Provider Work Up of Positive Findings in CT Lung Screening

LuCa National Training Network

August 25, 2020

Andrea McKee, MD and Shawn Regis , PHD

Rescue Lung Rescue Life

Beth Israel Lahey Health
Lahey Hospital & Medical Center

Disclosure

- Astra Zeneca Educational Materials

Rescue Lung Rescue Life

Beth Israel Lahey Health
Lahey Hospital & Medical Center

Background

- Lung cancer screening (LCS) with low-dose CT improves survival in selected patients
  - National Lung Screening Trial (NLST)[1] – 20% relative risk reduction
  - NELSON trial[2] – 24% risk reduction in men, 48% in women
- Concern over false positive results and iatrogenic harm continue to limit LCS implementation
- Challenge for shared decision making

Rescue Lung Rescue Life

1. Aberle DR, et al. NEJM 2011.
2. de Koning HJ, et al. NEJM 2020

Beth Israel Lahey Health
Lahey Hospital & Medical Center

Positive Findings

- Lung
  - True positive
  - False positive

Andrea McKee, MD

- Incidental
- Significant Incidental
- Tracking

Shawn Regis, PhD

Rescue Lung Rescue Life

Beth Israel Lahey Health
Lahey Hospital & Medical Center

National Lung Screening Trial
What is Positive?

- Treatment Arms:
  - Low Dose Chest CT (1.5 mSv)
  - PA Chest Radiograph (0.02 mSv)

- Screening Intervals:
  - T0: Baseline prevalence screen
  - T1: Year 1 incidence screen
  - T2: Year 2 incidence screen

- Positive Test
  - Non-calcified nodule greater than or equal to 4mm in maximum diameter
  - Other findings suspicious for lung cancer (adenopathy, effusion…)
  - Workup of positives determined by PCPs not NLST
    - NLST reading radiologist recommendation available

Rescue Lung Rescue Life

Beth Israel Lahey Health
Lahey Hospital & Medical Center

National Lung Screening Trial Results: Rate of Positive Screenings

- CT (24.2%) > 3x more sensitive than CXR (6.9%)
  - T0 & T1 Rate: 27-28%
  - T2 Rate: 16.8%
    - 2 year stability → benign (Fleischner Guidelines)
    - Expected rate for ongoing CT lung screening?

- Significant incidental finding: 7.5%

Rescue Lung Rescue Life

National Lung Screening Trial Research Team (2011) Reduced lung-cancer mortality with low-dose computed tomographic screening. N Engl J Med 365(5):395–409.

Beth Israel Lahey Health
Lahey Hospital & Medical Center

NLST

Results: False Positive Workup/Adverse Events

- False Positive Rate:
  - 20-25%: Chance you will end up with a false positive
  - ~8-10% for Mammography (“Call back”)

- False Discovery Rate (1-PPV):
  - 96%: Chance if you are positive you do not have cancer
  - Same as mammography

- Intervention without disease:
  - 0.4-2.4%: Chance if screened you will have an unnecessary invasive procedure (LDCT)
  - ~1.5%: Chance if screened you end up having a negative biopsy (mammography)

Rescue Lung Rescue Life

Beth Israel Lahey Health
Lahey Hospital & Medical Center

National Lung Screening Trial

Results: Positive Workup/Adverse Events

- False Positives
  - Most have noninvasive imaging follow-up
    - CXR: 14.4%
    - Chest CT: 49.8%
    - PET/CT: 8.3%
  - Invasive diagnostic procedures: 2.6 %
  - Complication rate: 1.4%
  - Major complication rate: 0.06%

- True Positives
  - Invasive procedure major complication: 11.2%
  - Surgical resection mortality: 1%

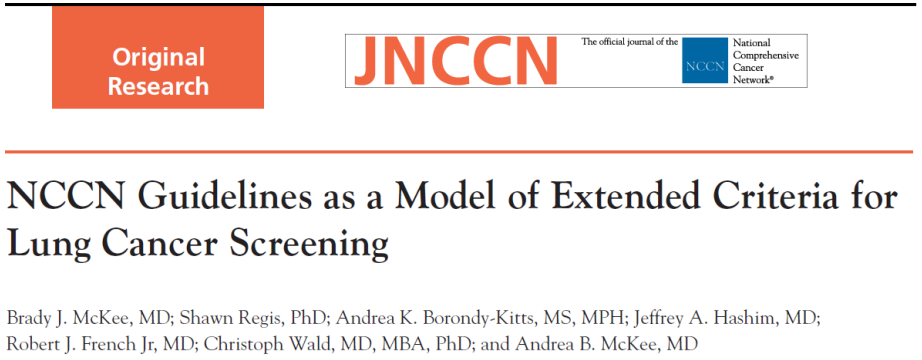
Rescue Lung Rescue Life

Beth Israel Lahey Health
Lahey Hospital & Medical Center

What **ARE** the False Positive Rates for CT Lung Screening?

T0: 26.3%
T1: 27.2%
T2: 15.9%
Overall: 23.3%

T0: 12.6%
T1: 5.3%
T2: 5.1%
Overall: 7.8%



T0: 10.6%
T1: 5.2%
T2: 5.0%
Overall: 7.6%

What **ARE** the False Positive Rates for CT Lung Screening?

T0: 26.3%
T1: 27.2%
T2: 15.9%
Overall: 23.3%

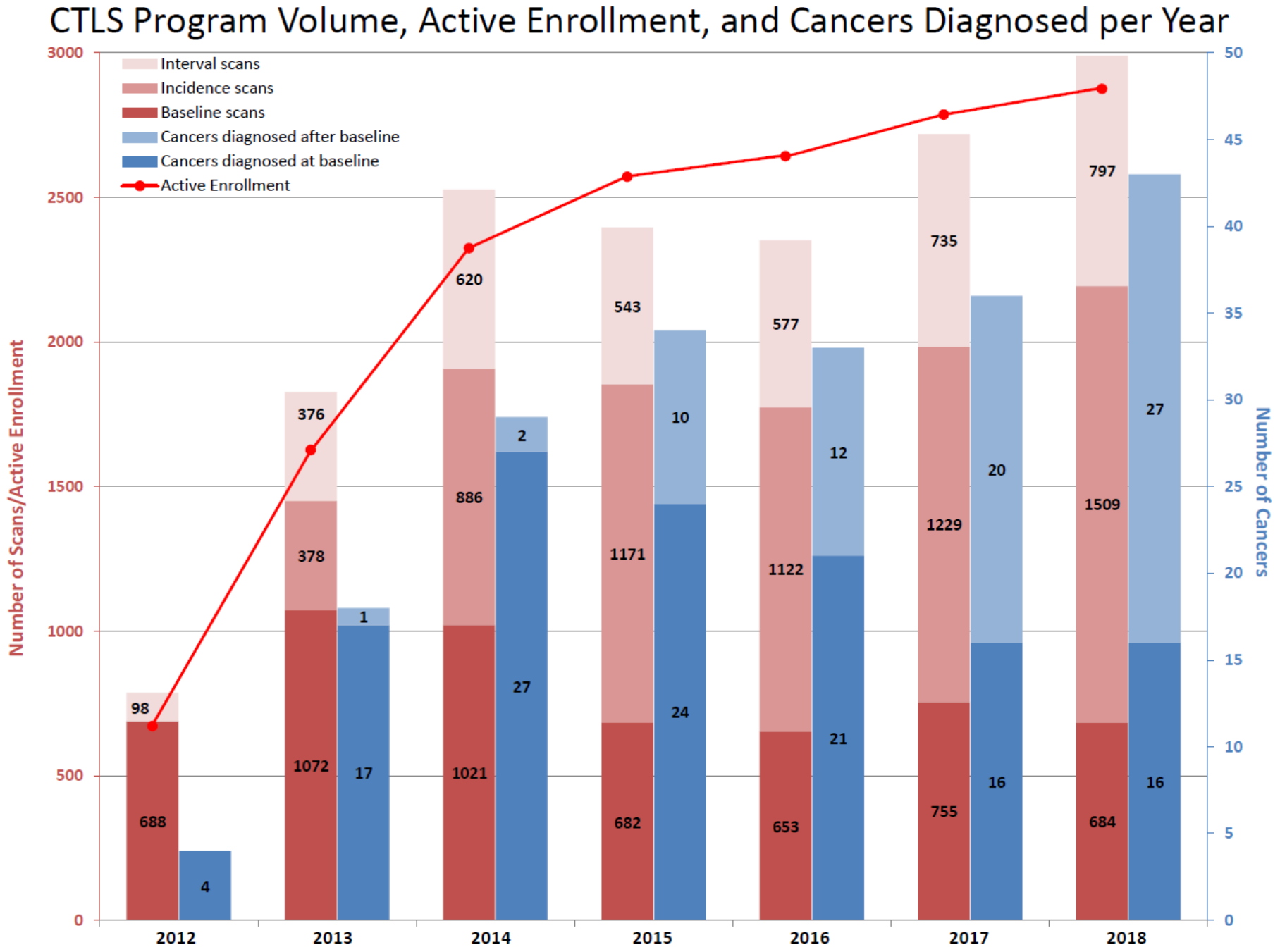
T0: 12.6%
T1: 5.3%
T2: 5.1%
Overall: 7.8%

T0: 10.6%
T1: 5.2%
T2: 5.0%
Overall: 7.6%

Covid-19?

Rescuing lives from lung cancer today and tomorrow

Numbers change as programs mature



Beth Israel Lahey Health
Lahey Hospital & Medical Center

Rescue Lung Rescue Life

Correction

FREE

February 2020

Clarification of False-Positive Reporting Language in an Editorial

JAMA Intern Med. 2020;180(2):338. doi:10.1001/jamainternmed.2019.7032

Editorial Comment

Editorial

Failing Grade for Shared Decision Making for Lung Cancer Screening

Rita F. Redberg, MD, MSc

In the Editorial titled "Failing Grade for Shared Decision Making for Lung Cancer Screening,"[1] published in the October 1, 2018, issue of *JAMA Internal Medicine*, language citing an Original Investigation by Kinsinger et al[2] reporting false-positive findings must be clarified. The phrase in the second paragraph of the Editorial that reads "these harms include a 98% false-positive rate" should more correctly read "the proportion of all positive tests that are falsely positive is 98%." This Editorial has been corrected online.

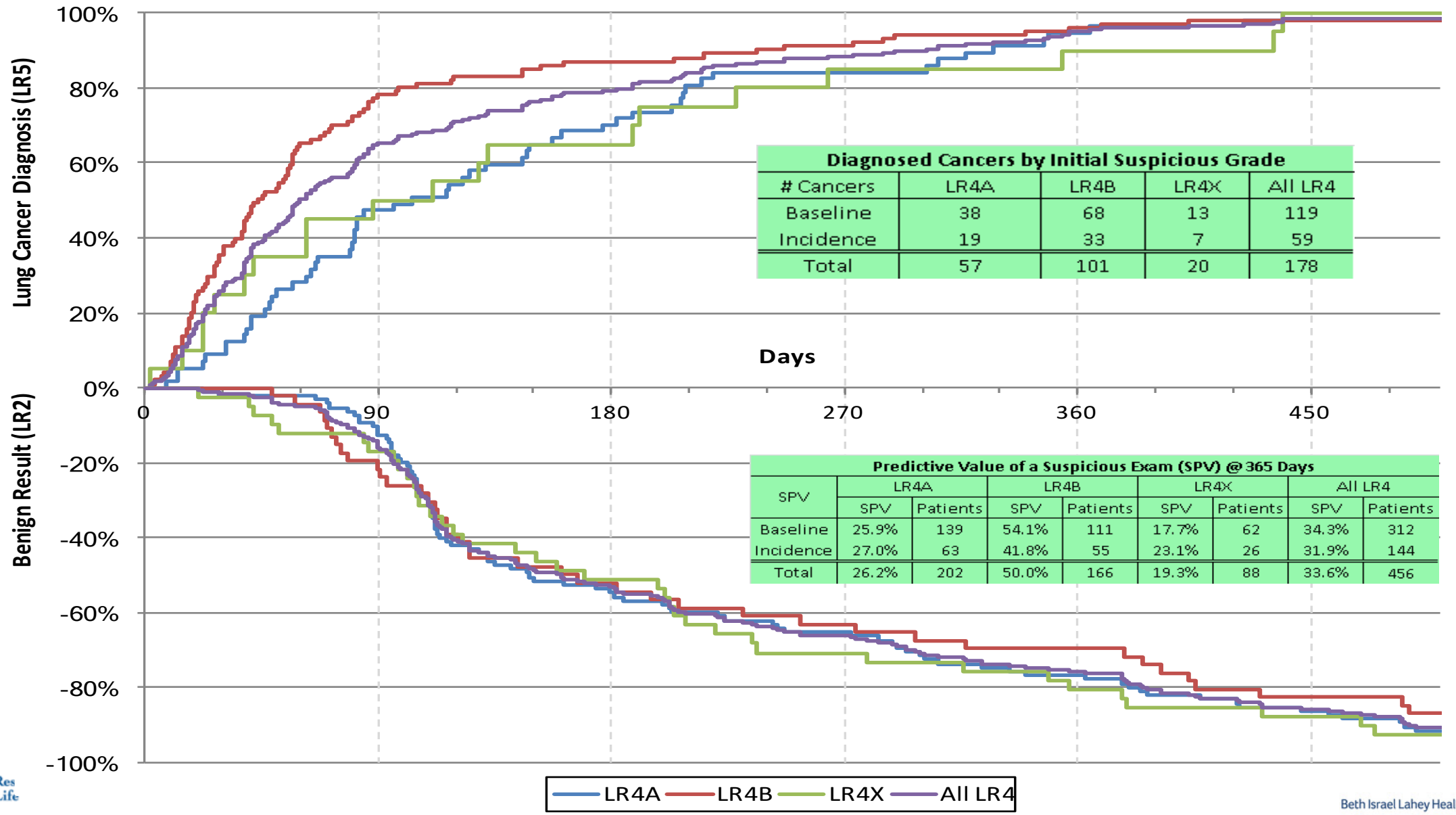
Methods & Demographics

- We aimed to evaluate the rates of intervention for benign findings in our large LCS program
  - As of April 2020, 19,158 LCS studies performed in 7521 patients
- Retrospective review of all Lahey LCS patients from January 2012 – June 2017
  - 4,490 screened patients
  - Follow-up through January 2019

Rescue Lung Rescue Life

Beth Israel Lahey Health
Lahey Hospital & Medical Center

Time to Lung Cancer/Benign Diagnosis from Initial Suspicious (LungRADS 4A/B/X) Exam



Diagnosed Cancers by Initial Suspicious Grade

# Cancers	LR4A	LR4B	LR4X	All LR4
Baseline	38	68	13	119
Incidence	19	33	7	59
Total	57	101	20	178

Predictive Value of a Suspicious Exam (SPV) @ 365 Days

SPV	LR4A		LR4B		LR4X		All LR4	
	SPV	Patients	SPV	Patients	SPV	Patients	SPV	Patients
Baseline	25.9%	139	54.1%	111	17.7%	62	34.3%	312
Incidence	27.0%	63	41.8%	55	23.1%	26	31.9%	144
Total	26.2%	202	50.0%	166	19.3%	88	33.6%	456

Rescue Lung Res Life

Beth Israel Lahey Health
Lahey Hospital & Medical Center

Methods & Demographics

- NCCN guidelines
- Patients with suspicious findings (Lung-RADS 4) were evaluated for interventions and outcomes

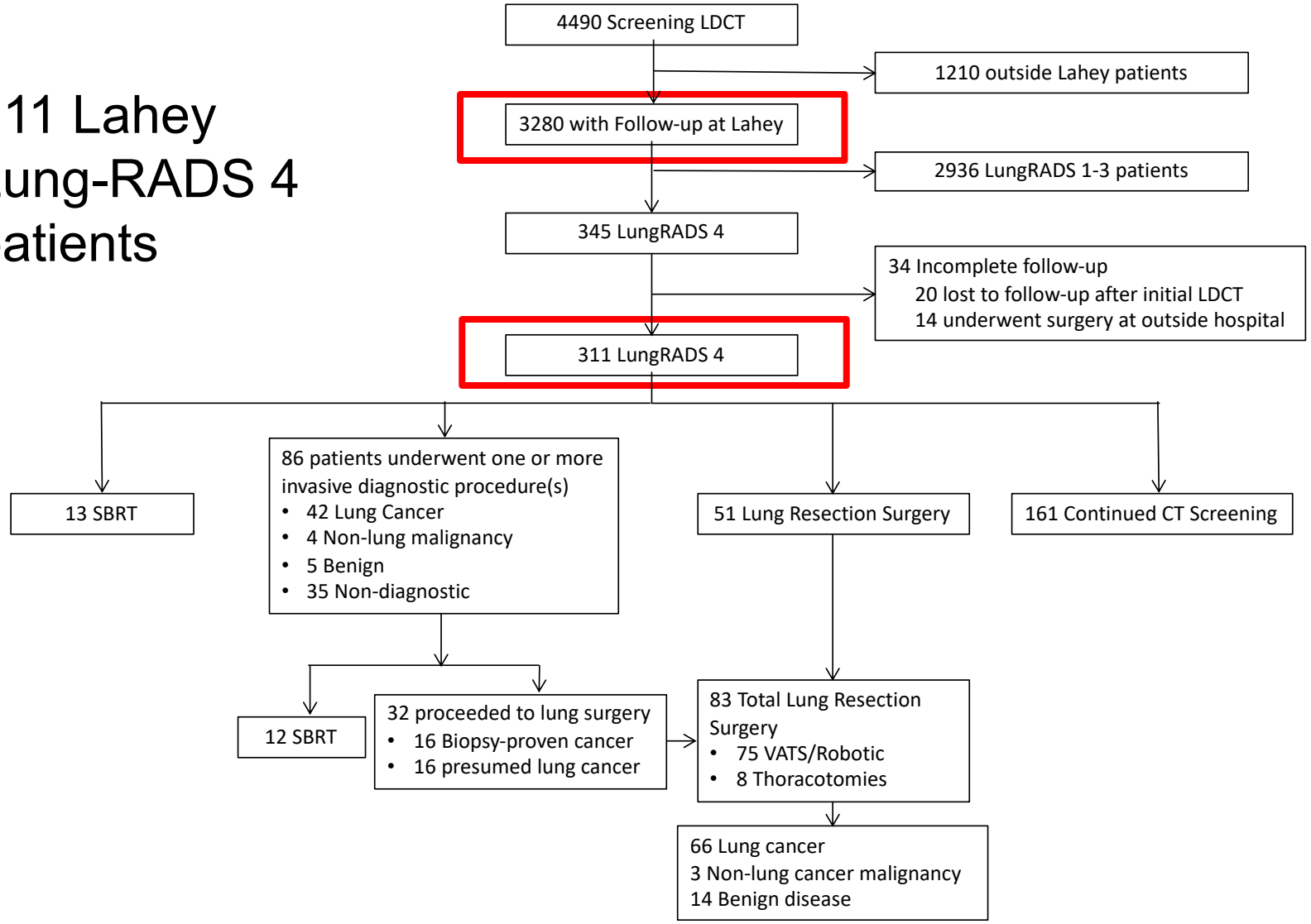
Characteristics of LungRADS-4 patients	Value
Sex – number (%)	
Male	169 (54.3)
Female	142 (45.7)
Age at enrollment – yr	
Median (IQR)	65 (60 – 69)
Range	50 – 77
NCCN Risk group – number (%)	
Group 1	252 (81.0)
Group 2	59 (19.0)
Smoking status – number (%)	
Current	167 (53.7)
Former	144 (46.3)
Pack-year of smoking	
Median (IQR)	43 (35 – 60)

Rescue Lung Rescue Life

Beth Israel Lahey Health
Lahey Hospital & Medical Center

Inclusion criteria

311 Lahey Lung-RADS 4 patients

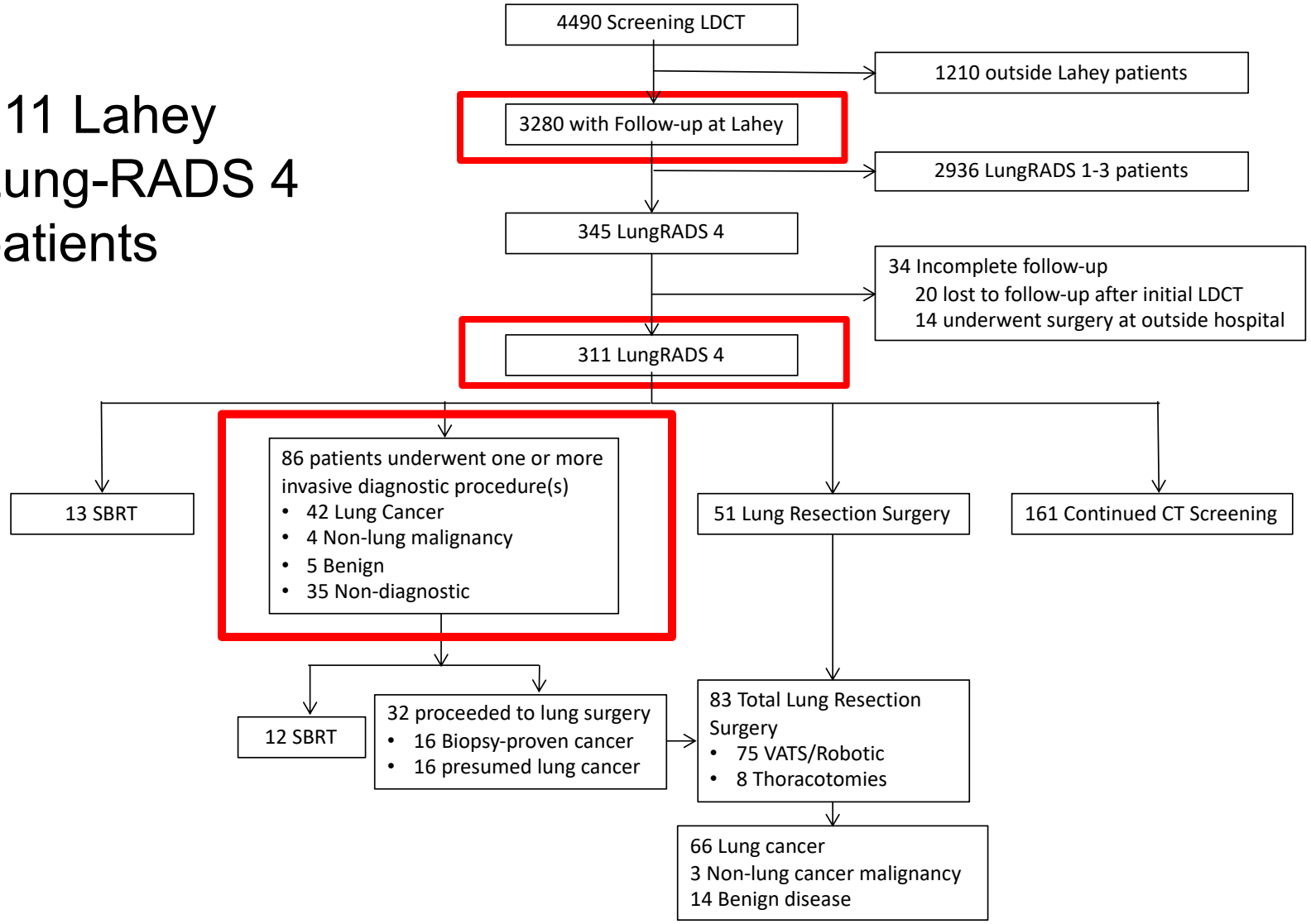


Rescue Lung Rescue Life

Beth Israel Lahey Health
Lahey Hospital & Medical Center

Inclusion criteria

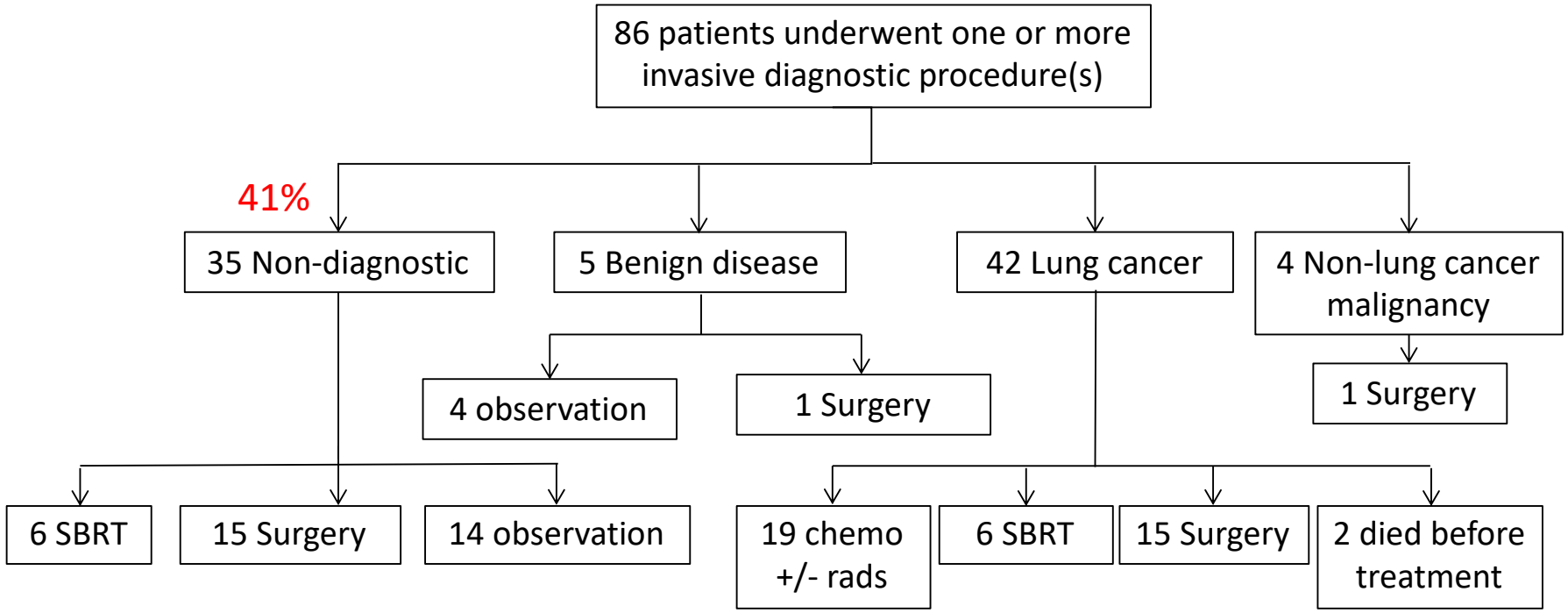
311 Lahey Lung-RADS 4 patients



Rescue Lung Rescue Life

Beth Israel Lahey Health
Lahey Hospital & Medical Center

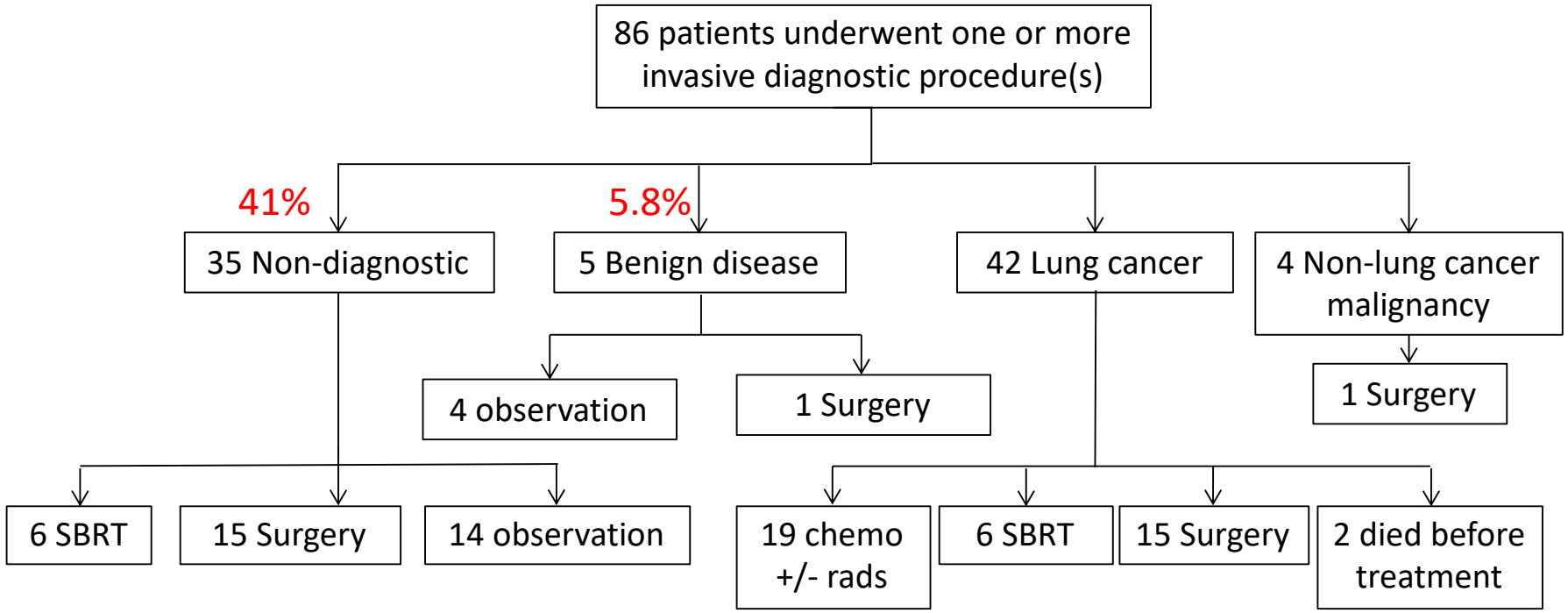
Invasive Diagnostic Procedures



Rescue Lung Rescue Life

Beth Israel Lahey Health
Lahey Hospital & Medical Center

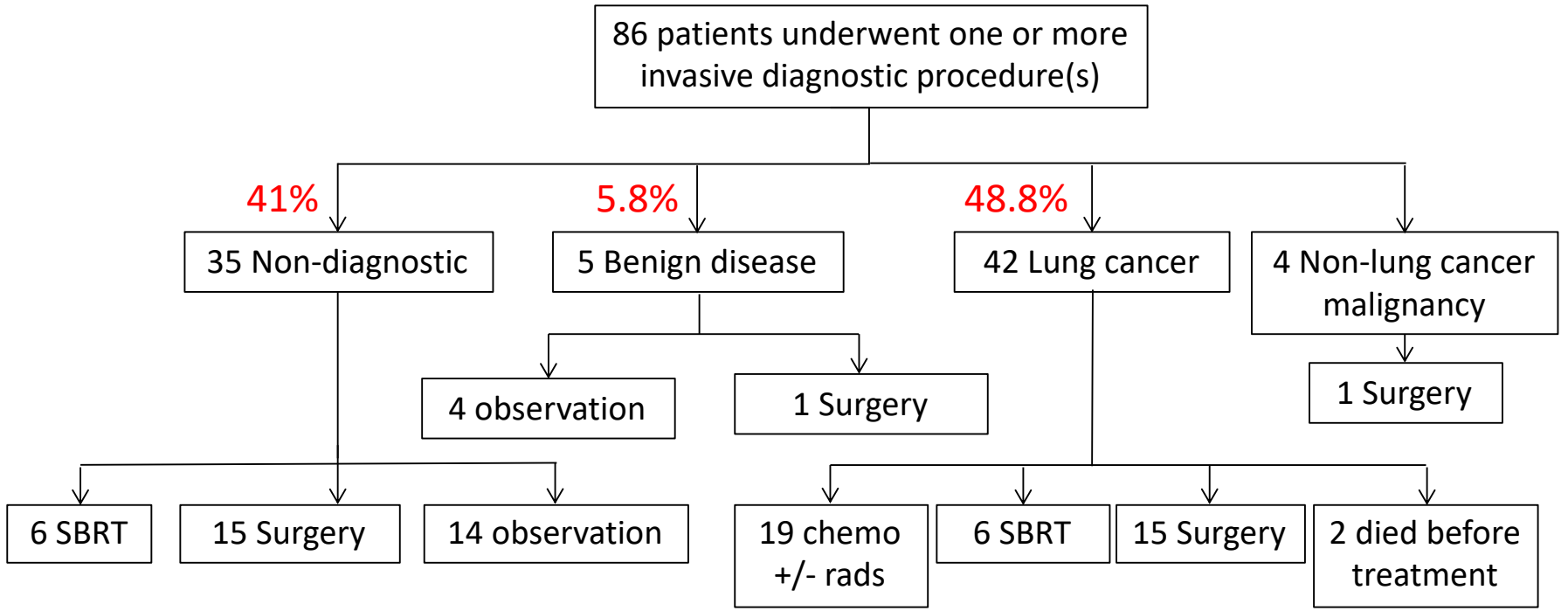
Invasive Diagnostic Procedures



Rescue Lung Rescue Life

Beth Israel Lahey Health
Lahey Hospital & Medical Center

Invasive Diagnostic Procedures



Rescue Lung Rescue Life

Beth Israel Lahey Health
Lahey Hospital & Medical Center

Results – Diagnostic interventions

Diagnostic study or procedure	Number of patients (% of Lung-RADS 4)
PET scan	192 (61.7)
CT-guided lung biopsy	31 (10.0)
Extrathoracic biopsy	6 (1.9)
Bronchoscopic-guided procedures	55 (17.4)
Navigational bronchoscopy	16 (5.1)
EBUS with transbronchial biopsy	47 (15.1)
Endobronchial biopsy	7 (2.3)
BAL/brushing	5 (1.6)
Medical thoracoscopy and pleural biopsy	2 (0.6)
Mediastinoscopy	26 (8.4)
Thoracentesis	3 (1.0)
Pericardiocentesis	1 (0.3)

- 86 patients underwent invasive diagnostic procedures
  - No periprocedural deaths or major complications
  - .95% for non-malignant disease

Therapeutic interventions

Therapeutic Intervention	Number of patients (%)	% Lung-RADS 4 patients
Surgical pulmonary resection	83	26.7
Tissue-proven lung cancer prior to surgery	16 (19.3)	5.1
Presumed lung cancer	67 (80.7)	21.5
SBRT	25	8.0
Tissue-proven lung cancer prior to SBRT	6 (24)	1.9
Presumed lung cancer	19 (76)	6.1
Chemotherapy	15	4.8
Adjuvant	9	2.9
Palliative	6	1.9
Chemoradiation	16	5.1
Neoadjuvant	2	0.6
Definitive	14	4.5
Palliative thoracic radiation	1	0.3

Lung resection surgery in LCS

- 83 patients underwent lung resection

Characteristic	Number of patients (%)
Extent of resection	
Wedge	28 (34.1)
Segmentectomy	12 (14.5)
Lobectomy	40 (48.2)
Bilobectomy	3 (3.6)
Pneumonectomy	0 (0.0)
Approach	
Thoracoscopy	75 (90.4)
Coil localization	9 (10.8)
Robotic assisted	22 (26.5)
Thoracotomy	8 (9.6)

Rescue Lung Rescue Life

Beth Israel Lahey Health
Lahey Hospital & Medical Center

Lung resection surgery in LCS

- 83 patients underwent lung resection

Characteristic	Number of patients (%)
Extent of resection	
Wedge	28 (34.1)
Segmentectomy	12 (14.5)
Lobectomy	40 (48.2)
Bilobectomy	3 (3.6)
Pneumonectomy	0 (0.0)
Approach	
Thoracoscopy	75 (90.4)
Coil localization	9 (10.8)
Robotic assisted	22 (26.5)
Thoracotomy	8 (9.6)

Rescue Lung Rescue Life

Beth Israel Lahey Health
Lahey Hospital & Medical Center

Surgical results

Characteristic	Number (%)
Diagnosis	
Lung cancer	66 (79.5)
Non-lung cancer malignancy	3 (3.6)
Benign disease	14 (16.9)
Lung cancer path stage (n = 64)	
Carcinoma in situ	2 (3.0)
IA	42 (63.6)
IB	11 (16.7)
IIA	8 (12.1)
IIIA	2 (3.0)
IV	1 (1.5)
Histology of benign disease	
Granuloma	6
Hamartoma	4
Organizing pneumonia	1
Other	3

- 0.43% of all Lahey LCS patients surgery for benign disease

Surgical results - complications

Complication Grade	Number of patients (%)
Clavien-Dindo Grade	
I	12 (14.5)
II	23 (27.7)
III	10 (12.0)
IV	2 (2.4)
V (death)	0
NLST Grade	
Major	5 (6.0)
Intermediate	42 (50.6)

- There were no deaths within 60 days of surgery
- 6.0% had “major” complications according to NLST criteria
  - Compared to 11.9% in NLST trial

SBRT in LCS

Characteristic	Number of patients (%)
Tissue-proven lung cancer prior to SBRT	6 (24.0)
Presumed lung cancer	19 (76.0)
Thoracic surgeon SBRT shared decision making	
Yes	24 (96.0)
No	1 (4.0)
Recurrence following SBRT	8 (32.0)
Patients initially with tissue-proven lung cancer	4
Patients initially presumed to have lung cancer	4
Median follow-up time from January 1, 2019 (months)	31.5

NLST

Results: False Positive Workup/Adverse Events

- False Positive Rate:
  - 20-25%: Chance you will end up with a false positive (7.8%)
  - ~8-10% for Mammography (“Call back”)

- False Discovery Rate (1-PPV):
  - 96%: Chance if you are positive you do not have cancer (85%)
  - Same as mammography

- Intervention without disease:
  - 0.4-2.4%: Chance if screened you will have an unnecessary invasive procedure (LDCT) (0.4%-0.95%)
  - ~1.5%: Chance if screened you end up having a negative biopsy (mammography)

Rescue Lung Rescue Life

Beth Israel Lahey Health
Lahey Hospital & Medical Center

National Lung Screening Trial

Results: Positive Workup/Adverse Events

- True Positives
  - Invasive procedure major complication: 11.2% (6%)
  - Surgical resection mortality: 1% 0

Rescue Lung Rescue Life

Beth Israel Lahey Health
Lahey Hospital & Medical Center

Challenges Shared Decision Making

False positive rate in modern clinical practice CTLS?

98%, 60%, 50%, 23%, 12%, 7%, 5%, 2%

Overdiagnosis

70%, 50%, 18%, 10%, 3%

Likelihood of surgery 0.4% or intervention 0.95%
for benign disease

Significant Incidental Findings

70%, 40%, 10%, 6%, 4%,2%

Rescue Lung Rescue Life

Beth Israel Lahey Health
Lahey Hospital & Medical Center

Shared Decision Making Conversation

- You are at high risk for lung cancer (2% baseline)
- New screening guidelines annual CTLS
- Finds early stage lung cancer 85% of the time
- Screen detected stage I lung cancer is 90% curable with surgery
- Less than 10% chance nodule is found that is not cancer – managed mainly with imaging follow up
- Surgery for benign disease .43%
- Invasive diagnostic intervention is rare .95%

Rescue Lung Rescue Life

Beth Israel Lahey Health
Lahey Hospital & Medical Center

Shared Decision Making Conversation

- If imaging follow up is recommended, and cancer ultimately found, it would be early stage
- No co-pay for annual screening exam
- Radiation exposure of a mammogram
- Smoking cessation for current smokers
- Small possibility we find something other than lung cancer requiring care escalation

Rescue Lung Rescue Life

Beth Israel Lahey Health
Lahey Hospital & Medical Center