FINDING LUNG CANCER EARLY SAVES LIVES: The Moffitt Lung Cancer Early Detection Program (LEAD)

Moffitt Grand Rounds
October 28, 2022

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Thoracic Surgery
Department of Thoracic Oncology
INDETERMINANT (UNDIAGNOSED) LUNG NODULES
The (Bad) Problem

- 236,000 new lung cancer cases yearly—130,000 will die from the disease (1 person every 4 minutes). Equals next 3 cancers combined.
- 1 of every 16 people (ignoring smoking status) will get lung cancer. Never smokers with lung cancer: 25% ♀ 10% ♂
- Only 24% are diagnosed early when survivals are highest.
1.6 million lung nodules found annually (95% found incidentally):
- CT angiograms in emergency rooms for dyspnea/chest pain
- CXRs and CT scans for trauma
- Abdominal CT scans for abdominal pain
- Calcium score CT scans
- 2/3 of these nodules are not followed.
- Lung nodule management guidelines are not followed by 60% of clinicians.
- Many unnecessary biopsies, with 38-44% of needle biopsies on benign nodules.
- Based on a SEER database study\(^1\): 43.7% of lung biopsies are unnecessary and do not follow NCCN guidelines.  
- Almost 1/3 of nodules removed at surgery are benign.
HOW CAN WE FIND LUNG CANCER EARLY?

- Randomized trial of 53,454 participants: Low dose chest CT versus chest x-ray screened annually for 3 years.
- 27% positive for lung nodules; 3.9% of them were lung cancer (1.05% of total scans).
- 80% of cancers found were early stage.
- Relative risk reduction in lung cancer mortality of 20%.
- Many subsequent RCT since then showing similar results.
- Current 2021 recommendations for eligibility for screening CT scans* by U.S. Preventive Services Task Force:
  - Adults aged 50 to 80 years
  - 20 pack-year smoking history
  - Currently smoke or have quit within the past 15 years.
  - Screen for lung cancer with low-dose computed tomography (CT) every year.
  - Stop screening once a person has not smoked for 15 years or has a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery.

* Cost Of CT scans covered by Medicare, Medicaid, and most Insurance plans for eligible people.
LOW DOSE SCREENING CHEST CT SCANS (LDCT):
The only proven way to find early-stage lung cancer and improve cure rates.

Eligibility Criteria

2021 United States Preventive Service Task Force (USPSTF) Recommendations:

- 50 – 80 years of age
- Currently smoking or quit within 15 years
- 20+ pack year smoking history

Pack year = 
# of years smoked
×
# of cigarette packs smoked per day

14.5 million people are eligible for screening – more people than reside in the state of Pennsylvania

60 thousand lives could be saved per year if every eligible person were screened – more people than can be held in Nationals Park

% ELIGIBLE PEOPLE WHO ARE SCREENED FOR:
Breast: 76%, Colon: 67%, Prostate: 40%, Cervical: 75%
LOW DOSE SCREENING CHEST CT SCANS (LDCT):
The only proven way to find early-stage lung cancer and improve cure rates. The Good…but.

HIGH SENSITIVITY (93.8%) BUT LOWER SPECIFICITY (73.4%)

27% LDCT SCANS ARE POSITIVE BUT FALSE POSITIVE RATE IS 96.1%

LDCT QUITE UNDERUTILIZED BY TARGET POPULATION

- ONLY 3% OF ELIGIBLE PEOPLE IN FLORIDA OBTAIN THE CT SCAN
- POSSIBLE REASONS:
  - NOT RECOMMENDED BY PCP (RARELY RECOMMENDED)
  - CONCERN ABOUT EXPENSE AND EFFORT TO OBTAIN TEST
  - CONCERN ABOUT RADIATION EXPOSURE
  - RELUCTANCE OF PERSON TO ADMIT THEY ARE AT RISK FOR LUNG CANCER.
  - STIGMA ASSOCIATED WITH SMOKING
  - CONCERN ABOUT POTENTIAL ADDITIONAL INVASIVE TESTS IF ABNORMAL SCREEN.
  - CLAUSTOPHOBIA
  - UNAWARE OF THE NEED FOR SCREENING AND ITS COST
  - LACK OF AVAILABILITY OF APPROPRIATE RADIOLOGY FACILITY
  - ANXIETY WAITING FOR CT SCAN RESULTS

% ELIGIBLE PEOPLE WHO ARE SCREENED FOR: Breast: 76%, Colon: 67%, Prostate: 40%, Cervical: 75%
STEREOTYPICAL IMAGE OF LUNG CANCER PATIENT (HOLLYWOOD VERSION)

THE MYTH OF LUNG CANCER

- **THE “INVISIBLE” CANCER.**
- **THE STIGMA ASSOCIATED WITH SMOKING.**
- **THE LAY PUBLIC AND HEALTH CARE PROVIDERS ASSUME THIS CANCER OCCURS ONLY IN A SET PATIENT POPULATION.**
- **IN REALITY, EVERYONE IS AT RISK...BUT SOME MORE THAN OTHERS!**
ACTUAL PEOPLE WHO DEVELOP LUNG CANCER

49 Y/O FORMER N.Y. MODEL AND MOM

68 Y/O WHO OWNS A BLUEBERRY FARM
(THIS PICTURE WAS TAKEN 3 WEEKS AFTER HER LUNG RESECTION
WHILE SHE WAS HIKING IN THE COLORADO MOUNTAINS)
POTENTIAL RISKS OF LOW DOSE SCREENING LUNG CT SCANS

• False Positive Screens:
  • 27% positive for a nodule on first screening CT, only 3.8% true positive.
  • Leads to further follow-up diagnostic procedures in 90%.
  • Of positive screens, 3.7% had an invasive procedure
    • 9.6% had a complication.
    • 2.4% had a major complication.
• Overdiagnosis: cancer detected through screening but never would have become symptomatic or clinically diagnosed otherwise. (Theoretical risk)
• Radiation Risk: with annual screens from 50-75 years, lung cancer estimated excess risk 0.07% for males and 0.14% for females.
  • But estimated 24 radiation-related lung cancer deaths compared with 459 lung cancer deaths averted by screening...1:20 ratio.
• Incidental Findings: >10% find emphysema, coronary artery calcifications, liver, kidney or adrenal lesions, infections, etc. (Actually a benefit)

FEAR OF RADIATION EXPOSURE
EFFECTIVE RADIATION DOSES

Effective doses in millisieverts:

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Dose</th>
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</thead>
<tbody>
<tr>
<td>Dental bite-wing</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Chest x-ray</td>
<td>0.02</td>
</tr>
<tr>
<td>U.S. coast to coast flight</td>
<td>0.035</td>
</tr>
<tr>
<td>Mammogram</td>
<td>0.4</td>
</tr>
<tr>
<td>Low dose chest CT</td>
<td>1.6</td>
</tr>
<tr>
<td>Annual flight crew dose</td>
<td>2.3</td>
</tr>
<tr>
<td>Diagnostic chest CT</td>
<td>7.0</td>
</tr>
<tr>
<td>Coronary CT angiogram</td>
<td>14.0</td>
</tr>
<tr>
<td>Natural ionizing radiation</td>
<td>3.0/year</td>
</tr>
<tr>
<td>Maximal allowable yearly dose</td>
<td>50/year</td>
</tr>
<tr>
<td>No increased cancer risk below</td>
<td>100/year</td>
</tr>
</tbody>
</table>
SCREENING CHEST CT SCANS

- Criteria (2021) for Screening Chest CT scans:
  1. Age 50-80 years
  2. Current smoker or former smoker with 20 pack-year history.
  3. Current smoker or quit smoking within the last 15 years


- Approximately 15 million Americans (4.5% of total population) are candidates for screening and only 5.5% obtain them (3% in Florida!).

- Therefore, for Florida with a population of 22 million, almost 1 million are candidates for screening.

- Since screening picks up approximately 1 cancer per 100 (twice the rate of mammography). 80% are early (potentially curable) stage cancers. Then if all Floridians were screened, we would find 10,000 cancers and 8,000 would be potentially curable.

- If the long-term cure rate for these early-stage cancers is 75%, then 6,000 Floridians could be theoretically cured yearly of lung cancer with 100% screening.

- Currently, there are 19,560 new lung cancer cases in Florida and only 23% or 4,500 will be cured.
**EARLY RESULTS OF SCREENING CHEST CT SCANS ON LUNG CANCER: DIAGNOSIS AND SURVIVALS**

- **STAGE SHIFT TO MORE STAGE I CANCERS**
  - Since low dose CT scans recommended in 2013, increase in stage I cancers.
  - More incidental lung nodules are being evaluated.
  
  \[1\] A. Potter. et.al. Brit Med J 2022;376:e069008

- **IMPROVING SURVIVALS IN LUNG CANCER**
  - Improved treatment.
  - Stage shift to more stage I lung cancers.\[1\]

  “…studies investigating treatments for lung cancer must take into account stage shift and the confounding association with survival and mortality outcome.”\[2\]

  \[2\] R. Flores, et. al. JAMA network Open 2021;4:e2137508
CO$T EFFECTIVENESS OF LOW DOSE CHEST CT SCANS FOR LUNG CANCER DISCOVERY

- Low-dose screening chest CT scans compared with no screening: $52,000 per life-year gained.¹
  ¹W. C. Black, et.al. NEJM, 2014;371:1793-1802
- Mammography screening compared with no screening biennial screening ages 40-69: $87,420 per life-year gained.²
- Colonoscopy screening compared with no screening: $6,783 per life-year gained.³
- Cervical Cancer Screening cost effectiveness: $23,900 per life-year gained.⁴
LOW DOSE CT SCREENING FOR LUNG CANCER IS EFFECTIVE

320 people need to be screened to prevent one lung cancer death

AND IT IS FAR CHEAPER TO TREAT AN EARLY-STAGE LUNG CANCER FOUND BY SCREENING!

Number Needed to Screen to Prevent One Death

<table>
<thead>
<tr>
<th></th>
<th>Lung</th>
<th>Cholesterol</th>
<th>Colon</th>
<th>Breast</th>
</tr>
</thead>
<tbody>
<tr>
<td>NNN</td>
<td>320</td>
<td>420</td>
<td>800</td>
<td>1500</td>
</tr>
</tbody>
</table>

NSCLC Treatment Costs Per Month by Stage

- Stage I: $7,239
- Stage II: $9,484
- Stage IIIa: $11,193
- Stage IIIb: $17,415
- Stage IV: $21,441
INCREASED RISK OF DEVELOPING LUNG CANCER (SECOND PRIMARY) AFTER A FEMALE HORMONE-RELATED CANCER (COMPARED TO THE GENERAL POPULATION)

- **Breast Cancer¹**
  - Breast cancer age at diagnosis 20-49.
    - HR Positive: 37% (SIR 1.37, C.I. 1.26-1.48). 1.72 Excess Absolute Risk per 10,000 person-years
      - Mean age at diagnosis of lung cancer: 57 years
    - HR Negative: 56% (SIR 1.56, C.I. 1.34-1.84). 2.5 Excess Absolute Risk per 10,000 person-years.
      - Mean age at diagnosis of lung cancer: 55 years
  - Breast cancer age at diagnosis 50-84.
    - HR Positive: N.S.
      - Mean age at diagnosis of lung cancer: 73 years
    - HR Negative: 17% (SIR 1.1.17, C.I. 1.09-1.25). 3.55 Excess Absolute Risk per 10,000 person-years.
      - Mean age at diagnosis of lung cancer: 71 years

²Additional Risk Factors in Breast Cancer Patients:
  - Smoking: 873% increased risk (SIR 9.73, p=0.002)
  - Radiotherapy: 40% increased risk (SIR 1.40, p<0.001)¹²

- **Cervical Cancer³**
  - Second primary Lung Cancer Risk: 124% (SIR 2.24, C.I. 2.06-2.43)
    - Mean age of cervical cancer: 56 years.
    - Mean age of subsequent lung cancer: 64 years.
    - The younger the age of cervical cancer predicted an increased risk.
    - Second cancers had a negative impact on overall survival.

# Increased Risk of Developing Lung Cancer (Second Primary) After a Female Hormone-Related Cancer

(Compared to the General Population)

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Pooled</td>
<td>25%</td>
<td>1.25 (1.16-1.35%)</td>
<td>40% (age effect)</td>
<td>1.40 (1.06-1.86)</td>
<td>50% (chemo and radiotherapy effects)</td>
<td>1.50 (1.10-2.05)</td>
<td>156% (2.56 (2.33-2.80))</td>
</tr>
<tr>
<td>&lt;5 Yrs.</td>
<td>N.S.</td>
<td>-- --</td>
<td>N.S.</td>
<td>-- --</td>
<td>N.S.</td>
<td>-- --</td>
<td>207% (3.07 (1.38-6.80))</td>
</tr>
<tr>
<td>≥5 Yrs.</td>
<td>49%</td>
<td>1.49 (1.23-1.81)</td>
<td>N.S.</td>
<td>-- --</td>
<td>N.S.</td>
<td>-- --</td>
<td>128% (2.28 (1.98-2.61))</td>
</tr>
<tr>
<td>≥10 Yrs.</td>
<td>55%</td>
<td>1.55 (1.25-1.93)</td>
<td>N.S.</td>
<td>-- --</td>
<td>N.S.</td>
<td>-- --</td>
<td>118% (2.18 (1.94-2.45))</td>
</tr>
<tr>
<td>≥20 Yrs.</td>
<td>139%</td>
<td>2.38 (1.66-3.45)</td>
<td>N.S.</td>
<td>-- --</td>
<td>N.S.</td>
<td>-- --</td>
<td>93% (1.93 (1.49-2.51))</td>
</tr>
<tr>
<td>≥30 Yrs.</td>
<td>77%</td>
<td>1.77 (1.34-2.33)</td>
<td>N.S.</td>
<td>-- --</td>
<td>N.S.</td>
<td>-- --</td>
<td>106% (2.06 (1.38-3.06))</td>
</tr>
</tbody>
</table>

2 Additional Risk Factors in Breast Cancer Patients:
- Smoking 873% increased risk (SIR 9.73, p=0.002)
- Radiotherapy 40% increased risk (SIR 1.40, p<0.001)


Management of indeterminant lung nodules require a great deal of detailed organization.

Many internists, pulmonologists and family practice physicians lack a reliable system to manage these patients.

Patients can easily get “lost” to follow-up.

Most physicians are not aware of the recommended management guidelines.

Physicians would rather not be primarily responsible for these patients.

Many physicians worry about medicolegal concerns.

Primary care physicians order screening low dose chest CT scans for only 3% of eligible patients.
62-year-old female current smoker with COPD and surveillance CT scans showing an enlarging lung cancer, watched outside for over 2 years. “Kickin’ the can down the road…”

October 5, 2021. Left upper lobectomy. Pathology: 1.9 cm Adenocarcinoma with all lymph nodes negative for cancer except a microscopic focus of cancer in one lymph node in the mediastinum...so unfortunately Stage IIIA disease.
HOW DO YOU DETERMINE WHETHER A NODULE IS BENIGN OR MALIGNANT?

- PET SCANS
- GUIDELINES (FLEISCHNER SOCIETY CRITERIA)
- MALIGNANCY CALCULATORS (MAYO CLINIC CALCULATOR)
- ANTIBIOTIC TRIAL, IF SUSPECTED INFECTION
- EXPERIENCE (It’s called the “practice of medicine” for a reason.)
- TIME, i.e., FOLLOWUP CT SCANS, WHEN LOW LIKELIHOOD OF CANCER

INVASIVE STUDIES:
- CT-GUIDED NEEDLE BIOPSY (Use Judiciously)
- BRONCHOSCOPY (STANDARD, NAVIGATION, ROBOTIC-ASSISTED)
- SURGICAL RESECTION
EXAMPLE OF LUNG NODULE EVALUATION

CT Scan June 9, 2021
2.05 cm RUL nodule

CT Scan June 23, 2022
3.70 cm RUL nodule

PET Scan July 8, 2022

RISK CALCULATOR

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

Predicts malignancy risk in solitary lung nodules on chest x-ray.

INSTRUCTIONS:
Do not use in patients with prior lung cancer diagnosis or with history of extrathoracic cancer diagnosed within 5 years of nodule presentation.

When To Use

Age
70

Years

Nodule diameter

1.5

mm

Current or former smoker

No

Yes

Yes

Former

Extrathoracic cancer diagnosis 15 years prior

No

Yes

Yes

Upper lobe location of tumor

No

Yes

Yes

Nodule spiculation

No

Yes

Yes

66.4%
Probability of malignancy

One study suggests watchful waiting only at very low post-test probabilities (<29%), biopsy at “lower” post-test probabilities (29% to 20%), and surgery at higher post-test probabilities (>70%). See Next Steps.

GUIDELINES

2017 Fleischner Society Guidelines for Management of Incidentally Detected Pulmonary Nodules

A: Solid Nodules

<table>
<thead>
<tr>
<th>Nodule Type</th>
<th>Nodules ≤5 mm (&lt;160 mm³)</th>
<th>Nodules 6–8 mm (160–250 mm³)</th>
<th>Nodules &gt;8 mm (250 mm³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single</td>
<td>Low risk: No routine follow-up</td>
<td>CT at 6–12 mo; then consider CT at 18–24 mo</td>
<td>Consider CT at 3 mo, PET/CT, or tissue sampling</td>
</tr>
<tr>
<td></td>
<td>High risk: Optional CT at 12 mo</td>
<td>CT at 6–12 mo; then consider CT at 18–24 mo</td>
<td>Consider CT at 3 mo, PET/CT, or tissue sampling</td>
</tr>
<tr>
<td>Multiple</td>
<td>Low risk: No routine follow-up</td>
<td>CT at 3–6 mo; then consider CT at 18–24 mo</td>
<td>Use most suspicious nodules as guide to management; follow-up intervals may vary according to size and risk (recommendation 2A)</td>
</tr>
<tr>
<td></td>
<td>High risk: Optional CT at 12 mo</td>
<td>CT at 3–6 mo; then consider CT at 18–24 mo</td>
<td>Use most suspicious nodules as guide to management; follow-up intervals may vary according to size and risk (recommendation 2A)</td>
</tr>
</tbody>
</table>

B: Subsolid Nodules

<table>
<thead>
<tr>
<th>Nodule Type</th>
<th>Nodules ≤5 mm (&lt;160 mm³)</th>
<th>Nodules ≥6 mm (200 mm³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single</td>
<td>Ground glass: No routine follow-up</td>
<td>CT at 6–12 mo to confirm persistence; if lesion is unchanged and solid component remains ≤6 mm, annual CT should be performed for 5 y</td>
</tr>
<tr>
<td></td>
<td>Partly solid: No routine follow-up</td>
<td>CT at 3–6 mo to confirm persistence; if lesion is unchanged and solid component remains ≤6 mm, annual CT should be performed for 5 y</td>
</tr>
<tr>
<td>Multiple</td>
<td>CT at 3–6 mos; if lesion is stable, consider CT at 2 y and 4 y; if solid component(s); develops or growth occurs, consider nodules (recommendations 5A and 4A)</td>
<td></td>
</tr>
</tbody>
</table>

In practice, partly solid nodules cannot be defined as such until they are ≥5 mm, and nodules ≤5 mm usually do not require follow-up; persistent partly solid nodules with a solid component ≥6 mm should be considered highly suspicious (recommendations 6A-4C).

Multiple ≤5 mm pure GGNs usually are benign, but consider follow-up at 2 y and 4 y in select patients at high risk (recommendation 4A).
CT-GUIDED LUNG BIOPSY

Technical success rate: 87%¹

Complications (mean % from recent literature)¹,²:

- 26% pneumothorax (6.5% required chest tube)
- 2% hemothorax
- 12-33% hemorrhage
- 3% hemoptysis
- 0.6% tumor seeding
- 0.06% air embolism
- 0.12% mortality


Dislodging circulating tumor cells:³

- Small series found circulating tumor cells in 33% of cases with after a percutaneous lung biopsy.²

³N. Sawabata, et.al. J Metastasis Treat 2017;3:16-20

Cost (2013): Medicare data for 8979 patients 2011-13 with abnormal CT scans.⁴

- Needle biopsy cost: median $1,071, mean $5,946.
- Cost of needle biopsy with a complication: median $14,824, mean $37,745.
- For comparison, surgical excision cost: median $15,623, mean $17,855.

WHEN IS A CT-GUIDED LUNG BIOPSY APPROPRIATE?

DO NOT ORDER LUNG BIOPSY:
• Just because the radiologist recommends it.
• Before a PET scan is obtained (to verify metabolic activity and to look for metastatic disease). NCCN Guidelines 2021.
• If metastases are apparent—biopsy the metastasis for highest stage.
• Where there is likely distal atelectasis.
• Just because a lung nodule is likely a lung cancer in a surgical candidate (a preop diagnosis is not necessary).
• To differentiate primary lung cancer vs. solitary lung metastasis from another prior cancer.

DO ORDER LUNG BIOPSY:
• Multiple PET positive nodules that not completely resectable but a diagnosis is needed.
• Apparent localized cancer and patient is not a surgical candidate (to have SBRT).
• A diagnosis is needed for neoadjuvant therapy (Pancoast tumor, clinical trial, etc.) and a lymph node biopsy (EBUS, EUS or mediastinoscopy) is not appropriate/feasible.
• Nodule with strong suspicion of granulomatous disease.
• A pneumonectomy will likely be required, although usually diagnosis is obtained by bronch.
CT-GUIDED NEEDLE BIOPSY: UNNECESSARY!

70-year-old female current smoker with emphysema and a 4.9 x 3.1 cm spiculated left upper lobe mass. No biopsy was needed before surgical resection of this obvious cancer. Surgical pathology: 4.0 cm adenocarcinoma with all lymph nodes negative, Stage IB.

PET Scan

Biopsy resulted in collapsed lung, hemoptysis, chest tube insertion and hospitalization.

**IMPRESSION:**
1. There is mild to moderate increased glucose metabolic activity in a 3.5 cm mass in the anterior left upper lobe which is highly suspicious for a primary lung malignancy. No evidence of metastatic mediastinal lymphadenopathy or distant metastatic disease is seen. A followup biopsy is recommended for further evaluation.
WHICH IS CANCER OR BENIGN?

BIOMARKERS MAY HELP WITH THIS DECISION

CT SCAN

PET SCAN

ANTIBIOTICS
3 MONTHS

Surgery

CT SCAN

PET SCAN

Adenocarcinoma
Stage IA
The Problem is the Health Care Providers that:

“Don’t Know They Don’t Know”

(Lack of Experience and Knowledge)
A clinic dedicated to evaluate and manage patients with pulmonary nodules for diagnosis of possible early stage, potentially-curable lung cancer.

Target providers for referrals: Internists, family practice, pulmonologists, oncologists, multi-specialty groups (FMC, FCS, etc.)

Target patients:
- Newly discovered indeterminant (no tissue diagnosis) lung nodules.
- Any age and sex.
- Clinic visit offered within one week of initial contact.
- Follow-up may be handled by virtual visits.

Initial Patient assessment:
- History & physical and review of all X-rays and lab work.
- Utilize the Mayo Clinic solitary pulmonary nodule malignancy risk calculator.
- Follow validated Fleischner Society Guidelines and NCCN Lung Cancer Guidelines.
LUNG NODULE CLINIC

- Create an evaluation and treatment plan for each patient.
- Order any appropriate imaging, biopsies and/or referral to a pulmonologist or thoracic surgeon.
- Manage the patient using a software program with regular, prompt feedback to referring provider.
- Reassure referring providers the lung nodule clinic will take full responsibility for evaluation/follow-up of their patient’s nodule.
- Reassure the referring provider that they continue to see their patient for all other health care needs.
- Nodule clinic patient population offers excellent research opportunities.
IMPORTANCE of the SURVEILLANCE CLINIC

- Second primary lung cancers are significant risk to lung cancer survivors.
- 4-6-fold risk of developing a second primary cancer after surgery for stage I.
- Of patients treated for lung cancer, a 2nd primary cancer is diagnosed 1-2% per year (incidence increases with time to >2%/year).
- Median time to diagnosis of second cancer 2.7 years.
- However, a second primary diagnosis 4 or more years later was more likely later stage (75%).
- “About 70% of patients in the NLST who developed second primary lung cancer currently smoked at the time of entry into the trial. Smoking cessation can help reduce patients’ risk of developing second primary lung cancers.”

PROGRAM OVERVIEW

Lung Cancer Early Detection Center (LEAD)
Dr. Lary Robinson

Three clinics dedicated to evaluate, detect & manage patients for early lung cancer

Lung Screening
Dr. Tawee Tanvetyanon
Haley Tolbert, MHA, CPH

Surveillance Program
Dr. Bob Keenan
Deanna Grubbs, PA-C

Lung Nodule Clinic
Dr. Lary Robinson
Sand Bryant, PA-C
CLINICAL RESEARCH OPPORTUNITIES

LUNG CANCER EARLY DETECTION CENTER (LEAD)
Biomarkers are defined as “any substance, structure or process measured in the body that will influence or predict outcome or disease.”
Blood test shows high accuracy in detecting stage I non-small cell lung cancer

Cherylle Goebel, Christopher L. Louden, Robert Mckenna Jr, Osita Onugha, Andrew Wachtel and Thomas Long

- **21 Biomarkers in Lung Cancer Detector Test 1 (LCDT1)**
- In 486 human plasma samples: 95.6% accuracy, 89.1% sensitivity, 97.7% specificity in detecting Stage I NSCLC on blind set.
- When only NSCLC cancers were analyzed, specificity 99.1%.
- Even with other cancer types are present, LCDT1 97.7% specific for stage I NSCLC.
NodifyXL2™

NODIFY XL2 TEST

Designed to Help Identify Patients with Likely Benign Lung Nodules

- **Clinical Risk Factors**
  - Location: 7.3%
  - Spiculation: 7.3%
  - Smoking History: 7.3%
  - Age: 18%
  - Nodule Size: 30%

- **Plasma Protein Levels Associated with Lung Cancer**
  - TGFβBP: 30%
  - C163A

- **Sensitivity**: 97%
- **NPV**: 98%

Reflected the median performance of Nodify XL2 test in the PANOPTIC study.
Patient: “Did you get it all, Doc?”

Surgeon: “I took out everything I could see.”

Unfortunately, what they heard is: “You’re cured!”

...however, that’s only true for some.
cT1cN0 (Stage IA3) Adenocarcinoma

- 76-year-old male former smoker (58 pk-yrs.), asymptomatic.
- Abnormal preop CXR.
- CT scan 2.9 cm LUL mass.
- PET positive SUV 18.5.
- PS 0
- PFTs mildly impaired (FEV₁ 81%)
- Stress test normal
- cT1cN0
- Surgery: LULobectomy
- Path: pT1cN0; lymphovascular invasion present.
- Estimated 5-year DFS: 66%
EARLY-STAGE LUNG CANCER IS STILL **DEADLY**

**40,000+** patients are diagnosed with early-stage non-squamous NSCLC in the U.S. annually\(^1\)

**20-50\%** of early-stage patients with NSCLC recur after surgical resection\(^2\)

**Recurrence** due to presence of occult distant metastases despite ‘early-stage’ diagnosis

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LUNG CANCER SURVIVAL IS JUST FAIR... EVEN AT EARLY STAGE

The majority of patients that recur do so within a year after surgical resection. Most of these recurrence events are due to distant metastasis.
### NCCN GUIDELINES FOR POSTOPERATIVE THERAPY

#### Post-Resection with Negative Surgical Margins

<table>
<thead>
<tr>
<th>Stage</th>
<th>Post-resection Treatment</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA (&lt;3cm)</td>
<td>Observe only</td>
<td>2A</td>
</tr>
<tr>
<td>IB (3-4 cm)</td>
<td>Observe or chemotherapy for high-risk patients</td>
<td>2A</td>
</tr>
<tr>
<td>IIA (4-5 cm)</td>
<td>Observe or chemotherapy for high-risk patients</td>
<td>2A</td>
</tr>
<tr>
<td>IIB (5-7 cm)</td>
<td>Chemotherapy</td>
<td>1</td>
</tr>
</tbody>
</table>

#### NCCN High Risk Features

- Poorly differentiated tumors
- Vascular invasion
- Wedge resection
- Tumors >4 cm
- Visceral pleural involvement
- Unknown lymph node status

“These factors independently may not be an indication and may be considered when determining treatment with adjuvant chemotherapy.”

DetermaRx is a 14-gene molecular classifier that stratifies patients into high-, intermediate-, or low-risk of disease recurrence. (FDA and Medicare approved)
post-resection, stage IA-IIA (node-negative) patients were prospectively stratified by DetermaRx.

- Test-identified **high-risk or intermediate-risk patients** who were treated with adjuvant platinum chemotherapy had 96.7% 5-year disease-free survival compared to 65.7% 5-year DFS for **high-risk patients** who did not receive chemotherapy.

- Test-identified **low-risk patients** had a 5-year DFS of 88.8%.

Log-rank $p=\ll 0.001$

Woodard, et al. 2020 IASLC World Lung Cancer Conference
CLINICAL RESEARCH STUDY TO COMBINE WITH LUNG NODULE CLINIC

- "USING BIOMARKERS FOR DIAGNOSIS, RISK STRATIFICATION OF POST-TREATMENT RECURRENCE AND LONG-TERM SURVEILLANCE OF LUNG CANCER" (Study supported by Foundation funds; DOD grant pending)

- Biomarkers are defined as "any substance, structure or process measured in the body that will influence or predict outcome or disease."

- Evaluate 3 key time points:
  - Initial Diagnosis of Nodule: Cancer or Benign
  - Risk Stratification for Recurrence after Surgery.
    - 15-50% of patients will have a cancer recurrence after a "curative" resection.
  - Long Term Surveillance for Cancer Recurrence or Second Primary Cancers.
Early Detection and Management of Resectable Stage I-III Lung Cancer

In a multi-disciplinary, case-based format, the speakers will discuss common presentations as well as screening, diagnosis and treatment pathways for patients diagnosed with stage I-III lung cancer as well as monitoring high risk patients for lung cancer.

Thursday, November 3, 2022

Season’s 52
204 Westshore Blvd., Tampa, FL 33609
Check in/Networking Reception: 6:00 – 6:30 PM
Program: 6:30 – 8:00 PM

Jacques Fontinha, MD, FACS, FRCSc(c)
Senior Member
Department of Thoracic and GI Oncology
Sobchak Head, M Idaho
Treatment & Research Center
Program Director, Robotic Thoracic Surgery Fellowship

Larry Robinson, MD
Senior Member
Cardiothoracic Surgeon
Medical Director for Lung Early Detection Center, Department of Thoracic Oncology

Stephen Rosenberg, MD, MS
Director of MRI Guided Radiation Therapy
Assistant Member, Department of Radiation Oncology

Michael Starfique, MD
Assistant Member
Medical Oncologist
Department of Thoracic Oncology

Registration is complimentary but required. Use this ink to register:
https://cvent.me/l5n3qP

For more questions, contact: Paula.Kiss@Moffitt.org

Provided By: USF Health

ACCREDITATION: This activity has been approved for AMA PRA Category 1 Credits™
QUESTIONS??