Keynote - Implementation of a High-Quality Lung Cancer Screening Program

David Tom Cooke, MD
Professor
UC Davis

Dr. David Tom Cooke is a Professor at the University of California, Davis School of Medicine. He is the founding Chief of the Division of General Thoracic Surgery, Director of the General Thoracic Surgery Robotics Program, the Vice Chair for Faculty Development and Wellness for the Department of Surgery, the Associate Director for the Office of Inclusivity, Diversity, Equity and Accessibility (IDEAL) and the Interim Physician-in-Chief, UC Davis NCI designated Comprehensive Cancer Center. Dr. Cooke specializes in the surgical treatment of malignant and benign lung and esophageal disease and is a national leader in robotic thoracic surgery. Dr. Cooke's research includes oncologic trials, surgical outcomes/health services research, patient-centered outcomes research, surgical education, medical social media, and public medical communication. He has authored over 100 peer-reviewed publications. He is president of the Thoracic Surgery Directors Association, a director of the American Board of Thoracic Surgery, a director of the Accreditation Council for Graduate Medical Education (ACGME), member of the American Surgical Association and an associate member of the American College of Surgeons Academy of Master Surgeon Educators. Dr. Cooke currently serves on the American Lung Association National Lung Cancer Expert Medical Advisory Panel. Dr. Cooke completed his cardiothoracic surgery training at the University of Michigan in Ann Arbor, general surgery residency at the Massachusetts General Hospital in Boston, medical school at Harvard Medical School and undergraduate at UC Berkeley.
Implementation of a High-Quality Lung Cancer Screening Program

California Thoracic Society Annual Educational Conference
March 8th, 2024

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Professor and Chief, Division of General Thoracic Surgery
Interim Physician-In-Chief, Comprehensive Cancer Center
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Disclosures

- **Bristol Meyers Squibb**
  - Speakers Honoraria

- **AMGEN and AstraZeneca**
  - Support for the UCLCC Screening & Prevention Taskforce
Lung cancer kills more Men AND Women...

Lung Cancer > Breast Cancer

Breast Cancer + Prostate Cancer + Colon Cancer
• Close to 238,000 people will be diagnosed with lung cancer this year, with the rate of new cases varying by state.
• Lung cancer has one of the lowest five-year survival rates because cases are often diagnosed at later stages, when the disease is less likely to be curable. The national average of people alive five years after a lung cancer diagnosis is 26.6%
• Nationally, only 26.6% of cases are diagnosed at an early stage.
### Menthol Cigarette Smokers

<table>
<thead>
<tr>
<th>Race and Ethnicity</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>African American</td>
<td>82.6%</td>
</tr>
<tr>
<td>Hispanic</td>
<td>32.0%</td>
</tr>
<tr>
<td>White</td>
<td>23.8%</td>
</tr>
</tbody>
</table>

among smokers 12 years of age and older, 2004 to 2008

Lung cancer is a leading cause of cancer mortality among AA populations

Rank (based on age-adj mortality rate) & % (of all cancer deaths) of top 5 cancer sites, 1990-2008

<table>
<thead>
<tr>
<th>Male (rank)</th>
<th>Asian Indian</th>
<th>Chinese</th>
<th>Filipino</th>
<th>Japanese</th>
<th>Korean</th>
<th>Vietnamese</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><strong>Lung 19.0%</strong></td>
<td>Lung 28.13%</td>
<td>Lung 30.7%</td>
<td>Lung 23.9%</td>
<td>Lung 22.8%</td>
<td>Lung 28.1%</td>
</tr>
<tr>
<td>2</td>
<td>Colorectal 8.3%</td>
<td>Liver 11.7%</td>
<td>Colorectal 10.8%</td>
<td>Colorectal 13.1%</td>
<td>Stomach 14.6%</td>
<td>Liver 22.3%</td>
</tr>
<tr>
<td>3</td>
<td>Prostate 8.1%</td>
<td>Colorectal 10.4%</td>
<td>Prostate 8.9%</td>
<td>Prostate 8.9%</td>
<td>Liver 12.9%</td>
<td>Colorectal 7.9%</td>
</tr>
<tr>
<td>4</td>
<td>Pancreas 7.0%</td>
<td>Stomach 6.5%</td>
<td>Liver 7.6%</td>
<td>Stomach 8.8%</td>
<td>Colorectal 11.0%</td>
<td>Stomach 6.5%</td>
</tr>
<tr>
<td>5</td>
<td>Leukemia 6.3%</td>
<td>Pancreas 5.9%</td>
<td>Pancreas 5.7%</td>
<td>Pancreas 8.4%</td>
<td>Pancreas 7.4%</td>
<td>Pancreas 4.4%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Female (rank)</th>
<th>Asian Indian</th>
<th>Chinese</th>
<th>Filipino</th>
<th>Japanese</th>
<th>Korean</th>
<th>Vietnamese</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Breast 19.8%</td>
<td><strong>Lung 22.2%</strong></td>
<td>Breast 19.5%</td>
<td>Lung 21.4%</td>
<td>Lung 18.5%</td>
<td>Lung 21.7%</td>
</tr>
<tr>
<td>2</td>
<td>Ovary 9.7%</td>
<td>Breast 11.8%</td>
<td><strong>Lung 18.1%</strong></td>
<td>Colorectal 12.9%</td>
<td>Stomach 11.6%</td>
<td>Breast 10.3%</td>
</tr>
<tr>
<td>3</td>
<td><strong>Lung 9.3%</strong></td>
<td>Colorectal 11.9%</td>
<td>Colorectal 9.0%</td>
<td>Breast 10.7%</td>
<td>Colorectal 11.4%</td>
<td>Colorectal 9.6%</td>
</tr>
<tr>
<td>4</td>
<td>Colorectal 6.8%</td>
<td>Pancreas 7.2%</td>
<td>Pancreas 6.7%</td>
<td>Pancreas 9.6%</td>
<td>Pancreas 8.2%</td>
<td>Liver 9.3%</td>
</tr>
<tr>
<td>5</td>
<td>Pancreas 5.9%</td>
<td>Stomach 5.4%</td>
<td>Ovary 6.0%</td>
<td>Stomach 6.5%</td>
<td>Liver 7.2%</td>
<td>Stomach 6.3%</td>
</tr>
</tbody>
</table>

# Cohort Description - Female Lung Cancer Cases (n=3867)

<table>
<thead>
<tr>
<th>Group</th>
<th>Cases (N)</th>
<th>Never</th>
<th>Ever</th>
<th>Missing</th>
</tr>
</thead>
<tbody>
<tr>
<td>AANHPI</td>
<td>613</td>
<td>38%</td>
<td></td>
<td>15%</td>
</tr>
<tr>
<td>NHPI</td>
<td>201</td>
<td></td>
<td>41%</td>
<td>14%</td>
</tr>
<tr>
<td>Native Hawaiian</td>
<td>160</td>
<td></td>
<td>14%</td>
<td>20%</td>
</tr>
<tr>
<td>Other Pacific Islander</td>
<td>41</td>
<td></td>
<td>20%</td>
<td>50%</td>
</tr>
<tr>
<td>Asian</td>
<td>412</td>
<td></td>
<td>50%</td>
<td>24%</td>
</tr>
<tr>
<td>Chinese</td>
<td>75</td>
<td></td>
<td>24%</td>
<td>79%</td>
</tr>
<tr>
<td>Filipina</td>
<td>80</td>
<td></td>
<td>53%</td>
<td>21%</td>
</tr>
<tr>
<td>Japanese</td>
<td>74</td>
<td></td>
<td>24%</td>
<td>79%</td>
</tr>
<tr>
<td>Other Asian (single grp)</td>
<td>67</td>
<td></td>
<td>53%</td>
<td>58%</td>
</tr>
<tr>
<td>Multiple Asian</td>
<td>116</td>
<td></td>
<td>53%</td>
<td>40%</td>
</tr>
<tr>
<td>Non-Hispanic White</td>
<td>1489</td>
<td>40%</td>
<td>14%</td>
<td>21%</td>
</tr>
<tr>
<td>Black</td>
<td>91</td>
<td>38%</td>
<td></td>
<td>14%</td>
</tr>
<tr>
<td>Hispanic</td>
<td>81</td>
<td></td>
<td>38%</td>
<td>14%</td>
</tr>
</tbody>
</table>

DeRouen, et al. CEBP, 2021
Compared with White patients, Black/African American patients were more likely to be diagnosed at late-stage disease. 

Late stage at diagnosis was examined for six screen-detectable cancers: female breast, cervical, colorectal, prostate, lung, and oropharyngeal cancers. A significantly higher percentage of Black/African American (vs. White) patients with lung (78.4 vs. 72.9 percent), and other cancers were diagnosed at late stage.
Decline in the death rate from Lung Cancer:

- Sped up from 3 percent per year during the 2008-2013 period to 5 percent annually for men for the following five-year period.
- For women, the decrease accelerated from 2 to almost 4 percent.
Cancer mortality rates among Black/African American men declined by 2.3 percent per year for all cancers combined.

Among Black/African American women, cancer mortality rates for all cancers combined declined as well, by 2.1 percent per year.
Why?
Why?

- **Population Health**
  - Prevention
    - Radon awareness
    - Tobacco Recovery and Prevention
  - Screening
- **Treatments**
  - Advances in Surgery
  - Stereotactic Body Radiotherapy
  - Precision Medicine
  - Immunotherapy
- **Patient Activation**
• Population Health
  – Prevention
    • Radon awareness
    • Tobacco Recovery and Prevent
  – Screening

• Treatments
  – Advances in Surgery
  – Stereotactic Body Radiotherapy
  – Precision Medicine
  – Immunotherapy

• Patient Activation
Lung Cancer Screening

UC Davis Comprehensive Lung Cancer Screening Program (CLSP)
Stage IV NSCLC

<5%

5 year Survival with Best Medical Management
Stage I NSCLC

>80%

5 year Survival After Surgery
Goal of Lung Cancer Screening

No Symptoms

Stage I
>80% 5 year Survival

Symptoms

Stage IV
<5% 5 year Survival
To determine whether screening with low-dose computed tomography (LDCT), as compared with chest radiography (CXR), reduces mortality from lung cancer among high-risk persons

- Eligible participants
  - 55-74 years old
  - History of cigarette smoking of at least 30 pack-years
    - If former smoker, had quit within the previous 15 years
National Lung Screening Trial: NLST

≥ 30 Pack years
Active Smoker or
Quit > 15 years
Aged 55-74
+50,000

Randomization

Low Dose CT
CXR

T0 T1 T2 7
T0 T1 T2 7

Years
### National Lung Screening Trial Results: Stage Shift

<table>
<thead>
<tr>
<th>Stage</th>
<th>Positive Screen</th>
<th>AJCC - NSCLC</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>63%</td>
<td>24%</td>
</tr>
<tr>
<td>II</td>
<td>7%</td>
<td>6%</td>
</tr>
<tr>
<td>IIIA</td>
<td>9%</td>
<td>23%</td>
</tr>
<tr>
<td>IIIB</td>
<td>8%</td>
<td>44%</td>
</tr>
<tr>
<td>IV</td>
<td>13%</td>
<td></td>
</tr>
<tr>
<td>Early (Stages I – II)</td>
<td>70% *</td>
<td>30%</td>
</tr>
<tr>
<td>Late (Stages III- IV)</td>
<td>30%</td>
<td>70%</td>
</tr>
</tbody>
</table>

* = for years T0-T3
20% reduction in lung-cancer specific mortality with LDCT
6.7% reduction in overall mortality with LDCT
NELSON - trial  ISRCTN 63545820

- Randomized Controlled Trial
- Recruitment through population-based registries
- CT screening vs. no screening
- Different screening intervals
- Volume & Volume Doubling Time of nodules
- Central reading of CT images
- Expert causes of death committee &
- Follow up through national registries

Trial, initially powered (80%) for high risk males, to detect a lung cancer mortality reduction of ≥ 25% at 10 years after randomization (individual FU)

And includes a small subgroup of women (16%)

Harry J. de Koning, Erasmus MC, Public Health Rotterdam

Presented at the 2018 WCLC
Lung Cancer Stage (males NL) 7th TNM

Cancer Registry NL - Control Arm - Screen Arm

up to December 2011

Yousaf-Khan et al., in preparation

Harry J. de Koning, Erasmus MC, Public Health Rotterdam
### NLST & NELSON: Lung cancer CT screening Mortality data

<table>
<thead>
<tr>
<th>Male v Female Ratio</th>
<th>Percent LC Mortality Decrease</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Trial</td>
</tr>
<tr>
<td>NLST+</td>
<td></td>
</tr>
<tr>
<td>NELSON</td>
<td></td>
</tr>
<tr>
<td></td>
<td>NLST*</td>
</tr>
<tr>
<td></td>
<td>NELSON**</td>
</tr>
</tbody>
</table>


**Effects of Volume CT Lung Cancer Screening: Mortality Results of the NELSON Randomised-Controlled Population Based Trial De Koning et al 2018**
Black/AA smokers have a higher risk of lung cancer and at lower levels of smoking intensity than White smokers\textsuperscript{1}

Latino/Hispanics who smoke accumulate fewer pack-years than White smokers\textsuperscript{2,3}

Women accumulate fewer pack-years than men\textsuperscript{4}

3. Tob Induc Dis. 2016;14:23
Southern Community Cohort Study participants found that 17% of Black/AAs who smoke were eligible for lung cancer screening based on the 2013 USPSTF eligibility criteria compared with 31% of White smokers.

Among those diagnosed with lung cancer, only 32% of Black/AA persons who smoke were eligible for screening compared to 56% of White smokers.

JAMA Oncol. 2019;5(9):1318-1324.
- African-Americans are more likely to die from Lung Cancer than White Americans. But African-Americans are screened less.

- However, African-Americans may have a higher incidence of positive screening exams.

- **When detected by screening, AA exhibit the same survival advantage and lower stage detection as their white counterparts.**

USPSTF New Recommendations

**What does the USPSTF recommend?**

Adults aged 50 to 80 years who have a 20 pack-year smoking history and 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 limits life expectancy or the ability to have lung surgery.

*Grade: B*

**How often?**

- Screen every year with low-dose CT.
- Stop screening once a person has not smoked for 15 years or has a health problem that limits life expectancy or the ability to have lung surgery.
New criteria would increase the relative percentage of persons eligible for screening by 87% overall
- 78% in White adults, 107% Black adults, and 112% in Hispanic adults compared with 2013 USPSTF criteria.

Increase the relative percentage of persons eligible for screening by 80% in men and by 96% in women.

Agency for Healthcare Research and Quality; 2021.
AHRQ publication 20-05266-EF-2.
Figure 1. U.S. Cancer Screening Rates

- ALA survey of over 1,000 people eligible for LCS, only 15% aware that LCS is an essential health benefit and covered by most healthcare plans with no or minimal costs.

- The top reason why not screened their doctor never recommended it.

- 3% of women cited lung cancer as a relevant health issue.

Rates of Physician-Patient Discussions About Lung Cancer Screening Very Low and Declining (American Association for Cancer Research)

- Prevalence of physician-patient discussions about lung cancer screening

**In 2012**
- 6.7% in the general population
- 12% among current smokers

**In 2017**
- 4.3% in the general population
- 8.7% among current smokers
Screening for High Risk:

- In California, 0.7% of those at high risk were screened, which was significantly lower than the national rate of 4.5%.
- It ranks 51st among all states, placing it in the bottom tier.
- Actual screening rates may be higher in states with large, regional managed care providers that did not share screening data.
New Measure Coming for Lung Cancer Screening

November 15, 2022 · Andy Reynolds

Description: The Healthcare Effectiveness Data and Information Set (HEDIS) is a tool used by more than 90 percent of U.S. health plans to measure performance on important dimensions of care and service. More than 190 million people are enrolled in health plans that report quality results using HEDIS. Since 2008, HEDIS has also been available for use by medical providers and practices. Because so many health plans use HEDIS and because the measures are so specifically defined, HEDIS can be used to make comparisons among plans. To ensure that HEDIS stays current, the National Committee for Quality Assurance (NCQA) has established a process to evolve the measurement set each year through its Committee on Performance Measurement.
Targeted Approach with Quality Goals

NCQA will look at how routine information shared in health encounters can help identify individuals who should get a lung cancer screening. Once implemented, this measure will help payers and providers steer a greater number of high-risk patients to lung cancer screenings, facilitate early detection, and ultimately reduce the number of deaths attributed to lung cancer.

We expect to develop the measure by the end of 2024.
- **Population Health**
  - Prevention
    - Radon awareness
    - Tobacco Recovery and Prevent
  - Screening

- **Treatments**
  - Advances in Surgery
  - Stereotactic Body Radiotherapy
  - Precision Medicine
  - Immunotherapy

- **Patient Activation**
IF YOU SMOKED:
This new lung cancer screening could save your life

SavedByTheScan.org
Hi Dr. Cooke,

As an African American female lung cancer survivor, I wanted to thank you for your article in Cure. I found it really informative and wish I had seen it before I was diagnosed. I’m actually one of the lucky ones. I saw the American Lung Association billboard on the side of Highway 880 as I drove home to Fremont from my job in San Jose. I’ll always say that billboard saved my life because it made me aware of such a thing as a low dose CT scan. Being stuck in traffic, I read that early detection is important.

I won’t go into how my PCP refused to order the test at first because she concluded that I “didn’t meet the criteria”. Suffice it to say “I persisted” and it saved my life. Although your interview was good, as a patient, I wish more doctors would mention that fear and stigma are just as much a barrier to getting screened and treated as a compromised health care system. I think we have to get people to realize and understand that early detection is key. Thank you for everything that you do.
Educating the Next Generation
Educating the Next Generation

AMERICAN LUNG CANCER SCREENING INITIATIVE

UC BERKELEY
UC DAVIS
UC IRVINE
UC LOS ANGELES
Patient Centered Outcomes Research
Direct Patient Contact

Eric Wai Chak, M.D., M.P.H.

Electronic Population Health Tools Enhance Preventive Care for Older Adults
Eric W. Chak, MD, MPH, Elizabeth Cortez-Toledo, MA, Randy Luna, BS, Scott MacDonald, MD, Susan L. Stewart, PhD, David T. Cooke, MD, Moon S. Chen Jr., PhD, MPH

Title: Enhancing Electronic Health Systems to Decrease the Burden of Colon Cancer, Lung Cancer, Obesity, Vaccine-Preventable Illness, and Liver Cancer (CLOVER)
Project: GRANT12965631 (Chak)
Agency: National Institutes of Health

<table>
<thead>
<tr>
<th>CLOVER Parameter</th>
<th>Outcome Measure</th>
<th>#At-Risk</th>
<th>Baseline Adherence (Prior to August 2020)</th>
<th>CLOVER Adherence (August 2020-May 2021)</th>
<th>Relative Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung Cancer</td>
<td>CT Lung Completion</td>
<td>280</td>
<td>6%</td>
<td>18.9%</td>
<td>315%</td>
</tr>
</tbody>
</table>
Dr. Chak's CLOVER Lung Screening component

- Scott MacDonald's team (Randy Luna) created custom Epic Workbench report
- Report contains all Smokers at Carmichael, for example, with upcoming appointments
- Staff member (pre-visit planner PVP) reaches out to patients with upcoming appointments with PCP (1-2 weeks in advance) to discuss and verify smoking History prior to upcoming appointment and updates smoking Hx in Epic
- Report is not granular enough to meet all the specific requirements to identify if the patient meets screening criteria and reason for staff needing to call pt to identify missing information.
- Once the staff member speaks to patient and verifies correct history and they meet criteria they are scheduled to either have a phone call by Dr. Chak or sent to the Cancer center Lung Ca screening staff for counselling/informational session
- If patient agrees to screening Dr. Chak places CT order. The PVP follows up to make sure the CT is completed, acts as a patient navigator.
- Results go to PCP and ordering provider.
- Results are followed up—PCP always involved.

Eric W Chak
I'll add here that it is the smoking history in the EHR that is usually inaccurate. It is not regularly updated so we are trying to update/correct it to ensure that are truly LCS candidates.

Eric W Chak
The results go to the ordering provider (may not be PCP), but we always forward result to PCP to keep them in the loop.
Strategic pillars

1. Develop a Regional System of Care
2. Deliver Exceptional Patient and Care Team Experiences
3. Advance Health Equity and Address Disparities
4. Develop and Grow Integrated, Patient-Centric Service Lines
What is an Integrated Service Line?

- An Integrated Service Line (ISL) is the organization of multidisciplinary clinical programs into an integrated care continuum around a population or disease state.

- Service lines reach beyond the traditional departmental structure in that the accountability and responsibility for optimizing clinical services, non-clinical operations, and capital and operational budgets reside with service line leadership (may be matrixed with clinical departments and operations).
Why Build a Patient-Centered Service Line?

- A service line structure is intended to provide a more integrated and focused patient experience while contributing to clinical efficiencies, clinical research, performance improvement, and expansion and integration of clinical areas with high market demand.
James gets a lung cancer screening CT and finds an early staged lung cancer.

Charles’ incidental lung cancer is diagnosed at an early stage and cured.

Linda and her family are happy with the speed of her diagnosis & ease of her care. They want to give back to UC Davis.

Sarah’s doctor is amazed how fast her referrals get into UC Davis.
This visual is designed to highlight areas of friction patients faced in their experiences. These colors correspond to report details and highlight areas of emotional stress specific to their experiences.
Lung Cancer ISL Care Continuum

Community-Based Care/Population Health
- Home
- PCP/ Specialist Office (e.g. pulmonology)

Initial Priority Areas
- NEW: Digital Davis AI
- NEW: Mobile Screening
- NEW: Al Lung Nodule Detection
- NEW: Second Opinion Program

Outpatient
- NEW: Comprehensive Patient Navigation /Care Coordination
- Lung Cancer - Lung Nodule Early Detection (Lung-LEAD) Clinic
  - Year 0-2 PCN
  - Year 3+ Community (mobile)
- Diagnostic Imaging/Pathology
- Cancer Center: Med Onc, Rad Onc, Interventional Pulmonary, Thoracic surgery
- Infusion/Clinical Trials
- Screening for clinical trials
- Infusion/Clinical Trials
- Radiation
- Palliative Care

Inpatient
- Surgery
- NEW: Surveillance/Survivorship Clinic
  - Care transition out of CC

Post-Acute
- Palliative Care

Integrated Service Lines Program
- Screening - Diagnosis
- Treatment
- Survivorship
Initial Priority Areas

1. Community-Based Care/Population Health
   - Lung Cancer - Lung Nodule Early Detection (Lung-LEAD) Clinic
     Increase the LDCT screening rate of patients, centralize management of incidental lung nodules, encourage active surveillance of LDCT screening patients and incidental findings, improve upon smoking cessation efforts.

2. Outpatient
   - Comprehensive Patient Navigation – Care Coordination
     Align and expedite testing and results to ensure meaningful treating provider and accelerated path from new patient referral, initiation of treatment, and navigation of care. Focused on patients diagnosed with lung cancer, and patients highly suspected of having lung cancer.

3. Post-Acute
   - Surveillance/Survivorship Clinic
     Transition long-term follow-up/surveillance patients from the treating provider schedule to APP, opening provider template to new patient appointments and expand access to the Cancer Center.
1. Patient Review Criteria
   - Established patients with an upcoming PCP appointment with UCDH will be flagged for review if they are aged 50-80 (77 Medicare) and have a history of smoking (as reported in EPIC)

2. Dedicated Lung Cancer ISL Care Navigators
   - Our Lung Cancer ISL Care Navigators will proactively engage with patients to update smoking history, determine patients for lung cancer screening eligibility (age, pack year history, current smoker/quit date), and schedule appointments with the Lung ISL APP in the Lung Early Detection Clinic.

3. Dedicated Lung Cancer ISL APPs
   - The Lung Cancer ISL APP will conduct a shared-decision making (SDM) visit and order a Low Dose CT (LDCT) for eligible patients who want to proceed with screening.
   - The Lung Cancer ISL APP will complete a follow-up visit with all patients to communicate results, ongoing follow-up (immediate or annual), and will order additional tests / referrals as needed based standardized clinical criteria

4. Communication and Results
   - The patient’s primary care physician will be cc’d on the Lung Cancer ISL APP provider chart note if the patient meets with the Lung Cancer ISL APP
   - If the LDCT shows significant screening results, these will be directly communicated to the patient’s primary care physician
Workflow: Lung - LEAD Clinic (Comprehensive Lung Cancer Screening Program)

Patient Review Criteria
- Established patients with an upcoming PCP appointment with UCDH are flagged for review if they are aged 50-80 (77 Medicare) and have a history of smoking (as reported in EPIC)

Dedicated Lung Cancer ISL Care Navigators
- Our Lung Cancer ISL Care Navigators proactively engage with patients to update smoking history, determine patients for lung cancer screening eligibility (age, pack year history, current smoker/quit date), and schedule appointments with the Lung ISL APP in the Lung – LEAD Clinic.

LVNs
- Terra Cruz
- Keilani Guevarra
- Ananeiri Medina
- Maria Quadra
- Christine Ramil-Francisco

Dedicated Lung Cancer ISL APPs

- The Lung Cancer ISL APP conduct a shared-decision making (SDM) visit and order a Low Dose CT (LDCT) for eligible patients who want to proceed with screening.
- The Lung Cancer ISL APP complete a follow-up visit with all patients to communicate results, ongoing follow-up (immediate or annual), and order additional tests / referrals as needed based standardized clinical criteria.

APPs
- Paola Velosa, NP
- Jennifer Aldred, NP
- Jaspreet Dhillon, NP
Workflow: Suspected Lung Cancer, Lung-LEAD Clinic patient w/ Findings

**Comprehensive Patient Navigation/Care Coordination**

- The patient’s primary care physician is cc’d on the Lung Cancer ISL APP provider chart note if the patient meets with the Lung Cancer ISL APP
- If the LDCT shows significant screening results, these are directly communicated to the patient’s primary care physician
- Highly suspicious nodules and suspected masses are managed by the Lung Cancer ISL and its Comprehensive Patient Navigation Team, including DGIM clinician, Nurse Coordinator/Patient Navigator and MA II Care Navigator.

Erin Noren, MD, MS  
Assistant Director,  
DGIM Cancer Center Initiatives

Angela Mackie, RN, Nurse Coordinator/Patient Navigator

Shalini Paul, MA II Navigator
## Lung - LEAD Clinic Results

<table>
<thead>
<tr>
<th>To Date</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calls Made</td>
<td>1147</td>
</tr>
<tr>
<td>Patients Called</td>
<td>721</td>
</tr>
<tr>
<td>Agree to SDM Appointment &amp; Screening</td>
<td>169 (48.29%)</td>
</tr>
</tbody>
</table>
As of 10/31/2023

Current smokers with LCS (CPT 71271) in the last 12 months

- 120 (17.5%)

Former smokers with LCS (CPT 71271) in the last 12 months

- 227 (19.3%)
Take Lessons Learned and Disseminate Statewide
University of California Lung Cancer Consortium (UCLCC)

- 5 NCI-designated comprehensive cancer centers
- 25 affiliated community clinics
- 20% CA lung cancer care
Specific Aims – Strategic Plan

UCLCC SCREENING INITIATIVE

Cultivating best practices

Addressing access

Facilitating research

Supporting cessation
• 5 Campus Screening and Tobacco Cessation Dashboard Project
• California Digital Health Project
Take the Lung Cancer Screening Questions

Two minutes could save your life. Find out if you should screen for lung cancer through UC Screen CA.

Start UC Screen CA  Learn More →

https://www.ucscreenca.org
Summary

- Lung cancer screening saves lives
- Eligible patients are not being screened
- Intentional efforts can move the needle to increase screening
Patient Promise: **Patients are at the center of everything we do.**

Thank you UC Davis. You saved my Dad, our Papa!
Advances in Smoking Cessation

Elisa Tong, MD, MA
Professor
UC Davis

Elisa Tong is a Professor of Internal Medicine at UC Davis. Her research focus is in tobacco cessation and policy, with special interests in cancer and population health. She completed her medical degree at Stanford University, residency training at Santa Clara Valley Medical Center, and research fellowship at UCSF. She is the Principal Investigator for CA Quits and Director for the Tobacco Cessation Policy Research Center.
ADVANCING TOBACCO CESSATION TREATMENT

Elisa Tong, MD, MA
Director, Tobacco Cessation Policy Research Center
Medical Director, Stop Tobacco Program, UC Davis Comprehensive Cancer Center
Professor of Internal Medicine, UC Davis
RELEVANT FINANCIAL DISCLOSURES

- I do not have relationships with ACCME defined ineligible companies

- I WILL NOT discuss off-label use and/or investigational use of any drugs or devices.

- Funding:
  - “CA Quits”, California Tobacco Prevention Program, California Department of Public Health 22-10340
  - “Tobacco Cessation Policy Research Center”, Tobacco-Related Disease Research Program T33PC6880
OBJECTIVES

- Understand the tobacco industry impact on public health
- Describe a framework for tobacco assessment and treatment
- Identify strategies for improving tobacco assessment and treatment
LEADING CAUSE OF DEATH AND DISEASE

Annual Deaths from Smoking, United States

- Lung Cancer: 137,989 (29%)
- Heart Disease: 158,750 (33%)
- Chronic Obstructive Pulmonary Disease: 100,600 (21%)
- Other Cancers: 36,000 (7%)
- Other Diagnoses: 31,681 (7%)
- Stroke: 15,300 (3%)

More Than 480,000 US Deaths Every Year Are From Cigarette Smoking


NEW PRODUCTS, NEW PROBLEMS

Vapes are sold in a variety of shapes and sizes.

THE E-CIGARETTE AEROSOL THAT USERS BREATHE FROM THE DEVICE AND EXHALE CAN CONTAIN HARMFUL AND POTENTIALLY HARMFUL SUBSTANCES:

New Nicotine Salts

Nicotine salts, which have a lower pH than free base nicotine, allow particularly high levels of nicotine to be inhaled more easily and with less irritation to the throat than freebase nicotine.

VAPING IS A YOUTH EPIDEMIC

“We must take action now to protect the health of our nation’s young people.”

— U.S. Surgeon General

Outbreak of Lung Injury Associated with E-Cigarette Use, or Vaping
BIOLOGICAL EFFECTS

Potential for release of pulmonary toxic ketene from vaping pyrolysis of vitamin E acetate

RESEARCH ARTICLE: Electronic Cigarettes: Not All Good News?
Cinnamaldehyde in flavored e-cigarette liquids temporarily suppresses bronchial epithelial cell ciliary motility by dysregulation of mitochondrial function

Risk Analysis for the Carcinogen Pulegone in Mint- and Menthol-Flavored e-Cigarettes and Smokeless Tobacco Products

September 16, 2019

CALIFORNIA: 3.2 MILLION TOBACCO USERS

Figure 3. Number of adults ≥18 years who reported current tobacco use—California Health Interview Survey, 2020-21

Tobacco use includes cigarettes, cigars, hookah, little cigars or cigarillos, smokeless tobacco products, or vapes. Racial groups include only non-Hispanic or Latino of a single race unless otherwise noted. Hispanic or Latino includes all racial groups. See Additional Notes section for more information.


TOBACCO USE = A HEALTH EQUITY ISSUE

African American/Black
There are up to 10 times more tobacco ads in African American/Black neighborhoods than in others.

American Indian
The tobacco industry appropriates American Indian cultures in marketing, using valued traditions to promote tobacco use.

Hispanic/Latino
Big Tobacco gave $75,000 to the Hispanic American Chamber of Commerce to mail 92,000 letters urging businesses to protest tobacco tax increases.

Asian/Pacific Islander
A Tobacco executive stated that Asian American populations would be a profitable target due to “this community being generally predisposed toward smoking.”

Low-income
Big Tobacco targeted children living in low-income housing projects by handing out free packs of cigarettes in the 50s.

LGBTQ
In 1995, a tobacco company created a targeted marketing plan for Lesbian, Gay, Bisexual, Transgender, Queer (LGBTQ) communities called “Project SCUM”.

People with Mental Challenges
Big Tobacco promoted cigarettes as a medicinal substance in behavioral health treatment facilities.

Rural Communities
Big Tobacco warps rural masculine ideals by depicting rugged images of cowboys, hunters, and racecar drivers in their advertising, making people living in rural communities some of Big Tobacco's best customers.

https://tobaccofreeca.com/story-of-inequity/
HARM TO NONSMOKERS & ENVIRONMENT

The U.S. Surgeon General has concluded that breathing even a little secondhand smoke poses a risk to your health.

Scientific evidence indicates that there is no risk-free level of exposure to secondhand smoke.

The U.S. Surgeon General Concluded that Aerosol from E-Cigarettes Can Contain Harmful Substances

Secondhand smoke and the harmful chemicals in it are known causes of Sudden Infant Death Syndrome, respiratory infections, ear infections, and asthma attacks in infants and children. They are also known causes of heart disease, stroke, and lung cancer in adult non-smokers.
QUITTING HAS IMMEDIATE HEALTH BENEFITS

What Happens When You Quit Smoking?

- Carbon monoxide levels return to normal
- Nerve endings begin to regenerate – You can smell and taste better
- Lung function begins to improve
- Coughing and shortness of breath decrease
- Risk of stroke decreases to that of a non-smoker
- Risk of coronary heart disease is half of a smoker's risk
- Risk of lung cancer is about half of a smoker’s risk

Smoking Cessation
A Report of the Surgeon General

U.S. Department of Health and Human Services

www.cdc.gov/tobacco/sgr/2020-smoking-cessation/index.html

https://smokefree.gov
OBJECTIVES

- Understand the tobacco industry impact on public health
- Describe a framework for tobacco assessment and treatment
- Identify strategies for improving tobacco assessment and treatment
STRONG EVIDENCE FOR TOBACCO TREATMENT

[Image of counseling and medications]

THE FIVE A’S → ASK ADVISE REFER

ASK
about tobacco USE and EXPOSURE

ADVISE
tobacco users to QUIT

REFER
to quitline or other resource

ASSESS
READINESS to make a quit attempt

ASSIST
with the QUIT ATTEMPT

ARRANGE
FOLLOW-UP care

Adapted from rxforchange.ucsf.edu
ASK: “HAVE YOU EVER USED TOBACCO OR NICOTINE PRODUCTS?” (CURRENT=PAST MONTH)

SMOKING

SMOKELESS

ECIGS or VAPES

*Now included in the CMS eCQI Tobacco quality metric

“Do you use nicotine, cannabis (THC, CBD), or flavors?”

CA Quits; Images: CDC, FDA, California Youth Advocacy Network
If you ask: “Do you smoke now?”
Patient answers: “No” → Former smoker?
Actually, nearly 1.5 million “Former Smokers” may be misclassified by asking this way and are actually “Current Tobacco Users”
- About 1 in 5 “Former Smokers” had recent tobacco use past 5 days or higher cotinine
- 53% of Former Smokers without recent tobacco use had recent exposure by cotinine
ASSIST: CESSATION MEDICATIONS

1 mg nicotine ~ 1 cigarette
20 cigarettes in 1 pack
1 smokeless can/week ~ 1 pack

Dose higher for “eye-opener” use (1st 5 min)

Combination Nicotine
Long-acting patch (7, 14, 21 mg)
Short-acting lozenge/gum (2 or 4 mg)

Rxforchange.ucsf.edu; veterans.smokefree.gov/tools-tips-vet/quit-for-good-with-nrt
REFER: “I’M GOING TO HAVE OUR FREE STATE QUITLINE CALL YOU”

Web-based referral: kickitca.org/patient-referral
Counseling doubles long-term abstinence rates (12 months)
Referred UC patients who completed intake (n=4264)

- 46% non-white
- 59% Medicaid
- 59% chronic disease
- 49% behavioral health condition

Quit rate of random sample
- 13% at 7-month follow-up
OBJECTIVES

- Understand the tobacco industry impact on public health
- Describe framework for tobacco assessment and treatment
- Identify strategies for improving tobacco assessment and treatment
QUALITY METRIC: TOBACCO

Non-users* + Current users

Clinic patients seen past year

1) % Patients Assessed

2) % Current Users Counseled

3) % Non-users* Assessed + Current Users Counseled
(Reflects the Non-user majority)

*Non-users = Never Users + Former Users
ecqi.healthit.gov/ecqm/ec/2024/cms0138v12

NCQA Quality Metric for Lung Cancer Screening (in process, late 2024)
• Free nicotine patch message got >6x more engagement than free help
  • Health messaging no difference

• 13,000 Californians got free nicotine patches mailed home during COVID shutdown
Among Californians diagnosed with 12 tobacco-related cancers (2014-2019), nearly 70,000 are current users (Maguire et al. *JAMA Network Open* 2023).

- NCI Cancer Center Cessation Initiative (3 of 5 UC, Stanford, City of Hope, USC)
- Commission on Cancer’s “Just ASK” and “Beyond ASK” tobacco QI projects
Mission

• Build capacity for health care access
• Promote excellence in health care delivery
• Facilitate health care engagement
• Achieve health plan coverage equity
To save African American lives, flavored tobacco ban must include menthol cigarettes

By David Tom Cooke and Phillip Gardner, Special to The Sacramento Bee
Updated March 14, 2019 12:15 PM

Join the Fight Against Underage Vaping

A new California law makes it illegal to sell most flavored tobacco, including vapes and menthol cigarettes, protecting our kids from a lifetime of deadly addiction.

LEARN MORE AT UNDO.ORG
GET FREE QUITTING SUPPORT AT KICKITCA.ORG

©2017 California Department of Public Health

Tobacco Cessation
Policy Research Center

tcpc.ucdavis.edu
SUMMARY

- The tobacco industry has new products, new problems
- Ask about tobacco and nicotine use
- Assist with FDA-approved cessation medications
- Refer to quitline or tobacco treatment program
- Tobacco assessment & treatment is a quality measure
- Engage by sharing your voice
**Multidisciplinary Approach to Lung Cancer**

Justine Ko, MD  
**Fellow**  
UC San Francisco-Fresno

Dr. Justine Ko received her medical degree from the Keck School of Medicine of USC. She completed her internal medicine residency at USC and was awarded resident of the year. Currently, she is a second year fellow at the UCSF-Fresno Pulmonary and Critical Care Fellowship Program. She has focused her education and research in interventional pulmonology under the mentorship of Dr. Pravachan Hegde. She will be applying for a fellowship position in interventional pulmonology this coming cycle.

David Tom Cooke, MD  
**Professor**  
UC Davis

Dr. David Tom Cooke is a Professor at the University of California, Davis School of Medicine. He is the founding Chief of the Division of General Thoracic Surgery, Director of the General Thoracic Surgery Robotics Program, the Vice Chair for Faculty Development and Wellness for the Department of Surgery, the Associate Director for the Office of Inclusivity, Diversity, Equity and Accessibility (IDEAL) and the Interim Physician-in-Chief, UC Davis NCI designated Comprehensive Cancer Center. Dr. Cooke specializes in the surgical treatment of malignant and benign lung and esophageal disease and is a national leader in robotic thoracic surgery. Dr. Cooke’s research includes oncologic trials, surgical outcomes/health services research, patient-centered outcomes research, surgical education, medical social media, and public medical communication. He has authored over 100 peer-reviewed publications. He is president of the Thoracic Surgery Directors Association, a director of the American Board of Thoracic Surgery, a director of the Accreditation Council for Graduate Medical Education (ACGME), member of the American Surgical Association and an associate member of the American College of Surgeons Academy of Master Surgeon Educators. Dr. Cooke currently serves on the American Lung Association National Lung Cancer Expert Medical Advisory Panel. Dr. Cooke completed his cardiothoracic surgery training at the University of Michigan in Ann Arbor, general surgery residency at the Massachusetts General Hospital in Boston, medical school at Harvard Medical School and undergraduate at UC Berkeley.
Elisa Tong, MD, MA
Professor
UC Davis

Elisa Tong is a Professor of Internal Medicine at UC Davis. Her research focus is in tobacco cessation and policy, with special interests in cancer and population health. She completed her medical degree at Stanford University, residency training at Santa Clara Valley Medical Center, and research fellowship at UCSF. She is the Principal Investigator for CA Quits and Director for the Tobacco Cessation Policy Research Center.

Brian Shaller, MD
Assistant Professor
Stanford

Brian Shaller is a Clinical Assistant Professor in the Division of Pulmonary, Allergy & Critical Care Medicine at Stanford University. He trained in Interventional Pulmonology at the Cleveland Clinic and helped establish Stanford’s Interventional Pulmonology fellowship program in 2022, for which he currently serves as Associate Program Director. Dr. Shaller's clinical and academic interests include advanced diagnostics for lung nodules, endoscopic management of central airway diseases, and procedural education.
Multidisciplinary Approach to Lung Cancer

California Thoracic Society
Friday, March 8, 2024

Brian Shaller, MD
David Tom Cooke, MD, FACS
Elisa Tong, MD, MA
Justine Ko, MD, MPH
COI/Disclosures

None
A 71 yo female is found to have an incidental nodule in the LLL during imaging for abdominal pain. Dedicated chest imaging is obtained and there is a 1.7 x 2.3 cm nodule with no hilar or mediastinal lymphadenopathy with no other nodules seen on imaging. Comparison to prior scan from 7 months prior show that there has been interval increase in size.

She is an active smoker and has a >20 pack year smoking history.
Case 1 Imaging

1.7 x 2.3 cm nodule in the left lower lobe
### Fleischner Society 2017 Guidelines for Management of Incidentally Detected Pulmonary Nodules in Adults (Radiology)

#### A: Solid Nodules*

<table>
<thead>
<tr>
<th>Nodule Type</th>
<th>Size</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;6 mm (&lt;100 mm³)</td>
<td>6–8 mm (100–250 mm³) &gt;8 mm (&gt;250 mm³)</td>
</tr>
<tr>
<td>Single</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low risk†</td>
<td>No routine follow-up</td>
<td>CT at 6–12 months, then consider CT at 18–24 months</td>
</tr>
<tr>
<td>High risk†</td>
<td>Optional CT at 12 months</td>
<td>CT at 6–12 months, then CT at 18–24 months</td>
</tr>
<tr>
<td>Multiple</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low risk†</td>
<td>No routine follow-up</td>
<td>CT at 3–6 months, then consider CT at 18–24 months</td>
</tr>
<tr>
<td>High risk†</td>
<td>Optional CT at 12 months</td>
<td>CT at 3–6 months, then at 18–24 months</td>
</tr>
</tbody>
</table>

Note.—These recommendations do not apply to lung cancer screening, patients with immunosuppression, or patients with known primary cancer.

* Dimensions are average of long and short axes, rounded to the nearest millimeter.

† Consider all relevant risk factors (see Risk Factors).
Question for Dr. Tong

- How does this patient’s smoking history change your approach to management?
Question for Dr. Shaller

- Who does the biopsy – IR or IP?
Question for Dr. Cooke

- When is empiric surgical resection appropriate for both diagnosis and treatment?
Case 1 Outcome

- Patient received a CT guided biopsy of the LLL nodule and was found to have squamous cell carcinoma of the lung
- Lymph node biopsies did not show hilar or mediastinal disease
- Due to her comorbidities, surgery was not offered
- She is currently seeing radiation oncology with plans for definitive SBRT with Cyberknife

https://www.pathologyoutlines.com/topic/lungtumorscc.html
Case 2

A 69 yo female with GOLD 1A COPD and 75 pack year smoking history has multiple subsolid lesions in her right lung. Her nodules were first detected on low dose CT in 2019 and have been slowly growing through 2023.
Classification and CT Appearance of Pulmonary Nodules

Pulmonary nodule

- Solid
- Sub-solid nodule (SSN)
  - Part-solid nodule (PSN)
  - Pure ground glass nodule (pGGN)

https://doi.org/10.1136/thoraxjnl-2015-207221
### B: Subsolid Nodules*

<table>
<thead>
<tr>
<th>Nodule Type</th>
<th>Size</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ground glass</td>
<td>No routine follow-up</td>
<td>CT at 6–12 months to confirm persistence, then CT every 2 years until 5 years</td>
</tr>
<tr>
<td>Part solid</td>
<td>No routine follow-up</td>
<td>CT at 3–6 months to confirm persistence. If unchanged and solid component remains &lt;6 mm, annual CT should be performed for 5 years.</td>
</tr>
<tr>
<td>Multiple</td>
<td>CT at 3–6 months. If stable, consider CT at 2 and 4 years.</td>
<td>CT at 3–6 months. Subsequent management based on the most suspicious nodule(s).</td>
</tr>
</tbody>
</table>

Note.—These recommendations do not apply to lung cancer screening, patients with immunosuppression, or patients with known primary cancer.

* Dimensions are average of long and short axes, rounded to the nearest millimeter.
† Consider all relevant risk factors (see Risk Factors).
Case 2

Nodules are measured as following:

- RLL anterior basal segment cystic ground glass nodule, 25 x 20 mm
- RLL superior segment subsolid nodule, 9 x 8 mm
- RML lateral segment subsolid nodule, 10 x 9 mm
Case 2 Imaging

- RML lateral segment subsolid nodule, 10 x 9 mm
Case 2 Imaging

- RLL superior segment subsolid nodule, 9 x 9 mm
Case 2 Imaging

- RLL anterior basal segment cystic ground glass nodule, 25 x 20 mm
What is your next step when you see a patient with ground glass nodules?
Case 2

The patient is referred to Thoracic Surgery for evaluation of the nodules.
Question for Dr. Cooke

- When should a patient be referred to thoracic surgery for management of lung nodules?
Case 2 Continued

The patient’s case was reviewed by the thoracic surgeon and the patient was referred to interventional pulmonology. She underwent robotic assisted, cone beam CT-guided bronchoscopy with biopsy of the nodules.

All 3 targets showed adenocarcinoma with acinar growth on pathology. Lymph nodes sampled from stations 7, 11R, and 11Ri were negative for malignancy.
Question for Dr. Shaller

- How does the management of ground glass nodules differ from the management of solid nodules?
The patient underwent a VATS-RLL lobectomy with lymph node dissection. Nodes were again confirmed negative on surgical pathology.

The patient was discharged home with plans to undergo SBRT to the RML nodule following recovery from surgery.
Case 3

A 82 yo female is referred to the lung nodule clinic for evaluation of a new PET avid right hilar lymph node identified on surveillance imaging.

Her medical history is significant for diagnosis of RUL squamous cell carcinoma in 2019 with bony metastases to the ribs. She has been treated with carboplatin, taxol, and Keytruda with restaging imaging showing excellent response to treatment. She was then maintained on Keytruda alone for several years before stopping in 2022 due to development of pneumonitis.

She has a prior 20 pack year smoking history but quit in 2007. Over the past few months, she has noted 10 lb weight loss.
Case 2 Imaging

- PET avid right hilar lymph node
Question for Dr. Tong

- How frequently do you get surveillance imaging after treatment of the malignancy?
Question for Dr. Shaller

- When is a biopsy indicated vs presuming recurrence of a prior confirmed diagnosis?
Question for Dr. Cooke

- Is there a role for surgery in recurrent disease?
Case 3 Outcome

- Stations 11R and 7 were sampled using EBUS and negative for malignancy.
- Station 10R biopsy using EBUS contains atypical cells positive for p40 and panCK which are suspicious for metastatic squamous cell carcinoma.
- Patient is referred by her oncologist to radiation oncology for consideration of CyberKnife radiation therapy.
### Guideline Recommendations and Invasive Mediastinal Staging

<table>
<thead>
<tr>
<th>Variable</th>
<th>CHEST</th>
<th>NCCN</th>
<th>CCO</th>
<th>NICE</th>
<th>ESTS/ERS/ESGE</th>
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</thead>
<tbody>
<tr>
<td><strong>Indications for invasive mediastinal staging</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tumor &gt; 3 cm</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>NS</td>
<td>Yes</td>
</tr>
<tr>
<td>Central tumor</td>
<td>Yes</td>
<td>Yes</td>
<td>NS</td>
<td>NS</td>
<td>Yes</td>
</tr>
<tr>
<td>Tumor without PET uptake</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>Yes</td>
</tr>
<tr>
<td>Lymphadenopathy</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Nodes showing positive PET results</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Definition of central tumor</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inner one third</td>
<td>Yes</td>
<td>...</td>
<td>Yes</td>
<td>NS</td>
<td>Yes</td>
</tr>
<tr>
<td>Inner two thirds</td>
<td>...</td>
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<td>...</td>
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<td>...</td>
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<td></td>
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<tr>
<td>EBUS</td>
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<td>...</td>
<td>...</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>EBUS/EUS</td>
<td>Yes</td>
<td>...</td>
<td>...</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Mediastinoscopy</td>
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<td>...</td>
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<td>...</td>
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<tr>
<td>Any method&lt;sup&gt;a&lt;/sup&gt;</td>
<td>...</td>
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<td>...</td>
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<td>Indication for repeat invasive mediastinal staging</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Negative or nondiagnostic first-line endosonography findings</td>
<td>Yes</td>
<td>Yes</td>
<td>NS</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Minimum extent of lymph node evaluation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Three mediastinal lymph node stations</td>
<td>NS</td>
<td>NS</td>
<td>...</td>
<td>NS</td>
<td>Yes</td>
</tr>
<tr>
<td>Five mediastinal lymph node stations</td>
<td>...</td>
<td>NS</td>
<td>Yes</td>
<td>NS</td>
<td>...</td>
</tr>
</tbody>
</table>

CCO = Cancer Care Ontario; CHEST = American College of Chest Physicians; EBUS = endobronchial ultrasound; ESGE = European Society of Gastrointestinal Endoscopy; ERS = European Respiratory Society; ESTS = European Society of Thoracic Surgeons; EUS = esophageal ultrasound; NCCN = National Comprehensive Cancer Network; NICE = National Institute for Health and Care Excellence; NS = not specified.

<sup>a</sup>EBUS, EUS, mediastinoscopy, mediastinotomy, CT scanning-guided nodal aspiration, or a combination thereof.
Q&A with the Audience
Thank you for joining us!
## Primary tumor (T)

<table>
<thead>
<tr>
<th>T category</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tx</td>
<td>Tumor that is proven histopathologically (malignant cells in bronchopulmonary secretions/washings) but cannot be assessed or is not demonstrable radiologically or bronchoscopically.</td>
</tr>
<tr>
<td>T0</td>
<td>No evidence of primary tumor.</td>
</tr>
<tr>
<td>Tis</td>
<td>Carcinoma in situ: Squamous cell carcinoma in situ. Adenocarcinoma in situ (pure lepidic pattern and ≤3 cm in greatest dimension).</td>
</tr>
<tr>
<td>T1</td>
<td>Size: ≤3 cm. Airway location: in or distal to the lobar bronchus. Local invasion: none (surrounded by lung or visceral pleura). Subdivisions: T1mi: Minimally invasive adenocarcinoma (pure lepidic pattern, ≤3 cm in greatest dimension and ≤5 mm invasion)—T1a (size ≤1 cm)→T1b (1 cm &lt; size ≤ 2 cm)—T1c (2 cm &lt; size ≤ 3 cm).</td>
</tr>
<tr>
<td>T2</td>
<td>Any of the following characteristics: Size: &gt;3 cm but ≤5 cm. Airway location: invasion of the main bronchus (regardless the distance to the carina) or presence of atelectasis or obstructive. Pneumonitis that extends to hilar region (whether it is involving part or the entire lung). Local invasion: visceral pleura (PL1 or PL2). Subdivisions: T2a (3 cm &lt; size ≤ 4 cm or cannot be determined) and T2b (4 cm &lt; size ≤ 5 cm).</td>
</tr>
<tr>
<td>T3</td>
<td>Any of the following characteristics: Size: &gt;5 cm but ≤7 cm. Local invasion: direct invasion of chest wall (including superior sulcus tumors), parietal pleura (PL3), phrenic nerve, or parietal pericardium. Separate tumor nodule(s) in the same lobe of the primary tumor.</td>
</tr>
<tr>
<td>T4</td>
<td>Any of the following characteristics: Size &gt;7 cm. Airway location: invasion of the carina or trachea. Local invasion: diaphragm, mediastinum, heart, great vessels, recurrent laryngeal nerve, esophagus or vertebral body. Separate tumor nodule(s) in an ipsilateral different lobe of the primary tumor.</td>
</tr>
</tbody>
</table>
**TNM Staging**

### Lymph nodes (N)

<table>
<thead>
<tr>
<th>Descriptor</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nx</td>
<td>Regional lymph nodes cannot be evaluated.</td>
</tr>
<tr>
<td>N0</td>
<td>No regional lymph nodes involvement.</td>
</tr>
<tr>
<td>N1</td>
<td>Involvement of ipsilateral peribronchial and/or ipsilateral hilar lymph nodes (includes direct extension to intrapulmonary nodes).</td>
</tr>
<tr>
<td>N2</td>
<td>Involvement of the ipsilateral mediastinal and/or subcarinal lymph nodes.</td>
</tr>
<tr>
<td>N3</td>
<td>Involvement of any of the following lymph node groups: contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular nodes.</td>
</tr>
</tbody>
</table>

### Distant metastasis (M)

<table>
<thead>
<tr>
<th>Descriptor</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>M0</td>
<td>No distant metastasis.</td>
</tr>
<tr>
<td>M1</td>
<td>Presence of distant metastasis.</td>
</tr>
<tr>
<td></td>
<td>Subdivisions: M1a (separate tumor nodule(s) in a contralateral lobe to that of the primary tumor or tumors with pleural or pericardial nodules or malignant effusion); M1b (single extrathoracic metastasis); M1c (multiple extrathoracic metastases to one or more organs).</td>
</tr>
</tbody>
</table>

*Note: Tumor’s size is determined by the greatest dimension of the lesion.*

*The uncommon superficial spreading tumor with invasive component limited to bronchial wall is classified as T1a regardless of size or extent to main bronchus.*
Dyssynchronous Waveforms

Rob Bautista, BSRT, RRT, RRT-ACCS
Respiratory Therapist
UC San Francisco

Roberto Bautista received his Baccalaureate Degree from Boise State University and is pursuing his Masters Degree at UCSF. He is a Clinical Specialist for the Respiratory Care Services department at UCSF with a focus on Adult Critical Care. Roberto is the CSRC-AARC Delegate and is a member of the CSRC Executive Committee.
Ventilator Asynchrony

Roberto Bautista BSRT, RRT, RRT-ACCS
Relevant Financial Disclosure(s)

Roberto Bautista BSRT, RRT, RRT-ACCS

- I have no conflicts of interest.
Ventilator Asynchrony

Introduction

- Mechanical ventilation is a supportive treatment for improving oxygenation and/or ventilation, unloading the respiratory muscles, and gaining time until the patient's condition improves.

- Patient-ventilator asynchrony can be defined as a mismatch between the patient and ventilator timing and/or effort.
Ventilator Asynchrony

Asynchronies can result in dyspnea, anxiety, delirium, cognitive alterations, and self-inflicted lung injury; they could also induce vigorous inspiratory efforts leading to high stress (i.e., elevated transpulmonary pressure), strain (i.e., global or regional lung overdistention), and consequent diaphragm and lung injury. Asynchronies are also associated with longer duration of mechanical ventilation.
Objectives
Ventilator Asynchrony

Objectives

- Interpret waveforms
- Identify and define type of asynchrony
- Discuss possible interventions and/or adjustments
- Evaluate efficacy of current plan
Physiology
Ventilator Asynchrony

Mechanisms

Main mechanisms of Asynchrony

Timing of the patient is mismatched with the timing of the ventilator

Imbalances in the amount work of breathing by the patient and the amount mechanical assist delivered during inspiration.
Neural/Ventilator Timing Mismatch
Respiratory Drive/Mechanical Assist Mismatch

**High Respiratory Drive**
(CNS, Metabolic, Respiratory Failure)

- Insufficient ventilatory assist
- Intrinsic to patient’s disease state

**Low Respiratory Drive**

- Excessive ventilatory assist
- Excessive sedation
Asynchrony Interactions

Neural/Ventilator timing mismatch

Unmatched respiratory drive needs
Ventilator Asynchrony

What Phase?

- When does the asynchrony occur?
  - Inspiratory Trigger
  - Inspiratory Limit
  - Inspiratory Cycle
  - Expiratory
Cases

Start of ventilator insufflation

Flow increase

Pressure drop

Start of patient’s effort

Wasted Effort: Ineffective breath

Intrinsic PEEP

Time (s)
Missed/Ineffective Trigger

- What phase is this in?
  - Inspiratory trigger

- Causes
  - Trigger sensitivity high
  - High set inspiratory pressure
  - Set frequency and/or I-time set too high
  - Presence of AutoPEEP
  - Low respiratory drive
  - Weak inspiratory effort
  - Sedation
Missed/Ineffective Trigger

- Interventions
  - Decrease trigger sensitivity
  - Decrease set inspiratory pressure
  - Increase PEEP
  - Decrease sedation
  - Increase pt strength
Flow asynchrony occurs when the set ventilator flow does not meet the patient inspiratory flow demand.
Generally recognized by concave pressure-time scalar. Also termed “Air Hunger”
Flow Asynchrony

- What phase is this in?
  - Inspiratory Limit

- Causes
  - Inappropriate vent mode
  - High Inspiratory Effort
  - Inappropriate Flow/ Time setting
  - Decreased Vt
Flow Asynchrony

- **Interventions**
  - Select appropriate mode
  - Increase Flow and/or Vt
  - Adjust time setting
0.6s
Premature/Short Cycling

Short cycling occurs when the inspiratory time set by the ventilator is less than the neural timing of the patient.

De Oliveira, B, Journal of Clinical Medicine 2021
Premature/Short Cycling

- When does this occur?
  - Inspiratory Cycle

- Causes
  - I-time set too low
  - High Inspiratory Effort
  - Vt set too low
Premature/Short Cycling

- Interventions
  - Adjust I-time
  - Increase Vt
  - Select to appropriate mode
  - Decrease cycle criterion
Double Triggering

Aka Breathstacking occurs when there is no expiration or very little expiration between breaths.
Double Triggering

- What phase is this in?
  - Inspiratory cycle

- Causes
  - High inspiratory demand
  - Inspiratory time too short
  - Vt too low
  - Cycle criterion too high
Double Triggering

- Interventions
  - Increase Vt
  - Increase peak flow to match demand
  - Increase I-time to match patient’s neural timing
  - Mode change to Pressure Support
  - Increase sedation
Delayed Cycling

- What phase is this in?
  - Inspiratory Cycle

- Causes
  - Cycle % set too low
  - I-time too long
  - Too much support/volume

Tassaux, D, AJRCCM 2005
Delayed Cycling

Delayed Cycling is active expiratory effort before the cycling criterion is met.
Delayed Cycling

- Interventions
  - Increase cycling criterion
  - Decrease I-time
  - Decrease support/volume
Auto-PEEP (Intrinsic PEEP) is incomplete emptying of the lungs occurs if the expiratory phase is terminated prematurely.

Hess, D, Respiratory Care 2014
Auto-PEEP

- What phase is this in?
  - Expiratory

- Causes
  - Inappropriate E-time
  - Inappropriate RR
  - Inappropriate Vt
Total PEEP = Set PEEP = Auto PEEP

3.7 cmH2O

45.0 Inspiratory flow

24.6 Expiratory flow
Auto-PEEP

- Interventions
  - Adjust E-time
  - Adjust RR
  - Adjust Vt
  - Increase PEEP
  - Bronchodilators
Summary

- Asynchronies are common
- Must be able to identify type of asynchrony
- Some can be resolved with vent interventions, others require chemical interventions
- Asynchronies if left untreated can be harmful
The capacity to learn is a **GIFT**; the ability to learn is a **SKILL**; the willingness to learn is a **CHOICE**.

Brian Herbert
Questions

Roberto.Bautista@ucsf.edu
Optimizing Lung Recruitment in Challenging Populations Post-Intubation

Alex Kristine Pearce, MD
Associate Physician Diplomate
UC San Diego

Dr. Alex Pearce received her medical degree from Tulane School of Medicine followed by residency in Internal Medicine at UC San Diego. She subsequently completed her clinical fellowship in Pulmonary and Critical Care and research fellowship at UC San Diego. She currently works as an intensivist at UC San Diego with a research focus on mechanical ventilation and Acute Respiratory Distress Syndrome.
OPTIMIZING LUNG RECRUITMENT IN CHALLENGING POPULATIONS POST-INTUBATION: INTRODUCTION TO ELECTRICAL IMPEDANCE TOMOGRAPHY (EIT)

CTS March 2024

Alex Kristine Pearce MD

UC San Diego, Division of Pulmonary and Critical Care
I have the following relationships with ACCME defined ineligible companies: N/A

I WILL discuss off-label use and/or investigational use of any drugs or devices.
Outline/Objectives

• Review pertinent background in VILI, pleural pressure gradients, distribution of ventilation.

• Recognize challenges in lung protective ventilation

• Introduction to principles of EIT

• Understand how EIT can be used in a clinical/research setting
Background: VILI (Ventilator induced lung injury)

- Several mechanisms
  - **Volutrauma**: injury from high volumes
  - **Barotrauma**: injury from high pressures
  - **Atelectrauma**: injury from repetitive opening/closing
  - **Dys-synchrony**: injury from pendelluft

Lung strain
(Tidal volume/FRC)

Lung Stress
(plateau or transpulmonary pressure)

Volu-trauma
Baro-trauma

↑ Mortality & morbidity

Dreyfuss and Saumon. AJRCCM 1998.
Lung protection (traditional)
Low tidal volumes $\rightarrow$ 6 cc/kg IBW
Plateau Pressure <30, Low Driving pressure <15 cmH2O
Open lung strategy (avoid cyclical atelectasis)
Prone positioning

Is this always enough? No
Can harm/VILI still occur? Yes

Why?– Current approaches only focus on global metrics and neglect assessment of regional stress/strain
Background: regional ventilation in health and disease

- Time-constants (resistance x compliance)
- Airway closure below FRC
- Pleural pressure gradients (transpulmonary pressure)
- Parenchymal heterogeneity
Pleural pressure

**Perfect world**: transpulmonary pressure would be the same throughout the lung

Pleural pressure (-10 cmH2O)

Transpulmonary pressure = Airway Pressure – Pleural Pressure

Inspiration
Pleural pressure gradients are complicated

Real world: Pleural pressure is WAY MORE complicated

Pleural pressure gradients + heterogeneity in lung injury

1. Gravity (both apical/basilar and Ventral/dorsal)
2. Lung injury make gradients worse


Pleural pressure gradients are complicated

Why does this matter?

heterogeneous lung parenchyma + uneven distribution of pleural pressure → variable transpulmonary pressure in different parts of the lung → difficult to ventilate all parts of lung safely

Options in a patient who is difficult to ventilate/oxygenate?

1. Esophageal manometry
2. Pressure volume curves
3. Recruitment maneuvers and best compliance

Only estimates pleural pressure at mid-thorax (at best the mid to dorsal lung- misses ventral, apex, base)

4. Electrical impedance Tomography? (EIT)

Treat the lung as a whole/average\(\rightarrow\) but injured lung tends to be heterogenous with complex pleural pressure gradients
EIT in ARDS: growing interest

Pubmed (EIT AND ARDS)

172 results

EIT: general principles

- Noninvasive real-time bedside technology

EIT General principles

- Every tissue has a different resistivity to current
- Estimates resistivity changes across lungs while breathing
  - Inspiration = \( \uparrow \) Resistivity
  - Expiration = \( \downarrow \) Resistivity

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Resistivity (( \Omega )m)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung during expiration</td>
<td>12.5</td>
</tr>
<tr>
<td>Lung during inspiration</td>
<td>25</td>
</tr>
<tr>
<td>Blood (50% hematocrit)</td>
<td>1.4–1.7</td>
</tr>
<tr>
<td>Cardiac muscle</td>
<td>2.5–5</td>
</tr>
</tbody>
</table>

Tomicic V and Cornejo R. Journal of Thoracic Disease, 2019

EIT plethysmogram

\[ \Delta Z \sim V_T \]

EIT: General principles

- Resistivity/change in resistivity correlates with volume of air that enters the lung
- Creates image and way to quantify/assess distribution of ventilation


Clinical/Research Applications

- Distribution of ventilation
- PEEP titration
- Pendelluft
- Other: patient-ventilator asynchrony, Ventilation/perfusion, NIPPV
Distribution of Ventilation

- EIT provides a ventilation map: can quantify distribution of ventilation several ways
- Can use to identify heterogeneity in distribution of ventilation
- Impedance change correlates with changes in air content

Example of mucus plugging on the left side

Distribution Ratio:

- Ventilation parameters:
  - $V_t$: 185 mL
  - PIP: 26.6 cmH$_2$O
  - PEEP: 14.1 cmH$_2$O
  - RR: 20 bpm
PEEP Titration

• How should we titrate PEEP?
  • Esophageal manometry: EP-VENT3 planning in progress= TBD
  • PEEP tables?
  • Best compliance?
  • WHO KNOWS?
  • What about EIT?
PEEP Titration with EIT

Balance between overdistension and collapse (Costa Method)


White = overdistension
Blue = collapse
PEEP Titration (example)

![Graph showing PEEP titration](image)

<table>
<thead>
<tr>
<th>PEEP (cmH2O)</th>
<th>Compliance (mL/cmH2O)</th>
<th>Hyperdist. (%)</th>
<th>Collapse (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>25.1</td>
<td>14</td>
<td>60</td>
<td>0</td>
</tr>
<tr>
<td>23.1</td>
<td>20</td>
<td>44</td>
<td>0</td>
</tr>
<tr>
<td>21.1</td>
<td>24</td>
<td>32</td>
<td>0</td>
</tr>
<tr>
<td>19.2</td>
<td>26</td>
<td>20</td>
<td>0</td>
</tr>
<tr>
<td>17.2</td>
<td>27</td>
<td>12</td>
<td>1</td>
</tr>
<tr>
<td>15.1</td>
<td>26</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>13.1</td>
<td>24</td>
<td>3</td>
<td>11</td>
</tr>
<tr>
<td>11.1</td>
<td>21</td>
<td>0</td>
<td>16</td>
</tr>
<tr>
<td>9.0</td>
<td>17</td>
<td>0</td>
<td>30</td>
</tr>
<tr>
<td>7.0</td>
<td>13</td>
<td>0</td>
<td>40</td>
</tr>
<tr>
<td>5.0</td>
<td>11</td>
<td>0</td>
<td>49</td>
</tr>
</tbody>
</table>
PEEP Titration with EIT offers individualized approach and may improve outcomes?

RECRUIT study (2023): Jonkman and Alcala et al. *AJRCCM*
- 171 Patients with ARDS due to COVID-19
- Used EIT based PEEP selection (Costa method) versus best compliance
- in 81% of patients EIT based PEEP selection yielded PEEP selection different from best compliance
- Offers personalized way to adjust PEEP in patients with different responses to PEEP
*Non COVID recruitment ongoing

EIT-Guided PEEP titration reduces mechanical power: a randomized crossover pilot study (2023): Jimenez et al. *Critical Care*
- High PEEP/FiO2 table versus EIT guided PEEP selection
- 16 patients with moderate to severe ARDS
- EIT guided PEEP titration resulted in lower mechanical power

Early Individualized PEEP guided by EIT in ARDS: a randomized controlled clinical trial (2021): He et al. *Critical Care*
- ARDS net PEEP/FiO2 table versus EIT guided PEEP selection
- 117 patients with moderate to severe ARDS
- Absolute mortality 27% (PEEP/FiO2 table) versus 21% (EIT guided)

Additional EIT studies upcoming
Pendelluft

General definition: movement of air from one region of the lung to another during a tidal breath

- Can lead to occult overdistension (potentially harmful)

Pendelluft

- EIT can be used to identify pendelluft

* Can use NMB or increase PEEP to minimize pendelluft

Future Directions

- Ventilation/perfusion mapping

- Asynchrony detection features

- HHFB, NIPPV, HFOV (measuring tidal volume, collapse/overdistention)

Take home messages

- EIT offers a continuous non-invasive bedside assessment of regional ventilation (and perfusion)
- Offers good temporal resolution; can see dynamic changes over time
- Can measure responses to changes like PEEP or paralytics
- Allows individualized patient management (when one-size fits all approaches have failed)
- Ongoing research will determine impact on clinical outcomes
Thank you!

• Special thank you to....
  • Marcelo Amato
  • Eduardo Costa
  • Caio Morais
  • Glasiele C. Alcala
  • Ewan Goligher
  • Atul Malhotra
  • Kim Prisk
  • Jim Butler
  • Stephen Loring
References

Pro: Non-Ventilator Based Techniques are Necessary for Optimization of Lung Mechanics in Ventilated Patients?

Brian M. Daniel, RRT, TCO
Respiratory Therapist
UC San Francisco

Brian M. Daniel is a respiratory care practitioner with more than 35 years of experience in academic health care, education, and research. Currently, he is a clinical specialist for Respiratory Care Services at UCSF Health as well as a clinical research coordinator for UCSF’s Cardiovascular Research Institute. Brian also serves as Director for Clinical Education, at Skyline College's Respiratory Care Program.
Let’s NOT forget the basics!

Non-Ventilator based techniques ARE necessary when optimizing lung mechanics...
Disclosures

• None relative to this presentation
Control System

\[
\text{Resistance} = \frac{\Delta \text{Transairway pressure}}{\Delta \text{Flow}}
\]

\[
\text{Compliance} = \frac{\Delta \text{Volume}}{\Delta \text{Transthoracic pressure}}
\]

\[
\text{Elastance} = \frac{\Delta \text{Transthoracic pressure}}{\Delta \text{Volume}}
\]

Equation of Motion for the Respiratory System

\[
P_{\text{vent}} + P_{\text{muscles}} = \text{elastance} \times \text{volume} + \text{resistance} \times \text{flow}
\]
Heightened sternomastoid activity is evidence of increased patient effort.

Recession may be seen in the suprasternal and supraclavicular spaces.

Intercostal space recession also indicates increased patient effort.

Tachycardia is an indicator of severe cardiopulmonary distress.

Diaphoresis and nasal flaring indicate increased patient effort.

Cyanosis is not a reliable physical sign.

Tachypnea determined over the course of a full minute is a sensitive sign of failure.

Paradoxical motion of the abdomen is also evidence of increased patient effort.
Patient/Ventilator Interaction

Underlying lung function, the acute process and effects of interventions
- Ventilator drive
- Muscle function
- Ventilator demand
- Airway resistance
- Lung volume
- Respiratory system compliance

The patient-ventilator interface

Effects of how the ventilator functions and how it is set by the clinician
- Mode
- Level of support
- Imposed WOB
- Tidal volume
- Trigger threshold
- Post-trigger work
- Inspiratory time
- Cycling
- Expiratory time

Problem recognition and response
- Symptoms
- Physical signs
- Problem recognition by clinician
- Response by clinician

Recognition and quantitation by
- ventilator
- Alarms
- Waveforms display
- Response by ventilator
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Setting</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sign off</td>
<td>Special</td>
<td>369</td>
</tr>
<tr>
<td>Disable TRC</td>
<td>Special</td>
<td>510</td>
</tr>
<tr>
<td>FlowPattern 4</td>
<td>Setting</td>
<td>312</td>
</tr>
<tr>
<td>Flowtrigger 5.0 l/min</td>
<td>Setting</td>
<td>304</td>
</tr>
<tr>
<td>Pause 0 %</td>
<td>Setting</td>
<td>308</td>
</tr>
<tr>
<td>TI 0.90 s</td>
<td>Setting</td>
<td>317</td>
</tr>
<tr>
<td>Oxygen 100 %</td>
<td>Setting</td>
<td>302</td>
</tr>
<tr>
<td>PEEP/CPAP 5.0 cmH2O</td>
<td>Setting</td>
<td>301</td>
</tr>
<tr>
<td>Vt 450 ml</td>
<td>Setting</td>
<td>315</td>
</tr>
<tr>
<td>Rate 28 b/min</td>
<td>Setting</td>
<td>314</td>
</tr>
<tr>
<td>Ventilation mode (S)CMV</td>
<td>Setting</td>
<td>224</td>
</tr>
<tr>
<td>Standard setup</td>
<td>Setting</td>
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<tr>
<td>Oxygen high is off</td>
<td>Setting</td>
<td>132</td>
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<tr>
<td>SpO2 right Off</td>
<td>Setting</td>
<td>118</td>
</tr>
<tr>
<td>SpO2 left Off</td>
<td>Setting</td>
<td>117</td>
</tr>
<tr>
<td>PetCO2 low 30 mmHg</td>
<td>Setting</td>
<td>112</td>
</tr>
<tr>
<td>PetCO2 high 60 mmHg</td>
<td>Setting</td>
<td>113</td>
</tr>
<tr>
<td>CO2 is on</td>
<td>Setting</td>
<td>116</td>
</tr>
<tr>
<td>O2 is on</td>
<td>Setting</td>
<td>111</td>
</tr>
<tr>
<td>Apnea time 20 s</td>
<td>Setting</td>
<td>110</td>
</tr>
<tr>
<td>Leak is off</td>
<td>Setting</td>
<td>109</td>
</tr>
<tr>
<td>Vt low 250 ml</td>
<td>Setting</td>
<td>108</td>
</tr>
<tr>
<td>Vt high 750 ml</td>
<td>Setting</td>
<td>107</td>
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<tr>
<td>Rate low 8 b/min</td>
<td>Setting</td>
<td>106</td>
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<tr>
<td>Rate high 23 b/min</td>
<td>Setting</td>
<td>105</td>
</tr>
<tr>
<td>ExpMinVol low 4.00 l/min</td>
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<td>104</td>
</tr>
<tr>
<td>ExpMinVol high 10.00 l/min</td>
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<td>103</td>
</tr>
<tr>
<td>Pressure low 5 cmH2O</td>
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<td>102</td>
</tr>
<tr>
<td>Pressure high 40 cmH2O</td>
<td>Setting</td>
<td>101</td>
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<tr>
<td>Reset Ventilation time 2856 min</td>
<td>Special</td>
<td>554</td>
</tr>
<tr>
<td>ETS 25 %</td>
<td>Setting</td>
<td>319</td>
</tr>
<tr>
<td>Standby Off</td>
<td>Special</td>
<td>507</td>
</tr>
<tr>
<td>Causes, clinical features, and management of respiratory distress in mechanically ventilated patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>---</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Etiology of respiratory distress</strong></td>
<td><strong>Clinical features, ventilator mechanics, bedside testing</strong></td>
<td><strong>Treatment</strong></td>
</tr>
<tr>
<td>Incorrect ventilator settings (eg, tidal volume, fraction of inspired oxygen, respiratory flow or pressure rate, positive and expiratory pressure, trigger sensitivity)</td>
<td>• Can occur when settings are inadequate or too high.</td>
<td>• Disconnect the ventilator from the ETT.</td>
</tr>
<tr>
<td></td>
<td>• Commonly found when ventilator settings are initiated or changed (eg, after intubation, procedures, or transport).</td>
<td>• If respiratory distress resolves, examine the ventilator including settings and connections for problems.</td>
</tr>
<tr>
<td></td>
<td>• May be less common with modern ventilators that automatically revert to previous settings when patients are temporarily removed from mechanical ventilation or settings are temporarily changed.</td>
<td>• Once resolved, resume mechanical ventilation.</td>
</tr>
<tr>
<td>Ventilator circuit leak or obstruction (including HME)</td>
<td>• Volume-controlled ventilation:</td>
<td>• If distress recurs, consider altering ventilator settings attempting to &quot;match&quot; patient effort (eg, increase the tidal volume or respiratory rate or switch to pressure support or pressure-controlled mode), ensuring new settings do not place the patient at risk of volutrauma or barotrauma.</td>
</tr>
<tr>
<td></td>
<td>Low peak pressures and low expired tidal volume may suggest a leak in the absence of a balloon cuff leak or segulated displacement of the ETT (refer to below).</td>
<td>• Consider replacement of the ventilator if distress persists.</td>
</tr>
<tr>
<td></td>
<td>High peak pressures, with widened delta PEEP-Pplat*, may suggest obstruction.</td>
<td>• Replace the tubing if a leak is suspected.</td>
</tr>
<tr>
<td></td>
<td>Pressure-controlled ventilation:</td>
<td>• Empty the ventilator tubing of secretions.</td>
</tr>
<tr>
<td></td>
<td>Airway pressure unchanged, increase in tidal volume, and respiratory flow that does not return to baseline may suggest an air leak.</td>
<td>• Replace the HME, if necessary.</td>
</tr>
<tr>
<td></td>
<td>Airway pressure unchanged; decrease in tidal volume, and respiratory flow that is slow to return to baseline, suggest increased airway resistance from obstruction.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>A sawtooth pattern on ventilator graphics may suggest secretions or water in ventilator tubing as a source of obstruction.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>If no secretions are present in ventilator tubing, consider an obstruction at the level of the HME.</td>
<td></td>
</tr>
<tr>
<td>Ventilator malfunction</td>
<td>• This issue is unusual but may be suspected when respiratory distress recurs despite resuming ventilation with the correct settings and no intrinsic parenchymal, airway, pleural, or extraordinary issues are suspected. May be determined during ventilator interrogation.</td>
<td>• Consider replacing components of the ventilator or the ventilator itself.</td>
</tr>
<tr>
<td><strong>Airway</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Most conditions are associated with the following ventilatory mechanics:</td>
<td>• Increased PEEP and a widened delta PEEP-Pplat (volume-controlled ventilation).*</td>
<td>• Attempt to identify and remove the obstruction.</td>
</tr>
<tr>
<td></td>
<td>or</td>
<td>• Suctioning thick secretions often sufficient.</td>
</tr>
<tr>
<td></td>
<td>Unchanged airway pressure, decreased tidal volume, respiratory flow slow to return to baseline (pressure-controlled ventilation).</td>
<td>• Reposition the head especially if a kinked tube is suspected.</td>
</tr>
<tr>
<td>ETT obstruction – Mucus, blood, foreign body, kinking, or biting</td>
<td>Known thick and voluminous secretions or hemorrhage.</td>
<td>• Place beta blocker if kinking of the ETT is suspected.</td>
</tr>
<tr>
<td></td>
<td>Foreign body such as a tooth may have been inhaled during intubation.</td>
<td>• If above measures fail, replace ETT.</td>
</tr>
<tr>
<td></td>
<td>Kinking in the ETT or biting may be obvious.</td>
<td>• Bronchoscopy if problem persists.</td>
</tr>
<tr>
<td></td>
<td>Resistance to manual ventilation and passage of a suction catheter through the ETT.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Maintenance of tidal volume, unless obstruction is complete.</td>
<td></td>
</tr>
<tr>
<td>Bronchospasm</td>
<td>Often occurs in those with underlying obstructive lung disease but can also occur due to trauma in the airways (eg, suctioning, bronchoscopy), or medications (eg, beta blockers, allergies).</td>
<td>• Urgent bronchodilution with beta-2 agonists.</td>
</tr>
<tr>
<td></td>
<td>Respiratory distress with wheeze or stridor.</td>
<td>• Glucocorticoids, antihistamines, histamine receptor blockers, and epinephrine and may be administered if allergy is suspected.</td>
</tr>
<tr>
<td></td>
<td>Maintenance of tidal volume.</td>
<td></td>
</tr>
<tr>
<td>Obstruction of lower airways by secretions, blood, airway mass, or foreign object</td>
<td>Secretions of blood may be evident.</td>
<td>• Attempt suctioning.</td>
</tr>
<tr>
<td></td>
<td>Respiratory distress with wheeze or stridor (may be unilateral or focal).</td>
<td>• saline bullae sometime required to break up thick mucus plugs.</td>
</tr>
<tr>
<td></td>
<td>Tidal volume is maintained. Increased PEEP* with widened delta PEEP-Pplat.*</td>
<td>• Urgent bronchoscopy may be needed for foreign body retrieval, preferably with adequate suction channel and the ability to retrieve a foreign body if necessary.</td>
</tr>
<tr>
<td>Caudal migration of the ETT to mainstem bronchi (typically right-sided)</td>
<td>Suspect in patients with agitation or in patients who have been repositioned.</td>
<td>• Deflate the cuff and pull the ETT back by a predetermined amount.</td>
</tr>
<tr>
<td></td>
<td>Air entry may be limited on the unaffected side and trachea may deviate away from the affected side.</td>
<td>• Re-image with chest radiography to confirm appropriate placement.</td>
</tr>
</tbody>
</table>
Summary

• Basic (non-ventilator based) patient assessment is essential when optimizing lung mechanics.

• Emerging mechanical ventilator tools and adjuncts lack significant evidence and consistency.
Con: Non-Ventilator Based Techniques are NOT Necessary for Optimization of Lung Mechanics in Ventilated Patients?

Pablo Gonzalez, RRT
Respiratory Therapist
Scripps Health

Pablo Gonzalez is currently a neonatal/pediatric/adult respiratory therapist at Scripps Memorial Hospital in La Jolla, San Diego, CA.

He has worked at a few facilities: Cedar Sinai Medical Center, CHOC, Loma Linda, Sharp Mary Birch, Sanford MN, and Regions Hospital in St Paul MN where he worked alongside Dr. John J. Marini which drove him to work at the Mayo Clinic and worked alongside Dr. Gustavo Cortes Puentes and worked along renowned physicians/nurses and respiratory therapist as a ECMO specialist.

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He has continued development of his skills and has started the Advanced Mechanical Ventilation Conference in San Diego. Bringing renowned speakers from all over the world. Currently he is working on a respiratory book that will help clinicians in the ICU.

Pablo earned a B.A. from laguna College of Art and Design in Laguna Beach, CA., and his associate science from California College San Diego.
“Ventilating Blindly
The Cons of External Tools”

My own religion has been to do all the good I could to my fellow man, and as little harm as possible.”

William Worrall Mayo
Conflict of interest

None
Objectives

1. Observe and understand ventilator settings and waveforms.
2. The cons of the advanced non and invasive ventilator tools.
3. Complexity of mechanical ventilation.
Lung settings
Driving Pressure and Survival in the Acute Respiratory Distress Syndrome

Marcelo B.P. Amato, M.D., Maureen O. Meade, M.D., Arthur S. Slutsky, M.D., Laurent Brochard, M.D., Eduardo L.V. Costa, M.D., David A. Schoenfeld, Ph.D., Thomas E. Stewart, M.D., Matthias Briel, M.D., Daniel Talmor, M.D., M.P.H., Alain Mercat, M.D., Jean-Christophe M. Richard, M.D., Carlos R.R. Carvalho, M.D., et al.

Median \( V_t \)
(10th–90th percentile) — mg/kg of predicted body weight

- 6.0 (5.9–7.5)
- 6.1 (5.8–9.2)
- 8.0 (5.7–12.1)
Estimation of Respiratory Muscle Pressure \( P_{\text{musc,est}} \) and dynamic transpulmonary Pressure \( \Delta P_L \)

\[
P_{\text{musc,est}} = -0.75 \times \Delta P_{\text{occ}}
\]

\(< 13-15 \text{ cmH}_2\text{O} \)

\[
\Delta P_L = \Delta P_{aw} - [2/3 \times \Delta P_{\text{occ}}]
\]

\(< 16.17 \text{ cmH}_2\text{O} \)

Bertoni et al. Critical Care (2019) 23;346
Lung Parameters

- \( \*VT/P_{\text{plat}} - \text{totalPEEP}= \text{Crs} \)
- \( \*VT/DP= \text{Crs} \)
- \( \*VT/PL=\text{Crs} \)
- \( \*P_{\text{plat}} - \text{totPEEP}= \text{DP} \)
- \( \*[(\text{PaO}_2 \times 10)/(\text{FiO}_2 \times \text{totPEEP})] \)
- \( \*\text{PaO}_2/\text{FiO}_2 \) ratio
- \( \*(\text{PEEP}_1 + \text{PEEP}_2)/2=\text{Average totPEEP (APRV)} \)
- \( \*\text{PHigh -Average totPEEP}= \text{DP} \) (APRV)
- \( \text{P}_{\text{musc}}, \text{estimated} = -0.75 \times \text{deltaP}_{\text{occ}} \) (<13-15 cmH2O)
- Dynamic \( \text{deltaPL} = \text{deltaP}_{\text{aw}} - [2/3 \times \text{deltaP}_{\text{occ}}] \) (<13-15 cmH2O)
- \( \*\text{Expiratory hold during APRV will give you totalPEEP} \) (do not do this on Drager vents)
- \( \*\text{Note-Without an Esophageal Balloon Monitoring device, driving pressure is an estimating number } \pm 3-4 \text{ cmH2O when compared with a true PL.} \)
The pressure to inflate the respiratory system is evaluated, but how do we calculate the stress/strain of the individual lung’s?

Mechanical Power = \( \frac{VE \times (\text{Peak Pressure} + \text{PEEP} + \frac{F}{6})}{20} \)

CONCLUSIONS:

In our study sample, mechanical ventilation with PEEP titrated by esophageal pressure monitoring resulted in unexpectedly high values of PEEP among patients with mild ARDS. Additionally, both $MP_{RS}$ and $MP_L$ seemed to track the higher mortality rate observed in the moderate ARDS group.
What is the local volume distribution? Using pressure-volume curves to set proper PEEP in acute lung injury.
Figure 4: Difference > 500 ml - high potential for recruitment
Electrical Impedance Tomography (EIT)

**Pros**
- Non-invasive, radiation-free monitoring tool to assess and visualize regional ventilation and perfusion.
- EIT is currently predominantly a research tool, but rapidly emerging data are helping to define its clinical role.
- EIT may prove to be a key component of a multimodal approach to individualizing ventilator management, as has been demonstrated by the Lung Rescue Team (MGH).

**Cons**
- >60 BMI: larger belt in development
- Implanted electronic devices (neurostimulators, cardioverter defibrillators or pacemakers)
- Pregnant or lactating patients
- Fragile skin, spinal cord injury (e.g., Burns)

---

### Esophageal Balloon Monitoring

**Pros**
- Excessive secretions
- Enlarge congenital anomalies
- Leakage in chest
- Anomaly in the esophagus
- Pneumomastectomy?

---

### Electrical Activity of the Diaphragm (EAdi)

- Easy to perform at bedside
- Reflects changes in respiratory muscle output
- Helpful for detecting asynchronies in PSV mode

---

The manuscript below for respiratory monitoring in ventilated patients: European Respiratory Review 2023; 32: 2300186. DOI: 10.1183/16000617.0186-2022

---

How do I know edema is not developing in the dependent reabsorption of intra-alveolar edema in nondependent

---

Transesophageal Echo
What would be your best clinical decision?

A. Change to PC-CMVs
B. Increase Vt up to 8ml/kg PBW
C. Decrease RR
D. Increase PEEP, prone, possibly sedate/paralyze
E. If ARDS, prone, sedate/paralyze
F. Lengthen i-Time
G. Change to PS/CPAP
High Positive End-Expiratory Pressure Renders Spontaneous Effort Noninjurious

Morais, Am J Respir Crit Care Med, 2018
### Blood gas values

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Measurement</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.429</td>
</tr>
<tr>
<td>( pCO_2 )</td>
<td>34.9 mmHg</td>
</tr>
<tr>
<td>( pO_2 )</td>
<td>251 mmHg</td>
</tr>
<tr>
<td>( cHCO_3^- )</td>
<td>23.1 mmol/L</td>
</tr>
</tbody>
</table>

### Oximetry values

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Measurement</th>
</tr>
</thead>
<tbody>
<tr>
<td>( sO_2 )</td>
<td>100.0 %</td>
</tr>
<tr>
<td>( cBase(Ecf) )</td>
<td>-1.2 mmol/L</td>
</tr>
<tr>
<td>ctHb</td>
<td>13.4 g/dL</td>
</tr>
<tr>
<td>( FO_2Hb )</td>
<td>&gt; 98.5 %</td>
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</tbody>
</table>

### Blood gas values (100% FiO2)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Measurement</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.468</td>
</tr>
<tr>
<td>( pCO_2 )</td>
<td>28.0 mmHg</td>
</tr>
<tr>
<td>( pO_2 )</td>
<td>77.8 mmHg</td>
</tr>
<tr>
<td>( cHCO_3^- )</td>
<td>20.3 mmol/L</td>
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</tbody>
</table>

### Oximetry values (100% FiO2)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Measurement</th>
</tr>
</thead>
<tbody>
<tr>
<td>( sO_2 )</td>
<td>96.5 %</td>
</tr>
<tr>
<td>( cBase(Ecf) )</td>
<td>-3.4 mmol/L</td>
</tr>
<tr>
<td>ctHb</td>
<td>14.7 g/dL</td>
</tr>
<tr>
<td>( FO_2Hb )</td>
<td>95.2 %</td>
</tr>
<tr>
<td>( FCOHb )</td>
<td>1.2 %</td>
</tr>
<tr>
<td>( FMetHb )</td>
<td>0.1 %</td>
</tr>
</tbody>
</table>

### Blood gas values (40% FiO2)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Measurement</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td></td>
</tr>
<tr>
<td>( pCO_2 )</td>
<td></td>
</tr>
<tr>
<td>( pO_2 )</td>
<td></td>
</tr>
<tr>
<td>( cHCO_3^- )</td>
<td></td>
</tr>
</tbody>
</table>

### Oximetry values (40% FiO2)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Measurement</th>
</tr>
</thead>
<tbody>
<tr>
<td>( sO_2 )</td>
<td></td>
</tr>
<tr>
<td>( cBase(Ecf) )</td>
<td></td>
</tr>
<tr>
<td>ctHb</td>
<td></td>
</tr>
<tr>
<td>( FO_2Hb )</td>
<td></td>
</tr>
<tr>
<td>( FCOHb )</td>
<td></td>
</tr>
<tr>
<td>( FMetHb )</td>
<td></td>
</tr>
</tbody>
</table>
Summary

1. Monitoring ventilator settings and parameters
2. Mechanical Power in PC and VC
3. PV tool maneuver
4. Driving pressure
5. Management of ventilator waveform asynchronies
6. Cons of external tools to assist ventilator management
Mayo Clinic Mechanical Ventilation Conference 2024
Oceanside, CA US
October 16, 2024 to October 19, 2024

Overview | Location | Faculty | Accreditation | Register

This course offers Live (in-person) and Livestream (virtual) attendance options.

Course summary
Available credit:
19.25 AMA PRA Category 1 Credit™
19.25 ANCC
19.25 Attendance
Event starts: 10/16/2024 - 6:15am
Event ends: 10/19/2024 - 12:00pm

2nd Advanced Mechanical Ventilation Conference 2024
June 29, 2024 – 8 CEU Event

“Sleep and Circadian Rhythm Disturbances: Respiratory Care in the Intensive Care Unit”
“Advanced Ventilation”, “Advances in Neonatal Respiratory Support”
“Precision medicine in critical care medicine: the implementation of a lung rescue team”
“Heart-Lung Interaction During Spontaneous and Passive Ventilation”
“Electrical Impedance Tomography Neonate/Peds/Adults”

Scripps Memorial Hospital La Jolla
Schaetzel Great Hall
9800 Genesee Ave
San Diego, CA 92037

https://www.scri.org/
Mortality rate is cut in half by a Lung Rescue Team at Mass General focused on patients with obesity and acute respiratory failure. The intervention tools they employ include esophageal manometry to determine the intrapleural pressure inside the chest; trans-thoracic echocardiography to determine cardiac function during mechanical ventilation manipulation; and electrical impedance tomography (EIT) to measure the regional distribution of ventilation and assess the degree of lung collapse and overdistension.
References


Hands-on Session:
ICU Ventilators and Ventilator Waveforms

Rob Bautista, BSRT, RRT, RRT-ACCS
Respiratory Therapist
UC San Francisco

Roberto Bautista received his Baccalaureate Degree from Boise State University and is pursuing his Masters Degree at UCSF. He is a Clinical Specialist for the Respiratory Care Services department at UCSF with a focus on Adult Critical Care. Roberto is the CSRC-AARC Delegate and is a member of the CSRC Executive Committee.

Lena Scotto, MD
Assistant Professor
VA Palo Alto/Stanford

After earning a B.S. from Stanford University, Dr. Scotto attended Johns Hopkins School of Medicine. She then returned to her native Bay Area to train in the combined Stanford University Anesthesiology Residency/Critical Care Fellowship program and served as a Chief Fellow in Critical Care Medicine (CCM). Following graduation, Dr. Scotto worked in private practice at a local hospital as an Anesthesiologist and Intensivist and later joined the Palo Alto VA in 2019 as an Attending in Anesthesiology and Critical Care Medicine. She is the hospital-wide Resuscitation Committee Co-Chair and heads the newly formed Green Anesthesia Committee. Furthermore, she is a member of the Anesthesia Patient Safety Foundation Advisory Group on Perioperative Brain Health. Outside of work, when she’s not chasing after her toddler, she enjoys trail running, reading mystery novels, and trying new cooking recipes.
Pablo Gonzalez is currently a neonatal/pediatric/adult respiratory therapist at Scripps Memorial Hospital in La Jolla, San Diego, CA.

He has worked at a few facilitates: Cedar Sinai Medical Center, CHOC, Loma Linda, Sharp Mary Birch, Sanford MN, and Regions Hospital in St Paul MN where he worked alongside Dr. John J. Marini which drove him to work at the Mayo Clinic and worked alongside Dr. Gustavo Cortes Puentes and worked along renowned physicians/nurses and respiratory therapist as a ECMO specialist.

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Pablo earned a B.A. from laguna College of Art and Design in Laguna Beach, CA., and his associate science from California College San Diego.
Hands-on Session:  
Electrical Impedance Tomography

Alex Kristine Pearce, MD  
Associate Physician Diplomate  
UC San Diego

Dr. Alex Pearce received her medical degree from Tulane School of Medicine followed by residency in Internal Medicine at UC San Diego. She subsequently completed her clinical fellowship in Pulmonary and Critical Care and research fellowship at UC San Diego. She currently works as an intensivist at UC San Diego with a research focus on mechanical ventilation and Acute Respiratory Distress Syndrome.
Hands-on Session:
Portable Bronchoscopy

Lindsey John, RRT
Respiratory Therapist
UC San Francisco

Lindsey John received her Associate of Respiratory Care in 2004 from Milwaukee Area Technical College and Bachelors of Psychology from Trinity International University in Deerfield, IL 2016. Over her 20 year career in Respiratory Care, Ms. John has worked in Level 1 and 3 Trauma Centers, Regional Burn Units, Level 3 NICUs and Critical Care ICUs. Currently, she is the Bronchoscopy Services Manager at UCSF for the Lung Transplant, Interventional Pulmonology and Pulmonary Consult Services.

Joon Chang, MD
Assistant Professor
Stanford University

Dr. Joon Chang received his medical degree from UCLA David Geffen school of medicine. He did her post-graduate medicine residency at NYU and pulmonary and critical care fellowship at Stanford. He completed his interventional pulmonology fellowship at the Hospital of University of Pennsylvania in 2022. Currently, he serves as an Assistant Professor of Medicine at Stanford and a member of interventional pulmonology group at Stanford.
Single-Use Bronchoscopy Cheat Sheet

Single-Use (Portable) Bronchoscope vs. Reusable Olympus Bronchoscope Considerations
- **Cost** of single use bronchoscope vs. repairing reusable bronchoscope
- Single use vs. sterile reprocessing for reusable
- **Workflow**: monitor and tower set up with processor
- **Bronchosampler**: single operator ease of use
- Infection risk
- **Environmental factors** (water, chemical energy)
- Location of working channel

<table>
<thead>
<tr>
<th>Single-Use Bronchoscopes</th>
<th>Working Channel Diameter (mm)</th>
<th>Scope Outer Diameter (mm)</th>
<th>Minimum Endotracheal (ET) Tube Size*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ambu aScope 4 Regular</td>
<td>2.2</td>
<td>5.0</td>
<td>6.0</td>
</tr>
<tr>
<td>Ambu aScope 4 Large</td>
<td>2.8</td>
<td>5.8</td>
<td>7.0</td>
</tr>
<tr>
<td>Ambu aScope 5 Ultra-Thin</td>
<td>1.2</td>
<td>2.7</td>
<td>4.0</td>
</tr>
<tr>
<td>Ambu aScope 5 Therapeutic</td>
<td>2.8</td>
<td>5.6</td>
<td>6.0</td>
</tr>
<tr>
<td>Boston Scientific EXALT Model B Slim</td>
<td>1.0</td>
<td>3.8</td>
<td>5.0</td>
</tr>
<tr>
<td>Boston Scientific EXALT Model B Regular</td>
<td>2.0</td>
<td>5.0</td>
<td>6.0</td>
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<tr>
<td>Boston Scientific EXALT Model B Large</td>
<td>2.6</td>
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<td>7.0</td>
</tr>
<tr>
<td>Verathon BFlex 2 Slim</td>
<td>1.2</td>
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</tr>
<tr>
<td>Verathon BFlex 2 Regular</td>
<td>2.2</td>
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</tr>
<tr>
<td>Verathon BFlex 2 Large</td>
<td>3.0</td>
<td>5.8</td>
<td>7.0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Reusable Olympus Bronchoscopes</th>
<th>Working Channel Diameter (mm)</th>
<th>Scope Outer Diameter (mm)</th>
<th>Minimum Endotracheal (ET) Tube Size*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapeutic Bronchoscope (BF-1TH190)</td>
<td>2.8</td>
<td>6.2</td>
<td>7.5</td>
</tr>
<tr>
<td>Diagnostic Bronchoscope (BF-H190)</td>
<td>2.0</td>
<td>5.5</td>
<td>7.0</td>
</tr>
<tr>
<td>Diagnostic Bronchoscope (BF-P190)</td>
<td>2.0</td>
<td>4.2</td>
<td>5.5</td>
</tr>
</tbody>
</table>

**Bronchosampler for Ambu**
1. Attach the flat portion of the sampler bridge to the flat portion of the Ambu scope.
2. Clamp the attachment lock into place for secure connection.
3. Attach the sample container to the port on the sampler bridge – it will click into place.
4. Place an introducer on the open port on top of the scope.
5. Connect IV Extension tubing to the introducer to allow for lidocaine to be administered through a 35cc syringe.
6. Attach suction tubing to the suction connector located on the sampler bridge.
7. The direction of the “Flow Switch” on the sampler bridge directs where sample is collected.
8. Press downward on the “Flip Top” of the sampler container and pull away to remove the sample from the bridge.
Catheter

Cooper Surgical

- 5 FR catheter
- Closed End
- Removable guide wire
- Extension tubing
- 3 way stopcock

Insertion

- Oral or Nasal Route (preference)
- Advance gently 1-2 cm at a time (avoids coughing)
- Don't advance during coughing, gagging, esophageal spasm.
- Apply jaw thrust or head tilt if needed
- Insert to 55-60 cm in gastric space
- Insert air into balloon
  - Cooper: 1 ml
  - Smartcath
- Perform stomach push

Withdrawal

- Withdraw catheter slowly until cardiac oscillations appear (25-40 cm at the incisor)

Indications

- Persistent Hypoxemia
- Prone to Atelectasis
- Intraabdominal Hypertension
- Early onset ARDS
- Morbid Obesity-Low chest wall compliance

Contraindications

- Contraindication to NG/OG tube
- Esophageal Varices, trauma, tumor
- Nasal/facial Fractures
- TE Fistula
- Severe Coagulopathy

Scalar Waveforms

Pressure/Time

Pes (Paux)

Ptraspulmonary
**Occlusion Test (Chest Push)**

- Adequate Depth
- Balloon To Low

\[ P_{\text{plat}} - P_{\text{es}} = \text{Transpulmonary Plateau (Insp. Hold)} \]

\[ 31.5 \text{ cmH}_2\text{O} - 20 \text{ cmH}_2\text{O} = 11.5 \text{ cm H}_2\text{O} \]

**P_{\text{PEEP}} - \ P_{\text{es}} = \text{Transpulmonary PEEP (Exp. Hold)}**

\[ 20.9 \text{ cmH}_2\text{O} - 17.9 \text{ cmH}_2\text{O} = +3 \text{ cm H}_2\text{O} \]

\[ TP \text{ Plateau} - \text{Transpulmonary PEEP} = \text{Transpulmonary } D_{PL} \]

\[ 11.5 \text{ cmH}_2\text{O} - 3.0 \text{ cmH}_2\text{O} = 8.5 \text{ cm H}_2\text{O} \]

**PEEP 12**
- Ptrans I = 9.6
- Ptrans E = -2.6

**PEEP 15**
- Ptrans I = 12
- Ptrans E = +.03

**Tidal Volume Adjustment**

- Tidal Volume decreased to lower Ptrans I (Inspiratory Transpulmonary Pressure) to ≤ 10 cm H2O.
- Ptrans E remained ≥ 0 cm H2O
- Goals for optimal Lung Protective Ventilation were optimized

Ptrans I goal ≤ 10  Ptrans E goal ≥ 0
CTS 2024 Annual Education Conference  
Hands-On Session: Ventilators and Ventilator Waveforms  
March 8, 2024

Hamilton C6 Ventilator

Features:

• Turbine driven – can transport patients on it, no air inlet necessary
• IntelliCuff – automated cuff manometer
  o Set desired cuff pressure & measure continuously
  o Cuff leak detection and compensation
• P/V tool – Protective Ventilation Tool
  o Generates a quasi-static P-V curve
  o Lung recruitability assessed by the differential volume between inspiration and expiration
  o Optional buy-in tool
• Esophageal manometry
  o Allows determination of transpulmonary pressure and appropriate PEEP titration
• ASV mode – Adaptive Support Ventilation, closed-loop ventilation
  o Adjusts rate & tidal volume based on Otis’ least work of breathing equation
  o Minimizes chance of autoPEEP, volutrauma, and barotrauma
  o Decreases work of breathing
• Intellisync+
  o Real-time measurements of patient effort and adjusts flow trigger and inspiratory/expiratory cycling to optimize patient comfort
  o Used for spontaneous or non-invasive modes
• Support HFO₂ up to 60 L/m
Draeger V800 Ventilator

Features:

- Tablet-like touch screen
- Supports HFNC up to 80 L/min
- Automatic weaning through SmartCare/PS
  - Automatically adjusts pressure support during spontaneous breathing
- Low Flow P-V loop maneuver
  - Determination of lung recruitability from inflation and deflation curves
  - Lower inflection point utilized for optimal PEEP
- Smart Pulmonary View
  - Graphic view of compliance and resistance
  - Displays ratio between spontaneous and mandatory ventilation
- PressureLink
  - Coupling of Pinsp and PEEP
  - Setting one parameter will adjust the other automatically
- Spontaneous-Proportional Pressure Support
  - Level of pressure support self-titrates based on patient inspiratory effort through Flow Assist and Volume Assist parameters
Small Airways Disease and Oscillometry

Catherine Sassoon, MD
Professor in Residence
UC Irvine/VA Long Beach

Dr. Sassoon is Emeritus Professor of Medicine at UC Irvine with specialty in Pulmonary, Critical Care and Sleep Medicine. She did her postgraduate work at Cook County Hospital, Chicago, and UCLA School of Medicine. She had previously served as Chief of Pulmonary and Critical Care Medicine at the VA Long Beach Healthcare System, and as member of the Editorial Board of the American Journal of Respiratory and Critical Care Medicine, CHEST, and Respiratory Care. Her research interest is in mechanical ventilation, lung physiology, and diaphragmatic structure and function.
SMALL AIRWAYS DISEASE AND OSCILLOMETRY

Catherine S. Sassoon, MD
Emeritus Professor of Medicine
University of California, Irvine
VA Long Beach Healthcare System
I have no relationships with any ACCME defined ineligible companies.

I will not discuss off-label use and/or investigational use of any drugs or devices.
OUTLINE

- What is Oscillometry?
- Physiology of Oscillometry
- Measured Variables and Interpretation
- Case presentation
- Clinical Application
- Limitation
- Summary
WHAT IS OSCILLOMETRY?

- Oscillometry is a **noninvasive method** to assess respiratory mechanics, by superimposing external small oscillatory pressure generated by a loudspeaker to the airway opening of **spontaneously breathing** subject.

- The delivered pressure waveform is a sine wave of a single frequency (e.g., 5 Hz), a combination of sine waves of multiple frequencies (5 Hz, 10/11 Hz, 19/20 Hz), pseudo-random noise, or a train of pulses (5 pulses/s).

- Two commercially available oscillometry instruments based on superimposed pressure delivery:
  - Forced oscillation technique (FOT, sine waveform)
  - Impulse oscillometry (IOS, train of pulses)

Adapted from Smith HJ et al. Eur Respir Mon, 2005, 31, 72-105
Kostorz-Nosal S et al. Respir Physiol Neurobiol 2023; 316:104135
BRIEF HISTORY OF OSCILLOMETRY

- Oscillometry was first introduced by A. Dubois and coworkers: Oscillatory mechanics of the lung and chest in man. J. Appl. Physiol. 1956; 8:587-594.

- Oscillometry has evolved from bulky equipment, manual calculation, paper tracings to plain mouth-piece and a small equipment of the size of a medium shipping box.

- Pressure generator (loudspeaker)
- Pressure
- Flow

Courtesy of C. Irvin, Ph.D. with permission; adapted from Oscillometry 101, ERS Channel 2022
METHOD OF MEASUREMENT WITH FORCED OSCILLATION TECHNIQUE

FOT

• Measured prior to spirometry
• Three acceptable tests, each of ≥ 30 sec duration
• Coefficient of variations <10% (adults); <15% (pediatrics)

Courtesy of R. Perissin, with permission MGC Diagnostic International, Italy
Kostorz-Nosal S et al. Respir Physiol Neurobiol 2023; 316:104135
PHYSIOLOGY OF OSCILLOMETRY
Courtesy of C. Irvin, PhD with permission; adapted from Oscillometry 101,
ERS Channel 2022
MEASURED VARIABLES AND INTERPRETATION
# PHYSICAL PROPERTIES OF THE RESPIRATORY SYSTEM

<table>
<thead>
<tr>
<th>IMPEDANCE (Zrs)</th>
<th>The ratio of effective Pressure to effective Flow ( \left( \frac{P}{V} \right) )</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. RESISTANCE (Rrs)</strong> (Real Component)</td>
<td><strong>2. REACTANCE (Xrs)</strong> (Imaginary component)</td>
</tr>
<tr>
<td>• Ratio of Pressure to Flow</td>
<td>• Ratio of Pressure to Flow</td>
</tr>
<tr>
<td>• Pressure and Flow are in-phase</td>
<td>• Pressure and Flow are out of phase</td>
</tr>
<tr>
<td>• Measure resistance of airways, tissue and chest wall</td>
<td></td>
</tr>
</tbody>
</table>

\[
Z_{rs} = \frac{P}{V} = R_{rs} + jX_{rs} \quad \text{where } j = \sqrt{-1}
\]

\[
Z_{rs} \sim R_{rs} \text{ ‘+’ } E_{rs} \text{ ‘+’ } I_{rs} \quad \text{(Equation of motion)}
\]

<table>
<thead>
<tr>
<th>2.a. ELASTANCE (Ers) (Capacitance)</th>
<th>2.b. INERTANCE (Irs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Elastic properties of peripheral airways, lung parenchyma, and chest wall</td>
<td>• Inertive force moving air column</td>
</tr>
<tr>
<td>• Negative component</td>
<td>• Positive component</td>
</tr>
<tr>
<td>• Dominates at low frequency</td>
<td>• Dominates at high frequency</td>
</tr>
</tbody>
</table>

Courtesy of C Cooper, MD, with permission; adapted from presentation at Spiromics 2022
Adapted from Kaminsky DA et al. Eur Respir Rev 2022; 31:210208
Pride NB. Thorax 1992; 47:317
OSCILLOMETRIC VARIABLES IN MEDIUM FREQUENCY RANGE (5-40 Hz) USED IN CLINICAL PRACTICE

- Zrs = Impedance of the respiratory system
- Rrs = Resistance of the respiratory system
- Frequency dependence of resistance (R5-R19/20Hz)
- Xrs = Reactance of the respiratory system
  (subscript numbers denote frequency in Hz)
- fres = Resonant frequency is the frequency where respiratory system elastance (Ers) and Inertance (Irs) make equal and opposite contributions to impedance (frs of healthy subjects is ~8-12 Hz; increases in lung disease)
- AX = Area under the reactance curve subtended by the Xrs curve at the lowest frequency (5Hz) and fres

Adapted from Kaminsky DA et al. Eur Respir Rev 2022; 31:210208
Low frequencies travel all the way to the small airways, thus, reflect the resistive properties of the entire airway tree, while high frequencies travel only proximally, reflecting mainly central airways.

Rentzhog CH et al. Clin Exp Allergy 2017; 47:1546

- **Respiratory system resistance (Rrs)** reflects frictional losses of gas flow along the airways, and in tissues of the lung and chest wall as they are stretched and deformed.

- **Rrs 5 Hz** reflects total airway resistance, increases in both peripheral and central airway obstruction.

- **Rrs 19/20 Hz** reflects changes in airway caliber (bronchoconstriction, mucus plug, airway inflammation) – central airways.

- **Rrs 5-19/20 Hz** considered to reflect small airway disease; but is not recommended given the lack of specificity. Impairment in **Xrs 5Hz** is more sensitive to peripheral airway disease.

Kaminsky DA et al. Eur Respir Rev 2022; 31:210208
INTERPRETATION OF RESISTANCE

Increased Central Airway Resistance

Increased Peripheral Airway Resistance

Increased Central and Peripheral Airway Resistance

Courtesy of C. Irvin, Ph.D. with permission; adapted from Oscillometry 101, ERS Channel 2022
Reactance (Xrs) expresses the energy storage, below the frs reflects respiratory system elastance (Ers) due to stiffness of the lung tissue, airways and chest wall and above frs reflects respiratory system inertance (Irs) due to the mass of gas in the central airways → [ Xrs = Ers + Irs ].

Xrs 5 Hz becomes more negative in lung disease, indicating the respiratory system becomes stiffer; reflects also small airway heterogeneity in obstructive lung disease.

AX (cm H2O/L): The area AX reflects the stiffness of the lung parenchyma, potentially more sensitive to changes in the elastic properties of the respiratory system than Xrs at single frequency.

Kaminsky DA et al. Eur Respir Rev 2022; 31:210208
Kostorz-Nosal S et al. Respir Physiol Neurobiol 2023; 316:104135
• Changes in intra-breath Xrs at 5Hz between inspiration and expiration are useful to detect expiratory flow-limitation.

\[ \Delta X_{rs_{5Hz}} = X_{rs_{5Hz \text{ insp}}} - X_{rs_{5Hz \text{ exp}}} \]

Threshold tidal EFL:
\[ \Delta X_{rs_{5Hz}} \geq 2.8 \text{ cm H2O/L/s} \]

• Xrs 5Hz is sensitive to airway closure, reflecting communicating lung volume (i.e., air trapping).

BRONCHODILATOR RESPONSE CRITERIA

Significant Bronchodilator Response Threshold:

- **ADULTS and CHILDREN**
  - $Rrs5Hz$: 40% decrease from baseline
  - $Xrs5Hz$: 50% increase
  - $AX$: 80% decrease

*King GG et al: Eur Respir J 2020;55:1900753*
CASE PRESENTATION NO. 1
CASE # 1: NORMAL SPIROMETRY WITH SYMPTOMS OF ASTHMA, DOES PATIENT HAVE ASTHMA?

32 yr old Hispanic Male
H 172 cm  W 72 Kg
BMI 24.3 Kg/m²
Dyspnea: walking < 91 m
Cough: non-productive
Tobacco: never smoke
Wheeze: frequent
Recent illness: Asthma exacerbation 3 months ago
Medications: Albuterol
ACT score: 9

**SPIROMETRY**

<table>
<thead>
<tr>
<th></th>
<th>Pre-BD</th>
<th>Post-BD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Actual</td>
<td>LLN</td>
</tr>
<tr>
<td>FVC (L)</td>
<td>4.63</td>
<td>4.01</td>
</tr>
<tr>
<td>FEV1 (L)</td>
<td>3.84</td>
<td>3.28</td>
</tr>
<tr>
<td>FEV1/FVC (%)</td>
<td>82.96</td>
<td>71.97</td>
</tr>
<tr>
<td>SVC (L)</td>
<td>4.74</td>
<td>4.01</td>
</tr>
</tbody>
</table>
## CASE # 1 OSCILLOMETRY DATA

<table>
<thead>
<tr>
<th></th>
<th>PRE-BD</th>
<th>POST-BD</th>
<th>CHG%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rrs 5Hz</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(cmH2O/L/s)</td>
<td>Mean±SD</td>
<td>Zscore</td>
<td>%Pred</td>
</tr>
<tr>
<td>Rinsp</td>
<td>3.86±0.35</td>
<td>0.97</td>
<td>131.27%</td>
</tr>
<tr>
<td>Rexp</td>
<td>4.26±0.04</td>
<td>1.32</td>
<td>144.90%</td>
</tr>
<tr>
<td>Rtot</td>
<td>4.04±0.21</td>
<td>1.13</td>
<td>137.22%</td>
</tr>
<tr>
<td><strong>Xrs5Hz</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(cm H2O/L/s)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Xinsp</td>
<td>-1.09±0.08</td>
<td>-0.04</td>
<td>101.29%</td>
</tr>
<tr>
<td>Xexp</td>
<td>-1.84±0.29</td>
<td>-1.89</td>
<td>170.79%</td>
</tr>
<tr>
<td>Xtot</td>
<td>-1.41±0.17</td>
<td>-0.88</td>
<td>131.58%</td>
</tr>
<tr>
<td><strong>Tidal EFL</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(cm H2O/L/s)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ΔXrs insp-exp</td>
<td>0.75±0.22</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Case #1 Interpretation

- $\text{Rrs}_{5\text{Hz}}$ is within normal limits with no significant response to bronchodilator.
- $\text{Xrsexp}_{5\text{Hz}}$ increased (more negative), suggests impaired mechanical properties of the peripheral airways due to peripheral airways inflammation, and/or ventilation inhomogeneities.
- Following bronchodilator administration, $\text{Xrsexp}_{5\text{Hz}}$ decreased >50% (less negative), with frs shifted to lower frequency, suggests a significant response to bronchodilator.
- Poor control asthma symptoms together with abnormal reactance ($\text{Xrsexp}_{5\text{Hz}}$) and response to bronchodilator are consistent with asthma.
# Relationship of Abnormal Spirometry and Abnormal Oscillometry to Poor Asthma Control

Lung Function Variable | Poor Asthma Control (ACT <20) |  
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>(n = 90)</td>
<td>Present (n)</td>
</tr>
<tr>
<td>Spirometric FAO</td>
<td>Present</td>
</tr>
<tr>
<td></td>
<td>Absent</td>
</tr>
<tr>
<td>Abnormal R&lt;sub&gt;5Hz&lt;/sub&gt;</td>
<td>Present</td>
</tr>
<tr>
<td></td>
<td>Absent</td>
</tr>
<tr>
<td>Abnormal X&lt;sub&gt;5Hz&lt;/sub&gt;</td>
<td>Present</td>
</tr>
<tr>
<td></td>
<td>Absent</td>
</tr>
<tr>
<td>Abnormal AX</td>
<td>Present</td>
</tr>
<tr>
<td></td>
<td>Absent</td>
</tr>
</tbody>
</table>

FAO: Fixed airflow obstruction; ACT: asthma control test

Adapted from Cottee AM et al. J Allergy Clin Immunol Pract 2022;10:1260
CASE PRESENTATION NO. 2
CASE #2: NORMAL SPIROMETRY, MILD OBESITY WITH AIR TRAPPING, DOES PATIENT HAVE COPD?

63 yrs old Caucasian Male  
H 169 cm W 97 Kg  
BMI 34 Kg/m²  
**Dyspnea:** with exertion  
**Cough:** yes, productive  
**Tobacco:** 5 pkyrs, quit 6 yrs ago  
**Wheeze:** no  
**Recent illness:** no  
**Medications:** Spiriva, ± Fluticasone/Salmeterol, ± Albuterol prn.

<table>
<thead>
<tr>
<th></th>
<th>Pre-BD</th>
<th>Post-BD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SPIROMETRY</strong></td>
<td>Actual</td>
<td>LLN</td>
</tr>
<tr>
<td>FVC (L)</td>
<td>3.13</td>
<td>3.03</td>
</tr>
<tr>
<td>FEV1 (L)</td>
<td>2.43</td>
<td>2.31</td>
</tr>
<tr>
<td>FEV1/FVC (%)</td>
<td>77.88</td>
<td>65.15</td>
</tr>
</tbody>
</table>

**SLOW VITAL CAPACITY**

|                      | Actual | LLN | ULN | Z-Score | Pred | %Pred |
| SVC (L)              | 3.57   | 3.03 | 4.99 | -0.74   | 4.00 | 89    |
| ERV (L)              | 0.22   |     |     |         | 1.35 | 16    |

**LUNG VOL (PLETH)**

|                      | Actual | LLN | ULN | Z-Score | Pred | %Pred |
| TLC (L)              | 6.80   | 5.12 | 7.70 | +0.51   | 6.40 | 106   |
| FRC (L)              | 3.45   | 2.23 | 4.47 | +0.33   | 3.22 | 107   |
| RV (L)               | 3.24   | 1.26 | 3.01 | +2.00   | 2.06 | 157   |
| RV/TLC (%)           | 47.58  | 21.62 | 42.01 | +2.50   | 31.59 | 150   |
| sGaw (L/cmH2O*s)     | 0.17   | 0.08 | 0.32 | -0.49   | 0.20 | 82    |
CASE #2 OSCILLOMETRY DATA

*EFL Threshold ≥ 2.8 cmH2O/L/s
CASE #2 INTERPRETATION

- $R_{rs_{5Hz}}$ is within normal limits with no significant response to bronchodilator.
- $X_{rsexp_{5Hz}}$ and $X_{rstot_{5Hz}}$ increased (more negative) suggests impaired mechanical properties of peripheral airways, ventilation inhomogeneity, airway closure, and increased chest wall stiffness (obesity).
- The presence of EFL leads to air trapping (increased RV/TLC).
- Following bronchodilator administration, both $X_{rsexp_{5Hz}}$ and $X_{rstot_{5Hz}}$ decreased >50% (less negative), with frs shifted to lower frequency, suggests a significant response to bronchodilator.
- The above findings are consistent with Chronic Bronchitis or Asthma.
INTRA-BREATH EFL DISCRIMINATE SURVIVAL IN MODERATELY SEVERE COPD (ECLIPSE TRIAL)

• In moderately severe COPD (FEV1 > 50% pred), oscillometry detected ~27% of patients with EFL.
• In this group of patients, EFL predicts high risk for mortality.
• In severe or very severe COPD (FEV1 <50% pred), FEV1 predicts high risk of mortality irrespective of EFL.
• Detection of EFL leads to early intervention, e.g., pulmonary rehabilitation may be of benefit.
CLINICAL APPLICATION IN OSCILLOMETRY
DIAGNOSTIC POTENTIAL OF OSCILLOMETRY
LEAD [LUNG HEART SOCIAL BODY] STUDY

- General population 18-90 yrs (total n: 7560; with symptoms /disease n = 2171)
- Abnormal Oscillometry detected in 20% (1506/7560) of population
- Abnormal Spirometry detected in 13% (985/7560) of population
- Abnormal oscillometry alone identified 27% (587/2171) of subjects with respiratory symptoms/disease
- Abnormal spirometry alone identified 22.2% (483/2171) of subjects with respiratory symptoms/disease
- Combined abnormal oscillometry and spirometry identified 38.8% (840/2171) of subjects with respiratory symptoms/disease

LIMITATIONS OF OSCILLOMETRY

- No extensive reference normal values comparable to Global Lung Function Initiative (GLI) reference values for spirometry, lung volumes and DLCO [e.g., Rrs5-19Hz].
- Unable to determine the degree of severity similar to the degree of obstruction with GOLD’s percent predicted FEV1.
- Resistance and Reactance are volume dependent, yet, unable to correct for lung volume. Since bronchodilation reduces lung hyperinflation, this would potentially cause paradoxical increase in Rrs and decrease Xrs, therefore, the interpretation of bronchodilator responses of Rrs and Xrs may not be straightforward and could cause some disparity with spirometry response.
SUMMARY OF OSCILLOMETRIC RESISTANCE AND REACTANCE PATTERN IN NORMAL AND DISEASE

Adapted from Komarow HD et al. Ann Allergy Asthma Immunol 2011; 106: 191
Oscillometry complements existing conventional pulmonary function tests.

Oscillometry is useful for longitudinal monitoring of lung function from the very young to the very old, essentially throughout life.

Increased Rrs5Hz is consistent with peripheral airway obstruction.

Increased Rrs at all frequencies is consistent with central airway obstruction.

Reactance at 5 Hz is sensitive to detect impaired mechanical properties of the peripheral airways, however, it increases (more negative) in both obstructive disease (due to parenchymal inhomogeneity, peripheral airway wall stiffness, or air trapping from dynamic airway closure) and restrictive disease (due to increased stiffness of lung parenchyma or chest wall), hence clinical correlation is necessary.
thank you
REFERENCES

Resmon Pro Full V3
DEMONSTRATION VIDEO:
“Measuring FOT with the Resmon Pro Full V3 FOT-Oscillometry system, a product demonstration, 7:30 minutes (Jan 2023)”
LINK: https://vimeo.com/788556136
Password: “ResmonV3DEMO”

“DESCRIPTION: Two good acceptable FOT and one one non-acceptable measurements have been already performed, and to complete the FOT session (as per 2020 ERS international guidelines) a THIRD acceptable measurement is now added. This video shows how to perform a measurement, complete a session, and analyze the results.

NOTE: This is an extract from the video (OPEN ACCESS, no password required) - Intro to Forced Oscillation Technique (FOT) or Oscillometry, using the Resmon PRO FULL V3 System – JAN 2023 (35 min) https://www.youtube.com/watch?v=mpdcqvrPnfU

Perissin R. With permission.
Dr. Christenson is an Associate Professor at the University of California, San Francisco in the Division of Pulmonary, Critical Care, Allergy, and Sleep Medicine. She serves as an attending physician on the Pulmonary Consult Service and in the Pulmonary Clinic. Dr. Christenson obtained her undergraduate degree at the University of Wisconsin, Madison and her medical degree at the Medical College of Wisconsin. She completed her residency training as well as a year of research training in computational biology at Boston Medical Center. She then came to UCSF for fellowship in Pulmonary and Critical Care Medicine where she also obtained a Master’s in Clinical Research, after which she joined faculty.

Dr. Christenson’s research program integrates her expertise in genomics/bioinformatics and clinical research to study chronic airway disease and the associated risk factors. Her research emphasizes innovative computational tools, systems biology approaches, and ‘omics biomarkers to better inform our understanding of the biology underlying clinical traits and outcomes in asthma, smoking, and COPD. Dr. Christenson also serves in multiple leadership roles for multi-center studies and advises industry on trials of biologic and inhaled therapies for COPD. Leadership roles include co-director of the Genetics and Genomics Subcommittee for the multi-center SPIROMICS and SOURCE studies, the UCSF site PI for the American Lung Association (ALA) Airway Clinical Research Consortium, and a Disease Study Site PI for the NHGRI-funded Multi-Omics in Health and Disease (MOHD) Consortium.
Biologic Therapies in COPD

Stephanie Christenson, MD MAS
California Thoracic Society
March 8th, 2024
Faculty Disclosures

I have the following relationships with ACCME defined ineligible companies:

- AstraZeneca: Consultant, Speaker (non-branded)
- GlaxoSmithKline: Consultant, Speaker (non-branded)
- Glenmark: Consultant
- Sanofi: Consultant, Speaker (non-branded)
- Regeneron: Consultant, Speaker (non-branded)
- UpToDate: writer
- Verona: Consultant

I WILL discuss off-label use and/or investigational use of any drugs or devices.
Outline

- Overview of T2 inflammation
- Evidence for T2 inflammation in COPD before biologics: blood eosinophils and corticosteroids
- Biologics in COPD
Type 2 Inflammation in the Airway

Fahy, Nat Rev Immun. 2015
Initial Pharmacotherapy

**Initial Pharmacological Treatment**

- **GROUP E**: LABA + LAMA*
  - Consider LABA+LAMA+ICS* if blood eos ≥ 300

- **GROUP A**: A bronchodilator
  - mMRC 0-1, CAT < 10

- **GROUP B**: LABA + LAMA*
  - mMRC ≥ 2, CAT ≥ 10

*single inhaler therapy may be more convenient and effective than multiple inhalers*
Follow-up Pharmacotherapy

Follow-up Pharmacological Treatment

1. IF RESPONSE TO INITIAL TREATMENT IS APPROPRIATE, MAINTAIN IT.
   - Check adherence, inhaler technique and possible interfering comorbidities
   - Consider the predominant treatable trait to target (dyspnea or exacerbations)
     - Use exacerbation pathway if both exacerbations and dyspnea need to be targeted
   - Place patient in box corresponding to current treatment & adjust follow indications
   - Assess response, adjust and review
   - These recommendations do not depend on the ABE assessment at diagnosis

DYSPEANEA

LABA or LAMA

LABA + LAMA*

- Consider switching inhaler device or molecules
- Implement or escalate non-pharmacologic treatment(s)
- Investigate (and treat) other causes of dyspnea

LABA + LAMA + ICS*

ExACERBATIONS

LABA or LAMA

LABA + LAMA*

LABA + LAMA + ICS*

- Consider de-escalation of ICS if pneumonia or other considerable side-effects. In case of blood eos > 300 cells/μL de-escalation is more likely to be associated with the development of exacerbations

*Single inhaler therapy may be more convenient and effective than multiple inhalers

**Consider de-escalation of ICS if pneumonia or other considerable side-effects. In case of blood eos > 300 cells/μL de-escalation is more likely to be associated with the development of exacerbations
Endotyping in COPD: Blood Eosinophils and Inhaled Corticosteroids

- Improved Exacerbation Prevention in Post-Hoc analyses of blood eos in ICS/LABA trials:
  - FORWARD → AECOPD rate reduction, Δ FEV1, SGRQ
  - INSPIRE → AECOPD rate reduction
  - TRISTAN → AECOPD rate reduction
  - 3 RCTs of Budesonide/Formoterol → AECOPD rate reduction, Δ FEV1, SGRQ
  - 2 RCTs of Fluticasone/Vilanterol → AECOPD rate reduction
  - WISDOM → Increased Moderate/Severe Exacerbations after ICS withdrawal
Endotyping in COPD: Blood Eosinophils and Inhaled Corticosteroids

Equipoise in Inhaled Therapy Trials:

LABA/LAMA vs ICS/LAB A
- **FLAME (2016):** indacaterol/glycopyrronium superior/similar to salmeterol/fluticasone regardless of blood eosinophil levels

Triple Therapies (ICS/LABA/LAMA)
- **IMPACT (2018):** fluticasone/umeclidium/vilanterol decreased exacerbations more than LAMA/LABA (umeclidium/vilanterol) or ICS/LABA (fluticasone/vilanterol) regardless of eosinophil counts
- **ETHOS (2020):** budesonide/glycopyrrolate/formoterol decreased exacerbations more than LAMA/LABA (glycopyrrholate/formoterol) or ICS/LABA (fluticasone/vilanterol) regardless of eosinophil counts

Endotyping in COPD:
Triple Therapy Post-Hoc Analyses of Eosinophils

**IMPACT**

Pascoe S et al, Lancet Respir Med 2020

**ETHOS**

Bafhadel M et al, Int J Chron Obstruct Pulmon Dis 2022
ICS containing regimens may not have an effect with Blood Eos <100
Blood Eosinophil counts in IMPACT

Pascoe S et al, Lancet Respir Med 2020
Biologics in COPD
# Biologics in Development in COPD

***None of these are FDA approved***

<table>
<thead>
<tr>
<th>Biologic</th>
<th>Target</th>
<th>Trial</th>
</tr>
</thead>
</table>
| Mepolizumab    | IL-5            | **METREX & METREO** *(Pavord ID, et al NEJM 2017)*  
|                |                 | **MATINEE** *(Ongoing, Est Completion: 8/24)* |
| Benralizumab   | IL-5R           | **GALATHEA & TERRANOVA** *(Lipson D, et al NEJM 2018)*  
|                |                 | **RESOLUTE** *(Ongoing, Est Completion: 6/25)* |
| Dupilumab      | IL4R (IL-4 & IL-13) | **BOREAS** *(Rabe KF, et al NEJM 2023)*  
|                |                 | **NOTUS** *(not yet reported)* |
| Tezepelumab    | TSLP            | **COURSE** *(Phase 2a, Ongoing, Completed: 1/24)* |
| Itepekimab     | IL-33           | **AERIFY-1 & 2** *(Ongoing, Est Completion: 11/25)* |
| Tozorakimab    | IL-33           | **OBERON & TITANIA** *(Ongoing, Est Completion: 8/25)* |
| Astegolimab    | ST2             | **ARNASA** *(Ongoing, Est Completion: 6/25)* |
Type 2 Inflammation in the Airway

Fahy, Nat Rev Immun. 2015
### Eosinophils as a Therapeutic Target: Anti-IL-5 Biologics

**Mixed Results to Date**

<table>
<thead>
<tr>
<th>Mepolizumab (anti-IL-5)</th>
<th>Benralizumab (anti-IL-5Rα)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Eligibility</strong></td>
<td><strong>Eligibility</strong></td>
</tr>
<tr>
<td>• 10 pack year smoking history</td>
<td>• 10 pack year smoking history</td>
</tr>
<tr>
<td>• Triple therapy x3 months</td>
<td>• Dual or Triple Therapy</td>
</tr>
<tr>
<td>• ≥ 2 moderate or ≥ 1 severe exacerbation</td>
<td>• ≥ 2 moderate or ≥ 1 severe exacerbation</td>
</tr>
<tr>
<td>• Current diagnosis of asthma excluded</td>
<td>• Symptomatic: MMRC ≥ 1</td>
</tr>
<tr>
<td>• Blood Eos: ( \geq 150/\mu L ) at screening <strong>OR</strong> ( \geq 300/\mu L ) during previous year</td>
<td>• Current diagnosis of asthma excluded</td>
</tr>
<tr>
<td>• Blood Eos: ( \geq 220/\mu L ) at baseline</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>METREX</strong></th>
<th><strong>METREO</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Statistically significant 18% reduction in exacerbations</td>
<td>• Did not reach significance for exacerbations</td>
</tr>
<tr>
<td>• No difference in symptom scores</td>
<td>• No difference in symptom scores</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>GALATHEA</strong></th>
<th><strong>Terranova</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Neither reached significance for exacerbations</td>
<td>• Both showed improvement in lung function</td>
</tr>
</tbody>
</table>

Lipson D, NEJM 2018   Pavord ID, NEJM 2017
Eosinophils as a therapeutic target: Anti-IL-5 Biologics

Post-Hoc Analyses: Potential efficacy with higher eos?

Mepolizumab (anti-IL-5)

Benralizumab (anti-IL-5Rα)

**METREX**

**METREO**

**GALATHEA**

**Terranova**

Lipson D, NEJM 2018  
Pavord ID, NEJM 2017
IL-4 and IL-13 as a therapeutic target: Dupilumab

BOREAS Trial

Eligibility

- 10 pack year smoking history
- triple therapy for ≥ 3 months
- ≥ 2 moderate or ≥ 1 severe exacerbation
- Chronic bronchitis
- No history of asthma
- Blood Eos: ≥300/µL at screening

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Placebo (N=423)</th>
<th>Dupilumab (N=460)</th>
<th>Total (N=883)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>63.2±6.1</td>
<td>65.0±6.0</td>
<td>64.1±6.1</td>
</tr>
<tr>
<td>Male sex (%  )</td>
<td>332 (61.4)</td>
<td>298 (65.4)</td>
<td>630 (69.8)</td>
</tr>
<tr>
<td>Race or ethnic group (%  )</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>367 (86.4)</td>
<td>359 (80.8)</td>
<td>726 (82.1)</td>
</tr>
<tr>
<td>Black</td>
<td>2 (0.5)</td>
<td>3 (0.6)</td>
<td>5 (0.6)</td>
</tr>
<tr>
<td>Asian</td>
<td>67 (15.9)</td>
<td>67 (14.3)</td>
<td>134 (15.3)</td>
</tr>
<tr>
<td>American Indian or Alaska Native</td>
<td>6 (1.5)</td>
<td>7 (1.5)</td>
<td>13 (1.5)</td>
</tr>
<tr>
<td>Native Hawaiian or other Pacific Islander</td>
<td>1 (0.2)</td>
<td>0</td>
<td>1 (0.1)</td>
</tr>
<tr>
<td>Multi-ethnic</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Hispanic or Latino ethnic group (%  )</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>129 (29.4)</td>
<td>137 (29.7)</td>
<td>266 (29.9)</td>
</tr>
<tr>
<td>Non-Hispanic or non-Latino</td>
<td>294 (69.6)</td>
<td>333 (71.6)</td>
<td>627 (72.1)</td>
</tr>
<tr>
<td>Unknown</td>
<td>0</td>
<td>1 (0.2)</td>
<td>1 (0.1)</td>
</tr>
<tr>
<td>Smoking status (%  )</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Former smoker</td>
<td>323 (76.6)</td>
<td>314 (73.4)</td>
<td>637 (72.0)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>149 (34.8)</td>
<td>146 (32.6)</td>
<td>295 (33.0)</td>
</tr>
<tr>
<td>Smoking history — pack y</td>
<td>60±42±4.4</td>
<td>89±62±22.4</td>
<td>108±53±23.4</td>
</tr>
<tr>
<td>Body mass index</td>
<td>27±6±7</td>
<td>27±6±6.4</td>
<td>27±6±6.6</td>
</tr>
<tr>
<td>Background medication — no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triple therapy</td>
<td>461 (99.7)</td>
<td>453 (97.2)</td>
<td>914 (97.6)</td>
</tr>
<tr>
<td>Inhaled high dose glucocorticoid</td>
<td>129 (28.6)</td>
<td>121 (26.0)</td>
<td>250 (27.4)</td>
</tr>
</tbody>
</table>

Baseline values for SOT outcomes at randomization:

<table>
<thead>
<tr>
<th>Outcomes (µM/L)</th>
<th>Placebo</th>
<th>Dupilumab</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>40±42±3</td>
<td>25±3±2</td>
<td>45±2±9</td>
</tr>
<tr>
<td>Median (interquartile range)</td>
<td>200 (200-400)</td>
<td>200 (200-400)</td>
<td>200 (200-400)</td>
</tr>
<tr>
<td>Postbronchodilator FVC — % predicted</td>
<td>23.5±3±20.0</td>
<td>25.3±3±22.7</td>
<td>24.3±3±22.4</td>
</tr>
<tr>
<td>Distribution — % (dp/di)</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>0-40 %</td>
<td>188 (44.2)</td>
<td>155 (44.3)</td>
<td>343 (44.3)</td>
</tr>
<tr>
<td>40-80 %</td>
<td>216 (43.3)</td>
<td>218 (43.3)</td>
<td>434 (43.7)</td>
</tr>
<tr>
<td>No. of moderate or severe COVID-19 exacerbations in previous yr</td>
<td>2.3±1.0</td>
<td>2.2±1.1</td>
<td>2.3±1.0</td>
</tr>
</tbody>
</table>

Baseline values for SOT outcomes at randomization:

<table>
<thead>
<tr>
<th>Outcomes (µM/L)</th>
<th>Placebo</th>
<th>Dupilumab</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>1.3±0.4</td>
<td>1.3±0.4</td>
<td>1.3±0.4</td>
</tr>
<tr>
<td>Median (interquartile range)</td>
<td>1.3±0.4</td>
<td>1.3±0.4</td>
<td>1.3±0.4</td>
</tr>
<tr>
<td>Postbronchodilator FVC — % predicted</td>
<td>58.6±13.0</td>
<td>58.6±13.3</td>
<td>58.6±13.2</td>
</tr>
<tr>
<td>Distribution — % (dp/di)</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>0-40 %</td>
<td>65±9±1</td>
<td>65±9±1</td>
<td>65±9±1</td>
</tr>
<tr>
<td>40-80 %</td>
<td>46±17±7</td>
<td>46±17±7</td>
<td>46±17±7</td>
</tr>
<tr>
<td>No. of moderate or severe COVID-19 exacerbations in previous yr</td>
<td>2.3±1.0</td>
<td>2.2±1.1</td>
<td>2.3±1.0</td>
</tr>
</tbody>
</table>
IL-4 and IL-13 as a therapeutic target: Dupilumab

**BOREAS Trial**

**Exacerbations: 30% reduction**

**Pre-Bronchodilator FEV1**

---

Bhatt, et al. NEJM 2023
**Table 2. End Points Corrected for Multiplicity (Intention-to-Treat Population)**

<table>
<thead>
<tr>
<th>End Point</th>
<th>Placebo (N=423)</th>
<th>Dalilumab (N=460)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary end point</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Annualized rate of moderate or severe exacerbations of COPD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adjusted annualized rate of moderate or severe exacerbations — events per yr (95% CI)</td>
<td>1.10 (0.93 to 1.30)</td>
<td>0.78 (0.64 to 0.93)</td>
<td></td>
</tr>
<tr>
<td>Rate ratio vs. placebo (95% CI)</td>
<td>—</td>
<td>0.70 (0.58 to 0.86)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Secondary and other end points</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change in prebronchodilator FEV₁ from baseline to wk 12</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Least-squares mean change (95% CI) — liters</td>
<td>0.077 (0.042 to 0.112)</td>
<td>0.160 (0.126 to 0.195)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Least-squares mean difference vs. placebo (95% CI) — liters</td>
<td>—</td>
<td>0.083 (0.042 to 0.125)</td>
<td></td>
</tr>
<tr>
<td>Change in prebronchodilator FEV₁ from baseline to wk 52</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Least-squares mean change (95% CI) — liters</td>
<td>0.070 (0.033 to 0.107)</td>
<td>0.153 (0.116 to 0.189)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Least-squares mean difference vs. placebo (95% CI) — liters</td>
<td>—</td>
<td>0.083 (0.038 to 0.128)</td>
<td></td>
</tr>
<tr>
<td>Change in prebronchodilator FEV₁ from baseline to wk 12</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>among patients with a baseline FeNO ≥20 ppb</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Least-squares mean change (95% CI) — liters</td>
<td>0.108 (0.058 to 0.177)</td>
<td>0.232 (0.164 to 0.299)</td>
<td></td>
</tr>
<tr>
<td>Least-squares mean difference vs. placebo (95% CI) — liters</td>
<td>—</td>
<td>0.124 (0.043 to 0.203)</td>
<td>0.002</td>
</tr>
<tr>
<td>Change in prebronchodilator FEV₁ from baseline to wk 52</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>among patients with a baseline FeNO ≥20 ppb</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Least-squares mean change (95% CI) — liters</td>
<td>0.120 (0.047 to 0.192)</td>
<td>0.247 (0.176 to 0.318)</td>
<td></td>
</tr>
<tr>
<td>Least-squares mean difference vs. placebo (95% CI) — liters</td>
<td>—</td>
<td>0.127 (0.042 to 0.212)</td>
<td>0.003</td>
</tr>
<tr>
<td>Change in SGRQ total score from baseline to wk 52</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Least-squares mean change (95% CI) — liters</td>
<td>-6.4 (-8.0 to -4.8)</td>
<td>-9.7 (-11.3 to -8.1)</td>
<td></td>
</tr>
<tr>
<td>Least-squares mean difference vs. placebo (95% CI) — liters</td>
<td>—</td>
<td>-3.4 (-5.5 to -1.3)</td>
<td>0.002</td>
</tr>
<tr>
<td>SGRQ total score improvement ≥4 points at wk 52</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percentage of patients (95% CI)</td>
<td>43.1 (38.6 to 47.7)</td>
<td>51.5 (46.9 to 56.1)</td>
<td></td>
</tr>
<tr>
<td>Odds ratio vs. placebo (95% CI)</td>
<td>—</td>
<td>1.4 (1.1 to 1.9)</td>
<td>0.009</td>
</tr>
<tr>
<td>Change in ERS-COPD from baseline to wk 52</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Least-squares mean change (95% CI) — liters</td>
<td>-7.5 (-2.1 to -1.1)</td>
<td>-2.7 (-3.2 to -2.2)</td>
<td></td>
</tr>
<tr>
<td>Least-squares mean difference vs. placebo (95% CI) — liters</td>
<td>—</td>
<td>-1.1 (-1.8 to -0.4)</td>
<td>0.001</td>
</tr>
<tr>
<td>Annualized rate of moderate or severe exacerbations of COPD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>among patients with a baseline FeNO ≥20 ppb</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adjusted annualized rate of moderate or severe exacerbations — events per yr (95% CI)</td>
<td>1.12 (0.83 to 1.50)</td>
<td>0.70 (0.51 to 0.96)</td>
<td></td>
</tr>
<tr>
<td>Rate ratio vs. placebo (95% CI)</td>
<td>—</td>
<td>0.62 (0.45 to 0.87)</td>
<td>0.005</td>
</tr>
</tbody>
</table>
## Biomarker Responses in BOREAS

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Placebo (N=470)</th>
<th>Dupilumab 300 (N=469)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Blood eosinophils, cells/µL</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percent change from baseline at week 52</td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>376</td>
<td>372</td>
</tr>
<tr>
<td>Median</td>
<td>-9.45</td>
<td>-11.95</td>
</tr>
<tr>
<td><strong>Fibrinogen, mg/dL</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percent change from baseline at week 52</td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>391</td>
<td>399</td>
</tr>
<tr>
<td>Median</td>
<td>-1.3</td>
<td>-2.6</td>
</tr>
<tr>
<td><strong>FeNO, ppb</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percent change from baseline at week 52</td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>358</td>
<td>350</td>
</tr>
<tr>
<td>Median</td>
<td>-6.9</td>
<td>-28.6</td>
</tr>
</tbody>
</table>

**Figure S8. Fractional Exhaled Nitric Oxide from Baseline to End of 52-Week Treatment Period and Follow-Up 12-Week Off-Treatment Period in the Safety Population**

Mean change ± 95% CI (parts per billion)

BL baseline, CI confidence interval. Error bars represent 95% confidence intervals. 95% CIs have not been adjusted for multiplicity and should not be used for hypothesis testing.
IL-33 as a therapeutic target in COPD: Itepikimab phase 2 trial

Eligibility
- 10 pack year smoking history
- Dual or triple therapy
- ≥ 2 moderate or ≥ 1 severe exacerbation
- Chronic bronchitis
- Symptomatic: CAT >10
- Blood Eos: any

**No Significant Differences**
IL-33 as a therapeutic target in COPD: Itepikimab phase 2 trial

Former Smokers

FEV1

Exacerbations

Current Smokers

FEV1

Exacerbations

## Biologics in Development in COPD

***None of these are FDA approved***

<table>
<thead>
<tr>
<th>Biologic</th>
<th>Target</th>
<th>Trial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mepolizumab</td>
<td>IL-5</td>
<td>METREX &amp; METREO <em>(Pavord ID, et al NEJM 2017)</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td>MATINEE <em>(Ongoing, Est Completion: 8/24)</em></td>
</tr>
<tr>
<td>Benralizumab</td>
<td>IL-5R</td>
<td>GALATHEA &amp; TERRANOVA <em>(Lipson D, et al NEJM 2018)</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td>RESOLUTE <em>(Ongoing, Est Completion: 6/25)</em></td>
</tr>
<tr>
<td>Dupilumab</td>
<td>IL4R (IL-4 &amp; IL-13)</td>
<td>BOREAS <em>(Rabe KF, et al NEJM 2023)</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td>NOTUS <em>(not yet reported)</em></td>
</tr>
<tr>
<td>Tezepelumab</td>
<td>TSLP</td>
<td>COURSE <em>(Phase 2a, Ongoing, Completed: 1/24)</em></td>
</tr>
<tr>
<td>Itepekimab</td>
<td>IL-33</td>
<td>AERIFY-1 &amp; 2 <em>(Ongoing, Est Completion: 11/25)</em></td>
</tr>
<tr>
<td>Tozorakimab</td>
<td>IL-33</td>
<td>OBERON &amp; TITANIA <em>(Ongoing, Est Completion: 8/25)</em></td>
</tr>
<tr>
<td>Astegolimab</td>
<td>ST2</td>
<td>ARNASA <em>(Ongoing, Est Completion: 6/25)</em></td>
</tr>
</tbody>
</table>
Conclusions

- There is evidence that T2 inflammation plays a major role in a subset of patients with COPD.
- Patients with T2 inflammation, as measured by blood eos, appear to respond better to inhaled corticosteroids than those without T2 inflammation.
- There are multiple T2 biologics in the pipeline for COPD with clinical trials ending in 2024 and 2025.
- Dupilumab is currently the only biologics with strongly positive results in COPD, but there is promise that others will work in COPD subgroups with blood eosinophils >300.
- Alarmin-based therapy, targeting IL-33 or TSLP, is being studied in both T2 low and T2 high individuals.
Bronchoscopic Management of Airways Diseases

Brian Shaller, MD
Assistant Professor
Stanford

Brian Shaller is a Clinical Assistant Professor in the Division of Pulmonary, Allergy & Critical Care Medicine at Stanford University. He trained in Interventional Pulmonology at the Cleveland Clinic and helped establish Stanford’s Interventional Pulmonology fellowship program in 2022, for which he currently serves as Associate Program Director. Dr. Shaller’s clinical and academic interests include advanced diagnostics for lung nodules, endoscopic management of central airway diseases, and procedural education.
RELEVANT DISCLOSURES

- I have the following relationships with ACCME defined ineligible companies:
  - None pertinent to this topic

- I WILL discuss off-label use and/or investigational use of any drugs or devices
  - Bronchial rheoplasty, cryospray, and targeted lung denervation have breakthrough device designation from the FDA and are approved for use in clinical trials only
OBJECTIVES

- Identify benign airway diseases for which there are bronchoscopic interventions
- Describe general mechanisms of action of different interventions
- Discuss clinical evidence and eligibility criteria for different interventions
- Assess the role of bronchoscopic interventions in broader context of patient care
### LIMITATIONS OF THERAPEUTIC BRONCHOSCOPY

#### Do I have a bronchoscopic intervention?

<table>
<thead>
<tr>
<th>Generation</th>
<th>Diameter, cm</th>
<th>Length, cm</th>
<th>Number</th>
<th>Total cross-sectional area, cm²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trachea</td>
<td>1.80</td>
<td>12.0</td>
<td>1</td>
<td>2.54</td>
</tr>
<tr>
<td>Bronchi</td>
<td>1.22</td>
<td>4.8</td>
<td>2</td>
<td>2.33</td>
</tr>
<tr>
<td>2</td>
<td>0.83</td>
<td>1.9</td>
<td>4</td>
<td>2.13</td>
</tr>
<tr>
<td>3</td>
<td>0.56</td>
<td>0.8</td>
<td>8</td>
<td>2.00</td>
</tr>
<tr>
<td>4</td>
<td>0.45</td>
<td>1.3</td>
<td>16</td>
<td>2.48</td>
</tr>
<tr>
<td>Bronchioles</td>
<td>0.35</td>
<td>1.07</td>
<td>32</td>
<td>3.11</td>
</tr>
<tr>
<td>Terminal bronchioles</td>
<td>0.06</td>
<td>0.17</td>
<td>$6 \times 10^4$</td>
<td>180.0</td>
</tr>
<tr>
<td>Respiratory bronchioles</td>
<td>0.05</td>
<td>0.10</td>
<td>$5 \times 10^5$</td>
<td>$10^3$</td>
</tr>
<tr>
<td>19</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T₃</td>
<td>0.05</td>
<td>0.10</td>
<td>$5 \times 10^5$</td>
<td>$10^3$</td>
</tr>
<tr>
<td>T₂</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T₁</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alveolar sacs</td>
<td>0.04</td>
<td>0.05</td>
<td>$8 \times 10^5$</td>
<td>$10^4$</td>
</tr>
</tbody>
</table>

- **Definitely**
- **Possibly**
- **I guess I can take a look . . .**
- **Wait, what?**
- **Isn’t there an inhaler for that?**
## LIMITATIONS OF THERAPEUTIC BRONCHOSCOPY

<table>
<thead>
<tr>
<th>RANK</th>
<th>ICD-10 CODE</th>
<th>ICD-10 DESCRIPTION</th>
<th>PERCENT OF PULMONOLOGIST VISITS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>J449</td>
<td>Chronic obstructive pulmonary disease, unspecified</td>
<td>8.90%</td>
</tr>
<tr>
<td>2</td>
<td>J069</td>
<td>Acute upper respiratory infection, unspecified</td>
<td>7.00%</td>
</tr>
<tr>
<td>3</td>
<td>J301</td>
<td>Allergic rhinitis due to pollen</td>
<td>5.90%</td>
</tr>
<tr>
<td>4</td>
<td>J9601</td>
<td>Acute respiratory failure with hypoxia</td>
<td>5.40%</td>
</tr>
<tr>
<td>5</td>
<td>J029</td>
<td>Acute pharyngitis, unspecified</td>
<td>5.10%</td>
</tr>
<tr>
<td>6</td>
<td>J45909</td>
<td>Unspecified asthma, uncomplicated</td>
<td>4.80%</td>
</tr>
</tbody>
</table>

https://www.definitivehc.com/resources/healthcare-insights/top-conditions-pulmonologist-visits
EVOLUTION OF BRONCHOSCOPIC THERAPEUTICS

- **First 100+ years**: therapeutics limited to central-lobar-segmental airways

- **Last 10-15 years**: multiple new treatment options for peripheral obstructive lung diseases
  - **2010**: bronchial thermoplasty for asthma
  - **2018**: endobronchial valves for emphysema
  - **2019**: bronchial rheoplasty and cryospray for chronic bronchitis
  - **2020**: targeted lung denervation for COPD
APPROVED INTERVENTIONS

Bronchial thermoplasty (asthma)

Bronchoscopic lung volume reduction (emphysema)
BRONCHIAL THERMOPLASTY (BT)

- Delivery of radiofrequency (RF) energy to intermediate-size airways for the treatment of severe asthma
- Alair system (Boston Scientific) FDA-approved since 2010
BRONCHIAL THERMOPLASTY (BT)

- Post-BT airway phenomena:
  - Decreased airway smooth muscle mass
  - Decreased type I collagen deposition
  - Disrupted autonomic innervation
  - Depletion of neuroendocrine cells
  - Increased distal airways volume on HRCT


BRONCHIAL THERMOPLASTY (BT)

- **Course of treatment:**
  - 3 sessions (RLL, LLL, both upper lobes)
  - 3 weeks apart
  - Treat all airways from 3 → 10 mm in diameter
BRONCHIAL THERMOPLASTY (BT)

- **AIR2 (2010)** – multicenter, double-masked, sham-controlled randomized trial
  - Pre-BD FEV$_1$ ~78%p, Asthma QoL Questionnaire score ~4.4
  - Small but statistically significant improvements in AQLQ, severe exacerbations, ED visits @ 12 mo
  - Sustained improvements over median 12 yrs (BT10+, 2021)

BRONCHIAL THERMOPLASTY (BT)

- **Risks/complications:**
  - Asthma exacerbation (*increased* x 3 mo post-tx), upper respiratory tract infection
  - Lower respiratory tract infection, atelectasis, hemoptysis (*uncommon*)

- **AIR2 (2010):**
  - 85% experienced an adverse event (~1 event/session)
  - 8.4% required hospitalization

Eligibility criteria:
- ≥ 18 years old
- Severe asthma
- GINA step ≥ 4 treatment
- $T_H^2$-low phenotype
- ACT score ≤ 19

Exclusion criteria:
- Smoker
- Life-threatening exacerbations/24 mo
- ≥ 3 LRTIs/12 mo
- FEV$_1$ < 50%p
- Implanted electronic device
BRONCHIAL THERMOPLASTY (BT)

- **Criticisms of BT:**
  - Study patient characteristics not clearly representative of severe asthma
  - Racial/ethnic homogeneity (80% white in AIR2)
  - High rate of AEs, increased exacerbations over 3 months
  - Magnitude of benefit may not be clinically meaningful
  - Degree of benefit in sham arm (placebo effect)
  - Lack of long-term follow-up for sham controls

BRONCHIAL THERMOPLASTY (BT)

- **Role of BT in asthma treatment:**
  - Uncontrolled at Step 5, referred to specialty center, no access/eligibility for biologics (GINA 2023)

- **Biased opinion:**
  - Consultation with asthma specialist and consideration of clinical trials should come first
  - Failure of advanced medical management should prompt reevaluation of diagnosis
  - BT is becoming treatment of last resort

https://ginasthma.org/2023-gina-main-report/
BRONCHOSCOPIC LUNG VOLUME REDUCTION (BLVR)

- Bronchoscopic procedure to treat hyperinflation in patients with emphysema

- Various modalities have been/are being studied
  - Endobronchial coils
  - Airway bypass stents
  - Thermal vapor ablation
  - One-way endobronchial valves

Zephyr

Spiration
BRONCHOSCOPIC LUNG VOLUME REDUCTION (BLVR)

- One-way valves placed in airways let air out but not in
- Gradual collapse of lobe(s)
- Reduced hyperinflation

https://www.accessdata.fda.gov/cdrh_docs/pdf18/P180002B.pdf
BRONCHOSCOPIC LUNG VOLUME REDUCTION (BLVR)

- Physiologic outcomes of BLVR:
  - Improved diaphragm length-tension relationship $\rightarrow$ better muscle mechanics
  - Less V/Q mismatch
  - Improved FEV$_1$
BRONCHOSCOPIC LUNG VOLUME REDUCTION (BLVR)

- Clinical trial data:
  - 2003 NETT
  - 2010 VENT
  - 2015 BeLieVeR STELVIO
  - 2016 IMPACT*
  - 2017 TRANSFORM
  - 2018 LIBERATE
  - 2019 EMPROVE

*Homogeneous emphysema
BRONCHOSCOPIC LUNG VOLUME REDUCTION (BLVR)

- **LIBERATE (Zephyr, 2018)**
  - FEV\(_1\) 28%p
  - RV 224.5%p
  - 6MWD 311 m
  - Emphysema destruction 70.9%
  - Heterogeneity 25.5%

- **EMPROVE (Spiration, 2019)**
  - FEV\(_1\) 30.8%p
  - RV 207.5%p
  - 6MWD 303.5 m
  - Emphysema destruction 63.6%
  - Heterogeneity 25.3%

12-month outcomes:

<table>
<thead>
<tr>
<th></th>
<th>Valves</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV(_1) improvement ≥ 15%</td>
<td>37.2</td>
<td>5.1</td>
</tr>
<tr>
<td>SGRQ reduction ≥ 4 pts</td>
<td>50.5</td>
<td>22.0</td>
</tr>
<tr>
<td>mMRC reduction ≥ 1 pt</td>
<td>48.9</td>
<td>7.3</td>
</tr>
</tbody>
</table>

BRONCHOSCOPIC LUNG VOLUME REDUCTION (BLVR)

- **Risks/complications:**
  - Pneumothorax (26.6% in LIBERATE)
  - No significant differences in other adverse events

76% of all PTX in Day 0-3

BRONCHOSCOPIC LUNG VOLUME REDUCTION (BLVR)

- **Eligibility criteria:**
  - ≥ 18 years old
  - Emphysema with hyperinflation
    - RV ≥ 150-175%p (heterogeneous)
    - RV ≥ 200%p (homogeneous)
  - FEV$_1$ 15-50%
  - 6MWD 100-500 m
  - Quit smoking ≥ 4 months ago
  - Completed pulmonary rehab

- **Exclusion criteria:**
  - ≥ 2 AECOPD hospitalizations in past year
  - ≥ 2 PNA in past year
  - Recent MI or LVEF < 45%
  - Bullae > 30% of hemithorax
  - Prior major chest surgery (LVRS, transplant, bullectomy, lobectomy, pleurodesis)
  - Significant sputum production
  - DL$_{CO}$ < 20%p
  - PASP > 45-50 mm Hg
  - PaCO$_2$ ≥ 50 mm Hg
  - PaO$_2$ ≤ 45 mm Hg
BRONCHOSCOPIC LUNG VOLUME REDUCTION (BLVR)

- Additional testing:
  - CT analysis to assess lobe volumes, % destruction, heterogeneity and fissure-integrity
  - Balloon occlusion test during bronchoscopy to confirm fissure-integrity (*Zephyr only*)

StratX Report (Zephyr)

Chartis assessment for fissure-integrity (Zephyr)

- No collateral ventilation (CV-)
  - Complete fissure

- Collateral ventilation (CV+)
  - Incomplete fissure

Bronchoscopic Lung Volume Reduction (BLVR)

- **Emerging long-term data:**
  - Sustained improvements in RV, FEV₁, and SGRQ at 3 years
  - Improved median survival in 1 study (+1.7 years vs “controls”)

- **BLVR vs LVRS:**
  - Nonsurgical
  - Similar efficacy (CELEB, 2023)
  - Does not complicate future chest surgery
  - Not limited to upper lobes*


BRONCHOSCOPIC LUNG VOLUME REDUCTION (BLVR)

- **When to consider BLVR in treatment of severe emphysema:**
  - Symptomatic despite maximal medical therapy + pulmonary rehab
  - Avoid LVRS
  - Delay time-to-transplantation
  - Potential future chest surgery (e.g., transplantation)

- **Biased opinion:**
  - Few interventions address hyperinflation or poor muscle mechanics
  - Pulmonary rehab, NIV, and BLVR should be considered *early* for emphysema patients
FUTURE INTERVENTIONS

Bronchial rheoplasty (chronic bronchitis)

Cryospray (chronic bronchitis)

Targeted lung denervation (COPD)
COPD WITHOUT SIGNIFICANT EMPHYSEMA

- Epithelial inflammation
- Mucus overproduction
- Cholinergic hyperreactivity
BRONCHIAL RHEOPLASTY

- Pulsed electric field (PEF) energy to ablate goblet cells

- RheOx system (Gala Therapeutics) granted breakthrough device status in 2019

BRONCHIAL RHEOPLASTY

- High-frequency, short-duration nonthermal, pulsed energy field
- Disrupts cellular homeostasis $\rightarrow$ apoptosis
- Preserves tissue architecture $\rightarrow$ mucosal regeneration, but with fewer goblet cells

BRONCHIAL RHEOPLASTY

- **Target patient population:**
  - FEV₁ 30-80%
  - Chronic productive cough ≥ 3 mo/yr x 2 consecutive years
  - ≥ 10 pack-year smoking history

- **Observational data:**
  - Sustained improvements in CAT, SGRQ, sputum production

- **Adverse events:**
  - Moderate AECOPD, hemoptysis (self-limited)

- **RheSolve:** multi-center, double-masked RCT (completed June 2023)

CRYOSPRAY

- Metered-dose LN$_2$ sprayed in airways to denude bronchial epithelium

- RejuvenAir system (CSA Medical) granted breakthrough device status in 2019

CRYOSPRAY

- Temperature-drop (-196 °C) penetrates into submucosa
- Entire epithelium is ablated
- Repopulation with healthy/normal epithelium
CRYOSPRAY

- **Target patient population:**
  - Same as rheoplasty

- **Clinical data:**
  - Improved symptoms and sputum production relative to baseline at 9 mo
  - Mean SGRQ -9.6 points relative to sham arm in study of 31 patients at 6 mo

- **Adverse events:**
  - AECOPD, PNA, worsening cough

- **SPRAY-CB:** multi-center, sham-controlled RCT (underway)

Orton CM, et al. ERJ 2022 (abstract).
TARGETED LUNG DENERVATION

- Radiofrequency ablation (RFA) of vagal branches to the mainstem bronchi

- dNerva system (Nuvaira, Inc.) granted breakthrough device status in 2020

https://nuvaira.com/technology/
TARGETED LUNG DENERVATION

- RFA disrupts peribronchial branches of vagus nerve
- Disruption of parasympathetic reflex in the airways
- Decreased smooth muscle tone and airway resistance
TARGETED LUNG DENERVATION

- **Target patient population:**
  - FEV1 30-60%
  - ≥ 2 moderate AECOPD or ≥ 1 severe AECOPD/12 mo

- **Clinical data:**
  - Improved symptom-control, fewer overall respiratory events, greater time-to-severe AECOPD vs sham controls
  - Benefit sustained up to 3 yrs

- **Adverse events:**
  - Esophageal complications

- **AIRFLOW-3:** multi-center, sham-controlled RCT (underway)

SUMMARY

- Interventional bronchoscopy no longer limited to the central airways
  - Several interventions for clinical use or under investigation for treatment of benign small airway obstructive disease

- BT somewhat fraught with uncertainty, losing ground to biologics

- Robust data in support of BLVR for advanced emphysema

- New bronchoscopic treatments for non-emphysematous COPD under investigation
THANK YOU!

Brian Shaller
bshaller@stanford.edu
(917) 626-0277