Management of stage II Lung Cancer (NSCLC)

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Chittaranjan National CI
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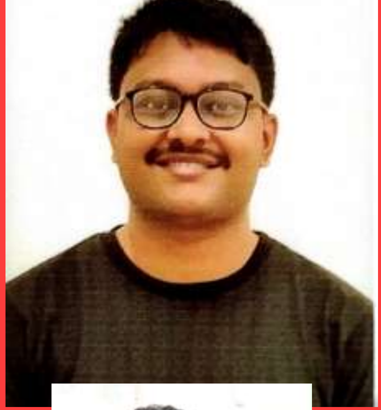
Govt MC, Kadapa
AP

Dr. Vasanthapriya
Registrar, MMC
TN

Case History

- 62 year male, smoker
- DM,CAD,Pacemaker,EF40%
- Cough x 1week
- CXR: Opacity Lt UL
- Sputum AFB –ve
- CT chest: Lt UL mass.
- Referred to U
- PETCECT: Mass + Node(4L)





How will you proceed- Basic framework? Investigation/workup?

- Pathological and Molecular Diagnosis
- Metastatic workup
- Staging
- Deciding Treatment
- Fittness for treatment

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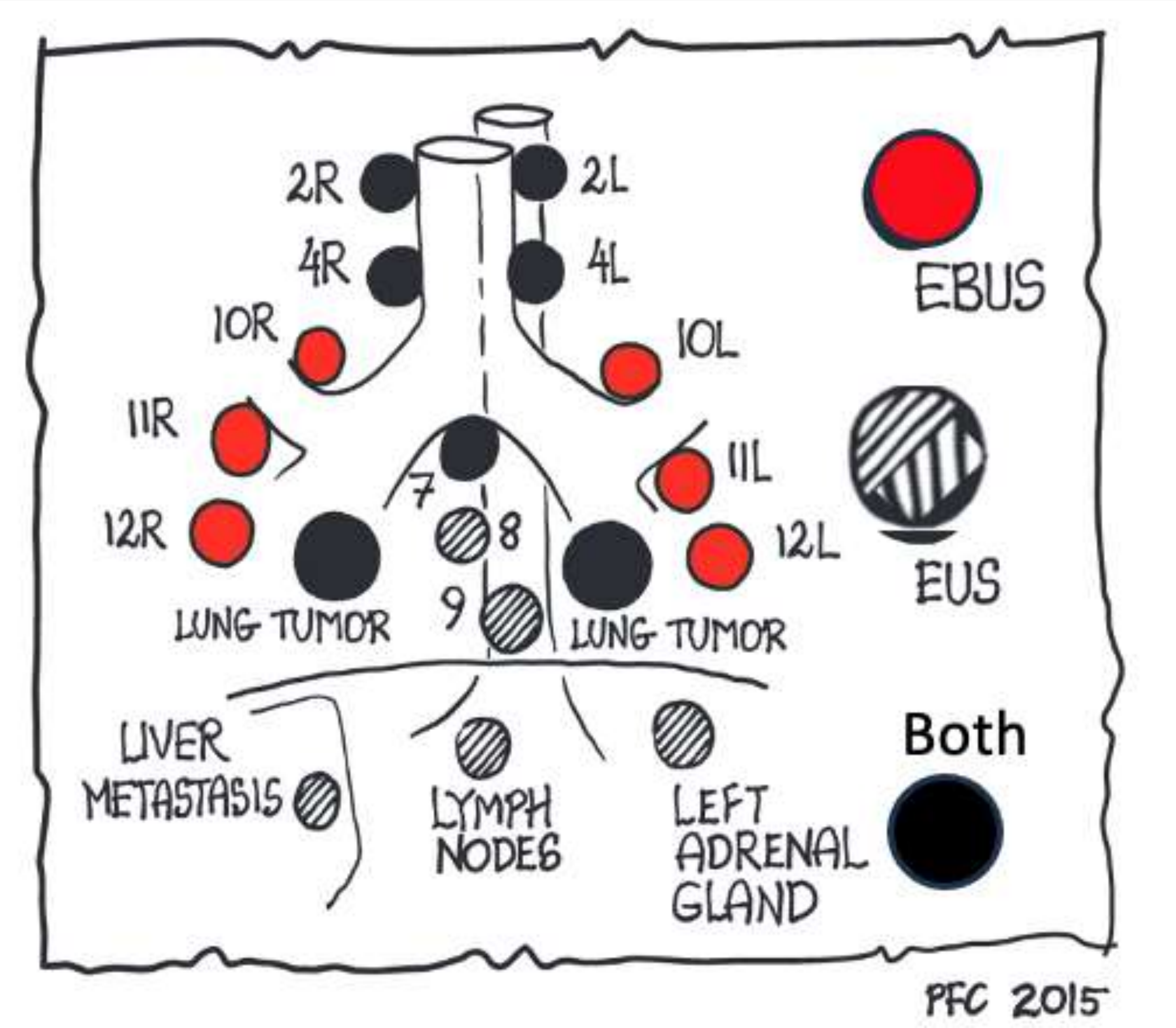
Patho Intervention: Type(FNAC/Biopsy) ; Site(s)?

- Biopsy always preferred > FNAC-FN(30%?);
- Tissue for HPE/Molecular analysis.

- Lung and Mediastinum(Co-existance of TB/Granuloma & Malignancy: 4-7%
  - Beyhan et al. https://doi.org/10.1016/j.rmcr.2017.11.004
  - Ramamoorthy et al. PMID: 36815938

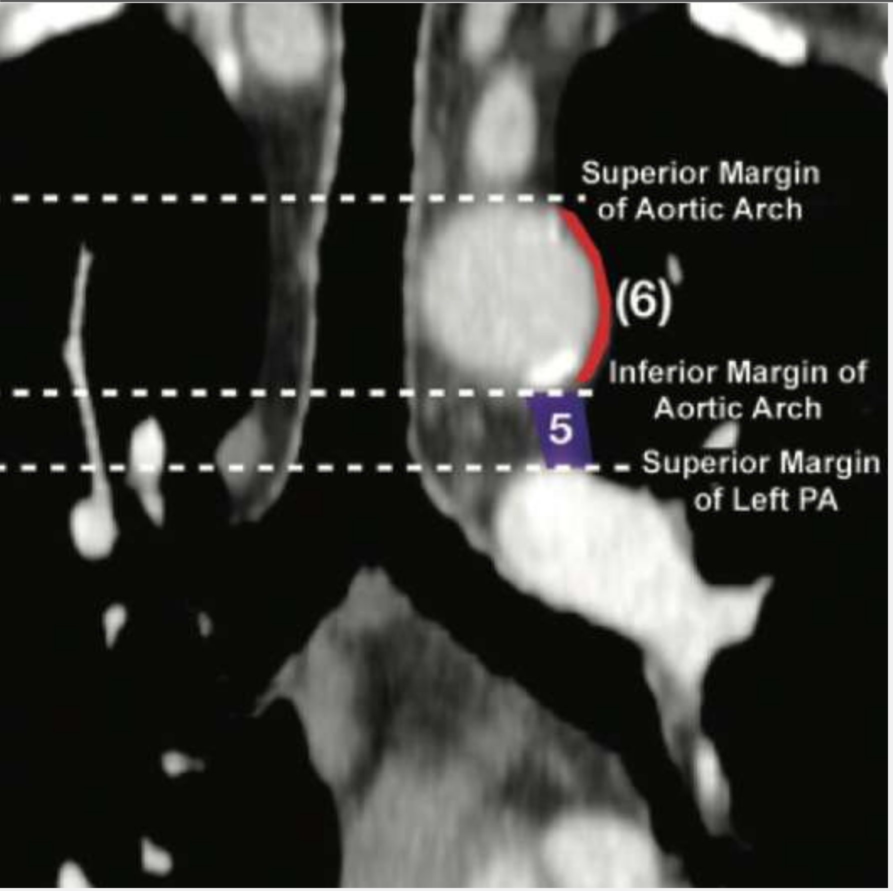
Station 4L- Technique?

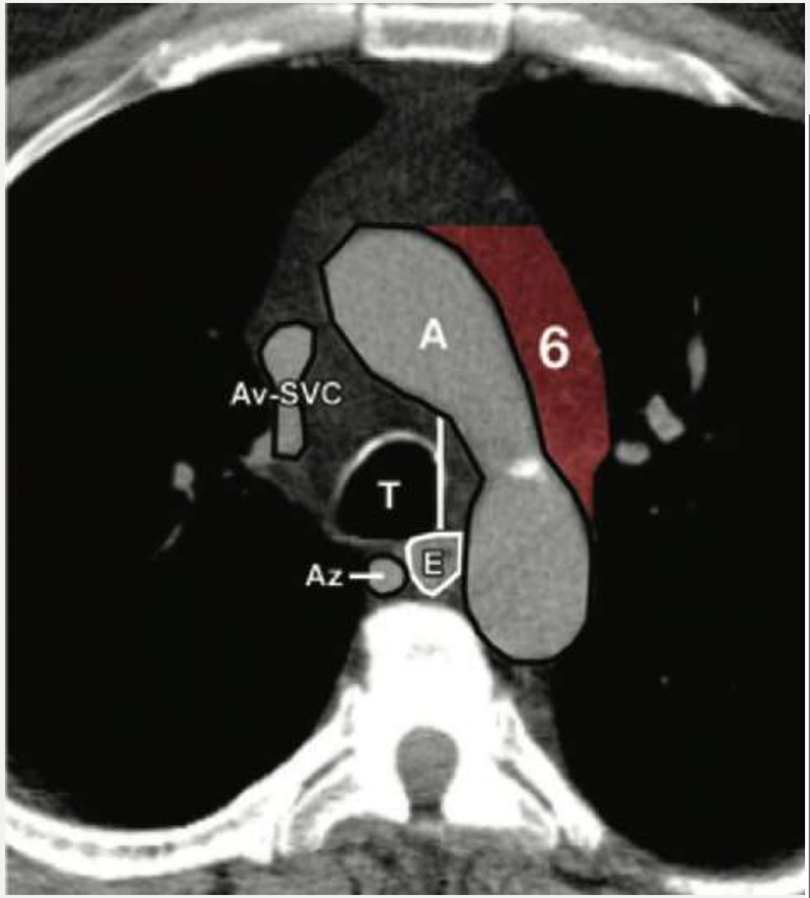


Lung Biopsy: Adenocarcinoma, TTF1 +ve

Node: Granuloma; No AFB

St 4,6,5,


Superior Margin of Aortic Arch
(6)
Inferior Margin of Aortic Arch
5
Superior Margin of Left PA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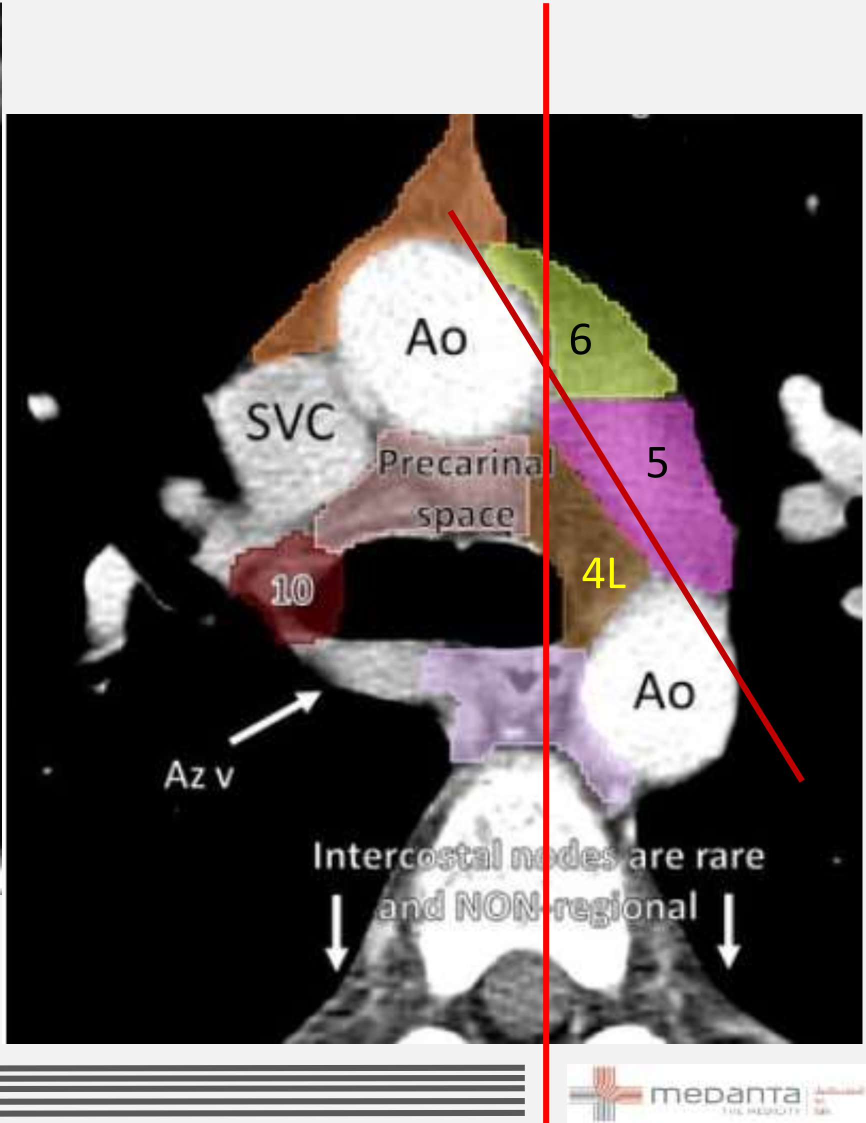
Ao
6
SVC
Precarinal space
5
4L
10
Ao
Az v
Intercostal nodes are rare and NON-regional

Molecular testing - current standard?

- EGFR, ALK, ROS1, **BRAF, MET, RET**
- NGS Lung Panel
- PDL1 by IHC

- ALK:Crizotinib/Ceritinib,Alecitinib, Brigatinib/Lorlatinib
- EGFR:Erlotinob,Geftinob/ Afatinib/ Osimertinib
- ROS1 rear: Crizotinib/Entrectinib
- BRAFV600E: Dabrafenib(BRAF inh), Trametinib (MEK inh)
- MET Ex14Skip: Capmatinib, Tepotinib
- RET : Selpercatinib, Pralsetinib

Non mutated; PDL-1: 40%

Staging

SAD or Longest diameter?

T -4.3 x 3.2cm

Pleural reflection or Invasion!!! NO

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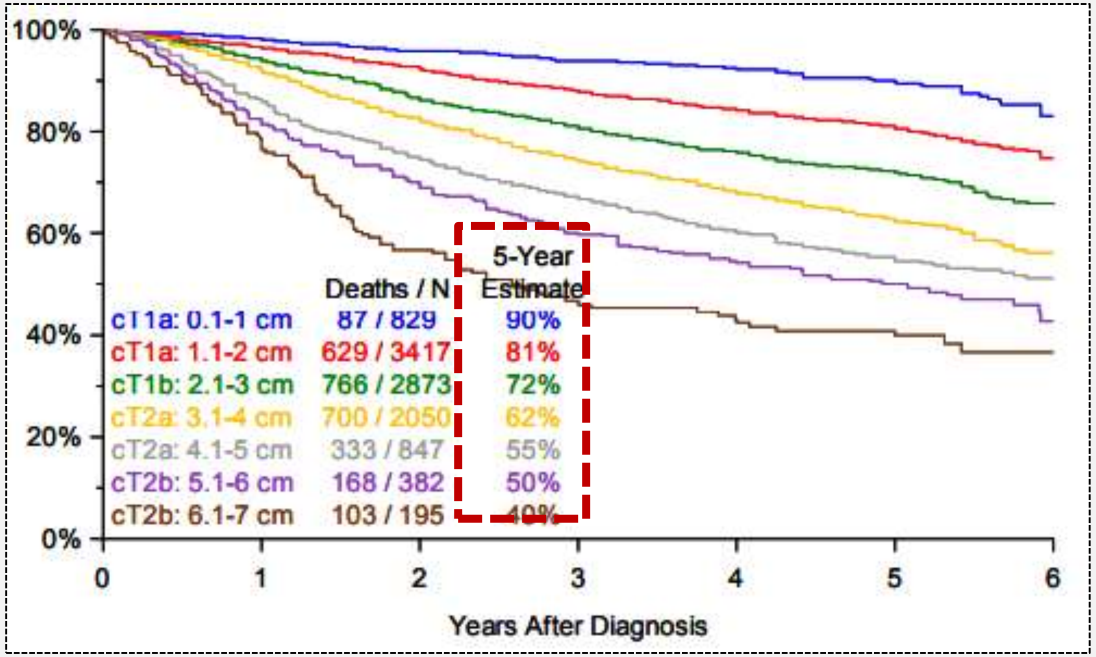
T2	Tumor >3 but ≤5 cm or tumor involving:	
	visceral pleura[b],	T2 *Visc Pl*
	main bronchus (not carina), atelectasis to hilum[b]	T2 *Centr*
T2a	Tumor >3 but ≤4 cm	T2a *>3-4*
T2b	Tumor >4 but ≤5 cm	T2b *>4-5*

3-4cm, N0: stage IB
4-5cm, N0: IIA

35

Bronchus main **A**telectasis **V** pleura **O**bs pneumonitis



When survival was analyzed by 1-cm increment in T size :
progressive degradation of survival was observed for each 1-cm cutpoint

STAGE	T	N	M
Occult	TX	N0	M0
0	Tis	N0	M0
IA1	T1a(mi)/T1a	N0	M0
IA2	T1b	N0	M0
IA3	T1c	N0	M0
IB	T2a	N0	M0
IIA	T2b	N0	M0
IIB	T1a-T2b	N1	M0
	T3	N0	M0
IIIA	T1a-T2b	N2	M0
	T3	N1	M0
	T4	N0/N1	M0
IIIB	T1a-T2b	N3	M0
	T3/T4	N2	M0
IIIC	T3/T4	N3	M0
IVA	Any T	Any N	M1a/M1b
IVB	Any T	Any N	M1c

International Association for the Study of Lung Cancer, 2015

3-4cm Tumor is stage IB
4-5:IIA

What treatment is recommended in this stage? (assuming fit pt)

STAGE IIA (T2b N0 M0)

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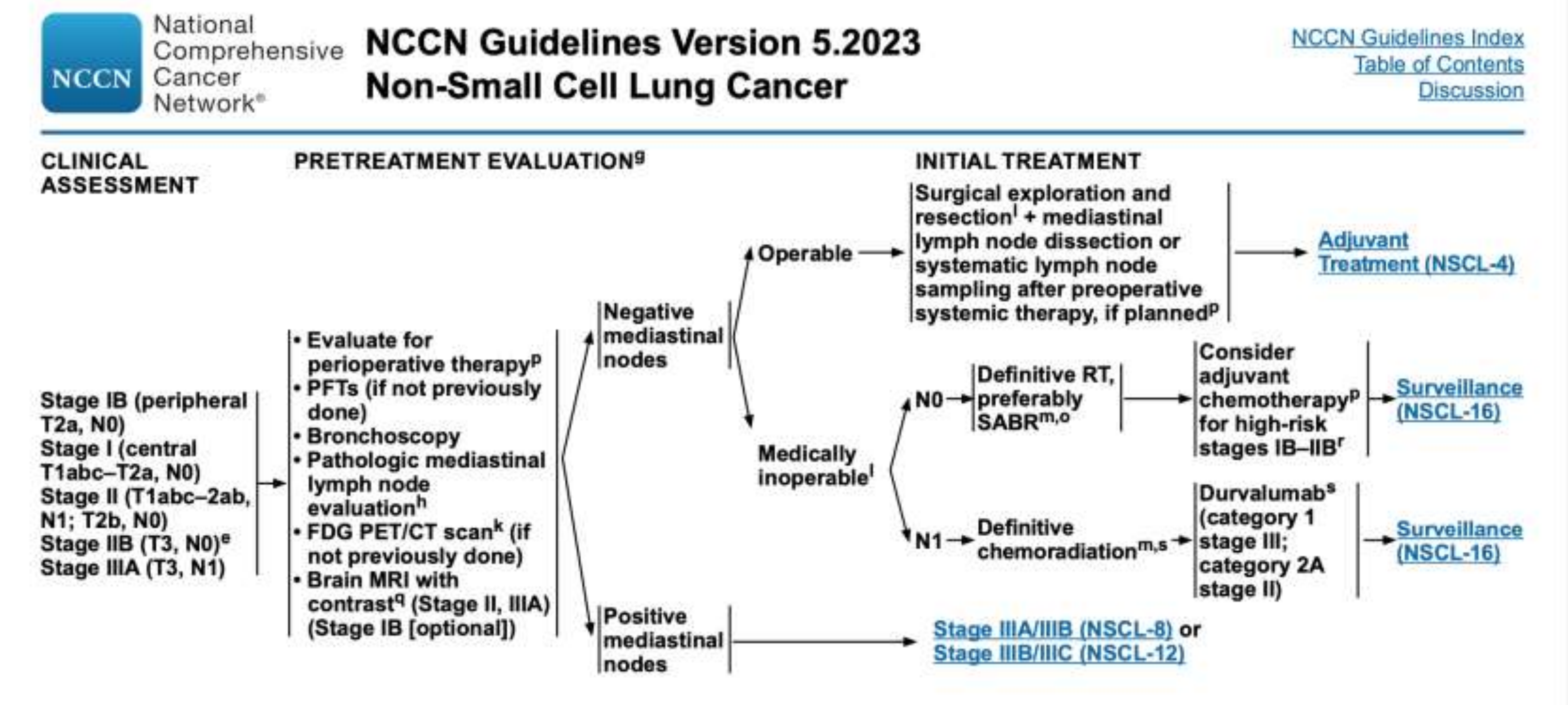
4-5cm: T2b (Stage IIA)

- Surgery- Lobectomy + complete Lymphadnectomy
- Evidence (Level C);

Surgical intervention remains the gold standard for the approximately 30% of NSCLC patients who present with resectable stage I and II disease [18] and who are functionally operable (level C evidence) [5, 15, 19]. The extent of resection and precise surgical approach are the subject of discussion. Additionally, with the



Stage IA (<=2cm,PeripheralT1a): Lobectomy vs Limited Rx

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 9, 2023 VOL. 388 NO. 6

Lobar or Sublobar Resection for Peripheral Stage IA Non–Small-Cell Lung Cancer

Nasser Altorki, M.D., Xiaofei Wang, Ph.D, David Kozono, M.D., Ph.D., Colleen Watt, B.S.,

CALGB 140503 multicenter, international, randomized, noninferiority, phase 3 trial

PIII RCT; 2007- 2017, n= 697
sublobar resection(Segement, wedge) vs lobar resection
T Upto 2cm

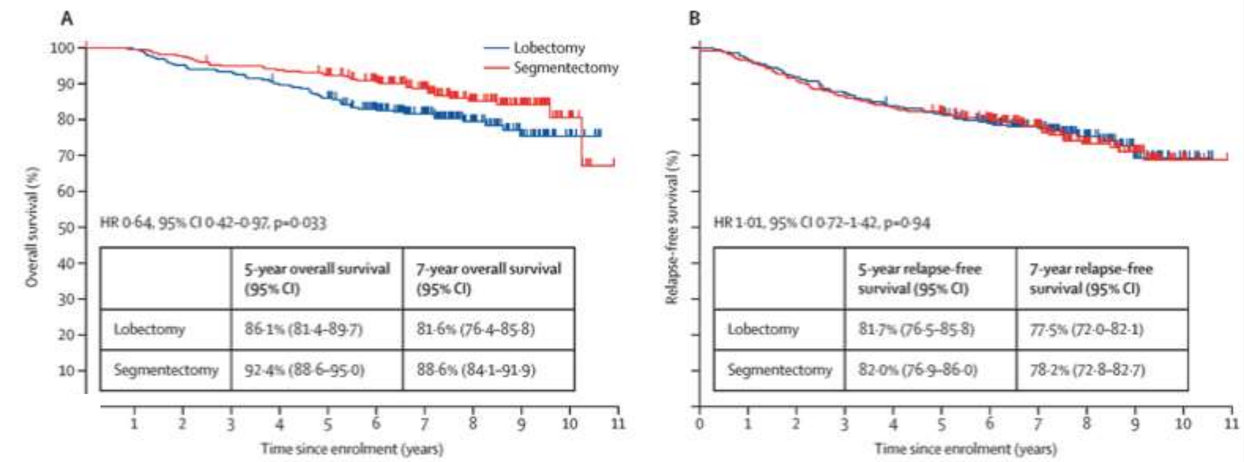
Conclusion: In peripheral NSCLC (t<= 2 cm) sublobar resection was not inferior to lobectomy with respect to DFS, OS.

Stage IA (<=2cm,PeripheralT1a): Lobectomy vs segment Rx

ARTICLES · Volume 399, Issue 10335, P1607-1617, April 23, 2022 Download Full Issue

Segmentectomy versus lobectomy in small-sized peripheral non-small-cell lung cancer (JCOG0802/WJOG4607L): a multicentre, open-label, phase 3, randomised, controlled, non-inferiority trial

Prof Hisashi Saji, MD [a] · Morihito Okada, MD [b] · Masahiro Tsuboi, MD [c] · Ryu Nakajima, MD [d] · Kenji Suzuki, MD [e] · Keiju Aokage, MD [c] · et al. Show more



Evaluation by Thoracic Sx: Very High-risk surgery in view of CAD, Pacemaker, Poor EF

What next?

Why not cf - RT? Any evidence...

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Why not conventional RT?

Dose Escalation in Non–Small-Cell Lung Cancer Using Three-Dimensional Conformal Radiation Therapy: Update of a Phase I Trial

By James A. Hayman, Mary K. Martel, Randall K. Ten Haken, Daniel P. Normolle, Robert F. Todd III, J. Fred Littles, Molly A. Sullivan, Peter W. Possert, Andrew T. Turrisi, and Allen S. Lichter

J Clin Oncol 19:127-136. © 2001 by American Society of Clinical Oncology.

- University of Michigan , 3-D CRT
- dose escalation as high as **102.9 Gy** .

DOSE ESCALATION IN NON–SMALL-CELL LUNG CANCER

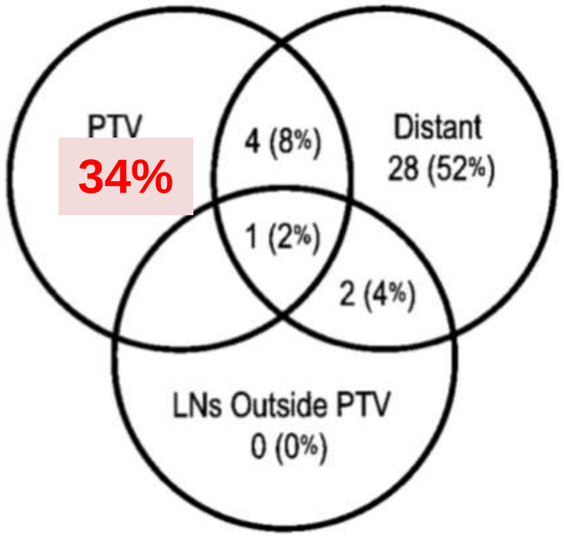

Fig 3. Pattern of first failure. Abbreviation: LNs, lymph nodes.

- Stage I/II NSCLC receiving conventional RT**: LF upto70%.**
  (Rowell and Williams 2001)

Pattern of Failure: Locoregional failure (30% -50%)---Auperin MA

ELSEVIER

Int. J. Radiation Oncology Biol. Phys., Vol. 42, No. 3, pp. 469–478, 1998

0360-3016/98 $19.00 + .00

PII S0360-3016(98)00251-X

- *Clinical Investigation*

RESPONSE, TOXICITY, FAILURE PATTERNS, AND SURVIVAL IN FIVE RADIATION THERAPY ONCOLOGY GROUP (RTOG) TRIALS OF SEQUENTIAL AND/OR CONCURRENT CHEMOTHERAPY AND RADIOTHERAPY FOR LOCALLY ADVANCED NON–SMALL-CELL CARCINOMA OF THE LUNG

R. W. Byhardt, M.D.,* C. Scott, Ph.D.,† W. T. Sause, M.D.,‡ B. Emami, M.D.,§ R. Komaki, M.D.,‖ B. Fisher, M.D., FRCPC,¶ J. S. Lee, M.D.# and C. Lawton, M.D.*

- Failure:
  - in-field (95% of rGTV was within the 95% IDL)
  - marginal (20–95% of rGTV was within the 95% IDL)
  - out-of-field (<20% of rGTV was within the 95% IDL)

Majority of local recurrences within 95% isodose line

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

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Original article

Patterns of locoregional failure in locally advanced non-small cell lung cancer treated with definitive conformal radiotherapy: Results from the Gating 2006 trial

Original Report

Patterns of locoregional failure in stage III non-small cell lung cancer treated with definitive chemoradiation therapy

Shalini Garg MD[a,*], Benjamin T. Gielda MD[a], Krystyna Kiel MD[a], Julius V. Turian PhD[a], Mary Jo Fidler MD[b], Marta Batus MD[b], Philip Bonomi MD[b], David J. Sher MD, MPH[a]

[a]Department of Radiation Oncology, Rush University Medical Center, Chicago, IL
[b]Section of Medical Oncology, Rush University Medical Center, Chicago, IL

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Stereotactic ablative radiotherapy versus standard radiotherapy in stage 1 non-small-cell lung cancer (TROG 09.02 CHISEL): a phase 3, open-label, randomised controlled trial

David Ball, G Tao Mai, Shalini Vinod, Scott Babington, Jeremy Ruben, Tomas Kron, Brent Chesson, Alan Herschtal, Marijana Vanevski, Angela Rezo, Christine Elder, Marketa Skala, Andrew Wirth, Greg Wheeler, Adeline Lim, Mark Shaw, Penelope Schofield, Louis Irving, Benjamin Solomon, on behalf of the TROG 09.02 CHISEL investigators

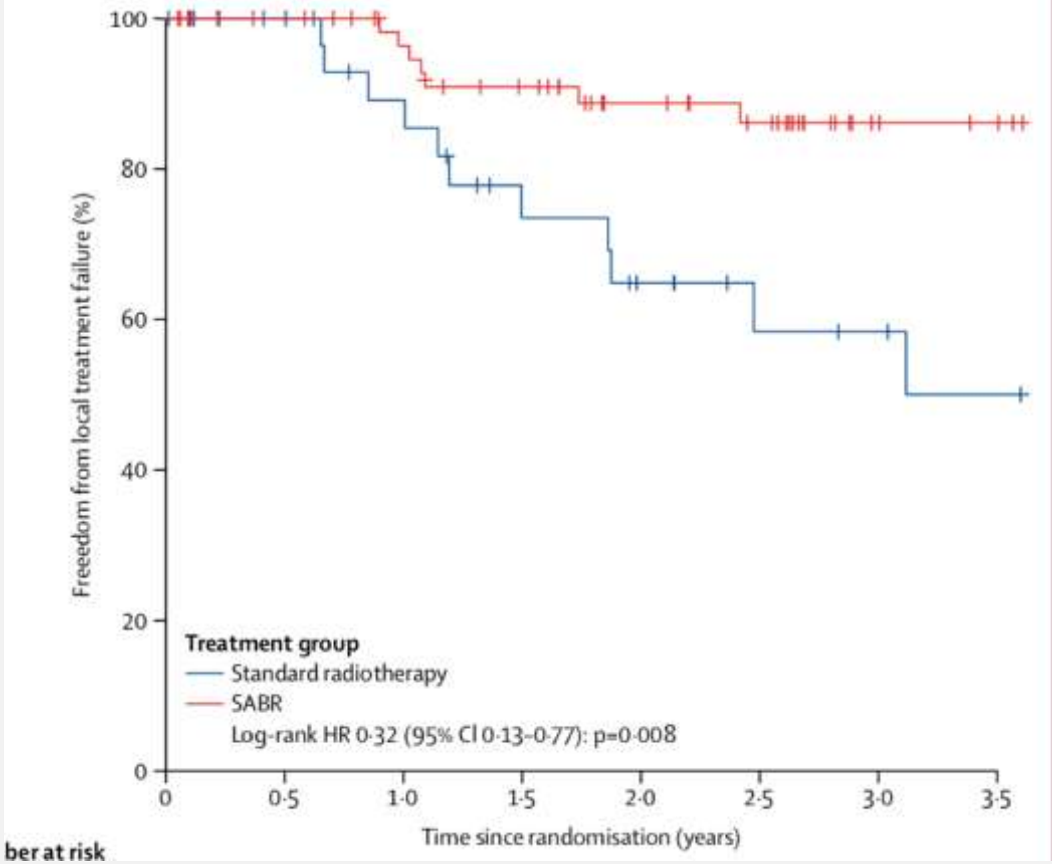
Systematic Review and Meta-Analysis
Medicine
OPEN

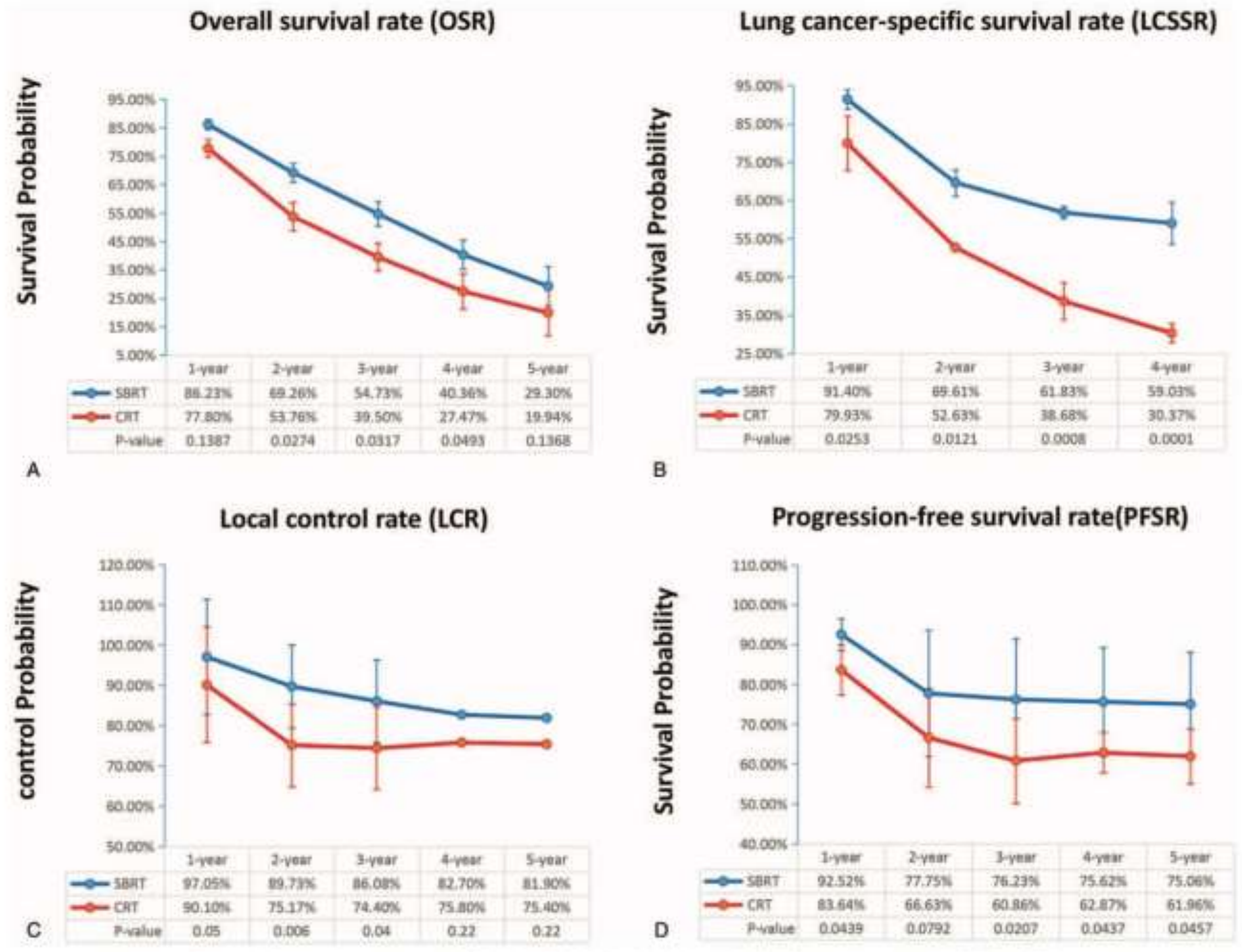
A meta-analysis comparing stereotactic body radiotherapy vs conventional radiotherapy in inoperable stage I non-small cell lung cancer

Can Li, MD, Li Wang, MD, Qian Wu, MD, Jiani Zhao, MD, Fengming Yi, MD, Jianjun Xu, MD, Yiping Wei, MD, PhD, Wenxiong Zhang, MD

Li et al. Medicine (2020) 99:34

- **PIII**
- **SABR (54 Gy/3# or 48 Gy/4#, vs**
- **RT (66 Gy/ 33# or 50Gy/ 20#)**
- **2 Fx per week.**





A – Overall survival rate (OSR)

	1-year	2-year	3-year	4-year	5-year
SBRT	86.23%	69.26%	54.73%	40.36%	29.30%
CRT	77.80%	53.76%	39.50%	27.47%	19.94%
P-value	0.1387	0.0274	0.0317	0.0493	0.1368

B – Lung cancer-specific survival rate (LCSSR)

	1-year	2-year	3-year	4-year
SBRT	91.40%	69.61%	61.83%	59.03%
CRT	79.93%	52.63%	38.68%	30.37%
P-value	0.0253	0.0121	0.0008	0.0001

C – Local control rate (LCR)

	1-year	2-year	3-year	4-year	5-year
SBRT	97.05%	89.73%	86.08%	82.70%	81.90%
CRT	90.10%	75.17%	74.40%	75.80%	75.40%
P-value	0.05	0.006	0.04	0.22	0.22

D – Progression-free survival rate (PFSR)

	1-year	2-year	3-year	4-year	5-year
SBRT	92.52%	77.75%	76.23%	75.62%	75.06%
CRT	83.64%	66.63%	60.86%	62.87%	61.96%
P-value	0.0439	0.0792	0.0207	0.0437	0.0457

Figure 3. Broken-line graphs of OSR (A), LCSSR (B), LCR (C) and PFSR (D) associated with SBRT vs CRT.

Guidelines?

preliminary report

Extracranial Stereotactic Radioablation*

Results of a Phase I Study in Medically Inoperable Stage I Non-small Cell Lung Cancer

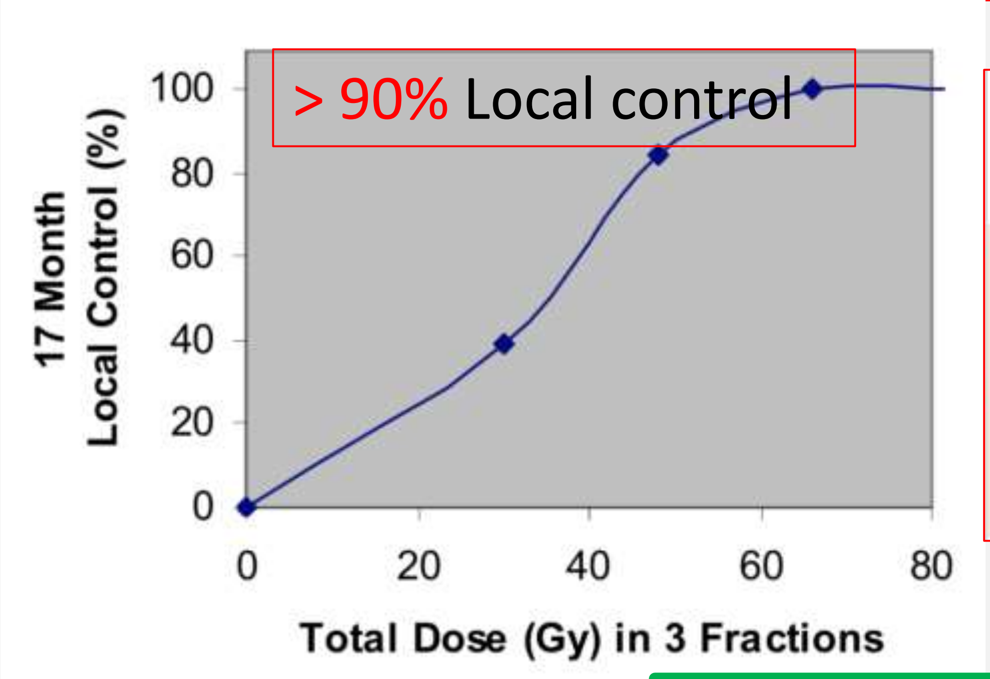
Robert Timmerman, MD; Lech Papiez, PhD; Ronald McGarry, MD; Laura Likes, RT; Colleen DesRosiers, MS; Stephanie Frost, MS; and Mark Williams, MD

pro

Special Article

Stereotactic body radiation therapy for early-stage non-small cell lung cancer: Executive Summary of an ASTRO Evidence-Based Guideline

Gregory M.M. Videtic MD, CM, FRCPC, FACR, Jessica Donington MD, Meredith Giuliani MBBS, John Heinzerling MD, Tomer Z. Karas MD, Chris R. Kelsey MD, Brian E. Lally MD, Karen Latzka, Simon S. Lo MB, ChB, FACR, Drew Moghanaki MD, MPH, Benjamin Movsas MD, Andreas Rimner MD, Michael Roach MD, George Rodrigues MD, PhD, FRCPC, Shervin M. Shirvani MD, MPH, Charles B. Simone II MD, Robert Timmerman MD, Megan E. Daly MD



(CHEST 2003; 124:1946–1955)

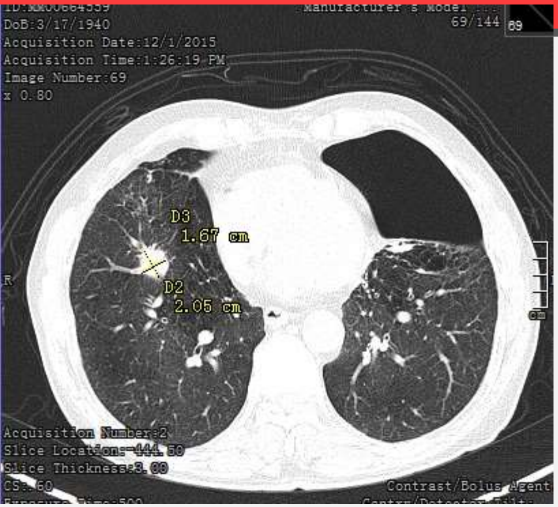
RTOG 0236

Stereotactic Body Radiation Therapy for Inoperable Early Stage Lung Cancer

- 3-year Primary tumor control rate: 97.6% ,
- Tumor,involved lobe control rate : 90.6% ; LRC:: 87.2%
- 3-year rate of disseminated failure was 22.1%
- OS at 3 years were 55.8%; Median OS: 48.1 months

SBRT:Standard of Care in Medically Inoperable (stage I, II)

Empirical SBRT?



Biopsy: very high risk

Age	80	years
Nodule diameter	18	mm
Current or former smoker	No 0	**Yes +1**
Extrathoracic cancer diagnosis ≥5 years prior	**No 0**	Yes +1
Upper lobe location of tumor	No 0	**Yes +1**
Nodule spiculation	No 0	**Yes +1**

FDG-PET
Optional, if performed

- PET not performed
- No uptake
- Faint uptake
- **Moderate uptake**
- Intense uptake

93.8 %
Probability of malignancy

Translational Lung Cancer Research, Vol 8, No 1 February 2019

Table 3 Proposed acceptable pretest probability thresholds for empiric therapy for clinical stage I

Study	Proposed acceptable pretest probability thresholds (%)
Gould *et al.* (34)	65
Louie *et al.* (42)	85
IASLC (8)	85
Senan *et al.* (43)	85

Solitary Pulmonary Nodule (SPN) Malignancy Risk Score (Mayo Clinic Model)

>85%----→SBRT
65-85%--→ PET Avidity---->SBRT

Decided for SBRT.

Contraindications?

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Contraindications for Lung SBRT?

~~SBRT~~: Infiltration to central structures

- Minimum ECOG 3
- Life Expectancy at least 1 year
- Severe COPD: GOLD III (FEV1 30-50%), GOLD IV (<30%)
- ILD : high risk

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journal homepage: www.thegreenjournal.com

Original article

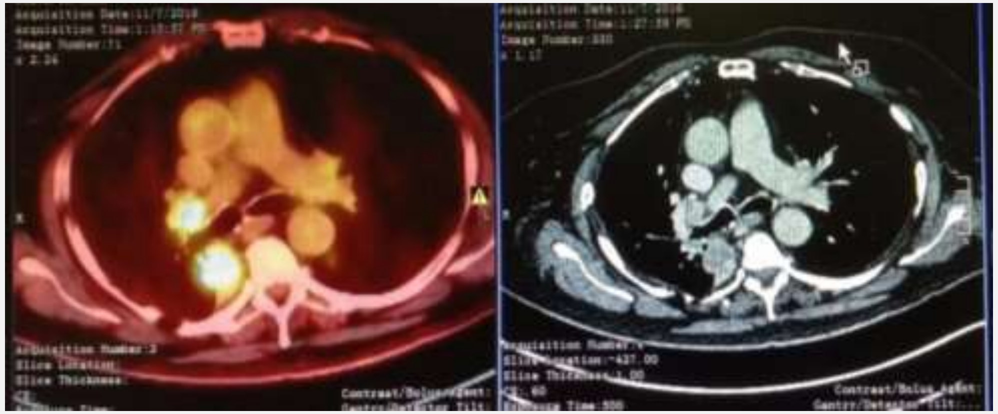
ESTRO ACROP consensus guideline on implementation and practice of stereotactic body radiotherapy for peripherally located early stage non-small cell lung cancer

Matthias Guckenberger, Nicolaus Andratschke, Karin Dieckmann, Mischa S. Hoogeman, Morten Hoyer, Coen Hurkmans, Stephanie Lang, Eric Lartigau, Alejandra Méndez Romero, Suresh Senan, Dirk Verellen

Review > Int J Radiat Oncol Biol Phys. 2012 Mar 1;82(3):1149-56.
doi: 10.1016/j.ijrobp.2011.03.005. Epub 2011 Jun 2.

Curative treatment of Stage I non-small-cell lung cancer in patients with severe COPD: stereotactic radiotherapy outcomes and systematic review

David Palma [1], Frank Lagerwaard, George Rodrigues, Cornelis Haasbeek, Suresh Senan



SBRT for T >5cm- Safe & effective

Clinical Investigation

Stereotactic Body Radiation Therapy for Non-Small Cell Lung Cancer Tumors Greater Than 5 cm: Safety and Efficacy

Neil M. Woody, MD, Kevin L. Stephans, MD, Gaurav Marwaha, MD, Toufik Djemil, PhD, and Gregory M.M. Videtic, MD, CM, FRCPC

Department of Radiation Oncology, Taussig Cancer Institute, Cleveland Clinic, Cleveland, Ohio

Received Dec 19, 2014, and in revised form Jan 27, 2015. Accepted for publication Jan 28, 2015.

Original Article

Multi-Institutional Experience of Stereotactic Body Radiotherapy for Large (≥5 Centimeters) Non–Small Cell Cancer Lung Tumors

February 15, 2017

Vivek Verma, MD[1]; Valerie K. Shostrom, MS[2]; Sameera S. Kumar, MD[3]; Weining Zhen, MD[1]; Christopher L. Hallemeier, MD[4]; Steve E. Braunstein, MD, PhD[5]; John Holland, MD[6]; Matthew M. Harkenrider, MD[7]; Adrian S. Iskhanian, MD[8]; Hanmanth J. Neboori, MD[8]; Salma K. Jabbour, MD[9]; Albert Attia, MD[10]; Percy Lee, MD[11]; Fiori Alite, MD[7]; Joshua M. Walker, MD, PhD[6]; John M. Stahl, MD[12]; Kyle Wang, MD[13]; Brian S. Bingham, BS[10]; Christina Hadzitheodorou, BS[9]; Roy H. Decker, MD, PhD[12]; Ronald C. McGarry, MD, PhD[3]; and Charles B. Simone II, MD[14]

pro

Special Article

Stereotactic body radiation therapy for early-stage non-small cell lung cancer: Executive Summary of an ASTRO Evidence-Based Guideline

Gregory M.M. Videtic MD, CM, FRCPC, FACR[a,*], Jessica Donington MD[b], Meredith Giuliani MBBS[c], John Heinzerling MD[d], Tomer Z. Karas MD[e], Chris R. Kelsey MD[f], Brian E. Lally MD[g], Karen Latzka[h], Simon S. Lo MB, ChB, FACR[i], Drew Moghanaki MD, MPH[j], Benjamin Movsas MD[k], Andreas Rimner MD[l], Michael Roach MD[m], George Rodrigues MD, PhD, FRCPC[n], Shervin M. Shirvani MD, MPH[o], Charles B. Simone II MD[p], Robert Timmerman MD[q], Megan E. Daly MD[r]

Local control with SBRT >85%

MC pattern of failure is regional/systemic

Relatively infrequent >5cm with N0; Limited trials

Larger irradiated volumes- Higher treatment toxicities as well as treatment failures (Regional, systemic > Local)

ASTRO conditionally recommend SBRT for > 5 cm. (higher risk of regional/ distant failures)

Consenting: Control, failure & toxicity to discuss?

- Response-LC; Failure
- Rib Fracture
- Chestwall Pain
- Pneumonitis
- Fibrosis

Table 2 Toxicity results

Study	Grade 3 + toxicity	Reported adverse events
Miyakawa *et al*[20], 2017	Grade 3-5, 5.6%	Radiation pneumonitis
Sun *et al*[80], 2017	Grade 3, 5%	Dermatitis, radiation pneumonitis, chest wall pain
Singh *et al*[22], 2017, I-124407	Grade 3, 30%	NA
Bezjak *et al*[24], 2016, RTOG 0813	Grade 3-5, 16%-21%	Respiratory and cardiac toxicities, esophageal perforation, pulmonary hemorrhage
Navarro-Martin *et al*[11], 2016	Grade 3, 10%	Cough, dyspnea, dermatitis
Nyman *et al*[14], 2016, SPACE	Grade 3, 14%	Dyspnea, cough, skin reactions
Chang *et al*[15], 2015, STARS and ROSEL	Grade 3, 10%	Chest wall pain, cough, fatigue, rib fracture
Lindberg *et al*[19], 2015	Grade 3-4, 30%	Rib fracture, dyspnea, ventricle tachycardia, cough, fatigue, fibrosis, lung infection, pain, pericardial effusion
Nagata *et al*[12], 2015, JCOG 0403	Grade 3-4, 13% (inop) Grade 3, 6% (op)	Inop: Dyspnea, hypoxia, pneumonitis, chest pain, cough Op: Dyspnea, hypoxia, pneumonitis, chest pain
Shibamoto *et al*[6], 2015	Grade 3, < 10%	Radiation pneumonitis, pleural effusion, esophagitis, rib fracture, dermatitis
Videtic *et al*[13], 2015, RTOG 0915	Grade 3-5, 12%	DLCO changes, pneumonitis, PFT changes, 2 treatment-related deaths
Timmerman *et al*[18], 2014, RTOG 0236	Grade 3-4, 31%	Hypocalcemia, hypoxia, pneumonitis, PFT decreased
Taremi *et al*[26], 2012	Grade 3, 11%	Fatigue, cough, chest wall pain, rib fracture
Bral *et al*[46], 2011	Grade 3, 20%	Pneumonitis, cough
Ricardi *et al*[16], 2010	Grade 3-4, 3%	Radiation pneumonitis
Fakiris *et al*[17], 2009	Grade 3-5, 16%	Apnea, pneumonia, pleural effusion, hemoptysis, respiratory failure, skin erythema
Koto *et al*[10], 2007	Grade 3, 3%	Pneumonitis
McGarry *et al*[7], 2005	Grade 3-4, 15%	Pneumonitis, hypoxia, dermatitis, pericardial effusion, tracheal necrosis
Nagata *et al*[8], 2005	None	None

Excellent Local Control with SBRT

World Journal of Clinical Oncology

Submit a Manuscript: https://www.f6publishing.com

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DOI: 10.5306/wjco.v10.i1.14

ISSN 2218-4333 (online)

MINIREVIEWS

Stereotactic body radiation therapy for non-small cell lung cancer: A review

Kavitha M Prezzano, Sung Jun Ma, Gregory M Hermann, Charlotte I Rivers, Jorge A Gomez-Suescun, Anurag K Singh

Table 1 Study characteristics and tumor control results

Study	No.	F/u (median)	Age (median)	Loc	Stage	Dose/fx	OS	LC	RC	DC
Miyakawa et al, 2017	71	44	77	C + P	T1-2N0M0	48-52 Gy/ 4 fx	5-yr 65%	5-yr 85%	NA	NA
Sun et al, 2017	65	86	71	C + P	T1-2N0M0	50 Gy/4 fx	7-yr 48%	7-yr 92%	7-yr 86%	7-yr 86%
Singh et al, 2017, I-124407	98	27	NA	P	T1-2N0M0	30 Gy/1 fx and 60 Gy/3fx	2-yr 71% (30 Gy) 2-yr 61% (60 Gy)	NA	NA	NA
Bezjak et al, 2016, RTOG 0813	71	33 (57.5 Gy) 30 (60 Gy)	NA	C	T1-2N0M0	57.5-60 Gy/5 fx	2-yr 70% (57.5 Gy) 2-yr 88% (60 Gy)	2-yr 90% (57.5 Gy) 2-yr 88% (60 Gy)	2-yr 95% (57.5 Gy) 2-yr 88% (60 Gy)	2-yr 84% (57.5 Gy) 2-yr 85% (60 Gy)
Navarro-Martin et al, 2016	38	42	74	P	T1-3N0M0	54 Gy/3 fx	3-yr 66%	3-yr 94%	3-yr 79%	3-yr 87%
Nyman et al, 2016, SPACE	102	37	74 (mean)	P	T1-2N0M0	66 Gy/3 fx	3-yr 54%	3-yr 86%	3-yr 93%	3-yr 76%
Chang et al, 2015, STARS and ROSEL	31	40	67	C + P	T1-2N0M0	54 Gy/3 fx, 50 Gy/4 fx, 60 Gy/5 fx	3-yr 95%	3-yr 96%	3-yr 90%	3-yr 97%
Lindberg et al, 2015	57	42	75 (mean)	P	T1-2N0M0	45 Gy/3 fx	5-yr 30%	5-yr 79%	3-yr 81% for regional/distant control	NA
Nagata et al, 2015, JCOG 0403	169	47 (inop) 67 (op)	78	NA	T1N0M0	48 Gy/4 fx	3-yr 60% 5-yr 43% (inop) 3-yr 77% 5-yr 54% (op)	3-yr 87% (inop) 3-yr 85% (op)	3-yr 92% (inop) 3-yr 75% (op)	3-yr 78% (inop) 3-yr 67% (op)
Shibamoto et al, 2015	180	53	77	C + P	T1-2N0M0	44-52 Gy /4 fx	5-yr 52%	5-y 83%	5-yr 84%	5-yr 76%
Videtic et al, 2015, RTOG 0915	94	30	75	P	T1-2N0M0	34 Gy/1 fx and 48 Gy/4 fx	3-yr 56%	3-yr 98%	NA	NA
Timmerman et al, 2014, RTOG 0236	55	48	72	P	T1-2N0M0	54 Gy/3 fx	5-yr 40%	5-yr 80%	5-yr 62% (local-regional control)	5-yr 79%
Taremi et al, 2012	108	19	73 (mean)	C + P	T1-2N0M0	48 Gy/4 fx or 54-60 Gy/3 fx (P) 50-60 Gy /8-10 fx (C)	4-yr 30%	4-yr 89%	4-yr 87%	4-yr 83%
Bral et al, 2011	40	16	73 (mean)	C + P	T1-3N0M0	60 Gy/3-4 fx	2-yr 52%	2-yr 84%	2 nodal recurrences	6 distant recurrences
Ricardi et al, 2010	62	28	74	P	Stage 1	45 Gy/3 fx	3-yr 57%	3-yr 88%	3-yr 94%	3-yr 76%
Fakiris et al, 2009	70	50	70	C + P	T1-2N0M0	60-66 Gy/ 3 fx	3-yr 43%	3-yr 88%	3-yr 91%	3-yr 87%
Koto et al, 2007	31	32	77	C + P	T1-2N0M0	45 Gy/3 fx or 60 Gy/8 fx	3-yr 72%	3-yr 78% (T1) 3-yr 40% (T2)	3-yr 94%	3-yr 81%
McGarry et al, 2005	47	27 (Stage IA)	71 (Stage IA)	C + P	T1-2N0M0	24-72 Gy/ 3 fx	NA	2-yr 81%	2-yr 81%	2-yr 79%

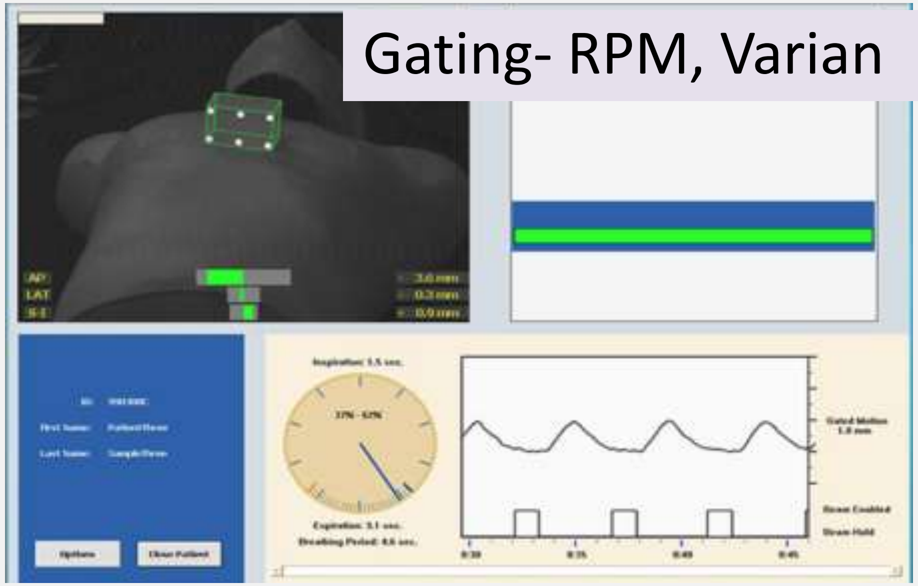
M/C type of failure in SBRT

Cancer 2017

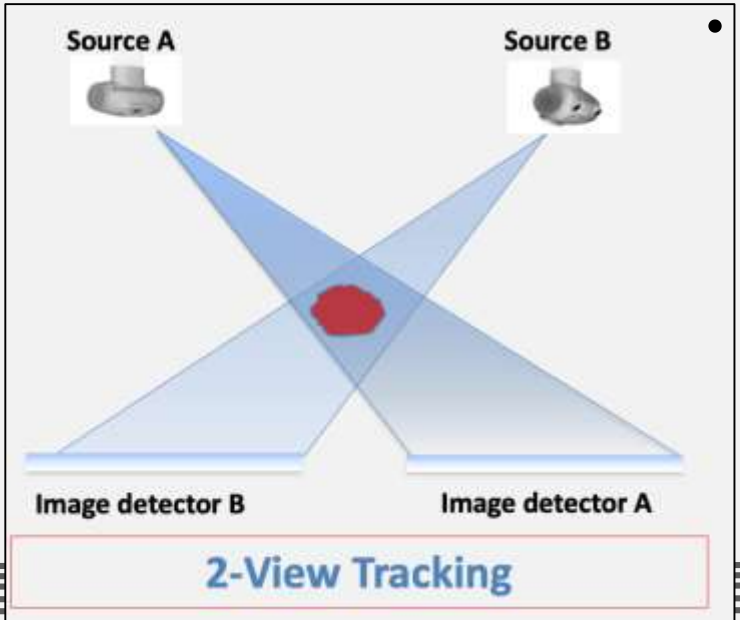
TABLE 2. Patterns of Failure, Survival, and SPLC >7 Years After SABR

Event[a]	Estimated Cumulative Incidence (95% CI), %			
	1 Year	3 Years	5 Years	7 Years
Local disease recurrence	1.5 (0.2-10.8)	4.6 (1.5-13.9)	8.1 (3.5-18.8)	8.1 (3.5-18.8)
Regional disease recurrence	4.6 (1.5-13.9)	9.2 (4.3-19.8)	10.9 (5.4-21.8)	13.6 (7.0-26.5)
Locoregional disease recurrence	6.2 (2.4-15.9)	12.3 (6.4-23.6)	17.4 (10.1-29.8)	20.0 (11.9-33.7)
Distant metastases	7.7 (3.3-17.9)	9.2 (4.3-17.8)	11.0 (5.5-22.2)	13.8 (7.1-26.8)
Any disease recurrence	12.3 (6.4-23.6)	18.5 (11.1-30.8)	25.3 (16.6-38.8)	30.9 (20.7-46.0)
PFS[b]	81.5 (76.7-86.3)	64.6 (58.7-70.5)	49.5 (43.2-55.8)	38.2 (31.2-45.2)
OS[b]	92.3 (89.0-95.6)	70.8 (65.2-76.4)	55.7 (49.4-62.0)	47.5 (40.6-54.4)
SPLC	4.6 (1.5-13.9)	9.2 (4.3-19.8)	16.2 (9.2-28.6)	20.7 (12.4-34.5)

Motion management strategies at your center?



Gating- RPM, Varian



Motion management

- **Tracking**
- **Gating**
- **Motion freeze**
- **Free breathing** with ITV
- **Abdominal compression**

Contouring

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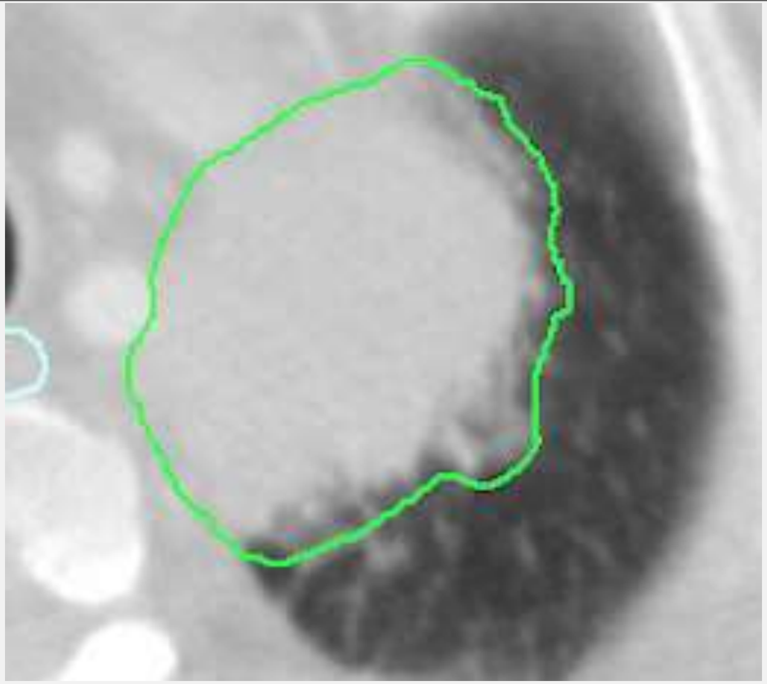
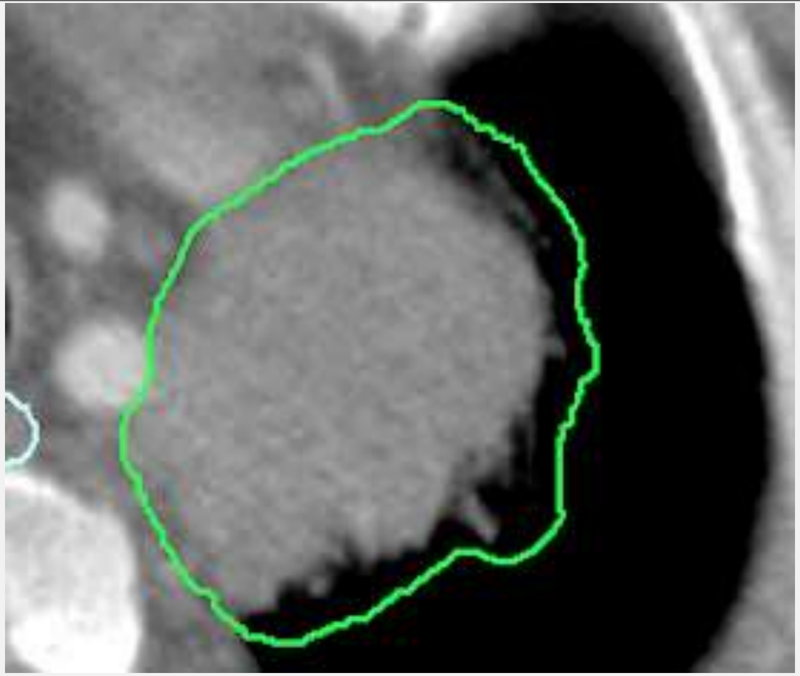
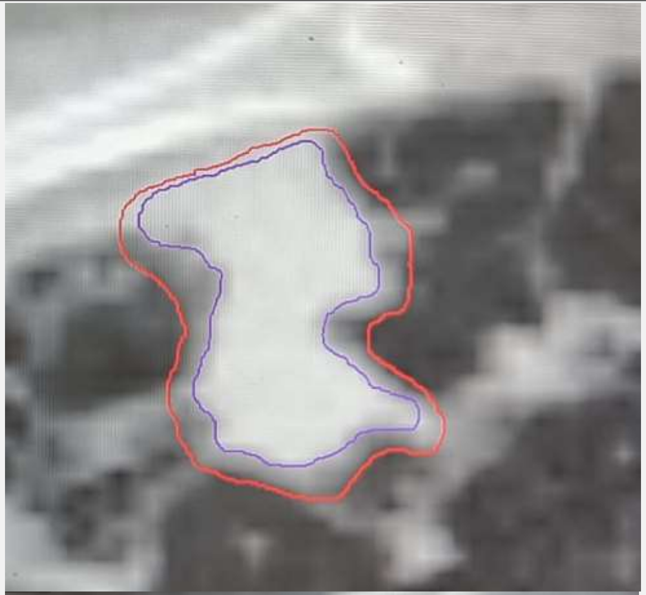
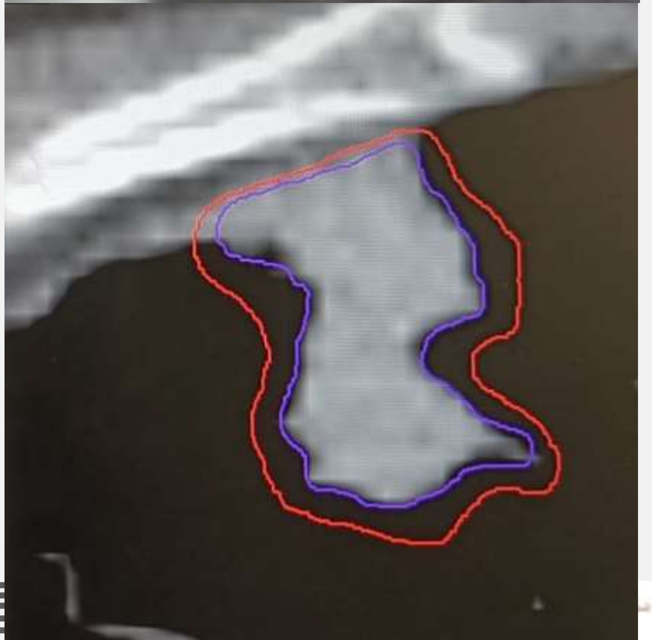
Contour?









Measurements of tumor on CT - highly dependent on W/L setting.

Best concordance b/w GTV_CT and tumor: W:1600 L:-600

Include spicules
Don't keep changing WL

Who all give CTV?

Radiotherapy and Oncology

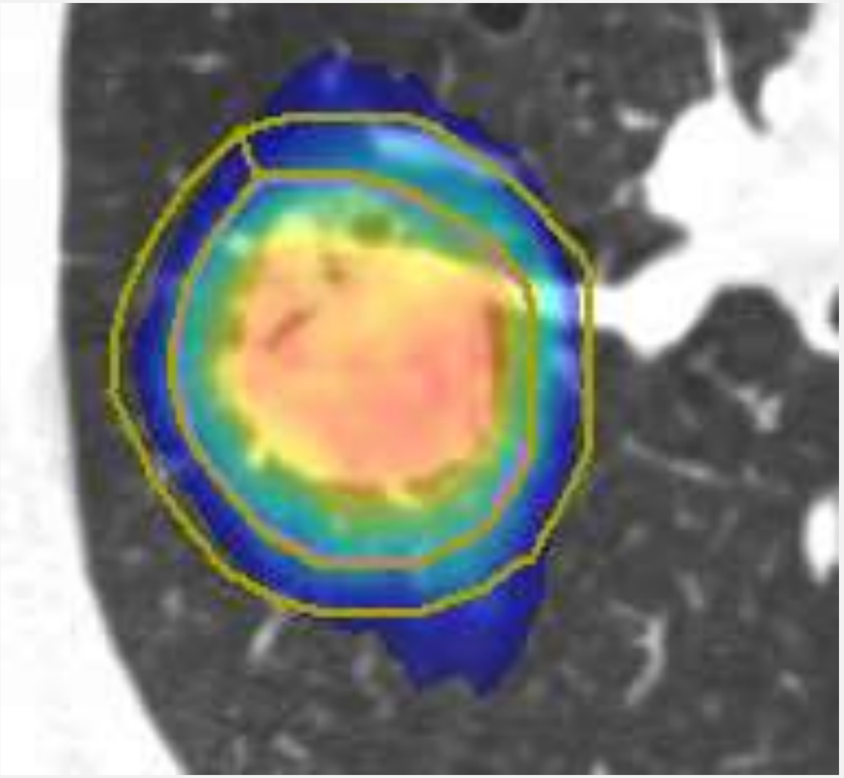
journal homepage: www.thegreenjournal.com

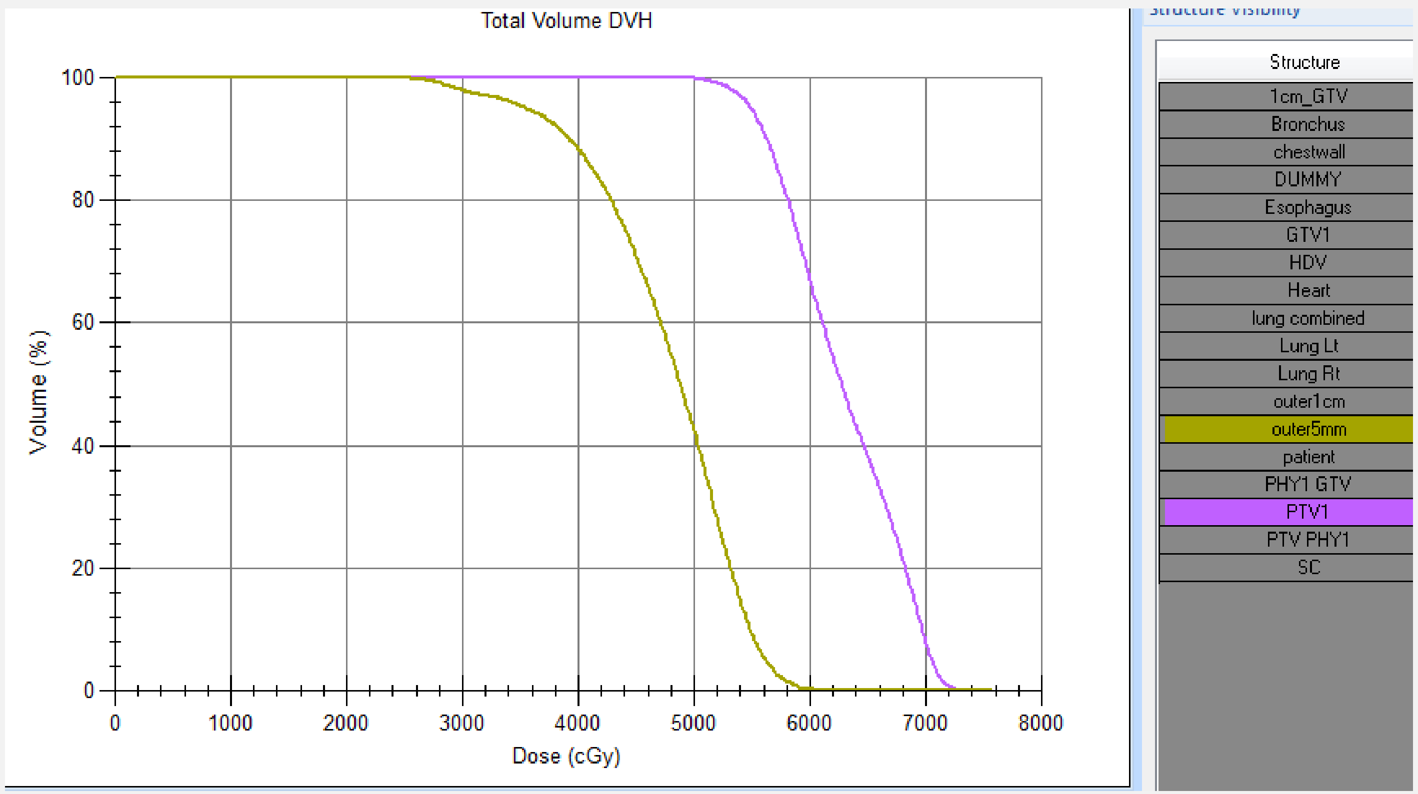
Meta-analysis

Is high-dose stereotactic body radiotherapy (SBRT) for stage I non-small cell lung cancer (NSCLC) overkill? A systematic review

Angela van Baardwijk, Wolfgang A. Tomé, Wouter van Elmpt, Søren M. Bentzen, Bart Reymen, Rinus Wanders, Ruud Houben, Michel Öllers, Philippe Lambin, Dirk De Ruysscher

Dose to "nontarget" tissues immediately adjacent to PTV receive a relatively high





PTV: 54Gy/ 3 Fx @ 76% Isodose

5mm Ring outside PTV : Dmean : BED125

Dose prescription methods?

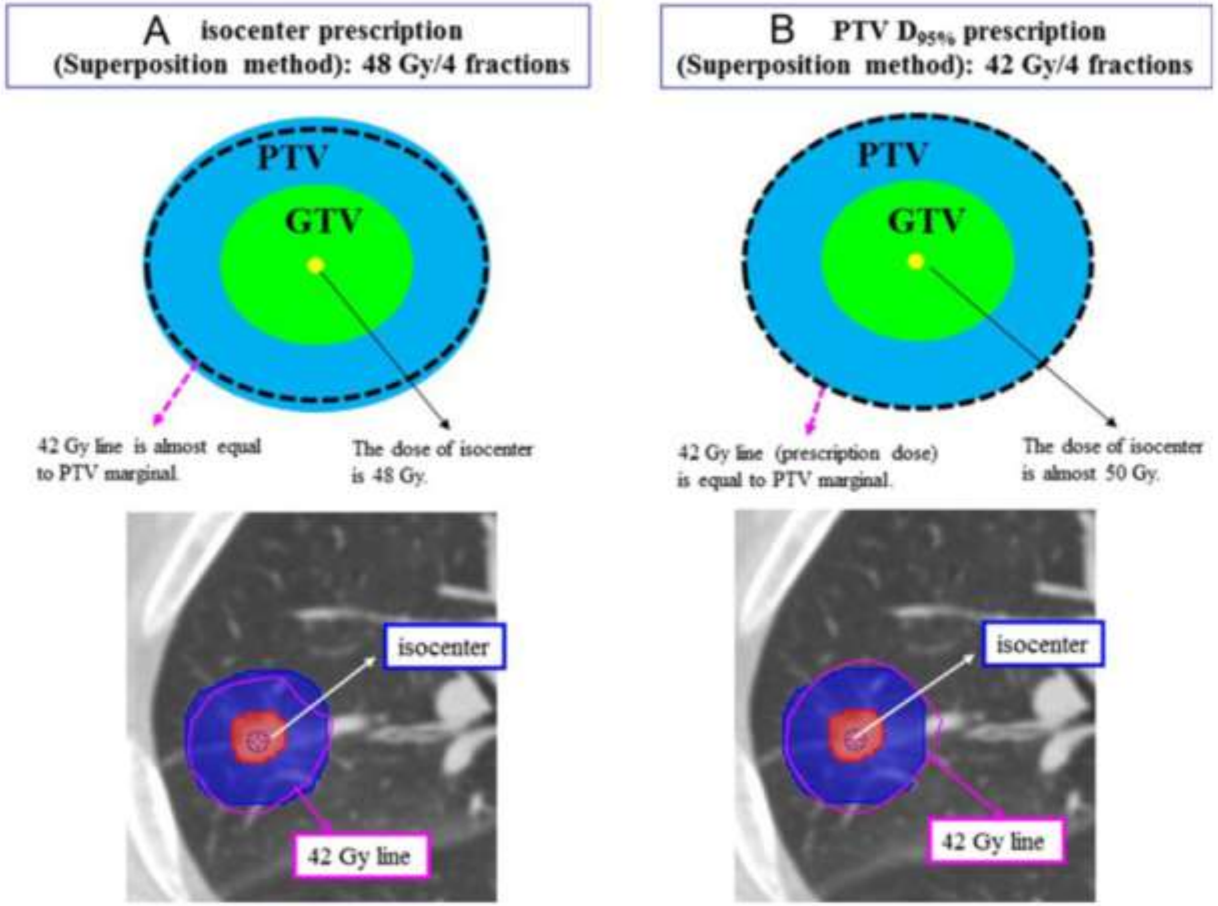


Figure 2. The difference of dose distribution by dose prescription method. (A) The isocenter prescription of 48 Gy/4 fractions. The 48 Gy in four fractions dose was evaluated at the isocenter using a new dose calculation algorithm (superposition method). The 42 Gy isodose line is covered PTV. (B) PTV D95% prescription of 42 Gy/4 fractions. The 42 Gy isodose line is also covered PTV, and marginal dose of PTV is almost equivalent to that of isocenter prescription.

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Original article

ESTRO ACROP consensus guideline on implementation and practice of stereotactic body radiotherapy for peripherally located early stage non-small cell lung cancer

Matthias Guckenberger[a,*], Nicolaus Andratschke[b], Karin Dieckmann[c], Mischa S. Hoogeman[d], Morten Hoyer[e], Coen Hurkmans[f], Stephanie Lang[b], Eric Lartigau[g], Alejandra Méndez Romero[d], Suresh Senan[h], Dirk Verellen[i]

[a] Department of Radiation Oncology; [b] University Hospital Zurich, Switzerland; [c] Medical University of Vienna, Austria; [d] Erasmus MC Cancer Institute, Rotterdam, Netherlan[ds]; [e] Aarhus University Hospital, Denmark; [f] Catharina Hospital, Eindhoven, Netherlands; [g] Centre Oscar Lambret, Lille, France; [h] VU University Medical Center, Amsterdam, Netherlan[ds]; [i] UZ Brussel (VUB), Belgium

Strahlenther Onkol
https://doi.org/10.1007/s00066-018-1416-x

REVIEW ARTICLE

ICRU report 91 on prescribing, recording, and reporting of stereotactic treatments with small photon beams

Statement from the DEGRO/DGMP working group stereotactic radiotherapy and radiosurgery

Lotte Wilke[1] · Nicolaus Andratschke[1] · Oliver Blanck[2] · Thomas B. Brunner[3] · Stephanie E. Combs[4] · Anca-Ligia Grosu[5] · Christos Moustakis[6] · Daniela Schmitt[7] · Wolfgang W. Baus[8] · Matthias Guckenberger[1]

Received: 17 August 2018 / Accepted: 13 December 2018

Volumetric + Isodose approach :

Dose is prescribed to isodose surface which should cover the optimal % of PTV Volume .

Ex: 50Gy/5Fx @ 70% Isodose;

D95% Volume- 100%Dose

D99% Volume 90%Dose

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What will be Target BED_{10}?

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BED_{10} atleast 100Gy needed....

Stereotactic Hypofractionated High-Dose Irradiation for Stage I Nonsmall Cell Lung Carcinoma

Clinical Outcomes in 245 Subjects in a Japanese Multiinstitutional Study

Onishi et al. 2004, Cancer

Patterns of First Disease Recurrences According to Stage and BED

Site of disease recurrence[a]	BED < 100 Gy (%)	BED ≥ 100 Gy (%)
Local disease recurrence	19/72 (26.4)	14/173 (8.1)
Regional lymph node recurrence	8/72 (11.1)	12/173 (6.9)
Distant metastasis	14/72 (19.4)	22/173 (12.7)

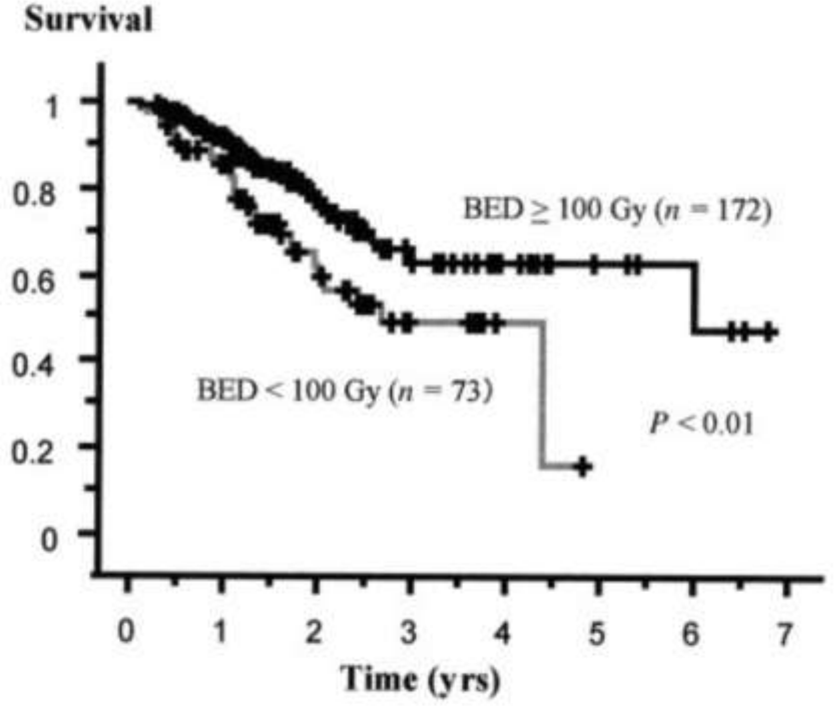


FIGURE 4. Overall survival rate according to the biologic effective dose in all patients.

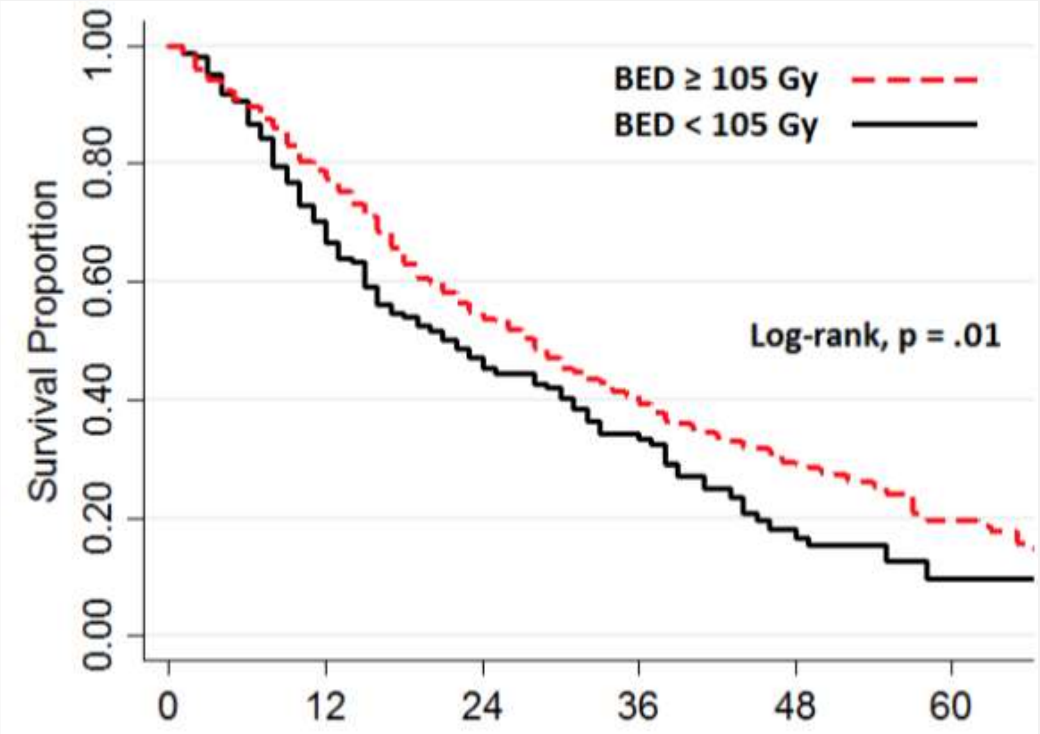
Dose response continue to rise beyond BED > 100

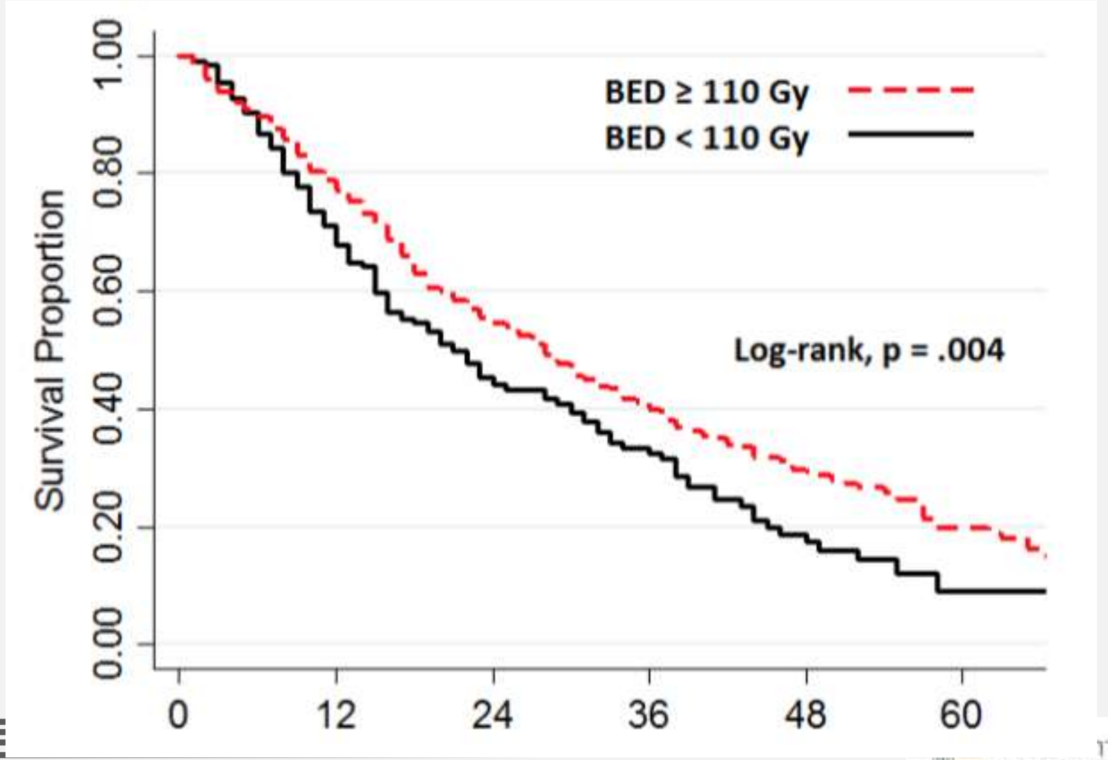
The association between biologically effective dose (BED) and radiation treatment schedule on overall survival in stage I non-small cell lung cancer (NSCLC) patients treated with stereotactic body radiation therapy (SBRT)

John M. Stahl. MD. Rudi Ross. BS. Eileen M. Harder. MD. Brandon R. Mancini. MD.

10.1016/j.ijrobp.2016.08.033

- 65 centers in US; 2006-2014
- T1-2; 921 patients





BED > 150Gy

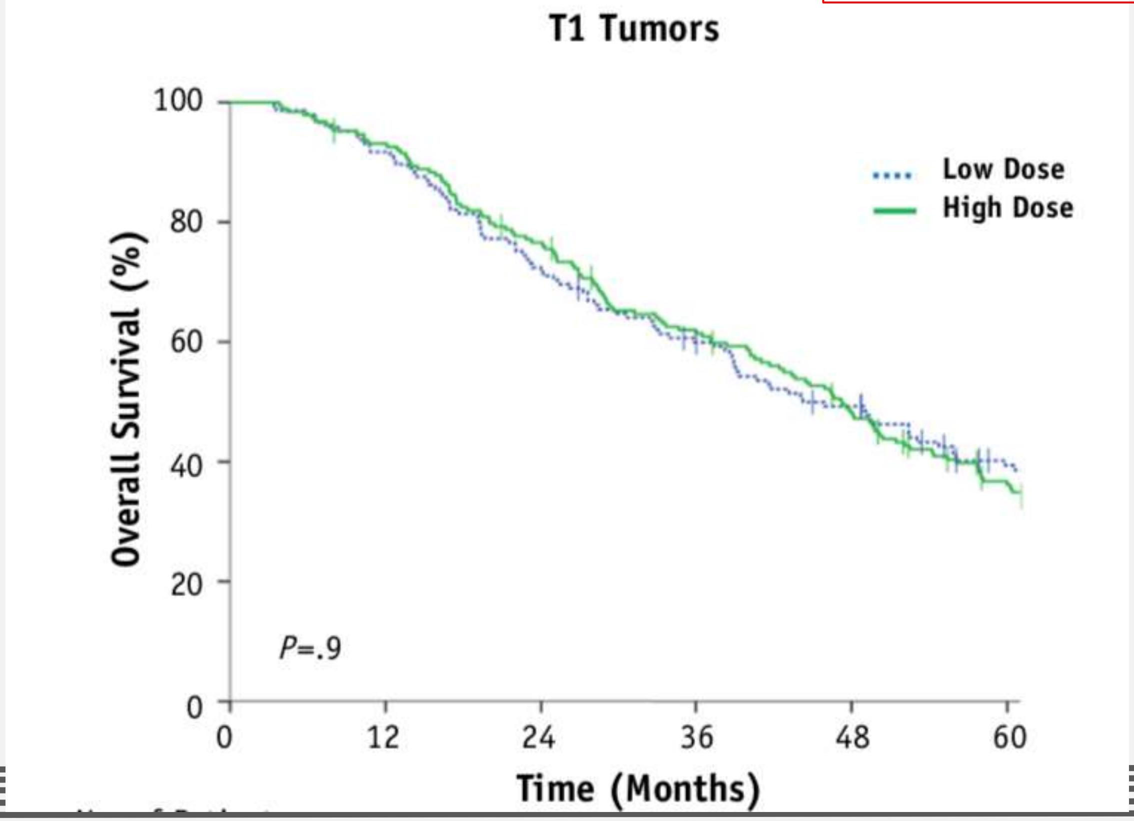
Increasing Radiation Therapy Dose Is Associated With Improved Survival in Patients Undergoing Stereotactic Body Radiation Therapy for Stage I Non–Small-Cell Lung Cancer

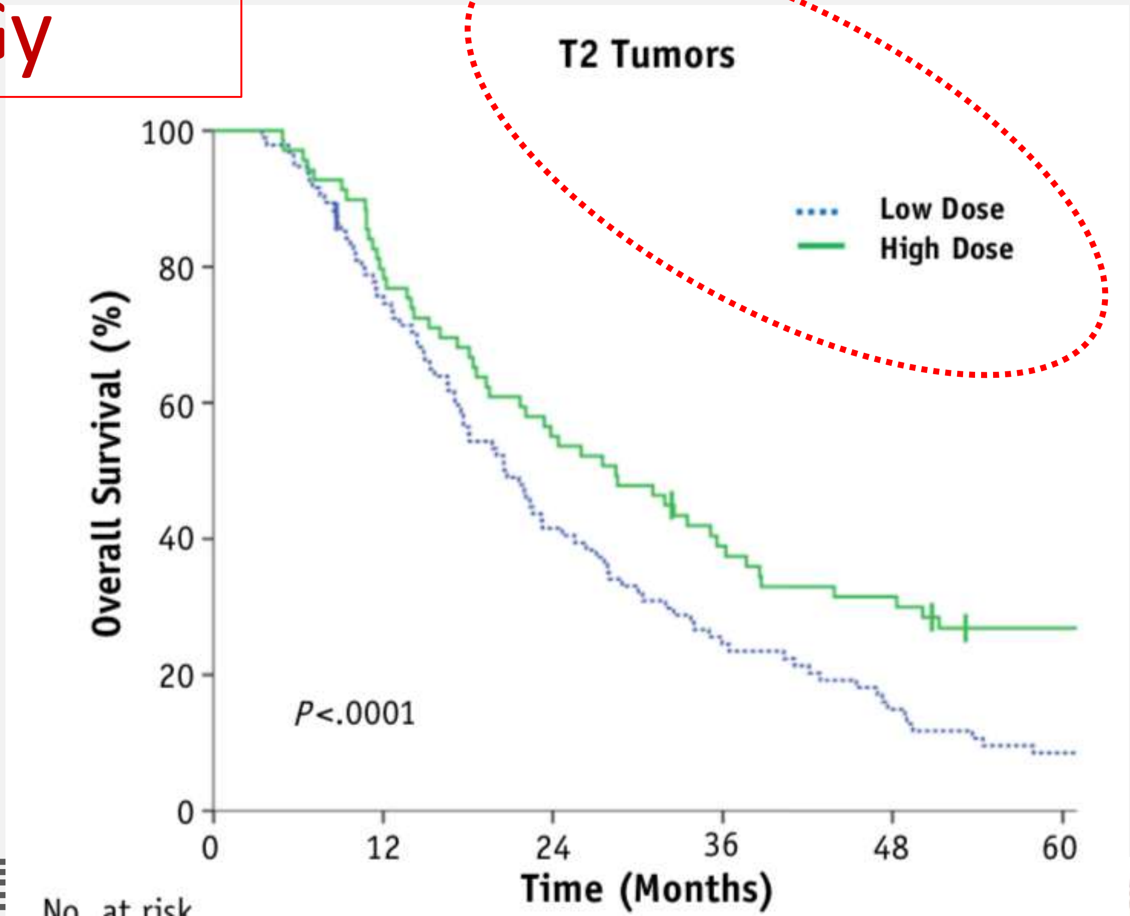
Matthew Koshy, MD,*,† Renuka Malik, MD,† Ralph R. Weichselbaum, MD,*,† and David J. Sher, MD, MPH‡

IJROBP, Vol. 91, 2015

National Cancer Database from 2003 to 2006 with T1-T2N0M0 inoperable lung cancer (n=498).

BED >/< 150Gy





HyTEC Organ-Specific Paper

Local Control After Stereotactic Body Radiation Therapy for Stage I Non-Small Cell Lung Cancer

Percy Lee, MD,* Billy W. Loo, Jr, MD, PhD,† Tithi Biswas, MD,‡

Table 1 Required physical doses (Gy) at isocenter and covering PTV with the 80% isodose line to reach the maximum TCP, calculated from the 3 models with the parameters determined in section "Mathematical and Biological Models."

Isocenter dose (Gy)		3 fractions	4 fractions	5 fractions
Regrowth	T1	52 ± 1	57 ± 1	60 ± 1
	T2	56 ± 1	62 ± 1	66 ± 1
	T1 + T2	54 ± 1	59 ± 1	63 ± 1
LQ	T1 + T2	55 ± 1	59 ± 1	63 ± 1
USC	T1 + T2	55 ± 1	59 ± 1	63 ± 1
PTV dose (Gy)		**3 fractions**	**4 fractions**	**5 fractions**
Regrowth	T1	42 ± 1	46 ± 1	48 ± 1
	T2	45 ± 1	50 ± 1	53 ± 1
	T1 + T2	43 ± 1	47 ± 1	50 ± 1
LQ	T1 + T2	44 ± 1	47 ± 1	50 ± 1
USC	T1 + T2	44 ± 1	47 ± 1	50 ± 1

Cautioned 42/3

T2 > 110 BED

"For pt with long OS expectancy, 18Gy x 3 Fx should be considered"

Dose/Fraction?

Peripheral: (<1cm away)

<2cm: 1 Fx: 25-34Gy

<3cm: 3 Fx : 45-60Gy /3Fx

3-5cm, : 4-5 Fx: 48/4

Close/chestwall- 55-60Gy/5

>5cm 60-64/8Fx

Central:

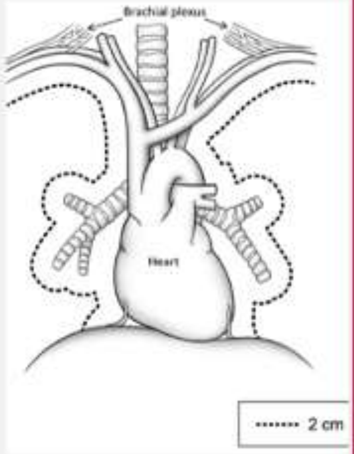
50Gy/5Fx

54Gy/6Fx

56GY/7 Fx

60Gy/8 Fx

70 /10 Fx



$BED_{10}>100$, $BED_{3}<210$:

Local control > 85%; Tx related mortality < 1%.

Ultrace

PTV overlap trachea or main bronchi

56Gy/8Fx

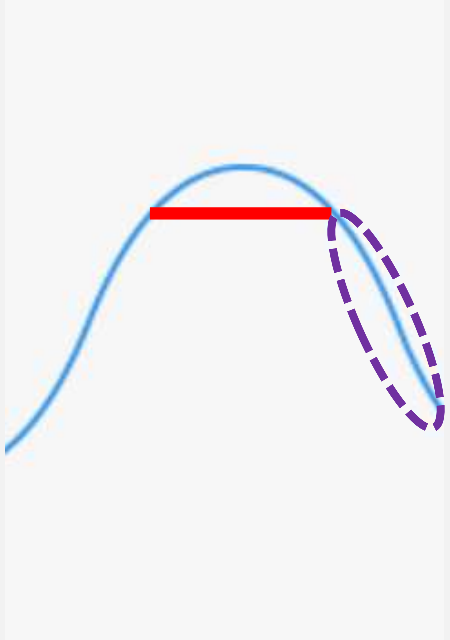
60Gy/10Fx

60Gy/12 Fx

Invasion of central structures:

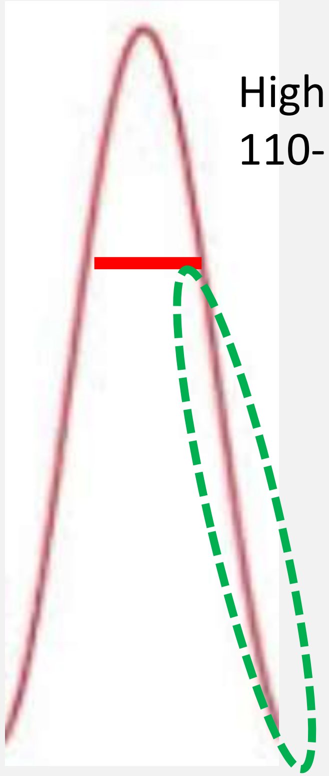
-------NO------

Prescription Isodose? Lower or Higher…



Homogenous Dose within PTV (95%-107%)

Slow dose falloff outside Target



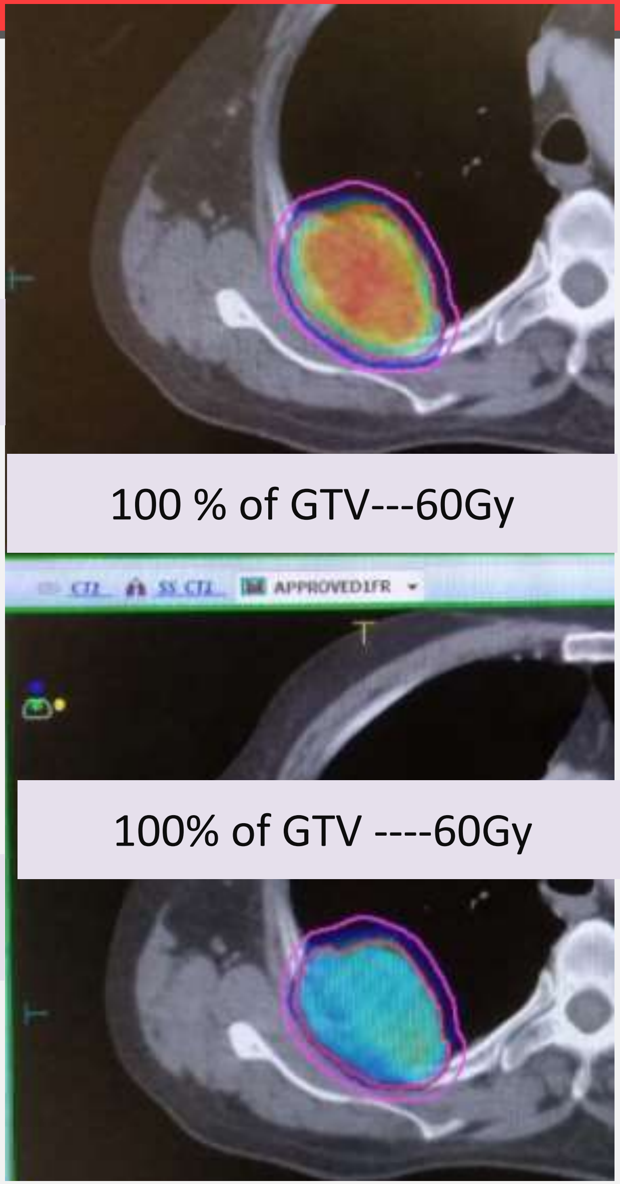
High doses within PTV 110-150%

Rapid dose falloff outside Target

- Radiobiological advantage
- Dosimetric advantage

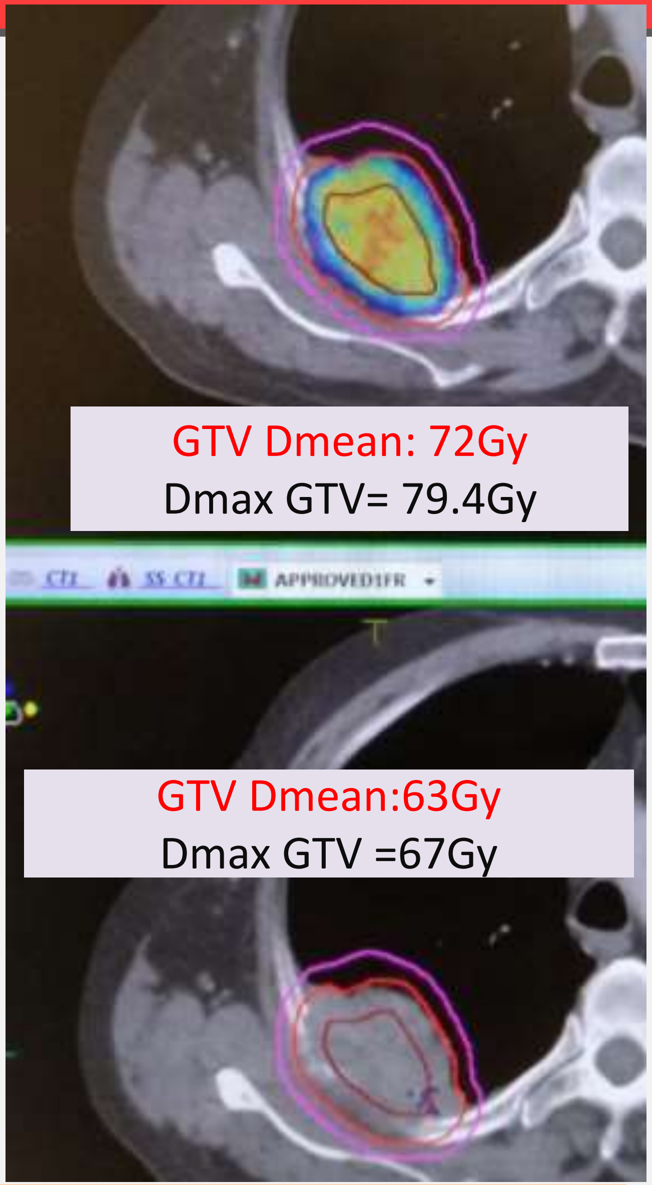
Effect of Prescription Isodose

GTV: 60Gy/5Fx **@ 75% Isodose**



100 % of GTV---60Gy

100% of GTV ----60Gy



GTV Dmean: 72Gy
Dmax GTV= 79.4Gy

GTV Dmean:63Gy
Dmax GTV =67Gy

GTV: 60Gy/5Fx **@ 90% Isodose**

Avoid using homogenous dose distribution within the target

Priority OAR for dose Constraints?

Clinical Investigation

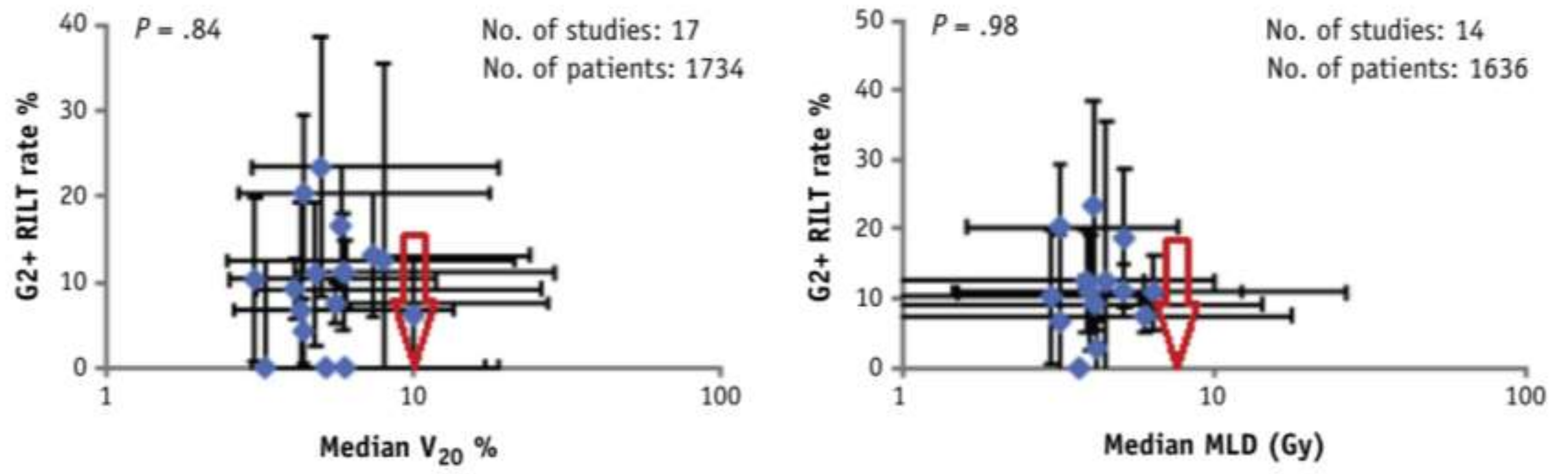
Organs at Risk Considerations for Thoracic Stereotactic Body Radiation Therapy: What Is Safe for Lung Parenchyma?

Feng-Ming (Spring) Kong, MD, PhD,* Vitali Moiseenko, PhD,†

Int J Radiation Oncol Biol Phys, Vol. ■, No. ■, pp. 1–16, 2019

HyTEC

there are no apparent “thresholds” for risk



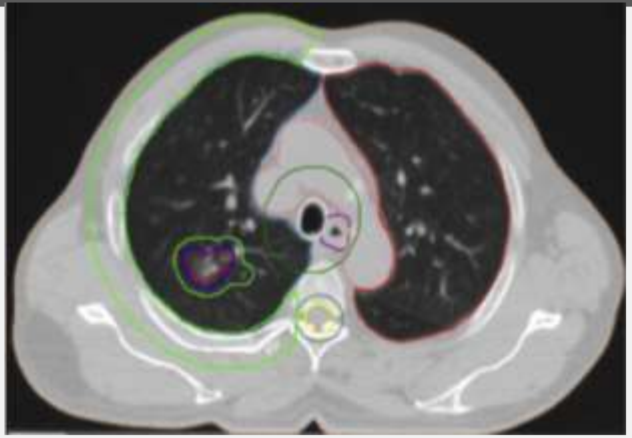
	Combined	I/L
MLD	6 Gy	10 Gy
V5Gy	30%	-
V10Gy	17%	35%
V20Gy	12	25
V30Gy	7	15

Combined lung **V20Gy 10- 12%**

Combined lung **MLD <6- 8Gy**

Combined Lung MLD EQD2: 9.9(Guckenberger et al)

Chestwall



2cm chest wall is most robust

Dose-Response Model for Chest Wall Tolerance of Stereotactic Body Radiation Therapy

	Low Risk Limits			
	D50% Limit (Gy)	D20% Limit (Gy)	D70cc Limit (Gy)	D2cc Limit (Gy)
1 fx	6.0	12.1	9.3, 10.0%	22.9, 10.0%
2 fx	7.8	16.3	12.4, 10.0%	31.5, 10.0%
3 fx	9.0	19.3	14.6, 10.0%	37.8, 10.0%
4 fx	10.0	21.6	16.2, 10.0%	43.0, 10.0%
5 fx	10.5	23.6	17.6, 10.0%	**50.0, 11.2%**

Grade 2 or higher

Type of Algorithms

- Type A: Pencil beam , TAR, BATHO—overestimation of Target dose
- Type B: Convolution/superposition: CCC, AAA-- Improved accuracy.
- Type C:
  - Acuros XB dose calculation algorithm
  - MC dose calculation algorithm

Parameter	Edge	Truebeam	Versa HD (Agility Head)	Cyberknife
Algo	AAA, Acuros	AAA, Acuros	MC	RT, MC
TPS	Eclipse Ver15.5	Eclipse Ver15.5	Monaco Ver 5.1	Precision

Planning Algorithm?
Why?

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RTOG 0236. (20 x 3=60)

Heterogeneity correction evaluation for RTOG 0236 ● Y. Xiao *et al.*

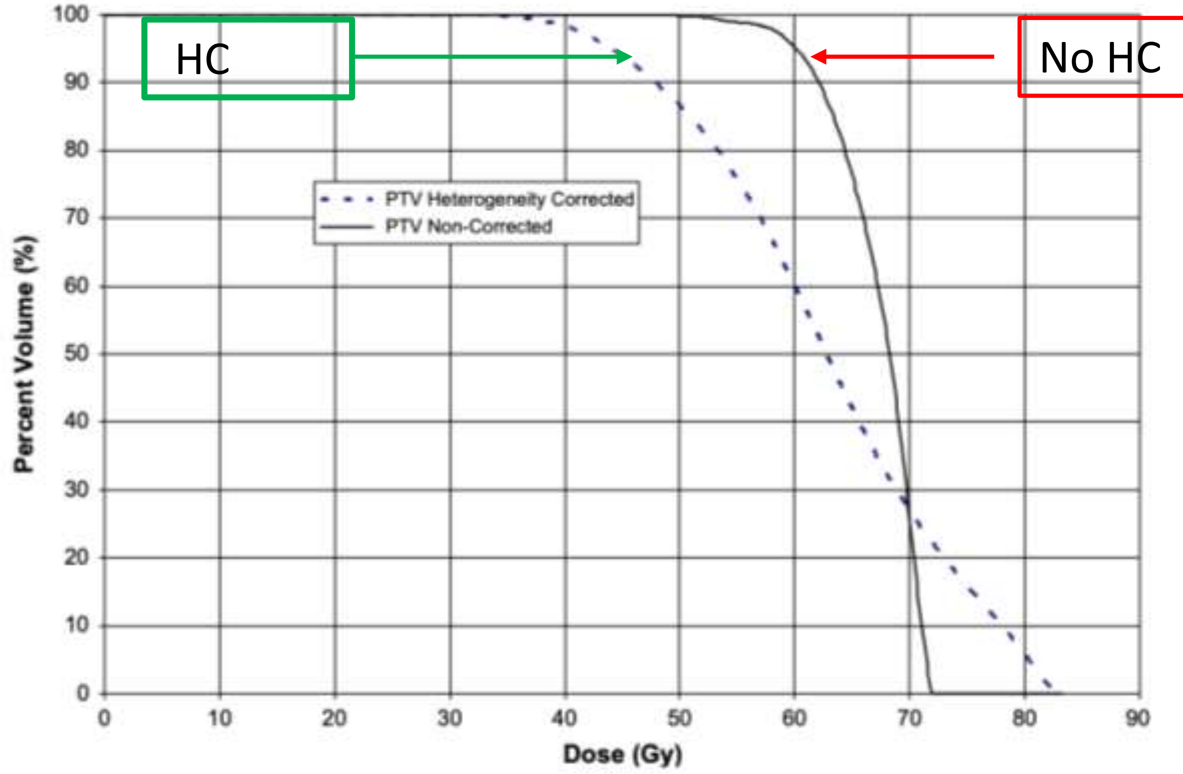


Fig. 4. Dose–volume histograms for planning target volume (PTV) coverage with unit density and density correction for case shown in Fig. 3, 1 of cases with larger than average differences between heterogeneity-corrected and unit density plans chosen for illustration.

ELSEVIER

Int. J. Radiation Oncology Biol. Phys., Vol. 73, No. 4, pp. 1235–1242, 2009

0360-3016/09/$–see front matter

doi:10.1016/j.ijrobp.2008.11.019

PHYSICS CONTRIBUTION

DOSIMETRIC EVALUATION OF HETEROGENEITY CORRECTIONS FOR RTOG 0236: STEREOTACTIC BODY RADIOTHERAPY OF INOPERABLE STAGE I-II NON–SMALL-CELL LUNG CANCER

Ying Xiao, Ph.D.,* Lech Papiez, Ph.D.,† Rebecca Paulus, B.S.,‡ Robert Timmerman, M.D.,† William L. Straube, M.S.,§ Walter R. Bosch, D.Sc.,§ Jeff Michalski, M.D.,§ and James M. Galvin, D.Sc.*

- Non-HC algorithms OVERESTIMATED target dose
- UNDERESTIMATED dose to normal tissues

OncoTargets and Therapy

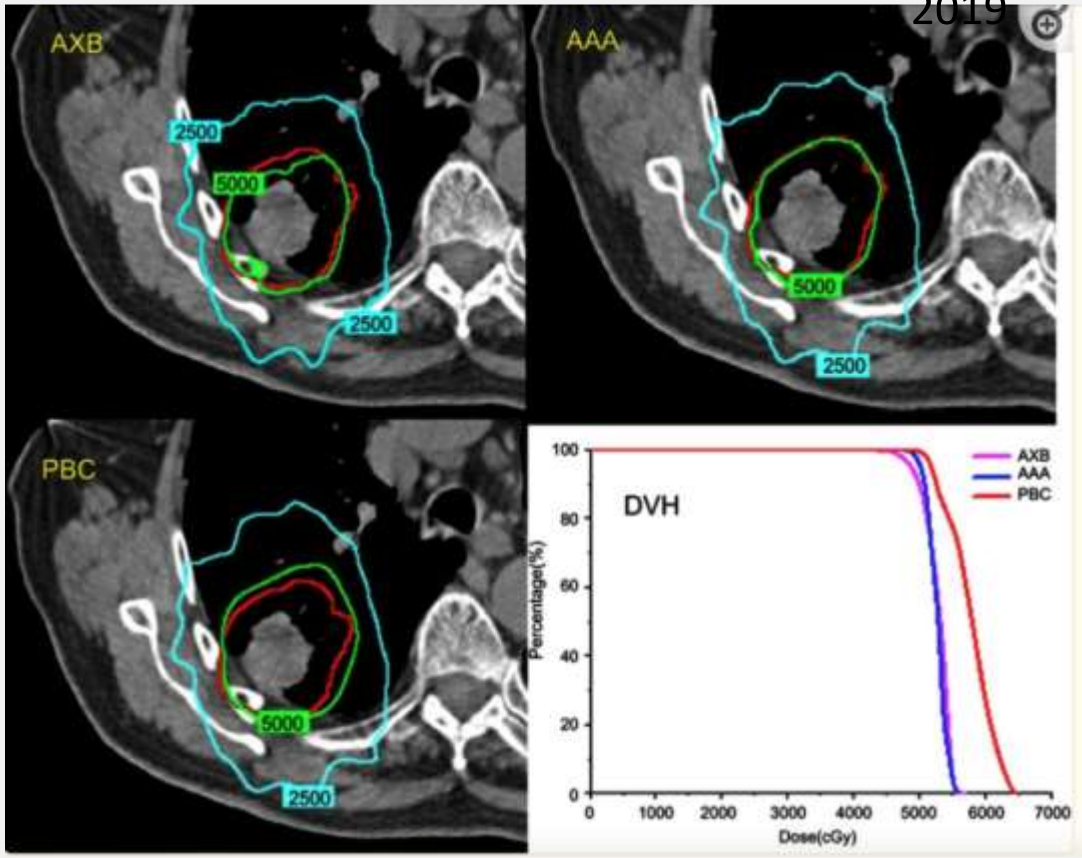
Dovepress

ORIGINAL RESEARCH

Dosimetric comparison of different algorithms in stereotactic body radiation therapy (SBRT) plan for non-small cell lung cancer (NSCLC)

This article was published in the following Dove Press journal: OncoTargets and Therapy

2019



Type C algorithm is recommended for Lung SBRT

Stereotactic Ablative Body Radiation Therapy (SABR): A Resource

SABR UK Consortium

Version 6.1, January 2019

Type B or MC are mandatory for lung SBRT

Plan evaluation:
essential component:



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Plan Evaluation:

- Target receive Px dose

Coverage:

- Hottness and location.

Dmax : 110% - 140%

- Px dose closely hugging PTV: HD spill

Conformity of Px dose to PTV

- Compact Intermediate Dose spill

Gradient Index(Steep dose fall)

- OAR constraints meet

OAR constraints

- 95% of PTV shud receive 100% Px dose (50Gy)
- 99% of PTV shud receive minimum of 90% Px dose (45.7Gy)

Conformity Index & R50%, Gradient Index

RTOG 0813

PTV Volume (cc)	Ratio of Prescription Isodose Volume to the PTV Volume		Ratio of 50% Prescription Isodose Volume to the PTV Volume, $R_{50\%}$	
	Deviation		Deviation	
	None	Minor	None	Minor
1.8	<1.2	<1.5	<5.9	<7.5
3.8	<1.2	.<1.5	<5.5	<6.5
7.4	<1.2	<1.5	<5.1	<6.0
13.2	<1.2	<1.5	<4.7	<5.8
22.0	<1.2	<1.5	<4.5	<5.5
34.0	<1.2	<1.5	<4.3	<5.3
50.0	<1.2	<1.5	<4.0	<5.0
70.0	<1.2	<1.5	<3.5	<4.8
95.0	<1.2	<1.5	<3.3	<4.4
126.0	<1.2	<1.5	<3.1	<4.0
163.0	<1.2	<1.5	<2.9	<3.7

Table 6.1. Prescription dose spillage requirements for lung and non-lung sites

Vol(PTV) (cc)	Vol(100%) / PTV V100%
	Target
<20	1.20*
20-40	1.10*
>40	1.10*

Table 6.2. Modified Gradient Index and other requirements for lung sites

Vol(PTV) (cc)	Vol(50%) / PTV V100%	
	Target	Tolerance
<20	7*	9*
20-40	5.5*	6.5*
40-60	5*	6*
60-90	4**	5
>90	4**	4.5

$$R100\% = \frac{Vol\ (100\%)}{Vol\ (PTV)} \rightarrow Prescription\ dose\ spillage = \frac{Vol\ (100\%)}{PTV\ V100\%}$$

$$R50\% = \frac{Vol\ (50\%)}{Vol\ (PTV)} \rightarrow Modified\ Gradient\ Index = \frac{Vol\ (50\%)}{PTV\ V100\%}$$

Followup –Aim; when and how?

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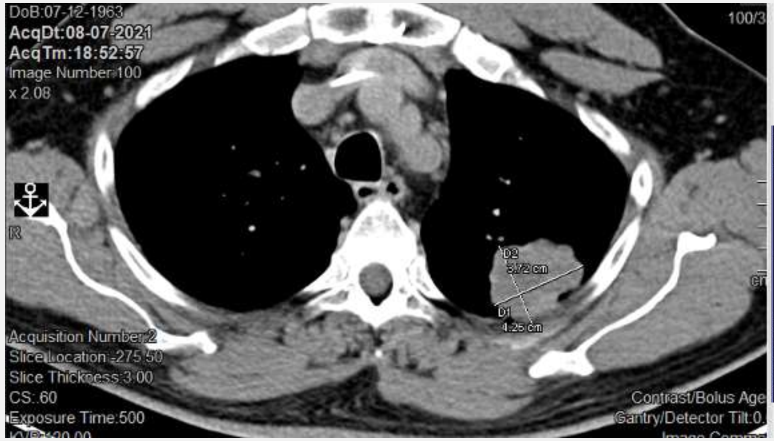
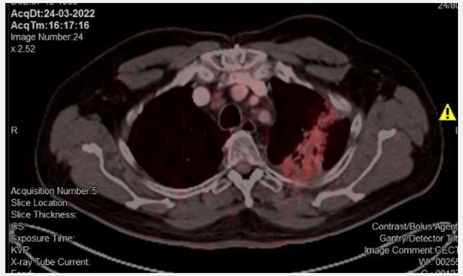
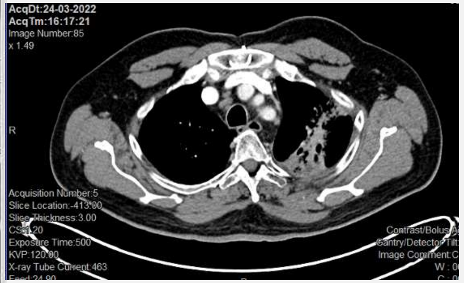
2021



2022





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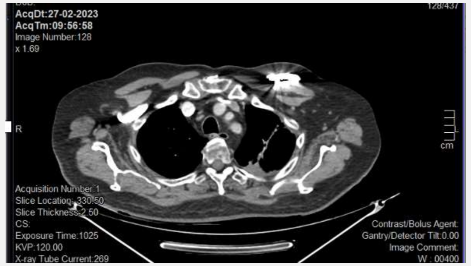

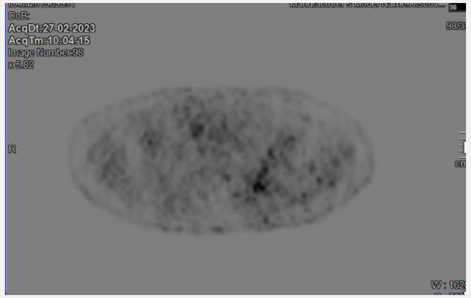

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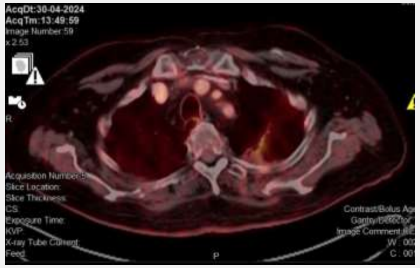

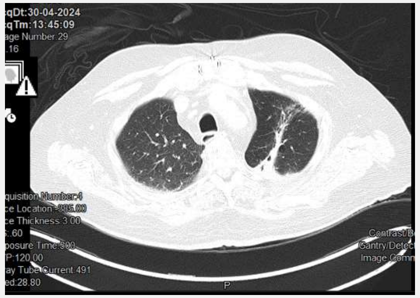

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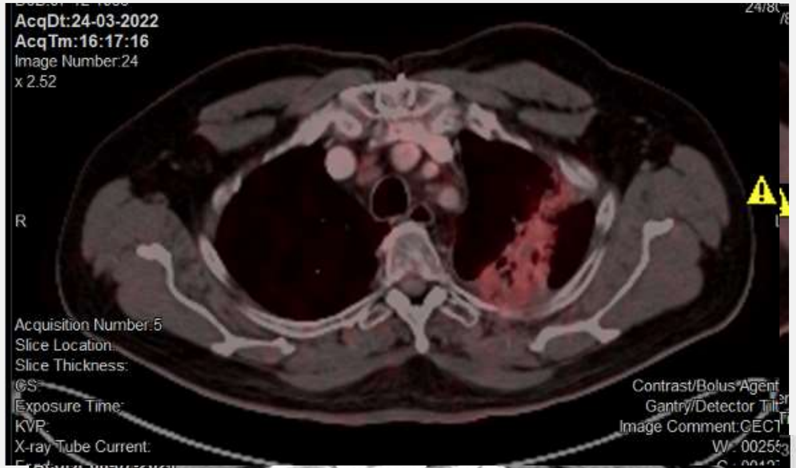

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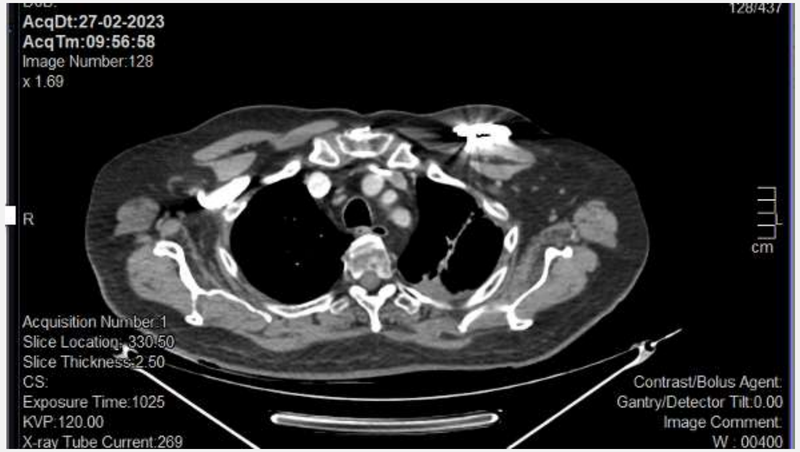

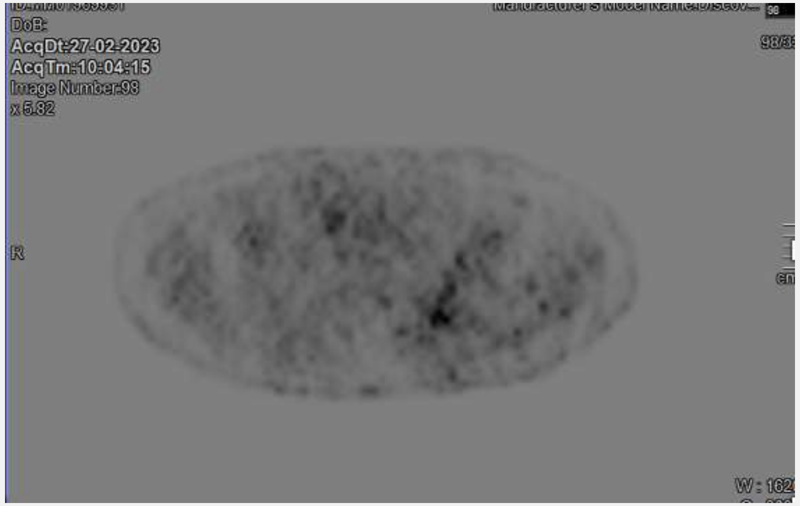

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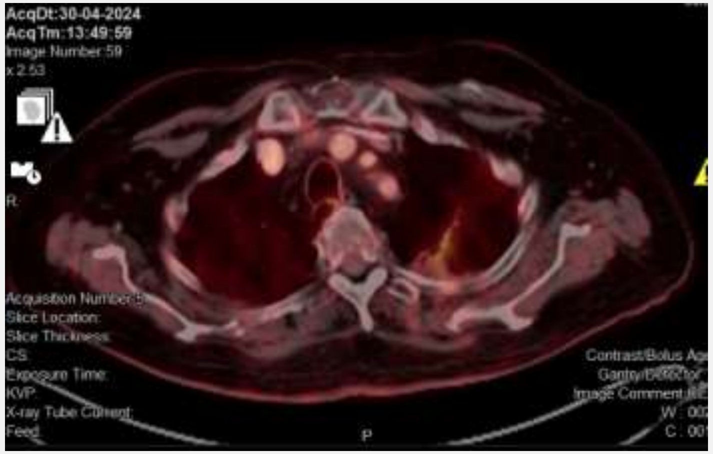
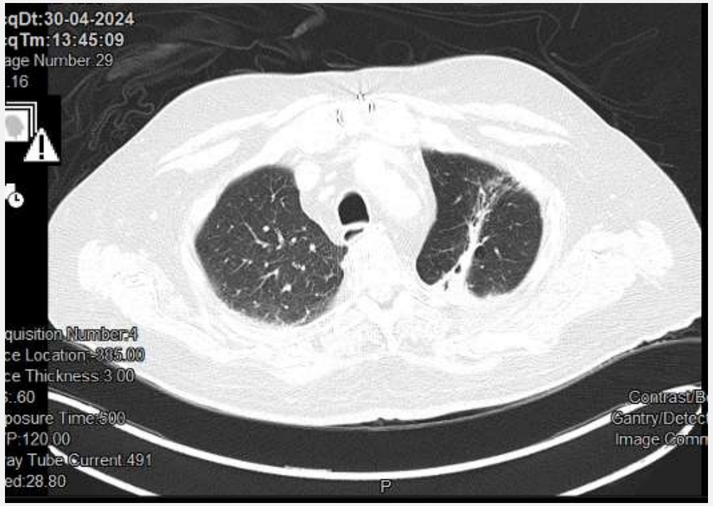
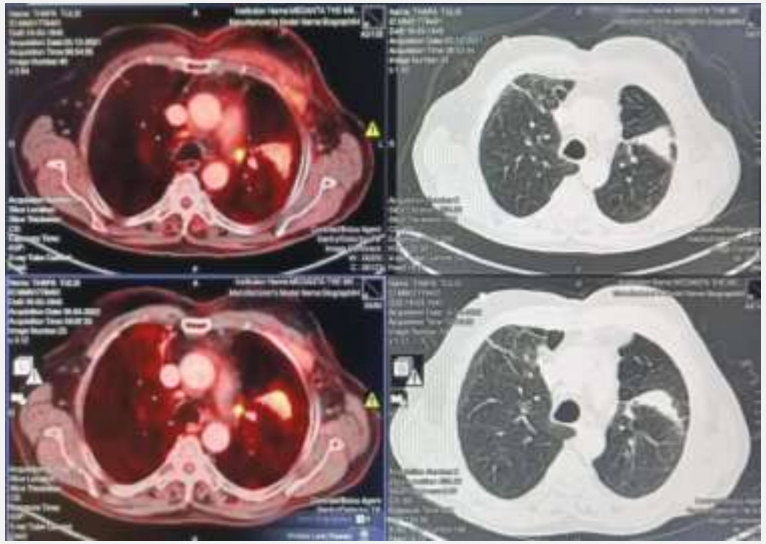




Criteria	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
CTCAE v4.0	Asymptomatic	Symptomatic; Required medical intervention; Limits ADLs	Severe symptoms; Oxygen indicated; Impairs ADLs	Life threatening respiratory dysfunction	Death
RTOG	Mild symptoms	Persistent symptoms requiring symptomatic treatment	Severe symptoms, possibly requiring intermittent O_2 or steroids	Severe symptoms requiring continuous O_2 or assisted ventilation	-

Other S/E in tumor close to chestwall?



When to suspect failure?

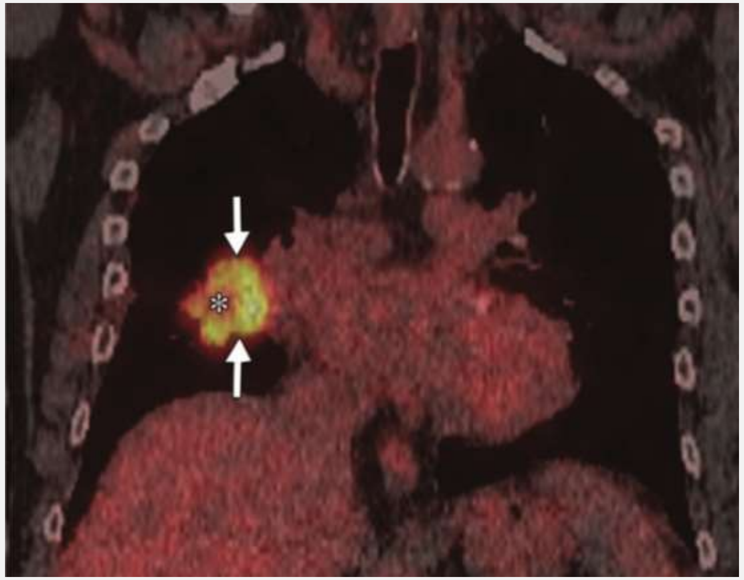


TABLE 1. High-Risk Features on CT Predictive of Local Recurrence[43]

High-Risk Feature	Sensitivity (%)	Specificity (%)
Enlarging opacity at primary site	92	67
Sequential enlargement	67	100
Enlargement after 12 months	100	83
Bulging margin	83	83
Linear margin disappearance	42	100
Loss of air bronchogram	67	96
Cranio-caudal growth of ≥5 mm and ≥20%	92	83

SUVs >5 on PET , more than 6 months after SABR should raise suspicion for Recurrence

Huang K, Senthi S, Palma DA, et al. High-risk CT features for detection of local recurrence after stereotactic ablative radiotherapy for lung cancer. Radiother Oncol. 2013

Radiologist will report as residual disease
Bx done

Thorax: There is no significant change in the primary residual ill defined plaque like pleural based mass in the medial aspect of apicoposterior segment of left upper lobe, measuring approximately 2.3 x 1.6 as before with insignificant metabolic activity; and merging with surrounding post RT related changes in the form of fibro-atelectatic bands with consolidation in the apicoposterior segment of left upper lobe and superior segment of left lower lobe, showing low

Histopathology Report

CLINICAL DIAGNOSIS: Carcinoma Lung

SPECIMEN: Plaque Like Apical Thickening

GROSS: Received multiple linear cores measuring 2 to 8 mm. All processed in A and B block.

MICROSCOPIC EXAMINATION:
Sections studied shows multiple linear tissue cores composed of predominantly necrotic tissue.
Very few viable tissue is identified which is unremarkable.

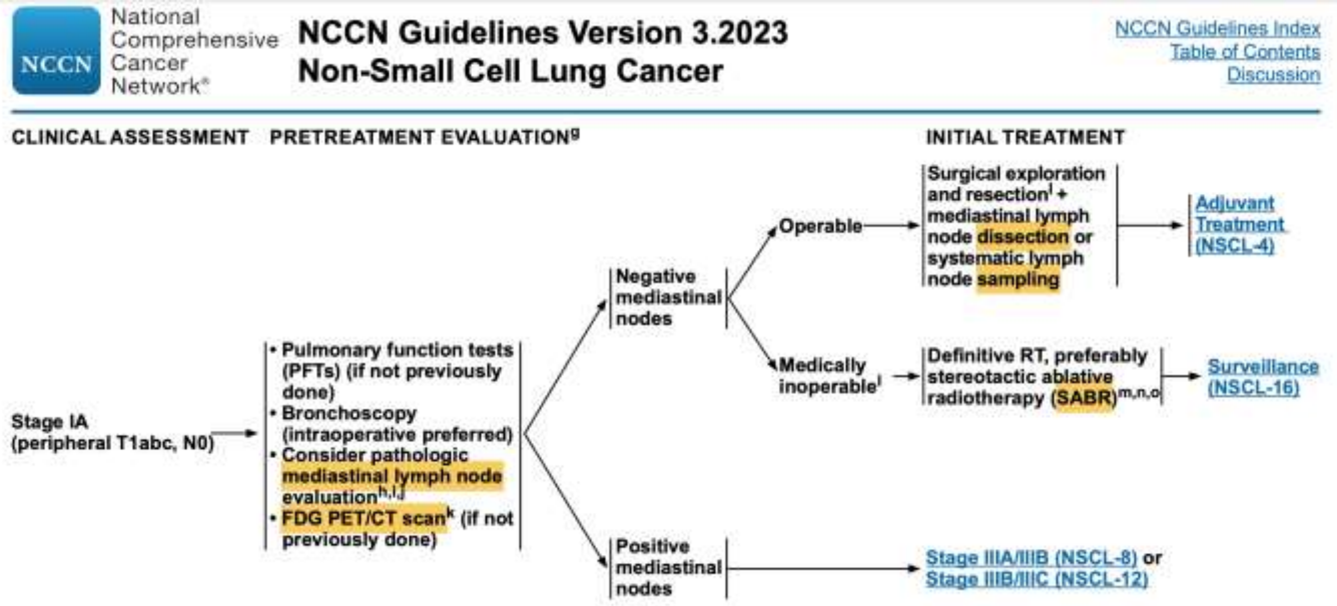
p-40- Negative
TTF-1- Negative
AFB- Non contributory

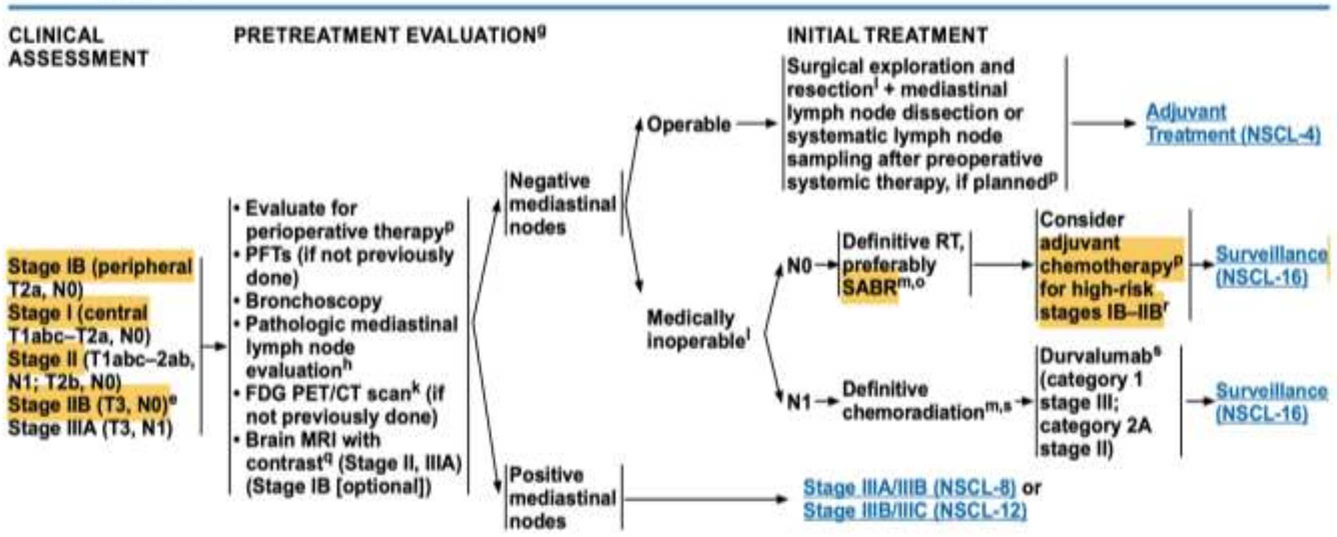
IMPRESSION: Plaque Like Apical Thickening: Pl see description

Any subsequent Therapy (chemo/immune)

MEDANTA THE MEDICITY dedicated to life

SBRT + "extra" in High Risk





High risk Features→ "extra"

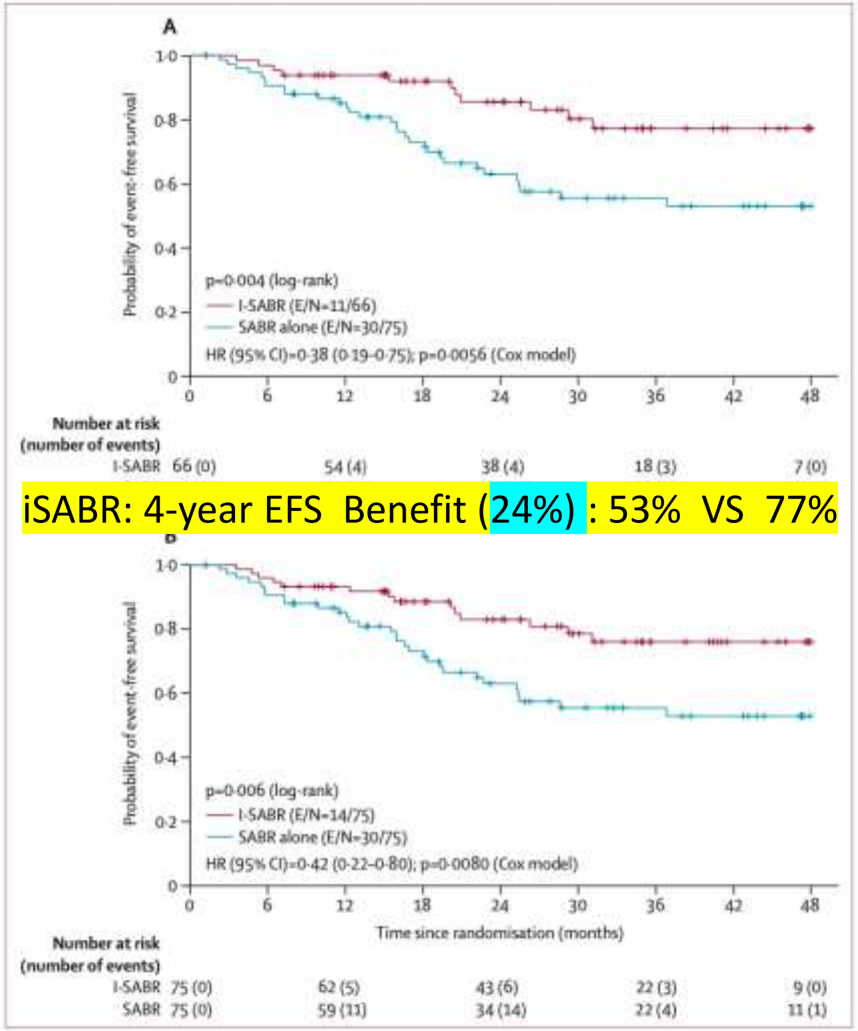
- Micropapillary, solid patterns
- LVSI
- Visceral pleural involvement
- Tumor size > 4 cm
- Wedge resection

SABR+ Nivo. Vs SBRT

Stereotactic ablative radiotherapy with or without immunotherapy for early-stage or isolated lung parenchymal recurrent node-negative non-small-cell lung cancer: an open-label, randomised, phase 2 trial

Joe Y Chang, Steven H Lin, Wenli Dong, Zhongxing Liao, Saumil J Gandhi, Carl M Gay, Jianjun Zhang, Stephen G Chun, Yasir Y Elamin, Frank V Fossella, George Blumenschein, Tina Cascone, Xiuning Le, Jenny V Pozadzides, Anne Tsao, Vivek Verma, James W Welsh, Aileen B Chen, Mehmet Altan, Reza J Mehran, Ara A Vaporciyan, Stephen G Swisher, Peter A Balter, Junya Fujimoto, Ignacio I Wistuba, Lei Feng, J Jack Lee, John V Heymach

- T <7cm,N0
- SABR +/- 4x Nivolumab
- PE: 4-year EFS
- 60/5 to 80/10



iSABR: 4-year EFS Benefit (24%) : 53% VS 77%

Figure 2: **Kaplan-Meier plot of event-free survival**
(A) Event-free survival for the randomly assigned per-protocol population (n=141). (B) Event-free survival for the

iSABR: 4-year event-free survival Benefit (24%) from 53% VS 77%

- Local Control
  - 100% VS 87%
- Distant Control
  - 97% VS 84%

Take home…

- SBRT standard of Care for Stage I/II, N0 Medical Inoperable.
- Local control >85-90% (5 years).
- No absolute C/I except Invasion of central structures.
- AIM BED10 > 110Gy
- Motion Management a Must.
- Type B/C Algorithm a must for Lung SBRT.
- Larger tumors (>4cm) need Adjuvant- iSABR data is exciting.

5 D of SBRT: Diligent- Dare- Do it—Document-- Discuss