Reducing QNS Rates for Molecular Testing Among Patients With NSCLC

Less than 40% of eligible patients receive targeted therapy, with **15%** of this patient loss due to barriers with tumor sample sufficiency during tissue collection, handling, and stewardship.[1] Examining common barriers and solutions may help standardize molecular biomarker testing and improve patient access to targeted therapies.

Tissue Collection | **Tissue Handling** | **Tissue Stewardship**

Barrier: Diagnostic Yield vs Molecular Yield

Barrier: Processing Conditions

Barrier: Tumor Tissue Sufficiency

Most NGS platforms require a sample size of ≥**25 mm²** tumor surface area and ≥**20%** tumor content per sample.[2,3]

Each laboratory will have a minimal amount and concentration of tumor cells required for accurate detection of molecular alterations based on the specific tumor enrichment protocols available and assay platforms used for testing.[4]

Tip: When feasible, **1)** collect "molecular-only" biopsies that will not be processed for IHC[5] and **2)** track tissue blocks that are adequate for molecular testing by indicating percentage of viable tumor and flagging in the report for the tissue navigator and/or lab technician.[5,6]

Solution: Rapid OnSite Evaluation (ROSE)[7-11]

- Cytopathologic assessment of individual biopsy passes performed during a procedure
- Can help ensure adequacy for diagnosis and adequacy for molecular testing

Tip: When taking a biopsy sample, avoid central necrosis by targeting the tumor periphery.[5]

Solution: Implement Tissue-Specific Procedures

Collection technique affects diagnostic yield and downstream success of genomic testing[12-14] or "**molecular yield**."

An appropriate biopsy approach can render a diagnosis and provide comprehensive biomarker testing from a single procedure.[15] Considerations include[16]:

Technique
EBUS-TNAs > CT-TTCN

Needle gauge
18G+ > 20G or smaller

Solution: Audit QNS Rates

Thorough recordkeeping and quality improvement interventions can help identify root causes of insufficient and/or inadequate tissue.[5] Examples include:

- Assessment of biopsy quality across multiple locations and/or proceduralists
- Quality assurance implementation to ensure quality of future incoming biopsies

Key Takeaways

Implementing standardized, tissue-specific collection procedures can improve molecular yield and help reduce QNS rates and downstream sequencing failure.[2,5,7-16]

Solution: Optimize Pre-Analytic Conditions

Biopsy[18]
Cold Ischemia Time
≤60 minutes

Fixation[18]
Fixative Type
10% phosphate-buffered formalin, pH 7.0
Formalin: Tissue Volume
≥4:1, with 10:1 preferred
Total Time in Formalin
6-36 hours; high-fat tissue may require 48 hours

Sectioning[18]
Paraffin type
Pure, low-melt (<60°C)

Embedding[18]
Tissue Thickness
Not to exceed 4-5 mm

Storage[18]
Block Storage Temperature
18°C-25°C (room temperature)

Optimizing pre-analytic conditions may help reduce QNS rates and downstream sequencing failure.[6,17]

Solution: Cutting Protocol to Preserve Tissue

When possible, limit IHC to[4-6]:

- PD-L1 status
- TTF-1 or Napsin A (adenocarcinoma markers)
- P40 or P63 (squamous markers)

Avoid recuts and bank unstained slides[4]

- Embed biopsy specimens into individual blocks[19]
- Cut 15-20 unstained slides upfront for later use (eg, IHC, FISH, NGS)

Maximally preserve tissue in block

- Use shallow facing of tissue block to maximize slide-mounted tissue[19]
- Pick up all tissue cut from the block onto glass slides[4] (no sections should be discarded from the water bath)

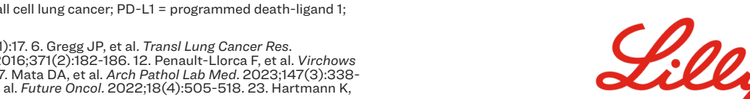
Key Takeaways

Optimizing pre-analytic conditions and sample handling may help reduce QNS rates.[6,17,18]

Solution: Use Alternative Specimens

Guidelines advise that ctDNA testing can be ordered concurrently with tissue NGS.[20]

If QNS is anticipated for a tumor tissue sample, consider alternative specimens for molecular testing, such as[21]:

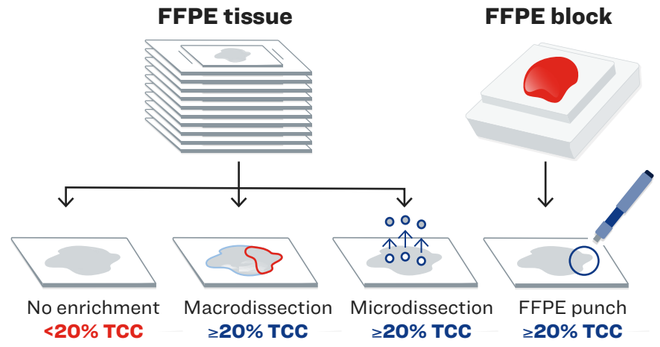


Solution: Comprehensive NGS vs SGTs

Tumor tissue may be insufficient to test all recommended biomarkers with sequential SGTs, while NGS can test for all established and emerging biomarkers.[22]

Solution: Section and Enrich Tumor Nuclei

Enrich for tumor within the sample to be tested and increase the likelihood of successful molecular testing.[6,23,24]



Key Takeaways

Using an NGS-based approach for genomic profiling can help limit the tissue consumption associated with multiple SGTs while providing the most comprehensive biomarker information.[20-24]

CT = computed tomography; ctDNA = circulating tumor DNA; EBUS = endobronchial ultrasound; FFPE = formalin-fixed, paraffin-embedded; FISH = fluorescence in situ hybridization; G = gauge; IHC = immunohistochemistry; NGS = next-generation sequencing; NSCLC = non–small cell lung cancer; PD-L1 = programmed death-ligand 1; P40 = isoform of P63 (ΔNp63); P63 = tumor protein p63; QNS = quantity not sufficient; SGT = single-gene test; TCC = tumor cell content; TNA = transbronchial needle aspiration; TTCN = transthoracic core needle biopsy; TTF-1 = thyroid transcription factor-1.

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