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Advancements in Intra-Nodal Forceps Biopsy: A Two-Decade Review of Techniques, Yield, and Future Directions

Kothwala Dr. Deveshkumar Mahendralal[1], Pathak Vipulkumar[2], Bhandari Ami Nejas[3], Kapadia Mahima Pragneshkumar[4]
Meril Medical Innovations Private Limited, Bilakhia House, Survey No.879, Muktanand Marg, Chala, Vapi, Dist.-Valsad, Gujarat, 396191

Abstract: ***Testing for granulomatous diseases, lymph proliferative disorders, and thoracic cancers requires precise sample of the mediastainal and Hilar lymph nodes. Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) has long been the accepted minimally invasive procedure; nevertheless, in diseases like lymphoma that need maintained tissue architecture, its reliance on cytological sample reduces the accuracy of the diagnosis. Intra-nodal forceps biopsy (IFB), which allows for the acquisition of histopathological core tissue through a transbronchial tract made under EBUS guidance, has become a useful complement or substitute for TBNA throughout the past 20 years.***

This review aims to synthesize two decades of clinical and technological advancements in IFB, evaluating its diagnostic performance, safety, and integration into current thoracic diagnostic algorithms. A systematic literature review was conducted using four major databases, identifying relevant studies from 2003 to 2024. The results show that IFB has a low complication rate (<1.5%) and a better diagnostic yield (85-90%) and sample adequacy (90-96%) than TBNA. Notwithstanding its efficacy, its broad adoption is hampered by drawbacks such operator dependence, procedural complexity, equipment variability regulations.

Future developments include sensor-integrated forceps for increased precision, robotic bronchoscopy, and AI-assisted targeting. IFB is also anticipated to play a bigger position in technologies. IFB is positioned to develop into a primary diagnostic tool for the assessment of Lymphadenopathy as training programs and regulatory frameworks change. This review underscores IFB's clinical relevance and potential to reshape the landscape of minimally invasive pulmonary diagnostics.

Keywords: Intra-nodal forceps biopsy (IFB), Endobronchial ultrasound (EBUS), Mediastainal Lymphadenopathy, Lymphoma diagnosis, minimally invasive diagnostics.

I. INTRODUCTION

A variety of thoracic disease, such as primary lung tumours, metastatic cancers, lymphhoproliferative disorders, and granulomatous ailments involving sarcoidosis and tuberculosis, require precise evaluation of mediastainal and Hilar Lymphadenopathy in order to be diagnosed and treated [1, 2]. Transbronchial needle aspiration (TBNA) has been the accepted minimally invasive method for reaching these lymph nodes for number of decades, particularly when directed by endobronchial ultrasonography (EBUS) [3-5]. While granulomatous inflammation and lung cancer staging have shown satisfactory diagnostic performance with EBUS-TBNA [6, 7], its dependence on cytological materials has significant drawbacks. Specifically, in conditions where tissue architecture is critical—such as in lymphoma sub typing or granulomatous disease characterization—cytological samples obtained via TBNA are frequently inadequate for a conclusive diagnosis [8–10]. Consequently, a significant diagnostic gap has persisted in patients for whom histological confirmation is imperative.

Intra-nodal forceps biopsy (IFB) has been developed as a supplementary or alternative method to get beyond the drawbacks of cytology-based sampling. This method allows core tissue specimens to be obtained under EBUS supervision [11, 12] In order to get histology tissue, this method entails creating a transbronchial route with a large-bore needle, usually 19G, through which flexible have advanced significantly during the last 20 years, leading to better diagnostic yields, especially in lymphoma and non-cascading granulomatous disorders [14, 15]. However, despite encouraging outcomes from various clinical studies, IFB has not been universally adopted into standard diagnostic algorithms. Barriers such as procedural complexity, the need for specialized training, heterogeneity in equipment availability, and regulatory ambiguity continue to limit its widespread implementation [16,17].

A growing body of literature has explored the diagnostic utility, safety profile, and technological developments associated with IFB, yet a comprehensive review that consolidates these findings across a two-decade timeline remains absent [18]. Given the rising demand for tissue-based diagnostics in the context of personalized medicine and the increasing reliance on molecular and immunohistochemical assays [19], it has become imperative to evaluate IFB's evolving role in the diagnostic landscape. This narrative review has therefore been undertaken to systematically examine the technological advancements, clinical performance, and regulatory progression of IFB since its inception.

The purpose of the review is to evaluate the diagnostic yield, tissue adequacy, and complication rates of IFB in comparison to traditional techniques such surgical mediastinoscopy and TBNA. We'll also talk about integration into current practices recommendation clinical accessibility, and economic ramifications. Additionally, unresolved issues and constraints will be noted, with a focus on equipment variability, procedural risks, and training shortages. Lastly, future views will be examined, including the development of innovation biopsy tools, robotics bronchoscopy, and AI-assisted targeting. When appropriate, the review uses a modified PECO framework, taking into account IFB (Exposure) in comparison to TBNA or surgical biopsy (Comparator). Outcomes are measured in terms of safety, cost-effectiveness, sample adequacy, and diagnostic yield [20]. Through this comprehensive analysis, the review seeks to clarify IFB's clinical value, technological trajectory, and potential to redefine diagnostic strategies in thoracic medicine.

II. METHODOLOGY

A. *Literature Search Strategy*

Four electronic databases-PubMed, Embase, Scopus, and Web of Science-were used to conduct a thorough literature search for the years January 2003 through March 2024 [21-24]. "Intranodal forceps biopsy," "EBUS-guided biopsy," "mediastainal lymph node sampling." "EBUS-TBNA and lymphoma diagnosis" were among the keywords and Boolean operators used. To restrict the results to human research published in English, filters were used. To guarantee openness in the screening and inclusion procedure, the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) criteria were adhered [25].

B. *Selection Criteria*

Articles included in this review were clinical trials, cohort studies, observational studies, review articles, and meta-analyses that assessed the efficacy, safety, or technical advancements in intra-nodal forceps biopsy (IFB) for mediastinal lymphadenopathy. Studies focusing on device innovation, sample adequacy, diagnostic yield, or comparisons with TBNA and mediastinoscopy were included [26–28].

III. CURRENT STATE OF THE ART

A. *Historical Background and Evolution*

Intra-nodal forceps biopsy (IFB) was developed to overcome the limitations of transbronchial needle aspiration (TBNA), particularly its inability to obtain adequate tissue architecture for diagnoses like lymphoma [31,32]. Introduced as an adjunct to EBUS-TBNA, IFB allows retrieval of core samples through a tract created by a 19G needle [33]. Its role has expanded over the past two decades due to its minimally invasive nature and improved diagnostic yield in select conditions [34].

B. *Current Technologies, Techniques, and Evidence*

Modern IFB employs flexible mini-forceps inserted via an EBUS-guided TBNA tract [35,36]. Devices feature blunt or serrated jaws, with innovations such as ultra-slim designs for 21G compatibility, improved sheaths, and Doppler-enhanced targeting [37]. Studies report sample adequacy of 93–96%, diagnostic accuracy for lymphoma at 82–89%, and a low complication rate (<1.5%) [38–40]. IFB has proven effective in conditions requiring histological diagnosis, including sarcoidosis and Hodgkin lymphoma [41,42].

C. *Comparative Analysis*

Table No [01]:- Comparative Analysis of Biopsy Techniques

Methods	Specimen Adequacy	Clinical Accuracy	Risk complication Rate
TBNA	~70%	65–75%	<1%
IFB	90–96%	85–90%	~1.5%
Mediastinoscopy	98%	95–98%	3–5%

IFB offers a less invasive, cost-effective alternative to mediastinoscopy, reducing hospitalization by up to 70%. However, it remains technique-sensitive and less available in low-resource settings.

D. Limitations in Current Approaches

Key challenges include operator dependency, lack of standardized forceps design, and limited training exposure [43]. IFB also cannot replace surgical biopsy in cases involving deep, non-accessible lymph nodes [44]. Regulatory variation and lack of uniform reimbursement further hinder widespread adoption [45].

E. Emerging Trends and Future Directions

Future developments include robotic bronchoscopy, AI-assisted targeting, and sensor-equipped forceps [46]. Ongoing trials such as NCT04529861 are expected to strengthen the evidence base [47]. Expanded training programs and molecular-compatible biopsy tools are likely to enhance IFB's role in personalized diagnostics [48].

IV. FUTURE PERSPECTIVES

The integration of robotic bronchoscopy is expected to improve stability and reach during IFB procedures, particularly for difficult-to-access lymph nodes [49]. AI-assisted targeting, using real-time EBUS imaging, is being developed to enhance node selection and reduce operator variability [50]. Advancements in sensor-integrated, ultra-fine forceps are anticipated to offer real-time feedback, improving safety and sample precision [38].

Biopsy tools capable of preserving RNA and protein integrity are under development to support molecular diagnostics in personalized medicine [41]. Additionally, simulation-based training programs are being proposed to standardize procedural skills and expand global access [46]. Future studies should explore IFB's utility in genomic and immunologic profiling for targeted therapies [48].

V. DISCUSSION

In the assessment of mediastainal Lymphadenopathy, intra nodal forceps biopsy has evolved during the past 20 years from an auxiliary to a nearly primary diagnostic method [31, 33]. IFB provides far better sample adequacy and diagnostic accuracy than TBNA, especially in diseases where histological architecture is crucial, such lymphoma, sarcoidosis, and reactive hyperplasia EBUS platforms make it clinically attractive options [34, 42]

Despite its advantages, challenges remain. These include operator dependence, training gaps, and non-standardized device designs, all of which contribute to variable outcomes [43,45]. Furthermore, geographic disparities in regulatory approval and reimbursement hinder global adoption [44]. While IFB cannot fully replace surgical biopsy, particularly in inaccessible or bulky nodal disease, it provides a less invasive alternative in many cases with comparable diagnostic value [46].

VI. CONCLUSION

Intra-nodal forceps biopsy represents a transformative leap in the diagnostic evaluation of mediastainal Lymphadenopathy. Over the past 20 years, the technique has evolved from an adjunct to a near-primary diagnostic tool in selected indications [31,34]. Its superior yield in diseases demanding histological architecture, low complication rates, and integration with EBUS platforms make it a valuable addition to the bronchoscopes' toolkit [36,41]. As technologies converge with robotics, AI, and molecular diagnostics, IFB is poised to further redefine minimally invasive diagnostics in pulmonary medicine [46,49].

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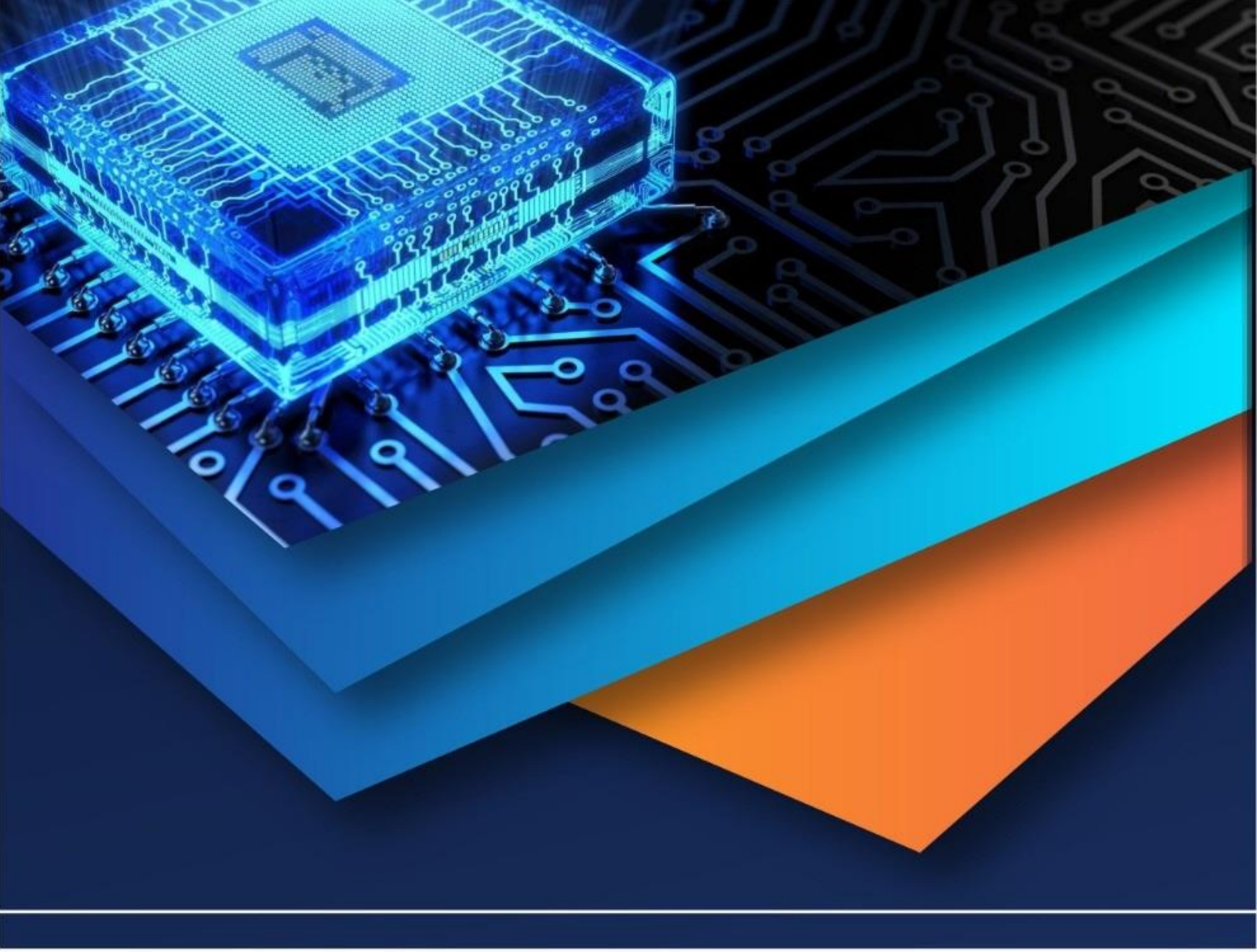

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