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REVIEW ARTICLE

Fiberoptic Bronchoscopy and Management of Lung Cancer

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Abstract

Lung cancer has the greatest mortality rates among both men and women and is the primary cause of cancer-related fatalities globally. Roughly 85% of occurrences of lung cancer are caused by smoking, making it the primary cause of the disease. Lung lesion analysis and, in the event that cancer is proven, therapy are becoming more and more necessary due to the rising usage of chest CT scans and lung cancer screening programs. The one-stop outpatient bronchoscopic technique, which includes tumor navigation, confirmation of malignancy, and prompt treatment, is a desirable future concept. A number of innovative ideas for bronchoscopic diagnosis and treatment are presently being considered in order to add to this idea. Better bronchoscopic navigation to the target lesion is crucial since most suspected malignant lung lesions originate in the lung's periphery. Thankfully, sophisticated bronchoscopic navigation techniques are becoming clinically available, and the discipline of interventional pulmonology is fast developing, allowing for an increasingly accurate tissue diagnosis of lung abnormalities. Furthermore, a number of bronchoscopic therapy techniques are presently being researched.
Keywords: Fiberoptic Bronchoscopy, Lung, Cancer.

INTRODUCTION:

It's critical to discover lung nodules early in order to diagnose treatable lung cancer **[1].** The effectiveness of low-dose computed tomography (CT) scans in promoting early diagnosis and lowering mortality from malignant tumors was shown by the National Lung Screening Trial. According to this experiment, 39.1% of participants in the low-dose CT screening group saw at least one favorable outcome **[2].**

The Nader Lands Leuvens Loker Skrecrinqs Ondarzoek (NELSON) trial and the National Lung Screening Trial estimate that peripheral pulmonary lesions (PPLs) accounted for almost 80% of these lesions. The need for tissue diagnosis has become more essential due to the rise in incidental lung nodule discoveries **[3].**

According to a prior study, transthoracic biopsy for malignant lesions has a 25% complication rate, 100% specificity, and 93% sensitivity; 24% of complications were pneumothorax **[4].** When diagnosing malignant lesions, conventional bronchoscopy is less sensitive and less effective for lesions smaller than 20 mm in diameter. While CT-guided transthoracic needle biopsy (TTNB) is a more effective method for diagnosing peripheral pulmonary lesions than conventional bronchoscopy, it carries a substantially lower risk of complications **[5].**

As a result, numerous cutting-edge technical modalities have been developed, enabling pulmonologists to safely and effectively access the lung's perimeter. These methods include fluoroscopy, radial probe endobronchial ultrasound (RP-EBUS), thin/ultrathin bronchoscopes, and navigation bronchoscopy, which includes electromagnetic and virtual navigation bronchoscopy (ENB) and VNB. In order to facilitate navigation to PPLs, more recent technologies have been used, such as augmented fluoroscopy (AF), cone-beam CT (CBCT), and robotic-assisted bronchoscopy (RAB) **[5].**

Bronchoscopy and Lung Tissue Biopsy:

A bronchoscopy is an endoscopic technique in which an optical instrument is inserted into the airways to visualize the tracheobronchial tree. In order to remove a foreign body from the airway, Gustav Killian conducted the first bronchoscopy in 1897 using a rigid bronchoscope**[6].**

In the early 1970s, Shikedo İkeda invented flexible bronchoscopy (FB), which gained its flexibility by being applicable through the nasal or oral passages **[7].** While it is debatable, sedation can help make patients more comfortable during bronchoscopies. It is possible to inject sedative medications intravenously, including morphine sulfate, fentanyl, midazolam, lorazepam, and diazepam. In order to avoid coughing, lidocaine at a dosage of 1% or 2% is typically applied topically to the airways. For the safety of the process, enough hemodynamic stability and oxygenation supply must be supplied during FB **[8].**

With each passing day, advancements in interventional pulmonology technology are starting to take the position of diagnostic thoracic surgery. The diagnostic and therapeutic use of bronchoscopy has increased, necessitating that clinicians understand the current state of technology and its related clinical applications. In order to maximize the diagnostic or therapeutic benefits of bronchoscopy, the appropriate technique should be selected prior to the procedure **[9].**

The introduction of fluorescence bronchoscopy removed this restriction. Though early invasive and in situ tumors may be localized with this approach, dysplasia detection remained a challenge. Furthermore, issues with tissue autofluorescence interference and sensitization hindered the development of photodynamic diagnostic systems. To get around this, a novel laser photodynamic diagnostic method that uses tumor-specific medication fluorescence at 630 nm wavelength was created. The usual endogenous fluorescence of the tissues, which spans 500–580 nm, is well separated from this wavelength. The development of the LIFE-lung Fluorescence Endoscopy was based on the idea that malignant and dysplastic tissues exhibit lower autofluorescence signals than normal tissues. This was achieved by utilizing a superior charge-coupled device and a novel algorithm **[10]**.

Lung Tissue Biopsies:

It involves making a tiny incision and using a needle to remove a lump or nodule in its entirety. This is employed in the diagnosis of specific diseases of the stomach, colon, lungs, and other organs. It is an extremely intrusive procedure that results in low patient compliance. Figure (1) illustrates the many types of biopsies that have been performed. Needle biopsy is the most often utilized biopsy method for LC detection. Lung nodules can be biopsyed transthoracicly to check for cancer. The size of the nodule (2 cm or more) determines the diagnostic method. It is employed to identify the tumor located in the lung parenchyma, mediastinum, or pleura. According to a study, 82.7% of malignant tumors, 80% of lung nodules, 90% of mediastinal lesions, and 83% of pleural masses could be diagnosed using CT guidance **[11]**.

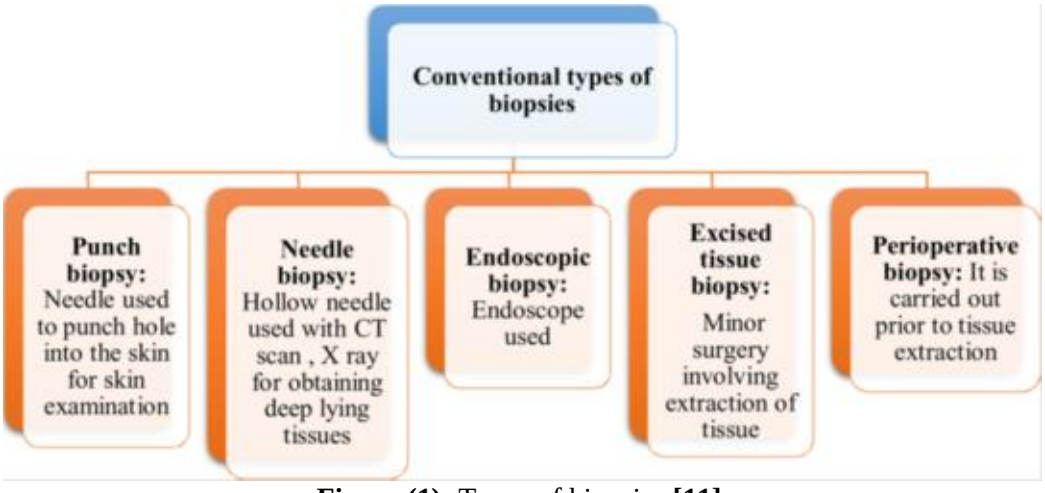

Figure (1): Types of biopsies **[11]**.

Basic flexible bronchoscopy:

Therapeutic and diagnostic indications for flexible bronchoscopy can be broadly separated into two categories (Table 1). Visual examination of the upper and "central" lower respiratory tracts is possible with flexible bronchoscopy. One important

role of flexible bronchoscopy should not be overlooked: inspection of the larynx and nasal passageways. Vocal cord polyps, nasal polyps, and nasal crusting are important diagnostic indicators for correctly identifying respiratory diseases **[12].**

Flexible bronchoscopy enables direct visibility from the subglottis to the fourth or fifth order bronchi within the lower respiratory system. Many illnesses can be identified by it, such as endobronchial tumors, subglottic stenosis, and endobronchial sarcoidosis, which is commonly referred to as a "cobblestone mucosa." Thus, the diagnosis of primary lung cancer is a basic skill of flexible bronchoscopy, which is mostly used to detect endobronchial abnormalities inside accessible large to medium-sized airways **[13].**

A biopsy, bronchial brush, or bronchial wash can be used to obtain a sample of any endobronchial abnormality seen during a bronchoscopy under direct view. Peripherally situated nodules or masses, extrabronchial abnormalities, and the peripheral lung parenchyma cannot be seen or examined with it. Nevertheless, broncho-alveolar lavage and transbronchial lung biopsy are two methods for easier peripheral lung sampling that basic flexible bronchoscopy can help with. These approaches are very helpful for certain indications and diseases (Table 2) **[13]**.

Basic flexible bronchoscopy is a safe procedure, performed under conscious sedation and usually as a day case, with a very low complication rate. The British Thoracic Society has produced detailed guidelines on the use of basic flexible bronchoscopy that serve as an excellent reference document for further reading **[14].**

Table (1): Indications for flexible bronchoscopy **[12]**

Diagnostic
Evaluation of symptoms:
Persistent cough
Unexplained breathlessness
Haemoptysis
Stridor
Hoarseness
Evaluation of clinical findings:
Suspected malignancy
Suspected bronchial obstruction e recurrent pneumonia, persistent atelectasis
Pneumonia of unknown aetiology, non-responding pneumonia
Suspected tuberculosis
Hilar/mediastinal lymphadenopathy
Suspected bronchopleural fistula
Excessive dynamic airway collapse
Suspected lung transplant rejection or infection
Therapeutic
Mucus impaction
Foreign body removal
Blood clot removal
Endotracheal intubation in patients with difficult airway
Tumour ablation e cryotherapy, laser, argon plasma coagulation
Balloon dilatation
Airway stenting
Airway valves in persistent air leak
Bronchoscopic lung volume reduction with valves, coils, thermal vapour ablation
Bronchial thermoplasty

Table (2): Description of the two available techniques for sampling the peripheral lung during basic flexible bronchoscopy **[12]**

	Broncho-alveolar lavage	Transbronchial lung biops
Technique	• Instillation of sodium chloride 120-240ml with the bronchoscope wedged in a distal bronchus and suctioning fluid back	Passing the biopsy forceps beyond the maximal reach and vision of the scope and performing a biopsy at the point of resistance
Tests available	• Microscopy and culture Polymerase chain reaction Differential cell count • Cytology	Histology
Conditions with a good diagnostic yield	• Atypical infection,e.g Pneumocystis jirove cli pneumonia • Eosinophilic pneumonia2% eosinophils abnormal • Interstitial lung disease– lymphocytosis in non–specific interstitial pneumonia and hypersensitivity pneumonitis 20% lymphocytes- abnormal • Sarcoidosis-lymphoocytosis • Adenocarcinoma presenting as consolidation-previously known as broncho-alveolar cell carcinoma	Lymphangitis carcinomatosis Sarcoidosis Cryptogenic organizing pneumonia Eosinophilic pneumona
Complications	• Transient hypoxia • Fever	Pneumothorax(approximately1%) Higher risk of major bleeding than endobronchial biopsy Can be perf
Additional comments		Can be performed under fluoroscopic guidance for focal lesion and cryobiopsy for interstitial lung disease

Conventional transbronchial needle aspiration (cTBNA):

The procedure known as TBNA involves inserting a needle into the surrounding tissue through the tracheal or bronchial wall. This can be utilized to take a sample from a peribronchial mass or nearby lymph node. When endobronchial markers are used to guide the sampling site during computed tomography (CT) to confirm the presence of an extrabronchial abnormality, cTBNA with a Wang needle is frequently referred to as "blind" TBNA. cTBNA is an inexpensive, safe procedure with a 0.3% major complication rate **[15].**

This method can be used to sample the lymph nodes in the hilar, subcarinal, and paratracheal regions. Additionally, it can be utilized to collect necrotic and submucosal masses, for which endobronchial biopsies would not be diagnostically useful. on skilled hands, this technique's diagnostic yield for lymph node sample is about 75%; nevertheless, its application is limited to lymph nodes that are noticeably enlarged, typically measuring more than 2 cm on the short axis **[16].**

Advanced flexible bronchoscopy:

Endobronchial ultrasound-transbronchial needle aspiration (EBUS-TBNA)

A convex-shaped ultrasonic transducer at the bronchoscope's tip is integrated with the Convex Probe Endobronchial Ultrasound System (CP-EBUS). By pressing the bronchoscope's end up against the airway wall or by pumping saline solution into the balloon, the doctor may see the walls of the airways and the structures around them. The needle's passage through the lesion of interest and the bronchial wall can be seen in real time. Using a needle aspiration, the doctor diagnoses the

pathology by using the tissue. Blood vessels can be avoided by using the ultrasound-equipped power Doppler mode **[17].**

When a patient exhibits positron emission tomography uptake or lymph node enlargement indicative of mediastinal lymph node involvement, EBUS-TBNA is the preferred main diagnostic method above surgical staging. Positive predictive value (NPV), specificity, sensitivity, and specificity were 89%, 100%, 100%, and 91%, respectively, for the entire sample. The pooled median sensitivity, specificity, PPV, and NPV when combined with endoscopic ultrasonography (EUS)-needle aspiration were 91%, 100%, 100%, and 96%, respectively **[18].**

When EBUS-TBNA was used in conjunction with EUS with bronchoscope-guided fine needle aspiration (EUS-B-FNA) to sample lesions that were inaccessible or when bronchoscopy was challenging because of coughing or dyspnea, it yielded significant diagnostic benefits **[19].**

Compared to bronchoscopy or CT-guided core biopsy, EBUS-TBNA yielded a greater amount of RNA extraction, and the feasibility of molecular profiling utilizing samples produced from this procedure was found to be acceptable **[20].** Rebiopsy by EBUS-TBNA was also a good sampling approach for the investigation of acquired resistance to epidermal growth factor receptor-tyrosine kinase inhibitor **[21].** For mediastinal staging in patients with suspected lung cancer, at least three needle aspirations per lymph node station are advised in the absence of prompt on-site examination **[22].**

Most central lung tumors can be diagnosed by FB; however, certain central tumors are not easily detected since they are not noticed by FB. When a central tumor is in contact with the bronchus and cannot be accessed by FB, CP-EBUS-TBNA can be used to perform a direct tissue inspection **[23].**

In EBUS-TBNA, complications were rare, ranging from 1% to 5%. Serious side effects have sporadically been documented, including sepsis, pericarditis, mediastinal abscess, mediastinitis, and bronchogenic cyst infection **[24].**

Endobronchial ultrasound and a guide sheath:

Physicians can perform a biopsy and identify peripheral pulmonary lesions with radial probe endobrochial ultrasound (RP-EBUS). Following the search of peripheral pulmonary lesions using an RP-EBUS inside guide sheath (GS), the RP is removed, leaving the GS in situ. Following the introduction of bronchial brush and biopsy forceps into the GS, brushings and biopsy specimens are gathered **[25].**

Based on the internal anatomy of the lesion, three groups of lesions were identified by RP-EBUS: type I (homogeneous pattern), type II (hyperechoic dots and linear arcs pattern), and type III (heterogeneous pattern). The information obtained from endobronchial ultrasonography indicates the lung lesions' histology **[25].**

After the fifth biopsy specimen was obtained, the total diagnostic yield plateaued. Thus, in order to improve the diagnostic yield, a minimum of five biopsy specimens are required **[26].**

Autofluorescence bronchoscopy (AFB):

The bronchoscopist has an extra way to examine the bronchial tree with this technique. It is based on the idea that when a particular wavelength of light is applied to aberrant and normal tissue, there would be a differential fluorescence emission. White light is used by a typical bronchoscope to illuminate and examine the bronchial tree (white light bronchoscopy) **[27].**

The bronchial tree in AFB receives blue light illumination, which causes normal mucosa to glow strongly green. The vascularity and thickness of abnormal tissue are enhanced, preventing blue light from penetrating and changing the fluorescence from green to magenta. AFB makes aberrant tissue apparent that would be invisible under a typical white light inspection, enabling focused biopsies to be carried out. This can help identify pre-invasive diseases like carcinoma-in-situ and pre-neoplastic conditions like metaplasia and dysplasia **[28].**

Management of malignant endobronchial disease:

Malignant endobronchial disease can also be treated with specialized bronchoscopic procedures. For the treatment of lung cancer, they can be used either alone or in conjunction with other therapies such external beam radiation **[29].**

The primary goals of treatment are symptom relief and airway maintenance; but, in certain circumstances, such as the management of radiologically occult but endobronchially evident tumors, treatment may be curative (Tx N0 M0) **[30].**

Photodynamic therapy (PDT) and high-dose brachytherapy

These biological treatments kill tumor cells one by one. Porphyrin is an intravenous sensitizer used in PDT that is taken up specifically by tumor cells. A hazardous reaction takes place in the sensitizer-containing cells upon exposure to a certain light wavelength, leading to instantaneous cell death. A

probe is used to provide this light, which is then positioned next to the tumor and seen through the bronchoscope. **[31].**

The surrounding tissue is not severely harmed by the sensitizer since it is only selectively absorbed by the tumor cells. The patient needs to avoid sunlight exposure for six weeks following PDT because the skin and cornea absorb the sensitizer as well. Blockage is a possible consequence due to the bronchial lumen airway's fast cell death and debris sloughing **[32].**

Intraluminal radiotherapy is administered to endobronchial lesions with high-dose brachytherapy. When a tumor cell tries to undergo mitosis, the radiation destroys the DNA inside the cell, resulting in cell death. Because tumor cells divide quickly, radiation therapy affects them more deeply than it does the surrounding normal tissue **[33].**

In brachytherapy, an iridium radioactive source is positioned very next to an endobronchial tumor. The 2 centimeter radius surrounding the radioactive source is the only area that receives radiation. The tumor is found using a flexible bronchoscope, and an applicator with surface markings per centimeter is positioned with the tip distal to the tumor **[34].**

After securing the applicator and removing the bronchoscope, a chest radiograph (CXR) is taken. The required field of treatment is identified using the CXR (the applicator and its graded markings are easily visible on CXR) and the applicator's graded markings. Following that, the applicator is fastened to a "safe" e a protective device that contains the radioactive source **[35].**

For the duration of the programmed duration, this machine feeds the radioactive source through the applicator to the targeted places. Since this procedure is entirely automated, every member of the medical team may stay safe and away from the radioactive source. Very uncommon side effects include bleeding, persistent radiation bronchitis, and the strictures that follow **[36].**

Electrocautery and cryotherapy

Typically, these methods are employed as debulking tactics. The application of heat generated by an electrical current during electrocautery can result in vaporization, cutting, or coagulation depending on the power setting. While a probe can be used to coagulate the surface of a lesion with a wider base, a snare can be used to cut through the base and remove polypoid lesions **[37].**

A similar method of non-contact coagulation that penetrates a tumor to a depth of two to three millimeters is argon plasma coagulation. Rare side effects include stricture formation, airway fire, and perforation of the airway **[38].**

Extreme cold is used in cryotherapy to kill tumor cells. Cell death results from a quick cooling to -70 C followed by a gradual thaw. There is minimal chance of perforation because cooling has no effect on collagen or cartilage. Since there is early tissue swelling, near-total obstruction is not treated with this approach. Nonetheless, malignant endobronchial blockage can be rapidly and efficiently debulked using a modified form of cryo-recanalization **[39].**

This entails using the cryoprobe to freeze the endobronchial tumor and then removing it while the tissue is still adhered to the probe, without thawing. However, to address any potential issues like hemorrhage, the airway must be securely sealed **[40].**

Tracheobronchial stenting:

Using a flexible bronchoscope to implant a stent can quickly restore impaired lung function brought on by malignant blockage and effectively safeguard an airway prior to tumor-reducing therapy **[30].**

Patients with viable distal airways and lung tissue with central airway obstruction (i.e., in the right main bronchus, bronchus intermedius, or left main bronchus) must be carefully chosen. Tracheo-oesophageal fistulae and tracheal blockage respond well to this treatment method as well. Stent fracture, granulation tissue, migration, and tumor growth are among the complications **[41]. Declaration of interest**

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