Best of 19th IASLC World Conference on Lung Cancer (WCLC) 2018



INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER

ΔΙΟΡΓΑΝΩΣΗ



Εταιρεία Μελέτης Πνευμονοπαθειών & Επαγγελματικών Παθήσεων Θώρακος Hellenic Society of Respiratory & Occupational Chest Diseases

17-18 Μαΐου 2019 Mediterranean Palace Hotel Θεσσαλογίκη

Diagnostic Dilemma in Lung Cancer

Μπαλιάκα Αγγελική

Παθολογοανατόμος, Επικουρική Επιμελήτρια Β' Παθολογοανατομικό Εργαστήριο Γ.Ν.Θ. «Γ. Παπανικολάου»





IASLC 19th World Conference on Lung Cancer

September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018

Diagnostic Dilemma in Lung Cancer: Biopsy Diagnosis and Classification



Andre L. Moreira MD, PhD. New York University Langone Health, USA





IASLC 19th World Conference on Lung Cancer September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018

Role of Biopsy in the diagnosis of Lung cancer

Approximately 70% of patients with lung cancer are diagnosed at advanced stages.

Cytology (FNAB, EBUS-TBNA, etc) and small biopsies (endobronchial, transbronchial, Core biopsy) are the only available diagnostic material for these patients.







IASLC 19th World Conference on Lung Cancer September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018

Role of Biopsy in the diagnosis of Lung cancer

Accurate diagnosis and tissue preservation:

- 1. Directs patient clinical management (Small cell carcinoma versus NSCLC)
- 2. Directs chemotherapeutic regimen in NSCLC
- 3. Guides the Identification of targetable mutations in adenocarcinoma
- 4. Tissue preservation for future discoveries of new targetable mutations and appropriate biomarkers for prognosis and therapies







IASLC 19th World Conference on Lung Cancer

September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018

Approach:

- 1. How to subtype Non-Small Cell Carcinoma in small biopsy specimen including cytology specimen?
- 2. Diagnosis of neuroendocrine tumor
- 3. Challenging cases







IASLC 19th World Conference on Lung Cancer

September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018

Adenocarcinoma



Small biopsy: Lepidic, acinar, papillary, micropapillary formation







IASLC 19th World Conference on Lung Cancer

September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018

Adenocarcinoma



Cytology:

Tridimensional clusters, delicate/vacuolated cytoplasm, fine chromatin, prominent nucleoli







IASLC 19th World Conference on Lung Cancer September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

Squamous cell carcinoma



Biopsy:

Evidence of keratinization

Presence of intracellular bridges



#WCLC2018





IASLC 19th World Conference on Lung Cancer September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018

Squamous cell carcinoma



Cell Block (Cytology):

Evidence of keratinization

Presence of intracellular bridges (cannot be seen on smears)

Dense cytoplasm

Flat sheets

Delicate nucleoli







IASLC 19th World Conference on Lung Cancer

September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018

NSCLC, Poorly differentiated









IASLC 19th World Conference on Lung Cancer September 23–26, 2018 Toronto, Canada

INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER

WCLC2018.IASLC.ORG

#WCLC2018

Adenocarcinoma versus Squamous cell carcinoma









IASLC 19th World Conference on Lung Cancer September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018

Literature on the subject

There have been a lot of publications on an IHC panel that can efficiently differentiate adenocarcinoma from squamous cell carcinoma

Most common markers: CK7, TTF-1, Napsin-A, p63, p40, 34be12 CK 5/6 etc.

Use of many markers defeats the idea of tissue preservation for prognostic/predictive markers

Travis WD, Brambilla E, Noguchi M, et al. Arch Pathol Lab Med 2013; 137: 668-684.





*

IASLC 19th World Conference on Lung Cancer

September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018

INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER

Minimal panel

	p40-	p40+
TTF-1+	ADC	ADC*
TTF-1-	NSCLC* (favors ADC)	SQCC (diffuse)

*If tissue is available other markers such as napsin-A and CK 5/6 can be added to the panel Always compare TTF-1 to p63/p40. Performing one stain only has very low predictive value







IASLC 19th World Conference on Lung Cancer

September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018

IASLC/ATS/ERS classification of NSCLC in small biopsy

	Histologic Criteria	2 markers IHC profile
Adenocarcinoma	Presence of acinar, papillary, lepidic, or micropapillary patterns	Not recommended
Squamous cell carcinoma	Presence of keratinization and intracellular bridges	Not recommended
NSCC, favor adenocarcinoma	Solid pattern, no other evidence of differentiation	Any TTF-1 positivity, negative for p63/p40
NSCC, favor squamous cell carcinoma	Solid pattern, no other evidence of differentiation	Diffuse and strong positivity for p63 or p40. Negative for TTF-1
NSCLC, not otherwise specified (NOS)	Solid pattern, no other evidence of differentiation	Double positivity for TTF-1 and p63 or p40 either focal or diffuse







IASLC 19th World Conference on Lung Cancer September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018

Double positive tumors

Pay attention to where the double positive cells are!!

- -Double positivity for TTF-1/p40 in the same cells
- P40 Diffuse: NSCLC- NOS
- P40 Focal: NSCLC- favor adenocarcinoma
- -Double positivity in different areas of the tumor
- NSCLC, favor adenosquamous carcinoma







IASLC 19th World Conference on Lung Cancer

September 23–26, 2018 Toronto, Canada

INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER

WCLC2018.IASLC.ORG

#WCLC2018

Adenosquamous carcinoma



Images provided by Dr Saqui, Columbia University, USA



WCLC 2018



*

IASLC 19th World Conference on Lung Cancer September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018

The diagnosis of adenosquamous carcinoma is difficult in biopsy specimens

In a biopsy both components need to be present

More frequently the diagnosis can be suspected in a biopsy diagnosis of SQCC in a non-smoker





*

IASLC 19th World Conference on Lung Cancer September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG



2018

Cytology Cell block

Images provided by Dr Saqui, Columbia University, USA

TTF-1 (+)







IASLC 19th World Conference on Lung Cancer September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018

Double negative tumors

- In double negative tumor, consider other primaries
 including non-epithelial tumors
- Add other markers such as napsin-A, keratins
- Large cell carcinoma cannot be diagnosed by biopsy /cytology







IASLC 19th World Conference on Lung Cancer

September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018

64 y.o. old woman, remote history of smoking.Presented with coughCT scan showed a single pulmonary noduleA biopsy was performed







IASLC 19th World Conference on Lung Cancer

September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018

IHC

Negative for p40, TTF-1, napsin A, and other organ specific marker. Positive for keratin

DX: Non-small cell carcinoma, NOS Send for molecular pathology







IASLC 19th World Conference on Lung Cancer

September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018

81 y.o, man, smoker, history of leukemia S/P chemotherapy Presents with a lung nodule

A biopsy of the nodule was obtained







IASLC 19th World Conference on Lung Cancer

September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018

IHC Negative for TTF-1, p40, NE markers

Keratin- NEGATIVE

Metastatic melanoma.

A remote history of melanoma was discovered after the biopsy2







IASLC 19th World Conference on Lung Cancer September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018

Take Home message

Solid adenocarcinomas of the lung can have a squamoid appearance, which may lead to misdiagnosis.

All adenocarcinomas or NSCLC, favor adenocarcinoma or NSCLC, NOS should be sent to molecular diagnosis

Squamous cell carcinoma or NSCLC, favor squamous cell carcinoma do not need to be sent for molecular studies, **unless in certain clinical conditions**, **such as non-smoker** (possibly a component of adenosquamous carcinoma)

Double negative add more markers









IASLC 19th World Conference on Lung Cancer September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018

Neuroendocrine tumors groups

High grade NET

- Small cell carcinoma
- Large cell Neuroendocrine carcinoma (LCNEC)

Low-intermediate grade NET (difficult to classify in small biopsy)

- Typical Carcinoid tumor
- Atypical carcinoid tumor







IASLC 19th World Conference on Lung Cancer

September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018

Reproducibility issues!

Moderate reproducibility among expert pathologists! Mostly due to small biopsies with crush artifact.

- Use of IHC is recommended to confirm diagnosis and avoid pitfalls with other NET
 - IHC work up should include KI-67 proliferation rate.

Thunissen E et al. J Thorac, Pathol. 2017; 12:334-46.





*

IASLC 19th World Conference on Lung Cancer

September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018

Carcinoid tumor











Journal of Thoracic Oncology 2017 12, 334-346DOI: (10.1016/j.jtho.2016.12.004) Copyright © 2017 International Association for the Study of Lung Cancer Terristica







IASLC 19th World Conference on Lung Cancer

September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018

LCNEC

Definition: NSCLC with NE morphology with IHC evidence of NE differentiation.

There is growing evidence that LCNEC is a heterogeneous group of tumors within a spectrum of small cell and adenocarcinoma

Biopsy diagnosis is difficult but can be made with caution.

There are overlapping features with adenocarcinoma and small cell carcinoma







IASLC 19th World Conference on Lung Cancer

September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018



Rekhtman et al Modern Pathol. 2018.31:111-121







IASLC 19th World Conference on Lung Cancer September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018

Carcinoid tumors

Typical carcnoid: less than 2 mitotic figures per 2mm², no necrosis. **Atypical Carcinoid**: 2 to 10 mitotic figures per 2mm², punctate necrosis

Ki-67 index is not helpful in differentiating Typical from atypical carcinoid, but is good to separate High grade NE tumors

Difficult to separate the 2 entities in biopsy or cytology material, focal mitotic figures





*

IASLC 19th World Conference on Lung Cancer September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018

72 year old woman, smoker, asymptomatic. Recent diagnosis of colon adenocarcinoma A work up CT scan showed a mass in the lung A PET CT showed in addition to the lung nodule, 2 PET avid nodules in the right breast.

A Biopsy of the lung nodule was performed.



IASLC-+-

INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER



IASLC 19th World Conference on Lung Cancer

September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018









IASLC 19th World Conference on Lung Cancer

September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018

2018









IASLC 19th World Conference on Lung Cancer

September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018







IASLC 19th World Conference on Lung Cancer

September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018

Combined SqCC and SCC

Small cell carcinoma can be combined with Sqcc, adenocarcinoma, and other types

Incidence is unreliable

SCC component may have the same mutation as the counterpart.







IASLC 19th World Conference on Lung Cancer September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018

Other carcinomas: Nut carcinoma



Poorly-differentiated with characteristic t(15;19) rearrangement leading to NUT fusion Rare tumor Poor prognosis Can be positive for p40 and TTF-1 (weakly) Often monotonous features with abrupt keratinization's Include in the differential diagnosis of poorlydifferentiated carcinomas Difficult in biopsy material!

Scholl LM et al. JTO. 2015, 10:951-9





IASLC 19th World Conference on Lung Cancer

September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018

Take home message

IHC is a very powerful method of identifying cell type of NSCLC

Awareness of the exact algorithm and its pitfalls is essential!

The minimal panel is only useful when the diagnosis is a primary lung carcinoma

Use of a limited panel of IHC markers saves tissue for molecular diagnosis Be aware of crush artifact in NE tumors, include KI 67 in your work up panel







IASLC 19th World Conference on Lung Cancer September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018

Staging and pathology of Multiple lung nodules

Alain C. Borczuk, MD

Weill Cornell Medicine

NYC, NY







IASLC 19th World Conference on Lung Cancer

September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018

Why is this an issue?

- Screening CT detects nodules with increasing frequency
- Overstaging multiple nodules leads to -
 - Under treatment by surgical approaches
 - Over treatment by systemic therapies







IASLC 19th World Conference on Lung Cancer

September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018

Why is this an issue?

- Survival data
 - Indicates further refinement resulted in better survival stratification



Table 3. Pathologic Criteria for Separate versus Related Pulmonary Tumors

Pathologic criteria (i.e., after resection)^a

- Tumors may be considered separate primary tumors if They are clearly of a different histologic type (e.g., squamous carcinoma and adenocarcinoma).
 - They are clearly different by a comprehensive histologic assessment.
 - They are squamous carcinomas that have arisen from carcinoma in situ.

Tumors may be considered to be arising from a single tumor source if Exactly matching breakpoints are identified by comparative genomic hybridization.

Relative arguments that favor separate tumors (to be considered together with clinical factors): Different pattern of biomarkers Absence of nodal or systemic metastases

Relative arguments that favor a single tumor source (to be considered together with clinical factors): Matching appearance on comprehensive histologic assessment The same biomarker pattern Significant nodal or systemic metastases

^aPathologic information should be supplemented with any clinical information that is available.

IASLC 19th World Conference on Lung Cancer

September 23–26, 2018 Toronto, Canada

> WCLC2018.IASLC.ORG

#WCLC2018

Except non-mucinous lepidic



IASLC-++



IASLC 19th World Conference on Lung Cancer

September 23–26, 2018 Toronto, Canada

#WCLC2018

AJCC 8th Edition - Springer

Table 36.11 Schematic summary of disease patterns and TNM classification of patients with lung cancer with multiple pulmonary sites of involvement¹⁶

	Second primary lung cancer	Multifocal GG/L nodules	Pneumonic-type adenocarcinoma	Separate tumor nodule
Imaging features	Two or more distinct masses with imaging characteristic of lung cancer (e.g., spiculated)	Multiple ground-glass or part-solid nodules	Patchy areas of ground glass and consolidation	Typical lung cancer (e.g., solid, spiculated) with separate solid nodule
Pathological features	Different histotype or different morphology based on comprehensive histologic assessment	Adenocarcinomas with prominent lepidic component (typically varying degrees of AIS, MIA, LPA)	Same histology throughout (most often invasive mucinous adenocarcinoma)	Distinct masses with the same morphologic features based on comprehensive histologic assessment
TNM classification	Separate cTNM and pTNM for each cancer	T based on highest T lesion, with (#/m) indicating multiplicity; single N and M	T based on size or T3 if in single lobe, T4 or M1a if in different ipsilateral or contralateral lobes; single N and M	Location of separate nodule relative to primary site determines whether T3, T4, or M1a; single N and M
Conceptual view	Unrelated tumors	Separate tumors, albeit with similarities	Single tumor, diffuse pulmonary involvement	Single tumor with intrapulmonary metastasis

AIS, adenocarcinoma in situ; GG/L, ground-glass/lepidic; LPA, lepidic-predominant adenocarcinoma; MIA, minimally invasive adenocarcinoma





IASLC 19th World Conference on Lung Cancer September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018

AJCC 8th Edition (paraphrased)

Table 36.9 – Pathological criteria identifying multifocal Ground glass or lepidic lung adenocarcinoma

Tumors should be considered multifocal lung adenocarcinoma if:

There are multiple foci of LPA, MIA or AIS

Foci of AAH are not counted

This applies regardless of detailed histologic assessment

Applies to clinical or pathology only detection of additional nodule



IASLC 19th World Conference on Lung Cancer





Left upper lobectomy

IASLC



IASLC 19th World Conference on Lung Cancer September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018





IASLC 19th World Conference on Lung Cancer







IASLC 19th World Conference on Lung Cancer September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018

Staging – AJCC 8th Edition

Tumor 1 - Lepidic predominant, 0.9 cm invasion or T1a (non-mucinous)

Tumor 2 - Lepidic predominant, 0.7 cm invasion or T1a (non-mucinous)

Tumor 3 – AIS

Tumor 4 – Minimally invasive, 0.3 cm





IASLC----

INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER

AJCC 8th Edition

IASLC 19th World Conference on Lung Cancer

September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018

Table 36.11 Schematic summary of disease patterns and TNM classification of patients with lung cancer with multiple pulmonary sites of involvement¹⁶

	Second primary lung cancer	Multifocal GG/L nodules	Pneumonic-type adenocarcinoma	Separate tumor nodule
Imaging features	Two or more distinct masses with imaging characteristic of lung cancer (e.g., spiculated)	Multiple ground-glass or part-solid nodules	Patchy areas of ground glass and consolidation	Typical lung cancer (e.g., solid, spiculated) with separate solid nodule
Pathological features	Different histotype or different morphology based on comprehensive histologic assessment	Adenocarcinomas with prominent lepidic component (typically varying degrees of AIS, MIA, LPA)	Same histology throughout (most often invasive mucinous adenocarcinoma)	Distinct masses with the same morphologic features based on comprehensive histologic assessment
TNM classification	Separate cTNM and pTNM for each cancer	T based on highest T lesion, with (#/m) indicating multiplicity; single N and M	T based on size or T3 if in single lobe, T4 or M1a if in different ipsilateral or contralateral lobes; single N and M	Location of separate nodule relative to primary site determines whether T3, T4, or M1a; single N and M
Conceptual view	Unrelated tumors	Separate tumors, albeit with similarities	Single tumor, diffuse putmonary involvement	Single tumor with intrapulmonary metastasis

AIS, adenocarcinoma in situ; GG/L, ground-glass/lepidic; LPA, lepidic-predominant adenocarcinoma; MIA, minimally invasive adenocarcinoma





IASLC 19th World Conference on Lung Cancer

September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018

Example 2a and 2b



IASLC-++

INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER



IASLC 19th World Conference on Lung Cancer

September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018





IASLC-++

INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER



IASLC 19th World Conference on Lung Cancer September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018









IASLC 19th World Conference on Lung Cancer

September 23–26, 2018 Toronto, Canada

INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER

> WCLC2018.IASLC.ORG

#WCLC2018

Table 36.11 Schematic summary of disease patterns and TNM classification of patients with lung cancer with multiple pulmonary sites of involvement¹⁶

	Second primary lung cancer	Multifocal GG/L nodules	Pneumonic-type adenocarcinoma	Separate tumor nodule
Imaging features	Two or more distinct masses with imaging characteristic of lung cancer (e.g., spiculated)	Multiple ground-glass or part-solid nodules	Patchy areas of ground glass and consolidation	Typical lung cancer (e.g., solid, spiculated) with separate solid nodule
Pathological features	Different histotype or different morphology based on comprehensive histologic assessment	Adenocarcinomas with prominent lepidic component (typically varying degrees of AIS, MIA, LPA)	Same histology throughout (most often invasive mucinous adenocarcinoma)	Distinct masses with the same morphologic features based on comprehensive histologic assessment
TNM classification	Separate cTNM and pTNM for each cancer	T based on highest T lesion, with (#/m) indicating multiplicity; single N and M	T based on size or T3 if in single lobe, T4 or M1a if in different ipsilateral or contralateral lobes; single N and M	Location of separate nodule relative to primary site determines whether T3, T4, or M1a; single N and M
Conceptual view	Unrelated tumors	Separate tumors, albeit with similarities	Single tumor, diffuse pulmonary involvement	Single tumor with intrapulmonary metastasis

AIS, adenocarcinoma in situ; GG/L, ground-glass/lepidic; LPA, lepidic-predominant adenocarcinoma; MIA, minimally invasive adenocarcinoma



*

IASLC 19th World Conference on Lung Cancer

September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018

Example 3 - Multiple nodules

Comprehensive histologic assessment







IASLC 19th World Conference on Lung Cancer

September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018

Radiologically Distinct















IASLC 19th World Conference on Lung Cancer

September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018

Example 4 - Multiple nodules -Resolvable

Integrate supportive molecular data







IASLC 19th World Conference on Lung Cancer

September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018



nodule 1 – acinar (clear cells)

KRAS G12D,EGFR wt

nodule 2 - acinar

KRAS wt, EGFR wt



IASLC 19th World Conference on Lung Cancer

September 23–26, 2018 Toronto, Canada

INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER

IASLC--+-

8th Editionwclc2018.IASLC.org

#WCLC2018

	Second primary lung cancer	Multifocal GG/L nodules	Pneumonic-type adenocarcinoma	Separate tumor nodule
Imaging features	Two or more distinct masses with imaging characteristic of lung cancer (e.g., spiculated)	Multiple ground-glass or part-solid nodules	Patchy areas of ground glass and consolidation	Typical lung cancer (e.g., solid, spiculated) with separate solid nodule
Pathological features	Different histotype or different morphology based on comprehensive histologic assessment	Adenocarcinomas with prominent lepidic component (typically varying degrees of AIS, MIA, LPA)	Same histology throughout (most often invasive mucinous adenocarcinoma)	Distinct masses with the same morphologic features based on comprehensive histologic assessment
TNM classification	Separate cTNM and pTNM for each cancer	T based on highest T lesion, with (#/m) indicating multiplicity; single N and M	T based on size or T3 if in single lobe, T4 or M1a if in different ipsilateral or contralateral lobes; single N and M	Location of separate nodule relative to primary site determines whether T3, T4, or M1a; single N and M
Conceptual view	Unrelated tumors	Separate tumors, albeit with similarities	Single tumor, diffuse pulmonary involvement	Single tumor with intrapulmonary metastasis

AIC







IASLC 19th World Conference on Lung Cancer

September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018

Example 5 - Multiple nodules difficult



IASLC-++

INTERNATIONAL ASSOCIATION FOR THE STUDY OF LUNG CANCER



IASLC 19th World Conference on Lung Cancer

September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018

Acinar patterns are common - Do they mean the same primary?





IASLC 19th World Conference on Lung Cancer September 23–26, 2018 Toronto, Canada MCCO24 CP OF OF OF WCCC2018 Nicholson et al, JTO 13:205, 2018



Strong agreement among observers Used nuclear features, pattern, cell size and mitoses as most helpful

Three separate tumors, high agreement







IASLC 19th World Conference on Lung Cancer

September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018

Summary

- Differences are easier to prove than similarity
- Unusual, distinctive (except non-mucinous lepidic) or uncommon features seen in two nodules may support same origin







IASLC 19th World Conference on Lung Cancer September 23–26, 2018 Toronto, Canada

> WCLC2018.IASLC.ORG

#WCLC2018

TAKE HOME MESSAGE

- Multiple nodules may be more frequently independent primaries than previously thought
- Staging has incorporated these concepts in AJCC 8th Edition
- Test strategies include combinations of radiology, pathology, and molecular features







IASLC 19th World Conference on Lung Cancer

September 23–26, 2018 Toronto, Canada

WCLC2018.IASLC.ORG

#WCLC2018

NYC – Columbia University?

NYC – 125th street?



No – Both are actually Toronto

