Low Dose Helical CT for Lung Cancer Screening

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Lung Cancer

- 213,000 new cases per yr
- #1 cause of cancer death
- 164,000 deaths/yr
- 5 yr survival approx 15 %, unchanged over 20 yrs
- Stage I, 60% 5 yr survival
  - 80-90% if < 3 cm
- Stage I can have unknown metastatic at Dx

Stages and Survival

No Conflicts. No Disclosures.
Begs The Question

- If we can discover lung cancer at an earlier Stage I and smaller size, can we improve survival?
- Can we effectively do lung cancer screening with imaging? CXR or CT?

Imaging Methods

- CXR
- CT
- MRI
- MR Spectroscopy
- Nuclear Medicine
- PET-CT
- Molecular Imaging
- Biomarkers

CXR Screening

- Mayo Lung (MLP)
- Johns Hopkins/ Sloan Kettering
- 10,000 cases each
- Discovered smaller, more Stage I and more resectable cancers
- Better 5 yr survival
- But no decrease in cancer specific mortality

CXR Screening

- Relatively inexpensive
- Fast, readily available
- Good for mass screening
- Relatively low radiation dose
- Not tomographic
- 25 cm of lung
- Overlapping structures
CXR vs CCT

Helical CT Screening
- Tomographic
- Higher contrast (ca+)
- Thin sections
- Single breath hold
- Better characterization
- Detects more and smaller nodules
- More radiation and $$

Helical CT Screening
- ELCAP, early 1990’s
- ALCA, Japan, 1990’s
- Mayo CT Project
- I-ELCAP
- NCI, LSS
- NCI, ACRIN
- NLST
- Others

Early Lung Cancer Action Project (ELCAP)
- 1000 high risk pts
- Baseline and annual
- 1st scan, 233 pos for SPN
- 16 (17%) lost
- 217 remained with 27 lung Ca (2.7%) prevalence
- 23/27 (81%) Stage I, 96% resectable
- CT >> CXR for smaller, Stage 1
- ? Up to 80% mortality reduction
Mayo CT Project

- 1999, 1520 hi risk pts
- In 2 yrs, 2832 nodules in 1049 pts
- 40 lung Ca (1.4%), (98.6% B9) 26 baseline (prevalence), 10 on subsequent CT (incidence)
- 25 Stage I (68%), potentially curable surgery in 31 (78%)
- 8 subjects surgery for B9 disease

International: I-ELCAP

- >30,000 pts, research and clinical world wide
- 15% positive baseline and 6% on repeat screening
- 8 yr cure rate 95% for Stage I on initial screen, 98% for resected lesions after annual screen
- 90% Stage I on repeat scans
- 70% “cure rate” for CT diagnosed cancers vs 20% for CXR vs 10-15% for clinical cases

Lead Time Bias

- Screening and non-screening cases not adjusted for the time of diagnosis
- If screening detects disease earlier, pt may survive longer from time of Dx even if death is not delayed
- Survival from Dx is inadequate measure of effectiveness of screening, and has no predictable relationship to mortality

Length Time Bias

- Screening and non-screening exams are not adjusted for rate of cancer progression, and for the tendency of screening to detect slow-growing cancers
- Screening tends to discover slower growing cancers that are asymptomatic
- Slower growing cancers are more likely detected
- So screening tends to detect slow growing, indolent cancers which are more survivable
Overdiagnosis Bias

- Screening tends to discover slow growing cancers that are asymptomatic
- Phenomena of detecting pseudodisease, eg. a lung cancer that would have remained subclinical, and Pt may have died from other causes leaving the cancer undiscovered

NCI LSS and ACRIN (NLST)

- 10 screening centers for Lung Screening Study (LSS), pilot
- ACRIN: 23 centers, Apr 2002 thru Apr 2004: National Lung Screening Trial (NLST)
- 53,472 hi risk volunteers, randomly assigned to CT for experimental gp or CXR for control gp,
- 1:1 randomization
- 55-74 yo, > 30 pk yrs

Over-dagnosis Bias

"I'll have someone come in and prep you for the bill."

ACRIN, NLST Trial

- 8 yr Randomized Control Trial (RCT) to determine if CT screening of high risk subjects can reduce lung cancer specific mortality and is compared to CXR screening
- Prevalence screen, followed by 2 annual incidence screens
- Secondary objective to bank specimens (blood, sputum, urine) at initial and 2nd, 3rd screens for future potential biomarkers
ACRIN: Secondary Aims

- To compare all cause mortality between screening with CT versus chest radiographs.
- To compare differences in stage distribution between the two arms of the study.
- To compare lung-cancer related medical resource utilization between the two arms of the study.
- To compare issues of quality of life and psychological impact associated with annual screening and with a positive screening test between the two arms of the study.
- To assess the economic consequences of screening with CT versus chest radiographs.
- To develop a tissue bank from individuals at high risk of lung cancer both with and without pathologically proven lung cancers. This bank will be a rich resource for determining biomolecular markers of high predictive value in stratifying levels of lung cancer risk such as premalignancy (risk of future development of lung cancer), subclinical lung cancer, and advanced disease.
- To assess the impact of screening on smoking behaviors.

What We Know Now

- CXR screening discovers smaller and earlier stage lung cancers than waiting for Sxs
- CXR screening may not save lives, but data being re-evaluated
- CT screening discovers smaller, earlier stage lesions than CXR screening or waiting for discovery
- CT screening has more benign or “false positive” lesions than CXR also
- Improving surgical resectability and survival does not necessarily improve lung cancer specific mortality
- Need RCT results from the NCI ACRIN study

Comments?