

**OPTN Kidney Committee
Biopsy Best Practices Workgroup
Meeting Summary
March 22, 2021
Conference Call**

Andrew Weiss, MD, Chair

Introduction

The Biopsy Best Practices Workgroup (the Workgroup) met via teleconference on 03/22/2021 to discuss the following agenda items:

1. Policy Oversight Committee Presentation Update
2. Summary of February 22 Meeting
3. Discussion: Develop a Standardized Pathology Report
4. Finalize Recommendations and Determine Policy or Guidance Development

The following is a summary of the Workgroup's discussions.

1. Policy Oversight Committee Presentation Update

The Committee Chair provided a brief overview of the update presented to the Policy Oversight Committee and the feedback that committee provided.

Summary of Discussion:

The Workgroup had no questions or comments.

2. Summary of February 22 Meeting

The Committee briefly reviewed the last Workgroup meeting, including discussions to develop minimum donor kidney criteria appropriate for biopsy and to incorporate recommendations into either a policy proposal or guidance document.

Summary of discussion:

The Workgroup had no questions or comments.

3. Discussion: Develop a Standardized Pathology Report

The Workgroup reviewed examples of pathology reports currently in use and developed recommendations for a standardized pathology report, discussing what renal biopsy criteria is critical to evaluating organ quality and what information is critical to determining the quality of a biopsy.

Data summary:

A pathologist Workgroup member presented a prepared sample standardized report to organize group discussion around. The example standardized report included the following categories, and a scoring system used by a research group studying biopsy reproducibility and quality.

- Biopsy type: Wedge or Core Needle
- Tissue preparation technique: Frozen section or Formalin-Fixed Paraffin-Embedded (FFPE)
- Number of Glomeruli

- Percent of globally sclerotic glomeruli: less than 5 percent, 5-10 percent, 11-25 percent, more than 25 percent
- Nodular Sclerosis: present or absent
- Interstitial Fibrosis and Tubular Atrophy (IFTA): less than 5 percent, 5-10 percent, 11-25 percent, 26-50 percent, and greater than 50 percent
- Vascular disease (percent lumina narrowing): none, mild (less than 25 percent), moderate (25-50 percent), or severe (greater than 50%)
- Other: infarction with percent cortical involvement, etc.
- For consideration: inflammation, fibrin thrombi, acute tubular injury

Summary of discussion:

One of the Workgroup members, a renal pathologist, remarked that a standardized biopsy form should have key data points needed to make clinical decisions with clear categories to improve reproducibility. The Workgroup member asked the Workgroup whether wedge or core needle biopsies should be recommended, noting that a wedge biopsy is more likely to overestimate subcapsular scarring, while core needle biopsies can better estimate the degree of vascular disease and obtaining an appropriate size of vessel in the sample. Another member remarked that the core needle method is generally higher risk, and that issues like arterial ureteral fistula can develop as a result of core needle sampling. One member agreed, noting there is risk if the needle is inserted incorrectly. Workgroup members agreed that wedge biopsies were far more common generally. A Workgroup member noted that core needle biopsies performed on recipients generally have ultra sound guidance, while most procurement biopsies do not. The member also noted that common issues like overestimating degree of fibrosis with wedge biopsies are exacerbated by overly conservative sampling, and can be significantly reduced with improved sampling. Another member agreed that the core needle method often may need to be performed by someone with training to ensure the needle is through the cortex, and that wedge sampling is often a simpler method for surgeons.

One Workgroup member, a renal pathologist remarked that tissue preparation technique can be critical to the quality of the biopsy, as many characteristics assessed in a biopsy are distorted in frozen sections. The member continued that while formalin-fixed tissue preparation is more ideal, frozen tissue sections are much more common and accessible, so indication of preparation technique is critical. Another member agreed that formalin-fixed paraffin-embedded samples produced more accurate biopsies, but are both more time consuming and less likely to be available to smaller or rural hospitals, making the logistics infeasible. A member agreed and noted that FFPE could be recommended as an ideal technique, not required. The member suggested that the limitations of frozen samples can be mitigated by creating clearly defined categories to allow non-renal pathologists to more easily define characteristics into data points.

The Workgroup agreed that mandating the use of FFPE and core needle methods that are not universally available could negatively impact access to biopsy information overall.

One member noted that cortical necrosis should be included, and typically described as focal (10 percent or less) or diffused (11 percent or more) if present. Another member agreed, adding that cortical necrosis, also known as infarction, is appreciable on both frozen and FFPE tissue samples. The member continued that fibrin thrombi should also be included, particularly as even non-renal pathologists can easily identify and characterize. Fibrin thrombi could utilize similar categories as cortical necrosis, with none (0 percent), focal (10 percent or less), and diffuse (11 percent or greater). Another member agreed with the inclusion of cortical necrosis and fibrin thrombi.

The presenting Workgroup member noted the scoring system was developed for research purposes on the predictive outcome and reproducibility of procurement biopsies, and shared that it was included to show how strategic granularity can be used to detect differences in outcome, but can also reduce reproducibility of a biopsy, particularly if performed by a non-renal pathologist. Another member noted some centers extrapolate biopsy data to score the report, but that any kind of scoring system should not be utilized in this standardized pathology report. Other members agreed, and one workgroup member noted that the pathologist's role is to provide values, not determine organ quality, and that the main question should be defining the characteristics through rating categories – the size of the degrees used to describe each characteristic. The Workgroup Chair agreed, and noted that the degrees presented in the scoring system to describe glomerulosclerosis, interstitial fibrosis and tubular atrophy, and vascular disease seemed appropriate.

A member asked if the interstitial fibrosis and tubular atrophy (IFTA) characteristic could be split up, and it was noted that IFTA is usually both read and reported as its own cumulative score.

One member recommended including the number of sclerosed glomeruli as well as the number of glomeruli, particularly as it is already commonly reported and absolute numbers can be critical information. Another member agreed, and noted this would be particularly important for biopsies with a low number of glomeruli. A member countered that for non-renal pathologists reading larger wedge sections, estimating a percentage can be easier than counting individual glomeruli and utilizing percentage categories can improve inter-observer reproducibility, but otherwise asking for absolute numbers of glomeruli is very feasible. The Workgroup Chair recommended including both the total number of sclerosed glomeruli and the percentage categories.

A member asked if a minimum number of glomeruli should be given to establish sample adequacy. Another member disagreed as most surgeons can glean on the number of glomeruli the adequacy of a sample.

4. Finalize Recommendations and Determine Policy or Guidance Development

A member remarked that the standardized pathology form and information needed to evaluate the biopsy, such as core versus wedge, should become a policy requirement. The member added that guidance could be provided on procedures like core needle or wedge biopsy, as well as FFPE or frozen preparation, but that providing information of sampling and tissue preparation methods should be required. The Workgroup Chair noted that the standardized report or policy proposal could include language like “preferred” to indicate a method was recommended but not required, and agreed with standardizing renal pathology reporting in policy.

A member remarked that a policy regarding the minimum criteria for biopsy could either be that every donor meeting the criteria is biopsied, or so that, in a situation where a donor meets the criteria *and* a biopsy is requested, then a biopsy is performed. The member continued that the latter option may be preferable, particularly as getting a biopsy reading can be difficult for some hospitals. Another member agreed, as getting a biopsy done in those cases can add a significant amount of cold time. The Workgroup Chair noted that the minimum criteria for biopsy could be guidance, but that any kind of policy development around the criteria would benefit from more consistent data to support the criteria recommendation. The Workgroup Chair also reminded the Workgroup that a previous comment expressed that incorporating minimum criteria into policy would be more impactful and ensure organ procurement organizations (OPOs) compliance. Another member agreed that more data-driven evidence would be important to require biopsy performance, particularly when literature points to an excess of biopsies being done. One member noted that feedback from the OPTN OPO Committee could be helpful as well.

Upcoming Meeting

TBD

Attendance

- **Committee Members**
 - Andy Weiss
 - Catherine Kling
 - Dominick Santoriello
 - Jim Kim
 - Julianne Kemink
 - Malay B. Shah
- **HRSA Representatives**
 - Marilyn Levi
- **SRTR Staff**
 - Bryn Thompson
 - Jonathan Miller
 - Nick Salkowski
- **UNOS Staff**
 - Lindsay Larkin
 - Kayla Temple
 - Tina Rhoades
 - Amanda Robinson
 - Ben Wolford
 - Lauren Motley
 - Nicole Benjamin
 - Leah Slife
 - Matthew Prentice