Improving Cancer Diagnosis and Care: Patient Access to Oncologic Imaging and Pathology Expertise and Technologies: A Workshop

Diagnostic Management Teams (DMT)
The Vanderbilt University Medical School Experience

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Cancer Diagnosis and Management

• Where we are today
• Vanderbilt “end-to-end” process engineering examples
  • Diagnostic Management Teams for cancer
• The future: Where we want to go
• Lessons and recommendations
Different Views of Cancer
The Traditional Model of Pathology: Limitations for Modern Medicine

Clinician orders individual tests

Lab(s) perform ordered tests and return simple results

Clinician collates and interprets results alone
Patient referred from outside clinician
Re: abnormal CBC/smear, suspect AML

Patient seen in clinic
18% blasts confirmed

Clinicin orders bone marrow biopsy with:
Flow cytometry
Karyotype
FISH (MDS and AML Panels)
Molecular tests (FLT3 and NPM1)

Clinician receives and interprets reports

Induction Chemotherapy Initiated

Unclear History

Bone Marrow Biopsy

Multiple Laboratories

Aspirate

Biopsy

Flow Cytometry

Hematopathology

Immunopathology

Morphologic exam

AML, with MDS features

Multiple, Asynchronous Reports

No Evidence-Based Testing Guidelines

Large Test Menu

Unclear History

Multiple Laboratories

Bone Marrow Biopsy

Aspirate

Molecular Pathology

FLT3

NPM1

Flosit (MDS and AML Panels)

Molecular tests (FLT3 and NPM1)

No Comprehensive Interpretation

Normal

Negative

Positive

Induction Chemotherapy Initiated

No Evidence-Based Testing Guidelines

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The Traditional Model of Pathology: Limitations for Modern Medicine

<table>
<thead>
<tr>
<th>Challenges</th>
<th>Consequences</th>
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<tbody>
<tr>
<td>• Large, complex, rapidly expanding test menus</td>
<td>• Unnecessary tests = increased costs</td>
</tr>
<tr>
<td>• Few if any evidence-based guidelines for test selection</td>
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<tr>
<td>• Multiple laboratories</td>
<td>• Inefficient work-flow = wasted time</td>
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<tr>
<td>• Multiple asynchronous reports</td>
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<tr>
<td>• Complex diagnostic outcomes.</td>
<td>• Difficult to correlate and interpret results</td>
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The Diagnostic Management Team (DMT)

A collaborative effort amongst pathologists, clinicians, and biomedical informatics.

1. To develop the right pattern of diagnostic testing for the patient, using standard test ordering algorithms.

2. To create a single, evidence-based, comprehensive report of integrated diagnostic data to guide therapy and disease monitoring.

3. To iteratively improve the algorithms as evidence based practices evolve and change.
The Diagnostic Management Team (DMT)

Standard Ordering Protocols (SOPs)

Unnecessary tests deleted

Essential tests added

Comprehensive Reports
### Secondary Testing Standards: MDS/AML

<table>
<thead>
<tr>
<th>Diagnosis or Morphologically Overt Disease</th>
<th>No Overt Disease (multiple encounters)</th>
<th>Pre-SCT</th>
<th>Post-SCT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Flow Cytometry</strong></td>
<td><strong>Karyotype</strong></td>
<td><strong>FISH</strong></td>
<td><strong>Molecular</strong></td>
</tr>
<tr>
<td><strong>AML or MDS</strong></td>
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SOPs Developed for:
- Acute Myeloid Leukemia
- Myelodysplastic Syndrome
- Acute Lymphoblastic Leukemia
- Myeloproliferative Disorders, including CML
- B cell, Acute lymphoblastic leukemia
- T cell, Acute lymphoblastic leukemia
- Non-Hodgkin and Hodgkin Lymphoma
- Multiple Myeloma
- Bone Marrow Failure Syndrome

**AML includes MDS in evolution to AML**

The hematologist retains the option to order tests “a la carte.”
<table>
<thead>
<tr>
<th>Comprehensive Diagnosis</th>
<th>Acute myeloid leukemia (47% blasts) with myelomonocytic differentiation, positive for NPM1 and FLT3-ITD mutations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical History</td>
<td>73-year old male with new onset cytopenias and circulating blasts</td>
</tr>
<tr>
<td>Morphologic Diagnosis</td>
<td>Hypercellular marrow (80-90% cellularity) with decreased trilineage hematopoiesis; involved by acute myeloid leukemia (47% blasts) with myelomonocytic differentiation</td>
</tr>
<tr>
<td>Flow Cytometry</td>
<td>Increased myeloblasts Gating on blasts (47% of total cells) identified on CD45/side scatter histograms, immature cells have the following immunophenotype: CD2 (negative), CD4 (heterogeneous dim), CD7 (dim), D11b (partial moderate), CD13 (dim), CD14 (negative), CD15 (dim), CD16 (negative), CD19 (negative), CD33 (bright), CD34 (partial moderate), CD45 (dim), CD56 (partial dim), CD64 (moderate), CD117 (partial moderate), HLA-DR (bright), MPO (partial moderate)</td>
</tr>
<tr>
<td>Karyotype</td>
<td>Abnormal male karyotype 46,XY,del(9)(q13q22)[12]/46,XY[8]</td>
</tr>
<tr>
<td>FISH</td>
<td>Normal for the tested MDS and AML panels nuc ish 8q22(RUNX1T1x2),21q22(RUNX1x2)[200] nuc ish 15q22-24(PMLx2),17q21(RARAx2)[200] nuc ish 16q22(CBFBx2)[200] nuc ish 11q23(KMT2Ax2)[200] nuc ish 5q15.2(D5S23,D5S721x2),5q31(EGR1x2)[200] nuc ish 7cen(D7Z1x2),7q31(D7S486x2)[200] nuc ish 8cen(D8Z2x2)[200] nuc ish 20q12(D20S108x2)[200]</td>
</tr>
<tr>
<td>Molecular Studies</td>
<td>NPM1 mutation detected 0.73 FLT3-ITD mutation detected 0.12 CEBPA mutation not detected c-KIT mutation not detected</td>
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</table>
Hemato-malignancy DMT was accepted by users and “a la carte” ordering fell significantly.

The DMT saves 10 minutes per patient for the clinician.
The providers trust that the right tests will be ordered.

Fractional weekly utilization of the bone marrow testing panel vs. a la carte ordering after DMT implementation.

A retrospective analysis predicted that DMT guidance of laboratory testing improves concordance and reduces testing.

Baseline Missing Tests Unnecessary Tests Optimal

<table>
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<th>Tests per bone marrow sample</th>
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<tbody>
<tr>
<td>Baseline</td>
<td>3.7</td>
</tr>
<tr>
<td>Missing</td>
<td>0.4</td>
</tr>
<tr>
<td>Unnecessary</td>
<td>1.3</td>
</tr>
<tr>
<td>Optimal</td>
<td>2.8</td>
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Saves ~1 test per bone marrow sample using real-time decision guidance integrated into clinical practice.


140,000 Americans will be newly diagnosed with leukemia, lymphoma or myeloma this year, while 1,000,000 are in remission/actively treated.

Scaling nationally, this represents a $0.5B/year savings opportunity.
Using the DMT to guide testing continues to improve test concordance and reduces testing year after year.

Evolution of the SOPs: An Example of a Learning Health Care System
Mutation testing for 36 genes by NGS was incorporated into the DMT algorithms in 2014:

*Only cases with suspected myeloid malignancies*

Results of NGS Testing by Concordance with DMT
(673 tests / 6,223 marrows)

- Concordant with DMT (86%)
  - 81% positive
- Discordant with DMT (14%)
  - 18% positive

Seegmiller AC (Unpublished results)
Ongoing Work:

- Scale to Vanderbilt Health Affiliated Network Partners
  First partner: Jackson Madison Hospital in Jackson, TN
  Implemented Hematopathology DMT in 2014

Vanderbilt Affiliated Systems
- >50 Hospitals
- ~4800 Physicians (VHAN)
- 12 Health Systems

VHAN Advisory Clients
- 4 Health Systems with 13 hospitals across Mississippi
Next Steps and Challenges:

- Develop similar processes
  - Currently developing: GI
  - On deck: lung and breast
- Challenges of solid tumors
  - Imaging is critical
  - Metastatic and non-metastatic disease
  - Multiple time points of entry into system
  - Multiple different tumor sites with different characteristics:
    - Colorectal, Stomach, Small intestine, Pancreas, Liver
  - Multiple providers involved:
    - Gastroenterologists, Surgeons, Radiologists, Oncologists,
  - Multiple different sample types:
    - Biopsies of primary or metastatic lesions, Full or partial resections,
In Summary

• Introduction
  • Discussed traditional pathology practice.
  • Developed the use case for innovation in practice.

• Description of the Hematopathology Diagnostic Management Team (DMT)
  • Defined the requirements for a DMT
  • Highlighted the team approach
  • Reviewed a “learning health care” system approach

• Presented on-going work and next steps
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