

Önleyebiliriz... doğrular için birşeyler yap

İletişim Toplantılar 🗸 Yayınlar 🗸 Linkler Dernek v Kurullar ~ Marmara Bölge Toplantısı 7 Kasım 2017 The Seed İstanbul Detaylı Bilgi 1 1 1 1 ------Toplantılar



Yayınlar



İletişim







Onsite Program

 IASLC 18TH WORLD CONFERENCE ON LUNG CANCER

 October 15–18, 2017 | Yokohama, Japan



Educational

Surgical Skills

The strategy for surgical treatment of IIIA –N2 non-small cell lung cancer

International Association for the Study of Lung Cancer

October 17, 2017

Joe B. Putnam, Jr., MD, FACS

Medical Director Baptist MD Anderson Cancer Center Jacksonville, Florida



Making Cancer History®



Stage IIIA is heterogeneous

Subset classification:

- IIIA₁ "Surprise" N2 found after resection (microscopic)
- IIIA₂ Single station N2 found at thoracotomy

IIIA₃ N2 found during preoperative staging » Single station » Multiple (ipsilateral)

IIIA₄ Bulky/fixed N2 disease

Robinson LA, et al. Chest 2003; 123:202S-220S



Mediastinal down-staging & complete resection (R0) needed for best survival

Betticher DC et al. J Clin Oncol. 2003: 21:1752-9; Brit J Cancer 2006: 94:1099-1106



Mediastinal downstaging (N0–1 v N2)

Complete vs incomplete resection

86 pts; 3 cycles cisplatin+docetaxel; CME (+) N2; mediastinal LN downstaging provided 61% 3 year survival vs. 11% for persistent N2.



Nodal pathological complete response has best survival after C+RT \rightarrow S



FIGURE 1. Overall survival as a function of treatment and nodal response. TMT, trimodality therapy; N-PCR, nodal pathologic complete response; RND, residual nodal disease.

MDAnderson Cancer Center

Multiple treatment options for IIIA-N2 NSCLC

- C→S
- C \rightarrow acc RT \rightarrow S
- C + RT
- $C \rightarrow RT$
- C+RT \rightarrow S
- C \rightarrow C+RT \rightarrow S

From Eberhardt WE Lancet 2015. 386: 1018-1019; https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf

BAPTIST MDAnderson Cancer Center

Making Cancer History

Multiple treatment options for IIIA-N2 NSCLC

- $C \rightarrow S$
- C \rightarrow acc RT \rightarrow S
- C+RT
- $C \rightarrow RT$
- C + RT \rightarrow S
- C \rightarrow C+RT \rightarrow S
- Better pCR rates: 25 30% in some series
- More likely to achieve R0 resectionOptimizes each treatment modality

From Eberhardt WE Lancet 2015. 386: 1018-1019; https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf

Conclusions

- Stage IIIA N2 NSCLC is complex and heterogeneous
- Selected cIIIA-N2 patient likely to benefit from resection
- Multidisciplinary treatment planning is required
- Accurate staging pretreatment, after induction, and intraoperative – is necessary
- Benefits of resection + induction therapy must exceed the benefits expected of induction therapy alone.



Potential future clinical trials for surgically resectable stage IIIA N2 NSCLC



1. Phase II: Surgery for single station N2 followed by chemotherapy

- FDG PET avidity uptake in at least one mediastinal nodal station
- Single station N2 by surgical staging
- EXCLUSION
 - Multi-station (≥ 2) mediastinal lymph node involvement
 - Bulky mediastinal disease



2. Phase III: C+RT vs. C+RT -> lobectomy

- Prospective randomized trial comparing definitive C+RT vs. C+RT →S (lobectomy) for cStage IIIA (N2) resectable by lobectomy.
 - "Cross-over" to resection after progression with C+RT
- EXCLUSION: Patients who require or are likely to require pneumonectomy



3. Phase II: Induction with biologicals

• cStage IIIA – N2 / Resectable

Induction for patient with PDL1 expression; or genetic 'targets'



Superior Sulcus Non Small Cell Lung Cancers "Pancoast tumors"

Valerie W. Rusch, M.D. Attending Thoracic Surgeon and Member Miner Family Chair in Intrathoracic Cancers Vice Chair for Clinical Research, Dept. of Surgery Memorial Sloan-Kettering Cancer Center

SWOG 9416 (INT 0160) Schema

```
T3-4, N0-1, M0 NSCLC of the superior sulcus
                     (n = 110)
        2 cycles cisplatin + etoposide
             RT (45 Gy,5 weeks)
       Repeat Extent of Disease Evaluation
                 N = 102 (92\%)
                 CR, PR or Stable
               Surgical Resection
                  N=83 (75%)
                                    Rusch et al. JCO 2007;25:313-318.
```

SWOG 9416 (INT 0160): Surgical Resection Data

Completeness of Resection	No. Pts.	% All Pts
Surgically complete (R0, R1)	76	91.6
T3	55/60	92.0
T4	21/23	91.0
Pathologically complete (R0)	75	90.4
T3	55/60	91.3
T4	20/23	87.0

Southwest Oncology Group Study S9416 Overall Survival by Pathologic Response

Eligible Patients Who Underwent Surgery



Rusch et al. JCO 2007;25:313-318.

MRI Classification Scheme



Pancoast Tumors Important advances in past 30 years

Improvements in resection technique and patient selection

Improvements in multimodality therapy



Management of Early Stage Lung Cancer

Norihiko Ikeda

Department of Surgey Tokyo Medical University

Lung Cancer Surgery in Japan (2014)

- No. of operations: 38085 cases [^]
- Lobectomy: 72.5%,
- Sublobar: 25.2% ↑
- VATS:70%↑
- Stage IA: 51.6% ↑
- Age ≧80: 12% ↑

Gen Thorac Cardionasc Surg 2016

Management of early cancer

• Diagnosis, Localization

- Minimal Invasive Surgery
- Biological Malignancy

Navigation

0 mm

30 mm

EBUS-GS







Diagnosic sensitivity of lung ca≦ 2cm

Conventional TBLB 54% (34% CHEST 2013)

Navigation + EBUS-GS





Minimal Invasive Surgery

VATS Sublobar resection

Safety Surgical simulation using 3D-CT

Ann Thorac Cardiovasc Surg 2013; 19: 1-5

doi: 10.5761/atcs.ra.12.02174

Review Article

Three Dimensional Computed Tomography Lung Modeling is Useful in Simulation and Navigation of Lung Cancer Surgery

Norihiko Ikeda, MD, PhD,¹ Akinobu Yoshimura, MD, PhD,² Masaru Hagiwara, MD,¹ Soichi Akata, MD, PhD,³ and Hisashi Saji, MD, PhD¹

European Journal of Cardio-Thoracic Surgery 46 (2014) e120-e126 doi:10.1093/ejcts/ezu375 Advance Access publication 23 October 2014 **ORIGINAL ARTICLE**

High-quality 3-dimensional image simulation for pulmonary lobectomy and segmentectomy: results of preoperative assessment of pulmonary vessels and short-term surgical outcomes in consecutive patients undergoing video-assisted thoracic surgery[†]

Masaru Hagiwara^a, Yoshihisa Shimada^{a,*}, Yasufumi Kato^a, Kimitoshi Nawa^a, Yojiro Makino^a, Hideyuki Furumoto^a, Soichi Akata^b, Masatoshi Kakihana^a, Naohiro Kajiwara^a, Tatsuo Ohira^a, Hisashi Saji^c and Norihiko Ikeda^a





Nodal Upstaging During Lung Cancer Resection Is Associated With Surgical Approach

Quality	Reference and Approach	Number	cN0–pN1 (%)	cN0–pN2 (%)	Overall (%)
Quality	Boffa 2012 [9]				
	Thoracotomy	7,137	9.3	5.0	14.3
	VATS	4,494	6.7	4.9	11.6
lodal Unstaging	Licht 2013 [10]				
voual upstaging	Thoracotomy	796	13.1	11.5	24.6
	VATS	717	8.1	3.8	11.9
Thoracotomy	Merritt 2013 [15]				
> VATS	Thoracotomy	69	17.4	7.2	24.6
	VATS	60	8.3	1.8	10.1
	Wilson 2014 [16]				
nsufficient nodal	Robotic	302	6.6	4.3	10.9
dissection in	Present study				
////	Thoracotomy	797	8.2	5.8	13.9
AIJ!	VATS	187	5.9	3.2	9.1
	Robotic	130	6.9	6.2	13.1

Martin JT ATS 2016

Minimal Invasive Surgery

VATS Sublobar resection ✓ Clinical trial ✓ Biological malignancy

JCOG/WJOG trials for small-sized (≤2 cm) NSCLC

JCOG0804: 0%<Solid<25%





JCOG0802:

25%<Solid<100%







Lobectomy vs. Segmentectomy (phase III)

Biological malignancy

SUVmax and Pathology

		Sq (n=140)		Adeno (n=870)			
		n	SUVmax	T-test P value	n	SUVmax	T-test P value
p stage	IA IB IIA IIB IIIA IIIB IV	54 44 20 7 13 1 1	7.14±4.66 11.20±6.21 14.82±5.55 15.58±8.47 16.18±7.46 20.32 6.36	<0.001	526 182 62 27 67 - 6	2.03 ± 2.71 5.42 ± 5.72 6.88 ± 4.97 7.40 ± 4.26 8.91 ± 6.53 - 4.00 ± 2.11	<0.001
LN meta	N0 N1 N2	107 23 10	9.53±6.27 14.78±5.06 16.09±8.46	<0.001	752 60 58	3.18±4.20 7.42±5.90 8.03±5.86	<0.001
Relapse	(-) (+)	120 20	10.32±6.45 14.11±7.24	0.018	782 88	3.29±4.26 8.25±6.13	<0.001

WCLC2015

SUVmax of Adenocarcinoma

Classification	No. of cases	SUVmax	P value
AIS+MIA	76	0.51±0.58 ⊺	TTT
Lepidic	206	1.46±1.51	
Papillary	317	4.37±4.70	
Acinar	163	4.49±4.22	<0.001
Solid	76	8.71±6.81	
Micropapillary	8	6.65±5.19	
Others	24	5.34±7.39	

unpublished ³⁴

RFS according to revised SUVmax on Squamous and Adeno



Volumetic analysis of CTR





Adenocarcinoma 170 cases Stage IA 128 Stage IB 18




Smoking Survival Stage

"Radiomics" ✓ Clinical information Stage **Prognosis** ✓ Image CT PET ✓ Pathology

✓ Translational Oncology

Lee G Eur J Radiol 2017



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MINIMALLY INVASIVE SURGERY FOR LUNG CANCER INCLUDING ROBOTIC

Giulia Veronesi





Diversion of true and virtual operating field



Lack of 3D vision

Bad ergonomics

Tremors amplification

Fulcrum effect

Instable surg field (camera assistant)

Counteractive movements

ADVANTAGES ROBOTIC APPROACH

Technical improvements:

Intuitive movements Tremor filtration Increased degrees of freedom Motion scaling Stereoscopic vision Stable camera platform Equivalence between the dominant and non-dominant hands Eye-hand-target alignment

Clinical improvements

NODAL UPSTAGING SEGMENTS OCCULT N2 LOCALLY ADVANCED

WI. 2014

NENI

	0 0 1 '		<i>J</i>	5 5	0
Outcome	Open (n = 466)	VATS (n = 555)	Robotic (n = 391)	p Value ^a	p Value ^b
Mortality	12 (2.6%)	7 (1.2%)	1 (0.3%)	0.062	0.003
LOS (mean)	8.0	6.4	6.0	0.454	0.001
Routine discharge	301 (64.6%)	343 (61.8%)	250 (63.9%)	0.502	0.843
Prolonged LOS	46 (9.9%)	42 (7.6%)	18 (4.6%)	0.055	0.003
Any complication	236 (50.6%)	275 (49.5%)	170 (43.4%)	0.065	0.036
Bleeding complication	12 (2.6%)	8 (1.4%)	7 (1.8%)	0.678	0.430

Current on Outcomes of Functions Charles Open, $VAIS$, of Nobolic Functionary Resections Fertormed Only by Robolic S

^a Between robot and VATS resections. ^b Between robot and open resections.



Surgical robot device market \$3.2 billion in 2014 \$20 billion by 2021

WinterGreen Research new study: Market Shares, Strategy, and Forecasts, Worldwide, 2015 to 2021





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TAKE HOME MESSAGE

VATS is the standard treatment for stage I and selected II disease

Rats introduced indusputable technical advantages

- No clear benefit of RATs is demonstrated compared to expect a trend in mortality reduction and better lymph node dissection
- Higher cost is the main limitation to wide diffusion and adoption of RATS, costs are expected to be reduced when competitors will enter the market
- Most advantages of RATS are expected in more complex procedures (pretreated N1 or N2 diseases or anatomical segmentectomies)
- More studies and longer fup are required to define the role of VATS and RATS



There is diffuse awareness that robotic surgery will become the minimally invasive approach of the future



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Lung Cancer Surgery for High Risk Patients

Claudio Suárez Cruzat Head Thoracic Surgery Clinica Santa Maria, Santiago de Chile





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Challenge in thoracic oncology

-heavy smokers

-cardiovascular and/or respiratory diseases

-prevents for getting optimal results in lung cancer treatment





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3.- If the patient persists in the high or moderate-risk group(VO2 10-15ml/kg/min with VE/VCO2 <35) we prefer sublobar resections



3.1

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• If the tumor is:

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a pure GGO or predominantly GGO (<50% solid) less than 2 cms

- VATS wide wedge resection + lymph node sampling.
- Frozen section must confirm:

<50% is invasive or invasion area is smaller than 5mm and Margins >1cm To persevere with wedge resection.





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3.- If the patient persists in the high or moderate-risk group (VO2 10-15ml/kg/min with VE/VCO2 <35), we prefer sublobar resections.



3.2

- If these pathological requirements are not met: (or for)
 - Solid tumors >10 mm or mostly solid/GGO tumors or
 - GGO tumors >20 mm with >25-50% solid, or
 - Invasive component >5 mm
- Perform an anatomic segmental resection, VATS/ thoracotomy, associated with hilar and mediastinal lymphadenectomy.

*Asamura H et al. Oncology Group 0201. J Thorac Cardiovasc Surg 2013;146:24-30 *Hattori A et al. JTO 2017;12(6):954-962 *Aokage K et al. Jpn J Clin Oncol,2017,47(1):7-11





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Even in larger tumors, we will attempt sublobar resection in high-risk patients. We consider that although the risk of local recurrence is high, the lower morbidity and mortality rate of sublobar resections justifies this approach in this patients.

We believe that a sublobar resection with margins >1 cm, grant better quality of life than a patient who becomes oxygen dependent, dies in the postoperative period or has not been resected due to the impossibility of lobectomy. Male, 77yo,heavy smoker, COP, SUV 11,7, EBUS(-) DLCO-VEF1>60%, CPETVO2 9 slope 46 After Training 13-42



Pathology: squamous cell ca 35mm, PL1. Fibrous adherence, margin 12 mm. Lymphovascular invasion (+), CPL(-)





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Stratified log-rank test for equality of survivor functions

vo2maxgood	Events observed	Events expected(*)
0 1	6 6	2.47 9.53
Total	12	12.00
(*) sum over	r calculations	within stage
	chi2(1) Pr>chi2	= 7.14 = 0.0075

Survival in Resected NSCLC Lung Cancer by VO2 max, adjusted by TNM Patiens with VO2 peak <15 ml/kg/min present a worse survival (obtained in series of 55 patients in the last preoperative evaluation, after training) 2017, Clinica Santa María, Santiago, Chile





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Surgical Skills:

Salvage Surgery

Hans Hoffmann

Dept. of Thoracic Surgery, Thoraxklinik, University of Heidelberg, Germany







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Salvage Thoracic Surgery...

...is defined as surgical resection of persistent or recurrent primary lung cancer after previous *local treatment without surgery*





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Indications for Salvage Surgery

Persistent or recurring primary lung tumor or specific complications

➢after stereotactic radiotherapy (SBRT) or other ablative therapies

"Salvage surgery after SBRT may be rather straightforward and in many cases even feasible by a minimally invasive approach." ➤after *definitive* chemoradiation therapy for Stage III non-small cell lung cancer

> "Surgery after a full dose of chemoradiation can be quite challenging and the dissection of the anatomical structures is technically demanding."





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Indications for Salvage Surgery

Persistent or recurring primary lung tumor or specific complications

➢after stereotactic radiotherapy (SBRT) or other ablative therapies ➢after *definitive* chemoradiation therapy for Stage III non-small cell lung cancer

- Common to all indications is that they are always individual case decisions.
- The published series are all retrospective, comprise only a small number of patients and refer to a long period at a single institution.





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Indications for Salvage Surgery

Persistent or recurring primary lung tumor or specific complications

➢after stereotactic radiotherapy
(SBRT) or other ablative therapies

Whereas in the past SBRT was typically considered an alternative to surgery for patients unfit or at high risk for surgery, the modality is now being used more often also for healthier, potentially operable patients.





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Indications for Salvage Surgery

Persistent or recurring primary lung tumor or specific complications

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	Total	R0	R1/2
	Ν	N (%)	N (%)
Interval RT-Surgery			
0-3 mo	12	8 (66.7)	4 (33.3)
≥3 mo	23	19 (82.6)	4 (17.4)
Resection		· · ·	
Explorative thoracotomy	6	0 (0.0)	6 (100.0)
Lobectomy	9	9 (100.0)	0 (0.0)
Extended* lobectomy	3	3 (100.0)	0 (0.0)
Pneumonectomy	7	7 (100.0)	0 (0.0)
Extended* pneumonectomy	10	8 (80.0)	2 (20.0)
30-day mortality			
No	33	25 (75.6)	8 (24.2)
Yes	2	2 (100.0)	0 (0.0)
90-day mortality		. ,	
No	31	24 (77.4)	7 (22.6)
Yes	4	3 (75.0)	1 (25.0)

Single Institution series of **35 cases** that underwent salvage surgery after definitive chemoradiation therapy for locally advanced non– small cell lung cancer over a period of 10 years, representing **1.2% of all lung resections** for lung cancer performed at their institution.







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Take Home Message: Salvage Thoracic Surgery...

- …after local failure of SBRT in highly select individuals is feasible and safe, and has an overall acceptable morbidity and mortality.
- …after a full dose of chemoradiation in advanced stages can be quite challenging and surgically demanding. Retrospective data show acceptable morbidity, mortality and promising outcome.
- Each individual case should be reviewed in a multidisciplinary tumor board (MTB) and the surgery should be performed by an experienced team.



Meet the Expert



do extended resections improve T4 lung cancer outcomes?

Dominique H. Grunenwald, MD Professor Emeritus Thoracic and Cardiovascular Surgery Pierre&Marie Curie University, Paris. F





SVC / great vessels left atrium trachea / carina satellite nodules vertebral bodies

heart / ventricle pleural effusion esophagus

technical resectability

yes

no



is there a role for surgical resection in T4 lung tumors? (" surgical " stage IIIA when N0-1)

- T4 nsclc is an heterogeneous group of patients
- decision making needs a case by case discussion
- surgery must perform an en bloc excision of invaded structures
- it needs a particular expertise of the surgical team
- serious perioperative complications can occur
- long-term outcome depends on nodal status
- adequate surgery has demonstrated ability to achieve long term survivals

critical point of view

a surgical procedure which would not be reproducible in other centers would never be recognized as an option for practice

it is important to distinguish the real progress that could be applied throughout the world, from the simple reports of individual performances or exploits





take home messages (2)

encouraging long-term survival rates can be expected, despite non negligible postoperative mortality rates

the 8th edition of TNM staging system confirmed its adaptation to these progress, by classifying T4N0-1 tumors in a "surgical" category, the stage IIIA

given the negative prognostical influence of N2 nodal status observed in any T4 situation, a thorough mediastinal evaluation is highly recommended to preclude these patients from surgery



Technical Issues after Neoadjuvant Chemoradiation For Stage IIIA N2 NSCLC A Surgeon's Perspective

Gail Darling MD FRCSC FACS Professor Thoracic Surgery Kress Family Chair in Esophageal Cancer gail.darling@uhn.ca







Contraindications to surgery for Stage IIIA NSCLC

- Extracapsular N2
- Fixed bulky nodes
- Inability to achieve an R0 resection
- T4N2
- Patient not fit for planned resection (right pneumonectomy required?)





Restaging after Induction therapy

- CT scan: to assess response but primarily to confirm resectability and exclude progression
- PET: to rule out progression; assess response to determine if surgery is required?





Restaging after Induction therapy

Int0139 best survival for pN0 but pN1-3 still better than no surgery!







Doctors of Thoracic Surgery[®]



Surgery has a role in Select Stage IIIA N2





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What type of surgery should be selected for GGO-containing tumors?

P. De Leyn, H. Decaluwé and W. Dewever Department of Thoracic Surgery and Radiology University Hospitals Leuven



Pure GGO lesions

- Etiology : Non-specific inflammation
 Fibrosis
 Neoplasm
- Recent guidelines (2017) : pure GGO ≥ 6 mm CT scan at 6-12 months and then every 2 years

Fleischner Society; Radiology 2017;153:462-9

A nomogram for predicting the risk of invasive pulmonary adenocarcinoma for patients with solitary subsolid nodules



FIGURE 2. A nomogram predicting the risk of IPA for patients with solitary peripheral sub-solid nodules. The value of each of variable was given a score on the point scale axis. A total score could be easily calculated by adding each single score and, by projecting the total score to the lower total point scale, we were able to estimate the probability of IPA.

Jin et al., J Thoracic Cardiovasc Surg 2017;153:462-9





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TAKE HOME MESSAGE

- Pure GGO lesions are often a challenge for the surgeon.
- Repairing techniques are essential
- Size and pleural retraction are predictive factors for invasive adenocarcinoma. Growing lesions > 10 mm, or appearance of solid component should be resected
- If peripheral and small, wedge resection is enough. When lesion is deep, segmentectomy is indicated







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• **Mixed nodules** : C/T ratio is important to predict aggressiveness of adenocarcinoma (both local and lymphatic spread)

 Lesion ≤ 2 cm with C/T ratio ≤0.25 : very good prognosis with limited resection (segmentectomy) with LN dissection (margin = tumor size). Whether wedge could be sufficient will depend on results of prospective randomized trials




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- For Mixed nodules ≤ 2 cm with C/T ratio > 0.5 results of prospective randomized studies need to be awaited. So far lobectomy with nodal resection is recommended.
- Limited role of TTP and frozen selection in subtyping aggressive types of adenocarcinoma (micropapilarry and solid patterns) which necessitate lobectomy. High specificity, low sensitivity

Resection of GGOs: How, When and Why?

David H. Harpole, M.D. **Professor of Surgery** Associate Professor of Pathology Duke University Durham, NC, USA **Co-chair NCI Thoracic Malignancy Steering Committee** Bethesda, MD, USA

Summary

- GGO-containing CT lesions require a multi-modality team including Thoracic Imaging to select most appropriate surgical candidates
- Localization techniques are often useful for minimizing resection size for diagnosis
- Minimally-invasive approaches to resection predominate in 2017
- Resections with node dissection required for TNM:
 - >3.0 cm size: Lobectomy
 - 1.0-3.0 cm size: Consider segmentectomy or lobectomy
 - <1.0 cm size with significant solid component: Wedge resection may be adequate (small pure GGOs should be followed)
- Resection margins should be > 1.0 cm from CT-sized mass (Do not use palpation to estimate margin of resection)