COLLEGE of AMERICAN PATHOLOGISTS

How Should We Integrate Biomarker Datasets into Cancer Reports

Lessons Learned from the US Experience with Biomarker Reporting

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The Landscape of Cancer Care

- **Key Points:**
  - Cancer care is complex and can extend over multiple years
  - Cancer care is often provided at multiple facilities with multiple providers
  - Enrollment in clinical trials is becoming *routine* part of care for some tumors
  - Clinical decision support at point of care and patient-facing technologies are rapidly becoming standard tools in cancer care

The Landscape of Cancer Care

- **Key Points:**
  - Big data and rapid learning systems: Evolving role in cancer care
  - Tumor registry as intersection of research, population health and clinical care
  - Targeted therapies as mainstay of cancer treatment
  - Evidence-clinical practice gaps
  - Tumor staging expanding to include personal survival outcomes by utilizing risk assessment models and clinical trial stratification

The Landscape of Cancer Care

- **Pathology cancer reporting:**
  - Needs to follow patient through entire continuum of care (i.e. portable)
  - Needs to be complete enough to allow patient to appropriately navigate continuum of care:
    - Include biomarker testing for treatment purposes as well as prognosis
    - Allow patient to be appropriately considered for enrollment in clinical trials
    - Support CDS and patient-facing technologies
    - Support tumor registry collection
    - Support rapid learning systems

The US Experience

- **Cancer Protocols introduced in 1986**
  - Identifies the minimum data set for cancer reporting on pathology specimens to *allow the patient to navigate the entire continuum of care*
  - Alternatively described as ‘checklist’ for cancer reporting (i.e. ensure completeness)
  - Widespread use and adoption driven by Commission on Cancer (CoC) accreditation requirements (2004)

The US Experience: Cancer Protocols

- **Cancer Protocols introduced in 1986**
  - Introduction of CAP Laboratory Accreditation Program requirements for use in 2015 required refinement of definitions and process:
    - ***Minimum data set*:** Contains information necessary for patient to navigate entire continuum of care

The US Experience: Cancer Protocols

- **Cancer Protocols introduced in 1986**
  - Introduction of CAP Laboratory Accreditation Program requirements for use in 2015 required refinement of definitions and process
    - **'*Synoptic format*': ** Standardized format to improved readability of report and reduce input and output interpretive errors.
      - Four simple rules:
        - All data elements together in one place in pathology report
        - Use of paired format (data element: response)
        - Each data element : response pair on separate lines
        - All core elements reported whether applicable or not

The US Experience: Cancer Protocols

- **Cancer Protocols introduced in 1986**
  - Introduction of CAP Laboratory Accreditation Program requirements for use required refinement of definitions and process:
    - **Applying the concepts of high quality clinical practice guideline development to protocol revision**
      - Institute of Medicine standards for high quality clinical practice guideline development and revision (2011)
      - Focus on transparency and evidence-based development and revision

The US Experience: Electronic Checklists

- **Introduction of the electronic checklist (eCC)**
  - Introduces structured data capture as a key feature of cancer reporting
  - Allows for improved reporting
    - Different input and output formats
    - Reduces errors in cancer reporting (both input and output interpretive errors)
    - Encourages use of standardized terminology for reporting

The US Experience: Electronic Checklists

- **Introduction of the electronic checklist (eCC)**
  - Allows for downstream uses:
    - Easy integration into electronic health records
    - Clinician dashboards and integrated disease reporting
    - Clinical decision support at the point of care
    - Patient-facing technologies
    - Tumor registries
    - Rapid learning systems
    - Accreditation and quality program compliance

The US Experience: Biomarker Reporting

- **Biomarker Reporting**
  - Prior to 2013: biomarker testing incorporated as part of Cancer Protocol
  - 2013: College of American Pathologists (CAP) Biomarker Committee established
    - Initial goal :
      - Standardize biomarker reporting and
      - Separate biomarkers from cancer reporting to address pathology workflow issues
    - Published 12 templates separate from the Cancer Protocols
    - Historical data shows not widely used with the exception of breast biomarkers
  - 2017: Committee dissolved and function re-incorporated into Cancer Committee

The US Experience: Biomarker Reporting

- **Biomarker Reporting: Lessons Learned**
  - A ‘one-size-fits-all’ approach to standardization suboptimal
  - Separate reporting of biomarkers from cancer reporting
    - Addresses pathologist workflow issues but NOT output
    - Results in fragmentation of cancer reporting from clinician perspective
  - Expanded panel testing, WES, WGS, etc. brings significant challenges to cancer reporting
  - Challenges with keeping protocols current with rapid pace of biomarker testing
  - Challenges with using the appropriate nomenclature for reporting
  - No easy answer to whether to or how to incorporate methodology into report

Issues and Challenges

- **Defining biomarkers**
  - Does reporting of methodology matter: Clinical vs molecular oncology perspectives
  - Actionable vs. non-actionable mutations: ‘variants of unknown significance’:
    - Hotspot mutation testing
    - Actionable gene panels
    - Disease focused gene panel
    - Comprehensive gene panel
    - Whole exome sequencing (WES)
    - Whole genome sequencing (WGS)

Issues and Challenges

- **Challenges with reporting biomarkers**
  - Often not available at time of cancer reporting
  - Outside laboratory testing
  - Fragmented reporting increases risk of clinical error
  - Reporting of methodology
  - The rapidly expanding landscape of biomarker testing and keeping cancer reporting current

Way Forward

- **Challenge: to create a comprehensive cancer report that includes ALL information necessary for patient to navigate the entire continuum of care**
  - Should include
    - histologic and anatomic staging information from specimen that informs clinical management
    - All relevant biomarker information to inform treatment and prognosis
    - Any relevant biomarker information that is definitional

Way Forward

- **Challenge: to create a comprehensive cancer report that includes ALL information necessary for patient to navigate the entire continuum of care**
  - Continuum of care may span months to years
    - Histologic information/staging information represents a single point in continuum
    - Biomarker data may
      - Be requested at a later time in the continuum of care
      - Variants of unknown significance may become actionable at a later time in the continuum of care

Way Forward

- **Challenge: to create a comprehensive cancer report that includes ALL information necessary for patient to navigate the entire continuum of care**
  - Challenges:
    - Biomarker testing often performed at external labs and reported separately
    - Pathology reporting of biopsy or definitive resection often cannot wait for biomarker testing to be completed
    - Reporting of biomarkers separate from histologic reporting creates opportunity for interpretative error

Way Forward

- **Challenge: to create a comprehensive cancer report that includes ALL information necessary for patient to navigate the entire continuum of care**
  - Challenges:
    - Biomarker testing may be extensive and problematic to incorporate into report
    - Issues with reporting of variants of unknown significance; what if it becomes actionable at a later date?

Way Forward

- **The ‘Layered’ approach:**
  - Utilizing a multi-tiered approach to reporting
    - Integrated disease reporting (‘integrated diagnosis’)
    - Histologic diagnosis
    - Biomarker testing
  - Concept first articulated by ICCR based on new WHO schema for CNS tumors
  - Allows for use by resource limited facilities
  - CAP protocols to be released utilizing approach:
    - CNS tumors
    - Leukemias and lymphomas

Way Forward

- **The ‘Layered’ approach:**
  - Unanswered questions:
    - Approach not field-tested for input and output i.e. *Is this approach actually an improvement over prior formats?*

Way Forward

- **Any long term solution will likely require utilizing structured data capture and focusing on true 'integrated disease' reporting**
  - Allows for creation of a patient-specific output format that includes:
    - Defined histologic data set from resection or biopsy specimens
    - Biomarker data that includes data pulled from external lab
    - Fields for updated diagnosis and additional testing performed at later date
    - Ability to integrate and update actionable mutations at a future point in continuum of care
    - Ability to integrate or utilize large data sets from WGS/WES

Way Forward

- **Any long term solution will likely require utilizing structured data capture and focusing on true ‘integrated disease’ reporting**
  - Allow for methodology to be incorporated and utilized as metadata.
  - Will require widespread standardization of biomarker reporting across external labs
  - A complicated solution: Will require extensive stakeholder input

Way Forward

- **Any long term solution will likely require utilizing structured data capture and focusing on true 'integrated disease' reporting**
  - *Ultimate goal should be to create an output report that is:*
    - Current at any given time in the continuum of patient care AND
    - Contains the complete set of data necessary for the patient to appropriately navigate the continuum of care