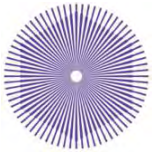
SBRT bei NSCLC

No conflict of Interest



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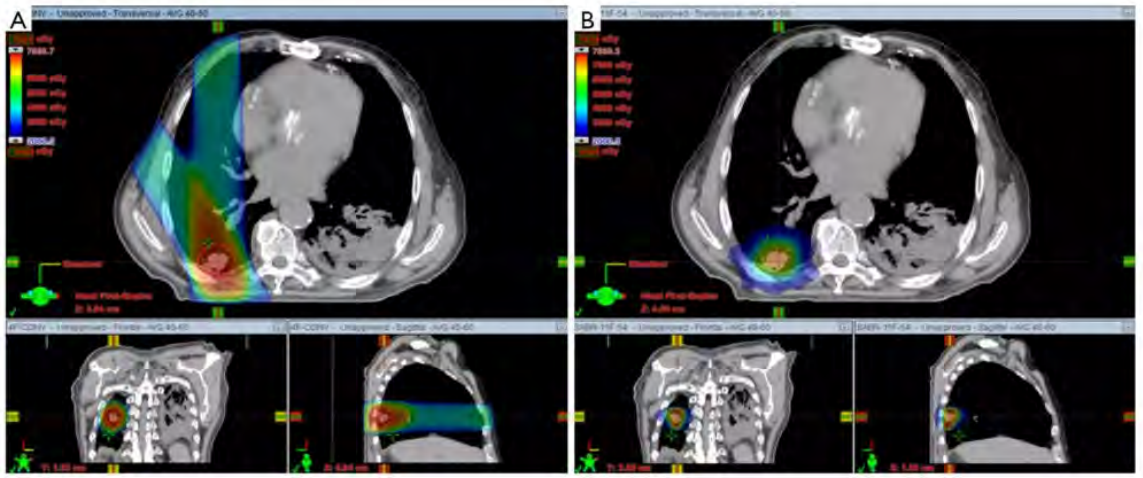
3D-CRT vs. SBRT



Pro	Con
Higher Precision	Higher technical effort with respiratory motion management
Short treatment time	
Higher biological effect	

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Respiratory Motion Management

Conventional (ITV-based)

- Contour and treat full tumor ROM

Accelerator beam gating

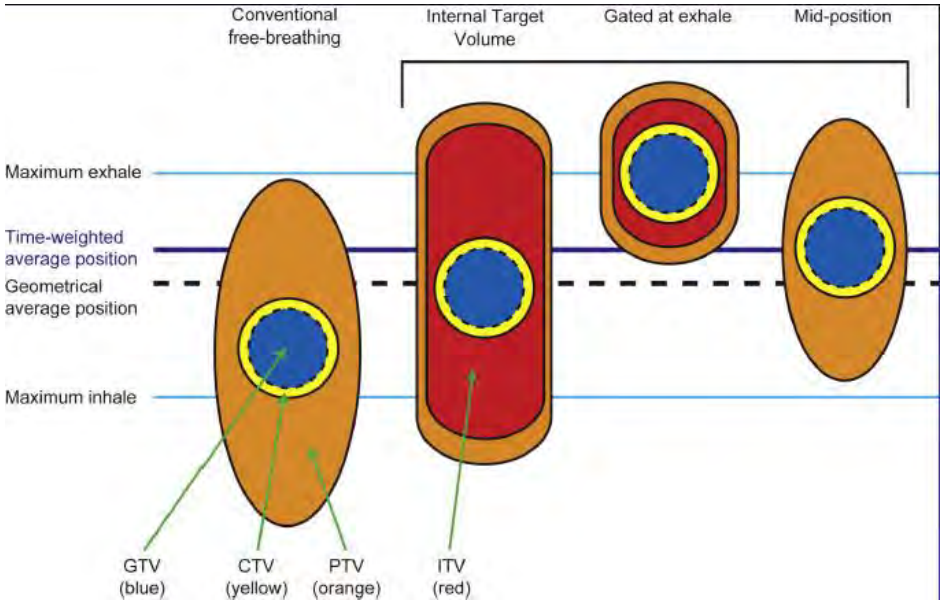
- Patient breathes normally; beam only on while patient is in a certain phase of the respiratory cycle

Active breathing control

- Patient holds breath in a certain position; beam only on in that phase of the respiratory cycle

Dynamic tumor tracking

- Patient breathes normally; tumor is tracked; beam always on and moves with tumor



Regardless of the motion management used, an additional "CTV/PTV" margin around our target is needed to ensure that we hit it.

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	3DCRT/IMRT	SBRT/SABR
Target Type	≥1 target (e.g., primary + nodes) Any size Close proximity to (or overlapping) critical organs	Single well-defined target Small-medium size Sufficient distance from critical organs
Dose/Fraction	Low	High
# Fractions	30-35	1-5
Biologically Effective Dose	70-90 Gy	≥ 100 Gy
Dose Conformity	Moderate - High	Very High
Immobolization	Secure	Very Secure
Image-Guidance	Should be performed daily, especially IMRT/PT	Required Daily
5 Year Local Control	50-75%	85-95%

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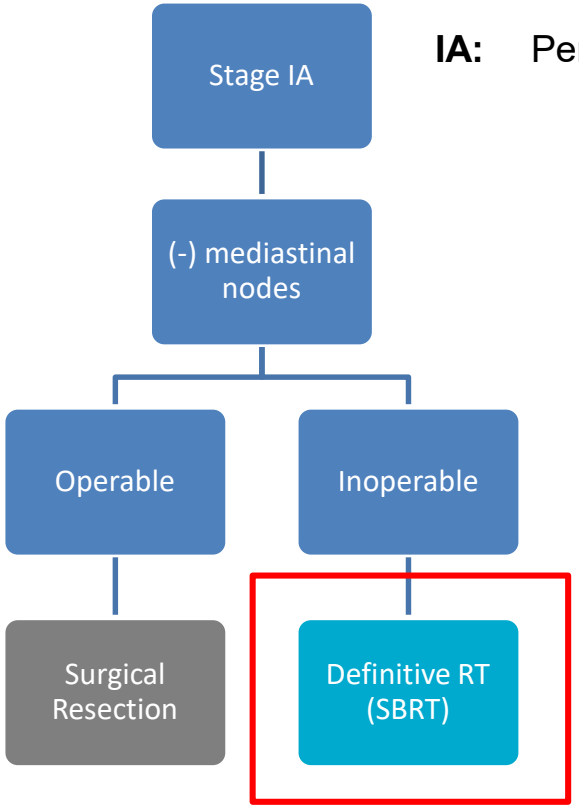
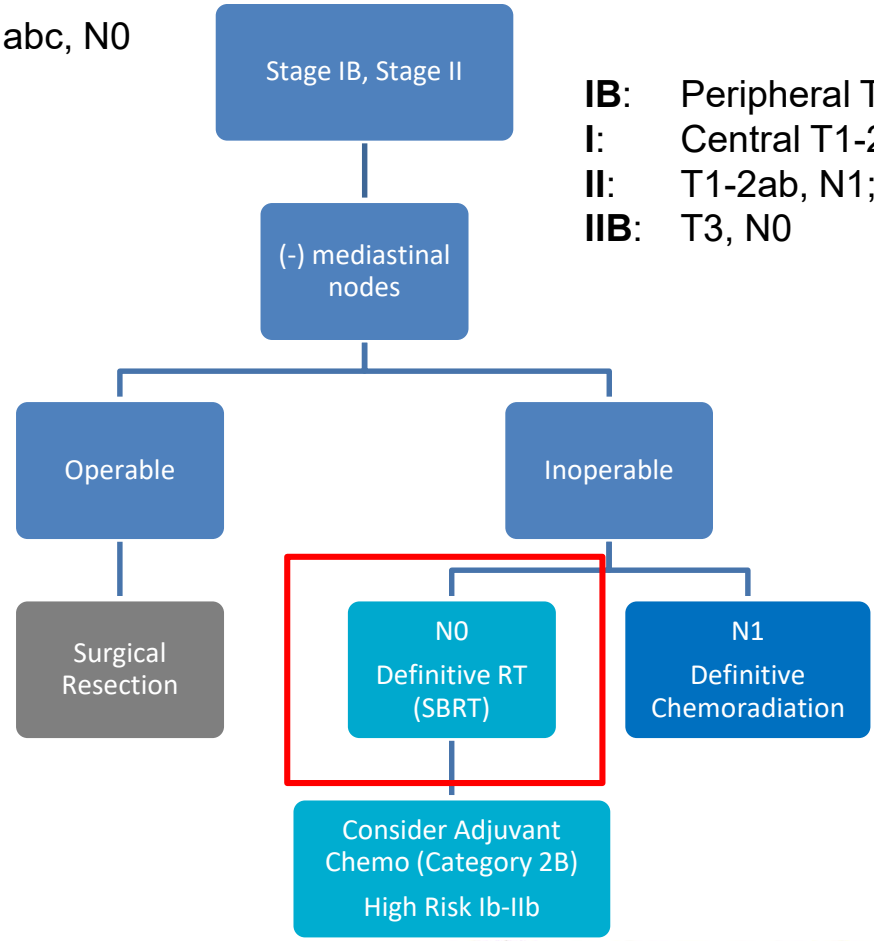
Curative Indication
NCCN Guidelines - NSCLC



IA: Peripheral T1abc, N0



IB: Peripheral T2a, N0
I: Central T1-2a, N0
II: T1-2ab, N1; T2b, N0
IIB: T3, N0

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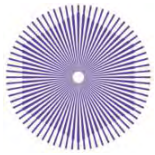
RADIOTHERAPY

Early-Stage Node-Negative NSCLC

- **Surgical resection** is the preferred local treatment
  - An anatomical resection with lobectomy or segmentectomy is preferred to wedge resection
  - Includes sampling of at-risk ipsilateral hilar and mediastinal LN

- **SBRT** for patients who are ***medically inoperable*** or ***refuse surgery***
  - **Limitations**: High ***volume*** (DM > 5cm) and "***ultra-central***" tumors should be treated more cautiously (e.g. 10 instead of 3 fractions)
  - Limited data yet supporting the addition of systemic therapy to SBRT



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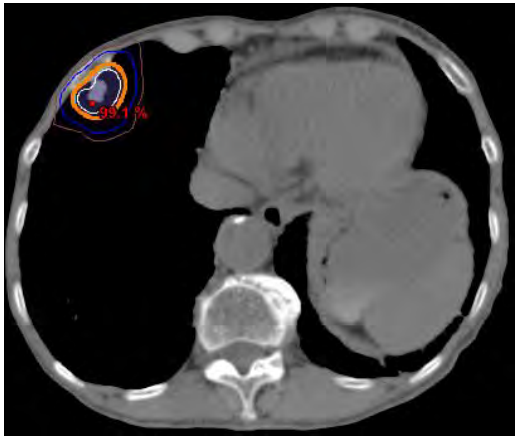
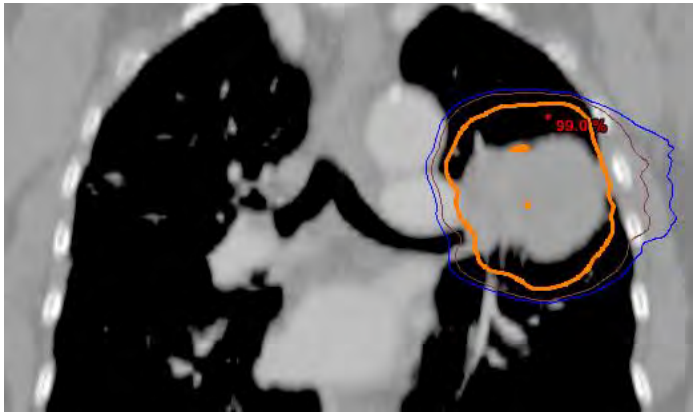
Potential SBRT Toxicity Depends on Tumor Site





- Fatigue
- Rib fracture, chest wall pain
- Skin Erythema/fibrosis

- Fatigue
- Pneumonitis, atelectasis hemoptysis, fibrosis
- Rib fracture, chest wall pain

Risk of toxicity can be reduced through risk-adapted dose-fractionation

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Outcomes of SBRT for Early Stage NSCLC

	RTOG 0236	RTOG 0915	RTOG 0813
Prospective Study Type	Single Arm Phase II	Randomized Phase II	Single Arm Phase I/II
# of patients	55	94	120
Medically Operable?	No	No	No
TNM Stage	cT1-2N0M0	cT1-2N0M0	cT1-2N0M0
Tumor Location	Peripheral	Peripheral	Central
RT Dose/Fx	54Gy/3fx	34Gy/1fx vs. 48Gy/4fx	50-60Gy/5fx
Local Control	93% @ 5 years	89-93% @ 5 years	88% @ 2 years
Overall Survival	40% @ 5 years	30-41%@ 5 years	70% @ 2 years

- **Most recurrences are distant** (~30%); **most deaths are not cancer related**
- ***Toxicity*** using risk-adapted dosing:
- **Grade 3 in 10-15%,** grade 4 in 3-5%, **grade 5 in < 1%**

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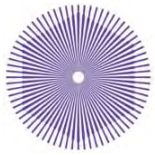
Take Home Pearl and *Further Indications* of SBRT for NSCLC

1. **SABR for Node-Negative Early-Stage NSCLC**
    1. BED ≥100 Gy are associated with significantly better local control and survival
    2. For central and ultra-central tumors 4 to 10 fraction regimens are effective and safe
    3. SABR is most commonly used for tumors up to 5 cm in size
2. **SBRT has a Developing role**
    1. Boost following definitive chemoradiation in management of LA-NSCLC
    2. Re-irradiation of locally recurrent disease
    3. Intrathoracic oligometastases from various primary histologies



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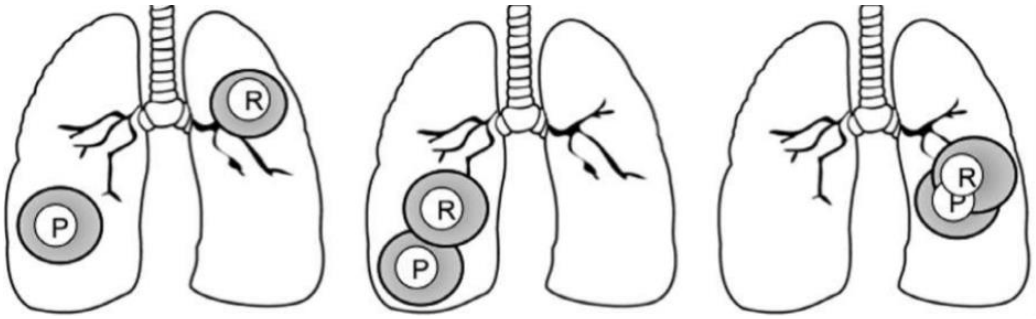
Reirradiation of Recurrent disease



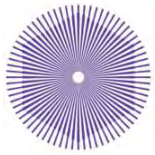
- Feasibility of treating with curative intent depends on site of primary (P) and recurrent (R) tumors

- Advanced treatment techniques are particularly useful for sparing normal tissue (e.g., IMRT, SBRT, protons)
  - Reirradiating central structures (e.g., esophagus, airway) most challenging
  - Long-term toxicity is the major concern – impacted by dose/fraction

SBRT in the Management of Stage IV NSCLC

Palliative Radiation For Symptom Relief

- Pain
  - Bone metastases
- Neurologic symptoms
  - Spinal cord compression
  - Brain metastases
- Bleeding
  - Endobronchial tumor
- Dyspnea/Dysphagia
  - Tumor obstruction causing SVC, respiratory distress or esophageal narrowing



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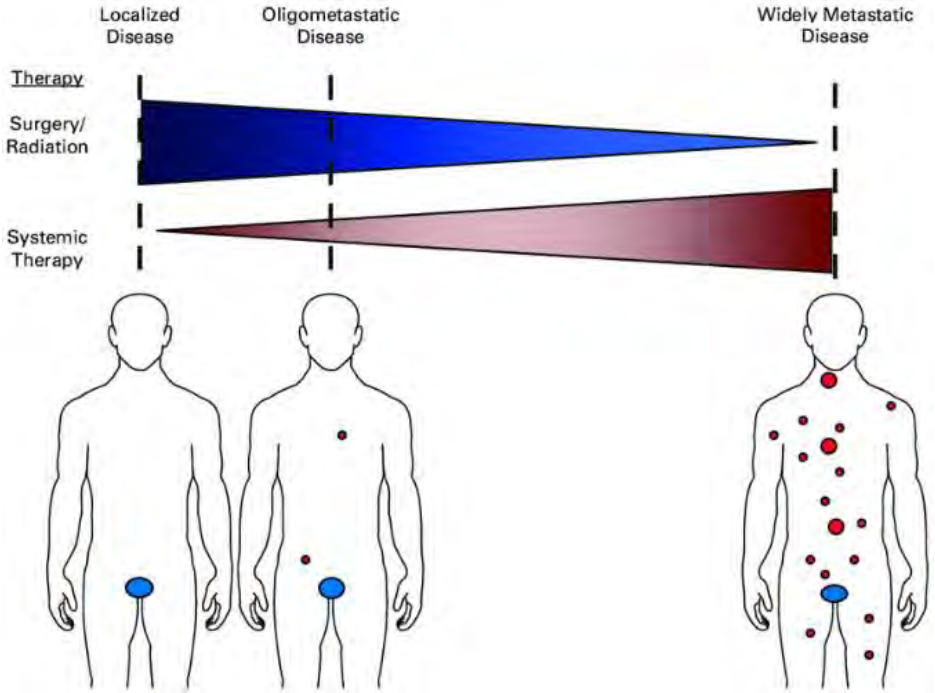
RADIOTHERAPY

Is all metastatic disease the same?

- **No!** Lung cancer has M1a, M1b and M1c designations because the metastatic state at diagnosis impacts prognosis; **a small subset of patients may be cured**

- **"Oligometastatic"** refers to a situation where distant metastases may be limited in number (typically defined as ≤ 5 mets in ≤ 3 organs), and potentially curative treatment can be delivered prior to the development of widespread disease



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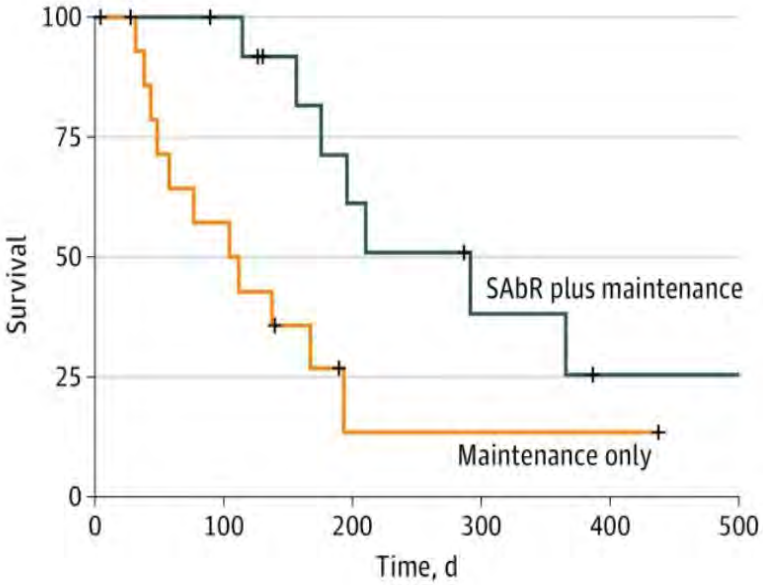
UT Southwestern Randomized Phase II Trial

- Iyengar *et al*, JAMA Oncol, 2018
- 29 patients, oligometastatic NSCLC with ≤ 5 sites of diseas (EGFR/ALK negative), PR or SD after induction chemo, randomized to +/- SAbR
- SAbR → ↑ M-PFS (3.5→9.7mo)



No. at risk					
SAbR plus maintenance	14	12	6	3	1
Maintenance only	15	8	1	1	1

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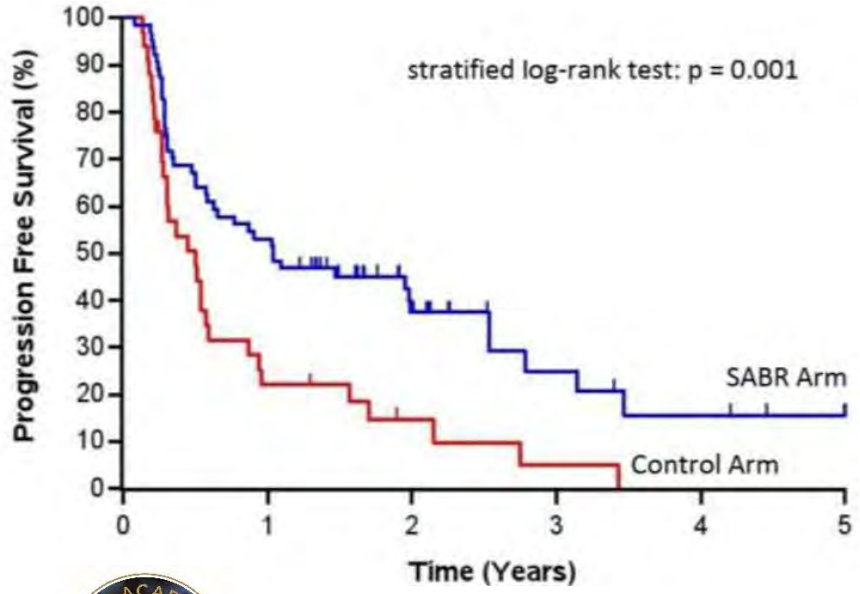
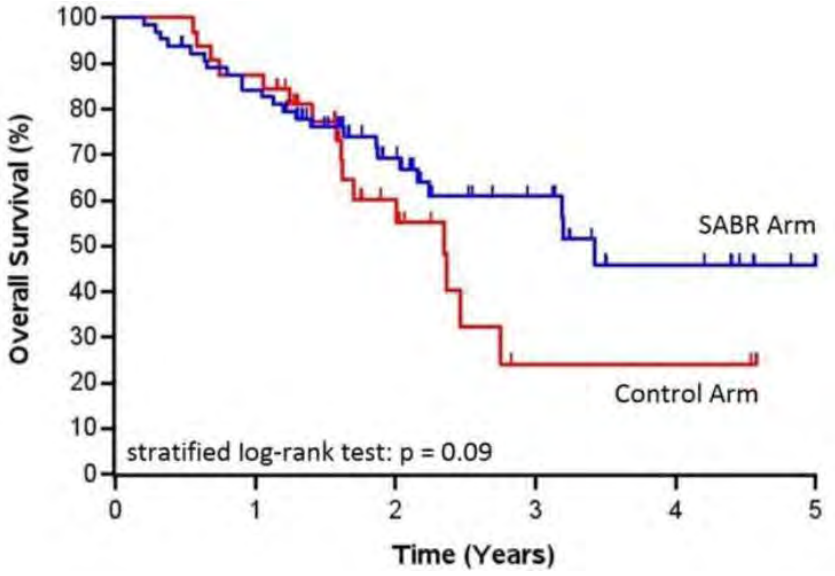
SABR-COMET Randomized Phase II Trial

- Palma *et al*, Lancet, 2019
- 99 patients, **variety of oligometastatic cancers** with ≤ 5 sites of disease, PR/SD on systemic therapy, randomized 1:2 to +/- SAbR (at ablative doses)
  - Most common histologies: breast, lung, colorectal, prostate
- SAbR → ↑ M-PFS (6→12mo, p<0.001) & M-OS (28→41mo, p=0.09)
  - Also ↑ G2 or higher toxicity, but no difference in QOL





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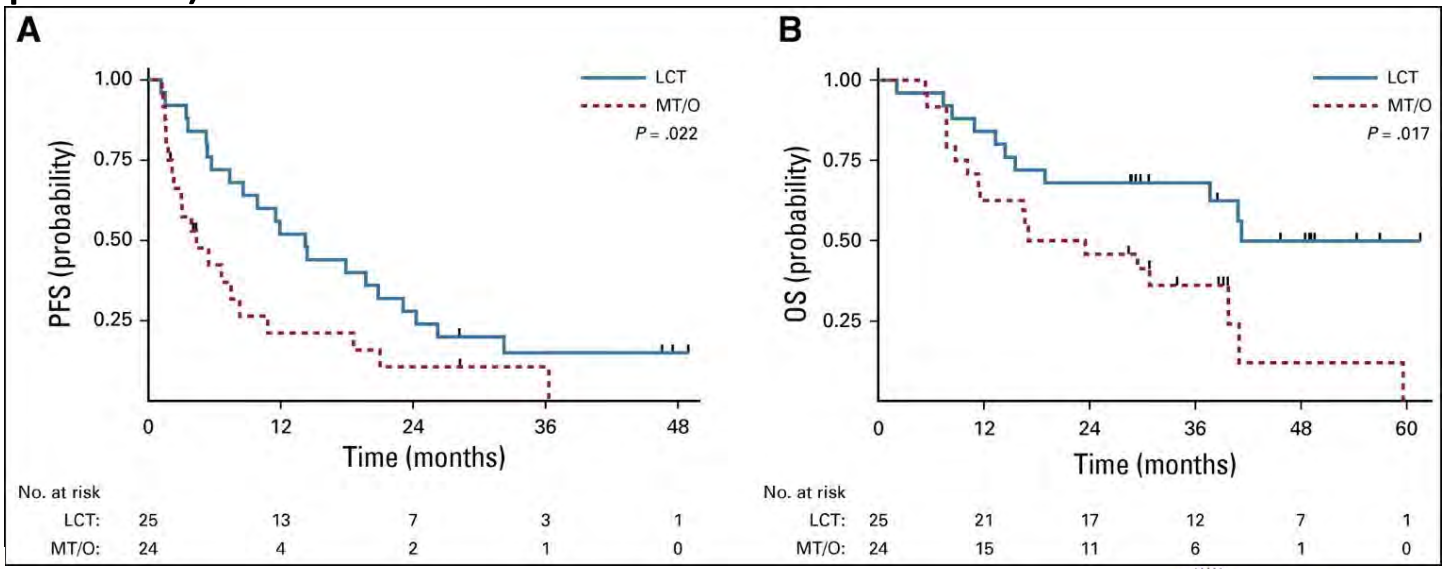
Multi-Institutional Randomized Phase II Trial

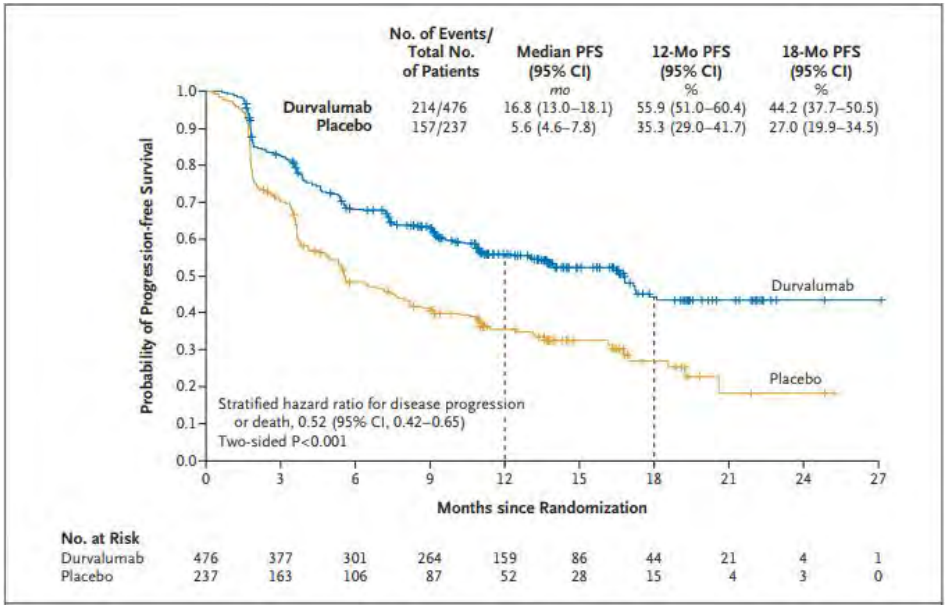
- Gomez *et al*, J Clin Oncol, 2019
- 49 patients with oligometastatic NSCLC with ≤ 3 sites of disease, SD/PR after Pt-based doublet or EGFR/ALK inhibitor, randomized to maintenance systemic therapy +/- local consolidative surgery/RT
- RT → ↑ M-PFS (4.4→14.2mo) and M-OS (17→41mo, p=0.02)

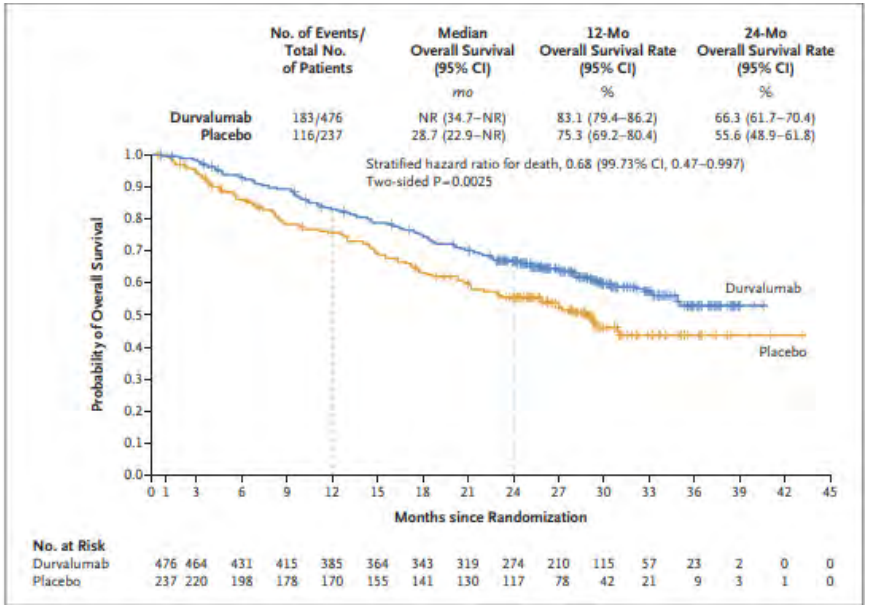


The Future…

Immunotherapy May Change Our Approach to Locoregional Management Too

- A stronger immune response ***may*** be elicited by leaving a tumor in and irradiating it, rather than removing the largest source of antigenic stimulation





PACIFIC Trial, *NEJM,* 2017

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Ergebnisse klinischer Studien: NSCLC – SBRT und IT mit ICI
PROSPEKTIV - Wirksamkeit

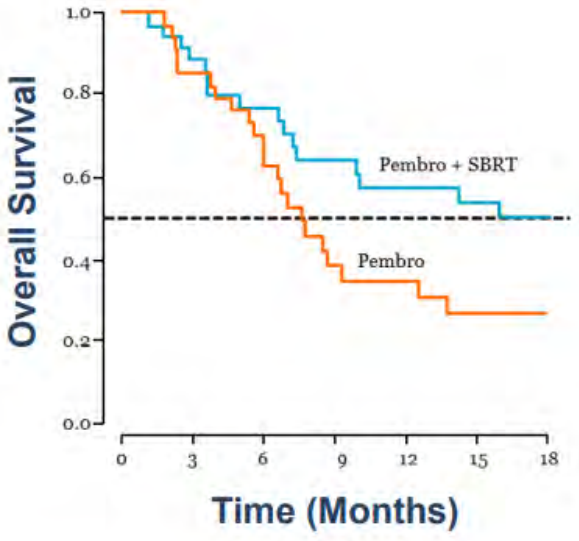
Effect of Pembrolizumab After Stereotactic Body Radiotherapy vs Pembrolizumab Alone on Tumor Response in Patients With Advanced Non-Small Cell Lung Cancer: Results of the PEMBRO-RT Phase 2 Randomized Clinical Trial.
Thelen et al. JAMA Oncol. **2019**

Results

doubled response rate @ 12 weeks,
18% vs 36 P = .07

tripled median PFS
1.9 vs 6.6 months hazard ratio, 0.71; P = .19

doubled median OS
7.6 vs 15.9 hazard ratio, 0.66; P = .16



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Ergebnisse klinischer Studien: NSCLC – SBRT und IT mit ICI
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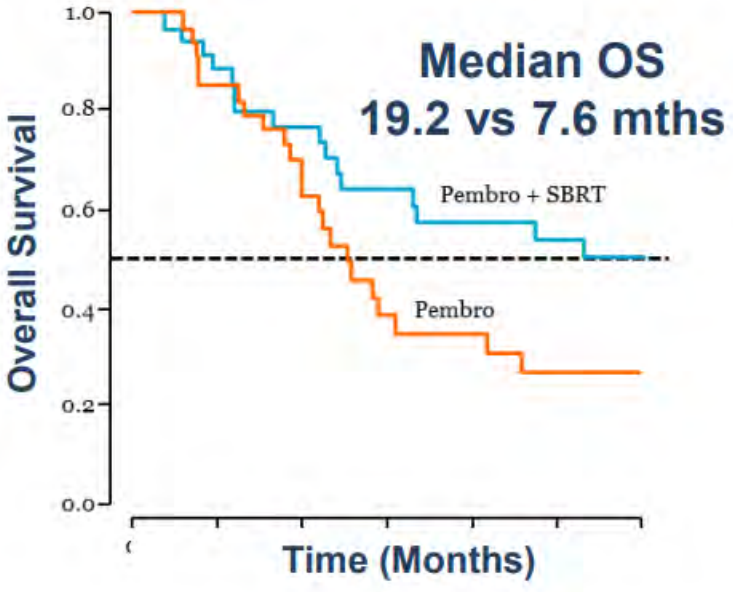
Thelen et al. JAMA Oncol. **2019**

	Pembrolizumab + SBRT (n=36)	Pembrolizumab (n=36)
Best overall response, n (%)		
Complete response	3 (12)	1 (3)
Partial response	14 (39)	7 (19)
Stable disease	9 (25)	9 (25)
Progressive disease	10 (28)	19 (53)
ORR at 12 weeks, n (%)		
Overall*	13 (39)	7 (21)
PD-L1 0%	4 (22)	1 (5)
PD-L1 1–49%	3 (38)	3 (38)
PD-L1 ≥50%	6 (60)	3 (75)
DCR at 12 weeks	23 (64)	15 (42)



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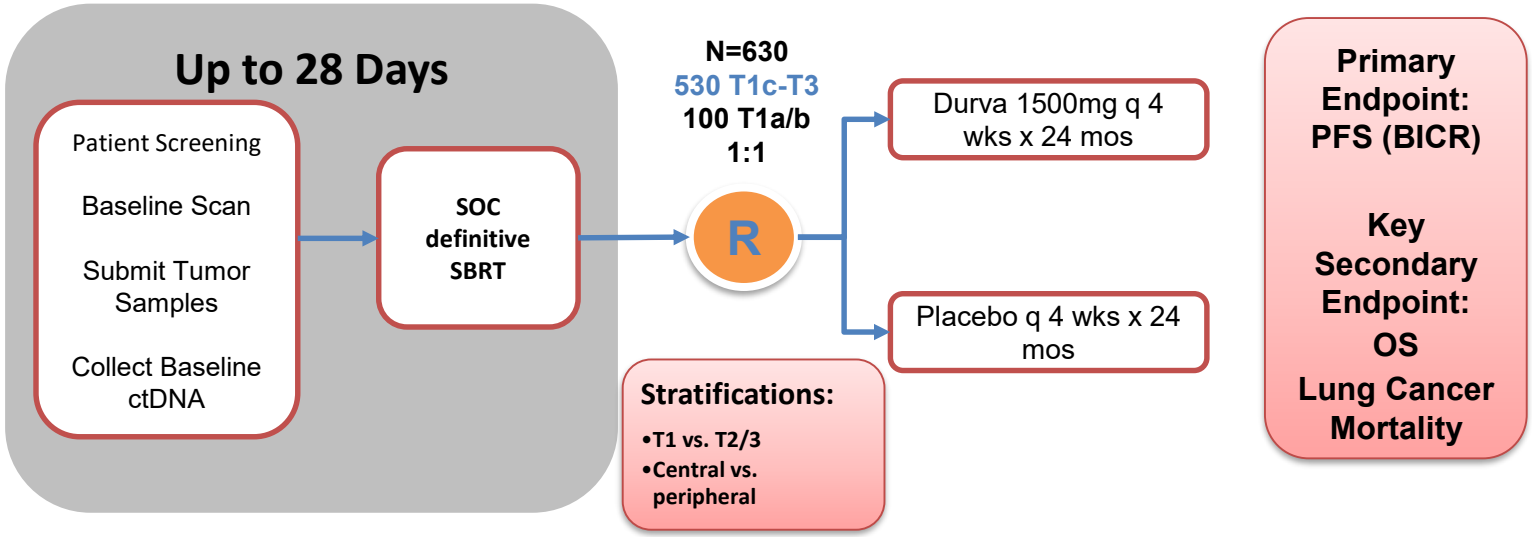
The Future……Aktive Protokolle

PACIFIC-4 / RTOG 3515

Inclusion Criteria

- **Clinical Stage I/II node negative (T1 – T3 N0)**
- **Medically inoperable or refuse surgery**
- **ECOG PS 0-2**
- **All comers for histology and PDL-1 status**
- **Sync/Metach allowed**



SBRT Dose Reflects Int'l Variability

50-60 Gy/8, 50-55 Gy/5,
42-48 Gy/4, 54 Gy/3

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The Future…A Few Examples of Active Clinical Trials in Lung Cancer

***CAVE*: Not all new substances proofed to be safe with SBRT. Additional surveys needed!**

- NRG LU002: Adds RT (to all sites of disease) to systemic therapy for oligometastatic NSCLC
- NRG LU004: Adds immunotherapy to IMRT or 3-D CRT for stage II-III NSCLC with high PD-L1 expression (instead of chemotherapy)
- PACIFIC 4 and NRG/S1914: Adds consolidative immunotherapy to SBRT for stage I NSCLC
- AEGEAN: Adds neoadjuvant immunotherapy to surgery for resectable stage II-III NSCLC
- ALCHEMIST: Evaluating adjuvant use of targeted agents for resected NSCLC
- RTOG 1308: Compares proton therapy to photon therapy for LA-NSCLC
- NRG LU005: Adds immunotherapy to chemoradiation for limited-stage SCLC
- NRG CC003: Hippocampal avoidance PCI for SCLC

Quellen

- David S. Buchberger et al. Stereotactic Body Radiotherapy for the Management of Early-Stage Non–Small-Cell Lung Cancer: A Clinical Overview. *JCO Oncol Pract* 19, 239-249(2023).DOI:10.1200/OP.22.00475
- DrAyush GargRole of SBRT in lung cancer 8. Okt. 2019•, A topic with precide information regarding role of SBRT in Lung Cancer, https://de.slideshare.net/DrAyushGarg/role-of-sbrt-in-lung-cancer
- Kanhu CharanLUNG SBRT A LITERATURE REVIEW 27. Feb. 2023•, https://de.slideshare.net/kanhucpatro/lung-sbrt-a-literature-review

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„CHALLENGES IN SBRT“,
22. November 2019

SBRT bei NSCLC

VIELEN DANK!

Dr. Kuczer & Partner

Radiation Oncology

Vienna PrIvate Clinic/ Amethyst Radiotherapy