Sixth International Joint Meeting on THORACIC SURGERY

Barcelona - 20th, 21st and 22nd November 2024
Auditorio Foment del Treball Nacional. Barcelona (Spain)

11th International Meeting on General Thoracic Surgery
Clínic Barcelona | Universitat de Barcelona | Hospital Universitari Sagrat Cor

5th Meeting of the Thoracic Oncology, Thoracic Surgery, Techniques & Transplant, Respiratory Nursing and Respiratory Physiotherapy Areas of the Spanish Society of Pneumology and Thoracic Surgery (SEPAR)
Sociedad Española de Neumología y Cirugía Torácica (SEPAR)

10th International Workshop on Surgical Exploration of the Mediastinum and Systematic Nodal Dissection
Hospital Universitari Mútua Terrassa | Universitat de Barcelona

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3rd Joint Meeting of the Spanish Society of Thoracic Surgery (SECT)
SECT Sociedad Española de Cirugía Torácica

30th Congress of the "Asociación Iberoamericana de Cirugía Torácica" AIACT

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AN ARTEFACT IN THE TNM CLASSIFICATION? REALLY?

Erik Thunnissen
Dept. Pathology, Amsterdam UMC, Amsterdam, NL

Historically, in 1995 the evolution of the invasion concept in pulmonary adenocarcinoma was initiated with the landmark paper of Masayuki et al.[1] described two patterns of adenocarcinoma *in-situ* (AIS). In 1997 the important original description of papillary carcinoma was published by Silver and Askin[2]. Remarkably, the 1999 (and subsequent 2014 and 2022) WHO classifications copied most of the criteria, except desmoplastic stroma with arbitray invasion connected to 'papillary' carcinoma. Not surprisingly, after a sufficiently long period two studies[3,4] reported a subgroup of invasive adenocarcinomas with mixed subtype and <0.6 cm invasion and excellent prognosis (100% 5-year recurrence free survival) In the 2011 adenocarcinoma classification this subgroup was incorporated as "minimally invasive adenocarcinoma (MIA)" and in the subsequent WHO. In 2012 the *pathology committee(PC)* of IASLC reported low reproducibility for the assessment of invasion in pulmonary adenocarcinomas. In 2016 the *IASLC Staging and Prognostic Factor Committee* (SC) proposed codes for the primary tumor categories of AIS, MIA, including invasive size of non-lepidic components[5]. Further research was encouraged on "what is the best method and **reproducibility of measuring size of invasive versus lepidic components"** and "how this could be improved". In 2023 the IASLC-PC confirmed the poor reproducibility of invasion assignment. In 2023 the reason for the low reproducibility was uncovered: during iatrogenic collapse infolding of the alveolar wall occurs: the morphology of the underlying lung changes. Collapsed AIS will show pseudo-papillary and pseudo-acinar patterns, which overlap with the patterns as described by the experts of the WHO as invasive acinar and papillary adenocarcinoma. Thus, in resection specimen AIS is overdiagnosed as invasive adenocarcinoma[6]. Thus, invasion assessment according **the WHO is not trustworthy**.

Multiple Tumor Nodules

In 2016 the IASLC-SC proposed assessment of histologic type as well as within histologic type different by comprehensive histologic assessment (CHA)[7]. In those days molecular analysis has less of a value than in 2024, where DNA analysis is considered to be the gold standard. Remarkably, CHA metastases diagnosis is true 52% of the time compared to DNA analysis[8], similar to flipping a coin. CHA is not a **trustworthy** approach.

Spread through air spaces (STAS)

In the 2015 WHO classification of Lung Tumors, STAS has been described as a new form of invasion in the lung, namely “invasion through alveolar spaces”. Recently, the IASLC-SC incorporated STAS in the staging data base.

In 2022 after The Pulmonary Pathology Society meeting in Cork, Ireland a survey was held about STAS, more than 100 pathologists participated. 80% of the pathologists believed in STAS, and 100% of the responders said that the criteria should be improved. The IASLC-SC reports in 9th TNM staging on 124,581 cases, after exclusions the analysis starts with 76,518 cases of which 39,192 with pT stage. In 2024 the SC reported on STAS compared with pleural, lymphatic/vascular (LVI). Excluded were cases in which STAS was not evaluated, leaving 4061 cases, a small fraction (3-5%) with database-STAS, not excluding selection bias. Biological and pathological arguments support STAS as malignant, but not as **invasive based on expert opinion**.

In conclusion, three examples of an overrated expert approach, with lack of generalizability of WHO pulmonary adenocarcinoma classification and major consequences for the patient.

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3. Yim, J. *et al*. *Modern Pathology* **20**, 233–241 (2007).
4. Borczuk, A. C. *et al. Am J Surg Pathol* **33**, 462–9 (2009).
5. Travis, W. D. *et al*. *Journal of Thoracic Oncology* **11**, 1204–1223 (2016).
6. Filipello, F. *et al. In press*, 107987 (2024).
7. Detterbeck, F. C. *et al*. *J Thorac Oncol* **11**, 651–65 (2016).
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