Three-dimensional Invasiveness Analysis of Adenocarcinoma Presenting as pure GGN

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Introduction

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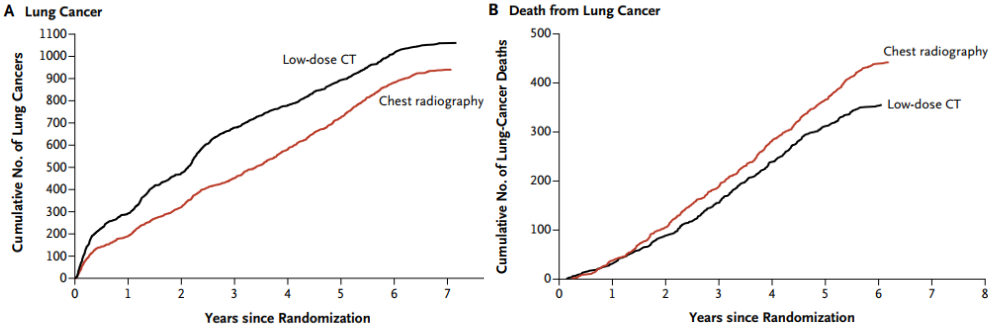
Reduced Lung-Cancer Mortality with Low-Dose Computed Tomographic Screening

The National Lung Screening Trial Research Team*



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ORIGINAL ARTICLE

Results of the Two Incidence Screenings in the National Lung Screening Trial

N ENGL J MED 369;10 NEJM.ORG SEPTEMBER 5, 2013

CONCLUSIONS

Low-dose CT was more sensitive in detecting early-stage lung cancers, but its measured positive predictive value was lower than that of radiography. As compared with radiography, the two annual incidence screenings with low-dose CT resulted in a decrease in the number of advanced-stage cancers diagnosed and an increase in the number of early-stage lung cancers diagnosed. (Funded by the National Cancer Institute; NLST ClinicalTrials.gov number, NCT00047385.)

Table 3. Frequency of Positive Screening Results and Positive Predictive Value at T2 Screening, According to Study Group.*

Variable	Low-Dose Computed Tomography						Chest Radiography					
	Confirmed Lung Cancer			Total	PPV†	PPV Range	Confirmed Lung Cancer			Total	PPV†	PPV Range
	yes	no	unknown				yes	no	unknown			
	number (percent)				*percent*		*number (percent)*				*percent*	
Size of nodule or mass‡												
<4 mm	0	7 (0.2)	0	7 (0.2)	0	0.0–0.0	2 (2.6)	11 (1.0)	0	13 (1.1)	15.4	0.0–37.5
4–6 mm	15 (7.1)	2007 (52.3)	1 (20.0)	2023 (49.9)	0.7	0.4–1.1	5 (6.4)	197 (18.0)	0	202 (17.2)	2.5	0.5–4.7
7–10 mm	58 (27.5)	1072 (27.9)	1 (20.0)	1131 (27.9)	5.1	4.0–6.4	9 (11.5)	335 (30.6)	0	344 (29.3)	2.6	1.1–4.4
11–20 mm	86 (40.8)	502 (13.1)	0	588 (14.5)	14.6	11.7–17.5	22 (28.2)	263 (24.0)	0	285 (24.3)	7.7	4.9–10.6
21–30 mm	23 (10.9)	77 (2.0)	0	100 (2.5)	23.0	14.1–31.7	19 (24.4)	47 (4.3)	0	66 (5.6)	28.8	18.2–40.0
>30 mm	20 (9.5)	41 (1.1)	1 (20.0)	62 (1.5)	32.8	21.0–45.1	2 (2.6)	22 (2.0)	1 (50.0)	25 (2.1)	8.3	0.0–20.9
Unknown	1 (0.5)	9 (0.2)	0	10 (0.2)	10.0	0.0–33.3	8 (10.3)	100 (9.1)	1 (50.0)	109 (9.3)	7.4	3.0–12.5

Zhang et al., *J Thorac Cardiovasc Surg* 2020;160:824-831

Kang et al., *J Thorac Oncol* 2019;14:436-444

Small nodule, GGN predominance

- Diagnostic accuracy
- Negative predictive value

- Complications

Choi et al., *Medicine (Baltimore)* 2016;95:e4359, Shimizu et al., *Lung Cancer* 2006;51:173-179

Preoperative diagnosis with CT is important

Malignancy favor CT parameter in pure GGN

Larger Size Irregular Spiculation Indentation Density

Robinson et al., *Ann Thorac Surg* 2020;109:270-279

Kitazawa et al., Clin Radiol 2019;74:922-929

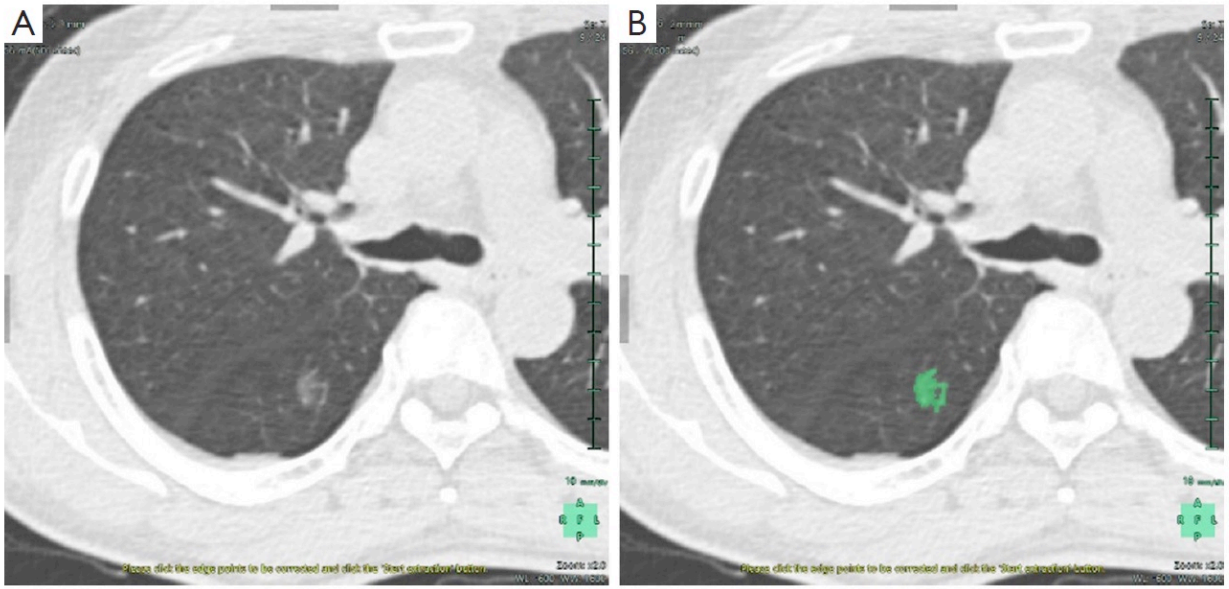
Fu et al., J Thorac Cardiovasc Surg 2021;162:451-459

3D CT volume rendering, HU adjustment

Method

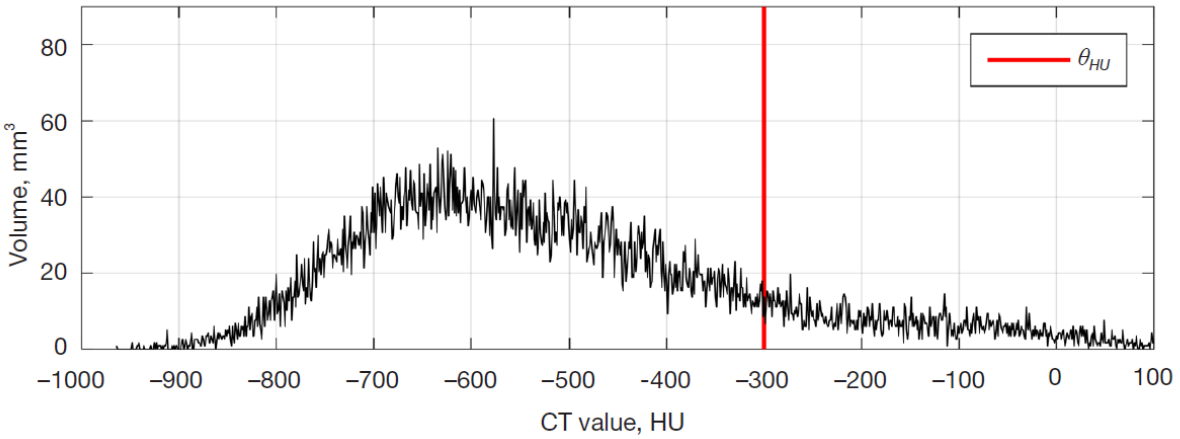
- Jan 2013 to Dec 2019, ENB-guided surgery of pure GGNs
- Retrospective review of medical records and prospectively re-assessed and analyzed the pathological and CT data
- Synapse Vincent system was used to analyze the images of pure GGNs
- CT Hounsfield units, size, volume
- Statistics: Student’s t-test, Mann-Whitney U-test

Method



θ_{HU}

= threshold high CT density



Method

$$\gamma = \frac{v_H}{v_H + v_L} \times 100\,\%$$

v_H Volumes with CT densities higher than θ_{HU}

v_L Volumes with CT densities lower than θ_{HU}

γ High density CT volume proportion

Result

- Forty-eight pure GGN were surgically resected in 45 patients
- Of the 48 pure GGNs, 40 were pathologically diagnosed as NSCLC and 8 as benign lesions
- 20 were diagnosed as NIAs (4 AISs and 16 MIAs) and 20 as IAs

Results

Table 1 Characteristics of the NIA and IA groups

Variable	NIA (N=20)	IA (N=20)	P value
Female, n [%]	11 [55]	9 [45]	0.539
Age (years), mean ± SD	63±9.9	62.8±9.5	0.949
Never smoker, n [%]	11 [55]	9 [45]	0.539
Operative method, n [%]			0.057
Lobectomy	7 [35]	11 [55]	
Segmentectomy	2 [10]	5 [25]	
Wedge resection	11 [55]	4 [20]	

NIA, non-invasive adenocarcinoma; IA, invasive adenocarcinoma; SD, standard deviation.

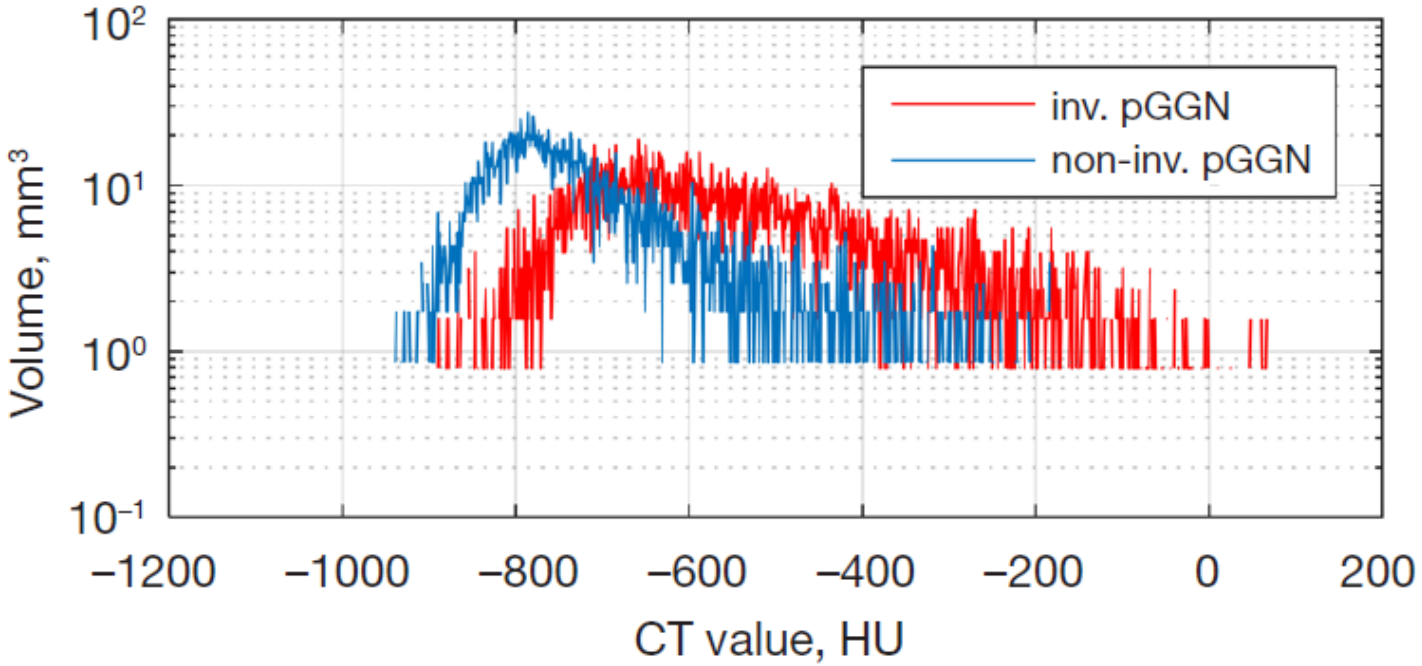
Results

Table 2 Three-dimensional analysis of lesions in the NIA and IA groups

Variable	NIA (N=20)	IA (N=20)	P value
CT size (mm)	15.1±8.6	17.1±7.3	0.459
≤10	6	4	
10–19	10	11	
≥20	4	5	
Distance from visceral pleura (mm)	10.3±10.7	8±6.7	0.442
Lesional volume (mm^3)	3,018 [361, 3,249]	2,765 [754, 2,977]	0.894
HU max	−102.8±239.4	83.6±178.7	0.010
HU min	−914.0 [−975.8, −871.3]	−900.5 [−959.5, −809.8]	0.644
HU mean	−651.8±76.9	−520.5±95.6	<0.005
HU SD	120.1±32.1	173.8±34.2	<0.005

Data were presented as mean ± SD, number, or median [range]. NIA, non-invasive adenocarcinoma; IA, invasive adenocarcinoma; CT, computed tomography; HU, Hounsfield unit; SD, standard deviation.

Results


10^2
10^1
10^0
10^{-1}
Volume, mm^3
inv. pGGN
non-inv. pGGN
−1200
−1000
−800
−600
−400
−200
0
200
CT value, HU

Results

- We evaluated the newly proposed CT parameter, the proportion of GGN voxels with high CT values
- This is denoted by γ , and it changes with the chosen high-CT threshold value θHU
- The γ distributions for IA and NIA at various thresholds were analyzed

$$\overline{\theta}_{HU} = (-500, -450, -400, -350 - 300, -250, -150, -100)[\mathrm{HU}]$$

Results

Table 3 The γ values associated with different θ_{HU} values in the NIA and IA groups

θ_{HU} value (HU)	γ of NIA (N=20), [95% CI]	γ of IA (N=20), [95% CI]	P value
−500	14.78 [4.35, 29.06]	40.46 [27.24, 58.19]	<0.001
−450	9.03 [2.45, 14.60]	32.57 [21.34, 49.00]	<0.001
−400	5.60 [1.10, 9.61]	25.67 [15.54, 40.64]	<0.001
−350	3.24 [0.67, 5.11]	19.87 [11.16, 31.33]	<0.001
−300	1.96 [0.23, 2.55]	14.66 [7.72, 19.95]	<0.001
−250	1.21 [0.00, 1.49]	10.85 [5.26, 13.95]	<0.001
−200	0.73 [0.00, 0.95]	7.61 [2.90, 8.77]	0.001
−150	0.38 [0.00, 0.55]	5.07 [1.36, 5.24]	0.006
−100	0.27 [0.00, 0.39]	3.10 [0.79, 3.13]	0.023

θ_{HU} is the threshold CT volume; volumes greater than θ_{HU} are v_H values; volumes less than θ_{HU} are v_L values. γ is $(v_H/v_H + v_L)\times 100$ [%]. HU, Hounsfield unit; NIA, non-invasive adenocarcinoma; IA, invasive adenocarcinoma.

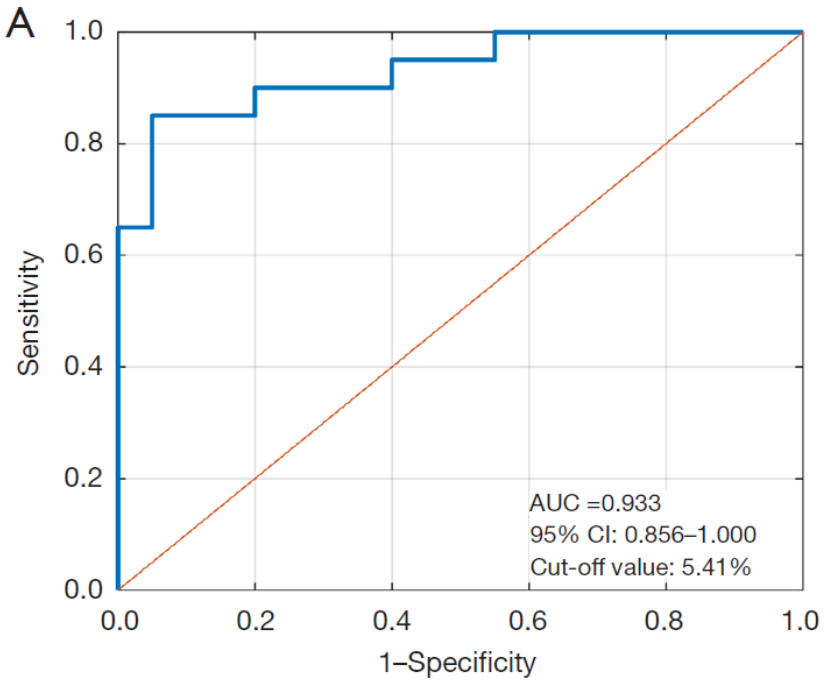
Results

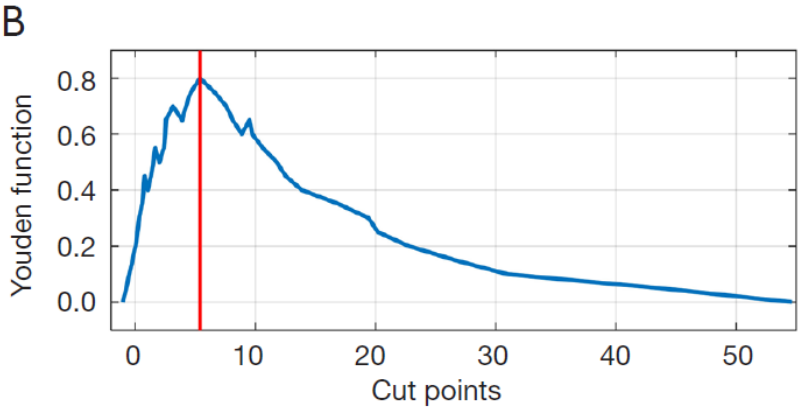
Table 4 The area under the receiver operating characteristic curves and the 95% confidence intervals for different θ_{HU} values

θ_{HU} value (HU)	AUC	95% CI
–500	0.855	0.742–0.968
–450	0.898	0.804–0.991
–400	0.915	0.831–0.999
–350	0.930	0.853–1.000
–300	0.933	0.856–1.000
–250	0.913	0.813–1.000
–200	0.919	0.822–1.000
–150	0.919	0.822–1.000
–100	0.875	0.755–0.995

θ_{HU} is the threshold computed tomography value. HU, Hounsfield unit; AUC, area under the curve; CI, confidence interval.

Results


A
1.0
0.8
0.6
0.4
0.2
0.0
Sensitivity
0.0
0.2
0.4
0.6
0.8
1.0
1–Specificity
AUC =0.933
95% CI: 0.856–1.000
Cut-off value: 5.41%


B
Youden function
0.8
0.6
0.4
0.2
0.0
0
10
20
30
40
50
Cut points

Results

Group	Nodule size	Predictive accuracy
A	0-9mm	90%
B	10-19mm	95.2%
C	>= 20mm	77.8%

Conclusions

- Analyses of CT volumes using the 3D system suggest a relationship between such as volumes and pure GGN invasiveness
- The pure GGN volume proportion of density >-300 HU may predict histological invasiveness; cutoff of 5.41% affords high sensitivity and specificity
- Multicenter prospective studies on pure GGNs are required to determine the clinical utility of the metrics