

Innovations in Bronchoscopy: Robotic-assisted Bronchoscopy

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Low-dose computed tomography screening for lung cancer has led to the increased detection of peripheral pulmonary nodules (PPN). Bronchoscopic modalities of PPN biopsy (ultrathin bronchoscope, radial endobronchial ultrasound, electromagnetic navigational bronchoscopy) have not consistently shown diagnostic yields as high as ultrasound- or computed tomography-guided transthoracic needle aspiration or surgical lung biopsy. Robotic-assisted bronchoscopy gained US Food and Drug Administration approval in 2018 and 2019, and preliminary data have shown an improvement in the ability to navigate to PPN, obtain a diagnosis and evaluate tissue for molecular markers, all while maintaining a safety profile similar to that of traditional bronchoscopic methods. In this article, we aim to briefly summarize the data available on this novel technology and its potential for future applications.

Keywords

Biopsy, bronchoscopy, computed tomography, lung cancer, peripheral pulmonary nodules, robotic-assisted bronchoscopy

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Lung cancer remains the leading cause of cancer-related death.¹ However, five-year survival in lung cancer varies greatly based on the stage of the disease at diagnosis.² Early lung cancer diagnosis through screening with low-dose computed tomography (CT) demonstrated a 20% reduction in lung cancer mortality in current or former smokers with a history of 30 or more pack-years.³ Tissue biopsy plays a crucial role in the diagnosis, staging and genomic evaluation of lung cancers. The detection of pulmonary nodules has increased significantly, owing to the increased use of CT and the institution of lung cancer screening programmes.⁴ The Fleischner Society guidelines are the most referenced guidelines for the management of pulmonary nodules detected incidentally on CT images.⁵ Other modalities for the risk stratification of nodules have gained traction, including the Lung Reporting and Data System assessment produced by the American College of Radiology to guide the management of nodules detected by low-dose CT screening for lung cancer, as well as calculators such as the Brock and Mayo models that take some clinical data into account.^{6,7} Estimates suggest that 1.6 million new pulmonary nodules are detected every year in the USA.⁸ Experts have identified three key steps in peripheral pulmonary nodule (PPN) sampling: (1) navigation to the lesion, (2) confirmation of the correct location and (3) acquisition of tissue. Robotic-assisted bronchoscopy (RB) is a novel tool that aspires to improve upon these aspects and thus achieve a better diagnostic yield.⁹

Over 50 years ago, the introduction of the flexible bronchoscope allowed for a minimally invasive endobronchial approach for diagnosing PPNs. While innovative, conventional bronchoscopy had a low sensitivity (14–63%) for diagnosing malignant lesions, which is even lower for those less than 20 mm in diameter.¹⁰ Radial endobronchial ultrasound (rEBUS) was introduced in the 1990s and slightly improved diagnostic yield, but navigation was still limited by the bronchoscopist, particularly in the setting of small (<2 cm) PPNs.¹¹ Electromagnetic navigational bronchoscopy (ENB) incorporated the use of a patient's CT scan for assistance with finding the lesion, but the yields of ENB alone were not a drastic improvement over rEBUS.¹² The combined use of rEBUS with ENB improved diagnostic yield to 88% compared with either technology alone.¹³ However, the interpretation of diagnostic yield across the innumerable different studies should be made with caution, as the different tools/technologies and definitions of 'diagnostic biopsy' are not standardized.¹⁴ Additionally, rEBUS, ultrathin bronchoscopy and ENB require an operator to navigate to a peripheral lesion and maintain the bronchoscope in a set position for many biopsies while accounting for motion of the breathing patient and other procedural factors that can lower diagnostic yields, such as CT-to-body divergence (CTBD) and atelectasis.¹⁵

These limitations in guided bronchoscopy led to the introduction of RB systems that allow operators to navigate through smaller airways under direct visualization.^{4,16} There are currently two RB platforms commercially available: the Monarch™ (Auris Health, Inc., Redwood City, CA, USA), which received US Food and Drug Administration approval in March 2018, and the Ion™ Endoluminal System (Intuitive Surgical, Sunnyvale, CA, USA), which received US Food and Drug Administration approval in February 2019. The key difference between these systems is their underlying technology, with the Monarch relying on electromagnetic navigation, whereas Ion

relies on fibreoptic 'shape-sensing' technology, which provides real-time feedback.¹⁷ The Monarch has a 6 mm outer sheath that can be locked in place with a 4.2 mm inner bronchoscope, while both have four-way steering control. Ion has a 3.5 mm fully articulating (180 degrees in any direction) catheter with a shape-sensing fibre and a 2.0 mm working channel. The Monarch allows for real-time visualization during a biopsy, whereas Ion requires the removal of the vision probe when placing the biopsy tools in the working channel of the scope. The scopes can be locked in position while instruments are advanced during the procedures, ensuring that the bronchoscopist remains in the target airway. There have been no head-to-head studies evaluating the performance of the different platforms.

The benefit of RB is primarily based on the ability of the robotic arm to navigate more peripherally in all airway segments compared with the conventional thin bronchoscope.¹⁸ The first safety and feasibility study of an RB system, the Robotic Endoscopy System (Auris Surgical Robotics, San Carlos, CA, USA), in humans showed great success in tissue acquisition while avoiding serious adverse events.¹⁹ The first multicentre trial in humans reported that RB is safe and feasible and should be offered to patients requiring PPN sampling.²⁰

The first comparative study across modalities in cadavers looked at the bronchoscopists' ability to navigate to the lesion and confirm tool-in-lesion positioning when using ultrathin bronchoscopy with rEBUS, ENB and RB.²¹ RB was superior for both navigation to lesions (successful navigation was achieved in 100% of RB, 85% of ENB and 65% of rEBUS) and puncture of lesions (localization and puncture were achieved in 90% of RB, 65% of ENB and 35% of rEBUS).²¹ Further multicentre prospective studies assessing the clinical safety and diagnostic accuracy of the Monarch and Ion are in the pipeline.

With the use of RB, CTBD has been found to be a significant problem in synching the patient and pre-determined plan. CTBD is the difference between the PPN location at the time of planning CT and the location at the time of the actual procedure and is mainly due to changes in lung volume.²² CTBD is being challenged with new technology, such as tomosynthesis, which allows the operator to correct for better target-lesion alignment and real-time positional correction, leading to improved diagnostic yields with minimal complications.²³

One modality for overcoming CTBD is the use of intra-procedural cone beam CT (CBCT). CBCT provides a real-time, three-dimensional image dataset that can be used to confirm tool in lesion with high confidence prior to biopsy and that has the potential to improve diagnostic yield.²⁴ This may likely be further optimized with RB, but further studies are

required to confirm whether this is the case. Image fusion of intra-procedural CBCT with live fluoroscopy (i.e. augmented fluoroscopy) in addition to ENB led to higher diagnostic yield in a preliminary study.²⁵ Augmented fluoroscopy exposes patients to acceptable doses of radiation and has the potential to be used with RB to better confirm tool in lesion and ensure diagnostic procedure.

In addition to improving diagnostic yield when sampling peripheral lung lesions, animal studies, as well as human case studies, have shown the potential of RB to perform therapeutic ablative therapies for inoperable peripheral lung lesions in the future.⁴ Several bronchoscopic ablation modalities are currently under development, with the ongoing clinical trial TARGET (Transbronchial biopsy assisted by robot guidance in the evaluation of tumors of the lung; ClinicalTrials.gov identifier: NCT04182815) and the PRECISE study (Clinical utility for Ion endoluminal system; ClinicalTrials.gov identifier: NCT03893539),^{26,27} and CBCT promises to play a prominent role in this growing field. CBCT can detect in real time the position of the ablating tools with respect to the target and provide a view of nearby anatomic structures, potentially preventing complications.²⁴

Another application of RB is a guided dye marking procedure that can successfully and safely aid in the localization of PPN during video-assisted thoracoscopic surgery, thus preventing unnecessary lobectomies.²⁸ The procedure is safe and can be performed in the operating theatre immediately prior to surgery, precluding transport and interdepartmental coordination. For inoperable or borderline surgical candidates, the placement of fiducial markers to assist in stereotactic body radiotherapy localization has proven to be feasible under ENB and will be expanded to robotic platforms.²⁹

Notable drawbacks of RB are similar to those noted at the early stages of the adoption of other robotic-assisted surgeries, such as increased unit cost compared with traditional approaches and additional training of staff to support robotic platforms.³⁰ We expect these factors to be further optimized as more experience is gained among providers and as the adoption of this technology by various medical facilities increases.

Conclusion

RB is an exciting new tool in the world of diagnostic bronchoscopy and has thus far proved very successful in navigating to PPNs and diagnosing pathology, all while maintaining an impressive safety profile. Next steps in technological development include comparing the efficacy of the two RB platforms, the Monarch and Ion, improving tool-in-lesion technology and the developing therapeutics for minimally invasive treatment at time of diagnosis. □

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