Banking AIDS-Related Malignancies in sub-Saharan Africa

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Worldwide Cancer Burden

- In 2010, Cancer is single greatest cause of mortality worldwide
  (> 1 million cases in sub-Saharan Africa)
- By 2020, 16 million new cancer cases
- By 2030, 27 million new cancer cases

SCO Ed ABook 670-674, 2009
Cancer incidence is increasing around the world

- Cancers are debilitating and lethal
- Treatment is resource intense
- Prevention requires energy, commitment, and financial resources
- Both treatment and prevention require knowledge
Platform for knowledge

- Top-down guidelines, methods and modalities
- Bottom-up platforms
Platform for knowledge

- Integrated
Basic Requirements for a HIV/AIDS Cancer Biorepository Platform

- HIV infected population
- Cancer prevalence
- Medical care conduits
- Cancer diagnosis/tissue preservation (pathologist)
- Established organization to support research (Universities/Institutes)
- Biorepository space
Adults and children living with HIV, by region, 1990–2007

The graph shows the number of people living with HIV by region, with the following trends:

- **Sub-Saharan Africa** shows the highest number of people living with HIV, with a significant increase from 1990 to 2007.
- **Middle East & North Africa** also shows a notable increase, though it remains lower than Sub-Saharan Africa.
- **Latin America and Caribbean**, **North America and W & C Europe**, and **Asia** have comparatively lower numbers, with moderate increases over the period.
- **Eastern Europe & Central Asia** and **Oceania** have the lowest numbers, with a steady increase.

The data highlights the ongoing global challenge of HIV/AIDS, with Sub-Saharan Africa bearing the brunt of the epidemic.
Malignancies in sub-Saharan Africa
Gender and Site, 2002

Source: WHO 2004
Mulago Hospital Complex, Kampala, Uganda

Makerere University
Uganda Cancer Institute, Kampala, Uganda
Uganda Cancer Institute, Kampala, Uganda
Histology Laboratory

- Trained personnel
- Laboratory space
  but
- Electrical outages
- Financial constraints
Preservation of Tissue
Pre-analytical barrier

**Formaldehyde**

34-40% gas by weight

10% formalin (4% formaldehyde)

- 40% formaldehyde: 100ml
- Distilled tap water: 900ml
# Formalin Fixation

- **Neutral buffered formalin**

  - 40% formaldehyde 100ml
  - Sodium Dihydrogen phosphate monohydrate 4g
  - Disodium hydrogen phosphate anhydrous 6.5g
  - Distilled water 900ml
Aged, poorly functioning equipment can be replaced. Electricity is unreliable.
Technical Challenges

pre-analytical barrier

- Laboratory supply shortages
Pathology Archives, a tissue biorepository
10% Formaldehyde
Proteins and DNA, RNA, other

- **Pre-analytical variability**
  - Selected samples
  - Selected analytes

- **Analytical variability**
  - Partial preservation analytes
  - Absence of analyte
    - Preservation failure
    - Destruction
### Immunohistochemistry (IHC) protein analytes

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<thead>
<tr>
<th></th>
<th>H&amp;E</th>
<th>CD20 (IHC)</th>
<th>CD10 (IHC)</th>
<th>BCL6 (ISH)</th>
<th>EBER (ISH)</th>
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<tbody>
<tr>
<td><strong>Case A</strong></td>
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<td><strong>Case B</strong></td>
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**Burkitt Lymphoma**
Plasmablastic Lymphoma

H&E  
CD20  CD44

MUM1

Ki67

HHV8-
## Plasmablastic Lymphoma

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<thead>
<tr>
<th>Test</th>
<th>Image 1</th>
<th>Image 2</th>
<th>Image 3</th>
<th>Image 4</th>
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**HHV8 (LANA-1)** negative
Diffuse large B-cell lymphoma (DLBCL) 
Germinal centre B-cell-like (GCB)
Diffuse large B-cell lymphoma (DLBCL)
Activated B-cell phenotype
Anaplastic Lymphoma

H&E

CD45RO

CD30

Ki67

p53

B cell markers negative NK
Conclusions

- Tissue biorepository offers a **bottom up** opportunity to implement pre-analytical controls.

- Frozen or specially preserved tissues (ex. RNA later) support isolation of DNA, RNA, proteins and other analytes **but**:
  - Fresh tissues are difficult to obtain outside of a research protocol.
  - Frozen or refrigerated tissues are expensive to maintain. (electricity unreliable)
Conclusions

- Fixed tissues are collected as part of patient care (<50% CA) and autopsy evaluations.
  - Optimally fixed tissues are a valuable resource.
  - Without pre-analytical controls, FFPE tissues have marginal value.
  - Current tissues can reveal scope of cancers not previously clearly documented.
Conclusions (continued)

- Non-toxic fixation methods needed
  - Support expanding molecular techniques
- Deploy with expanded quality assurance
- **Bottom-up** platforms required for cancer research
Collaborators

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Thank you