Treatment of disease detected post-SABR

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Organisers

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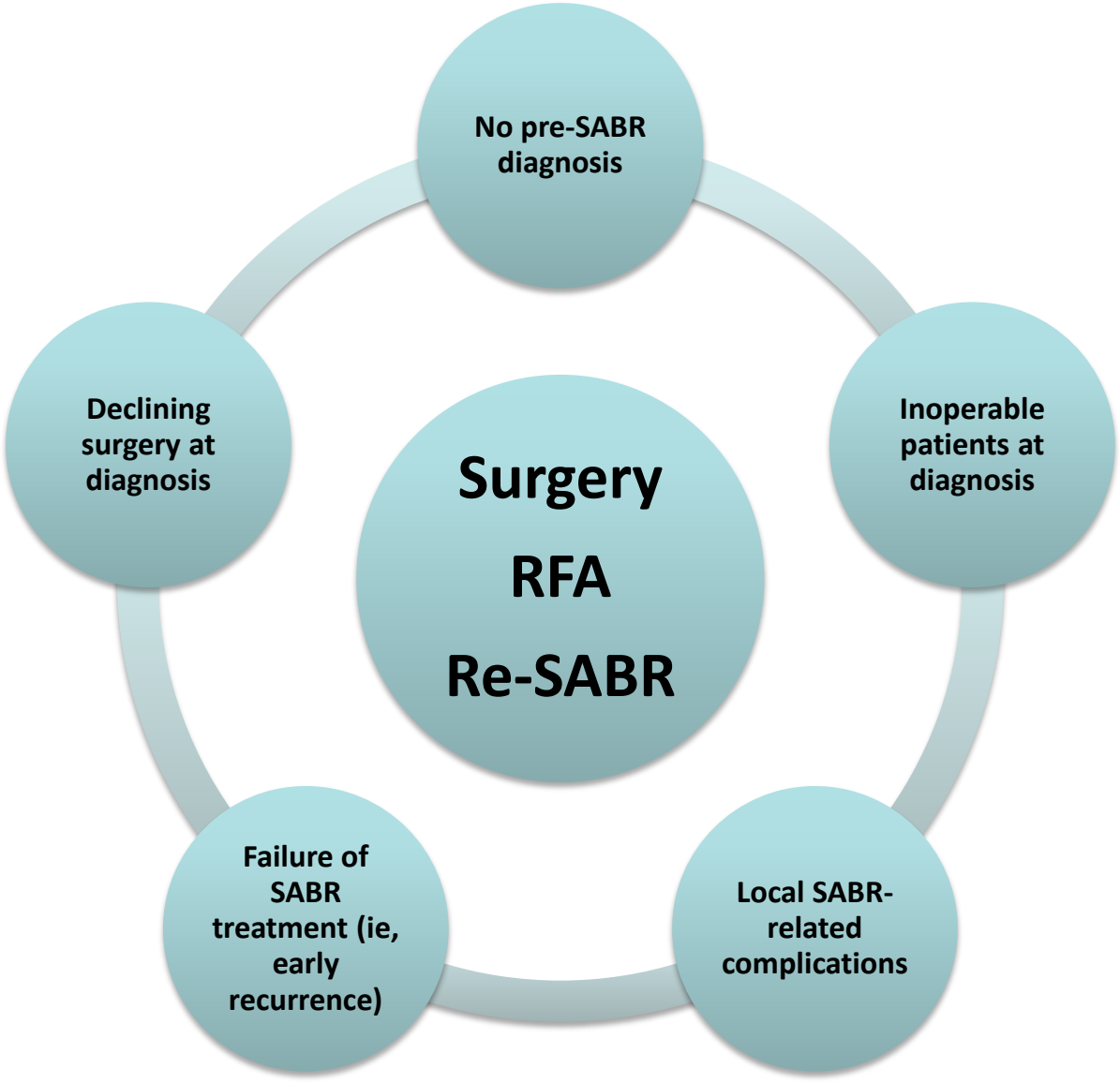
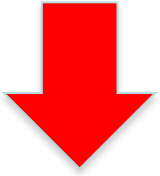
Disclosure slide

- Nothing to declare


No pre-SABR diagnosis
Inoperable patients at diagnosis
Local SABR-related complications
Failure of SABR treatment (ie, early recurrence)
Declining surgery at diagnosis
Surgery
RFA
Re-SABR

Stage-centered therapy

- Surgery for early stage NSCLC
- Surgery for locally advanced (stage) NSCLC
- Surgery for oligometastatic (stage IV) NSCLC



- No nodal sampling/dissection after SABR – Surgery for unknown stage

Van Schil PE, JTO 2010

Possible scenarios

- No pre-SABR histological diagnosis
- Inoperable patients at diagnosis
- Declining surgery at diagnosis
- Failure of SABR treatment (ie, early recurrence)
- Local SABR-related complications (ie, abscess)

No pre-SABR histological diagnosis

[Original Research **Lung Cancer**]

CHEST

When Is a Biopsy-Proven Diagnosis Necessary Before Stereotactic Ablative Radiotherapy for Lung Cancer?

A Decision Analysis

Alexander V. Louie, MD; Suresh Senan, PhD; Pretesh Patel, MD; Bart S. Ferket, MD, PhD; Frank J. Lagerwaard, MD, PhD; George B. Rodrigues, MD, PhD; Joseph K. Salama, MD; Christopher Kelsey, MD; David A. Palma, MD, PhD; and Myriam G. Hunink, MD, PhD

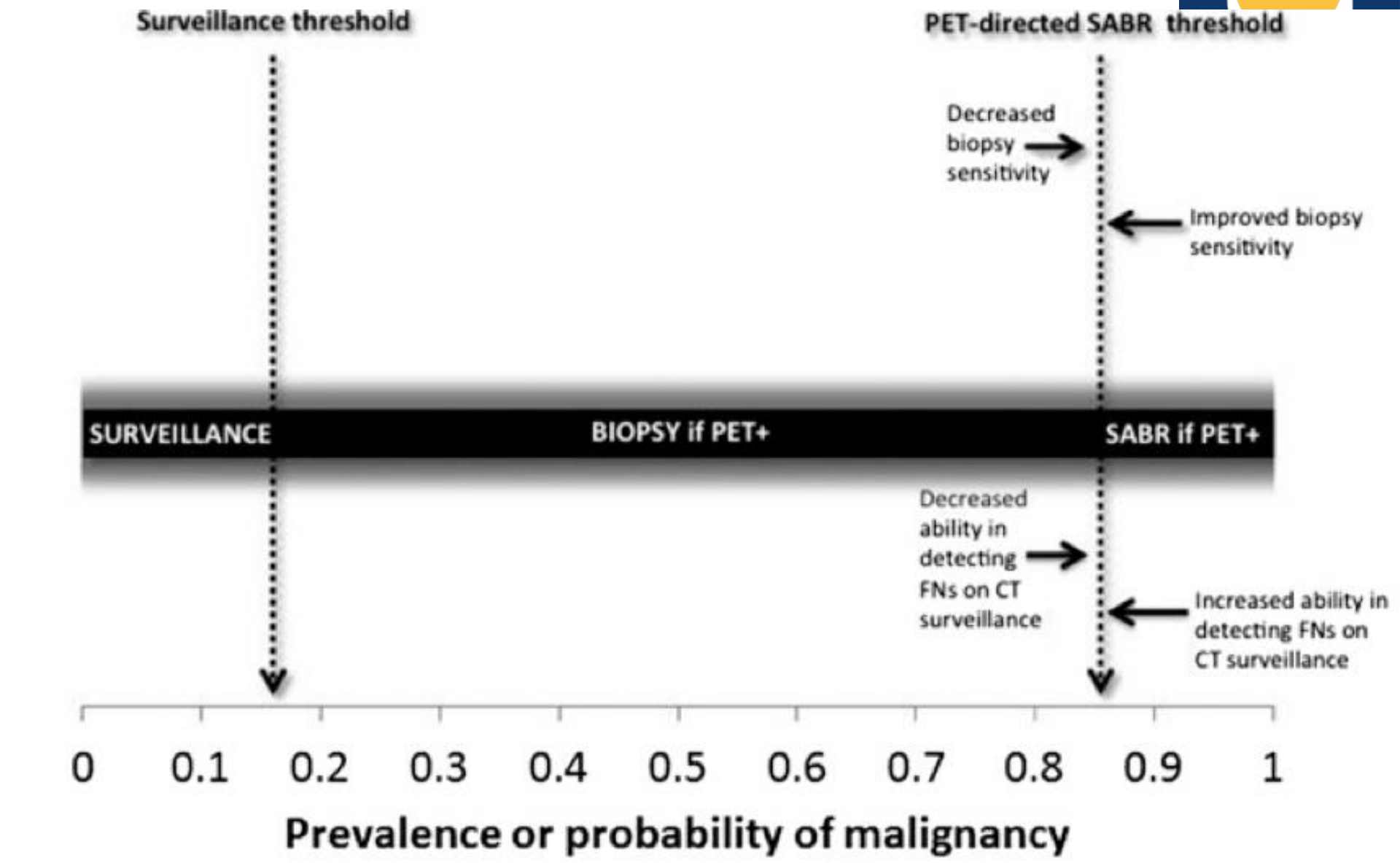
CONCLUSIONS: This model suggests that if there are concerns about morbidity related to biopsy for an SPN, a PET scan-directed SABR strategy is warranted when the prior probability of lung cancer exceeds a point estimate of 85%.

CHEST 2014; 146(4):1021-1028

TABLE 1] Biopsy Rates in a Sample of Studies Using SABR in Stage I NSCLC

Study	Institution	No. of Patients	Region	% Biopsy
Haasbeek et al[6]	Netherlands Cancer Registry	1,570	The Netherlands	72
Guckenberger et al[9]	Central European Multi-institutional	591	Germany	85
			Austria	
Grills et al[10]	Elekta Consortium	505	Detroit, MI	87
			Philadelphia, PA	95
			Toronto, Canada	72
			The Netherlands	41
			Germany	70
Onishi et al[11]	Japanese Multi-institutional	2,278	Japan	73
Baumann et al[12]	Scandinavian Multi-institutional	57	Sweden	67
			Denmark	
			Norway	
Timmerman et al[5]	RTOG 0236 Multi-institutional	55	North America	100

There appears to be a trend toward increased rates of biopsy in North America compared with other parts of the world. SABR = stereotactic ablative radiotherapy.

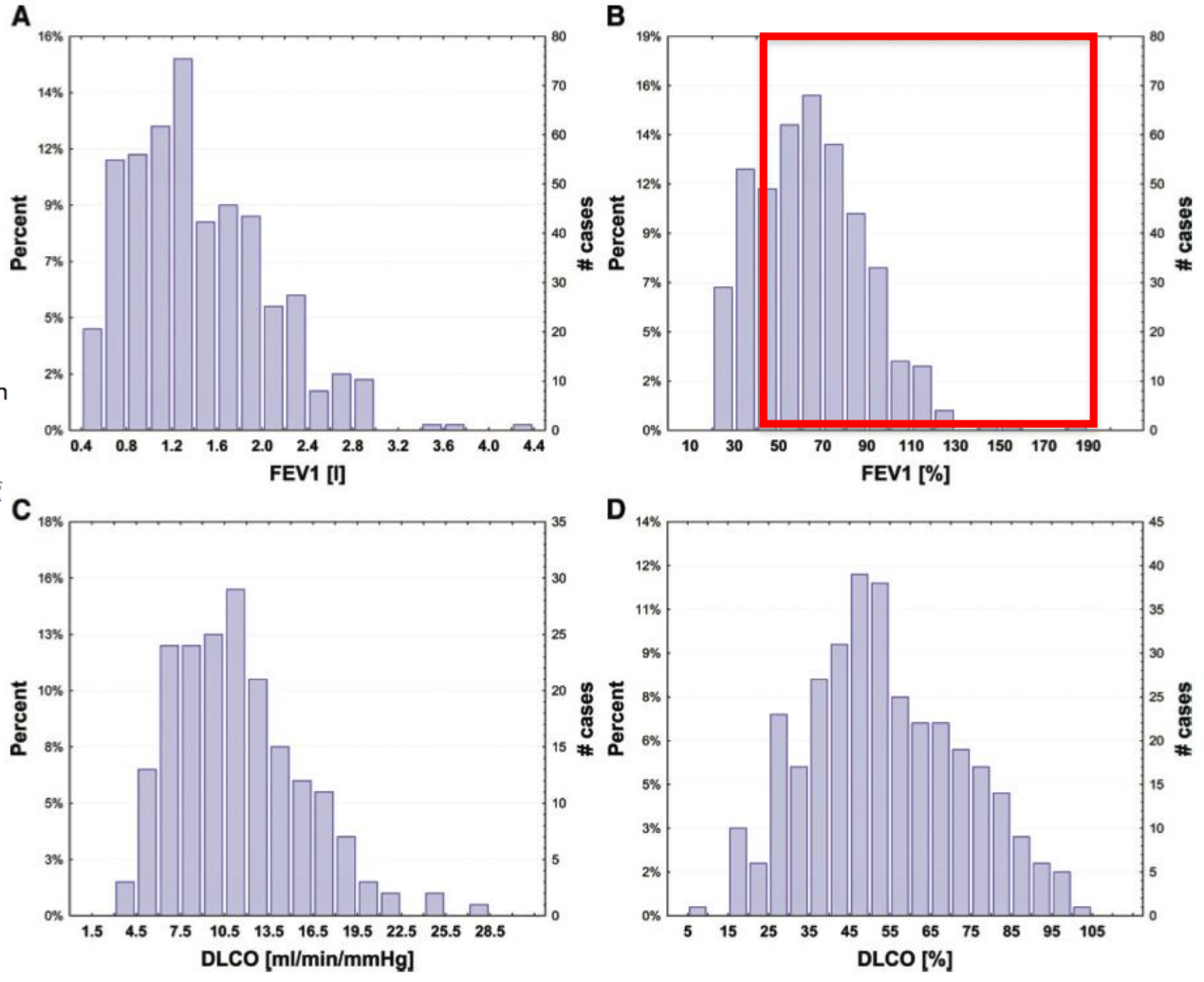

Surveillance threshold
PET-directed SABR threshold
Decreased biopsy sensitivity
Improved biopsy sensitivity
SURVEILLANCE
BIOPSY if PET+
SABR if PET+
Decreased ability in detecting FNs on CT surveillance
Increased ability in detecting FNs on CT surveillance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
Prevalence or probability of malignancy

Inoperable at diagnosis

Inoperable patients at diagnosis

Is There a Lower Limit of Pretreatment Pulmonary Function for Safe and Effective Stereotactic Body Radiotherapy for Early-Stage Non-small Cell Lung Cancer?

Matthias Guckenberger, MD, Larry L. Kestin, MD,† Andrew J. Hope, MD,‡ Jose Belderbos, MD,§ Maria Werner-Wasik, MD,‖ Di Yan, DSc,† Jan-Jakob Sonke, PhD,§ Jean Pierre Bissonnette, PhD,‡ Juergen Wilbert, PhD,* Ying Xiao, PhD,‖ and Inga S. Grills, MD†*



(*J Thorac Oncol.* 2012;7: 542–551)

Safety and Efficacy of Stereotactic Body Radiotherapy for Stage I Non–Small-Cell Lung Cancer in Routine Clinical Practice

A Patterns-of-Care and Outcome Analysis

Matthias Guckenberger, MD, Michael Allgäuer, MD,† Steffen Appold, MD,‡ Karin Dieckmann, MD,§ Iris Ernst, MD,‖ Ute Ganswindt, MD,¶ Richard Holy, MD,# Ursula Nestle, MD,** Meinhard Nevinny-Stickel, MD,†† Sabine Semrau, MD,‡‡ Florian Sterzing, MD,§§ Andrea Wittig, MD,‖‖ and Nicolaus Andratschke, MD¶¶*

Time trends in patient characteristics were analyzed and are summarized in Table 1. No time trend was observed for patient age, pretreatment performance status, pretreatment pulmonary function, and maximum tumor diameter.

(*J Thorac Oncol.* 2013;8: 1050-1058)

Predicted preop FEV1 < 50%
Predicted preop DLco < 50%
ppoFEV1 < 40%
ppoFEV1 < 35%
ppoDLco < 40%
ppoDLco < 35%
VO2max <15 ml/kg/min
VO2max <12 ml/kg/min
VO2max <10 ml/kg/min

2015

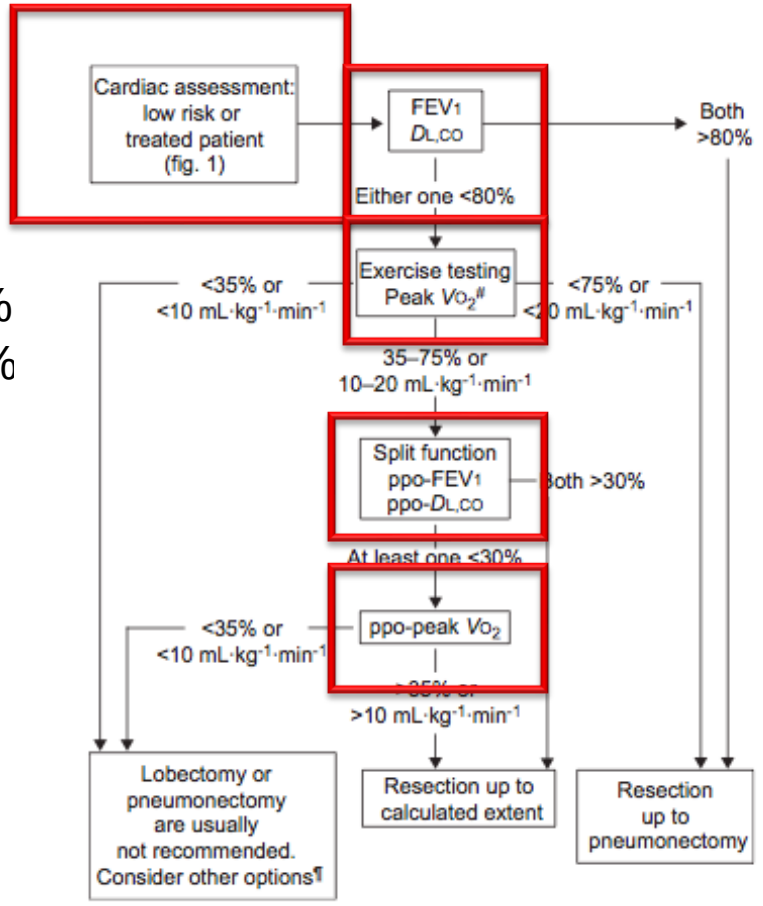


FIGURE 2. Algorithm for assessment of cardiopulmonary reserve before lung resection in lung cancer patients. FEV1: forced expiratory volume in 1 s; $D_{L,CO}$: diffusing capacity of the lung for carbon monoxide; V_{O_2}: oxygen consumption; ppo: predicted post-operative. #: If peak V_{O_2} is not available, cardiopulmonary exercise testing can be replaced by stair climbing (see subsection entitled Exercise tests); however, if altitude reaching during stair climbing is <22 m, cardiopulmonary exercise testing with peak V_{O_2} measurement is highly recommended; ¶: see sections entitled Surgical techniques in lung cancer and Chemo-radiotherapy in lung cancer. Modified from [59], with permission from the publisher.

Brunelli et al ERJ 2009

Patterns of disease recurrence after stereotactic ablative radiotherapy for early stage non-small-cell lung cancer: a retrospective analysis

Sashendra Senthi, Frank J Lagerwaard, Cornelis J A Haasbeek, Ben J Slotman, Suresh Senan

SABR indication	
General state	22 (3%)
Pulmonary insufficiency	237 (35%)
Cardiac insufficiency	99 (15%)
Previous chemoradiation	7 (1%)
Previous lung surgery	23 (3%)
Other comorbidity	81 (12%)
Potentially operable*	207 (31%)

Lancet Oncol 2012; 13: 802–09

Declining surgery at diagnosis

Features (7 pts)

- Usually operable patients who refused surgery
- Older than 75 years-old at surgery
- Peripheral tumors (average: 16 mm from pleura)
- 14 months between SBRT and surgery
- Lobectomy – only 1 by VATS; 1 BPF
- Viable tumor in all specimens

Neri S. et al JTO 2010

Features (5 pts)

- Borderline operable; SABR as per patient preference
- Average of 73 years-old at surgery
- Average: 23 mm in size
- 32 months between SBRT and surgery
- Lobectomy – open
- Viable tumor in all specimens

Chen F. et al JTO 2010

The patient should know…

- SABR may leave tumor behind
- The surgical approach after SABR is likely not to be minimally invasive
- Although he/she declines surgery, operation is to be considered in the future after SABR

Failure of SABR treatment

Long-term Results of RTOG 0236

- R. D. Timmerman[1], C. Hu[2], J. Michalski[3], W. Straube[3], J. Galvin[4], D. Johnstone[5], J. Bradley[3], R. Barriger[6], A. Bezjak[7], G. M. Videtic[8], L. Nedzi[1], M. Werner-Wasik[4], Y. Chen[9], R. U. Komaki[10], H. Choy[1]

Purpose/Objective(s): Patients with early stage but medically inoperable lung cancer historically had poor primary tumor control and high mortality with conventional radiotherapy. SBRT appeared to improve outcomes, as suggested by the initial published results of RTOG 0236. Herein, **we update those results with longer follow-up**.

Materials/Methods: The study was a Phase 2 North American multicenter study of patients aged 18 years or older with **biopsy-proven peripheral T1-T2N0M0** non-small cell tumors (measuring ≤5 cm in diameter) and **medical conditions precluding surgical treatment**. The prescription dose was 18 Gy per fraction X 3 fractions (54 Gy total) with entire treatment lasting between 1½ and 2 weeks. The study opened May 26, 2004, and closed October 13, 2006; data were analyzed through October 15, 2013. **The primary end point was 2-year actuarial primary tumor control**; secondary end points were disease-free survival (ie, primary tumor, involved lobe, regional, and disseminated recurrence), treatment-related toxicity, and overall survival.

Results: A total of 59 patients accrued, of which **55 were evaluable** (44 patients with T1 tumors and 11 patients with T2 tumors) with a median follow-up of 4.0 years (7.2 years for surviving patients). Four patients had an in-field/marginal (primary) tumor failure (range, 1.8-4.8 years after SBRT); the estimated 5-year primary tumor failure rate was 7%. Nine additional patients had recurrence within the involved lobe (range 0.1-5.9 years after SBRT); **the 5-year primary tumor and involved lobe (local) failure rate was 20%.** Seven patients experienced regional failure (range, 2.8-5.2 years after SBRT); **the 5-year local-regional failure rate was 38%**. Fifteen patients experienced disseminated recurrence; the 5-year disseminated failure rate was 31%. **The rates for disease free and overall survival at 5 years were 26% and 40%, respectively.** The median overall survival was 4 years. Protocol treatment-related grade 3 and 4 adverse events were reported in 15 patients and in 2 patients, respectively, modestly more than was described in the previous 3-year report. No grade 5 adverse events were reported.

Failure of SABR (ie, early recurrence)

ORIGINAL ARTICLE

Follow-Up of Patients after Stereotactic Radiation for Lung Cancer

A Primer for the Nonradiation Oncologist

Kitty Huang, MSc, MDCM, and David A. Palma, MD, MSc, PhD, FRCPC,*† on Behalf of the IASLC Advanced Radiation Technology Committee*

(*J Thorac Oncol.* 2015;10: 412–419)

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

CT, computed tomography.

Follow-up after SABR

- CT imaging at 3-6 months for the initial year
- Every 6-12 months for an additional 3 years, and annually thereafter
- MDT discussion, use of high-risk CT features for accurate detection of local recurrence, and positron emission tomography/CT SUVmax cutoffs
- Biopsy and/or surgical or nonsurgical salvage therapy can be considered if safe and when investigations are nonreassuring

J Thorac Oncol. 2015 Mar;10(3):412-9

Salvage Operation for Late Recurrence After Stereotactic Body Radiotherapy for Lung Cancer: Two Patients With No Viable Cancer Cells

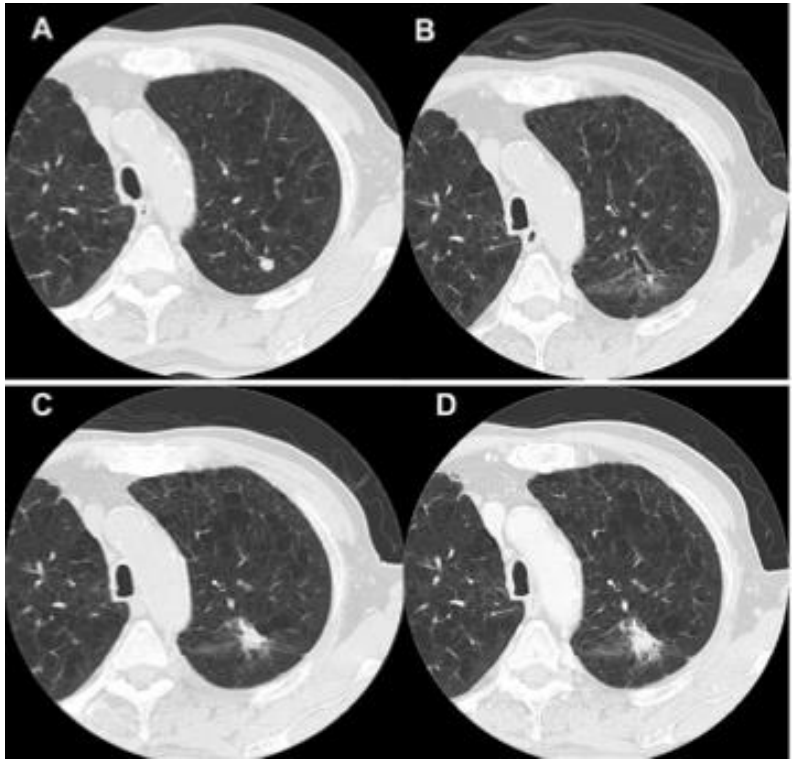
Naohiro Taira, MD, Tsutomu Kawabata, MD, PhD,
Takaharu Ichi, MD, Kazuaki Kushi, MD,
Tomofumi Yohena, MD, PhD,
Hidenori Kawasaki, MD, PhD,
Kiyoshi Ishikawa, MD, PhD, and Seiya Kato, MD, PhD

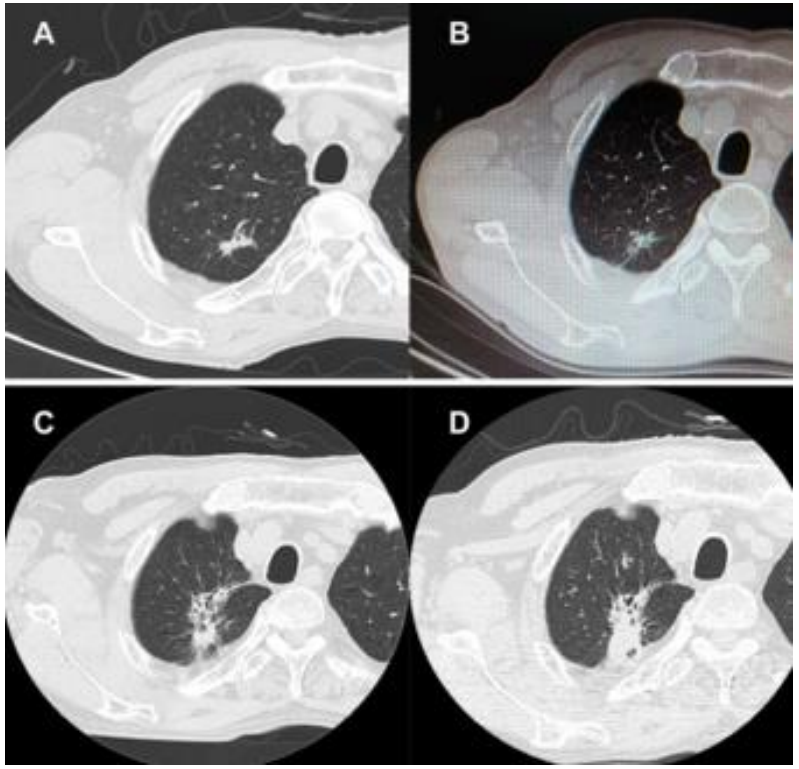
Department of General Surgery, National Hospital Organization, Okinawa Hospital, and Division of Pathology and Cell Biology, Graduate School of Medicine, University of the Ryukyus, Okinawa, Japan

S/P RLL lobectomy; further surgery declined

COPD – high risk;

Ann Thorac Surg
2014;97:2167–71





Local treatment-related complications

Severe Local Toxicity after Lung Stereotactic Body Radiation Therapy

Lesional Abscess Leading to Bronchocutaneous Fistula Requiring Surgical Marsupialization

Neil M. Woody, BS, Toufik Djemil, PhD,* David J. Adelstein, MD,† David P. Mason, MD,‡ Thomas W. Rice, MD,‡ and Gregory M. M. Videtic, MD**

Journal of Thoracic Oncology • Volume 5, Number 11, November 2010 *Lung Stereotactic Body Radiation Therapy*

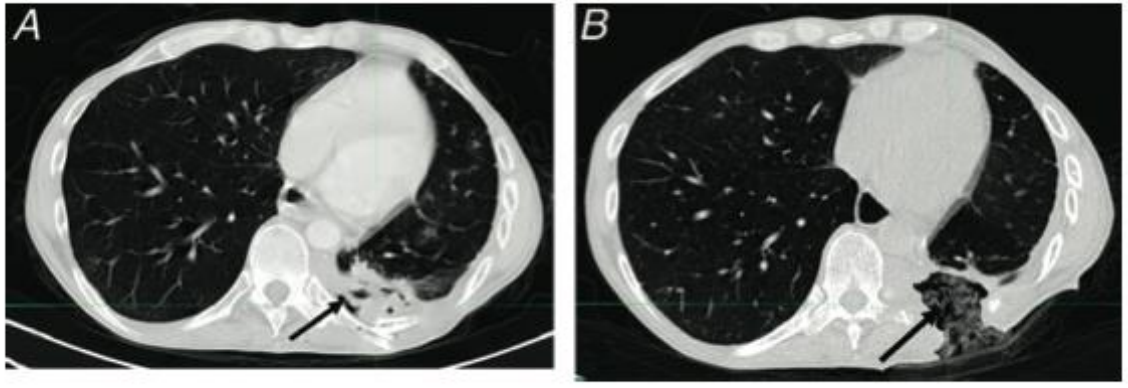
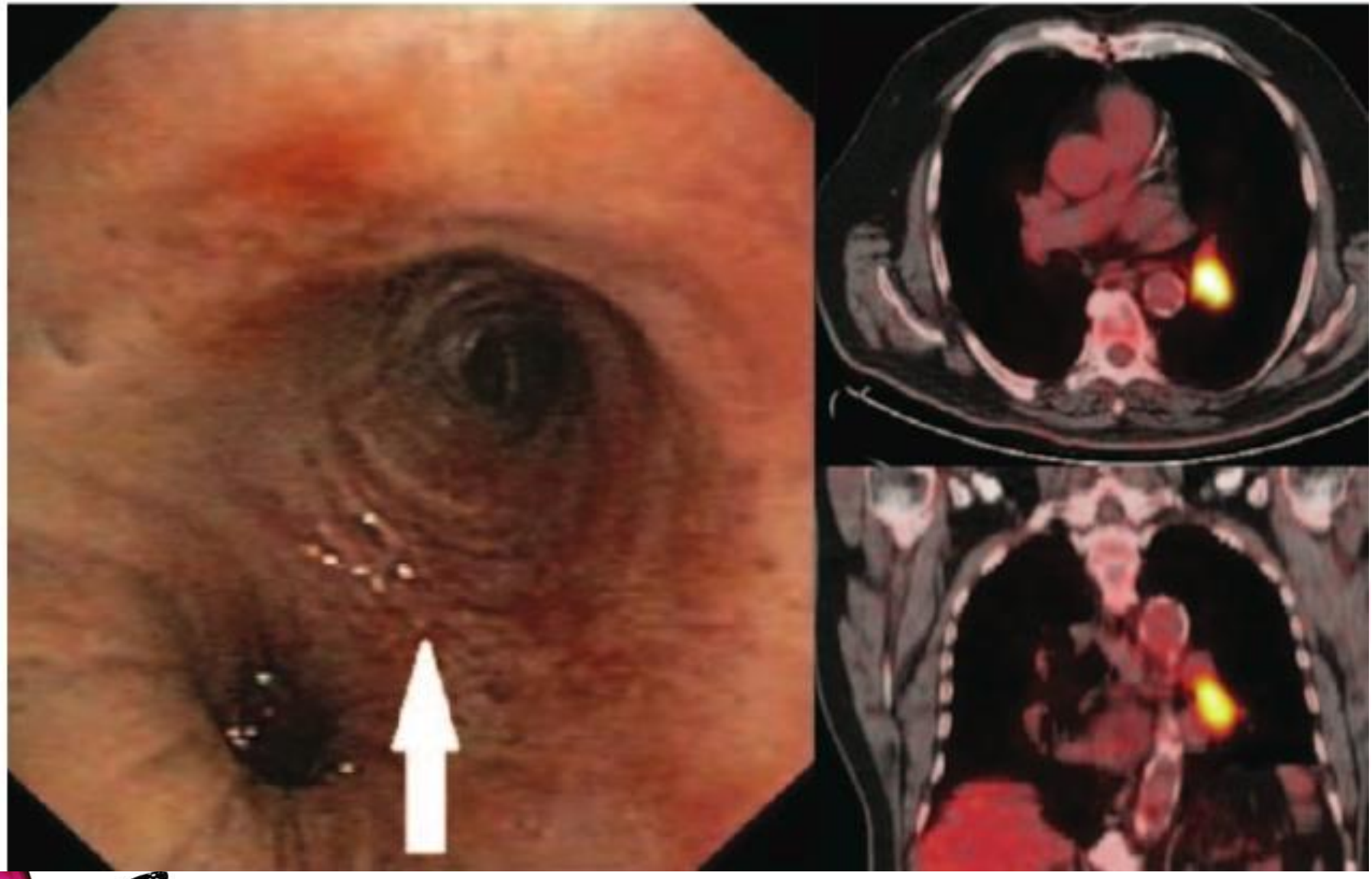
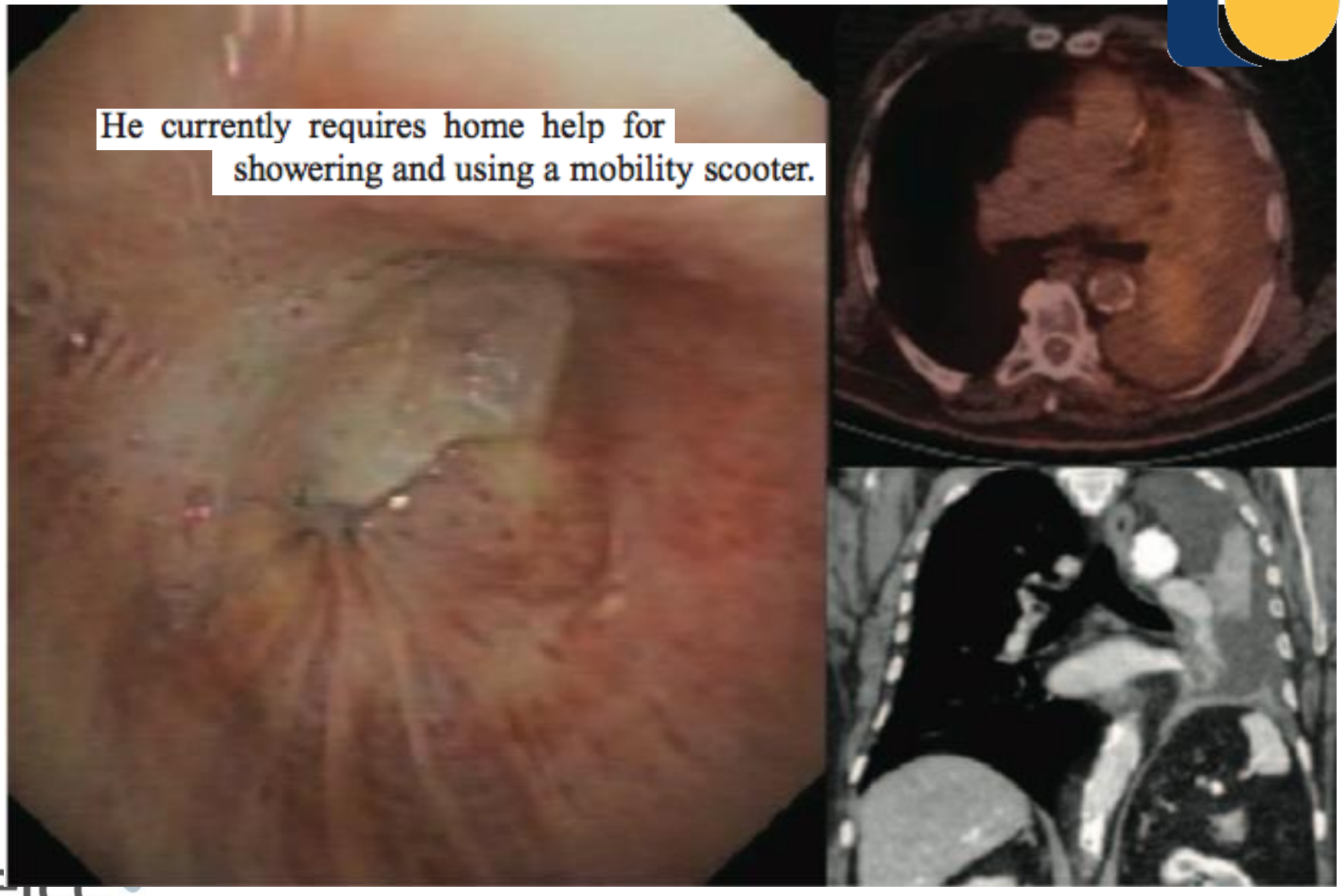


FIGURE 2. *A,* Representative axial computed tomography (CT) chest image without contrast at 17 months post-stereotactic body radiation therapy (SBRT). Arrow indicates air in lesion suggesting abscess. *B,* Representative axial CT chest image without contrast at 19 months post-SBRT. Arrow indicates abscess cavity after resection and marsupialization.

Journal of Thoracic Oncology® • Volume 8, Number 11, November 2013




He currently requires home help for
showering and using a mobility scooter.

Pathophysiology of SABR

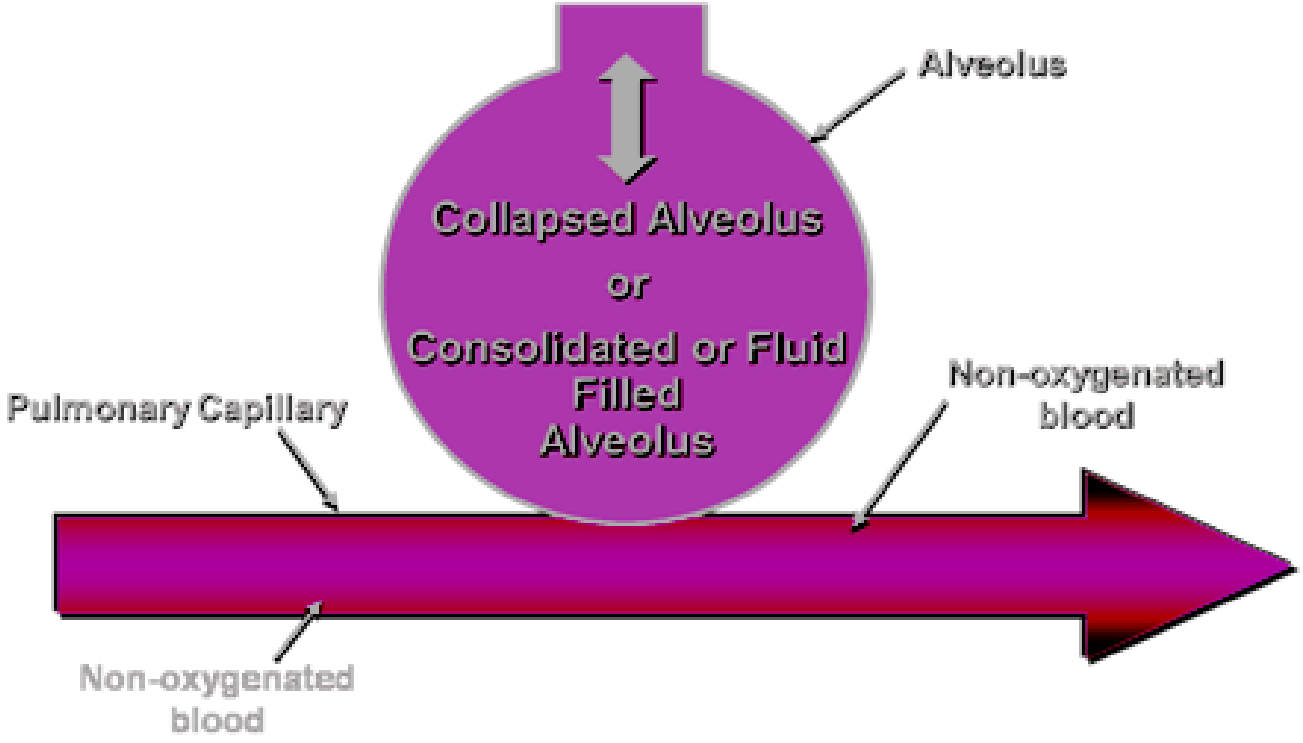


Figure 2-28. Types of Capillary Shunts.

http://media.lanecc.edu

Surgical referral after SABR for uncharacterized lesion

- Redo major surgery entails up to doubled operative risks
  - [Lobectomy 2.3%; pneumonectomy 5.8%] x 2
- Redo surgery may be forced to involve remaining lobe(s)
- Discrepancy between the need of parenchymal resection and residual cardiorespiratory function

Informed consent

- What are we operating on and which extension of resection are we proposing?
- What type of information (ie, operative risk) about possible surgery?
- No stage-specific survival data as a perspective to measure the operative risk against!
- How can we avoid casting shadows on the efficacy of primary line treatment (ie, SABR)?

MDT

Van Schil PE, JTO, 2010

Desiderata

- **Pre-treatment histological diagnosis**
- **MDT *evidence –based* decision based on internationally recognized risk assessment protocols:**
  - **Spirometry, DLco, *and* CPET (VO2max)**
  - **Split function (awareness of pathophysiology)**
- **For borderline patients, a pre-treatment visit with a board qualified thoracic surgeon should be arranged**