

## Precision in lung nodule biopsy: combining robotic bronchoscopy with real-time cone-beam CT scan

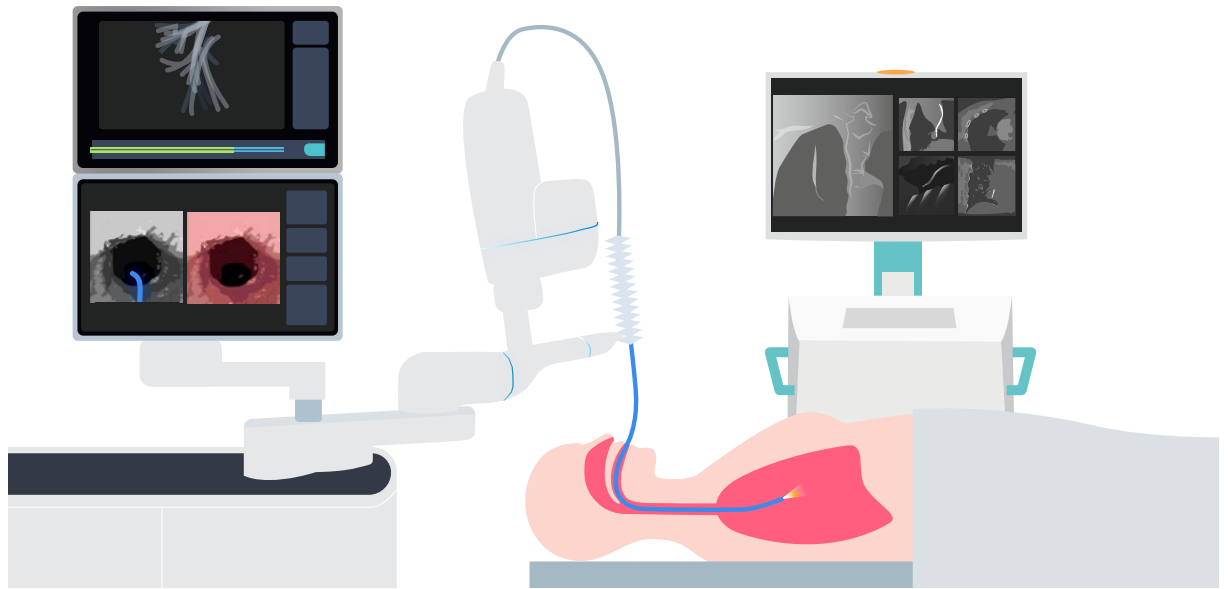
Lung cancer remains a major public health challenge both in the United States and globally. In the U.S., it is the second most commonly diagnosed cancer and the leading cause of cancer-related mortality among both men and women.<sup>1,2</sup> On a global scale, lung cancer is the most frequently diagnosed cancer and the leading cause of cancer-related deaths, accounting for approximately 1.8 million fatalities annually.<sup>3-5</sup> Modern imaging devices, such as computed tomography (CT) scanners and intraoperative cone-beam CT (CBCT) imaging devices like the Ziehm Vision RFD 3D, are important tools for the early detection of suspicious pulmonary nodules and for increasing the diagnostic yield in their biopsy.

Despite advancements in therapeutic strategies, the high mortality rate associated with lung cancer is largely due to its frequent diagnosis at advanced stages. Early-stage detection is critical, as patients diagnosed at this stage exhibit substantially higher survival rates compared to those diagnosed with late-stage disease. This underscores the importance of preventive measures and identifying lung cancer in its early stages to improve patient outcomes.<sup>1,4,6</sup>

Lung nodules, small rounded or irregularly shaped growths within the lungs, represent a common radiological finding with significant

public health implications worldwide. In the United States alone, over 1.6 million lung nodules are detected annually, predominantly via CT scans. The majority are identified incidentally, while the remainder are discovered through lung cancer screening programs.<sup>6,7</sup>

Globally, the prevalence of lung nodules varies, with studies estimating that up to 20% of adults may harbor these lesions.<sup>8</sup> The increasing identification is largely attributed to the growing adoption of lung cancer screening and the expanded use of low-dose CT scans.<sup>4,6,9</sup>



Schematic illustration of a bronchoscopy guided procedure; left: Intuitive Ion with robotic bronchoscopy; right: Intraoperative mobile 3D C-arm Ziehm Vision RFD 3D

Although the majority of lung nodules are benign, up to 6 % are found to be malignant. This underscores the critical importance of accurate diagnosis and effective management strategies to address this potentially life-threatening condition.<sup>10, 11</sup>

CT-guided transthoracic needle aspiration (TTNA) or biopsy has been the global standard of care for lung nodule evaluation due to its high diagnostic accuracy, exceeding 90 %.<sup>12</sup> However, TTNA carries a significant risk of complications, particularly pneumothorax, with an incidence exceeding 15–25 %.<sup>12–14</sup> Although traditionally less accurate, bronchoscopic biopsy offers key advantages, including being less invasive, carrying a lower complication risk – particularly a pneumothorax risk of <3 %<sup>12, 14, 15</sup> – and enabling concurrent mediastinal staging via endobronchial ultrasound.<sup>14, 16, 17</sup>

Over the past decade, peripheral bronchoscopy has experienced significant advancements. The introduction of electromagnetic navigation bronchoscopy, which utilizes real-time tracking of the bronchoscope's position within the lung, marked a pivotal milestone in its evolution.<sup>14–16</sup> More recently, the advent of robotic bronchoscopy has further improved navigation, maneuverability, and stability within the bronchial tree, enabling more precise targeting of peripheral lung nodules.<sup>16, 17</sup>

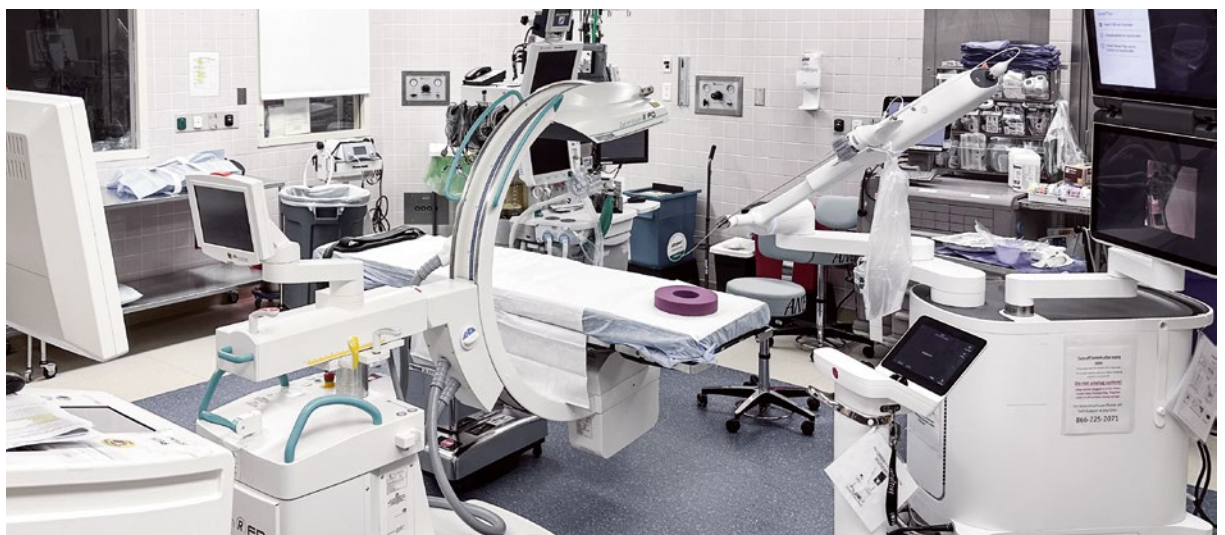
Robotic bronchoscopy offers enhanced control and stability compared to manual techniques, minimizing operator fatigue and improving tool precision. These advancements enable deeper access into the lung periphery, surpassing traditional bronchoscopes by up to three airway generations. The superior maneuverability and control contribute to more accurate biopsies, potentially leading to higher diagnostic yields and improved clinical outcomes.<sup>16–19</sup>

Robotic bronchoscopy currently achieves a diagnostic yield marginally lower than CT-guided transthoracic needle aspiration (TTNA); however, advancements in technology and techniques are poised to bridge this gap.<sup>12,17-21</sup> Notably, a study by Lee-Mateus et al. demonstrated that robotic bronchoscopy can match TTNA in accuracy for sampling pulmonary nodules.<sup>22</sup> Furthermore, robotic bronchoscopy offers a significantly lower complication rate, with pneumothorax occurring in <3 % of cases and bleeding in <1 %.<sup>20,21</sup> It also facilitates mediastinal lymph node staging during the same procedure, providing a comprehensive lung cancer assessment while minimizing patient discomfort and reducing healthcare costs.<sup>16-19,22</sup> Continued research and technological innovation may establish robotic bronchoscopy as the new standard of care for diagnosing peripheral lung nodules.

The integration of intraoperative real-time imaging modalities, such as cone-beam CT, significantly enhances the accuracy of robotic bronchoscopy. This is particularly critical as lesions detected through the expanded use of diagnostic CT scans are increasingly small,

often sub-centimeter in size. Without intraoperative cone-beam CT, reliably locating these small lesions would be challenging, increasing the risk of false-negative biopsy results.<sup>16,23-27</sup> The use of such advanced imaging techniques is therefore pivotal in improving diagnostic precision and ensuring more accurate outcomes in lung nodule evaluation.

A significant challenge in bronchoscopic biopsies is the discrepancy between the static location of a nodule on pre-procedure CT imaging and its actual position within the dynamic lung environment during the procedure, a phenomenon known as CT-to-body divergence. This divergence arises from factors such as lung volume changes, patient positioning, anesthesia-induced atelectasis, and respiratory motion. Cone-beam CT addresses this issue by providing real-time imaging, enabling precise confirmation of the biopsy tool's position relative to the lesion. This facilitates accurate adjustments and tool-in-lesion confirmation, reducing false negatives and enhancing biopsy accuracy.<sup>17,23-27</sup>



## Benefits of Ziehm Vision RFD 3D

With the 3D C-arm Ziehm Vision RFD 3D, a 3D C-arm is utilized, capable of performing a 3D scan in less than 3 minutes from setup to Multiplanar Reconstruction (MPR) creation. Several body size options (Pediatric/Low Dose, Adult, and Large) can be selected, impacting the radiation dose used. The CTDI values for the body region 'Spine' are 7.8 mGy for 'Adult' and 23.7 mGy for 'Large Patient', both below comparable C-arms. The variable isocenter (patented SmartScan technology) allows centering lesions in the lung's outer range, avoiding table collisions seen with isocentric C-arms. The Complementary Metal Oxide Semiconductor (CMOS) flat-panel Detector, with a pixel size of 100 µm, offers higher sensitivity, enabling the same image quality to be achieved with a lower radiation dose. With a 3D volume of 19.8 cm x 19.6 cm x 18 cm and a resolution of 512<sup>3</sup> voxels, every detail is captured. The metal artifact reduction technology (Ziehm Iterative Reconstruction ZIR) enables clear visualization of suspect tissue and precise localization of the biopsy tools within it. The compact 0.8 m<sup>2</sup> footprint ensures it fits seamlessly into any operation setting.

## Workflow for robotic bronchoscopy with intra-procedural cone-beam CT assistance

### Preprocedural planning

Preprocedural planning is typically conducted several days before the procedure. A high-resolution chest CT scan with thin slices (<2 mm) is uploaded to the PlanPoint software provided by Intuitive. After identifying the nodule of interest on the software-generated 3D airway tree, the software automatically creates a navigational path and anatomical borders. Operators

can review, edit, and finalize the plan according to their preferences, ensuring optimal guidance during the procedure. The software also generates a virtual bronchoscopy pathway, offering an endobronchial view leading to the nodule. Once finalized, the plan is saved on a thumb drive for use on the procedure day.

### Step 1 – Anesthesia and patient positioning

On the day of the procedure, the patient is positioned supine on a fluoroscopy-compatible operating bed. General anesthesia with a non-depolarizing neuromuscular blockade is administered, followed by endotracheal intubation. The patient is ventilated using a high-volume, high-PEEP, low-FiO<sub>2</sub> protocol to prevent atelectasis.

### Step 2 – Setting up Ziehm Imaging cone-beam CT

The patient's ventilation and associated tubing are adjusted to facilitate the rotation of the Ziehm Vision RFD 3D C-arm. The 3D fluoroscopy unit is positioned over the patient, with adjustments made to center the nodule in the anteroposterior view. A collision check is performed to ensure safe rotation of the C-arm without interference. As the C-arm reaches 90°, the operating table height is adjusted to align the nodule centrally in the lateral view, verified via fluoroscopy. The collision check is then successfully completed.

### Step 3 – Docking Ion robotic bronchoscopy

After completing the collision check, the robotic arm of the Ion robotic bronchoscopy system is attached to the proprietary swivel adapter on the endotracheal tube at the patient's head, ensuring it remains clear of the C-arm during the 3D fluoroscopy scan.

#### Step 4 – Navigation with robotic bronchoscope

After docking the robotic arm, the robotic bronchoscope is advanced into the patient's airways using a proprietary controller. The bronchoscope, with a 3.5mm outer diameter and a 2.0mm working channel, can articulate 180°, enabling access deep into the lung periphery and all 18 segments. It is equipped with shape-sensing technology, providing real-time, precise location, shape information and stability during navigation and biopsy.

Additionally, Ion's vision probe, inserted into the catheter's working channel, offers a 120° real-time airway view to guide navigation to the target. Initially, the catheter is driven through all lobar airways to complete registration, which synchronizes the virtual and live camera views by orienting the bronchoscope to the patient's airways.

Once registration is completed, the operator follows the pre-planned path to the target nodule. Upon reaching the virtual nodule, the catheter is positioned in front of the virtual center. The vision probe is then removed, and a radial endobronchial ultrasound (EBUS) is introduced into the working channel. Under live fluoroscopy, the radial EBUS is advanced toward the nodule. If a signal indicating the nodule is detected, a 21-gauge needle is inserted to the corresponding depth under fluoroscopic guidance, followed by a 3D scan using the Ziehm Vision RFD 3D.

If the radial EBUS does not detect a nodule signal, it is positioned based on the estimated virtual nodule distance, and a CBCT scan is performed to guide further adjustments.

#### Step 5 – CBCT scan and tool-in-lesion confirmation

After advancing the tool into the lung and aligning it with the virtual nodule, real-time imaging is performed to confirm tool-in-lesion placement, addressing CT-to-body divergence. Prior to the CBCT scan, the radiology technician repeats the collision check. Once confirmed, the patient is placed in an end-inspiratory breath hold for 40 seconds, during which the CBCT scan is performed. Ventilation resumes afterward.

The operator reviews the CBCT images on the Ziehm monitor cart to determine if the tool is positioned within the lesion. If confirmed, a biopsy can proceed.

If the tool is not within the lesion, the CBCT images are analyzed to identify the necessary adjustments to the robotic catheter. The Ion system's endoluminal compass aids in precise directional modifications. For instance, if the CBCT indicates that moving the tool superiorly aligns it with the lesion, the catheter can be adjusted solely in that direction using endoluminal compass. Once the correct position is achieved, a subsequent radial EBUS and/or CBCT scan is performed to reconfirm tool-in-lesion placement.

#### Step 6 – Biopsy of the lesion

If the tool is inside the lesion and is a needle, needle aspiration can be performed under 2D fluoroscopy guidance. If the tool is radial EBUS, a needle is advanced to the same location as the radial EBUS under 2D fluoroscopy guidance, and a biopsy is performed. In addition to needle aspiration, transbronchial biopsies can be performed using forceps or a 1.1 cryoprobe. Bronchoalveolar lavage can also be performed if infection is considered in the differential diagnosis.

### Example case

A 63-year-old woman with a history of hyperlipidemia and left amblyopia was referred from the outpatient ophthalmology clinic to the emergency room with concerns of left central retinal arterial obstruction and a need for stroke evaluation. Stroke was ruled out, but CT neck imaging incidentally revealed a pulmonary nodule. Dedicated CT chest imaging confirmed a 1.7 cm part-solid nodule with an 8 mm solid component in the right upper lobe, concerning for an adenocarcinoma spectrum lesion (Figure 1). The decision was made to pursue robotic bronchoscopy-guided biopsy of the right upper lobe lesion, along with mediastinal staging via endobronchial ultrasound under a single anesthesia.

On the day of the procedure, the patient was intubated with an 8.5 mm endotracheal tube under total intravenous anesthesia and non-depolarizing neuromuscular blockade, with a high-volume, high-PEEP ventilation protocol. The fluoroscopy and operating room table were adjusted to center the right upper lobe nodule in both the anteroposterior and lateral fluoroscopic views. After the Ziehm Vision RFD 3D collision check was completed, the Ion robotic arm and catheter were docked to the endotracheal tube. The robotic catheter was then navigated to the right upper lobe nodule along the pre-planned navigation pathway.

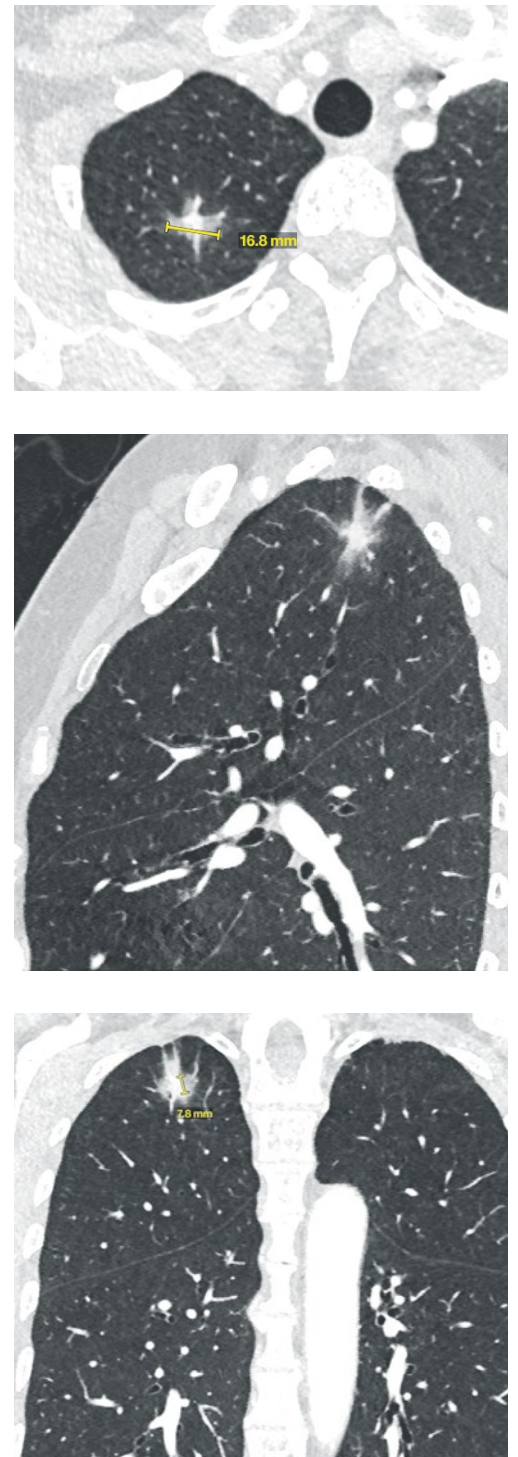


Figure 1: Diagnostic CT

Upon reaching the virtual nodule, a biopsy tool was advanced into the lesion. Under peak inspiratory breath hold, a 3D CBCT scan was performed. The CBCT images showed that the needle tip was lateral and anterior to the lesion (Figure 2). Using the endoluminal compass, the robotic catheter was adjusted medially and posteriorly. A 21-gauge needle was then advanced to the expected location of the nodule, and a repeat 3D CBCT scan was performed during an

end-inspiratory breath hold. The repeat scan confirmed the needle's position within the lesion in axial, coronal, and sagittal views (Figure 3). Multiple transbronchial needle aspirations and forceps biopsies were performed at the same location in the lung parenchyma. Additionally, endobronchial ultrasound-guided transbronchial needle aspiration of the right hilar lymph node was performed for staging.

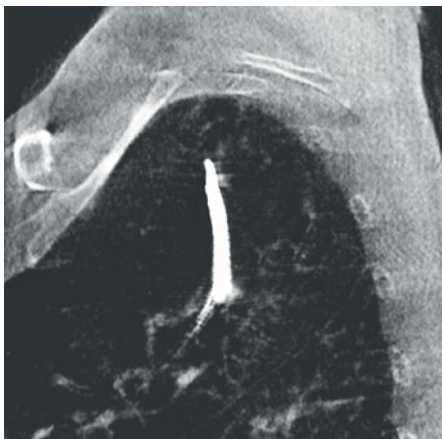
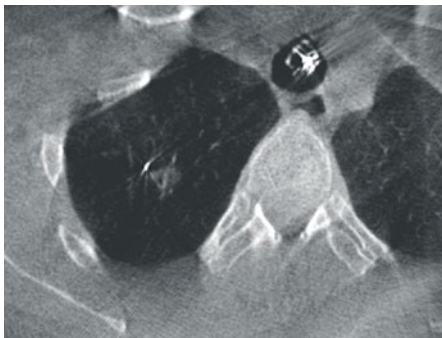


Figure 2: Initial CBCT scan for tool-in-lesion-confirmation (TILC) using Ziehm Vision RFD 3D. TILC not confirmed.

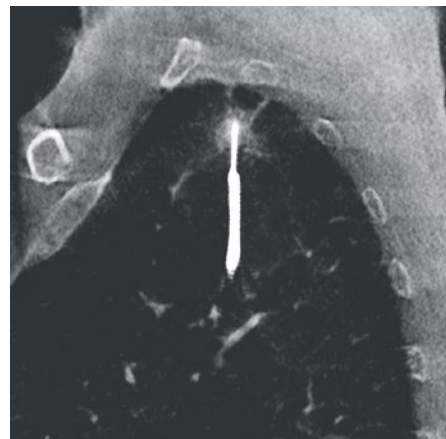
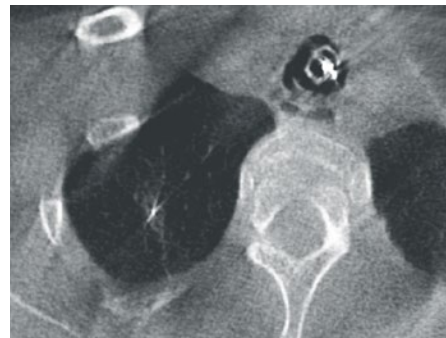


Figure 3: Second CBCT scan for TILC after successful repositioning of the needle. TILC confirmed.

The patient was discharged from the hospital and underwent PET/CT staging workup as an outpatient. She was diagnosed with stage 1A2 adenocarcinoma of the lung and underwent robotic-assisted right upper lobe wedge resection within four weeks of the discovery of the lung nodule.

In conclusion, the integration of robotic bronchoscopy with real-time cone-beam CT as provided by the Ziehm Vision RFD 3D C-arm has revolutionized the diagnosis and management of lung nodules. This technique allows for precise navigation to peripheral lesions, reduces complication rates, enables concurrent mediastinal staging, and offers a strong alternative to conventional methods like transthoracic biopsy. As technology continues to evolve, it is poised to become the standard of care, improving diagnostic yields, reducing patient discomfort, and providing a more comprehensive assessment of lung cancer, ultimately leading to better patient outcomes.

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