Title

Diagnostic Discrepancies in Small-volume Biopsy for the Initial Diagnosis, Recurrence, and Transformation of Follicular Lymphoma: A Multi-Institutional Collaborative Study.

Journal

The American Journal of Surgical Pathology, 47(2)

Authors

Volaric, Ashley
Lin, Oscar
Balassanian, Ronald
et al.

Publication Date

2023-02-01

DOI

10.1097/PAS.0000000000001985

Peer reviewed

Published in final edited form as:

Am J Surg Pathol. 2023 February 01; 47(2): 212–217. doi:10.1097/PAS.0000000000001985.

Diagnostic Discrepancies in Small-Volume Biopsy for the Initial Diagnosis, Recurrence, and Transformation of Follicular Lymphoma: A Multi-Institutional Collaborative Study

Ashley K. Volaric, MD[1,4], **Oscar Lin, MD, PhD**[2], **Sara L. Zadeh, MD**[4], **Srishti Gupta, MD**[4], **Daniel R. Reed, MD**[5], **Megan J. Fitzpatrick, MD**[6], **Amy Ly, MD**[6], **Robert P. Hasserjian, MD**[6], **Ronald Balassanian, MD**[7], **Annabel K. Frank, MD**[8], **Steven Long, MD**[7], **Roberto Ruiz-Cordero, MD**[7], **Linlin Wang, MD, PhD**[7], **Kwun Wah Wen, MD, PhD**[7], **Yi Xie, MD, PhD**[7], **Eric Mou, MD**[9], **Lorenzo Falchi, MD**[3], **Stephen Cook, MD**[10], **Joshua R. Menke, MD**[1], **Yasodha Natkunam, MD, PhD**[1], **Dita Gratzinger, MD, PhD**[1] **Cyto-Heme Institutional Collaborative (CHIC) consortium**

[1]Department of Pathology, Stanford University, Stanford, CA

[2]Department of Pathology, Memorial Sloan Kettering Cancer Center, New York, NY

[3]Department of Hematologic Malignancies, Memorial Sloan Kettering Cancer Center, New York, NY

[4]Department of Pathology and Laboratory Medicine, University of Virginia Medical Center, Charlottesville, VA

[5]Section on Hematology/Oncology, Wake Forest Baptist Health Comprehensive Cancer Center, Winston-Salem, NC

[6]Department of Pathology, Massachusetts General Hospital, Boston, MA

[7]Departments of Pathology and Laboratory Medicine, University of California San Francisco, San Francisco, CA

[8]Department of Hematology/Oncology, University of California San Francisco, San Francisco, CA

[9]Division of Hematology, Oncology, and Blood & Marrow Transplantation, University of Iowa Health Care, Iowa City, IA

[10]Department of Pathology, Veteran Affairs Medical Center, San Francisco, CA

Abstract

Small-volume biopsies (SVB) including fine needle aspiration (FNA), cell block, and needle core biopsies (NCB) are increasingly utilized to diagnose and guide the clinical management of lymphoma. We established a multi-institutional interdisciplinary collaboration of cytopathologists, hematopathologists, and oncologists focused on the role of SVB in the management of patients

Corresponding Author: Ashley K. Volaric, M.D., Hematopathology, University of Vermont Medical Center, Assistant Professor of Pathology and Laboratory Medicine, Robert Larner, M.D. College of Medicine at the University of Vermont, 111 Colchester Avenue, Burlington, VT 05401, ph (804) 916-0085, aek4f@virginia.edu.

DISCLOSURES: The authors have no financial disclosures.

with follicular lymphoma (FL). In order to assess the performance characteristics of SVB in this setting we evaluated all consecutive SVBs performed for clinical indications of initial diagnosis, recurrence, or transformation of FL over a 5-year period and focused on the 182 that had at least one subsequent biopsy within 3 months as part of the same clinical work-up. The most common outcome of a subsequent biopsy as part of the same clinical work-up was a more specific diagnosis usually assigning the pathologic grade (111/182, 61%), followed by complete agreement with the SVB (24/182, 13%), and change from non-diagnostic on initial biopsy to diagnostic on subsequent biopsy (21/182, 12%). A minority resulted in a diagnostic change from benign to lymphoma (17/182, 9%), change in follicular lymphoma grade (5/182, 3%), or change in lymphoma diagnostic category (4/182, 2%). There were no cases where an initial diagnosis of lymphoma was overturned. The distribution of discrepancies was similar across initial SVB types (FNA, FNA + cell block, needle core biopsy with or without FNA). Tissue limitations were noted in a minority of cases (53/182, 29%) and were enriched among initially non-diagnostic biopsies (16/21, 76%). Flow cytometry immunophenotyping was performed in the majority of cases both at the first and last biopsy (147/182, 81%). SVB can be a powerful method to detect FL in various clinical indications, with discrepant cases mostly resulting from a refinement in the initial diagnosis.

Keywords

follicular lymphoma; small volume biopsy; fine needle aspiration; needle core biopsy; discrepancy

Introduction

Fine needle aspiration (FNA) with or without subsequent cell block or needle core biopsy (NCB) define small-volume biopsies (SVB) and are increasingly used across various pathology practice settings in the clinical work-up of solid tumors and hematolymphoid neoplasms. The value of SVB in the initial diagnosis and work-up of non-Hodgkin lymphoma, in particular, has been well-established previously in single institutional studies.[1–3] Multiple studies have proven that SVB, when of sufficient quality and cellularity, can reliably provide a diagnosis of follicular lymphoma in the initial diagnostic, transformation, and recurrent disease settings.[1,4] When coupled with ancillary studies like flow cytometry, the sensitivity of the diagnosis increases.[2,4] Further, SVB as a clinical technique is cost-effective, minimally invasive, and well-tolerated by patients.[2,5,6] Given that majority of lymphadenopathies at presentation are reactive and that a small subset of patients with prior diagnosis of follicular lymphoma suspected to have transformation or recurrent disease can also have non-lymphomatous lymphadenopathy, SVB are an appropriate first step in the work-up of these patients.

The diagnostic limitations of SVB have also been investigated.[7] The main limitation of SVB is the fact that the lymph nodal architecture may not be fully evaluated, which can limit general diagnostic sensitivity.[1,7] Other factors that may affect the diagnostic sensitivity of SVB include the type and size of the lesion, performance of immediate adequacy assessment, biopsy needle gauge, experience of the operator, cellular preservation, and workflow of the cytologic specimen.[7] Despite these limitations, the diagnostic sensitivity of

SVB has drastically improved over the past decade.[7–9] The increased sensitivity has been made possible by the incorporation of flow cytometric, cytogenetic, and molecular studies as well as workflow improvements like ultrasound-guidance and cell block preparation techniques .[3,10–12]

Despite advances in the use and work-up of SVBs, there is still a relative dearth of robust data understanding the value of SVB in various clinical settings for hematolymphoid malignancy.[2] Our study was a multi-institutional collaborative effort that explored potential issues involving SVB in the diagnosis of follicular lymphoma when compared to subsequent biopsies in which a definitive diagnosis was rendered. We reviewed the diagnostic discrepancies between the initial SVB and the subsequent biopsy obtained within 3 months of the initial SVB. This review was done in the settings of primary diagnosis, disease recurrence, and assessment for potential transformation. Diagnostic discrepancies occurred when there was a diagnostic change upon subsequent biopsy and encompassed the following categories: benign to malignant, non-diagnostic to diagnostic, malignant to benign, change in lymphoma diagnosis, change in follicular lymphoma grade, and a more specific diagnosis.

Materials and Methods

A total of 676 biopsy work-ups of follicular lymphoma performed over a five-year period (1/1/2012–12/31/2016) were retrospectively analyzed from six academic institutions (Stanford University, University of California San Francisco, Memorial Sloan Kettering Cancer Center, Massachusetts General Hospital, University of Virginia, and the San Francisco Veteran’s Affairs Health Care System), which make up the Cyto-Heme Inter-Institutional Collaborative (CHIC) consortium.

The initial biopsy in all cases was an SVB, defined as fine needle aspiration (FNA) with or without cell block and/or needle core biopsy (NCB). The biopsy was performed for the clinical indications of initial diagnosis, ruling out recurrent disease, or ruling out transformation. Within this cohort, 182 SVB work-ups had a subsequent biopsy (SVB or surgical biopsy) performed less than 3 months from the initial biopsy to answer the same clinical question. The final biopsy served as the gold standard for comparison and was labeled as final diagnosis.

Data on discrepancy type was obtained from electronic medical records at each institution and entered by pathologists into a shared REDCap database. Discrepancy type was defined as a change in the diagnosis upon subsequent biopsy and included the categories: benign to malignant, non-diagnostic to diagnostic, malignant to benign, change in lymphoma diagnosis, change in follicular lymphoma grade, and a more specific diagnosis. Most SVB were collected in a preservative solution, either formalin or alcohol at the time of biopsy. If a sample was submitted for flow cytometry, then either a separate pass was submitted in cell culture media or the full sample was collected in cell culture media and reapportioned for fixation and flow cytometry. At most institutions, material collected for flow cytometry in cell culture media can stay in the refrigerator for up to 48 hours. Light chain restriction was assessed by flow cytometry immunophenotyping in most cases. Molecular clonality studies were not a subject of this study but were not routinely performed. Decisions regarding

selection of the anatomic site to biopsy were made by the patient's clinical team and were not analyzed in this retrospective study. There were no cases of non-hematologic malignancy or infectious etiology in this analysis. This study was approved by the Institutional Review Boards at each participating site.

Results

Work-up Characteristics

Among 676 work-ups beginning with SVB for initial diagnosis, recurrence, or transformation of follicular lymphoma, we identified 182 biopsy work-ups that required one or more subsequent biopsies as part of the same clinical work-up; demographic and clinical characteristics are summarized in Table 1. Most SVB work-ups requiring more than one biopsy began with an FNA with or without cell block (142/182, 78%), with the remainder being NCB with or without FNA (40/182, 22%) (see Figure 1). In marked contrast to initial biopsies, the final biopsies were very rarely FNA with or without cell block (7/182, 4%). The final biopsy was at the same site as the initial biopsy in the majority of cases (146, 80%), and the majority of work-ups were for initial diagnosis (131, 72%). FNA without cell block was most common in the initial diagnosis setting (56/131, 43%) and uncommon in the rule out transformation setting (2/26, 12%). FNA with cell block was relatively evenly distributed across clinical scenarios, whereas NCB with or without FNA was uncommon in the initial diagnosis setting (22/131, 17%) (see Table 2).

Diagnoses Rendered from Initial and Final SVB Specimens

Initial biopsies often resulted in B-cell lymphoma diagnoses without specification of the type of lymphoma (69/182, 38%), followed by follicular lymphoma without grade provided (29/182, 16%) (Figure 2). Most final diagnoses were of a specific type of lymphoma (174/182, 96%), most commonly follicular lymphoma, grade 1–2 (116/182, 64%) or diffuse large B-cell lymphoma (27/182, 15%). Non-diagnostic, limited, suspicious, and atypical diagnoses as a group were more common upon initial than final diagnosis (43/182, 24% vs 2/182, 1%). The diagnostic categories of limited sampling and non-diagnostic were made exclusively in the initial SVB, while diagnoses of follicular lymphoma grade 3A or 3B were only made in the final biopsy category.

Types of Discrepancies

Discrepancies were assessed between the initial and final biopsy in the work-up and were categorized as follows:

- *Agreement* - same diagnosis in initial and final biopsy, including grade
- *More specific diagnosis* – typically a refinement of the diagnosis; for example, assigning a grade to follicular lymphoma, most often grade 1–2
- *Change in follicular lymphoma grade* - for example, follicular lymphoma grade 1–2 to follicular lymphoma grade 3A
- *Change in lymphoma diagnosis* - for example, follicular lymphoma to diffuse large B-cell lymphoma

- *Benign to malignant* - for example, reactive follicular hyperplasia to follicular lymphoma
- *Malignant to benign* - for example, follicular lymphoma to reactive follicular hyperplasia
- *Non-diagnostic to diagnostic* - for example, insufficient or atypical to follicular lymphoma

There were no cases with an overdiagnosis of lymphoma on SVB (malignant to benign).

Discrepancies According to Initial Biopsy Type

Regardless of initial biopsy type (FNA, FNA + cell block, and NCB +/− FNA), the most common discrepancy was a more specific diagnosis or an agreement between the two biopsies, which in combination accounted for 74% (134/182) of total work-ups (see Table 3). The next most common discrepancy was an initial non-diagnostic specimen followed by a diagnostic specimen, which occurred in 12% (22/182) of cases. Benign to malignant discrepancies were seen in 9% (17/182) of cases and were low across all specimen types (3–15%). Changes in lymphoma grade and diagnosis were also low overall, each 5% or less across all specimen types.

Discrepancies by Clinical Indication

Types of discrepancies identified across clinical indications (initial diagnosis, rule out recurrence, rule out transformation) and according to whether the final diagnostic biopsy was at the same or a different site as the initial diagnostic biopsy are provided in Table 4. The most common outcome of a subsequent biopsy following initial SVB was a more specific diagnosis (111/182, 61%). Across all clinical indications, this category of discrepancy was most common in biopsies for initial diagnosis (92/131, 70%) and was also seen in about half of biopsies for an indication of rule out recurrence (13/25, 52%). However, it was less common among biopsies to rule out transformation (6/26, 23%). In contrast to work-ups for initial diagnosis or recurrence of follicular lymphoma, those where the biopsy was being undertaken to rule out transformation had a wider range of discrepancy types, with the most common diagnostic discrepancy being non-diagnostic to diagnostic (27%, 7/26).

Types of Discrepancy According to Site of Repeat Biopsy

Among the majority of work-ups where the last biopsy was at the same site as the initial SVB, the pattern of discrepancies was dominated by a more specific diagnosis (99/146, 67%) (see Table 4). Among these, the vast majority were repeat biopsies at initial diagnosis of follicular lymphoma (86/99, 87%). The pattern of discrepancies was more heterogeneous among the smaller group of work-ups where the final biopsy was of a different site. While more specific diagnosis was still common (12/36, 33%), the combination of categories initially not diagnostic of lymphoma - non-diagnostic to diagnostic and benign to malignant - comprised 14/36 (39%) of discrepancies.

Flow Cytometry Immunophenotyping

The majority of both initial and final biopsies were accompanied by flow cytometry immunophenotyping (see Figure 3). Across categories of discrepancy, flow cytometry was less commonly used in the first biopsy than the last in just two discrepancy categories: benign to malignant and non-diagnostic to diagnostic.

Diagnostic Interpretative Changes After Repeat Biopsy at the Same Site

Non-diagnostic to diagnostic discrepancies and more specific diagnoses reflect a clarification or refinement of the diagnosis. In contrast, diagnostic interpretative changes after repeat biopsy at the same site include those with discrepancy categories of benign to malignant, malignant to benign, change in lymphoma diagnosis, and change in follicular lymphoma grade. No malignant to benign cases were identified. There were 16 out of 146 work-ups (11%) resulting in a diagnostic interpretative change on a subsequent biopsy at the same site (see Supplementary Table 1).

Tissue Limitations

Tissue limitations included necrosis, fibrosis, crush artifact or non-intact cells, pauci-cellularity, and non-representative specimens. Tissue limitations according to these criteria were noted in 29% (53/182) of first biopsies and in 11% (20/182) of final biopsies.

Discussion

Small-volume biopsies (SVB) through fine needle aspiration (FNA) with or without cell block and/or needle core biopsy (NCB) are an increasingly employed practice in the diagnosis and clinical management of hematolymphoid neoplasms and in particular, follicular lymphoma. However, there is a lack of robust data to guide the management and interpretation of SVB in this setting. This is the first multi-institutional study to the authors' knowledge, specifically addressing the utility of SVB in refining the diagnosis of follicular lymphoma across three main clinical indications of initial diagnosis, ruling out recurrence, and ruling out transformation.

The diagnostic work-up of follicular lymphoma using SVB is challenging but can be a very sensitive and specific method to detect malignancy. McCroskey et al. determined that FNA can result in an 89% sensitivity for the initial diagnosis of follicular lymphoma and 66% sensitivity for low-grade follicular lymphoma.[4] We are not in a position to report overall sensitivity and specificity in this retrospective study as the majority of SVB were not followed by an additional biopsy (494/676, 73%). We focused on the minority of small volume biopsies where an additional biopsy was performed, and in this subset our cohort yielded a 70% sensitivity of the initial SVB for lymphoma, with 8% of initial biopsies resulting in a benign diagnosis and 7% non-diagnostic. There were no cases of overdiagnosis of lymphoma on the initial SVB, even in cases with limited tissue. Thus in our cohort, SVB methodology had a 100% specificity in the diagnosis of lymphoma in the initial diagnostic, ruling out recurrence, and ruling out transformation clinical scenarios.

Many factors influence the sensitivity of SVB in the diagnosis of follicular lymphoma across multiple disease settings. Some of these factors are pre-analytical including the experience of the aspirator, size of the biopsy needle, number of aspirations, preservation and cellularity of the sample, and even workflow of the sample processing.[7] Other factors are analytical and involve the processing and analysis of SVB samples.

At presentation most lymphadenopathies are reactive in nature or secondary to infection or metastasis. Even in patients with prior history of lymphoma, the presence of lymphadenopathy is not always due to recurrence or transformation. Because of this and the high cost and potential morbidity of lymph node excision, SVB and early inclusion of cytopathologists in the triage, processing, and analysis of the limited biopsy material is essential, allowing for the optimal use of the tissue.[5] Furthermore, the use of SVB for the diagnosis of lymphoproliferative disorders requires an integrated effort of cytopathologists, hematopathologists, and hematologic oncologists.

The majority of diagnostic changes between initial and final biopsies was a more specific diagnosis of follicular lymphoma. This most often involved assigning a grade to the follicular lymphoma classification. Refining the diagnosis of follicular lymphoma by assigning a grade can be especially challenging on SVB, and additionally, determination of follicular architecture typically requires observing at least 10 follicles.[1,13,14] A more specific diagnosis occurred in the majority of cases where limited tissue was noted in the initial SVB. Nearly 40% of the initial diagnoses were B cell lymphoma, NOS, suggesting that a more definite diagnosis could not be rendered due to limitations in terms of quality or quantity of diagnostic tissue or absence of ancillary studies.

The most common final biopsy type was surgical excision, with FNA with or without cell block occurring more often at the initial biopsy. These data reflect the role of SVB as an initial screening test for diagnosing follicular lymphoma, despite its limitations in fully classifying the lesion. In addition, the need for more tissue, as reflected in the increased surgical excisions upon final biopsy, is compatible with the diagnostic limitation of SVB to provide a definite classification and/or grading. A recent study by the authors' consortium evaluated time to final diagnosis in the setting of a history of follicular lymphoma with suspected transformation and determined that initial biopsy type, whether FNA, needle core biopsy, or surgical excision, did not significantly impact time to final diagnosis.[15] Further, another study by the authors' consortium, as a companion to the current study, determined that SVB results in high diagnostic yield for the evaluation of recurrence or transformation of follicular lymphoma.[16] This reflects the utility of SVB as a screening diagnostic modality in evaluating follicular lymphoma.

Ancillary studies, particularly flow cytometry, are important in diagnosing follicular lymphoma in SVB. Flow cytometry complements cytomorphologic analysis of SVB by simultaneously assessing light scatter characteristics which correlate with cell size, immunophenotype, and light chain restriction.[1,17] Flow cytometry studies were performed at most initial and final biopsies. However, the use of flow cytometry at the time of initial diagnosis was less common in non-diagnostic SVB and in those with an initial benign diagnosis found to be lymphoma in the final biopsy. Thus, lack of flow cytometry may

increase the risk of non-diagnostic or even false negative SVB. However, flow cytometry accompanying a SVB may not be sufficient to establish a definite lymphoma classification, as all cases in the cohort with a change in lymphoma diagnosis had flow cytometry performed at both initial and final biopsies.

There are notable statistical limitations to the present study. Gold-standard determination of sensitivity and specificity would require matched SVB and surgical biopsies for all work-ups. In clinical practice, only a subset of SVB is followed by another biopsy, and this likely enriches for cases where the initial SVB either did not result in a diagnosis in keeping with clinical expectation, did not provide enough specific information to support clinical decision-making, or was not deemed sufficient by the oncologist as a definitive diagnostic modality to support clinical decision-making. In our series, this represented a minority of biopsy work-ups, starting with small volume biopsy (182/676, 27%). Since in the other 73% no subsequent biopsy was performed, the work-ups reviewed here likely represent the "worst case scenario" for sensitivity and specificity, as they select for the minority of cases where the initial SVB was not sufficient to support clinical decision-making.

Notably, we structured this study in an "intention to diagnose" manner - i.e., we included all work-ups with more than one biopsy, even when the subsequent biopsy was at a different site. This is a retrospective exploratory study, and confounders are numerous, including unknown variations in practice patterns, reasons for repeat biopsy, and limited focus on the evaluation for follicular lymphoma. While this is a multi-institutional study, clinical practice varies between these institutions and could significantly impact the quality of the SVB analysis as well as the decisions to perform a subsequent biopsy across the various clinical scenarios.[18] We therefore present cohort data to the pathology and oncology communities as a snapshot of the current state but do not provide p-values or statistical analyses.

Multiple types of diagnostic changes can occur when a SVB is followed by another biopsy in the diagnostic evaluation of follicular lymphoma across various clinical settings (initial diagnosis, rule out recurrence, rule out transformation). The most common change was a more specific diagnosis, which usually entailed assigning a follicular lymphoma grade. There were no cases where an initial malignant diagnosis was subsequently downgraded to a benign diagnosis, supporting 100% specificity of SVB for the diagnosis of lymphoma in this setting. Future directions to expand upon the present study include evaluating the effect of different clinical practice and workflow parameters on the quality of SVB and resultant discrepancy type upon subsequent biopsies. Additionally, further exploration of how flow cytometry affects the refinement of the diagnosis versus other biopsy discrepancy types is needed.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

References

1. Young NA. Grading follicular lymphoma on fine-needle aspiration specimens - A practical approach. Cancer 2006;108(1):1–9. doi:10.1002/cncr.21350 [PubMed: 16400642]

2. Jin M, Wakely PE. Endoscopic/Endobronchial Ultrasound-Guided Fine Needle Aspiration and Ancillary Techniques, Particularly Flow Cytometry, in Diagnosing Deep-Seated Lymphomas. Acta Cytol 2016;60(4):326–335. doi:10.1159/000447253 [PubMed: 27414717]
3. Jin M, Wakely PE. FNA diagnosis of deep-seated lymphoma: an institutional experience. J Am Soc Cytopathy 2017;6:114–119. doi:10.1016/j.jasc.2017.03.002
4. Mccroskey Z, Khoury JD, Stewart JM, Caraway NP. Sensitivity of fine-needle aspiration biopsy for diagnosing and grading follicular lymphomas using a multiparameter approach in a cancer center 2017. doi:10.1016/j.jasc.2016.12.001
5. Shah A, Ross C, Sur M. An approach to small lymph node biopsies: pearls and pitfalls of reporting in the real world. J Am Soc Cytopathol 2021;10(3):328–337. doi:10.1016/J.JASC.2020.12.006 [PubMed: 33812794]
6. Paul T, Gautam U, Rajwanshi A, et al. Flow cytometric immunophenotyping and cell block immunocytochemistry in the diagnosis of primary Non-Hodgkin's Lymphoma by fine-needle aspiration: Experience from a tertiary care center. J Cytol 2014;31(3):123–130. doi:10.4103/0970-9371.145577 [PubMed: 25538379]
7. Caraway NP. Evolving role of FNA biopsy in diagnosing lymphoma: past, present, and future. Cancer Cytopathol 2015;123(7):389–393. doi:10.1002/CNCY.21551 [PubMed: 25924600]
8. Campo E, Harris NL, Jaffe ES, Pileri SA, Stein H, Thiele J, & Vardiman JW. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues Volume 2. Lyon, France: International Agency for Research on Cancer; 2008.
9. Swerdlow SH, Campo E, Harris NL et al. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues Vol 117. 4th, revised ed. International Agency for Research on Cancer, 2017; 2017. https://books.google.com/books?id=Qdt9swEACAAJ&source=gbs_book_other_versions. Accessed December 19, 2020.
10. Dey P Role of ancillary techniques in diagnosing and subclassifying non-Hodgkin's lymphomas on fine needle aspiration cytology. Cytopathology 2006;17(5):275–287. doi:10.1111/j.1365-2303.2006.00331.x [PubMed: 16961657]
11. Mathew EP, Nair V. Role of cell block in cytopathologic evaluation of image-guided fine needle aspiration cytology. J Cytol 2017;34(3):133–138. doi:10.4103/JOC.JOC_82_15 [PubMed: 28701825]
12. Sumana BS, Muniyappa B. Ultrasonography Guided Fine Needle Aspiration Cytology with Preparation of Cell Blocks in the Diagnosis of Intra- Abdominal Masses. J Clin Diagn Res 2015;9(12):EC08–EC12. doi:10.7860/JCDR/2015/16490.6869
13. Young NA, Ehya H. Grading Follicular Lymphoma. Acta Cytol 2004;48(2):117–118. doi:10.1159/000326302 [PubMed: 15085739]
14. Choi SM, Betz BL, Perry AM. Follicular Lymphoma Diagnostic Caveats and Updates doi:10.5858/arpa.2018-0217-RA
15. Mou E, Falchi L, Sundaram V, et al. Impact of initial biopsy type on the time to final diagnostic biopsy in patients with follicular lymphoma and suspected histologic transformation doi:10.1080/10428194.2021.1941936
16. Megan JF, Vandana S, Amy L, et al. Small Volume Biopsy Diagnostic Yield at Initial Diagnosis versus Recurrence/Transformation of Follicular Lymphoma: A Retrospective Cyto-Heme Inter-Institutional Collaborative (CHIC) Study. Am J Surg Pathol 2022; Under Review.
17. Gong JZ, Williams DC, Liu K, Jones C. Fine-Needle Aspiration in Non-Hodgkin LymphomaEvaluation of Cell Size by Cytomorphology and Flow Cytometry. Am J Clin Pathol 2002;117(6):880–888. doi:10.1309/16UL-W4PX-HRL7-7V88 [PubMed: 12047139]
18. Zadeh SL, Balassanian R, Cheung MC, et al. Global Cytopathology-Hematopathology Practice Trends. Am J Clin Pathol 2022;157(2):196–201. doi:10.1093/AJCP/AQAB111 [PubMed: 34508545]

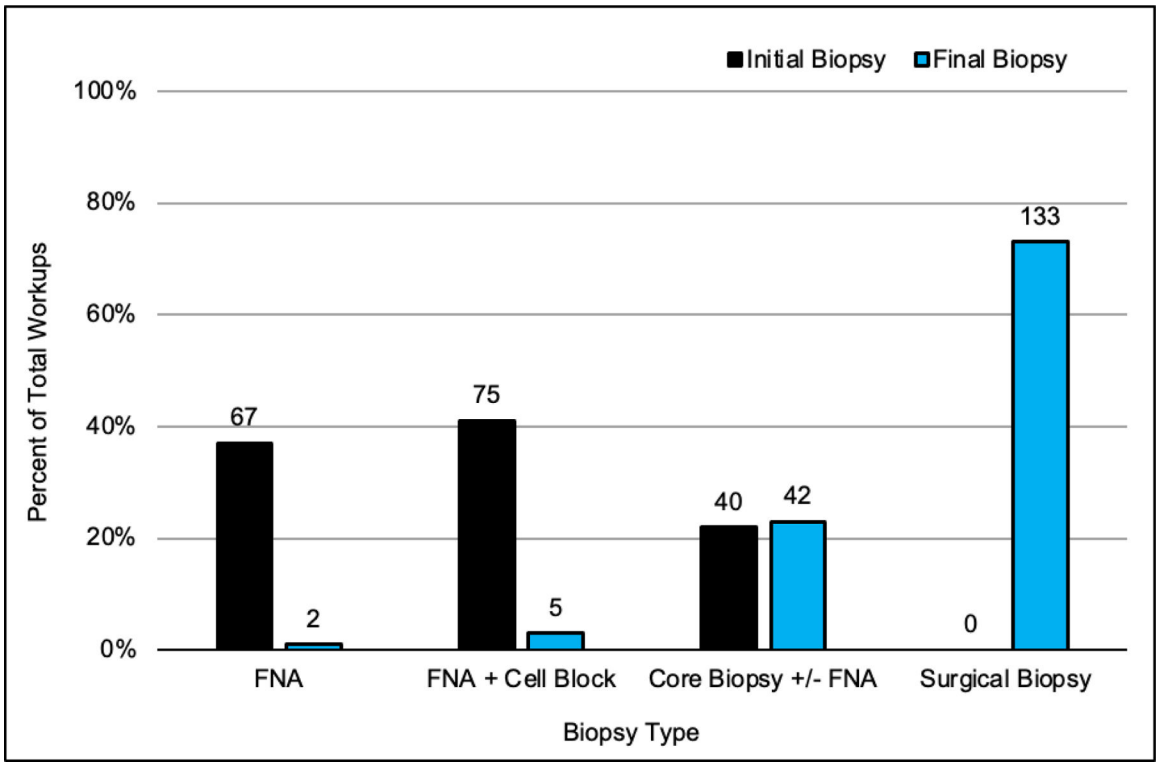

Figure 1.

Biopsy Types at Initial and Final Biopsy, All Work-ups (n=182).

N.B. Initial surgical biopsies (incisional or excisional) were excluded per study inclusion criteria. Numbers above each bar graph indicate absolute case numbers.

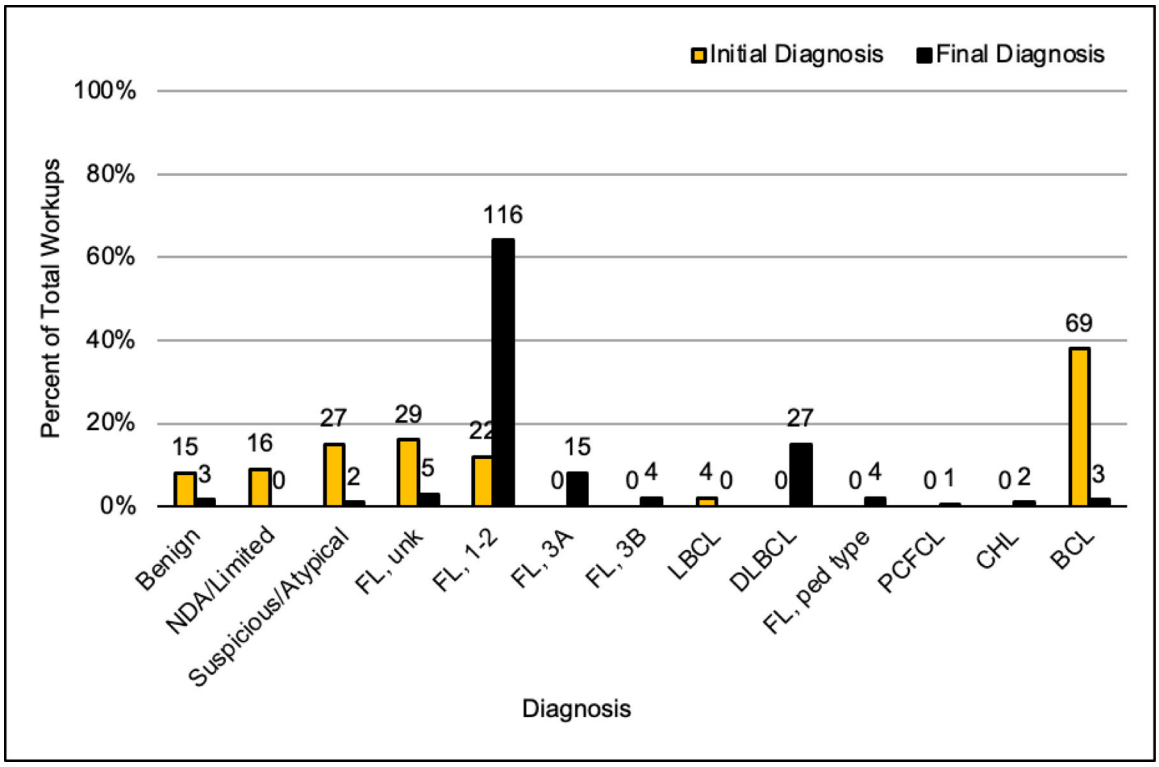

Figure 2.

Diagnoses at Initial and Final SVB Biopsy, All Work-ups (n=182).

N.B. Numbers above each bar graph indicate absolute case numbers

NDA, Non-diagnostic; Limited, Limited Sample; Suspicious, Suspicious for Malignancy; Atypical, Atypical Cells Present; FL, unk, Follicular Lymphoma, Unknown Grade; FL, 1-2, Follicular Lymphoma, Grade 1-2; FL, 3A, Follicular Lymphoma, Grade 3A; FL, 3B, Follicular Lymphoma, Grade 3B; LBCL, Large B cell Lymphoma; DLBCL, Diffuse Large B cell Lymphoma; FL, ped type, Pediatric-Type Follicular Lymphoma; PCFCL, Primary Cutaneous Follicle Center Lymphoma; CHL, Classic Hodgkin Lymphoma; BCL, B cell Lymphoma

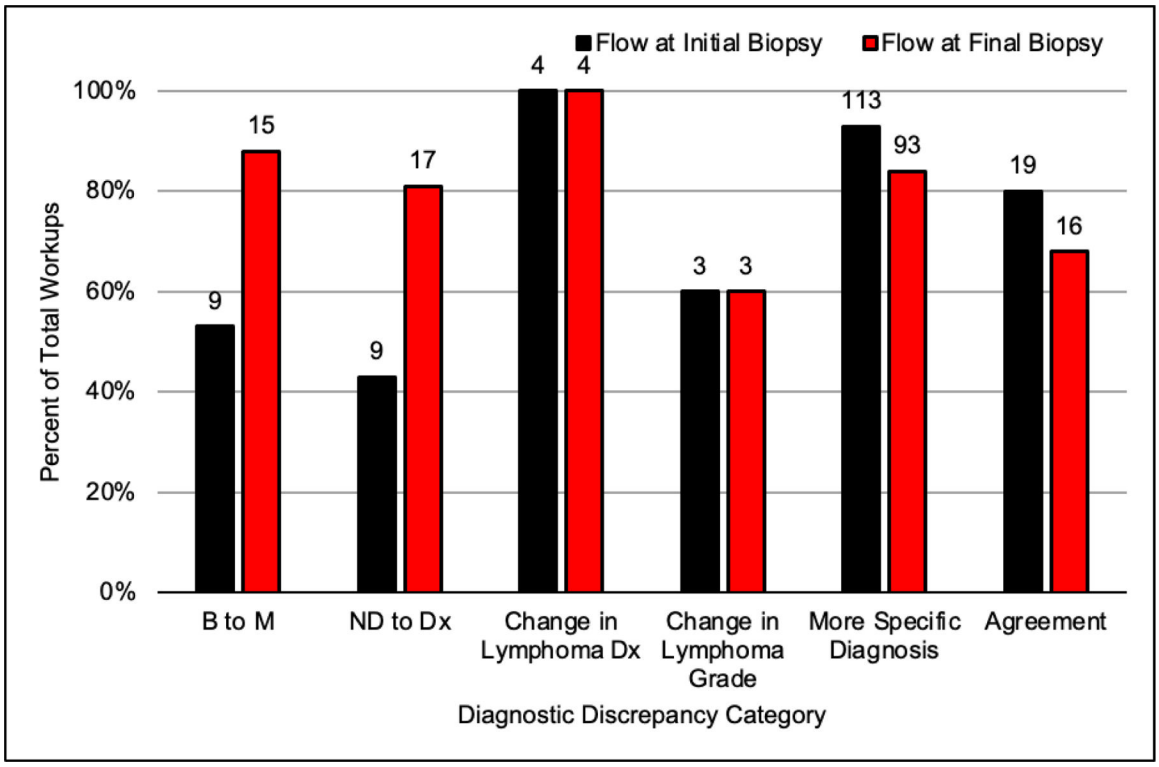

Figure 3.

Flow Cytometry Performed at Initial and Final Diagnosis per Diagnostic Discrepancy Category, All Work-ups (n= 182).

N.B. Numbers above each bar graph indicate absolute case numbers.

B to M, Benign to Malignant; ND to Dx, Non-Diagnostic to Diagnostic

Table 1.

Demographics and Clinicopathologic Features of All SVB Work-ups.

	All work-ups (n = 182)	
	n	%
Age at initial biopsy: mean (SD)	61.5 (14.0)	
Last biopsy same site as first?		
Yes	146	80%
No	36	20%
Reason for biopsy		
Initial diagnosis	131	72%
Rule out recurrence	25	14%
Rule out transformation	26	14%
Type of Initial Biopsy		
FNA	68	37%
FNA + cell block	74	41%
Needle core biopsy +/− FNA	40	22%
Final diagnosis		
Benign	3	1%
FL, grade 1–2	116	64%
FL, grade 3A	15	8%
FL, grade 3B	4	2%
FL, unknown grade	5	3%
FL, special type *	5	3%
Large B-cell lymphoma	0	0
DLBCL **	27	15%
Other ***	7	4%

* 4 pediatric type FL, 1 primary cutaneous follicle center lymphoma

** Of DLBCLs, 3 also had a component of FL grade 1–2, 3 also had a component of FL 3A, and 5 also had a component of FL grade 3B

*** 3 B cell lymphoma, 2 classic Hodgkin lymphoma, 1 suspicious for lymphoma, 1 atypical

DLBCL, diffuse large B cell lymphoma; FL, follicular lymphoma; FNA, fine needle aspiration; SD, standard deviation

Table 2.

Initial Biopsy Types FNA, FNA with Cell Block, and Needle Core Biopsy with or without FNA According to Clinical Indication and Biopsy Site.

	Clinical Indication (n=182)				Biopsy Site (n=182)	
	Initial Diagnosis (n=131)	Rule Out Recurrence (n=25)	Rule Out Transformation (n=26)	Total (n=182)	Same (n=146)	Different (n=36)
FNA	56 (43%)	9 (36%)	3 (12%)	68 (37%)	58 (40%)	10 (28%)
FNA + cell block	53 (40%)	8 (32%)	13 (50%)	74 (41%)	61 (42%)	13 (19%)
NCB +/− FNA	22 (17%)	8 (32%)	10 (38%)	40 (22%)	27 (18%)	13 (36%)

FNA, fine needle aspiration; NCB, needle core biopsy

Table 3.

Types of Diagnostic Discrepancy Across Initial Biopsy Types FNA, FNA with Cell Block, and Needle Core Biopsy with or without FNA.

	FNA (n=68)	FNA + cell block (n=74)	NCB +/− FNA (n= 40)	Total (n=182)
Benign to Malignant	10 (15%)	2 (3%)	5 (12%)	17 (9%)
Non-diagnostic to Diagnostic	8 (12%)	6 (8%)	8 (20%)	22 (12%)
Change in Diagnosis	2 (3%)	2 (3%)	0 (0%)	4 (2%)
Change in Grade	0 (0%)	4 (5%)	1 (2%)	5 (3%)
More Specific Diagnosis	46 (68%)	45 (61%)	20 (50%)	111 (61%)
Agreement	2 (3%)	15 (20%)	6 (15%)	23 (13%)

FNA, fine needle aspiration; NCB, needle core biopsy

Table 4.

Types of Diagnostic Discrepancy Across Clinical Indications of Initial Diagnosis, Rule Out Recurrence, and Rule Out Transformation and Biopsy Site.

	Initial Diagnosis (n=131)	Rule Out Recurrence (n=25)	Rule Out Transformation (n=26)	Same Site (n=146)	Different Site (n=36)	Total (n=182)
Benign to Malignant	13 (10%)	2 (8%)	2 (8%)	10 (7%)	7 (19%)	17 (9%)
Non-diagnostic to Diagnostic	11 (8%)	3 (12%)	7 (27%)	14 (10%)	7 (19%)	21 (12%)
Change in Diagnosis	1 (1%)	0 (0%)	3 (12%)	3 (2%)	1 (3%)	4 (2%)
Change in Grade	2 (2%)	1 (4%)	2 (8%)	3 (2%)	2 (6%)	5 (3%)
More Specific Diagnosis	92 (70%)	13 (52%)	6 (23%)	99 (67%)	12 (33%)	111 (61%)
Agreement	12 (9%)	6 (24%)	6 (23%)	17 (12%)	7 (19%)	24 (13%)