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Letter to Editor: Interpretation and Application of the Likelihood Ratio to Clinical Practice in Thoracic Oncology

To the Editor:

A recent opinion piece entitled *Interpretation and application of the likelihood ratio to clinical practice in thoracic oncology* presents an incorrect description of the statistical approach used in the Nodify XL2 Proteomic Test and an erroneous view of the way the Nodify XL2 test results are used by clinicians.

Current clinical management of lung nodule patients is challenging for physicians because the available tools are insufficient. This insufficiency can lead to a misclassification of risk of malignancy and subsequently to delayed diagnosis or unnecessary procedures,[1] including invasive and painful biopsies, increased risk of complications for patients, and higher patient expenses. Because of this, we designed the Nodify XL2 test to help physicians make more informed decisions about the risk of malignancy of a lung nodule based on a simple blood draw.

The Nodify XL2 test, when used as intended, has been widely validated using multiple clinical studies. The test has been reviewed and approved by third-party statisticians and the New York State Department of Health Clinical Laboratory Evaluation Program/Wadsworth Center. Clinical studies evaluating the test have been reviewed by a centralized Institutional Review Board and local Institutional Review Boards at 30 different academic and community centers.[2]

The concept of likelihood ratios, as applied in the Nodify XL2 test, is widely used and understood. There are $>300{,}000$ publications[3] discussing the application of likelihood ratios and >8000[4] published papers that reference this same standard approach for determining likelihood ratio in conjunction with diagnostic tests. In fact, the Centre for Evidence-Based Medicine at Oxford, the industry global standards developer, advocates the use of this approach. By using a well-established likelihood ratio application and aggregate data modeling, not only does the Nodify XL2 test align more closely to the empirical data,[5] it reduces variance across the thresholds and thereby reduces patient risk as compared to the author's method. In contrast, the author's approach of a multilevel likelihood ratio increases variance, overestimates risk, and may lead physicians to recommend a more invasive procedure, all of which can lead to further complications and higher patient costs.

We continue to generate and incorporate emerging data and identify opportunities to further enhance the way physicians utilize this Nodify XL2 test. For example, a team of biostatisticians and clinical statisticians are currently analyzing results from over 1500 patients and samples from the prospective ORACLE Study and 2 major US cancer centers for continued assessment of the clinical utility and performance of the Nodify XL2 test. As the author states, we have also initiated a first-in-class,[6] prospective randomized, blinded, controlled clinical trial[7] (ALTITUDE). Interim results are anticipated in 2022.

Biodesix will continually assess and apply the data's learnings to our methodology and if necessary, make any changes needed to ensure the best possible performance of the test for patients with indeterminate pulmonary nodules.

It is important to note that Nodify XL2 results provide supplementary information to the standard of care patient risk assessment and are intended to assist physicians with decisions related to patient management. Physician recommendations, patient choice, other clinical information, and guideline recommendations are all used in combination with these test results to determine the best course of action for each patient.

Biodesix is committed to patient safety and improving health outcomes. The Nodify XL2 test, when used as intended, is a safe[8] and valuable tool, in combination with other important clinical factors, to provide supplemental information to aid physicians in treatment decision-making.

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REFERENCES

1. Tanner NT, Aggarwal J, Gould MK, et al. Management of pulmonary nodules by community pulmonologists: a multicenter observational study. *Chest*. 2015;148:1405–1414.
2. Clinical Trials (clinicaltrials.gov). Early diagnosis of pulmonary nodules

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using a plasma proteomic classifier. Identifier NCT01752114 [about 4 screens]. Bethesda, MD: National Library of Medicine (US); 2012. Available at: https://clinicaltrials.gov/ct2/show/NCT01752114?term=PANOPTIC&draw=2&rank=2. Accessed June 25, 2021.
3. PubMed.gov. Likelihood ratios. Available at: https://pubmed.ncbi.nlm.nih.gov/. Accessed June 25, 2021.
4. PubMed.gov. Likelihood ratios and diagnostics. Available at: https://pubmed.ncbi.nlm.nih.gov/. Accessed June 27, 2021.
5. Wikipedia. Brier Score; June 3, 2021. Available at: https://en.wikipedia.org/wiki/Brier_score. Accessed June 25, 2021.
6. Hariton E, Locascio JJ. Randomised controlled trials—the gold standard for effectiveness research: study design: randomised controlled trials. *BJOG*. 2018;125:1716.
7. Mazzone PJ, Sears CR, Arenberg DA. Evaluating molecular biomarkers for the early detection of lung cancer: when is a biomarker ready for clinical use? An official American Thoracic Society Policy Statement. *Am J Respir Crit Care Med*. 2017;196:e15.
8. International Organization for Standardization. Medical devices—Application of risk management to medical devices (ISO Standard No. 14971:2019). Available at: www.iso.org/standard/72704.html. Accessed June 26, 2021.

Flexible Bedside Bronchoscopy Using Closed Sheath System and COVID-19 Patients

To the Editor:

We would like to share ideas on the publication, "Flexible Bedside Bronchoscopy Using Closed Sheath System Devised from Ultrasound Probe Cover for Use in SARS-CoV-2 Patients."[1] Styrvoky et al[1] recommended the use of a new tool. There are many newly proposed tools for improving safety in endoscopy procedures. For infection control, the single-use tool is preferable, but there is still an issue on waste management.[2] It is necessary to control any tools that require washing or produce many wastes for possible spreading of the virus from contaminated surfaces. In addition, the procedure for a COVID-19 case should be performed in a well-controlled isolated place. Complex tools such as the newly proposed flexible bedside bronchoscopy might increase the chance of environmental contamination and the bedside procedure might also increase the chance of contamination in the ward. Although it is a closed system, it requires a material science study to prove that the pathogen cannot pass through the material that the tool is composed of.[2] Finally, the infection control for a bronchoscopy procedure has to start from the prebronchoscopy phase (good patient isolation) through the procedure performing period and the postprocedure period.

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REFERENCES

1. Styrvoky K, Dave S, Abu-Hijleh M. Flexible bedside bronchoscopy using closed sheath system devised from ultrasound probe cover for use in SARS-CoV-2 patients. *J Bronchol Interv Pulmonol*. 2021;28:e10–e11.
2. Wiwanitkit V. Use of a plastic banded bag over the control body of the endoscope for COVID-19 prevention: a comment. *Endoscopy*. 2020;52:1149.

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Keep it Clean

Novel Use of Sterile Disposable Flexible Bronchoscopes for Pleuroscopy

To the Editor:

Since its description in the early 20th century by Jacobaeus,[1] pleuroscopy has become an essential tool in the diagnosis and management of the pleural disease. Pleuroscopy has an important role as a minimally invasive diagnostic procedure for pleural effusions and tumor biomarker analysis as well as a therapeutic intervention through pleurodesis, adhesiolysis, and placement of indwelling tunneled pleural catheters (TPCs).[2]

Recently, a technique was described combining pleuroscopy with TPC placement using a peel-away sheath introduced through the Seldinger technique. Through this sheath, a standard flexible bronchoscope is introduced into the pleural space.[3] This technique allows for a simple procedure with a minimal incision and few equipment requirements. One noted limitation is the difficulty associated with sterilizing reprocessed bronchoscopes.[4]

We present here a report of 3 patients in which we used this previously reported method of pleuroscopy through the peel-away TPC sheath while using a disposable sterile flexible bronchoscope. This technique allows for a simpler and lower cost method for diagnostic and therapeutic pleuroscopy while minimizing infectious risk to the patient.

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