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# Challenges of Implementing Best Specimen Practices

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NATIONAL  
CANCER  
INSTITUTE



## Questions to be Answered

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- **Why are best practices imperative?**
- **How will we find the best ones?**
- **What are the implementation issues?**
- **How can they be addressed?**



# Best Practices Imperative

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- **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

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- **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

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- **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

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- **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

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- **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

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- **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

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- **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 study**
  - Rapidly obtained, fixed samples for ER on cohort of breast cancer patients
  - Same percent positive (70%) as in USA



## Case Study, Con't

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- 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

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- **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

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- **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

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- **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

# Data

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## Frequency of ER negative test results by hospital

Hospital	Cases	ER positive	ER negative	% ER negative
Hosp A	217	155	62	28.6%
Hosp B	196	154	42	21.4%
Hosp C	853	659	194	22.7%
Hosp D	570	435	135	23.7%
<b>Ref Hosp*</b>	<b>1555</b>	<b>1250</b>	<b>305</b>	<b>19.6%</b>
Hosp F	953	796	157	16.5%
Hosp G	733	563	170	23.2%
<b>ALL</b>	<b>5077</b>	<b>4012</b>	<b>1065</b>	<b>20.9%</b>

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



# Data Analysis

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- 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

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





# Communication

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- **All stakeholders has 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

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- **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

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- **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



## Pathologists as Team Leaders

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- **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**



## College of American Pathologist Role **OBBR** Office of Biorepositories and Biospecimen Research

- **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

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- **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