NLST

methodological considerations

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overview

- Process standardization
  - Image acquisition
  - Screen interpretations
  - Results communication
- Outcomes data collection
- Endpoint verification
- Implications for public policy

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imaging standardization

NLST CT Technique Chart
kV
Gantry rotation time
mA (Regular – Large patient values)
mAs (Reg – Lg)
Scanner effective mAs (Reg – Lg)
Detector collimation (mm) - T
Number of active channels - N
Detector configuration – N · T
Collimation (operator console)
Table incrementation (mm/rotation) - I
Pitch ([mm/rotation]/ beam collimation – I/NT
Table speed (mm/second)
Scan time (40 mm thorax)
Nominal reconstructed slice width
Reconstruction interval
Reconstruction algorithm
Images/data set (40 cm thorax)
CTDI vol (Dose in mGy)

- CT Technique Chart
  - Standardized 18 parameters
  - 14 CT scanners: 4-64 channels
  - 120-140 kV; mAs < 80 ($CTDI_{vol}$ 2-3mGy)
  - Nominal slice thickness: ≤ 2.5 mm
- Equipment certification annually
- Routine CT phantom calibration
- QC: DICOM headers | visual QC
- CXR techniques from CRFs and machine output: mR/mAs vs. kV

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Cagnon CH. Acad Radiol 2006; 13: 1431-1441.

NLST CT Technique Chart	Siemens 64 Sensation	GE – VCT (64)	Toshiba Aquilion	Philips MX8000 16 slice
kV	120	120	120	120
Gantry rotation time	0.50 sec	0.50 sec	0.50 sec	0.5 sec
mA (Regular – Large patient values)	50-100	50-100	80-160	75-150
mAs (Reg – Lg)	25-50	25-50	40-80	37.5-75
Scanner effective mAs (Reg – Lg)	25-50	27-53	26.7-53.3	25-50
Detector collimation (mm) - T	0.6 mm	0.625	2 mm	.75 mm
Number of active channels - N	32	64	16	16
Detector configuration – N · T	32 x 0.6 mm	64 x 0.625	16 x 2 mm	16 x .75 mm
Collimation (operator console)	64 x 0.6 mm	.625/.984/39.37	NA	NA
Table incrementation (mm/rotation) - I	19.2 mm	39.37 mm	48 mm	18 mm
Pitch ([mm/rotation]/ beam collimation – I/NT	1.0	0.984	1.5	1.5
Table speed (mm/second)	38.4 mm/sec	78.74 mm/sec	96 mm/sec	36 mm/sec
Scan time (40 mm thorax)	11 sec	5.1 sec	4.2 sec	11 sec
Nominal reconstructed slice width	2 mm	2.5 mm	2 mm	2 mm
Reconstruction interval	1.8 mm	2.0 mm	1.8 mm	1.8 mm
Reconstruction algorithm	B30	STD	FC 10	B or C
# Images/data set (40 cm thorax)	223	200	223	223
CTDI vol (Dose in mGy)	1.9 – 3.8 mGy	2.2 – 4.4 mGy	2.7 – 5.4 mGy	1.9 – 3.8 mGy

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= Modifiable parameters on technologist console

radiation dose

- Whole body effective dose (weighted average dose to each organ)
  - Low dose helical CT: 1.5mGy
  - Mammogram: 0.7mGy
  - CXR: 0.01 mGy
- Low dose helical CT: estimates of organ specific dose
  - Lung: 4 mGy
  - Breast: 4 mGy
  - Red bone marrow, stomach, liver and pancreas: each ~1 mGy
- Screening mammogram organ specific dose:
  - Breast : 4mGy
  - Other organs: < 0.1mGy
- CXR: effective dose ~ 0.1 mSv

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http://www.radiologyinfo.org/en/safety/index.cfm?pg=sfty_xray

image interpretation findings

- Non-calcified nodule(s) or masses ≥ 4 mm
  - Anatomic location, slice #; diameters; margins, attenuation

- Other findings:
  - Micronodules < 4 mm
  - Atelectasis, segmental or greater
  - Pleural thickening | effusion
  - Hilar | mediastinal adenopathy
  - Significant cardiovascular abnormality (CM, CAD, valvular calcification
  - Interstitial fibrosis
  - Significant other findings above | below diaphragm

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image interpretation findings

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interpretation results

- [-] Screen

  No significant findings –or –
  Minor incidental findings not significant for lung cancer

- [-] Screen

  Significant findings unrelated to lung cancer
  [Some form of diagnostic recommendation required; e.g., echocardiogram for suspected pulmonary hypertension)

- [+] Screen

  Findings potentially related to *lung cancer*
  [diagnostic recommendation of some form required]

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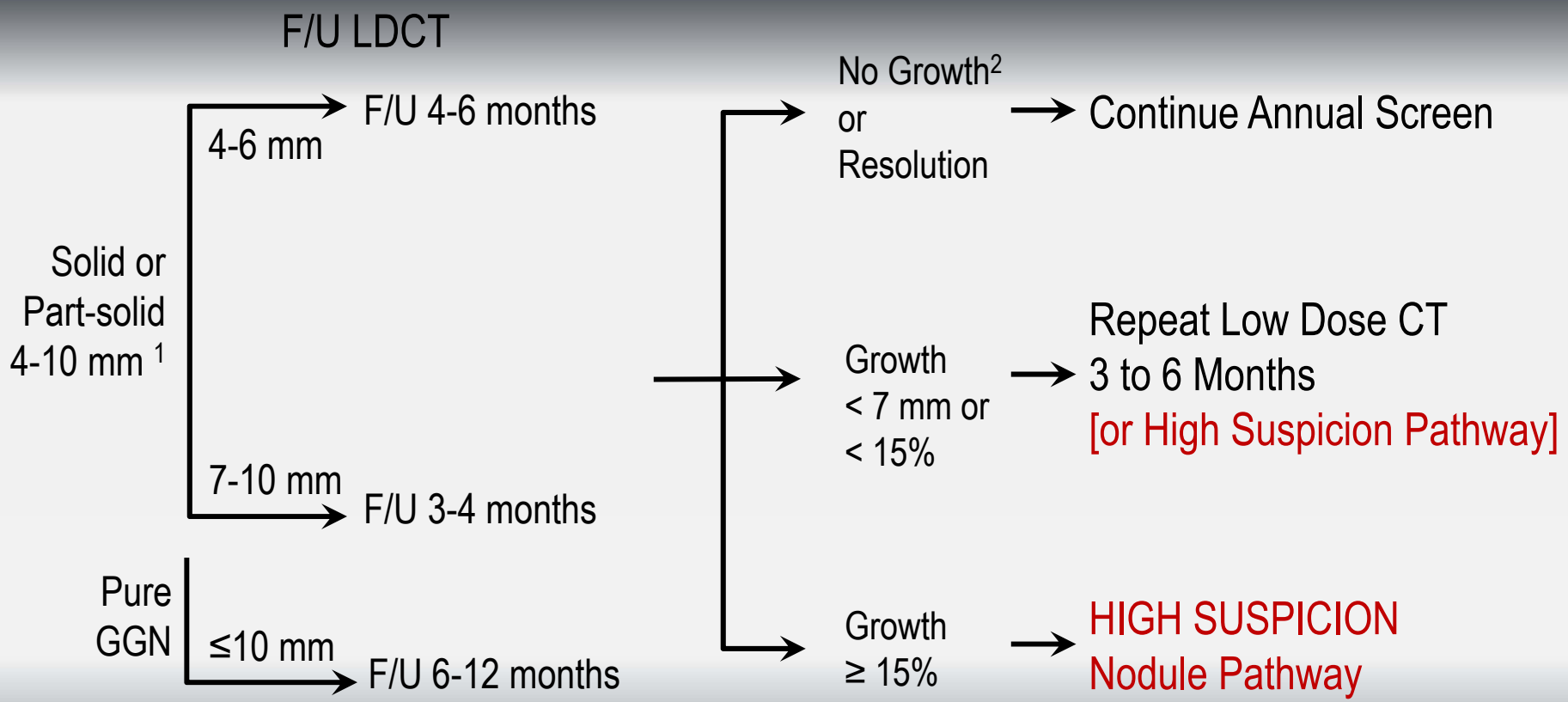
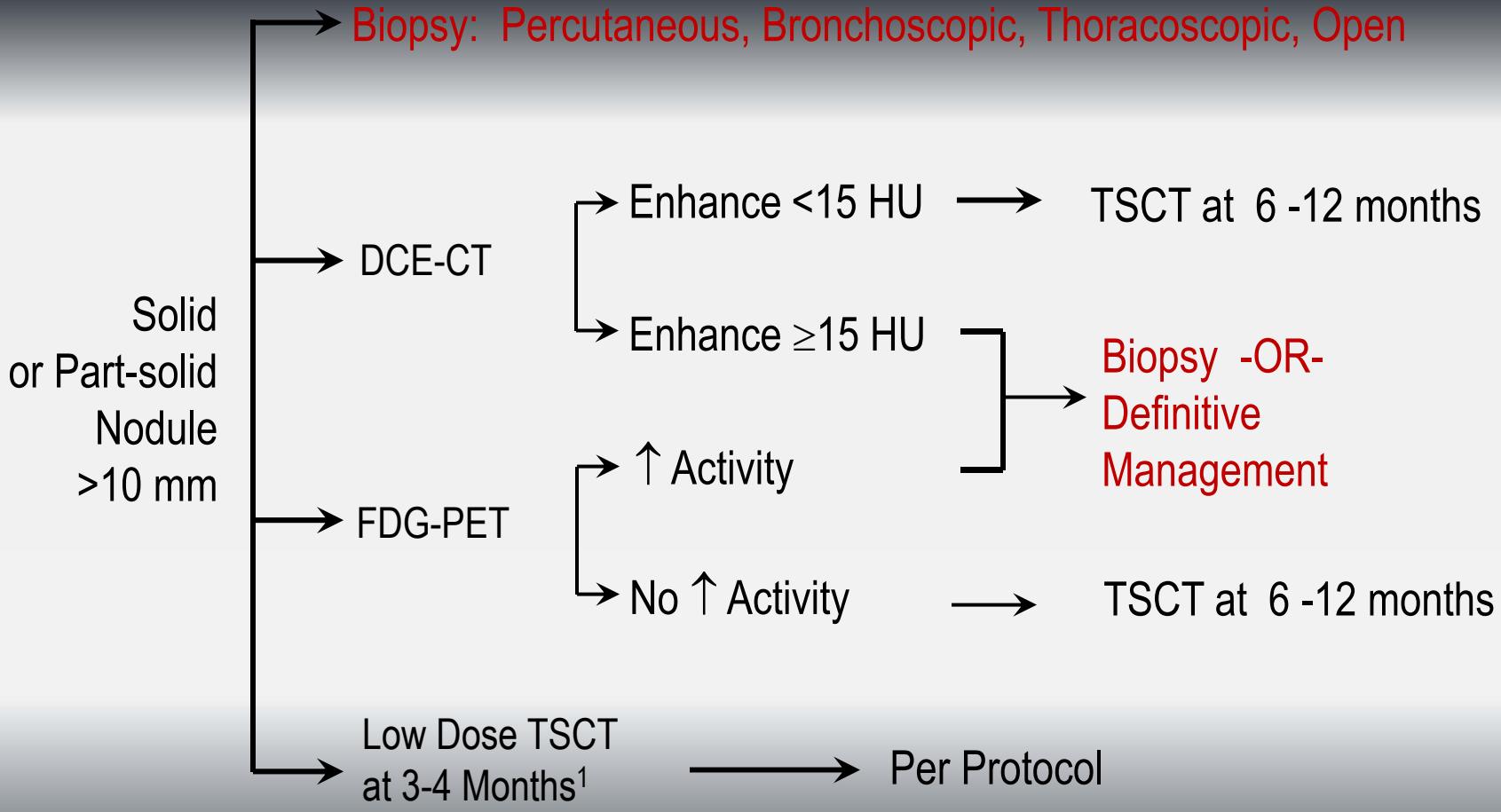
diagnostic pathways
nodule ≤ 4 mm



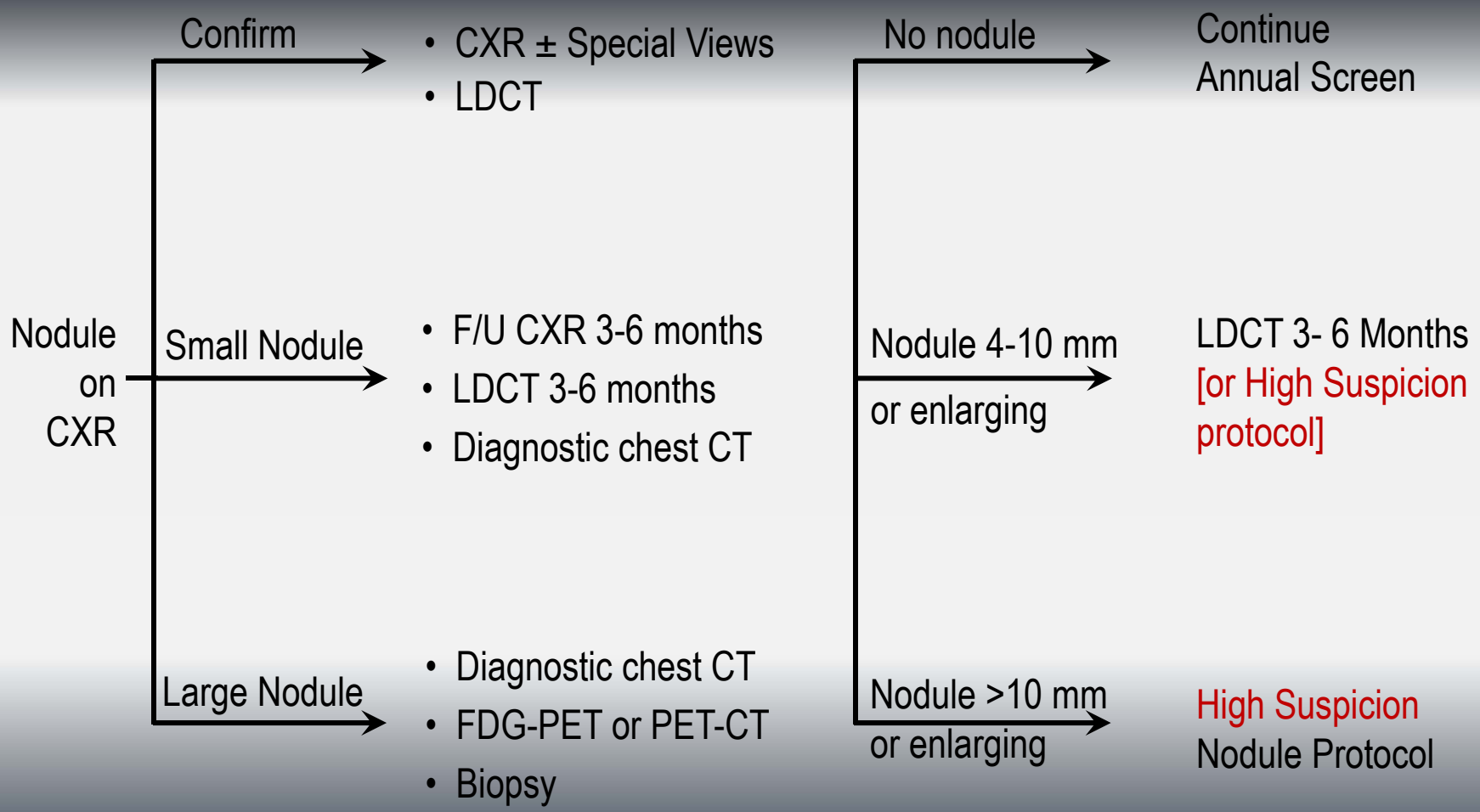
[1] Some nodules 4-10 mm may go directly to biopsy or other tests in ABNORMAL pathways.
[2] No growth is defined as < 15% increase in overall diameter OR no ↑ in solid component.

diagnostic pathways
high suspicion



[1] Reserved for nodules considered highly likely to be BENIGN [polygonal shape, 3D shape ratio > 1.78]

diagnostic pathways
[+] CXR



results communication | outcomes

- Study interpretation within 1 month
- Results reporting to
  - Participant
  - Primary physician (or documented participant refusal)
- Diagnostic algorithms served as guidelines
- 3-month | annual FU to determine management & results

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outcomes collection

- [+] screens
  - Diagnostic procedures (CPT) | complications (ICD.9)
  - Diagnoses: lung cancer | other cancer (ICD-0-3) | other Dx (ICD.9)
- Lung cancers
  - ICD-0-3 (histology and grade) | size | anatomic location
  - Clinical and pathologic stage (AJCC 6th Edition)
  - 1st line lung cancer treatment(s)
  - Time of progression or 2nd primary lung cancer
- Death certificates | time and cause of death
- Sample of [-] screen *significant other* & [-] screen no/minor abnl

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endpoint verification

- Independent endpoint verification committee (chair + 4 members)
- EVP review dictated by a selection algorithm
  - Cause of death (ICD-10) on death certificate
  - Review blinded to screening arm and official death certificate
  - Arbitration for disparity between: DC & chair | between EVP members
- Selection algorithm intended to capture
  - All lung cancer deaths (reported or death certificate)
  - Death following a [+] screen
  - Deaths following diagnostic evaluation of [+] screen
  - Cause of death = COPD
- Sub-sample of cases not included in the algorithm underwent EVP

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implications of NLST

- Efficacy proven under ideal conditions
  - Institutions with sophisticated medical resources
  - Multidisciplinary team for management follow-up
  - High risk population
  - Rigorous image quality
  - Standardized interpretation | communication
  - Systematic follow-up & outcomes collection
  - Endpoint verification

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implementation prerequisites

- Consistent definitions of [+] screen
  - All nodules | minimum size thresholds?
  - All evolving nodules?
- Controlled vocabulary & consistent feature description
  - Anatomic location
  - Size
  - Consistency
- Guidelines for work-up & communication of screening findings
- Types and degree of follow-up
- CAD | image analysis

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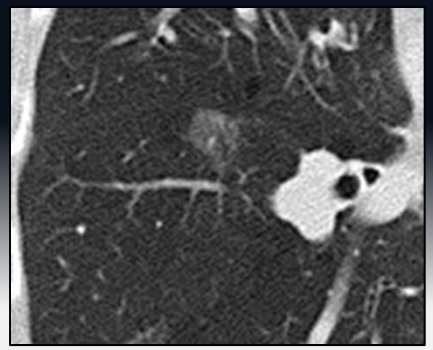
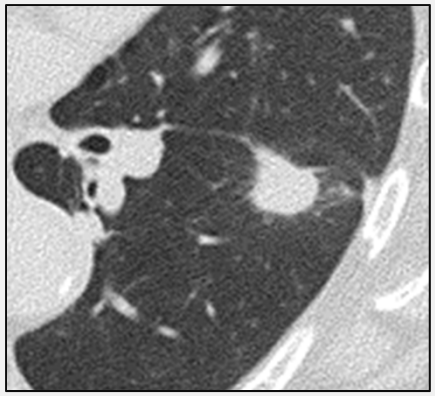
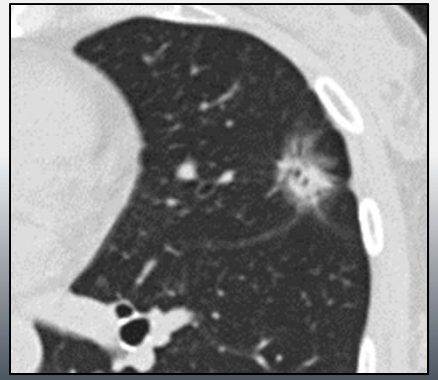
controlled vocabulary



GGN: Focal opacity of increased attenuation within which normal structures remain visible



Solid: Focal opacity of increased attenuation that completely obscures underlying structures



Part-solid: Focal opacity containing both solid and GG components

classification of adenocarcinoma

IASLC | ATS | ERS 2011	CT
AAH (typically ≤ 5 mm)	GGN
Adenocarcinoma in situ (AIS)[1]	GGN Part-solid
Minimally invasive ADC (MIA)[1,2,3]	Part-solid
Invasive ADC, lepidic predominant	Part-solid
Invasive ADC, acinar predominant Invasive ADC, papillary predominant	Part-solid to solid
Invasive mucinous adenocarcinoma	Solid

Godoy MCB, Naidich D. Radiology 2009; 253:606-622.
Travis WD et al. J Thorac Oncol 2011; 6:244-285.

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classification of adenocarcinoma

IASLC | ATS | ERS 2011	CT	Prognosis
AAH (typically ≤ 5 mm)	GGN	Pre-malignant
Adenocarcinoma in situ (AIS)[1]	GGN	100% survival
	Part-solid	100% survival
Minimally invasive ADC (MIA)[1,2,3]	Part-solid	~100% survival
Invasive ADC, lepidic predominant	Part-solid	~90 5-Yr progression free survival
Invasive ADC, acinar predominant	Part-solid to solid	multiple factors
Invasive ADC, papillary predominant		
Invasive mucinous adenocarcinoma	Solid	

[1] Rarely mucinous histology; [2] Maximum diameter ≤ 30 mm, [3] Invasive component ≤ 5 mm

Godoy MCB, Naidich D. Radiology 2009; 253:606-622.
Travis WD et al. J Thorac Oncol 2011; 6:244-285.

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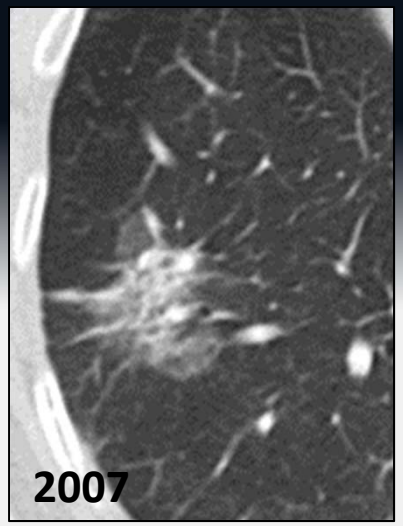
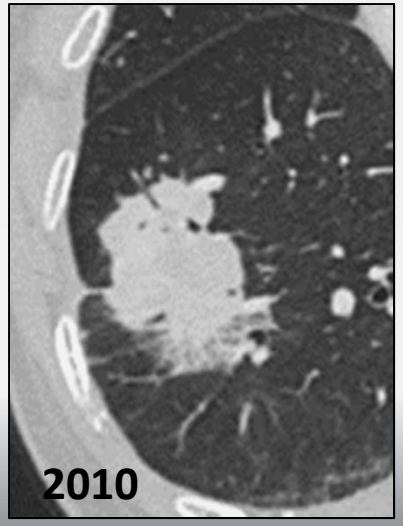
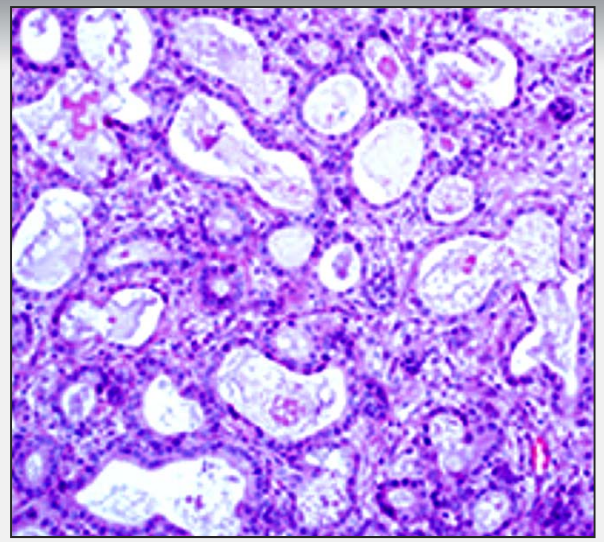
nodule characterization





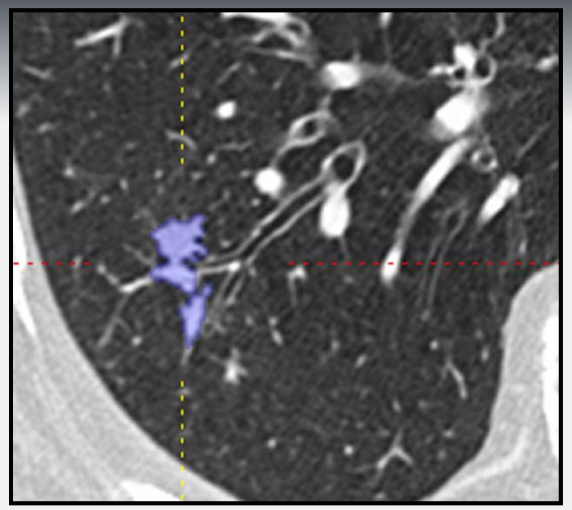
- 2007: Part-solid
- 2010: Part-solid | larger
  - Increasing opacification
  - Increasing “mass”
  - Linear reticulation
  - Cysts
  - Air bronchograms
  - Convex margins

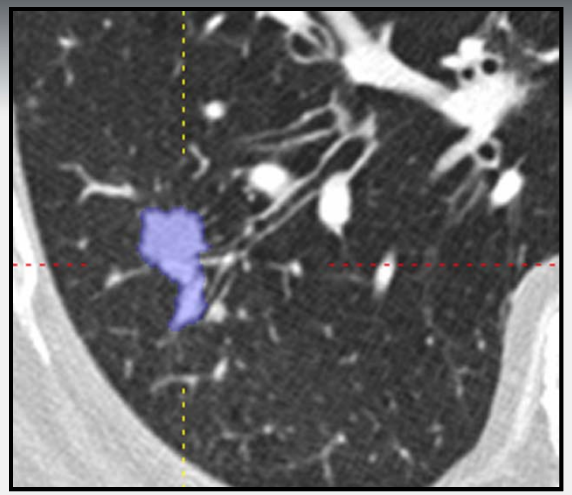


Invasive adenocarcinoma, acinar predominant

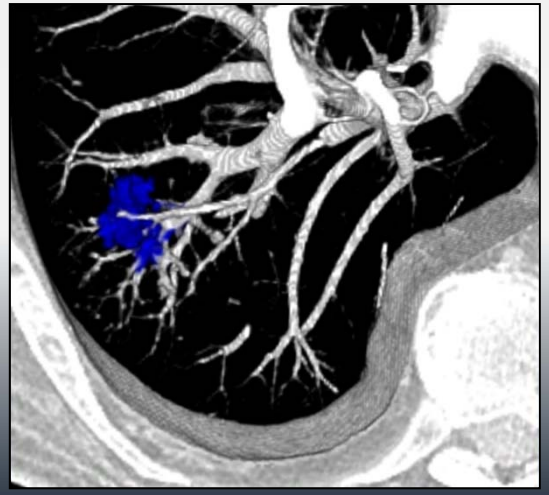
Round to oval-shaped malignant glands invading a fibrous stroma.

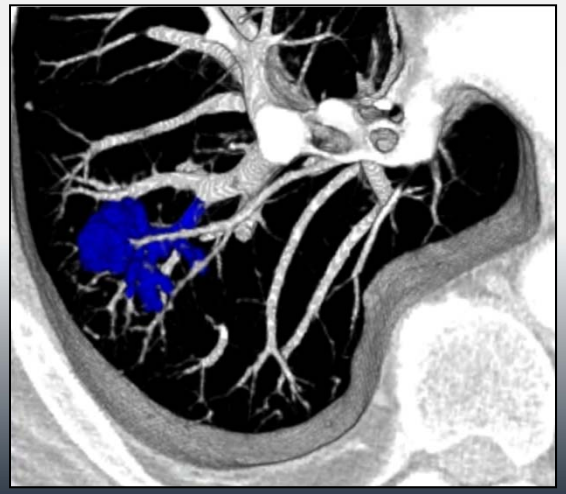
computer aided diagnosis





4-2006:
Diameters: 24 x 11 mm
Volume: 2805 mm^3





3-2007:
Diameters: 24 x 14 mm
Volume: 5955 mm^3

dD = 27% | dV = 112%

NLST ACRIN biospecimen repository

ACRIN web site: http://www.acrin.org/ACRIN-NLSTBIOREPOSITORY.aspx

- Specimens collected at 3 annual screening time points (N = 10,200)
- Purpose: validation of biomarkers of early detection
- Biorepository open to scientific community | 2-step peer-review process

Specimen Type	Samples	Number Participants	# Participants with ≥ 1 sample	% Participants with ≥ 1 sample
Plasma	108,666	10,218	10,133	99.17%
Buffy coat	108,891	10,218	10,132	99.16%
Urine	55,332	10,247	10,168	99.23%
Sputum cell pellet	39,544	8,336	8,173	99.04%
Remnant tissue TMA	(NLST trial wide)			

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looking forward

lessons from mammography implementation

- Establish cost-effectiveness
- Optimal risk cohorts for CT-screening
- Standardize practices
  - Acquisition parameters and radiation dose
  - Interpretation and communication practices
  - Follow-up documentation
- Determine what molecular biomarker(s)
  - Identify high risk individuals who may benefit from screening
  - Motivate more aggressive evaluation of [+] screen
- Establish appropriate venues for screening within broader programs of risk modification and smoking cessation

Thank you