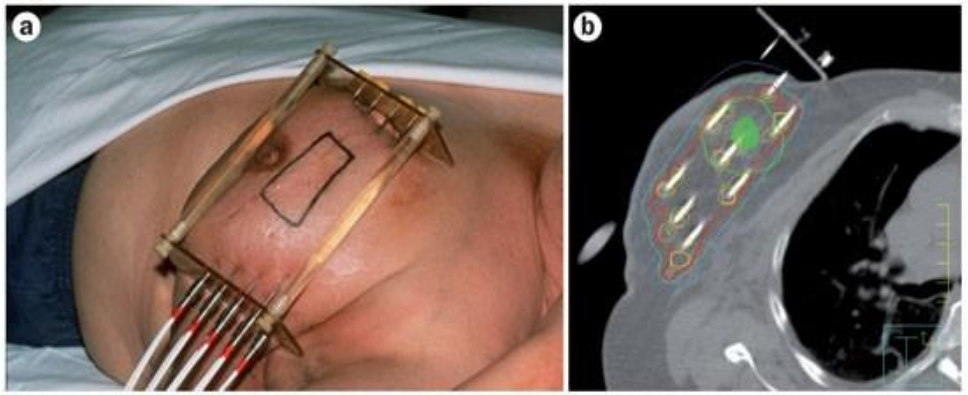
Partial Breast Irradiation

Selected patients: Suitable & Cautionary

smaller treatment volumes

=> reduces the volume of irradiated heart

as compared to whole breast irradiation
depending upon the location of the tumor bed.

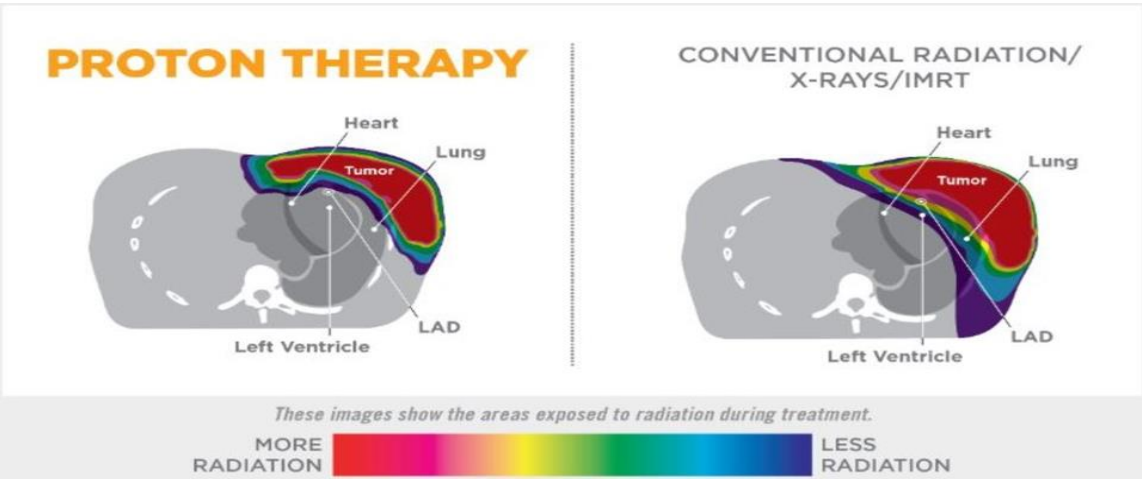


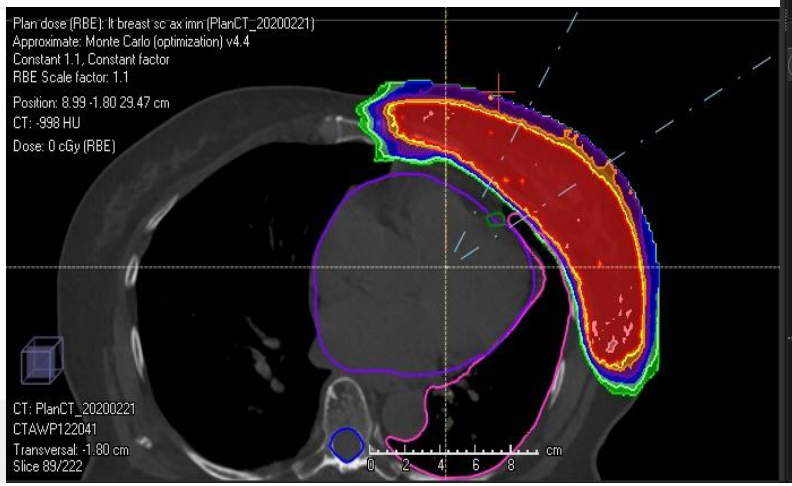
<u>Techniques:</u>

- Interstitial brachytherapy,
- Applicator-based brachytherapy,
- 3D-CRT external beam.

Proton Beam

- Reduce cardiac dose **by optimization of the Bragg peak**

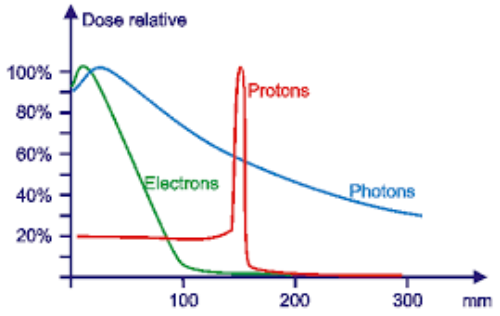




<u>Radiotherapy Comparative Effectiveness (RADCOMP) study will compare</u>

- cardiovascular morbidity and mortality,
- health-related quality of life,
- cancer control outcomes

<u>among women with LABC randomized to either proton or photon therapy</u>



Cardiac Dose Constraints

- **V25 < 10%**

  Cardiac mortality at 15 years <1%

- **Mean Heart Dose < 2 Gy**
  - 10% increase in the relative risk of major coronary events compared to mean cardiac dose of zero.
  - If MHD > 2 Gy : increased risk of major coronary events > 30%

	Left (No RLNI)	Left (with RLNI)	Right	Mean Heart Dose
NSABP B 51	V20 < 5% V10 < 30%	V25 < 5% V15 < 30%	V10 < 10%	< / = 4 Gy
Alliance A011202	V25<10%		V25 < 2%	</= 4 Gy

Cardiac Dose Constraints

- **LV – V5**
  - optimal probability model to predict for a radiation-induced acute coronary event includes LV–V5, age, and pre-existing cardiac risk factors.
- **Wall segments of left ventricle & Coronary artery segments**

  doses should be limited as much as possible without compromising target coverage.

Table 4.5 Cardiac tissue dose constraints for conventional fractionated radiotherapy

Structure	Dose/fraction	Dose	Volume
Whole heart (Breast radiotherapy)	2 Gy	<2.5 Gy	Mean
Left ventricle (Breast radiotherapy)	2 Gy	<3 Gy V_5 V_{23}	Mean <17% <5%
LAD (Breast radiotherapy)	2 Gy	<10 Gy V_{30} V_{40}	Mean <2% <1%

Follow-Up and Screening

Different guidelines proposed several types of screening:

1. Yearly physician visits and blood pressure control,
2. Twice a year lipid screening,
3. For patients with no additional risk factors: transthoracic echocardiography (TTE) 10 years after RT and repeat TTE every 5 years.
4. For patients with >1 additional risk factor: TTE 5 years after RT, repeat TTE every 5 years, noninvasive stress imaging every 5 years.
5. For patients with symptoms of chronic heart failure (CHF), angina, and new murmur: refer immediately for TTE and stress imaging.

Treatment:

- Referring the patient to a cardiologist.
- Treatments vary according to the disease type

Breast Cancer Related Pulmonary toxicity

Radiation pneumonitis

- >/= Grade 2 RP : 0–30%
- Modern era risk of <5%

Reasons:

- 2D vs. CT-based
- radiographic vs. clinically symptomatic
- breast/chest wall only vs. comprehensive regional nodes

RP: acute or subacute toxicity

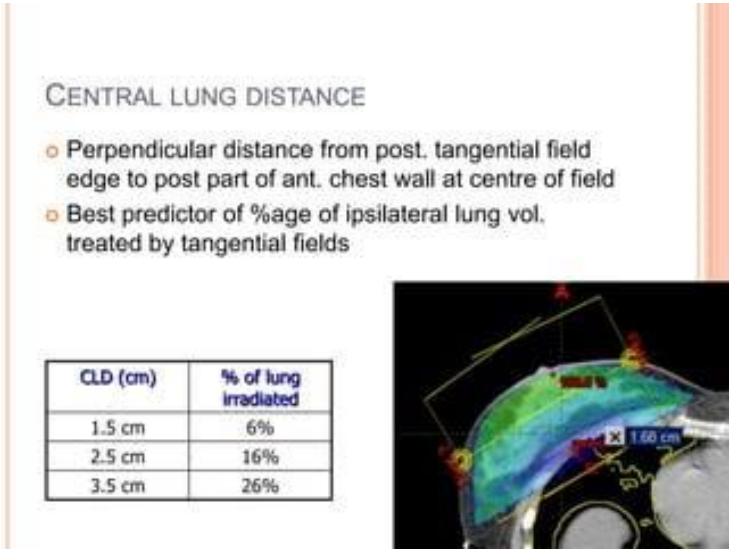
1 – 6 months following RT

Symptoms:

- cough,
- dyspnea,
- low-grade fever,
- increased sputum production,
- severe cases - hypoxia.

Radiation Pneumonitis: Risk factors

- Central Lung Distance



- V20 < 20% or <25%
- Mean Lung Dose <15%

- Higher risk with Inclusion of nodal areas
  - SCF: strong association with RP incidence (OR = 5.07) (95% CI = 1.95–13.22).
  - IMN: OR 1.04 (95% CI, 0.43–2.54)

- No significant effect
  - concomitant use of Hormone therapy
  - prior exposure to chemotherapy

Pulmonary fibrosis

- Uncommon
- Late toxicity
- 6–24 months post-RT, with stabilization at 2 years
- overall rate of grade ≥2 pulmonary fibrosis only 3%

Risk is higher (upto 29%) in patients, receiving

  - anastrozole
  - taxane agent

- However, no clinically meaningful decline in QoL

Methods to reduce risk:

- DIBH: With maximal inspiration, the lung volume is expanded => leading to a lower percent of total lung volume within the radiation field.
- Prone: Not suitable for L.N +ve pt

Dose Constraints

No regional nodal irradiation:

Per protocol: ≤15% of the ipsilateral lung should receive ≥20 gray (Gy)
Variation acceptable: ≤20% of the ipsilateral lung should receive ≥20 Gy
Per protocol: ≤35% of the ipsilateral lung should receive ≥10 Gy
Variation acceptable: ≤40% of the ipsilateral lung receives ≥10 Gy
Per protocol: ≤ 50% of the ipsilateral lung should receive ≥5 Gy
Variation acceptable: ≤55% of the ipsilateral lung receives ≥5 Gy

Regional nodal irradiation:

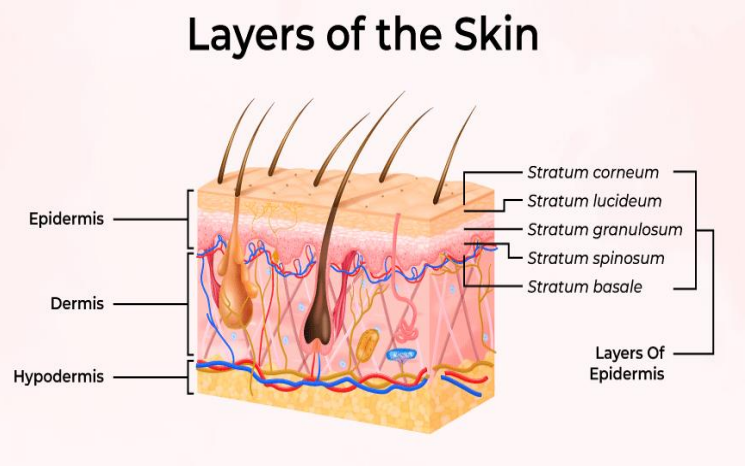
Per protocol: ≤30% of the ipsilateral lung should receive ≥20 Gy
Variation acceptable: ≤35% of the ipsilateral lung should receive ≥20 Gy
Per protocol: ≤50% of the ipsilateral lung should receive ≥10 Gy
Variation acceptable: ≤60% of the ipsilateral lung receives ≥10 Gy
Per protocol: ≤65% of the ipsilateral lung should receive ≥5 Gy
Variation acceptable: ≤70% of the ipsilateral lung receives ≥5 Gy

Breast Cancer Related Skin toxicity

Skin Toxicities: Breast Cancer

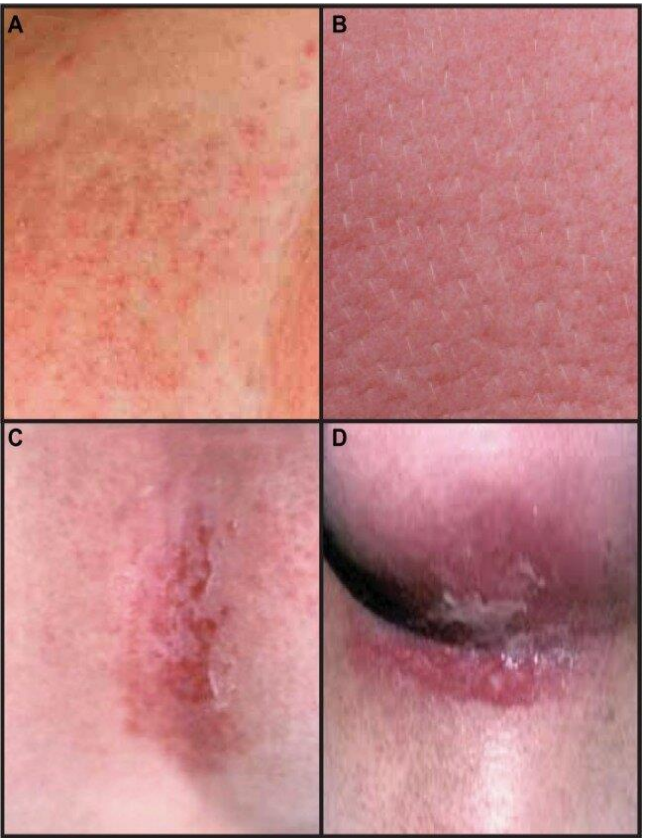
- The maturation process for these cells is about 2 weeks
- Complete reconstitution of the epidermis requires a period of 1–2 months

Layers	Function	Specific cells
Stratum corneum	Barrier to extrinsic pathogen	Dead keratinocyte
Stratum granulosum & lucidum		Keratinocytes get mature
Stratum spinosum	Immune response	Langerhans cells -
stratum basale	UV protective Melanin, Superficial Sensory information	highly proliferative keratinocytes , melanocytes, Merkel cells
Dermis	Thermoregulation, lymphatic vessels, sebaceous glands, nociceptors, tactile receptors, and hair follicles.	fibroblast-dominated, blood-rich area



Acute skin toxicity: Grading

	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
Acute	None	Follicular, faint or dull erythema/epilation/dry desquamation/decreased sweating	Tender or bright erythema, patchy moist desquamation/moderate edema	Confluent, moist desquamation other than skin folds, pitting edema	Ulceration, hemorrhage, necrosis



Generally start around the 2nd to 4th week of radiation treatment
Occur within 30 days from completion of therapy.
The maximal peak response occurs 1–2 weeks following the conclusion of radiotherapy

Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Faint erythema or dry desquamation	Moderate to brisk erythema; patchy moist desquamation, mostly confined to skin folds and creases; moderate edema	Moist desquamation in areas other than skin folds and creases; bleeding induced by minor trauma or abrasion	Skin necrosis or ulceration of full thickness dermis; spontaneous bleeding from involved site	Death

Grades of Radiation Dermatitis

Risk factors

Treatment factor

- Radiation technique
  - IMRT vs 3DCRT vs Conventional
- Dose / Fractionation
  - Hypo# vs Conventional #
- Dosimetric parameters
  - Dose inhomogeneity (>107%, V107%)
  - Skin dose (0.07 mm from the skin surface)
- BCS vs MRM
- RLNI vs No RLNI

Patient factor

- High BMI (larger breast size, greater body mass, and higher disease stage, larger treatment field size)
- Genetic Predisposition via Altered DNA Damage Repair
- Dysfunctional Immune Response
- Smoking

Anticipatory practices

- Smoking cessation
- Physical activities that irritate the skin within the radiation field should be avoided or pursued with caution
- Use of supportive undergarments
- General hygiene practices should be explored and optimized.
- No excess toxicity with the addition of soap (non-perfume) soap
- Use of deodorant during radiotherapy is controversial

  - concern that the metallic ingredients within some deodorant could lead to scatter and increased skin dose.

  - Studies have failed to show a significant increase in skin reactions with use of these products.

Prophylactic approaches

To moisturize the affected skin, reduce friction and possibly minimize local inflammation.

- Calendula cream
- Aloe vera
- Use of oil emulsions has generally been discouraged

  theoretically increase the dose to the skin by creating pseudobolus.
- **Topical steroids: Mometasone furoate and emollient care was found to result in less acute radiation dermatitis**

Non-scented and lanolin-free hydrophilic cream for potential prevention of radiation skin reactions

Treatment of Acute Skin Toxicity

- Continue to use their daily topical cream
  to increase skin moisture to support regeneration of the epidermis
- Cool air – high flow
- Topical Dye
- Mepilex dressings
- Hydrocolloid and hydrogen dressings.

- Biological membrane dressing
- Silver ion-based creams may be applied if there is concern for infection
- SCGG recommendations: low-dose topical steroids for the management of pruritus and irritation

Late Skin Toxicity: Grading

Figure 8 Total mastectomy patients 24 months post-RT skin atrophy, Clinical picture.

- Radiation-Induced Fibrosis
- Atrophy
- Hyperpigmentation
- Telangiectasia
- Morphea
- Radiation Recall

Table 1 Grading scales for fibrosis

Scale	Description	0	1	2	3	4	5
LENT-SOMA	Post-radiation fibrosis	None	Barely palpable/increased density	Definite increased density and firmness	Marked density, retraction, and firmness	N/a	N/a
RTOG	Subcutaneous tissue	None	Slight induration (fibrosis) and loss of subcutaneous fat	Moderate fibrosis but asymptomatic, slight field contracture, <10% linear reduction	Severe induration and loss of subcutaneous tissue, field contracture >10% linear measurement	Necrosis	Death
CTCAE	Fibrosis – deep or superficial connective tissue[a]	None	Mild induration, able to move the skin parallel to the plane (sliding) and perpendicular to the skin (pinching up)	Moderate induration, able to slide skin, unable to pinch skin, limiting instrumental ADL	Severe induration, unable to slide or pinch skin, limiting joint or orifice movement, limiting self-care ADL	Generalized, associated with signs or symptoms of impaired breathing or feeding	Death

[a]Deep and superficial connective tissue fibroses are measured on two separate scales, with the same grading rubric

Radiation related risk factors

- Increased radiation dose,
- Increased volume of radiated tissues,
- Presence of a radiation boost
- Technique

Patient related	Treatment related
Age	Radiotherapy
Breast size	Radiation dose
Genetics	Volume of radiated tissue
Connective tissue disorders	Use of a boost
TGF-B serum levels	Radiation technique
RILA	Surgery
	Surgical complications
	Chemotherapy
	Timing of chemotherapy

Breast hypofractionation has not been shown to increase the rate of fibrosis.

START A/B trials

Whelan hypofractionation trial

Radiation induced fibrosis

- Decreased tissue compliance,
- Atrophy,
- Skin retraction,
- Toughness to palpation
- Hyperpigmentation, dryness, and telangiectasia.
- Significant induration and rigidity or retraction of the breast or chest wall.
- Skin ulceration or necrosis may occur in severe cases.
- Extreme RIF resulting in a mass mimicking breast cancer recurrence

Treatment of Late Skin Toxicities:

- Options are limited, so their efficacy
- **Physical therapy**: exercise protocols
  - to maintain recovery,
  - movement of the impaired shoulder
  - massage therapy - *Deep friction massage may also be helpful*
- **Medical management**
  - Pentoxyphylline
  - Vit E
  - Oral and topical steroids may be considered
  - psoralen UVA (PUVA) therapy
  - Ultrasound phonophoresis combined with hyaluronidase
  - Hyperbaric Oxygen
- *Surgical interventions*: For extreme case

Morphea:

- Topical calcipotriol - vitamin D3 analog,
- UVA1 irradiation

Telangiectasia:

- pulse dye laser.

PMRT in Breast Reconstruction: Toxicities

PMRT in Breast Reconstruction:

Surgical factors

- **Implant + PMRT**:
  - capsular contracture,
  - compromises in the RT plan
  - asymmetry and impaired cosmesis,
  - infections,
  - incision breakdown
  - implant loss
- **Autologous + PMRT**:
  - compromises in the RT plan
  - fat necrosis,
  - vascular complications,
  - fibrosis,
  - contour deformities,
  - need for reoperation,
  - flap loss

Type	Time	Location
• Implant • Autologus	• Immediate • Delayed • 2 staged	• Sub pectoral • Subcutaneous

	Timing	Outcome
Yale	< 4 months	Higher infection Less capsular contracture
UCSF	< 6 months	Implant failure more
MD Anderson	7.1 m (median)	Flap based 20 % implant based

	Subcutaneous	Subpectoral
Pros	Less Post Op visits Faster expansion Lack of animation deformity	Decreassed Edge visibility Decreased Capsular contracture
Cons	Increased Edge visibility Increased Capsular contracture	Increassed pain Increased procedure time Risk of breast animation deformity

PMRT in Breast Reconstruction:

Surgical factors

- **Implant + PMRT**:
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  - compromises in the RT plan
  - fat necrosis,
  - vascular complications,
  - fibrosis,
  - contour deformities,
  - need for reoperation,
  - flap loss

Patient factors: increased risk poor outcome

- higher BMI
- smoking,
- diabetes

Type	Time	Location
• Implant • Autologus	• Immediate • Delayed • 2 staged	• Sub pectoral • Subcutaneous

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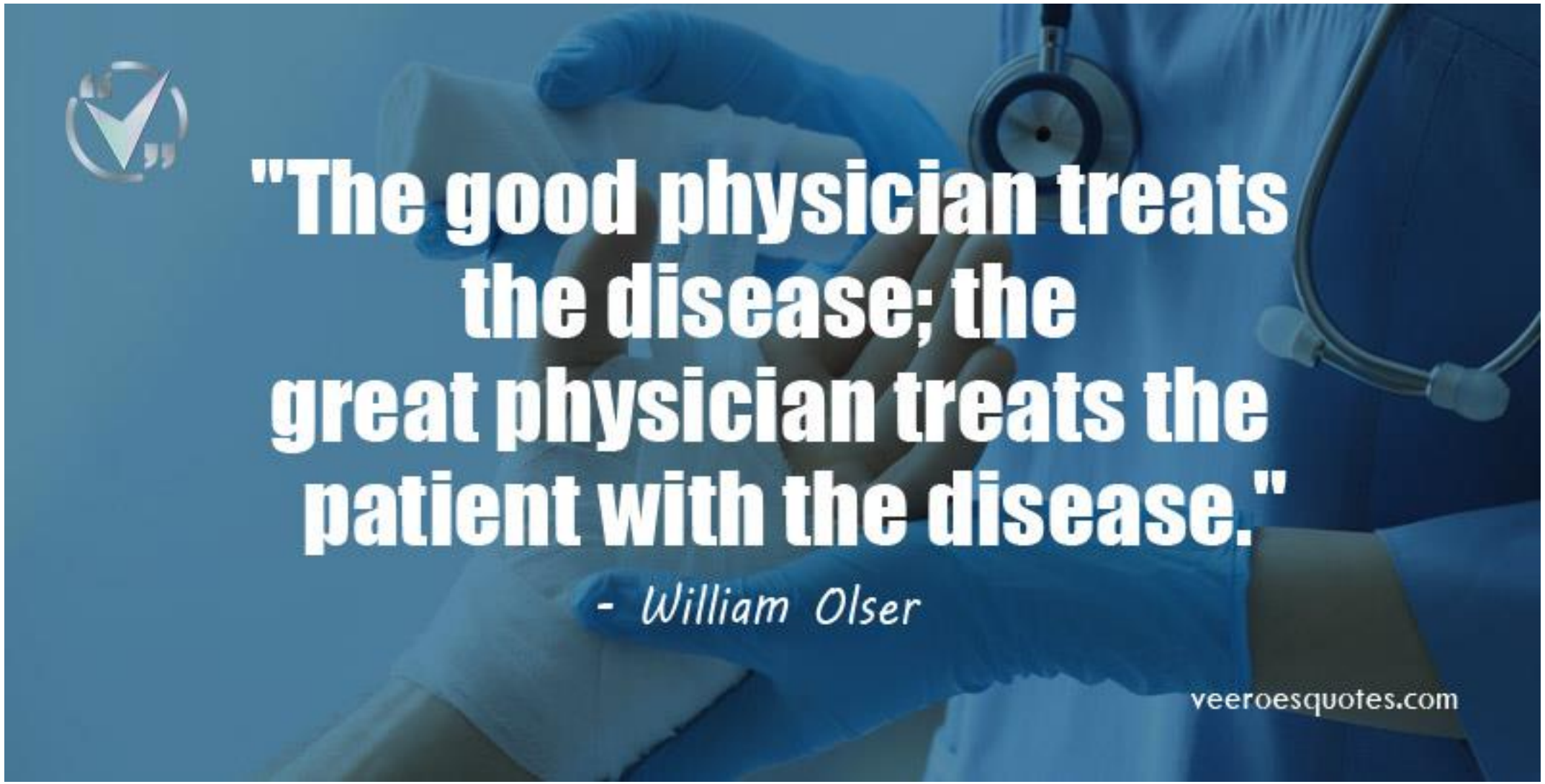
Others: Multifactorial

- **Pain**
- **Fatigue**

- Exercise: safe, effective, and low-cost measure
  - Improve both quality of life and quantity of life
  - reduce
    - ✓Pain
    - ✓Fatigue
    - ✓BCRL
- Nutrition:
  - Fruits , Vegetables
  - Avoid red meat, processed food, alcohol
- Mindfulness based intervention
  - ➢Yoga
  - ➢Stress reduction
  - ➢CBT


NOT ME
THEIR FAULT
HIS FAULT
HER FAULT


"The good physician treats the disease; the great physician treats the patient with the disease."
- William Olser
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