ADJUVANT RADIOTHERAPY - CARCINOMA LUNG

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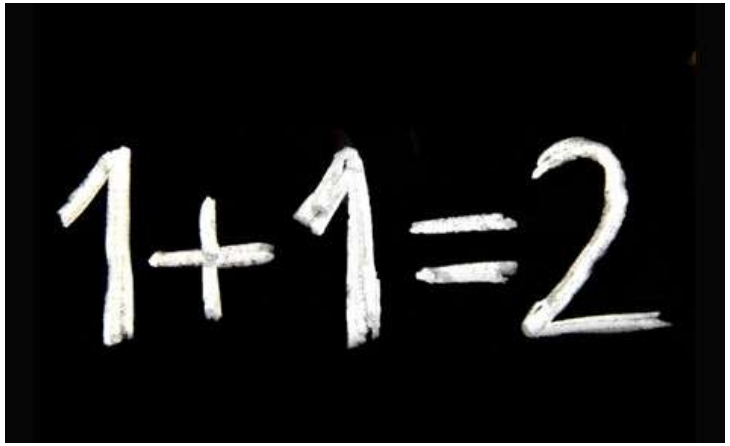
ADJUVANT THERAPY

Additional cancer treatment given **after primary treatment** to **control the microscopic disease** in order to **lower the risk** of recurrence.



National Cancer institute

TYPES

- Radiation therapy
- Chemotherapy
- Hormone therapy
- Biological therapy
- Combination any of the above

WHY ADJUVANT

- NSCLC constitutes 80% of Lung cancer
  - 30% complete surgical resection
  - long term survival.
- Post Surgery Recurrence rates
  - STAGE I - 20 %
  - STAGE IIIA - 50 %
- Intra thoracic recurrence
  - Along surgical stump
  - Mediastinal lymph nodes

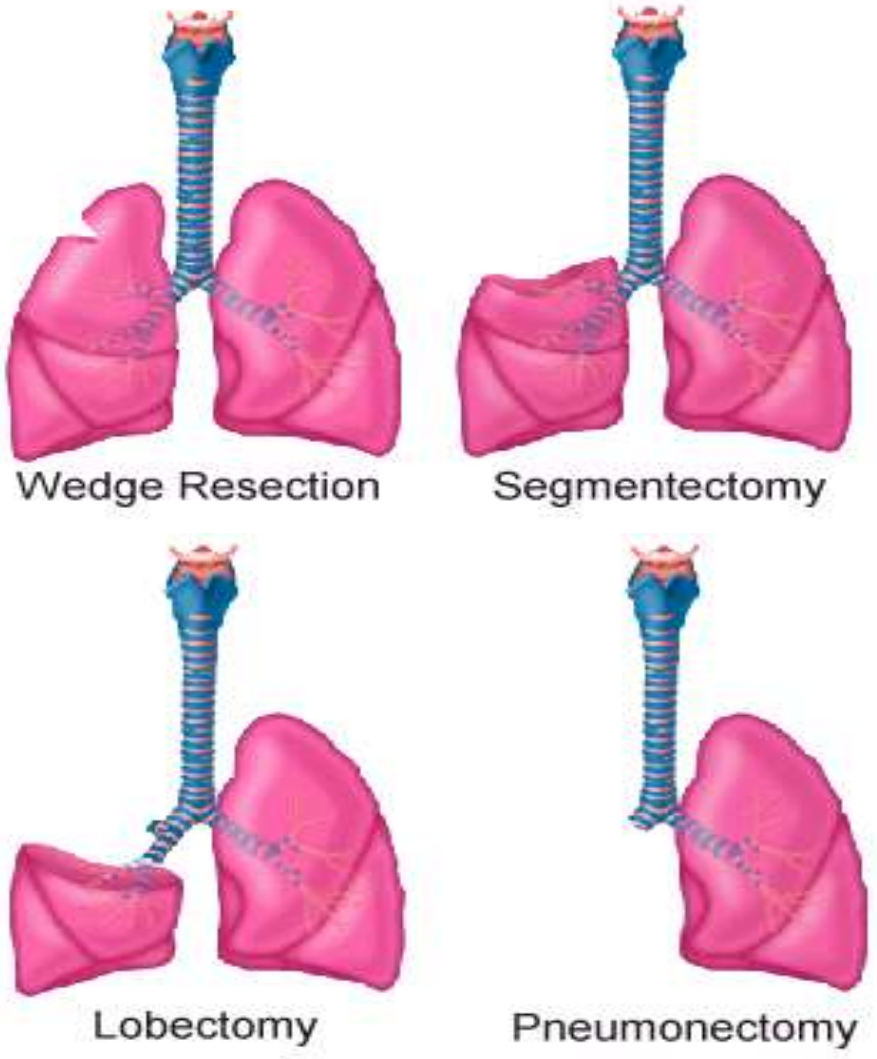
CONTD..

- Chemotherapy and Radiotherapy evaluated to improve prognosis.

- High rate of local failure after surgery & Post op Chemo
  - New interest on PORT came into picture.

SURGERY IN CA LUNG

- Wedge Resection
- Segmentectomy
- Lobectomy
- Pneumonectomy



INDICATIONS - PORT

- Stage I & II – close/positive margins.

- Stage IIIA
  - Close margin (<5mm),
  - Positive margin,
  - N2 disease,
  - Nodal ECE.

RT PLANNING

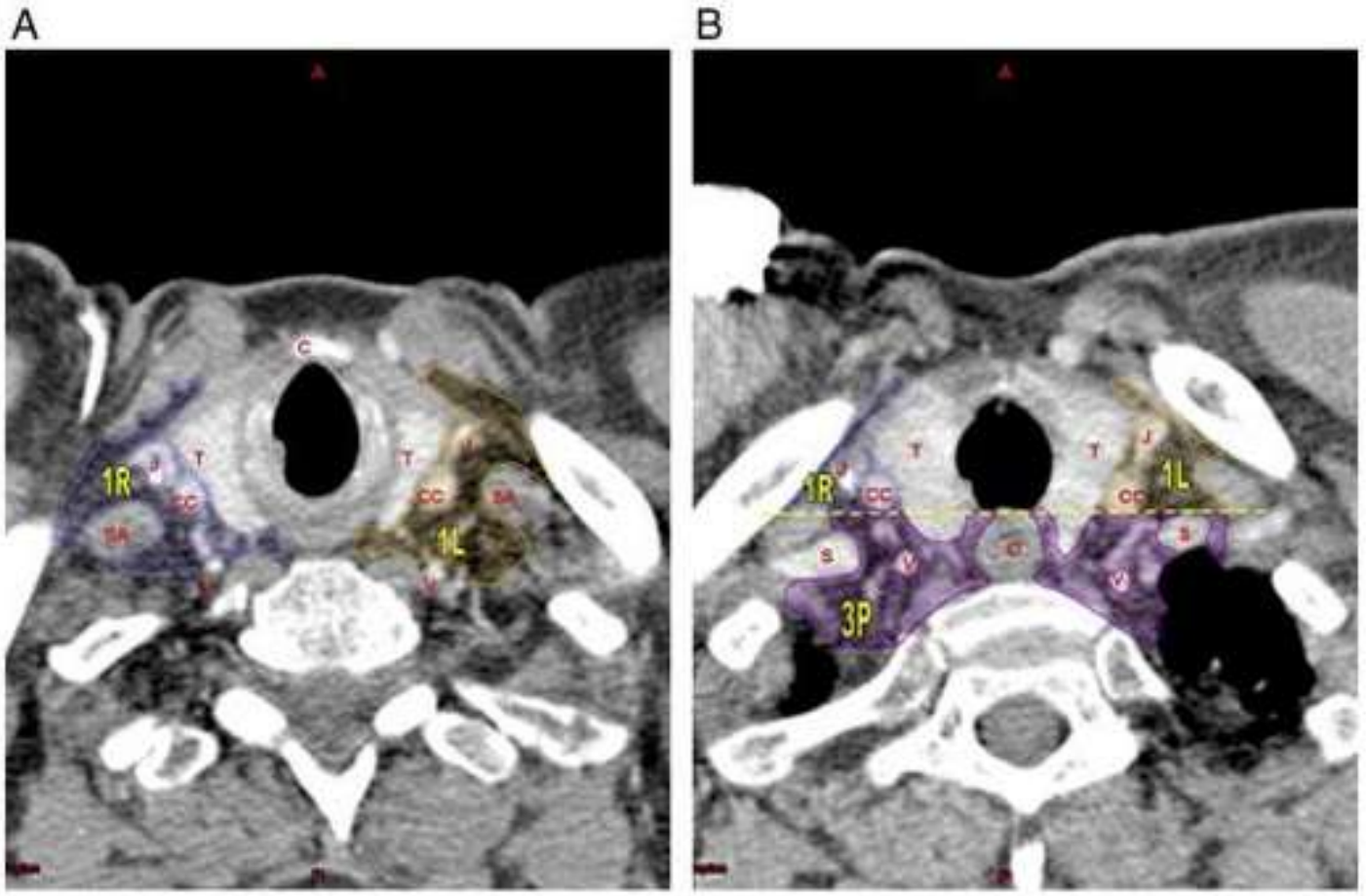
- Immobilization
- Simulation scan
- Transferring images to planning system
- Contouring
- Dose constraints to both target and OAR’s
- Plan approval
- Daily verification of treatment setup
- Plan execution
- Weekly review

IMMOBILIZATION

SIMULATION

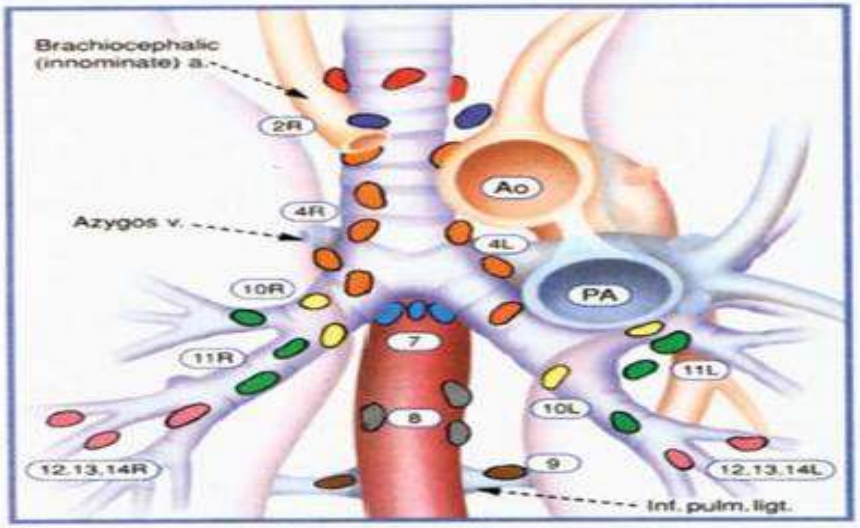
- Supine position
- Spine straight
- Hands above the head
- Lasers aligned
- Orfit cast
- Contrast+/_
- Serial CT
- Thickness <5mm

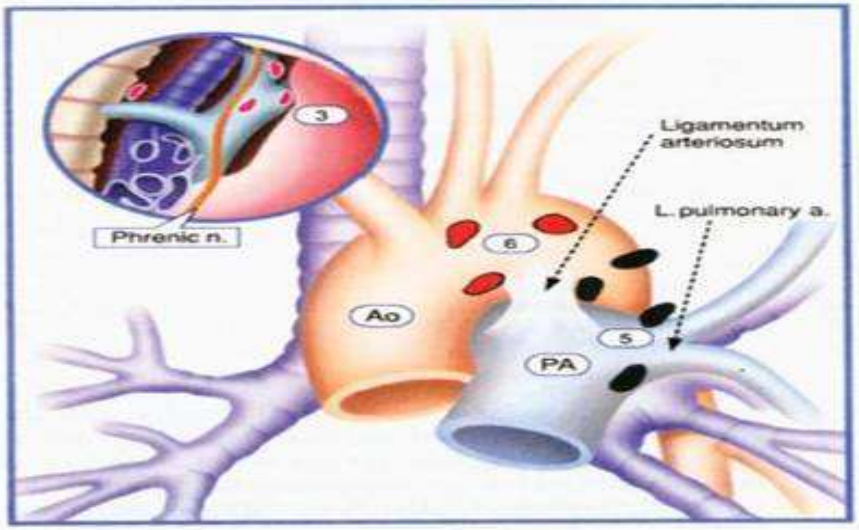
CONTOURING



Practical Radiation Oncology Jan-Mar 2013

MEDIASTINAL LYMPHNODES





Superior Mediastinal Nodes

- 1 Highest Mediastinal
- 2 Upper Paratracheal
- 3 Pre-vascular and Retrotracheal
- 4 Lower Paratracheal (including Azygos Nodes)

N_2 = single digit, ipsilateral
N_3 = single digit, contralateral or supraclavicular

Aortic Nodes

- 5 Subaortic (A-P window)
- 6 Para-aortic (ascending aorta or phrenic)

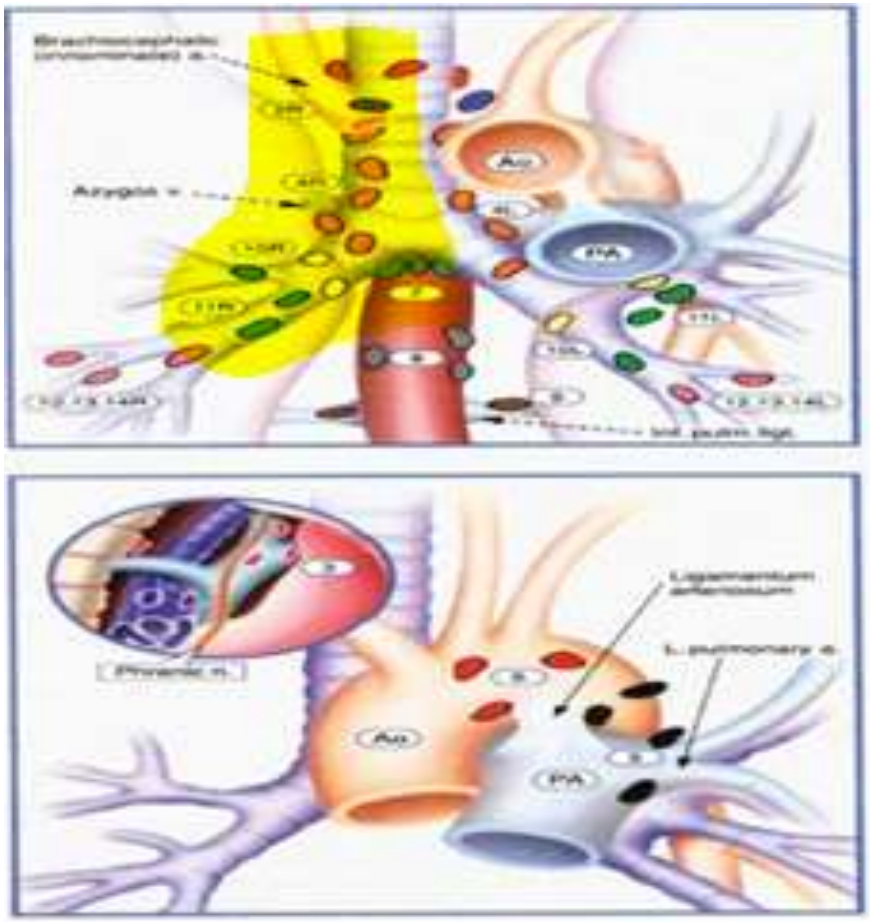
Inferior Mediastinal Nodes

- 7 Subcarinal
- 8 Paraesophageal (below carina)
- 9 Pulmonary Ligament

N_1 Nodes

- 10 Hilar
- 11 Interlobar
- 12 Lobar
- 13 Segmental
- 14 Subsegmental

MEDIASTINAL LN'S



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CTV for right lung cancers includes bronchial stump and LN stations 2R, 4R, 7, and 10 To 11R .

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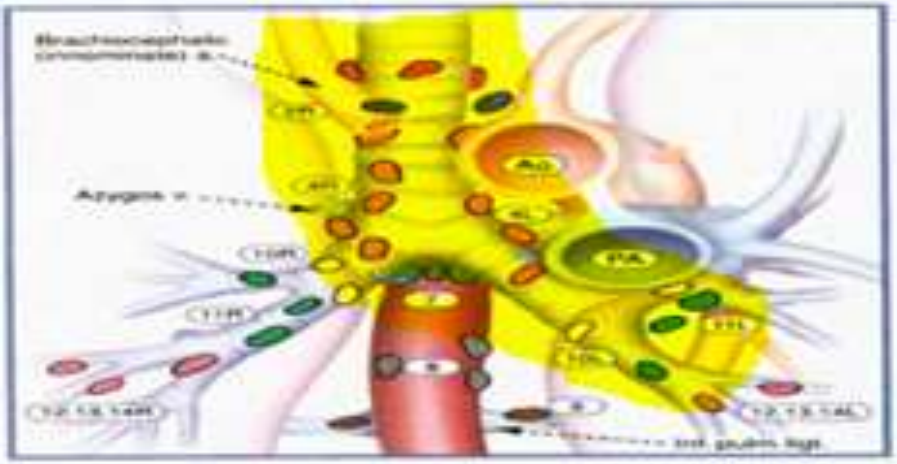

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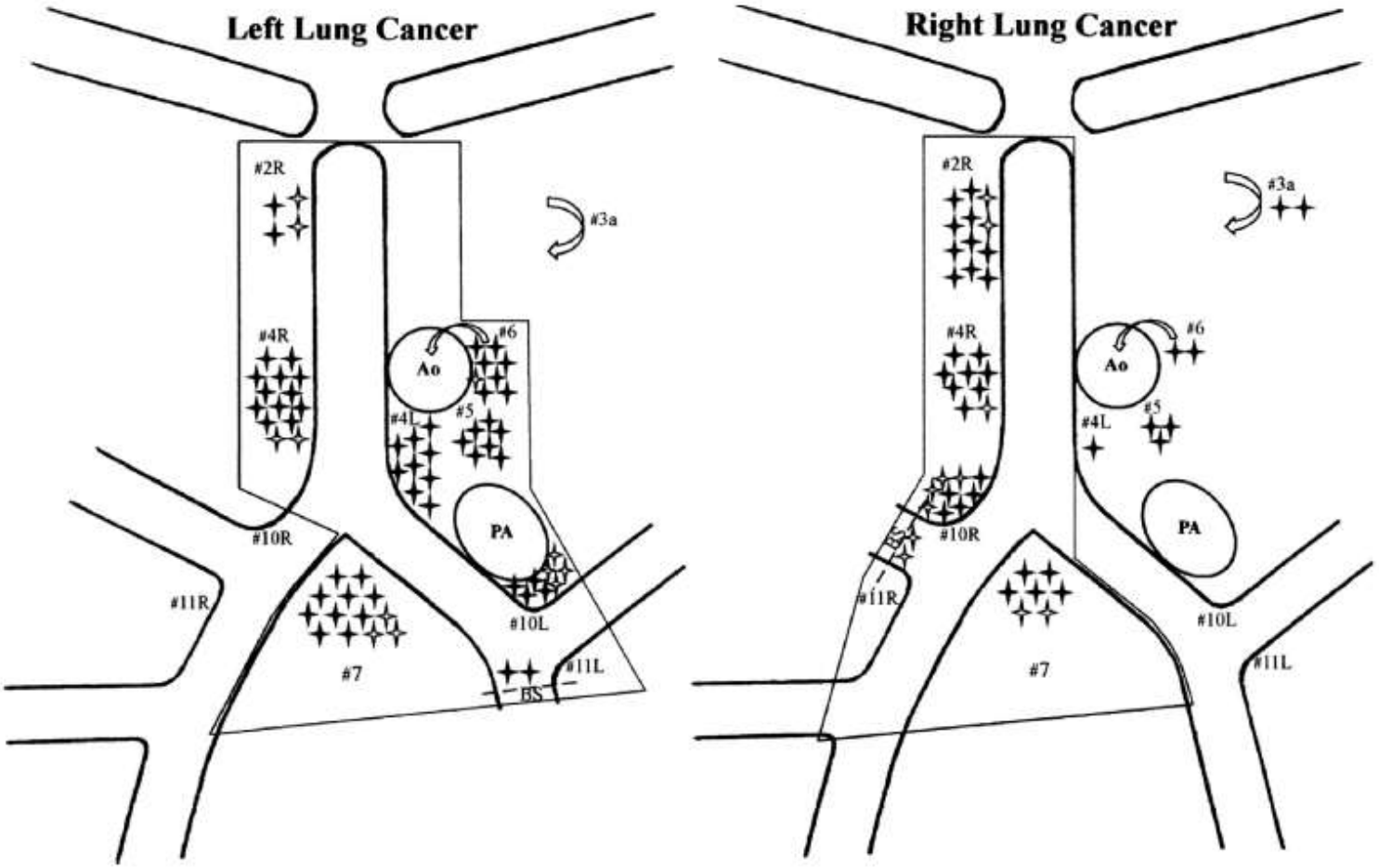
CTV for left lung cancers includes bronchial stump and LN stations 2R, 2L, 4R, 4L, 5, 6, 7, and 10 To 11R.

VOLUMES



LRF sites in left- and right-sided lung cancers are shown. The proposed PORT fields for left- and right-sided lung cancers are presented. Solid star symbols are multiple-site failures (patients failing in multiple LRF sites simultaneously); open star symbols are isolated failures (patients with a single LRF site). For patients with left-sided tumors, all LRF would have been covered by the proposed PORT CTV. For patients with right-sided tumors, 83% (39 of 47) LRF would have been contained in the PORT field; 17% (8 of 47) LRF were outside the proposed PORT field and observed in 6 patients (. CTV = clinical tumor volume; LRF = local-regional failure; PORT = postoperative radiation therapy.

- CTV to include
  - Positive margin or microscopic extension disease.
  - Surgical clips in positive margin Stage 1 & 2
- PTV – 1cm around CTV
- 3D CRT will improve the loco regional control rate compared to 2D.

STATUS OF LUNG PORT

- No clear cut consensus on definition of the extent of CTV

- After PORT meta analysis (1998) PORT in ca lung banned in many RT departments world wide.

PORT RESULTS RATIONALE

- In the previous trials most of the patients with stage I & II with NO/N1 were also included which showed detrimental effect.
- But for N2 patients there was no clear adverse effect.
- So the trials mainly started for those patients with N2 disease

REVIEW OF LITERATURE

Retrospective studies on postoperative radiation therapy

Study	Stage	*n* of patients	Dose (Gy)	Local recurrence (%)	Overall survival (%)	Follow-up method
Astudillo and Connill 1990	IIIA	60	–	20%	28%	3-yr actuarial
		86	45–50	13%	20%	
Green et al. 1975	I–IIIA	94	–	NR	16%	5-yr crude
		125	50–60	NR	31%	
Choi et al. 1980	IIIA	55		31%	8 %	5-yr actuarial
		93	40–56	14%	43%	
Chung et al. 1982	I–IIIA	68	–	32%	28%	3-yr crude
		50	46	10%	40%	
Paterson et al. 1962	T3N0–2	22	–	27%	30%	5-yr actuarial
		13	20–50	0	56%	
Kirsh et al. 1982	IIIA	20	–	NR	0%	5-yr crude
		110	50–60	NR	26%	
Sawyer et al. 1997	IIIA	136	–	60%	22%	4-yr actuarial
		88	45–66	17%	43%	

Risk of local recurrence lower with PORT (25%-35%) based on the above results

REVIEW OF LITERATURE

Results of certain randomized studies

Study	Stage	*n* of patients	Total dose/ fraction size	LRR (%)	*p*	5-yr SR (%)	*p* (in favor)
Van Houtte et al. 1980	T1–3N0	104	–	10.9%	NS	43%	<.05 (surgery)
		98	60/2 Gy	1.2%		24%	
Lung Cancer Study Group 1986	II–III SCC	120	–	41%	.001	40%	NS
		110	50.4/1.8	3%		40%	
Dautzenberg et al. 1999	I–II–III	355	–	28%	NS	43%	.002 (surgery)
		373	60/2–2.5	22%		30%	
Mayer et al. 1997	I–II–III	72	–	20%[a]	<.01	20.4%	NS
		83	50–56/2	7%[a]		29.7%	
Trodella et al. 2002	T-2N0	53	–	23%	0.19	58%	.048 (PORT)
		51	50.4/1.8	2.2%		67%	
Feng et al. 2000	II–III	182	–	33.2%	.01	40.5%	NS
		183	60/2	12.7%		42.9%	

[a]Cumulative rate of local recurrences.
[b]Study not included in the meta-analysis published in 1998.
Abbreviations: LRR, local recurrence rate; NS, nonsignificant; PORT, postoperative radiation therapy; SCC, squamous cell carcinoma; SR, survival rate.

Randomized trials showing the results of with / without PORT

SEER (JCO 2006)

- 7,400 patients, stage II–III NSCLC post op + PORT
- T3-T4 advanced nodal stage
  - Involved vs Sampled ratio of Lympnodes
- On multivariate analysis
  - older age T3,T4 N2 stage male,
  - fewer sampled LN greater no of LN involved had negative impact on survival.
- 5-year OS for
- N2 patients (20→27%, HR 0.85)
- N0 (41 → 31%, HR 1.2)
- N1 (34 → 30%, HR 1.1)

PORT META-ANALYSIS TRIALIST GROUP

- 2128 patients.
- 9 randomised trials of PORT vs Sur
- 21% relative increase in the risk of death with RT
- 2 yr reduced OS from 55% to 48%
- Adverse effect was greatest for Stage I,II
- St.III (N2): no clear evidence of an adverse effect

Lancet 1998;352:257

PORT TRIALS

- Postoperative RT should be used outside of a clinical trial in Stage I, II lung cancer when surgical margins are positive and repeated resection is not feasible.

VAN HOUTTE ET AL (1980):

- NSCLC Stage I–II
- Observation vs Post-op 60Gy to mediastinum.
- RT improved local-regional control,
- 5-year OS 24% RT vs. 43% with observation
- Increased pneumonitis.
- Study criticized because used Co-60 machines, large field size, and no CT planning.

ANITA TRIAL

(ADJUVANT NAVELBINE INTERNATIONAL TRIALIST ASSOCIATION)

- 1994- 2000. N = 840 , Stg IB to IIIA

- Post op adjuvant chemo or observation and RT was not randomised but decided before initiation of study.
- RT dose 45-60Gy at 2Gy/#

MEDIAN SURVIVAL	pN1 patients PORT to both arms for selected patients		pN2 patients PORT to both arms for selected patients	
	WITH OUT RT	WITH RT	WITH OUT RT	WITH RT
Chemotherapy	93.6m	46.6m	23.8m	47.4m
Observation	25.9m	50.2m	12.7m	22.7m

ECOG – 3590 TRIAL

- 488 pt's
- Stage II - IIIA NSCLC post op negative margins.
- RT Vs CT+RT
- RT – 50.4Gy/28#, CT- EP regimen.
- Result – No difference in LC or survival.

RTOG 9705 TRIAL – PHASE 2

- 88 pt's
- Stage II to IIIA NSCLC post operative CT+RT
- CT- carboplatin + paclitaxel
- RT – 50.4Gy/28Fr
- + Boost 10.8Gy/6Fr for Extra nodal extension or T3 lesions.

RTOG 9705

- Median F/U 56.7 months. Median OS 56.3 months

	OS	PFS
1YEAR	86%	70%
2YEAR	70%	57%
3YEAR	61%	50%

- RTOG conclusion- with acceptable toxicities there might be improvement in OS & PFS with chemoradiotherapy in resected NSCLC pt's.

PATTERNS OF FAILURE

- Rt lung – ipsilateral superior Mediastinal nodes.
- Lt Lung - bilateral superior Mediastinal nodes.
- Mediastinal CTVs
  - Involved LN's & a margin corresponding to the upper and lower LN's to the involved LN area and all LN's lie between two noncontiguous involved LN's.

TREATMENT TECHNIQUES

3D-CRT

- Target can be seen and contoured.
- Coverage can be assessed to the target.
- Dose to the OAR's can be verified and if required can be optimized by changing the weightage to the beams.

IM-IGRT

- Target coverage will be better at the same time the OAR's can be spared better than 3D-CRT.

- Daily verification can be done by either KVCT/MVCT image, which will improve the accuracy of treatment and reduces the chances of random errors

DOSES

- If R0 resection - 50-56Gy / 25-28#
- If N2 with ECE - 10-16Gy boost.
- If positive margin - 60Gy / 30#
- If gross residual disease - 66-70Gy / 33-35#

along with concurrent chemo.

CONCLUSION

- Radiotherapy is a proven adjuvant therapy in Stage 1,2 (+ margin) & 3A
- IM-IGRT >3D CRT > 2D treatment
- Volume delineation is of prime importance

THANK YOU