Emerging Issues with Quantitative Imaging

Prevent Cancer Foundation
Quantitative Imaging Workshop XIV

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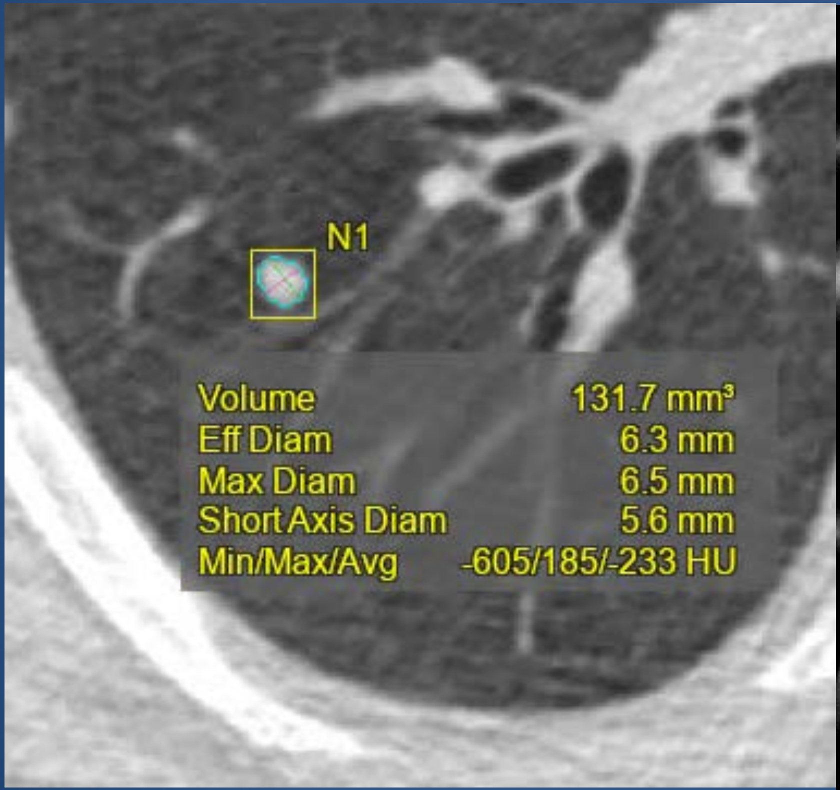
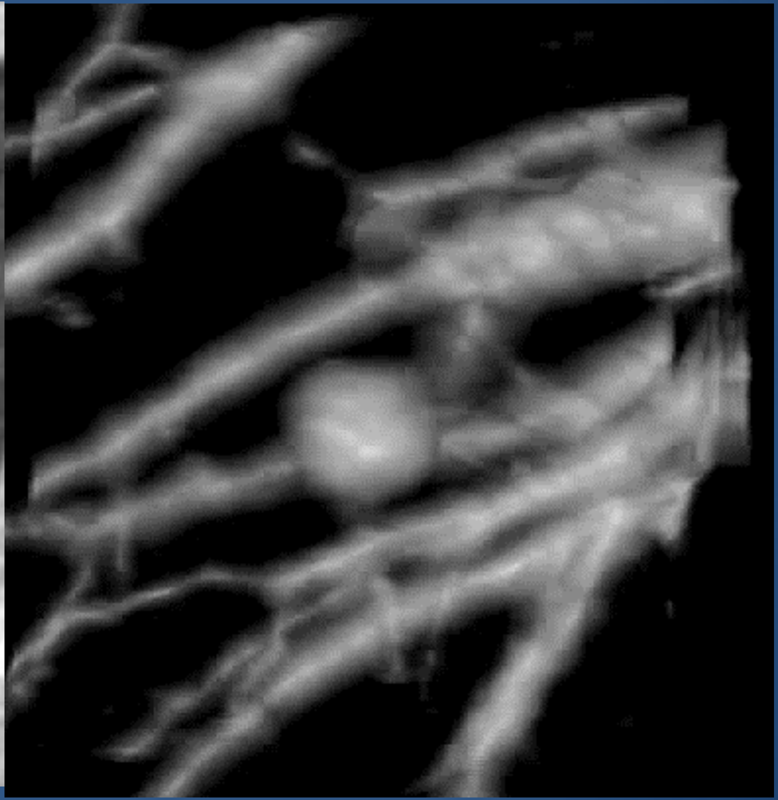
Quantitative Imaging in Lung Nodule Assessment

- CT volumetry
- Computer-aided diagnosis

CT Volumetry





Quantitative CT Nodule Volumetry

QIBA Small Nodule Profile Claims

Single measurement

True volume = $Y \pm 1.96 \times Y \times CV$

95% CI

Comparison at two time points

True change if $> 2.77 \times CV_1 \times 100\%$

- Amount of change = $(Y_2 - Y_1) \pm 1.96 \times \sqrt{(}[Y_1 \times CV_1]^2 + [Y_2 \times CV_2]^2$

- Y=measured volume
- CV=coefficient of variation
- 1=baseline scan
- 2=follow-up scan

Nodule Diameter	Nodule Volume	Coefficient of Variation (CV)	True Volume 95% CI Limits
6 mm	113 mm^3	0.29	± 64 mm^3 (57%)
7 mm	154 mm^3	0.23	± 69 mm^3 (45%)
8 mm	268 mm^3	0.19	± 100 mm^3 (37%)
9 mm	382 mm^3	0.16	± 120 mm^3 (31%)
10 mm	524 mm^3	0.14	± 144 mm^3 (27%)
11 mm	697 mm^3	0.12	± 164 mm^3 (24%)
12 mm	905 mm^3	0.11	± 195 mm^3 (22%)

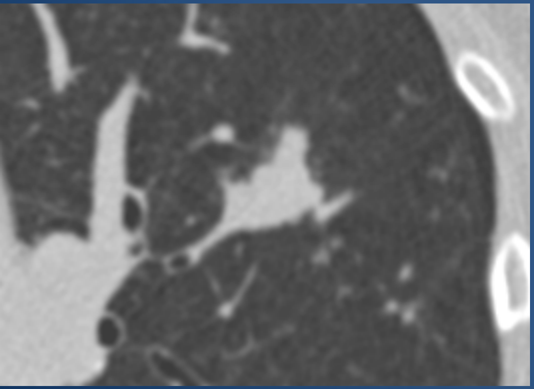
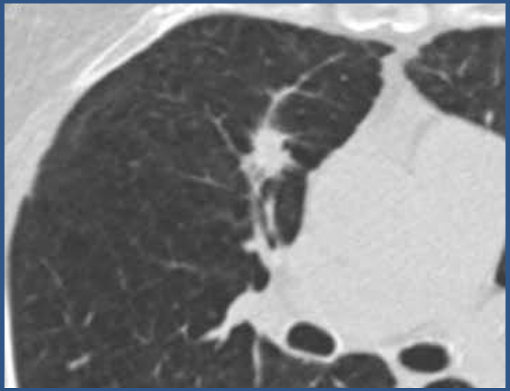
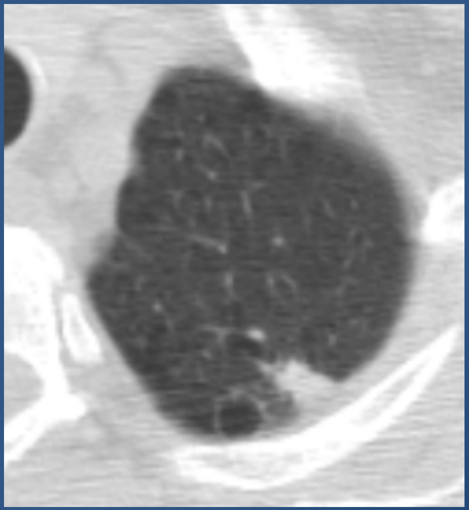
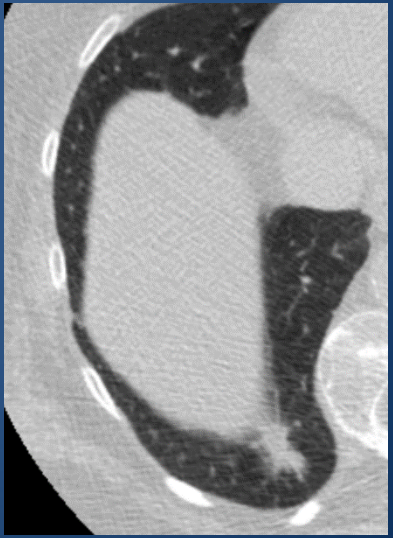
Quantitative Imaging Biomarkers Alliance
RSNA

Quantitative CT Nodule Volumetry
Open Issues

- Solid nonspherical and attached nodules
- Subsolid nodules
- Radiologist acceptance
- Clinical impact

Quantitative CT Nodule Volumetry
Nonspherical and Attached Nodules

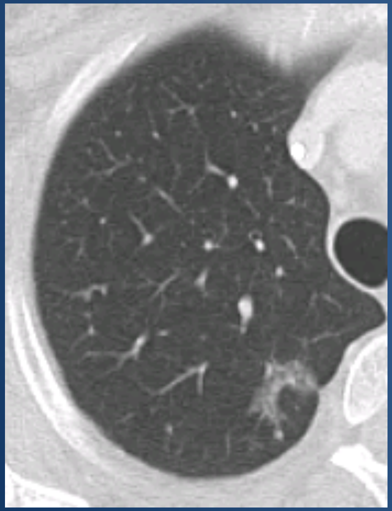
- Excluded from repeatability studies and clinical trials
- Multiple algorithms described
- FDA-approved software performance, interaction with technical parameters unknown

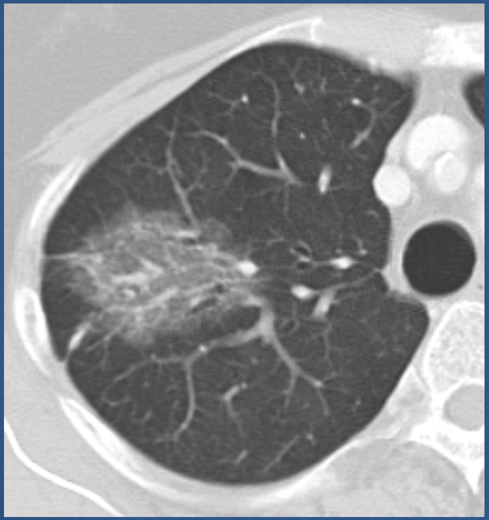
Quantitative CT Nodule Volumetry

Subsolid Nodules

- Nonsolid – usually indolent, lower risk
- Part solid – solid component size determines risk

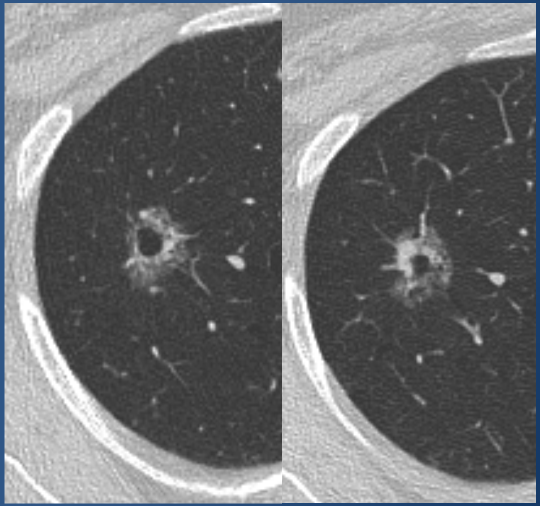


Nonsolid



Nonsolid

Part solid



Part solid with cystic lucency

Quantitative CT Nodule Volumetry
Subsolid Nodules

- >95% nodules segmented; Volume interscan var ±18%;
  - AJR 2010; 195:W408-414 (30 nonsolid, scan-rescan)
  - Radiology 2013; 269:585-593 (72 nonsolid, 22 part solid, scan-rescan)
- 100% nodules segmented; ICC=0.94 (2 obs)
  - PLOS ONE 2013; 8:e80249 (33 subsolid)
- Solid component detectable in 87%, segmentation volume dependent on HU threshold
  - Eur Radiol 2015; 25:488-496 (86 part solid)

Quantitative CT Nodule Volumetry
Nodule mass

- Mass=[Volume x (Mean Attenuation+1000)]/1000
- Radiology 2010;255:199-206
  - Kappa=0.38 for deciding if solid component (2 observers)
  - $CV_{mass} < CV_{volume} < CV_{diameter}$
  - Time for growth to exceed limits of agreement
    - Mass (425 days)<volume (673 days)<diameter (715 days)
- Radiology 2013; 269:585-593 (nonsolid and part solid)
  - Interscan variability -18% to 19%
  - Interobserver variability -18% to 12% (2 observers)

Quantitative CT Nodule Volumetry
Subsolid Nodules

- Effect of tube current (phantom studies)
  - Increased error with lower mAs
    - Acad Radiol 2009; 16:934-939
    - Br J Radiol 2014; 87:20130644
- Effect of reconstruction algorithm (phantom studies)
  - Decreased error with sharp kernel
    - Radiology 2003; 228:864-870
- Iterative reduces low-dose error (phantom study)
  - Br J Radiol 2014; 87:20130644

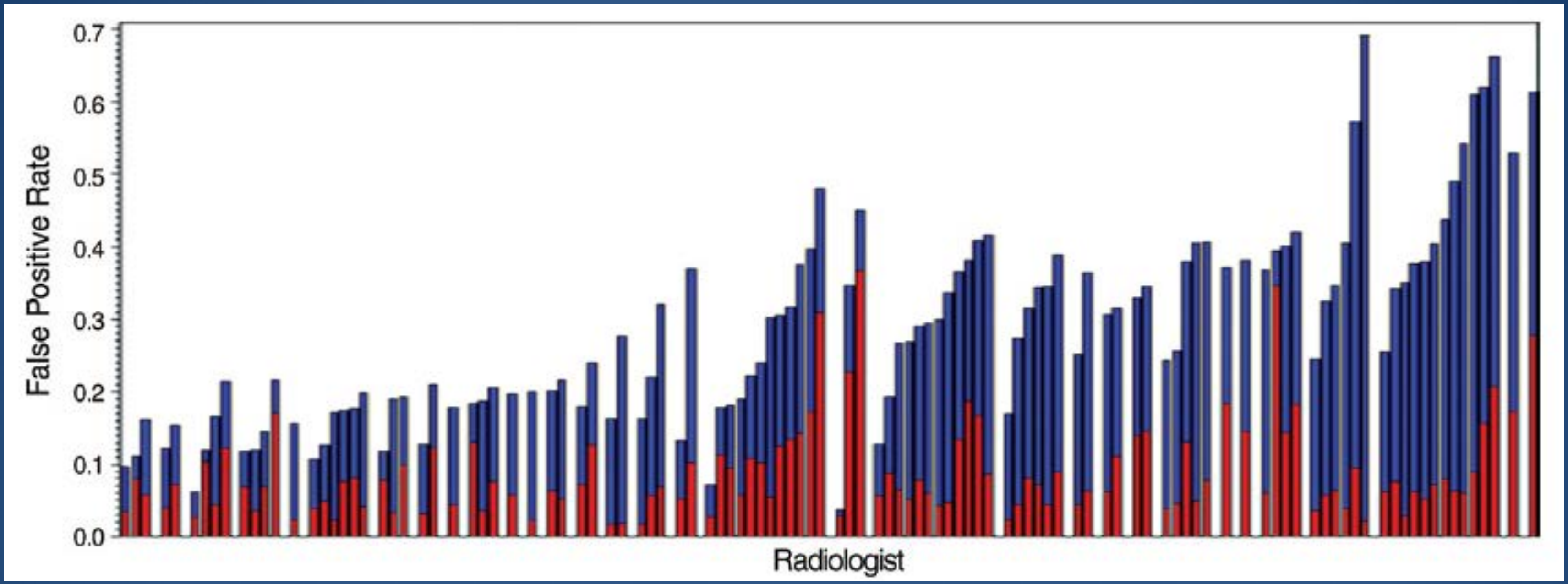
Quantitative CT Nodule Volumetry
Radiologist Acceptance

- Multiple FDA-approved programs
- Current use and impact unknown
- Better integration of analysis software into workflow may be essential

Quantitative CT Nodule Volumetry
Clinical Benefit?

- Observer variability
- Management decisions
- Patient outcomes

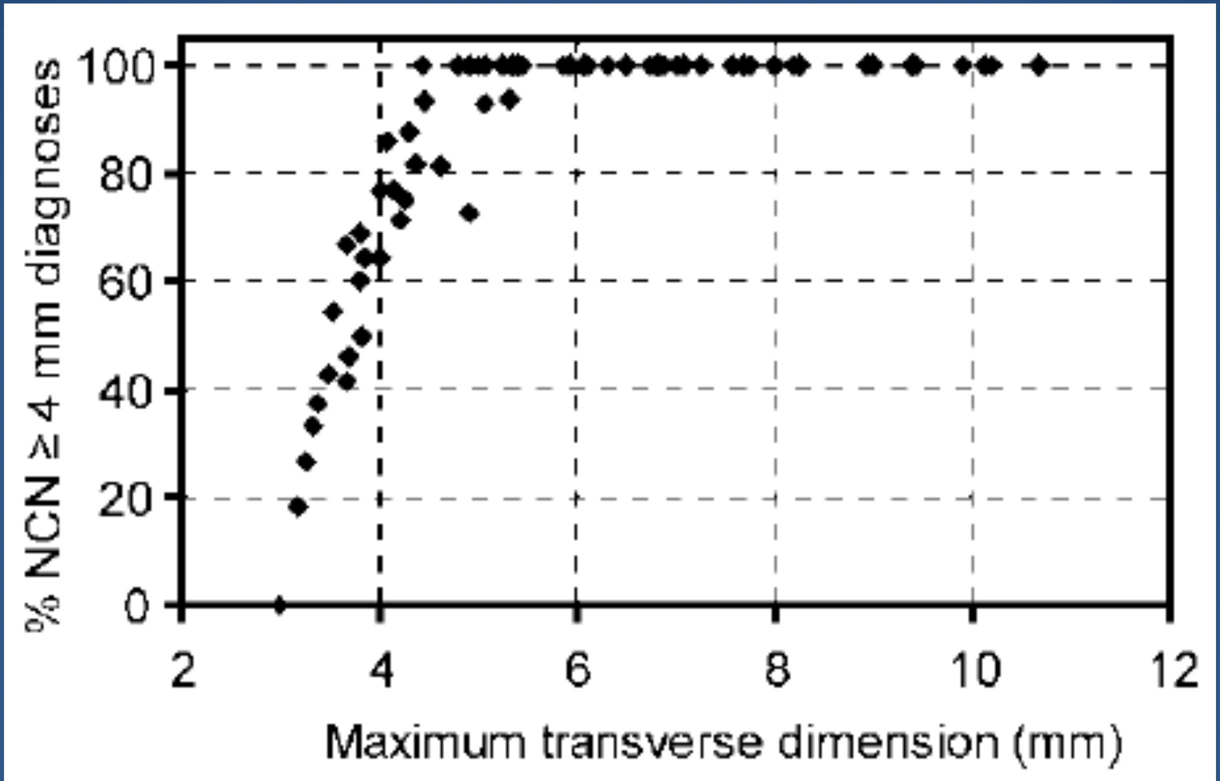
Observer variability in NLST: Classification



- 112 radiologists grouped by screening center
- At least 100 exams per radiologist
- 4 mm diameter positivity threshold
- Red bars=high level follow-up recommended (3 mo CT, PET, or Bx)

Radiology 2013; 268:865-873

Observer variability in NLST: Classification



- Image subsets of 135 nodules
- 16 radiologists
- 4 mm diameter positivity threshold

Radiology 2007; 247:265-272

Observer variability in NLST: Change

Number of Nodules Showing Changes in Growth, Attenuation, and/or Margins and Percentage of Positive Screening Results according to Reader

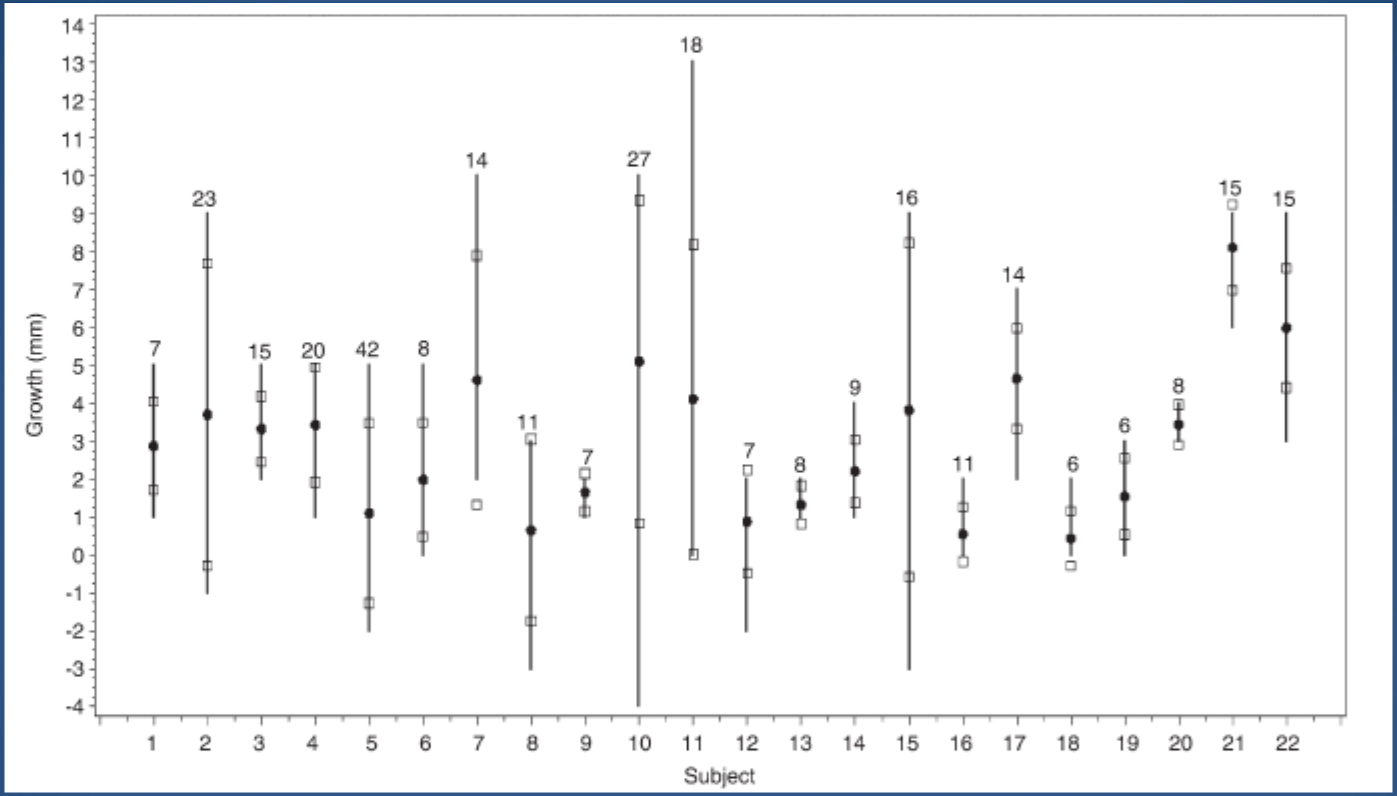
Reader	Growth	Change in Attenuation	Change in Margins	Any Change*	Positive Category *a* Screening Result
1	28 (37)	10 (13)	12 (16)	31 (41)	31 (41)
2	30 (39)	14 (18)	21 (28)	34 (45)	34 (45)
3	21 (28)	7 (9.2)	2 (2.6)	25 (33)	28 (37)
4	16 (21)	5 (6.6)	6 (7.9)	16 (21)	7 (9.2)
5	22 (29)	9 (12)	11 (14)	23 (30)	31 (41)
6	36 (47)	8 (10)	8 (10)	39 (51)	37 (49)
7	18 (24)	6 (7.9)	4 (5.3)	21 (28)	31 (41)
8	18 (24)	6 (7.9)	2 (2.6)	20 (26)	22 (29)
9	18 (24)	6 (7.9)	5 (6.6)	20 (26)	18 (24)
Median	21 (28)	7 (9.2)	6 (7.9)	23 (30)	27 (41)
Mean	23 (30)	8 (10)	9 (10)	25 (33)	27 (35)
CV (%)†	30	36	77	30	41

Note.—Except where indicated, data are numbers of nodules; numbers in parentheses are percentages. Data were obtained in the 76 nodules that were determined by all readers to be present at baseline.

- Sample of 76 nodules
- 9 study readers

Radiology 2011; 259:263-270

Observer variability in NLST: Change



- 22 nodules judged to have grown by at least 5 readers

Observer variability with volumetry

- Lower than reported for manual diameters
  - Radiology 2006: 241:251-257 (89% no diff, >10% in 3.7% of nodules)
  - Eur Radiol 2010; 20:187-1885 (diff >25% in 4% of nodules)
  - J Digit Imag 2010; 23:8-17 (95% CI = -13% to 12%)
  - AJR 2014; 202: W202-209 (95% CI = -33% to 35%, phantom nodules ≤5.5 mm)
- Direct comparisons of diameter and volume measurements lacking
  - Volumetry superior in pig lung phantom study (EurJRadiol 2007; 64:285-295)
- No studies comparing change

Quantitative CT Nodule Volumetry
Management Decisions

- Used in European trials
- Limited direct comparison with manual diameter-based management
  - Linear and volumetric growth correlated (r=0.84 for 25 smooth vs r=0.69 for all 87 nodules, 55 sub-cm); decision to Bx changed in 6.2% by volumetry (incl 3 of 7 cancers) (J Thorac Cardiovasc Surg 2011; 142:372-37)
- Standardized reporting algorithms current basis for management, should be comparison standard

Quantitative CT Nodule Volumetry
Patient Outcomes

- Sensitivity, specificity, PPV, NPV
  - Diagnostic follow-up testing rates
  - Time to diagnosis
    - Would have been reduced with volumetry for 8 screen-detected lung cancers: 183±158 vs 344± 84 days (Radiology 2011; 262:662-671)
- Stage distribution
- Mortality

Quantitative Imaging
Computer-aided diagnosis

- Radiomics
- Machine learning

Quantitative Imaging
Radiomics

- Characterization of tissue features by extracting quantitative parameters from radiologic images
- Categories: Size, Shape, Attenuation, Texture, Margins
- Dozens of predefined features obtained from segmented nodules
- Multivariable logistic regression or machine learning models developed from predictor variables

Quantitative Imaging
Radiomics

- AUROC for predicting malignancy around 0.8-0.9
  - Med Phys 2003; 30:387-394
  - Acad Radiol 2005; 12:570-575
  - AJR 2004; 183:1209-1215
  - Med Phys 2006; 33:2323-2337
  - J Med Imag 2015; 2:041004
  - J Computer Assist Tomogr 2016; 40:589-595
- Slightly higher including surrounding parenchyma
  - Journ Med Imag 2015; 2:041004
- No definitive model for clinical/trial use
- No assessment of variability or technical factors

Quantitative Imaging
Machine Learning for Nodule Classification

- Deep learning using convolutional neural networks
  - Assume elements of inputs have geometric relationship
- Many “neural layers” that perform different functions and can “learn” from images of known classification to discriminate images of unknown classification
- Open source and proprietary algorithms

Quantitative Imaging
Machine Learning

- Benefits
  - No need to define input features
  - No segmentation!
  - Less sensitive to technical factors?
- Limitations
  - Features used for discrimination unknown
  - Trial-and-error nature
  - Require large number of images

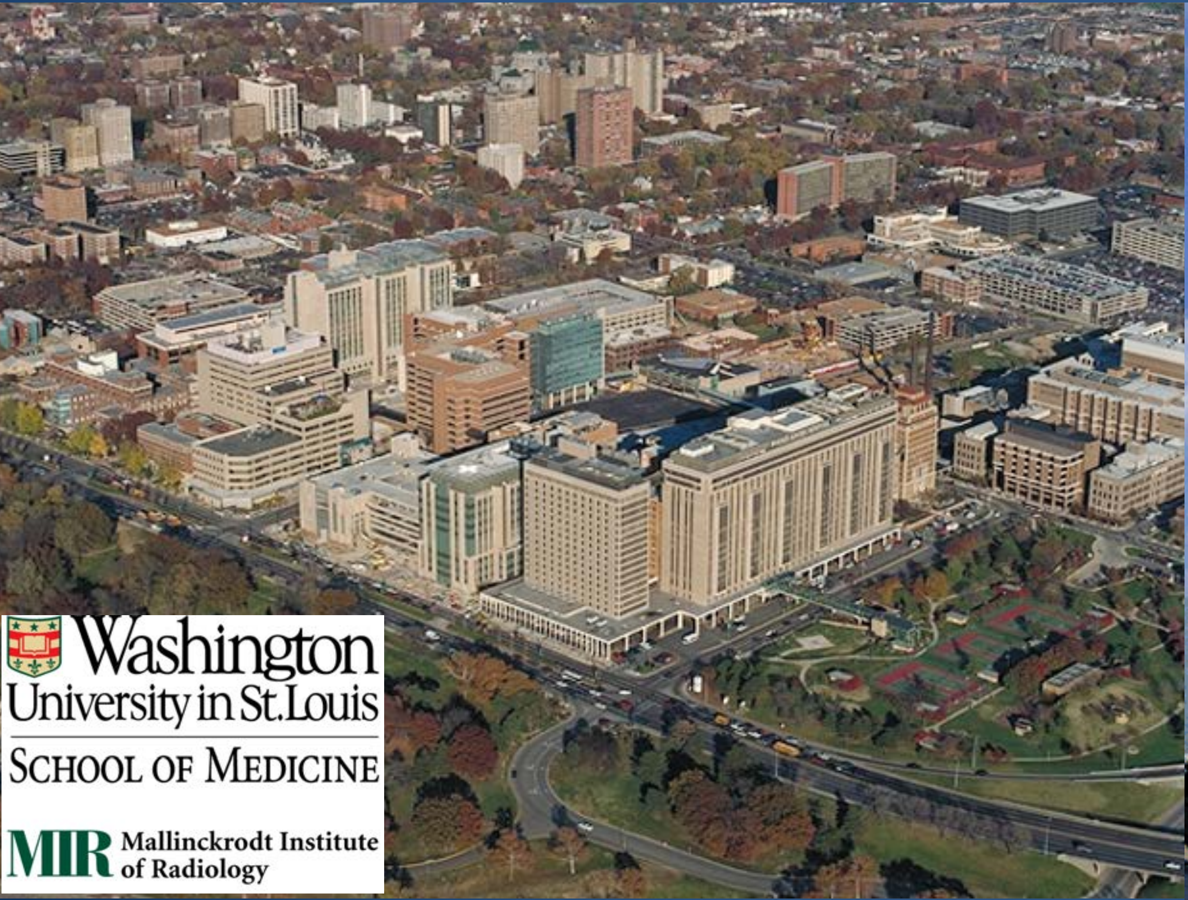
Quantitative Imaging
Machine Learning

- Benign vs malignant LIDC nodules:
  Accuracy 87%, Sensitivity 86%, Specificity 89%
  - Sci Rep 6, 24454; doi:10.1038/srep24454 (2016)
- Machine-observer variability equivalent to interobserver variability for classifying 6 nodule types (solid, perifissural, non-solid, part-solid, spiculated, Ca^{++})
  - Sci Rep 7, 46479; doi: 10.1038/srep46479 (2017)
- Data Science Bowl 2017 task

Emerging Issues with Quantitative Imaging
Summary

- Quantitative volumetry
  - Expand technical foundation to subsolid, nonspherical, attached nodules
  - Compare clinical effectiveness to current practice
- Computer – aided diagnosis
  - Need for larger image databases
  - Determine repeatability and dependence on technical factors

Thank You!



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