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Early View

Research Letter

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Edoardo Amante, Rocco Trisolini, Olivier Taton, Nicolas Guibert, Aurelien Brindel, Christophe Gut Gobert, Florian Guisier, Luc Thiberville, Mathieu Salaün, Samy Lachkar

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Direct endoscopic visualization of ground-glass opacities using a miniaturized videoendoscopy probe

Authors' full names: Edoardo Amante[a,b] , Rocco Trisolini[c] , Olivier Taton[d], Nicolas Guibert[e], Aurelien Brindel[e] , Christophe Gut Gobert[f], Florian Guisier[a] , Luc Thiberville[a] , Mathieu Salaün[a], Samy Lachkar[a]

Authors' affiliation(s):

[a] Normandie Univ, UNIROUEN, AIMS-QuantIF, CHU Rouen, Department of Pulmonology and Inserm CIC-CRB 1404, F-76000 Rouen, France

[b] Pulmonary Medicine Division, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Università Cattolica del Sacro Cuore, Rome, Italy

[c] Interventional Pulmonology Division, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Università Cattolica del Sacro Cuore, Rome, Italy

[d] Department of Pneumology, Hôpital Erasme, Université libre de Bruxelles (ULB), Brussels, Belgium

[e] Interventional Pulmonology Unit, Pulmonology department, Toulouse University Hospital

[f] Pulmonology Department, CHU Brest, Brest, France

Corresponding Author details:

Dr Samy Lachkar Department of Pulmonology, Thoracic Oncology, and Respiratory Intensive Care, Hôpital Charles Nicolle, CHU de Rouen, 1 rue de Germont, 76031 Rouen Cedex, France.

Email: samy.lachkar@chu-rouen.fr

The widespread use of chest computed tomography (CT), both through lung cancer screening programs and in other clinical contexts, has significantly improved the detection of pulmonary ground-glass opacities (GGOs) [1][2][3].

Although surgical resection and CT-guided biopsies provide high diagnostic yields for GGOs, they carry inherent risks [4, 5]. Bronchoscopy with radial endobronchial ultrasound (rEBUS) , while being a less invasive alternative, still shows suboptimal diagnostic yields for GGOs despite recent technological advances, , highlighting the need for novel tools. [6][7] This limitation stems from the subtle and indistinct features seen on the rEBUS probe, where slight increases in acoustic shadow intensity can be challenging to interpret[8][9].

A reusable, miniaturized videoendoscopy probe (Iriscope® probe, Lys Medical, Charleroy, Belgium) with a diameter of 1.3 mm has been recently developed, representing the thinnest videoendoscopy probe currently available [10, 11].

This retrospective multicentric study examines the use of direct endoscopic visualization with the Iriscope® in diagnosing both pure and mixed GGOs.

All consecutive patients undergoing r-EBUS and Iriscope® procedures for GGO diagnosis between May 2022 and November 2024 at Rouen University Hospital (France), Toulouse University Hospital (France), Brest University Hospital, and Bruxelles University Hospital (Belgium) were included. The study was approved by the Institutional Review Board of Rouen University Hospital (agreement number E2024-10).

As previously described, the procedure[11, 12], involved using virtual bronchoscopy software *(LungPoint®, Broncus, Medical Inc.)* to identify the pathway to the GGO and an r-EBUS probe *(1.4 mm, UM-S20-17S, Olympus)* to confirm lesion localization. r-EBUS views of GGOs were classified as "centered" (circumferent or *mixed blizzard* sign), tangential (signal adjacent to the

probe's center), or "unsuccessful" (no image)[13] . Even if r-EBUS failed to obtain an image, the probe was removed and replaced with the Iriscope® probe for direct endoscopic visualization. Two methods ensured the correct positioning of the Iriscope®: a guide sheath (GS) *(1.9 mm, K401, Olympus)*, or cone beam CT (CBCT) according to centers. Iriscope® images were recorded for further analysis.

Sampling was performed after Iriscope® removal using brushing, forceps biopsies, and/or cryobiopsies. Chest radiographs were not systematically obtained post-procedure.

GS was used in all procedures. CBCT was used exclusively at Erasme Hospital (24 cases), where it was systematically combined with the GS to confirm both the position of Iriscope® and of the sampling tool. Fluoroscopy was not used in any case.

The final diagnosis was based on cytology or histology, with benign lesions confirmed by negative biopsy and regression on follow-up CT scans, or specific microbiological findings responsive to treatment.

Based on endoscopic patterns established in previous studies, Iriscope® images were classified as malignant ("fish flesh aspect" – i.e whitish friable tissue, and/or mucosal outgrowth and/or stenosis) or benign (inflammation and/or secretions and/or normal bronchus appearance) **(Figure 1).**

A total of 63 GGOs (30 pure and 33 mixed) were analyzed. For pure GGOs, the long axis median diameter was 22.0 mm (IQR: 16.0–24.75 mm), with a median distance to pleura of 9.5 mm (IQR: 2.0–13.5 mm). For mixed GGOs, the median long axis diameter was 12.5 mm (IQR: 9.0–14.5 mm), with a median distance to pleura of 15.0 mm (IQR: 6.0–24.5 mm). The median size of the solid component was 9.0 mm (IQR: 6.0–13.0 mm). Lesions were distributed across

the right upper lobe (n=27), right lower lobe (n=8), left upper lobe (n=18), and left lower lobe (n=10).

The procedure was performed under local anesthesia in 30/63 patients. No complication was reported.

r-EBUS achieved visualization in 17/30 of pure GGOs (9 centered, 8 tangential), and 26/33 of mixed GGOs (20 centered, 6 tangential).

For pure GGOs, a final diagnosis was obtained in 29 of 30 cases via endoscopic sampling, including 21 lung cancers, 5 benign conditions and 2 B-cell lymphomas. The remaining case, diagnosed via surgical sampling, was identified as pulmonary adenocarcinoma. According to the most recent diagnostic criteria[14], the diagnostic yield of the endoscopic procedure was 83.3 %.

For mixed GGOs, a final diagnosis was obtained in 31 of 33 cases via endoscopic sampling, including 25 lung cancers and 6 inflammatory nodules (which regressed on follow-up CT scans). The remaining 2 cases diagnosed via surgical sampling were identified as pulmonary adenocarcinomas. The diagnostic yield [14] of the endoscopic procedure for mixed GGOs was 75.8%.

The Iriscope® detected a tumoral aspect in 17/30 pure GGOs (16 lung cancers, 1 B-cell lymphoma). The remaining cases with non-tumoral appearance corresponded to 7 lung cancers, 1 B-cell lymphoma, 1 inflammatory nodule, 1 case of cryptogenic organizing pneumonia (COP), 1 tuberculosis, and 2 aspergillosis. Sensitivity, Specificity, Positive Predictive Value (PPV), and Negative Predictive Value (NPV) of the Iriscope® were 68 %, 100%, 100%, and 38%, respectively. Among r-EBUS positive cases, the Iriscope® correctly predicted the final diagnosis in all 12 cases with tumoral appearances and in 3 out of 5 cases with non-tumoral

appearances. For r-EBUS-negative cases, the Iriscope® correctly identified 5 out of 5 tumor cases but only 2 out of 8 non-tumor cases **(Figure 1).** The location and diagnosis of the sixth tumoral case, which was negative on both r-EBUS and Iriscope®, was determined using CBCT.

For mixed GGOs, Iriscope® identified tumoral aspects in 19 cases, all of which were lung cancers. Non-tumoral appearances (n=14) included 8 lung cancers and 6 inflammatory nodules. Sensitivity, Specificity, Positive Predictive Value (PPV), and Negative Predictive Value (NPV) of the Iriscope® were 70 %, 100%, 100%, and 43%, respectively. Among r-EBUS positive cases, the Iriscope® correctly predicted the final diagnosis in all 15 cases with tumoral appearances and in 7 out of 11 cases with non-tumoral appearances. For r-EBUS-negative cases, Iriscope® correctly identified 4 out of 4 tumor cases but failed in all 3 non-tumor cases **(Figure 1).**

A Z-test comparison of sensitivity between pure (68%) and mixed GGOs (70%) showed no significant difference ($p = 0.79$).

We then analyzed whether Iriscope® performance differed based on the tool-in-lesion confirmation method. Among the 24 cases in which CBCT was used, Iriscope® correctly predicted the final diagnosis in 18/24 cases (Accuracy 75 %). In the 39 cases confirmed by r-EBUS and GS only, Accuracy was 28/39 (72 %). A Z-test comparison showed no statistically significant difference between the two groups ($p = 0.78$), suggesting that Iriscope® maintained comparable performance regardless of the confirmation strategy used.

This is the first study to evaluate a miniaturized videoendoscopy probe for real-time, in vivo exploration of GGOs. Iriscope® allowed direct visualization of GGOs with high specificity and PPV, providing diagnostic insights even when r-EBUS failed to provide clear images.

Indeed, Iriscope identified a tumoral aspect in 50% of cases (9/18) when the r-EBUS was negative.

This study has several limitations, including the small sample size, retrospective design, and procedural variability across centers (e.g., use of CBCT and different sampling tools). The lack of predefined inclusion criteria may also limit reproducibility. Moreover, Iriscope® allows lesion visualization but not real-time sampling.

In conclusion, Iriscope® represents a promising tool for GGO visualization, offering potential diagnostic refinement in cases where r-EBUS sampling is inconclusive. Standardized procedures and advanced imaging technologies could further improve outcomes in this challenging diagnostic field.

FIGURE 1: (A) CT scan image of a pure ground glass opacity (GGO); **(B)** No evident r-EBUS image of this pure GGO; **(C)** Tumoral aspect with 'fish flesh' appearance on Iriscope® (final diagnosis: Adenocarcinoma); **(D)** Flowchart of all GGO lesions.

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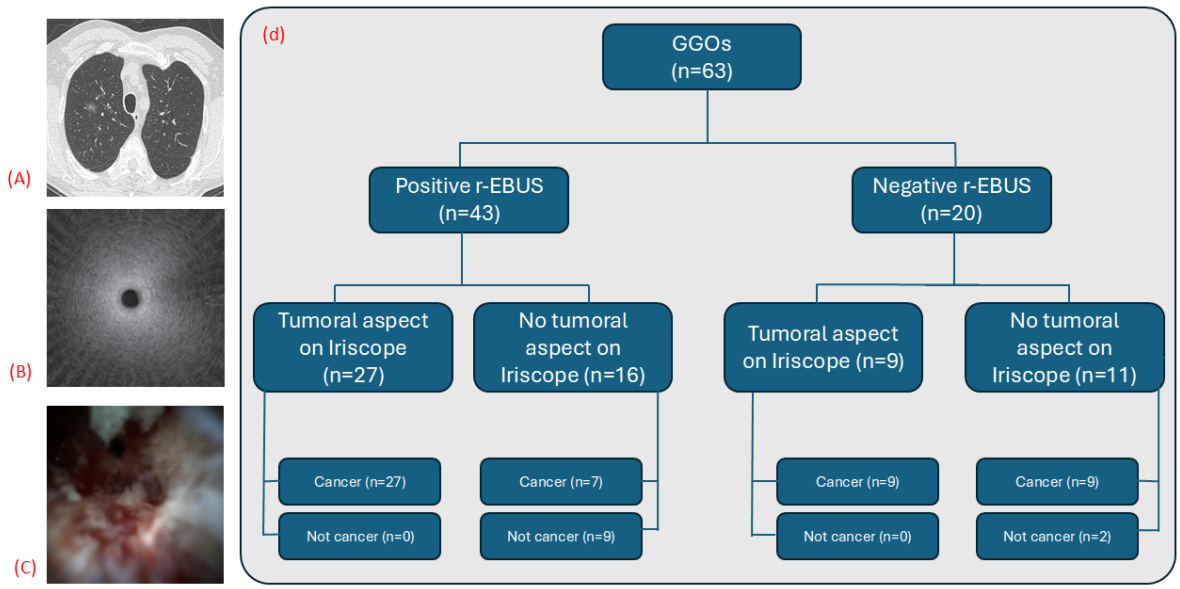

Figure 1