TIES Cancer Research Network
Y2 Face to Face Meeting
U24 CA 180921

Session III  Pilot Projects

October 29th, 2014
University of Pennsylvania
<table>
<thead>
<tr>
<th>Time</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>8:00-8:15</td>
<td>Goals for the Meeting, Overall Summary of Progress in Y1; Y2 Project Plan (Crowley-Jacobson)</td>
</tr>
<tr>
<td>8:15-8:30</td>
<td>University of Pittsburgh Update (Crowley-Jacobson)</td>
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<tr>
<td>8:30-9:00</td>
<td>University of Pennsylvania Update (Feldman)</td>
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<tr>
<td>9:00-9:30</td>
<td>Georgia Regents University (Bollag)</td>
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<tr>
<td>9:30-10:00</td>
<td>Roswell-Park Cancer Institute (Gaudioso)</td>
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<tr>
<td>10:00-10:30</td>
<td>Demonstration of Multi-Site Search; Discussion (Chavan and Crowley-Jacobson)</td>
</tr>
<tr>
<td>10:30-10:45</td>
<td>Break</td>
</tr>
<tr>
<td>10:45 – 11:15</td>
<td>Policies and Processes Subcommittee ~ Completed Work and Next Steps (Crowley-Jacobson, Bollag, Weaver, Murphy)</td>
</tr>
<tr>
<td>11:15 – 12:00</td>
<td>National Mesothelioma Virtual Brank (Amin)</td>
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<tr>
<td>12:00 – 12:15</td>
<td>Other emerging pilot projects (Feldman, Crowley-Jacobson)</td>
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<tr>
<td>12:15 – 12:45</td>
<td>LUNCH</td>
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NATIONAL MESOTHELIOMA VIRTUAL BANK (NMVB)
(HTTP://WWW.MESOTISSUE.ORG)
SUPPORTED BY CDC/NIOSH GRANT 2U24OH009077-08

Waqas Amin, MD
Senior Research Scientist
Department of Biomedical Informatics
University of Pittsburgh
Overview:

- The National Mesothelioma Virtual Bank (NMVB) provides de-identified annotated mesothelioma biospecimens to the mesothelioma research community.
- We collect retrospective and prospective mesothelioma cases at New York University (NYU), University of Pennsylvania (U Penn), University of Pittsburgh (U Pitt) and Rowell Park Cancer Institute (new collection site).
- Key to this resource is continued annotation of mesothelioma biospecimens including demographic, epidemiologic, clinicopathologic, follow-up and recurrence data for all biospecimens collected.
- The NMVB database allows a user to query the biospecimen resource to identify cohorts for translational research.
- We then provide well-annotated high quality mesothelioma biospecimens and data to approved researchers via a Letter of Intent – see [http://www.mesotissue.org/apply.cfm](http://www.mesotissue.org/apply.cfm)
NMVB Resource Organization:

- **STEERING COMMITTEE**
  - Member are Principle/Co-Investigator of NMVB & CDC/NIOSH

- **NMVB Resource Management Core**

- **RESEARCH EVALUATION PANEL (REP)**

- **MESO-FOUNDATION**
  - Mesothelioma Advocacy Group

- **WORKING GROUP**
  - Members are data managers, Tissue Bank Technicians, Cancer Registrars and Clinical Nurse Coordinators

- **NMVB-CENTRAL DATA MANAGEMENT CORE**

- **NYU**
- **U. Penn**
- **UPMC**
- **RPCI**
Common Data Elements (CDEs):

- With leadership of the MVB Coordinating Committee, established a CDE subcommittee to develop CDEs pertinent to mesotheliomas: demographic, epidemiologic, clinical, pathologic specimen and block annotation, follow up and outcome.

- Major standards used to build CDEs:
  - North American Association of Central Cancer Registry (NAACCR) core elements.
  - College of American Pathology (CAP) checklists.
  - American Joint Commission on Cancer (AJCC) staging.
  - Association of Directors of Anatomic and Surgical Pathology (ADASP) guidelines.
NMVB-CAE Model:

- Built upon the Clinical Annotation Engine (CAE) developed by DBMI as part of the caBIG project.
- Takes a UML Domain Model as input.
- Generates core application components:
  - Database
  - Metadata
  - Query capability
  - Data viewers
  - Data entry forms
- Iterative – model can change over time; system can be regenerated
- Extensible – models can be layered on top of one another
Human Subjects:

- Individuals to be approached for participation in the NMVB include all adult (age ≥ 18 years old) patients who are receiving or seeking medical care for mesothelioma.

- Participation in the NMVB does not involve a risk of physical harm, women of childbearing potential will not be queried as to pregnancy status or tested for pregnancy

- Prisoners-patients shall not be approached for participation in the NMVB Registry.

- This study will not include children.
Specimen Collection:

- Tissue bank protocols are followed in the collection and storage by tissue bank technicians.

- Specimen Types:
  - Tissue Microarray with Clinical Data Annotation
  - Fresh Frozen Tissues
  - Blood Products: Serum, RBC, Plasma, Whole blood, Buffy Coat, etc...
  - Paraffin embedded blocks
Nurse coordinator notifies Health Sciences Tissue Bank (HSTB) personnel prior to the patient’s surgery of NMVB tissue candidate and follows up by faxing a consent to the HSTB.

E-mail notification to Post Doc and Project Coordinator on the upcoming surgery.

Surgical tissue is picked up at the OR and brought to the Gross Dissection room and is triaged under the auspices of a Pathologists’ Assistant.

The Surgical tissue is assigned a NMVB Study number.

Each portion received from the Pathologists’ Assistant (determined by amount and size of tissue) is to be divided into three portions:

- Bulk Frozen
- Formalin Tissue
- Fresh frozen OCT

Bulk frozen is kept in bitran bag and stored in -80°C.

Taken to research histology lab for processing to formalin fixed paraffin embedded (FFPE)

FF OCT is stored in a heat sealed bag @ -80°C.
Blood Products Collection & Processing Protocol

Nuncs should be labeled and aliquot as shown below and record on specimen sheet:

- 2 WB (whole blood – purple top before spinning)
- 2 B (buffy coat)
- 2 R (red blood cells)
- 10-20 P (plasma)
- 10-20 S (serum)

Research nurse coordinator call the tissue bank when patient is consented and pre-op, operative and post-op blood samples are drawn.

Blood is tubed to Gross Dissection Room in the Department of Pathology.

Tissue bank tech. receives 2-3 small purple tops and 1-2 large red tops along with a consent for the patient.

Nunc vials for the separated blood products are labeled with the NMVB Study# by tissue bank technician.

Before the purple tops are centrifuged, aliquot 2 nuncs with whole red blood. All peripheral blood tubes are put through the centrifugation process.

Purple top yields plasma, buffy coat and red blood cell aliquots.

Red top yields serum aliquots.
Mesothelioma Consenting, Tissue Banking and Clinical Data annotation workflow

TBIS: Tissue Bank inventory System,
RIS: Registry Information System,
CTTK: Clinical Trial Tool Kit,
NMVB: National Mesothelioma Virtual Bank
http://www.mesotissue.org/
Mesothelioma Tissue Resources Available for Your Research

The National Mesothelioma Virtual Bank (NMVB) is a virtual biospecimen registry designed to support and facilitate basic science, clinical, and translational research that will advance understanding of mesothelioma pathophysiology with the goal of expediting the discovery of preventive measures, novel therapeutic interventions, and ultimately, cures for mesothelioma. The NMVB Data and Query tool is a Java based application designed using a Model-Driven Development framework. This approach begins with a UML class model which is then used to generate all the other aspects of the application from the data tables through to the User Interface components. The code was written and is supported by staff at the Department of Biomedical informatics at the University of Pittsburgh.

MVB database version 3.0 has been released that provides researchers real-time access to demographic, epidemiologic, pathologic, genotype, and follow-up data associated with biospecimens at no cost. Researchers interested in utilizing NMVB samples for their research may submit an application. All researchers (academic or commercial, United States or foreign) may apply for NMVB tissue specimens.

NMVB currently has 979 annotated cases and 1207...
NMVB Tissue Microarrays (TMAs):

- **Tissue Microarray** (TMA) is used to examine the distribution of marker molecules in hundreds of different tissues displayed on a single slide.

- **U Pitt TMA**: 41 Mesothelioma cases; 36 cases have tissue cores from the primary lesion, 4 patients have tissue cores from a metastatic lesion and 1 patient has tissue cores from both the primary and metastatic lesions.

- **U. Penn TMA**: 4 TMA slides contain 61 mesothelioma cases. The TMA slides hold tissue core of primary, metastatic mesothelioma and control samples.

- **NYU TMA**: 37 cases have been included in the development of TMA which included primary metastatic, mixed lesions and control sample.

- TMA data excel, XML and maps files are available on the website [http://mesotissue.org/TMA](http://mesotissue.org/TMA)
## Percentage of Contribution / Each Site:

<table>
<thead>
<tr>
<th>Institutions</th>
<th>Retrospective Cases</th>
<th>Prospective Cases</th>
<th>Overall NMVB Total</th>
<th>% Contribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>NYU</td>
<td>158</td>
<td>102</td>
<td>260</td>
<td>22%</td>
</tr>
<tr>
<td>U. Penn</td>
<td>128</td>
<td>162</td>
<td>290</td>
<td>25%</td>
</tr>
<tr>
<td>*MSSM</td>
<td>42</td>
<td>4</td>
<td>46</td>
<td>4%</td>
</tr>
<tr>
<td>U.Pitt</td>
<td>403</td>
<td>167</td>
<td>570</td>
<td>49%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>731</strong></td>
<td><strong>435</strong></td>
<td><strong>1166</strong></td>
<td><strong>100%</strong></td>
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*MSSM joined the resource in November 2012
### NMVB Accrual-Blood Products:

<table>
<thead>
<tr>
<th>Type of Blood Products</th>
<th>Number of Cases</th>
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<tbody>
<tr>
<td>Serum</td>
<td>400</td>
</tr>
<tr>
<td>Whole Blood</td>
<td>305</td>
</tr>
<tr>
<td>Buffy Coat</td>
<td>225</td>
</tr>
<tr>
<td>Plasma</td>
<td>401</td>
</tr>
<tr>
<td>Red Blood Cells</td>
<td>245</td>
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### NMVB Accrual-Surgical Specimens:

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Surgical Procedure Type</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Biopsy Specimen</td>
<td>166</td>
<td>362</td>
</tr>
<tr>
<td>Paraffin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fresh Frozen</td>
<td></td>
<td>42</td>
<td>360</td>
</tr>
<tr>
<td>Bulk Frozen</td>
<td></td>
<td>12</td>
<td>108</td>
</tr>
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NMVB Biospecimens Request Status Report:

- To date over 34 requests have been received and 29 have been fulfilled, representing 25 different Universities and Research Institutes.

- Represent a total of 531 patients material shared with the mesothelioma research community.

- This is comprised by 666 paraffin blocks, 196 fresh frozen tissue samples and 742 of blood product samples as well as 145 TMAs and 200 control samples.

- This represents a total of 897 biospecimens distributed with over 58,300 de-identified data elements collected on individual biospecimens on patients in the NMVB database.

- Average turnaround from initial request to getting specimens is about 6 weeks.
Sustaining the Expansion of the National Mesothelioma Virtual Bank (NMVB)

- **Ongoing Aim:** To continue to serve the needs of the mesothelioma cancer research community by collecting tissue, blood and clinical data and providing efficient access to these federated resources. We will continue to collect patients’ clinical data and enroll them in the biospecimen bank at the original NMVB partners.

- **Expansion Aim:** To expand the NMVB to the Rowell Park Cancer Institute (RPCI) as a collection site.

- **Sustainability Aim:** To automate the biospecimens annotation through electronic extraction of clinical and pathology data from electronic health record (EHR), cancer registry system and integrating the Text Information Extraction System (TIES). We will also be implementing a more sustainable informatics federation model by deploying i2b2 (Informatics for Integrating Biology and the Bedside) and SHRINE (Shared Health Research Information Network) to maximize the effectiveness of the data mining process across NMVB sites. This will leverage the existing funding and informatics infrastructure from three other funding sources (NCATS, NCI and PCORI).
Design Principles (Sustaining Aim):

- Existing informatics solution is expensive, laborious and quickly exhausts the resource available to sustain the operation of tumor bank.

- To automate the biospecimens annotation through electronic extraction of clinical and pathology data from electronic health record (EHR) and cancer registry system.

- Adopting the Text Information Extraction System (TIES), a clinical document search engine, to identify the cases and reports.

- Adopting a new informatics federated model by deploying i2b2 (Informatics for Integrating Biology and the Bedside) and SHRINE (Shared Health Research Information Network) to maximize the effectiveness of the data mining process across collaborations.

- New Informatics model will leverage the existing funding from three other funding sources (CTSA-ACTS, NCI and PCORI).
Adopting TIES for NMVB Pathology Data Extraction:

- TIES application adoption will help to automate the extraction of pathology data and bio specimen annotation process for NMVB cohort at all collection sites.

- We plan to do initial test TIES application utility on prospective cohort of mesothelioma cases at U. Pitt before extending the same to partner sites.

- Pathology data elements are prioritized in three categories as per their availability in the pathology reports and need for research purposes.

- TIES application will process the first pass of U. Pitt prospective cases through NLP/Info extraction.

- The extracted data will be manually reviewed by web based annotation tool by the pathologist and then exported in i2b2 instance at U. Pitt.

- Tentative date to for the test plan is by the end of March 2015 and full implantation will be extended to all collection sites of NMVB by the end of July 2015.
NMVB-Federated Database Model

NMVB Related and Supported Publications:


Acknowledgment:

Collaborators:
- Center for Disease Control and Prevention (CDC)
- National Institute of Occupational Safety & Health (NIOSH)
- Mesothelioma Foundation (Meso Fndn)
- Mount Sinai School of Medicine (MSSM)
- New York University (NYU), New York City, NY
- University of Pennsylvania (U Penn), Philadelphia, PA
- University of Pittsburgh (U Pitt), Pittsburgh, PA
- Roswell Park Cancer Institutes (RPCI), Buffalo, NY

Future Partners: NCI Meso SPORE Core to NMVB in 2014 with the University of Hawaii (UHCC) via Meso SPORE to also include Mayo Clinic.

Leadership:
- Michael J. Becich MD, PhD (U Pitt)  
- Harvey I. Pass MD (NYU)  
- Rebecca Jacobson MD, MS (U Pitt)  
- Steven Abelda, MD (U Penn)  
- Carl Morrison, MD (RPCI)  
- Angela R. Omilian (RPCI)  
- Mary Hesdorfer (Meso Fndn)  
- Raja Flores, MD (MSSM)  
- Michael Feldman MD (U Penn)  
- Jonathan Melamed MD (NYU)  
- Anil V. Parwani MD, PhD (U Pitt)  
- David Bartlett, MD (U Pitt)  
- Carmelo Gaudioso (RPCI)  
- James Luketich M.D (U Pitt)  
- James Pingpank, MD (U Pitt)
Thank you
Morning

Welcome

8:00-8:15 Goals for the Meeting, Overall Summary of Progress in Y1; Y2 Project Plan (Crowley-Jacobson)

Project Status

8:15-8:30 University of Pittsburgh Update (Crowley-Jacobson)
8:30-9:00 University of Pennsylvania Update (Feldman)
9:00-9:30 Georgia Regents University (Bollag)
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10:30-10:45 Break
10:45 – 11:15 Policies and Processes Subcommittee ~ Completed Work and Next Steps (Crowley-Jacobson, Bollag, Weaver, Murphy)

Pilot Projects

11:15 – 12:00 National Mesothelioma Virtual Brank (Amin)
12:00 – 12:15 Other emerging pilot projects (Feldman, Crowley-Jacobson)
12:15 – 12:45 LUNCH
PathoChip (Feldman)

Metagenomic Assay for Identification of Microbial Pathogens in Tumor Tissues

Don A. Baldwin, Michael Feldman, James C. Alvina and Erie S. Robertson

ABSTRACT

Screening for thousands of viruses and other pathogenic microorganisms, including bacteria, fungi, and parasites, in human tumor tissues will provide a better understanding of the contributory role of the microbiome in the predisposition for, causes of, and therapeutic responses to the associated cancer. Metagenomic assays designed to perform these tasks will have to include rapid and economical processing of large numbers of samples, supported by straightforward data analysis pipeline and flexible sample preparation options for multiple input tissue types from individual patients, mammals, or environmental samples. To meet these requirements, the PathoChip platform was developed by targeting viral, fungal, and
Rosai-Dorfman Disease Cases at Pitt and Penn
PathoChip Pilot in TIES (Feldman, Penn)

- Approved IRB at Penn
- Need to get collaborator and approved IRB at Pitt (this will test our ‘fast’ IRB process)
- 1st time through approval process at Pitt
  - Penn Admin will create the study and request access
  - Collaborators at Pitt (Rebecca, John Ozolek)
  - Upload IRB protocol and IRB approval
  - Request will arrive at Pitt
  - Routed to Approval Process (Rebecca, Anil Parwani, HSTB)
  - Pitt Admin signs on to request
  - At that point Mike can search Pitt Repository
  - At point where tissue is requested we’ll need the UBMTA and the mechanism for cost recovery at Pitt
Discussion

• Time for more Pilot Projects – We need 4 more by the end of Y2
  – Focus on projects that can go through the step up procedure
  – Not all need to go to tissue
  – How should we handle collaborators?
  – How can we simplify compliance process?

• What existing projects would be useful?

• What kinds of projects do we need to test the system?