2008 Assessment of the Department of Defense’s Tissue Repository
Located at the Armed Forces Institute of Pathology in Washington DC

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Agenda

2008 Assessment of the Department of Defense’s Tissue Repository Located at the Armed Forces Institute of Pathology in Washington DC

• Background
• Methods
• Results
• Recommendations
• Valuation
Background

- BRAC recommendation in 2005 to disestablish AFIP
- Consensus panel convened in August 2005
- DoD -USUHS commissioned a comprehensive study to evaluate repository and recommendation future directions
- Awarded to Asterand in October of 2007

Very honored to have been awarded this contract
RFP Tasks

1. Database accuracy (PIMS/Legacy)
2. Database assessment (BRAC)
3. Sampling plan
4. Effect of evolving terminology
5. Quality of accessioned materials
6. Quantification of viable versus exhausted material
7. Validity of blocks - lesions
8. Quantification of normal tissue
9. Valuation of holdings
10. Continuity of input for repository viability
AFIP tissue holdings

>7 million cases; >75 million samples
1917 to 2008

FFPE blocks, tissue slides, “wet tissue”
Four active databases, two collections
Climate controlled warehouses
Central Repository Sampling Strategy

1. AFIP Central Repository – Seven time bins
   - PIMS: 1999-2002

2. Disease Categories
   - Colorectal Cancer
   - Prostate cancer
   - Tuberculosis
   - Synovial Sarcoma

3. Wet Tissue – random sampling

4. Limited to human tissue specimens
Central Repository - Overview

Central Repository databases

- PIMS
- PANLARS
- SNDO

Total Number of Accessions: 4,193,219

Databases are suited for clinical care and pathology
Criteria for Analysis

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Possible Values</th>
<th>Sample Estimate</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retrievable</td>
<td>Yes/No</td>
<td>Retrieval %</td>
<td>Is the requested material retrieved (received or in use by a researcher at AFIP)</td>
</tr>
<tr>
<td>Relevant</td>
<td>Yes/No</td>
<td>Relevant %</td>
<td>If case is examined does clinical data represent the disease of interest; If H&amp;E slide is readable does it represent the disease of interest</td>
</tr>
<tr>
<td>Overall Recovery Rate</td>
<td></td>
<td>Overall Recovery %</td>
<td>Calculated as Retrieval%  Relevant%</td>
</tr>
</tbody>
</table>

**Clinical Data**
- Keyword search
- Retrievability & accuracy of clinical data records

**Pathology data**
- Physical presence of materials
- Presence of diseased tissue on slides
- Presence of normal tissue
- Size of block, mm³
Central Repository Clinical Data Results

A. Colorectal Cancer

<table>
<thead>
<tr>
<th>Time Period</th>
<th>Overall CD Pass Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1917-1951</td>
<td>65</td>
</tr>
<tr>
<td>1951-1959</td>
<td>70</td>
</tr>
<tr>
<td>1960-1969</td>
<td>75</td>
</tr>
<tr>
<td>1970-1979</td>
<td>80</td>
</tr>
<tr>
<td>1980-1989</td>
<td>85</td>
</tr>
<tr>
<td>1990-1999</td>
<td>90</td>
</tr>
<tr>
<td>1999-2002</td>
<td>95</td>
</tr>
<tr>
<td>( R^2 = 0.0002 )</td>
<td></td>
</tr>
</tbody>
</table>

B. Prostate Cancer

<table>
<thead>
<tr>
<th>Time Period</th>
<th>Overall CD Pass Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1917-1951</td>
<td>65</td>
</tr>
<tr>
<td>1951-1959</td>
<td>70</td>
</tr>
<tr>
<td>1960-1969</td>
<td>75</td>
</tr>
<tr>
<td>1970-1979</td>
<td>80</td>
</tr>
<tr>
<td>1980-1989</td>
<td>85</td>
</tr>
<tr>
<td>1990-1999</td>
<td>90</td>
</tr>
<tr>
<td>1999-2002</td>
<td>95</td>
</tr>
<tr>
<td>( R^2 = 0.009 )</td>
<td></td>
</tr>
</tbody>
</table>

C. SS & TB

<table>
<thead>
<tr>
<th>Time Period</th>
<th>Overall CD Pass Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1917-1951</td>
<td>65</td>
</tr>
<tr>
<td>1951-1959</td>
<td>70</td>
</tr>
<tr>
<td>1960-1969</td>
<td>75</td>
</tr>
<tr>
<td>1970-1979</td>
<td>80</td>
</tr>
<tr>
<td>1980-1989</td>
<td>85</td>
</tr>
<tr>
<td>1990-1999</td>
<td>90</td>
</tr>
<tr>
<td>1999-2002</td>
<td>95</td>
</tr>
<tr>
<td>( R^2 = 0.025 )</td>
<td></td>
</tr>
</tbody>
</table>
Central Repository Pathology Results

A. Colorectal Cancer

- Time Period: 1917-1951
- Overall Pathology Pass Rate (%): 55
- R² = 0.000003

- Time Period: 1951-1959
- Overall Pathology Pass Rate (%): 60

- Time Period: 1960-1969
- Overall Pathology Pass Rate (%): 65

- Time Period: 1970-1979
- Overall Pathology Pass Rate (%): 70

- Time Period: 1980-1989
- Overall Pathology Pass Rate (%): 75

- Time Period: 1990-1999
- Overall Pathology Pass Rate (%): 80

- Time Period: 1999-2002
- Overall Pathology Pass Rate (%): 85

- R² = 0.1

B. Prostate Cancer

- Time Period: 1917-1951
- Overall Pathology Pass Rate (%): 95

- Time Period: 1951-1959
- Overall Pathology Pass Rate (%): 90

- Time Period: 1960-1969
- Overall Pathology Pass Rate (%): 95

- Time Period: 1970-1979
- Overall Pathology Pass Rate (%): 100

- Time Period: 1980-1989
- Overall Pathology Pass Rate (%): 90

- Time Period: 1990-1999
- Overall Pathology Pass Rate (%): 80

- Time Period: 1999-2002
- Overall Pathology Pass Rate (%): 75

- R² = 0.001

C. SS & TB

- Time Period: 1917-1951
- Overall Pathology Pass Rate (%): 100

- Time Period: 1951-1959
- Overall Pathology Pass Rate (%): 95

- Time Period: 1960-1969
- Overall Pathology Pass Rate (%): 90

- Time Period: 1970-1979
- Overall Pathology Pass Rate (%): 85

- Time Period: 1980-1989
- Overall Pathology Pass Rate (%): 80

- Time Period: 1990-1999
- Overall Pathology Pass Rate (%): 75

- Time Period: 1999-2002
- Overall Pathology Pass Rate (%): 70

- R² = 0.1
<table>
<thead>
<tr>
<th>Presumed Disease</th>
<th>Clinical Data Recovery Rate*</th>
<th>Sample Recovery Rate*</th>
<th>Overall Recovery Rate*</th>
</tr>
</thead>
<tbody>
<tr>
<td>SNDO Total</td>
<td>80%</td>
<td>83%</td>
<td>67%</td>
</tr>
<tr>
<td>PANLARS Total</td>
<td>84%</td>
<td>90%</td>
<td>79%</td>
</tr>
<tr>
<td>PIMS Total</td>
<td>89%</td>
<td>95%</td>
<td>84%</td>
</tr>
<tr>
<td>Grand Total</td>
<td>83%</td>
<td>89%</td>
<td>74%</td>
</tr>
</tbody>
</table>
Description
Collections from 24 Military Treatment Facilities
Clinical records are scanned and converted to PDF document (AWARS)
Only 64% of cases have associated specimens

Methodology
13 Bases
Keyword search for breast cancer
Clinical data expected to have 100% retrievability

Pass/fail criteria for pathology was modified
Primary diagnosis did not have to match search criteria
At least one slide had to correctly represent the primary diagnosis stated on report
## BRAC Results

<table>
<thead>
<tr>
<th>Base</th>
<th>Clinical Data Recovery Rate</th>
<th>Sample Recovery Rate</th>
<th>Overall Recovery Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>97th General</td>
<td>83%</td>
<td>98%</td>
<td>81%</td>
</tr>
<tr>
<td>Carswell</td>
<td>53%</td>
<td>99%</td>
<td>52%</td>
</tr>
<tr>
<td>Fitzsimmons</td>
<td>37%</td>
<td>100%</td>
<td>37%</td>
</tr>
<tr>
<td>Fort Ord</td>
<td>86%</td>
<td>96%</td>
<td>83%</td>
</tr>
<tr>
<td>Homestead</td>
<td>57%</td>
<td>100%</td>
<td>57%</td>
</tr>
<tr>
<td>Letterman</td>
<td>54%</td>
<td>100%</td>
<td>54%</td>
</tr>
<tr>
<td>MacDill</td>
<td>89%</td>
<td>95%</td>
<td>85%</td>
</tr>
<tr>
<td>March</td>
<td>87%</td>
<td>98%</td>
<td>85%</td>
</tr>
<tr>
<td>Maxwell</td>
<td>54%</td>
<td>97%</td>
<td>52%</td>
</tr>
<tr>
<td>Millington</td>
<td>95%</td>
<td>98%</td>
<td>93%</td>
</tr>
<tr>
<td>Oakland</td>
<td>38%</td>
<td>99%</td>
<td>38%</td>
</tr>
<tr>
<td>Orlando</td>
<td>76%</td>
<td>97%</td>
<td>74%</td>
</tr>
<tr>
<td>Orlando</td>
<td>89%</td>
<td>98%</td>
<td>87%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>69%</strong></td>
<td><strong>98%</strong></td>
<td><strong>68%</strong></td>
</tr>
</tbody>
</table>
Quality of Specimens

Wet tissue quality was quite poor overall, with only 1% of the 438 samples measured still being in liquid.
IHC Results

- Colorectal cancer and prostate cancer cases with normal tissue slides selected
- Performed Pan-cytokeratin staining
- Good quality results overall for IHC tests
- No evidence of time-dependent decrease in stain specificity

Normal colon stained with Cytokeratin
Conclusions

THE COLLECTIONS ARE IN GOOD SHAPE

BREADTH, DEPTH, VOLUME OF SAMPLES

HOLD UNPARALLELED RESEARCH POTENTIAL

USEFUL FOR MODERN DISEASE RESEARCH AND EDUCATION

There is no other centralized tissue bank in the world with as many samples, representing such a wide breadth of diseases over so long a period of time.
Additional Steps to ready the Collection for research use

1. Assess the retrievability and quality of the RNA of tissues in both the Central and BRAC repositories

2. Modify the BRAC and Central Repository databases to ensure that appropriate information for research and retrieval is easily available

3. Enhance clinical data by adding data from external patient medical records (treatment and follow-up) where available

4. Classify and organize the tissue samples for efficient retrieval and reduce the number of samples that have no further value

5. Facilitate controlled access to the repositories and ethical protocols for the use of samples.
   
   Establish a scientific committee to oversee projects

6. Ensure that the inflow of useable materials into the repositories is equal to or greater than the outflow

Recommendations are best managed using a diseased-based approach
“Make an initial assessment of the value of the holdings to the research/commercial community at large, both in terms of current and emerging technologies. Recommendations for areas of improvement to increase value and usability are appropriate.”
Summary of Valuation

Commercial appraisal of Central and BRAC repositories places value between $423 million and $3.3 billion

Valuation is dependent upon

1. Cost recovery model
   1. Whole Sample Transfer Model
   2. Derivative Transfer Model
2. RNA qualification
3. Organizing collections by disease cohorts
4. Improved characterization and clinical annotation of clinical data and samples
5. Physical organization of BRAC material samples
6. Database improvements for BRAC and Central repositories
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