

# Commentary: Preoperative versus Intraoperative Tissue Diagnosis in Highly Suspicious Stage I Lung Cancer: Which Is the Superior Approach?

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Numerous studies have compared the efficacy of preoperative tissue biopsy versus intraoperative tissue biopsy for lesions suspected to be stage I lung cancer [1-5]. Previous research has identified key factors, including the impact of preoperative biopsy on prognosis. Major questions addressed include whether preoperative biopsy damages the tumor and leads to the dissemination of tumor cells, and whether the time spent on preoperative diagnosis affects prognosis. However, when evaluating the effectiveness of preoperative and intraoperative tissue diagnosis, it is also important to consider the limitations of intraoperative tissue diagnosis, such as potential constraints associated with frozen biopsy.

For upfront surgery to confer a survival benefit, as the authors of this article suggest [6], any significant delay in surgery or treatment due to preoperative diagnosis must be avoided, as it could worsen the patient's current stage [5]. While the extent of delay can vary based on the medical competency of each institution, in most lung cancer treatment centers, a preoperative biopsy rarely causes significant delays. However, the timing of lesion progression remains uncertain, and if early-stage cancer is suspected, surgical treatment is typically pursued. If imaging tests

with high diagnostic accuracy suggest a high probability of malignancy in a lung nodule, and the lesion's location, as determined by transbronchial lung biopsy (TBLB) or percutaneous needle aspiration (PCNA), indicates a low likelihood of successful preoperative diagnosis, investing time and resources in further diagnostic procedures is unnecessary. Conversely, if the lesion's characteristics are unclear and TBLB or PCNA can be easily performed, a preoperative biopsy is advisable to avoid unnecessary surgery. Thus, the necessity of performing a preoperative biopsy depends on the specific circumstances of each case [3]. When a lobectomy is required for tissue diagnosis, a preoperative biopsy should be conducted whenever feasible. However, if TBLB or PCNA is not possible, some reports suggest that proceeding with caution in lobectomy, based on comprehensive preoperative imaging tests and without preoperative tissue diagnosis, may still be a viable option [7]. The concern remains whether TBLB or PCNA could potentially damage the lesion and lead to implantation metastasis, although most studies have shown that these procedures do not impact survival [1,4,8]. Nonetheless, as the authors have noted, some studies have indicated potential harmful effects [9]. Therefore, if the lesion's location or the biopsy

method increases the risk of implantation metastasis, a more cautious approach should be considered when considering preoperative biopsy.

The National Comprehensive Cancer Network (NCCN) guidelines (version 7.2024) advise clinicians to consider risk factors, radiologic appearance, and current or prior residence in regions with prevalent endemic infectious lung diseases (e.g., fungal and mycobacterial) when planning a preoperative biopsy for suspected stage I lung cancer. In instances where there is a very high pre-test probability of stage IA lung cancer, a preoperative biopsy may be deemed unnecessary due to the associated costs, time, and risks, as it does not significantly contribute to treatment decisions. If a biopsy is needed during surgery, it is recommended to perform an intraoperative diagnosis using techniques such as wedge resection or needle biopsy before proceeding with more extensive operations like lobectomy, bilobectomy, or pneumonectomy, which are necessary for treatment. Furthermore, in situations where a diagnosis cannot be established through minimally invasive biopsy techniques, and if the suspected disease is stage IB or higher, necessitating preoperative systemic therapy, or if obtaining a preoperative diagnosis is particularly challenging or hazardous, stereotactic ablative radiotherapy may be planned as an alternative to surgery. The NCCN guidelines suggest that prioritizing a biopsy before surgery is appropriate whenever feasible [10].

Even when considering upfront surgery, it is crucial to acknowledge the limitations of frozen section biopsy. The challenges of intraoperative diagnosis include limited diagnostic accuracy, small sample sizes, issues with sample representativeness, difficulties in pathological interpretation, time constraints, and limitations associated with certain types of lesions. As a result, it can be challenging to determine the appropriate extent of surgery based on the results of a frozen section biopsy during the procedure, especially in cases where stage IA is strongly suspected. Consequently, it is difficult to dismiss preoperative tissue diagnosis as an unnecessary step in the management of highly suspected stage I lung cancer. Furthermore, some studies suggest that when intraoperative tissue diagnosis is conducted, there is a tendency to perform inappropriate extents of resection or to inadequately carry out lymph node staging [11]. This issue often arises because surgeons may proceed with surgery without comprehensive preoperative planning, which can lead to bias. Care must be taken to prevent the occurrence of this condition.

In summary, the authors suggest that while this study concluded upfront surgery does not affect overall survival

in patients with stage I lung cancer, preoperative biopsy for stage I lung cancer may negatively impact recurrence and overall survival [6]. Furthermore, intraoperative biopsy could be a beneficial intervention. I find this opinion compelling. However, given the limitations of intraoperative biopsy, prioritizing preoperative diagnosis may be necessary when the location and size of the lesion permit, even if stage I lung cancer is highly suspected.

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All the work was done by Jeong Su Cho.

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