Challenges of Implementing Best Specimen Practices

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Questions to be Answered

- Why are best practices imperative?
- How will we find the best ones?
- What are the implementation issues?
- How can they be addressed?
Many new tests are being developed whose accuracy is critical
- Predict patient likelihood of disease
- Predict patient response to treatment,
- Define appropriate dose or drug
- Exclude patients from treatment

Preanalytic variables have been poorly studied so much confusion exists about methods

Preanalytic variables are source of most variation in some test results
Proliferation of Testing

• 660 tests in 1690 diseases are commercially available for germline mutations/alterations of genes in 2009*

• There should be a similar number of tests which predict patient treatment responses
  • Currently about 30 tests which stratify patients and are used to define expensive and/or potentially toxic treatment
    • Number has gone up very slowly because of variation

• How can we quickly find the best tests to make drugs effective and safe for patients?

* Genetest.com
Case Example

- 1987 HER2 gene found to be important in breast cancer
- 1999 breast cancer drug targeting HER2 developed with companion diagnostic test
- 2002 clinical trials showed 13-18% false positive rate for testing
  - Many errors related to incorrect preanalytical handling
  - Poor information available about correct methods
- 2006 guideline tried to remedy by proposing standard methods…are they the best?
Data Conundrum

• Few papers published which define
  • Best fixatives for various specimen types
    to allow specific tests to be done
    • Same for DNA, RNA, Protein
      expression?
    • Same for cells, biopsy, resection?
  • How long should samples be fixed?
  • Does handling before fixation matter for every test?
The Reality is Improving

- Standardized methods of prospective collection of specimens will be addressed in BRN symposium
- Research underway but not complete to understand important collection variables among many possible ones
- Funding for prospective tissue collection has been offered through NCI
- CaTissue provides data base for collection parameters
- Publishing standards are being developed
Implementation Issues

- If protocols are defined and tested, will they be routinely used in laboratories?
- What are barriers to adoption?
- How can barriers be addressed?
- What other issues will delay implementation?
Case Study

- Incidence of breast cancer in Philippines is similar to USA
- All breast cancer was thought to be estrogen receptor (ER) negative
- Richard Love MD went to Philippines and did a study
  - Rapidly obtained, fixed samples for ER on cohort of breast cancer patients
  - Same percent positive (70%) as in USA
Case Study, Con’t

- Experience dictated result so no attempt to improve testing despite information about appropriate procedure
- Samples sat unfixed at room temperature for long periods
- Samples transported long distances before fixation
- Samples fixed without processing in batches
- No attempt to standardize anything except testing

*If you do what you have always done, you will get the result you have always gotten!*
Implementation Strategies

- Use data to encourage change
  - Research publications on best practices
  - Consensus opinion
  - Case studies of successful/unsuccessful performance
  - Measure own performance
  - Involve all stakeholders
- Consider defined process to implement new strategies
  - Clinical Quality Improvement tools
  - Behavioral management
Implementation Steps 1

- What is the standard you want to implement?
- Use data to understand variation in current process so that everyone will buy into effort
- Involve all stakeholders
- Define current process. Is there best implementation practice?
- Design new process
  - Practical and locally logical
  - Use best practice principles with local innovation
- Identify champions to carry the message
ER in Intermountain Healthcare

- All ER testing done in one location
- 27 hospitals where breast cancers could be removed
- Processes vary by site

**Question:**
- If all testing done in standard way, would outcomes be related to pre analytic variables at site?
- Outcome to test: ER negative rate
### Frequency of ER negative test results by hospital

<table>
<thead>
<tr>
<th>Hospital</th>
<th>Cases</th>
<th>ER positive</th>
<th>ER negative</th>
<th>% ER negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hosp A</td>
<td>217</td>
<td>155</td>
<td>62</td>
<td>28.6%</td>
</tr>
<tr>
<td>Hosp B</td>
<td>196</td>
<td>154</td>
<td>42</td>
<td>21.4%</td>
</tr>
<tr>
<td>Hosp C</td>
<td>853</td>
<td>659</td>
<td>194</td>
<td>22.7%</td>
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<tr>
<td>Hosp D</td>
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<td>435</td>
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<tr>
<td><strong>Ref Hosp</strong>*</td>
<td><strong>1555</strong></td>
<td><strong>1250</strong></td>
<td><strong>305</strong></td>
<td><strong>19.6%</strong></td>
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<tr>
<td>Hosp F</td>
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<td>796</td>
<td>157</td>
<td>16.5%</td>
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<tr>
<td>Hosp G</td>
<td>733</td>
<td>563</td>
<td>170</td>
<td>23.2%</td>
</tr>
<tr>
<td><strong>ALL</strong></td>
<td><strong>5077</strong></td>
<td><strong>4012</strong></td>
<td><strong>1065</strong></td>
<td><strong>20.9%</strong></td>
</tr>
</tbody>
</table>

*Surgical specimens removed and tested in house at the reference laboratory Sample from 27 hospitals processed at 6)*
Data Analysis

• We found that ER negative was significantly higher in some facilities and in most facilities on weekends (Friday/Saturday excisions)
• The findings in 5077 pts over 7 years during which the assay has been stable.
• Data was controlled for variation due to stage of disease, age of patient and tumor size.
• We concluded and reported that this increased ER negative rate was likely due to the more variable preanalytic variable handling on weekends and at remote sites.
Stakeholders

- Patients
- Surgeons
- Medical Oncologists
- OR staff
- Grossing room staff
- Histologists
- Pathologists
- Transcriptionists
- IS personnel
- Lab Administrators
Communication

- All stakeholders have data presentation of Intermountain data and literature
- Patients informed by caregivers only
- Data sharing and problem discussion in facility and specialty based manner
- Each facility was asked to identify a person to take responsibility for the local process
- Common strategies were discussed
  - Recording time of resection, time of fixation, fixation time, type of fixation
Implementation Steps 2

- Implement new process
- Get feedback about barriers
- Measure impact
- Share data with stakeholders
- Use teamwork to modify plan if necessary
- Remeasure impact
- Disseminate new plan
Barriers in ER Example

- **Time**
  - IS personnel took 3 months to create method to record times in Word macro
  - No APIS method for recording
  - Common solution was dictation and calling OR

- **Apathy**
  - Pathologists and OR personnel resisted changes in process
  - Some facilities would not comply because their pathologist also resisted
  - Surgeons initially resisted lengthening of fixation time but ultimately complied because of data review

- **Lack of leadership**
  - Some facilities had no champions who would step forward
  - Some facilities would not convene teams to work on issues
• **Some lack leadership skill and desire**
  - Not typically part of job of AP pathologists
  - Do not understand critical role of such variables as part of their job
• **Perception by some that this is unfunded mandate rather than necessary part of job**
  - Institutions should clearly define team leader efforts as part of job
  - CMS should provide pay for performance mandates
• **Some lack understanding of process of performance improvement**
  - Requires institutional commitment to CQI
  - Requires training and practice
• **Lack of data system support to provide data**
• **CAP understands the importance of standardizing practice**
  • Focus on Center for Best Practices
  • Widely supported by pathologist members
• **CAP understands natural reticence of pathologists**
  • Clearly articulated by president Jared Schwartz
  • Speaker training has been created
  • Team leader training has been modified
  • Self assessment modules will include this vital role
  • CAP Institute for specialized training will embark on training programs with awarding of certificates to those who comply
• Quality Improvement Programs need to also be developed
Summary

• BRN symposia will define best practice strategies
• OBBR will fund research and publication mandates to make sure literature supports best practice
• Future efforts must provide way for labs to share implementation strategies and understand necessary steps
• CAP will facilitate and participate
• APIS/EMR pressure needed to create simple data collection systems for the required elements
• Clinical Quality Improvement training will be needed in many institutions
  • Must involve leaders and team members
  • Must involve all stakeholders