

Telecytopathology as a component of ROSE

Poorva Singh, MD
Cytopathology Fellow, University of Minnesota

Jim Stewart, MD
Medical Director of Cytopathology, University of Minnesota

1

The flow of the talk

- ◆ History and basics of telepathology
- ◆ Rationale and background of telecytopathology
- ◆ Considerations for any telecytopathology system
- ◆ Challenges in telecytopathology for ROSE
- ◆ Telepathology versus telecytopathology
- ◆ UMN methods for ROSE
- ◆ Few real-life clinical cases
- ◆ Summary and take-aways

2



3

Telepathology - History

The first live telepathology system connected Boston Logan Airport and the Massachusetts General Hospital in 1968

4

Father of telepathology

- The term first coined by Dr. Ronald Weinstein of Rush Medical College in Chicago, IL in 1986
- He first published the steps needed for remote pathology diagnostic services



PMID: 30783545

5

Some more history.....



Live demonstration (in 1986) of the first operational robotic telemicroscopy system

6

Definition

- ◆ The American Telemedicine Association definition:
"the electronic multimedia communication across a network of pathology-related information between 2 or more locations for use-cases between pathologists and/or qualified laboratory personnel; and may include involvement by clinicians and/or patients."
- ◆ As defined by the CAP, telepathology is "the practice of pathology in which the pathologist views digitized slides or still images and renders an interpretation"

7

Terminology pertinent to telepathology

- ◆ 'Static Telepathology' – scan slides, store images and review later
- ◆ 'Dynamic Telepathology' – synchronous (real time slide viewing)
- ◆ 'Formal Telepathology' – diagnosis is rendered & report sent to patient chart
- ◆ 'Informal Telepathology' - informal/internal "curbside/hallway" opinion given; no report generated
- ◆ 'Adequacy' - no diagnosis given, but there is an action that affects patient care - a mention is needed in the final report!

8

Medical Record Statement for Report

Rapid Onsite Evaluation*

FNA Performance:

Fine needle aspiration was not performed by Fairview Pathology staff.

Aspirate immediate study/adequacy:

I, Jimmie Stewart, MD, attest that I immediately examined smears while the procedure was underway and determined or confirmed the adequacy of the specimens via telepathology.

It is of note that the final assessment and report may be performed and signed by a different pathologist.

Onsite adequacy/interpretation:

A: Adequate

9

Classic Purposes of Telepathology

- ◆ Education
 - Teaching from remote locations
 - Providing cases students otherwise might not see
- ◆ Quality of care
 - Expert consultation and review
- ◆ Accessibility of care
 - Providing services that would have been otherwise denied due to distance or other barriers
- ◆ Efficiency
 - Providing services in the best way possible!

10

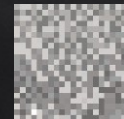
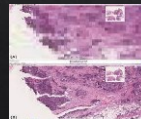
Telepathology Systems - Components

- ❖ Microscope and slide viewing system, on-site personnel
- ❖ Camera and imaging setup – static vs dynamic vs robotic
- ❖ Image sharing and management system – real-time vs teleconferencing vs Whole Slide Imaging
- ❖ Network for connectivity – wired vs wireless
- ❖ Data security and firewalls
- ❖ Computer hardware

11

Telepathology - System Challenges

- ◆ Cost of the system setup and implementation – in-house vs 3rd party?
- ◆ An appropriate network speed- wired is preferred!
- ◆ Data security and storage – DICOM standards, duration of image storage
- ◆ Location of scanners and mobility of the system
- ◆ Reconciliation with EHR, IMS and LMS software and updates
- ◆ Long-term maintenance and hardware upgrades



12

Telectytopathology for Rapid Onsite Evaluation (ROSE)

- ◆ Most common application of telectytopathology
- ◆ Extends the reach of cytopathologists
- ◆ Cytologists/trainees are onsite personnel
- ◆ Instrumental in ensuring adequacy & tissue triage
- ◆ Facilitates cost effectiveness in high-volume settings
- ◆ The cytopathologist provides preliminary diagnoses or adequacy statement
- ◆ Expertise of on-site personnel is paramount!



13

Rationale for Telectytopathology

- ◆ Efficiency
 - A pathologist can review multiple ROSE cases at disparate sites
 - ◆ Radiology at 1pm, endoscopy at 1:15pm and US at CSC at 1:40pm
- ◆ Educational
 - Assessment of trainees in university hospital settings
- ◆ Financial
 - Requires lower number of highly trained cytopathologists or cytology-trained pathologists for a service to function and grow
 - Keep cytopathologists focused on billable tasks with more attractive reimbursement

14

Telectytopathology systems



Video microscopy

Whole Slide Scanning

Robotic microscopy

15

Telectytopathology systems – Setup considerations

- ◆ Depending on the setup needs, a system can be either
 - home grown with help from IT, or
 - a purchased product with offsite support from a company
- ◆ Despite the origin, a telectytopathology system will **always** need hospital and/or department IT to assure all security parameters and compliances are met for your hospital or medical group
- ◆ **Validation** is required as per American Telemedicine Association
 - Simpler for 3rd party systems vs home grown systems
 - A universal approach to telectytopathology system validation (PMID – 35469774) –
 - ◆ 2-step validation process with training to validation data set ratio of 1:3
 - ◆ including "Nondiagnostic" cases to reflect a real-world scenario
 - ◆ overall, a 90% concordance rate is adequate for system competency
 - Monitors need to be 1080p or high definition at least, but **need not be 4K**

16

Telecytopathology – Significance of Resolution

- ◆ In a study performed by McMahon et al. on image resolution
 - 2 different systems of video microscopy for dynamic telecytopathology were used
 - ◆ High resolution systems (1920 x 1080 pixels)
 - ◆ Low resolution systems (800 x 600 pixels)
 - Cytopathologists looked at the slides remotely using a 3-tiered classification system
 - ◆ Negative
 - ◆ Atypical
 - ◆ Suspicious/malignant
 - Comparison to final diagnoses was made to determine which system gave a higher concordance rate

17

Low resolution screen shot



18

The million-dollar question –

Which system had higher
concordance?
?????

19

The study found that....

- ◆ They were roughly equally efficient with both having a 0.95 concordance index
- ◆ However, pathologists did profess a greater personal preference for the higher resolution system, gave them more confidence while assessing specimens
- ◆ Why no statistical difference?
 - Both arms of the study used the same cytologists (on-site personnel) to locate the cells
 - Cells of interest were presented to the pathologist at high magnification
- ◆ **Takeaway** – The cytologist locator skills seemed to be the key determinant !!!

20

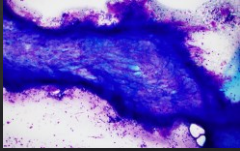
Issues of telecytopathology for ROSE

- ♦ **Quantity / quality of material** to examine
 - Not under the control of the cytopathologist
- ♦ **Quality of the smear**, and the ability to see diagnostic cells clearly and rapidly
 - Cytologists or trained cytopathology trainees (trained by cytologists)
- ♦ **Locator skills** – most significant variable!
 - Cytologists or trained cytopathology trainees (trained by cytologists)
- ♦ **Triage for definitive diagnosis**, ancillary investigations and patient management
 - The diagnosis of pancreatic adenocarcinoma on endoscopic ultrasound guided biopsies are usually based on morphology only
 - Endoscopic bronchial ultrasound guided lung biopsies for non-small cell carcinoma need additional studies including molecular analyses

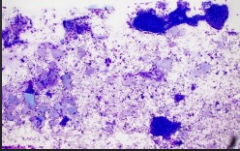
21

Issues of telecytopathology

Unreadable



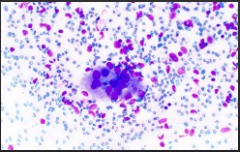
Need to locate the cells



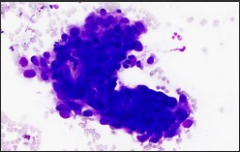
22

Issues of telecytopathology

Located cells



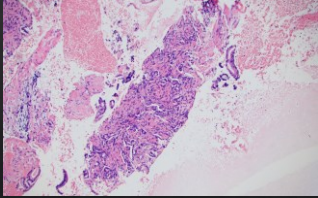
Located cells



23

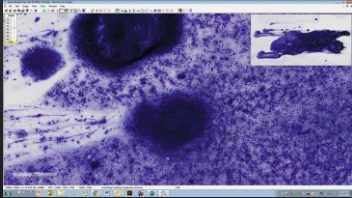
Issues of telecytopathology

Adequate triage of specimen to ensure an adequate cell block for molecular studies or immunohistochemistry



24

Telepathology vs Telectytopathology



25

Telepathology vs Telectytopathology

- ◆ **Rapid diagnoses comparison**
 - Telepathology today is moving or has moved to whole slide scanning for frozen section analysis and diagnosis
 - Telectytopathology mostly still utilizes an onsite operator (usually a cytologists or trainee) to transmit the images from the slide
- ◆ **Final diagnoses**
 - During the pandemic and otherwise there are biopsy cases and others that were/are diagnosed solely via telepath (direct microscopy review later)
 - Not many cytology cases were able to be diagnosed in this manner due to the depth of field or z-stack nature of cytopathology slides
 - ◆ Too long to generate an image representative of the slide (and too many slides)

26

Telepathology vs Telectytopathology

- ◆ Whole slide scanning in ROSE – **why not?**
 - Speed of scanning slides with Z-stacking, currently not quite ready for prime time
 - A paper from Yao et al in 2018 compared clinical light microscopy with two methods of whole slide scanning and found significant intermodality discordance (15% and 10.8%) between the standard of light microscopy and the two different methods
 - ◆ Issues were experienced with digital images for preliminary diagnoses
 - ◆ Network infrastructure difficulties were faced due to lag in the systems
 - ◆ They mentioned but did not test in “real world”, the need to coverslip

27

Telepathology vs Telectytopathology

Z-stacking for depth of field



- ◆ Stacking is done on some scanners today
- ◆ A study showed 21 Z-focal planes (at 1.5 micron intervals) showed high enough quality for their group
- ◆ The Panoptiq uses continual Z stacking in real time, but requires manual selection of areas

28

Telepathology vs Telecytopathology

- ◆ All current methods of WSI for ROSE are lacking
 - Z-stacking at a practical speed (fastest with a single Z-stack level takes 10-15 mins/slide)
- ◆ Future developments in digitization may yield faster scanning
- ◆ **BEWARE** - Faster scanning does not mean faster ROSE!!!
 - Slide preparation and simultaneous tissue triage – takes time
 - Adequately drying and staining the slides effectively – takes time
 - Locator skills are paramount, and time taken to locate diagnostic cells is highly dependent on specimen type and quality
 - WSI scanners may not be mobile enough to be carried to the ROSE site

29



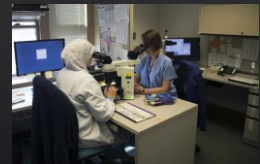
30



31


Telecytopathology - UMN method for ROSE

- ◆ Determine cases that will need ROSE for the day
 - Review history if necessary (fellow or house staff, and cytologists)
- ◆ When paged, move the telecytopathology setup to the bedside and obtain any further clinical history
 - Usually done by the trainees



32


Telecytopathology UMN style

- ◆ 64 year-old woman, longstanding smoker with a 3 cm mass centrally in her right middle lobe. An EBUS to be performed @ 9:45am.
- ▣ The EPIC OR list of possible ROSE cases with a 
- ▣ The above history is obtained
- ▣ Wait for a page around 9:30am
- ▣ Get paged at 11am and head down to the OR

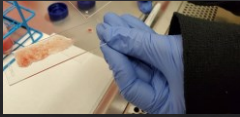
33

Telecytopathology UMN style

Aspirate material on slide



Move particulate material to the edge



34

Telecytopathology UMN style

Remove a small piece of particulate material with a slide



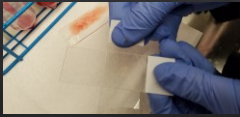
Place on clear charged slide




35

Telecytopathology UMN style

Smear lightly



Stain with Diff-Quik



Remainder is used to make an alcohol-fixed smear for Pap stain, and the rest is placed in formalin for cell block as a priority or divided between formalin and RPMI based on the clinical input.

36

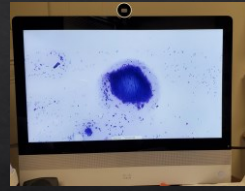
Telecytopathology UMN style



- UMN utilizes Cisco video sharing that sends a high-definition real-time video feed offsite
- A microscope with a video camera connected to a computer or codec box (Olympus)
- Monitor for viewing what the offsite pathologist is seeing
- Microphone for communication to offsite pathologist
- Receiving desktop monitor in the pathologist offices
- Wired high-speed LAN for efficient connectivity

37

Telecytopathology UMN style

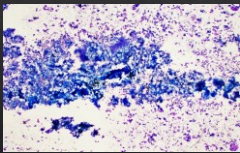


Monitors in our cytopathologist offices roughly 4K with higher capacity video card to obtain better color representation

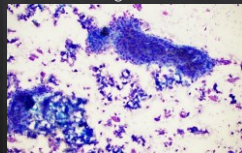
38

Telecytopathology UMN style

Low power of smear



20x shows adequate material for diagnosis

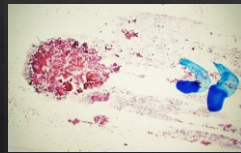


The attending asked for a Pap here as well as more for formalin

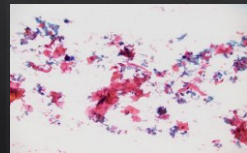
39

Telecytopathology UMN style

Low power Pap-stained smear



Diagnostic cells



40

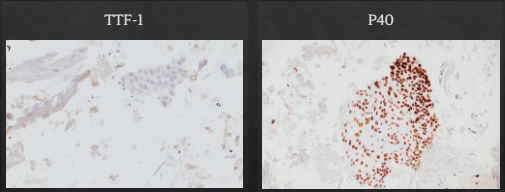
Telecytopathology UMN style



Cell block was further diagnostic

41

Telecytopathology UMN style



Material was present for immunohistochemistry and a full molecular workup

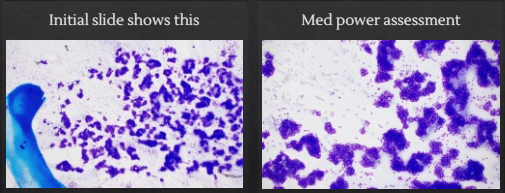
42

Telecytopathology UMN style – Case 2

◆ 54 year old man found incidentally to have a 2 cm mass in the body of the pancreas. An EUS is to be performed.

43

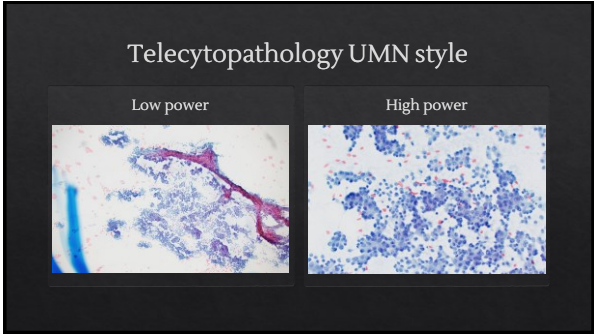
Telecytopathology UMN style



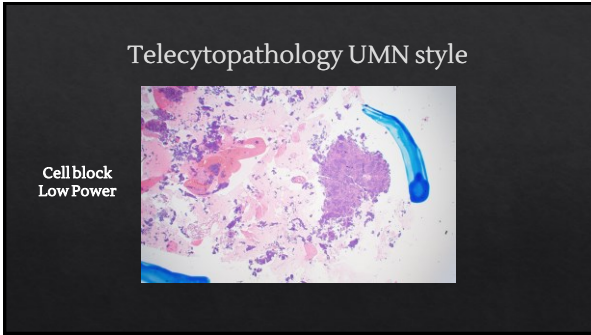
44



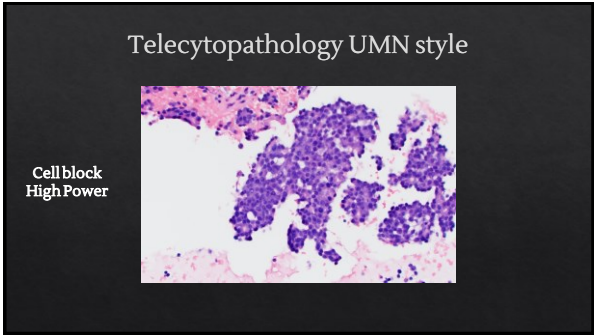
45



46



47

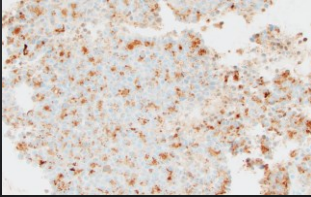


48

Telectytopathology UMN style

- Neuroendocrine stains - negative
- Beta catenin - negative
- Trypsin sent out - POSITIVE

Final Diagnosis was
Acinar Cell
Carcinoma



49

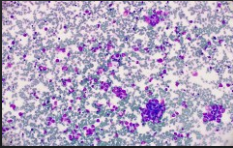
Telectytopathology UMN style – Case 3

◆ 45 year old woman with history of kidney transplant and smoking having multiple pulmonary nodules. EBUS is performed.

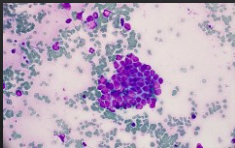
50

Telectytopathology UMN style

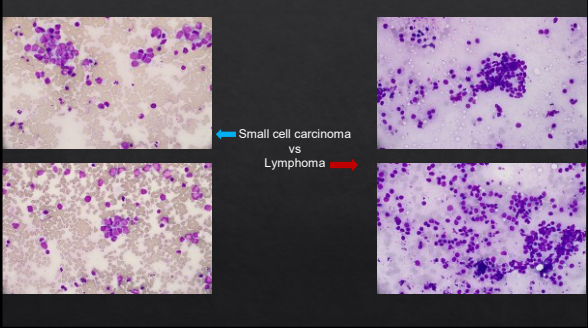
Low power



High power

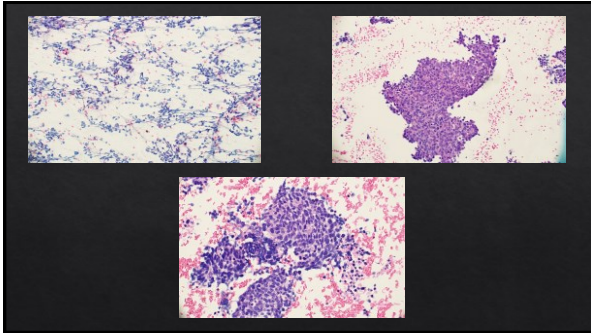


51

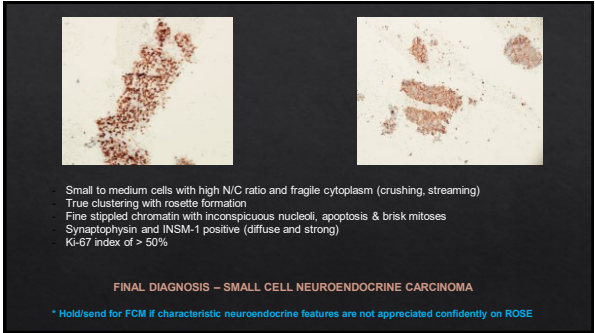


← Small cell carcinoma
 VS
 Lymphoma →

52



53

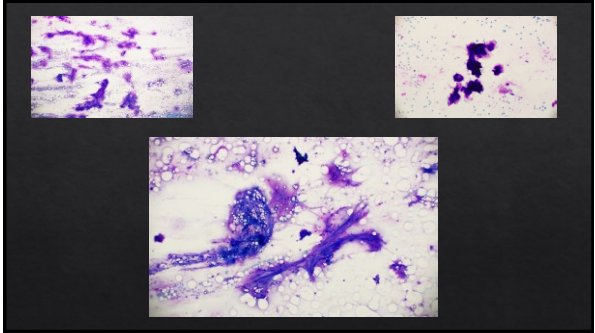


54

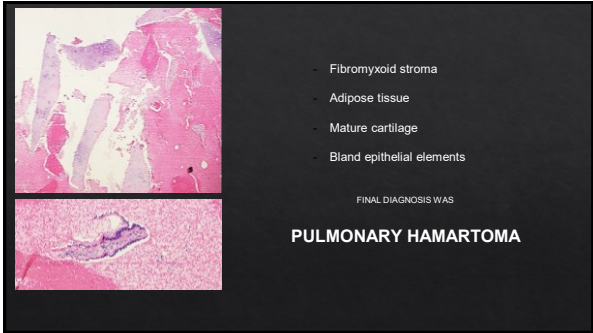
Telecytopathology UMN style – Case 4

◆ 54 year old man with a solitary lung nodule and long history of smoking. EBUS is performed.

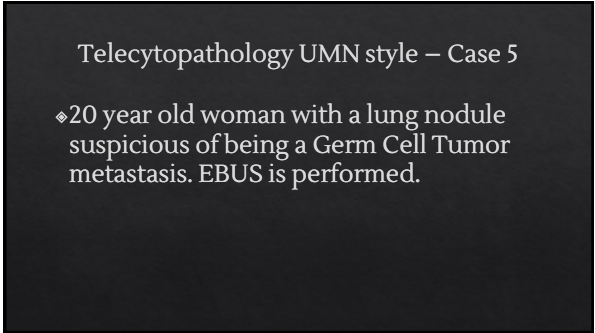
55



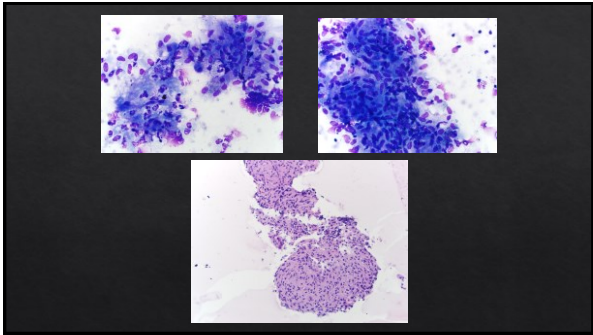
56



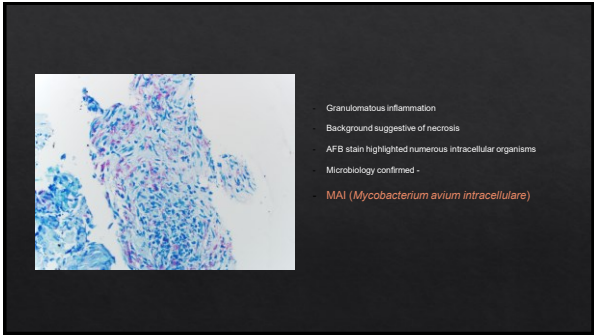
57



58



59



60

Telecytopathology UMN style - Effectiveness

- ◆ UMN abstract study (Chauhan et al.) examined EBUS cases for a year
 - 124 EBUS lung FNAs were studied
 - ◆ 117 cases or 88.7% had optimal cell block material for ancillary studies
 - ◆ 99 cases or 79.8% had adequate material for IHC
 - ◆ 65 cases or 52.4% had adequate material for PDL-1
 - ◆ 64 cases or 51.6% had adequate material for molecular testing
 - This diagnostic and prognostic information was made available to all these patients without the need for an additional sampling or a concurrent surgical biopsy
- ◆ UMN – one-stop shop which aids patients undergoing EBUS procedures by reducing the morbidity associated with core biopsies and repeat procedures
- ◆ More complete diagnoses using telecytopathology and ROSE aids EUS cases by giving clinicians more detailed information to guide patient management

61



62

Telecytopathology - Summary

- ◆ Extends the reach of the cytopathologists requiring less numbers of them on service at any given time
- ◆ Aids ROSE to assure adequacy and proper triage of the specimen
 - When paired with good preparatory methods, it can facilitate more definitive and complete diagnosis and treatment plans with just a single procedure
- ◆ Requires trained cytology personnel, either cytologists or cytology fellows or trained residents to make slides, stain them, locate diagnostic cells, drive the microscope and be the link between the clinical and diagnostic team.
- ◆ However, the technology for WSI is currently limited for ROSE, but the future holds great power!

63

References

- ◆ Park, Seung et al. "The history of pathology informatics: A global perspective" J Pathol Informatics 2018;4:97
- ◆ Yao K, Li Z. Review of different platforms to perform rapid onsite evaluation via telecytology. Cytopathology. 2020 Sep;31(5):379-384. doi: 10.1111/cyt.12871. McMahon RQ, McCarthy EE, Hetzel SJ, Das K, Stewart III J. **Focus on technology: How important is resolution in telecytopathology?** Cancer Cytopathology Volume 122, Issue 7 July 2014 pp546-52 Bui MM, Pantanowitz L (eds): Modern Techniques in Cytopathology.
- ◆ Bui MM, Pantanowitz L (eds): Modern Techniques in Cytopathology. Monogr Clin Cytol. Basel, Karger, 2020, vol 25, pp 75–83 (DOI: 10.1159/000496525). doi: 10.1159/000496525
- ◆ Chauhan, A., Rabe, K., Holler, J., Mettler, T., Amin, K., & Stewart, J. (2021). Optimization of Cytology Cell Blocks in EBUS Guided Lung FNA Cases: An Institutional Experience. Journal of the American Society of Cytopathology, 10(5), 358.
- ◆ Yan, Keluo et al. "Comprehensive Study of Telecytology Using Robotic Digital Microscope and Single Z-Stack Digital Scan for Fine-Needle Aspiration-Rapid On-Site Evaluation." Journal of pathology informatics vol. 9 49-24 Dec. 2018. doi:10.4103/jpi.jpi_75_18

64



66