

RADIATION INDUCED TOXICITY IN LUNG CANCER – **BALANCING EFFICACY & SAFETY**

DR. L. SOFIA RAJESH, MD (PGIMER CHD).,

GVN CANCER INSTITUTE

TRICHY

INTRODUCTION

- ▶ Radiation is the cornerstone in Lung Cancer treatment.
- ▶ Wide options – Conventional CRT ,SBRT , Immuno Consolidation, Re- irradiation
- ▶ Increases the toxicity - Balance with efficacy !!!
- ▶ Therapeutic ratio

► SPECTRUM OF TOXICITIES

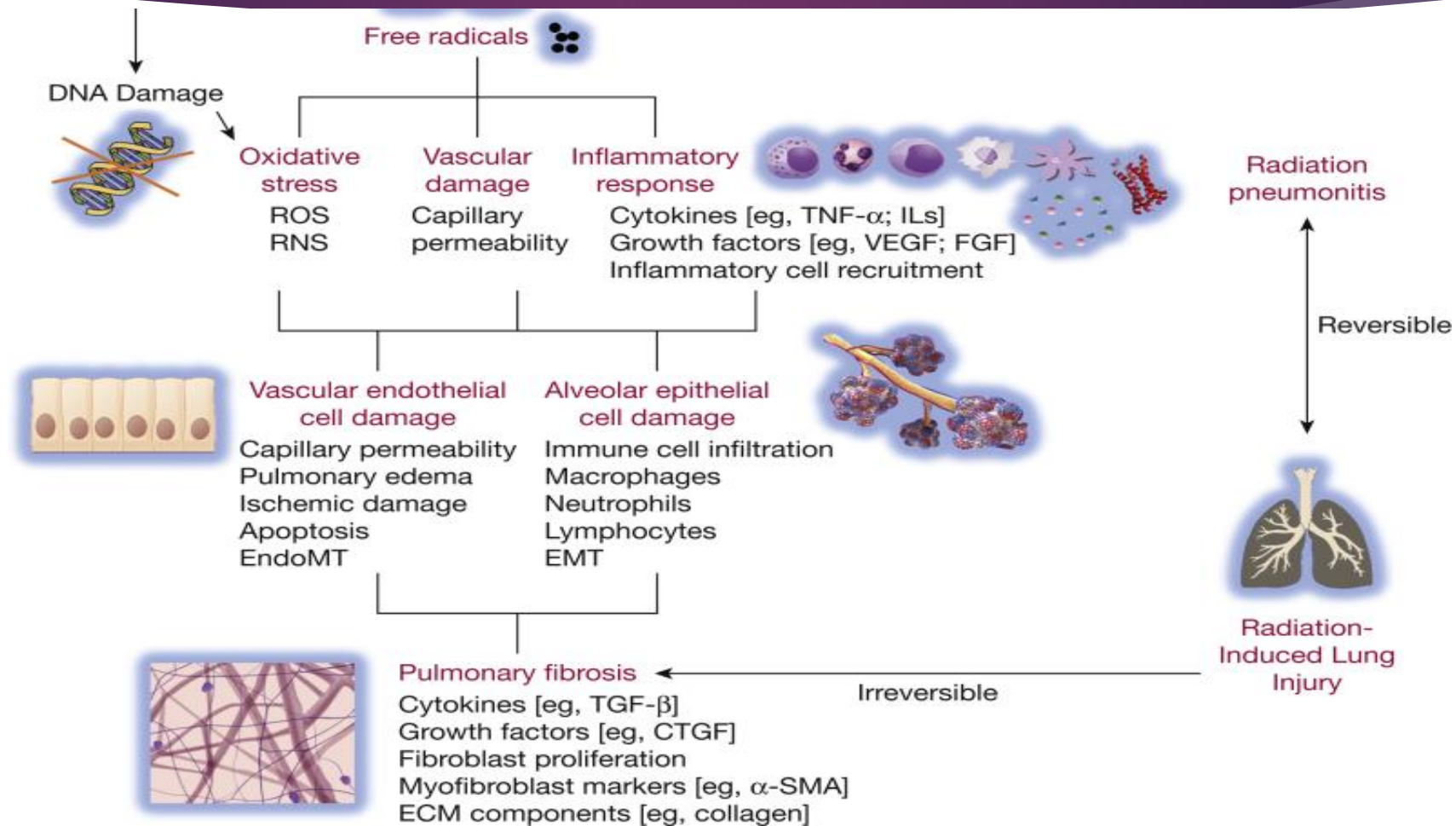
- PULMONARY
- CARDIAC
- ESOPHAGEAL
- CHEST WALL , DERM , NEURO , HEMAT

► RADIATION INDUCED LUNG INJURY (RILI) – 5 TO 25 % IN CA LUNG

PATHO - PHYSIOLOGY

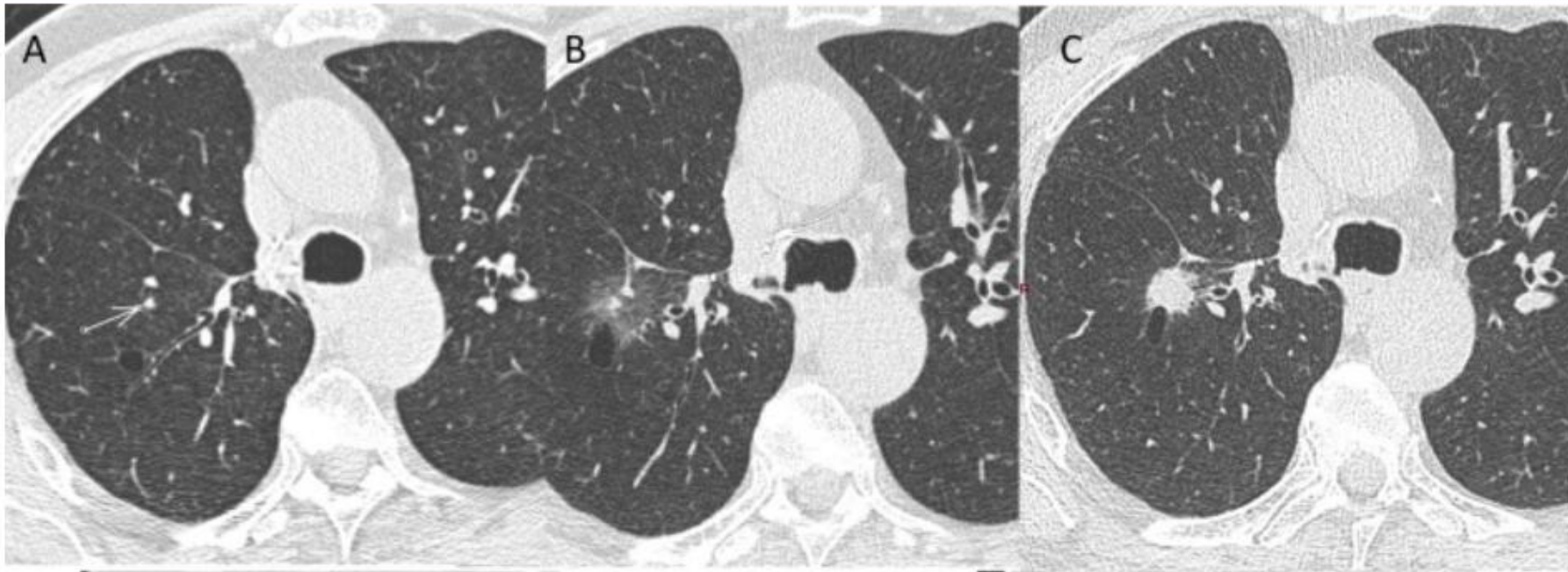
- ▶ THE EFFECT OF RADIATION ON LUNG
- ▶ DESCRIBED IN 1925 BY EVANS AND LEUCUTIA
- ▶ **ACUTE INJURY STATE** – RADIATION PNEUMONITIS
OCCURS WITHIN 6 MONTHS
- ▶ **CHRONIC INJURY STATE** – RADIATION PULMONARY FIBROSIS
OCCURS AFTER 1 YEAR

RADIATION PNEUMONITIS



MOLECULAR MECHANISMS

- ▶ ACUTE PHASE – Acute Reduction Of Endothelial Cells & Alveolar Epithelial Type 1 Cells
But ACE Type 2 Hyperproliferate And Compensate For Type I Cells
- ▶ SUB ACUTE – Functional Change Caused By Death Of Ace I / Endothelial Damage –
Increased Vascular Permeability & Interstitial Edema –Inflm Response
- ▶ CHRONIC – Pro Fibrotic Phase Occurs After Months –Activation Of Myofibroblasts,
Deposition Of Extra Cellular Matric– Chronic Fibrosis



QUANTEC Constraints (Conv RT)

- ▶ Mean Lung Dose (MLD) <20 Gy preferred
- ▶ V20 <30–35% lowers RP risk
- ▶ V5 <60% (especially IMRT)
- ▶ Risk rises sharply if MLD >20 Gy or V20 >35%



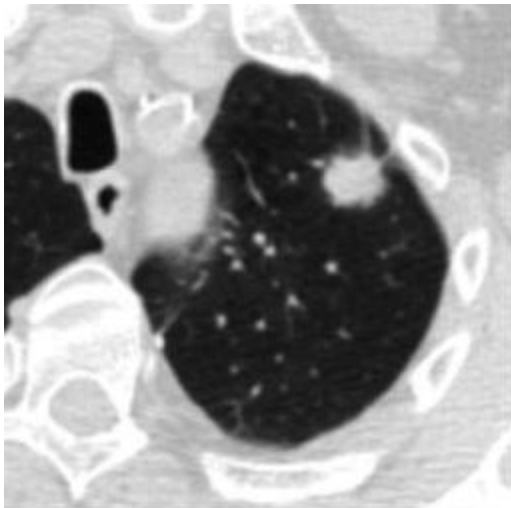
QUANTEC PNEUMONITIS Estimate

- ▶ MLD < 13 GY - less 10% Symp RP
- 13 – 20 GY - Intermediate risk
- > 20 GY - higher risk

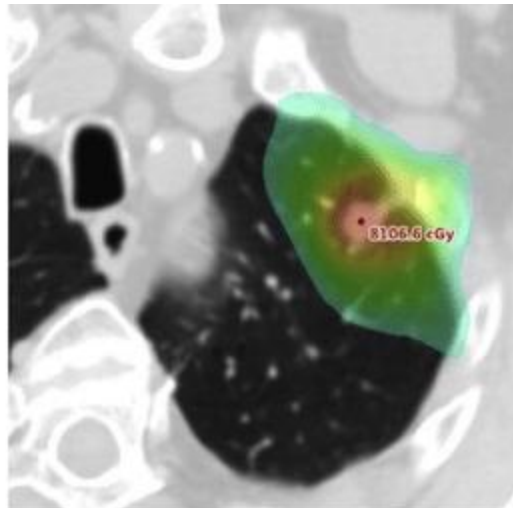
- ▶ RISK IS MODIFIED BY
 - Conc chemo / immune
 - Pre existing COPD
 - Baseline poor PFT
 - Re-irradiation

SBRT constraints

- ▶ Regimens – 54GY / 3# , 60GY / 5#
- ▶ LUNG – MLD < 8Gy , V20 < 10%, V5 – as minimal
- ▶ Heart – 0.5 cc < 32 Gy



Planning CT



Planning CT – Isodose colorwash 30Gy



40 months post-SABR

TECHNIQUES & DOSE CONSTRAINTS

- ▶ General Notion --- High V5 – Increased Risk Of Rp
- ▶ Secondary Analysis –RTOG 0617 Trial Showed, Lung V5 Was Not Associated With Grade 3 Toxicity, Whereas Lung V20 Was Associated With Increased Grade 3 Pneumonitis Risk In Multivariable Analysis.
- ▶ In Addition, The Rates Of Severe Pneumonitis Were Lower With IMRT Compared To 3DCRT

SBRT-related RILI

- ▶ Different biology vs conventional fractionation
 - ▶ More focal but can be severe if central/perihilar <2cm
 - ▶ Common patterns: patchy GGO, mass-like fibrosis
 - ▶ Chest wall and rib toxicity may coexist
-
- ▶ Mean ipsilateral lung dose matters
 - ▶ 5-fraction regimens carry lower toxicity than 3-fraction central SBRT

Immunotherapy Overlap

- ▶ PD-1/PD-L1 + RT increases pneumonitis risk
- ▶ PACIFIC trial highlighted this issue
- ▶ Timing matters: early IO after CRT may increase incidence
- ▶ Distinguish IO pneumonitis (multifocal/bilateral) vs RP (in-field)

CTCAE Grading (Practical)

- ▶ G0: No changes
- ▶ G1: Asymptomatic: radiologic only
 - no treatment
- ▶ G2: symptomatic, limits instrumental ADL
 - steroids
- ▶ G3: severe symp, self care ADL
 - oxygen required
- ▶ G4: life-threatening
 - ventilate
- ▶ G5: death

RADIOLOGICAL...

- ▶ CT / HRCT – LOW DOSE IMAGING
- ▶ ACUTE – GGO & consolidation
- ▶ CHRONIC -- radiation fibrosis emerge, such as volume loss, consolidation, and traction bronchiectasis

DIAGNOSIS OF RP

- ▶ COULD BE A DIAGNOSIS OF EXCLUSION – CONFOUNDING MEDICAL CONDITIONS
- ▶ ARRAY OF SYMPTOMS, CLINICAL, RADIOLOGICAL, TEMPORAL RELATIONSHIP OF RT TIMING etc
- ▶ PFT / BAL / Sr Procal
- ▶ X RAY / HRCT

TREATMENT

GRADE 2 RP

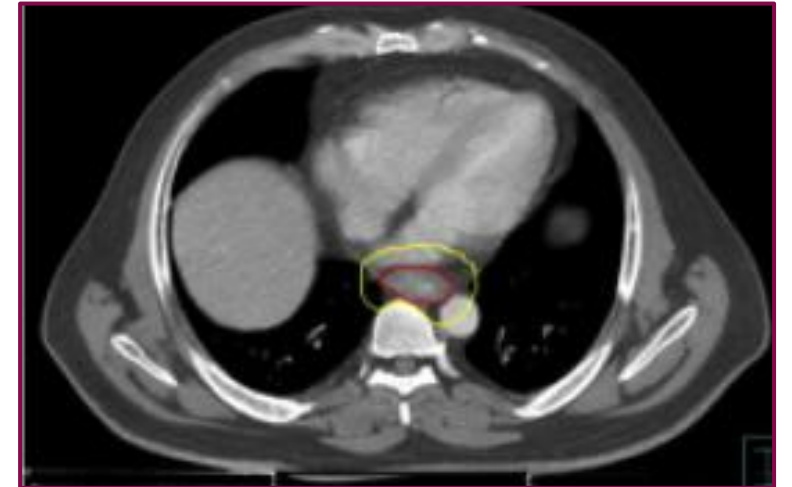
- Prednisolone 0.75- 1mg /kg/day
- Till 1 week after symp control
- Taper over 4 weeks

GRADE 3-4 RP

- IV methyl prednisolone 1-2 mg/kg/day
- Convert to oral – symp control
- Taper over 6 -12 weeks
- Consider PCP prophylaxis

ESOPHAGUS

- ▶ Odynophagia , dysphagia, weight loss
- ▶ Dose constraints - Mean dose , V60
- ▶ Analgesics, nutritional support



CHEST WALL / PROX. BRONCHUS

Conventional

- ▶ V 30 < 70cc
- ▶ Max rib dose < 60GY

SBRT

- ▶ V30 < 30cc
- ▶ Chw & rib in peripheral tumors

Pain , rib fracture

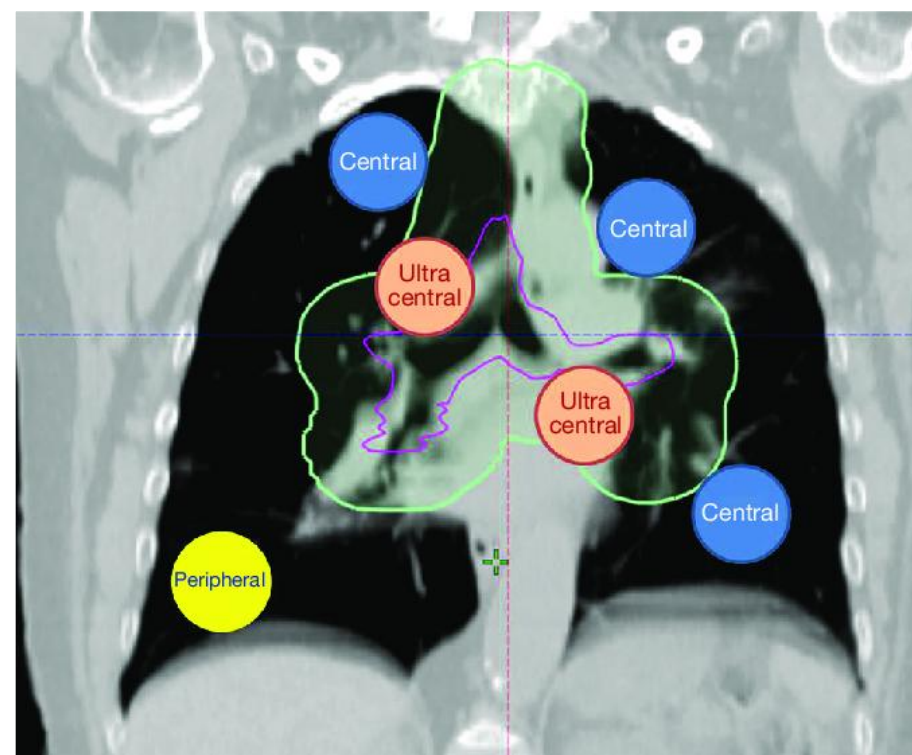
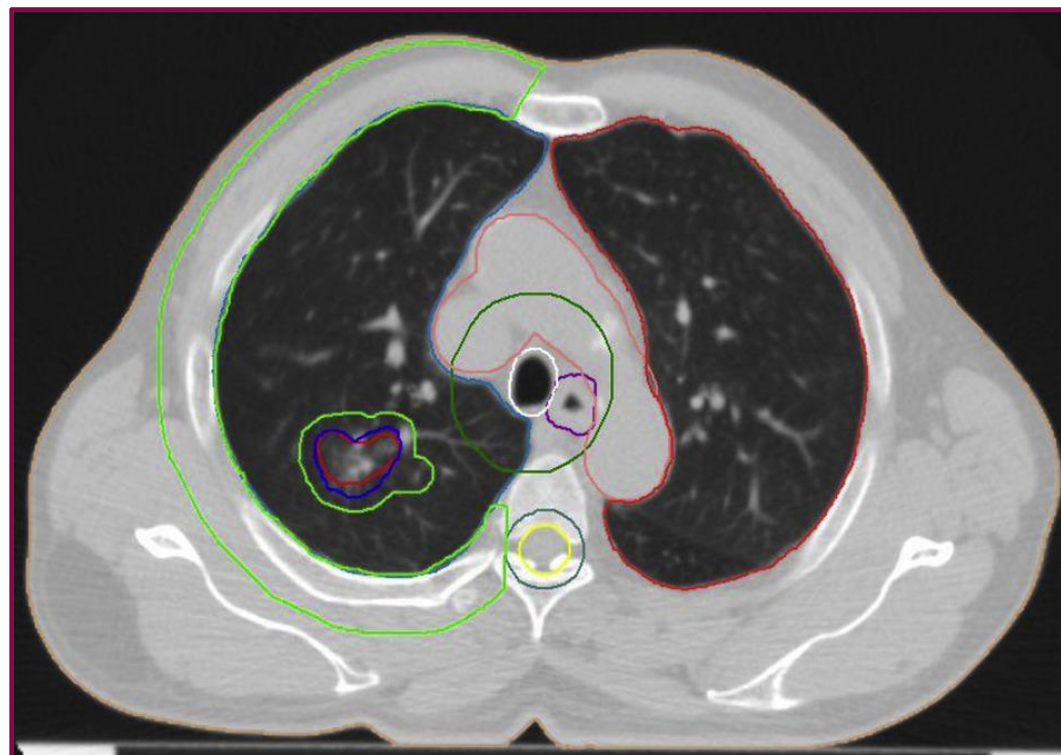
Conventional

- ▶ Dmax < 65GY
- ▶ Avoid hot spots

SBRT

- ▶ Dmax < 30GY
- ▶ 8# schedule in ultra central tumours

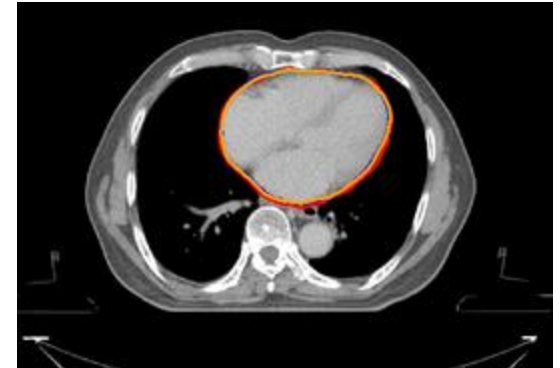
Necrosis, fibrosis, fistula, Hge



CARDIAC

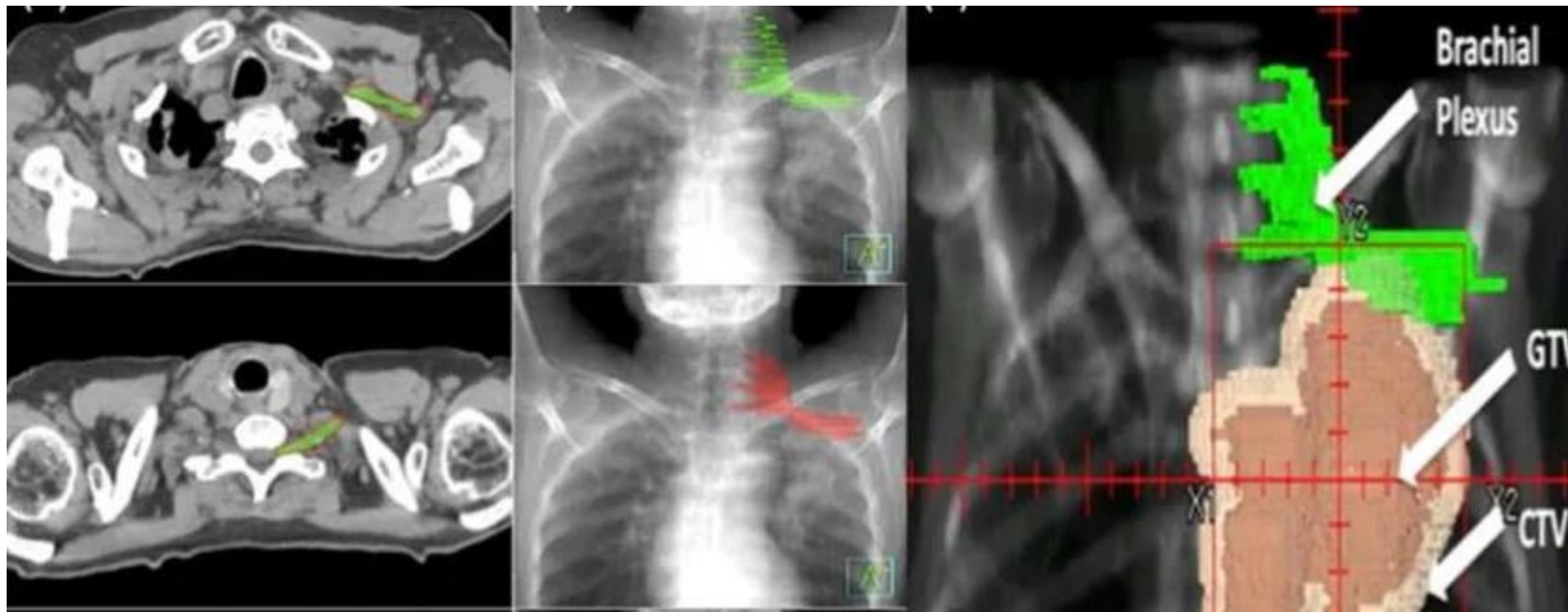
- ▶ After RTOG 0617 trial -- 60 GY vs 74 GY
- ▶ Emphasised on heart dose constraints
- ▶ Pericarditis, arrhythmias, CAD, CHF
- ▶ Mean heart dose < 10 GY
- ▶ V5 < 50% ideally (evolving)
- ▶ V30 < 30 %

Not Quantec



NEURO – Brachial plexus

- Dmax < 60 GY



PREVENTION STRATEGIES

- ▶ Prefer IMRT / IGRT over 3D CRT
- ▶ Adaptive RT
- ▶ Motion Management
- ▶ Adhere OAR Constraints
- ▶ Reduce low dose V5 - bath

FUTURE...

- ▶ Personalised Constraints
- ▶ Functional Lung avoidance RT
- ▶ PROTON therapy
- ▶ Radiomics Prediction in Toxicity
- ▶ AI toxicity modelling

TAKE HOME !!!

- ▶ RILI – remains Dose Limiting !
- ▶ QUANTEC constraints are critical in planning
- ▶ SBRT requires unique planning
- ▶ Vigilant if Immunotherapy is added
- ▶ Technology improves safety – but clinical Judgement matters most

THANK YOU

