

. Describe how advancements in diagnostic screening procedures require ever more specialized handling in real time 2. Recognize how these advancements increase the risk for operative morbidity, delay in diagnosis, and diagnostic error 3. Explain how an intraoperative protocol directing interventional procedures can prevent or mitigate these problems

# SITUATION

Rapid advancements in diagnostic screening methods combined with more effective therapeutic modalities have placed increasing pressure on clinicians to diagnose significant disease as early as possible. This has led to the growing use of minimally invasive interventional procedures on very early lesions to minimize morbidity. This has resulted in ever increasing numbers of specimens of ever decreasing size that harbor poorly representative and/or early borderline lesions.

This has lead to:

- Diagnostic inaccuracy and indeterminacy
- Paradoxical delay of diagnosis and so treatment
- Repeat procedures increasing risk for procedure related morbidity/mortality

# PROBLEM

How can we address the problems posed by earlier, smaller, and potentially nonrepresentative specimens so as to:

**RISK:** Maximize the patient's safety from repeat procedures, delay of treatment, and inappropriate therapy.

**QUALITY**: Minimize inconvenience, pain and suffering through multiple procedures magnified by missed or wrong diagnoses.

**UTILITY:** Maximize the yield of diagnosable samples on first procedure thereby reducing the additional cost of follow on procedures and their associated costs of increased morbidity.

# SOLUTION

Intraoperative microscopic review of Fine Needle Aspiration [FNA] smears and Needle Core Biopsy [NCB] touch preps provides a means of reducing sampling error while increasing yield to fully characterize lesions with just one procedure. This is achieved through the establishment of close cooperation between interventional physician, pathologist, and support personnel through implementation of a set of guidelines that direct these procedures to:

- Minimize the degree of intervention as measured in passes and repeat procedures.
- Maximize the volume of diagnosable tissue to assure accuracy.
- Assure appropriate handling, preservation, and processing of specimens.
- Assure correct battery of specialized testing is carried out.

# IMPLEMENTATION

I have developed a detailed protocol that includes rapid intraoperative microscopic review of initial fine needle aspirations and/or core biopsies by the pathologist. This protocol categorizes each specimen without necessarily requiring a specific diagnosis be made intraoperatively.

This categorization directs additional actions to be taken by the interventionist in acquiring a diagnosable specimen and the pathologist in properly preserving the specimen to assure successful follow on testing.

The goals are to minimize risk for morbidity and mortality from both the procedure and the diagnostic effort while maximizing the yield in specimen volume, quality, and diagnostic usefulness.

# **REDUCING DIAGNOSTIC ERROR**

# **Through an Intraoperative Protocol for Microscopic Examination of Small Biopsies** © 2015 Mark Gusack, M.D. **MANX Enterprises, Ltd.**®

# **OVERVIEW OF PROTOCOL WITH LUNG NODULE EXAMPLE**

### 1<sup>ST</sup> FNA/NEEDLE CORE BIOPSY NORMAL TISSUE Ben **NECROTIC DEBRIS** INFLAMMATION Inflammatory Inflammatory If final Advise movement of Infectious - Infectious biopsy needle to diagno - Tumor Necrosis attempt to obtain specia diagnostic specimen Advise move needle Advise move needle to obtain intact to obtain intact Advise at least three diagnostic specimen passes before diagnostic specimen discontinuing the If infection is a consid-If infection is a considprocedure unless the addit patient is high risk or eration, request one eration, request one pass in sterile cup for pass in sterile cup for experiencing an REQU culture. Residual is culture. Residual is SPEC adverse event placed in fixative placed in fixative Appr LUNG MASS OR NODU SMALL CELL Νει **A**DENOCARCINOMA SQUAMOUS CELL Poorly differentiated Immunohistochemical If moderate to well Immu **Genomic Studies** studies to confirm differentiated then: studie DONE! Additional specimen: Additional specimen Addit FNA: Variable FNA: Variable FNA: **Core**: Formalin **Core**: Formalin Core: PROCESSING - FNA **PROCESSING - FNA** PROCESSING - FNA Two **ETOH** fixed **H&E** Two **ETOH** fixed **H&E** Two **ETOH** fixed **H&E** Two I stained slides per pass stained slides per pass stained slides per pass stain **Residual passes** Residual placed in **Residual passes** Resid placed in Sacommand Cytolyte Preservative placed in Sacommano place for cytospin or thin Fixative for cell block Fixative for cell block Fixati prep slides and attempt at and CD56 immunoand C histochemical stain Synaj genomics PROCESSING - BX PROCESSING - BX PROCESSING - BX PROCESSING - BX **PROCESSING - BX** Target: three full core Target: three full core Target: three full core Target: six full core Target: one full core biopsy specimens biopsy specimens biopsy specimens biopsy specimens biopsy specimen confirmed as with one confirmed with one confirmed with one confirmed with one confirmed harboring SCC on on touch prep on touch prep on touch prep on touch prep examination placed in examination placed in examination. One in examination placed in touch prep formalin / five in flow examination placed in at least two cassettes at least two cassettes at least two cassettes in formalin in formalin in formalin one cassette in cytometry transport media if possible formalin **KEY TO SUCCESS: NEEDLE GAUGE AND DIAGNOSTIC YIELD ARE EXPONENTIALLY RELATED** CHANGE IN CROSS SECTIONAL AREA & VOLUME BY GAUGE 1.5 cm AREA VOLUME GAUGE ID [mm] follow on studies is 0.827 100.00% 0.838 the volume of intact 0.428 51.78% 0.603 0.286 tissue obtained. 0.311 37.62% 0.514 0.207 Notice the dramatic 0.201 24.29% 0.413 0.134 influence needle 0.260 0.053 0.080 9.63% gauge has on this. 26 0.250 0.049 0.074 8.90% lote that volume drops off by 50% from 18 to 20 gaug WE HAVE FOUND THAT 18 GAUGE IS OPTIMAL FOR BOTH FNA AND NCB. 20 – 22 GAUGE ARE ADEQUATE **REFERENCES – SELECTED:** 1. Travis WD et al.; Diagnosis of Lung Cancer in Small Biopsies and Cytology: Implications of the 2011 International Assoc. for the Study of Lung Cancer; Arch of Path & Lab Med 2013 Vol 137 668 - 684 2. Travis WD et al; Pathologic Diagnosis of Advanced Lung Cancer Based on Small Biopsies and Cytology: A Paradigm Shift; Journal of Thoracic Oncology 2010 Vol 5 411 – 414. 3. Cataluna JJ, Perpina M, Greses JV, et al. Cell Type Accuracy of Bronchial Biopsy Specimens in Primary Lung Cancer Chest 1996 Vol 109 1199 –1203. 4. Sanjay Mukhopadhyay; Utility of Small Biopsies for Diagnosis of Lung Nodules: Doing More with Less; Modern Pathology 2012 Vol 25 S43 – S57.

GN NEOPLASM	ATYPICAL CELLS	MALIGNANCY
type can be osed without I stains then:	Advise movement of biopsy needle to attempt to identify a nearby malignancy	If final type can be diagnosed without special studies and no genomics are needed:
DONE!	Advise at least three	DONE!
timen requires onal studies : JEST ADEQUTE IMEN VOLUME opriate fixative	discontinuing the procedure unless the patient is high risk or experiencing an adverse event	If special studies/ genomics required: <b>REQUEST ADEQUTE</b> <b>SPECIMEN VOLUME</b> Appropriate fixative
nohistochemical		Culture and special
s to confirm	/flow cytometry/	stains
onal specimen: Variable Formalin	FNA: Variable Core: Formalin + 0.5 cm <sup>3</sup> in flow transport media	At least one needle core or <b>FNA</b> pass in sterile cup. At least one additional in appropriate fixative
CESSING - FNA	PROCESSING - FNA	PROCESSING - FNA
ETOH fixed H&E ed slides per pass	Two <b>ETOH</b> fixed <b>H&amp;E</b> stained slides per pass	Two <b>ETOH</b> fixed <b>H&amp;E</b> stained slides per pass
ual passes d in Sacommano ve for cell block Chromogranin/ ptophysin	Residual placed in <b>RPMI</b> cytometry transport media to attempt flow cytometry studies	At least one pass into sterile cup /residual in Sacommano for cell block and <b>AFB</b> /Fungal stains

### PROCESSING - BX Target: four full core biopsy specimens with one confirmed on touch prep examination. One in sterile cup / residual in two cassettes in formalin



Critical to the success of the procedure and

- 5. Colby TV; Difficulties in the Pathologic Diagnosis of Lung Cancer (Especially in Small Biopsies); Mayo Clinic Arizona; Undated Power Point Presentation
- 6. Davidson MR, Gazdar AF, Clarke BE; The Pivotal Role of Pathology in the Management of Lung Cancer; Journal of Thoracic Diseases 2013 Vol 5 S463-S478. ACKNOWLEDGEMENTS: Huntington VAMC Departments of Radiology, Surgery, and Endocrinology for help and cooperation; and Dr. Nishi Dave, MBBS Indiana University Dept. of Laboratory Medicine

## Application of the protocol has resulted in:

### DIRECT PATIENT EFFECT:

- Reducing number of aspirations/biopsies per procedure.
- Reducing second procedures and associated costs.
- Reducing morbidity: pneumothorax, collapsed lung, hemorrhage, and hematomas

### **DIRECT SPECIMEN EFFECT**:

- Increasing quantity and quality of specimen produced.
- Increasing quality of touch preps to assure appropriate direction of procedure.
- Facilitating tumor characterization and staging to direct appropriate therapy.

# scans and additional interventions.

To the left is an abbreviated schema illustrating the key decision points for either a Fine Needle Aspiration [FNA] or a Needle Core Biopsy [NCB] of the lung nodule/mass. This is also used for mediastinal masses.

The key is to properly prepare and examine the first pass within five to ten minutes. This allows for the timely determination of:

The key to properly handling follow on passes is to determine:

- If additional specimens appear representative
- ➡ If additional specimens are adequate in condition
- When an adequate volume of diagnosable specimen has been obtained
- When attempting to obtain adequate volume will compromise patient safety

To do this the pathologist wears 2.5 - 3.5x magnifier lens to examine the specimen or, when necessary uses a dissecting microscope to examine intact needle core biopsies before making touch preps or allocating the specimen to one or more preservatives.

The presence of an experienced pathologist during interventional procedures utilizing a mutually agreed upon decision tree provides significant advantages. These include but are not limited to relieving the interventionist from having to do two separate tasks; real time guidance for adjustment of the biopsy or aspiration needle position; intraoperative diagnosis allowing early termination of the procedure, and indicating when additional specimen is need as well as which preservative to utilize.

Following an intraoperative protocol increases the number of definitive diagnoses, subclassifications, and stagings in a timely manner while reducing adverse outcomes secondary to the procedure itself by eliminating the need for a second procedure.

This **Reduces Diagnostic Error** in an affordable manner that increases quality of care.

RISK

GIILITY

OURINT

# **COST BENEFIT ANALYSIS**

# EXAMPLE

Interventional procedures to diagnose very small lung nodules that have grown slowly generally produce scant tissue upon which to make a diagnosis leading to follow up

Needle placement for the next specimen if additional material is needed Condition of the lesion which may require adjusting placement as well Inflammatory vs benign neoplasm vs malignancy to determine follow on passes What additional studies may be needed to direct total number of passes What type(s) of preservation will be carried out to do appropriate studies How specimen will be split if more than one form of preservation is required

# CONCLUSION