**Abstract**

**Background:** Archived formalin-fixed paraffin-embedded tissues (FFPET) are a resource for rapid translation from molecular target discovery to clinical disease application. NCIs AIDS Cancer and Specimen Resource (ACSR) provides HIV/AIDS-related malignancy tissue to approved investigators. Mid-Region ACSR has FFPET sampling techniques including field tissue microarrays (TMA) construction for cancer epidemiology or cancer molecular studies. TMAs facilitate high throughput immunohistochemistry (IHC) and in situ hybridization (ISH) evaluations and, with digital image analysis, allow cost-effective and time-efficient evaluation.

**Methods:** Sampling and FFPET block production standards were used in US and East African ACSR sites for several years. FFPET quality at collaborator laboratories was assessed. Source FFPET cores were inserted into TMA blocks. TMA sections were stained and digitized. TMAlab and ImageScope (Aperio) and AnalyzeTMA software facilitated image evaluation/sharing results. Quality of immunostaining, FISH, ISH, DNA and accuracy of pathology diagnosis/categorization were assessed.

**Results:** ACSR produced 8 TMA blocks (728 cores, 259 source blocks, various lymphomas). Cores for DNA isolation/characterization were also collected at the time of construction. RNA, DNA, IHC, and ISH were used for immunophenotyping and molecular genotyping. DNA isolated from samples was not of quality for molecular testing; signals from FISH probes were limited to few samples.

**Conclusions:** Digital imaging/software facilitated stained TMA tissue section evaluation. Resource poor sites were troubled by delayed fixation, poor quality formalin fixation, suboptimal tissue processing (particularly temperature control), poor slide preparation, and inconsistent quality pathology interpretation. Confusion of lymphoma with other small malignant tumor types and interpretations attempted from poorly produced H&E stained diagnostic slides.

**Acknowledgements:**

- David Nohle edited the poster.
- NCIC-CAG-CA6351

**References**


3. Ayers LW, Hackman BA, Notcha DG. Software-assisted Image Analysis for Administration of Tissue Specimens (TMA) Quality Control. Accepted for poster presentation at the 10th Annual Meeting of the Society for Biological and Environmental Repositories (SBER) 2006 Annual Meeting, Bethesda, MD, April 30-May 3, 2006.
4. AIDS and Cancer Specimen web site [www.acsr.ucsd.edu].

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**Image:**

- Figure 1: (left to right) Nairobi, Kampala, and Gulu sites.
- Figure 2: (left) Barb Hackman assists Dr. Robert Lukonde (Uganda) in making a TMA; (right) Dr. Leona Ayers phenotypes lymphomas using digital images from TMAs.
- Table 1: Selected Tissue Microarrays (TMA) Constructed by OSU.

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**Table 1: Selected Tissue Microarrays (TMA) Constructed by OSU**

<table>
<thead>
<tr>
<th>TMA ID</th>
<th># cores</th>
<th># donor blocks</th>
<th>core size (mm)</th>
<th>type of cores</th>
</tr>
</thead>
<tbody>
<tr>
<td>TA07-021</td>
<td>8</td>
<td>1</td>
<td>0.6</td>
<td>Burkitt Lymphoma, subset of TA07-020</td>
</tr>
<tr>
<td>TA07-022, 023</td>
<td>58</td>
<td>20</td>
<td>1</td>
<td>Burkitt Lymphoma, Kampala, Uganda 1997 - 2006</td>
</tr>
<tr>
<td>TA07-030</td>
<td>74</td>
<td>74</td>
<td>1</td>
<td>Burkitt lymphoma, Gulu 1993 - 2000</td>
</tr>
<tr>
<td>TA07-031</td>
<td>54</td>
<td>54</td>
<td>1</td>
<td>Burkitt lymphoma, Gulu 2001 - 2005</td>
</tr>
<tr>
<td>Total</td>
<td>728</td>
<td>259</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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**Objectives**

- Archived formalin-fixed paraffin-embedded tissues (FFPET) are a resource for rapid translation from molecular target discovery to clinical disease application. NCIs AIDS Cancer and Specimen Resource (ACSR) provides HIV/AIDS-related malignancy tissue samples and negative controls to approved investigators.
- The Mid-Region ACSR has developed FFPET sampling techniques including laboratory and whole tissue preparation, and inconsistent quality pathology interpretation. Confusion of lymphoma with other small malignant tumor types and interpretations attempted from poorly produced H&E stained diagnostic slides.

**Methodology**

- A standard for tissue sampling, fixation, processing and paraffin block production has been in use in ACSR operations in US and East African sites for several years.
- Collaborative laboratories have been assessed for tissue quality of collected stored FFPET.
- Source FFPET cores were inserted into TMA blocks and TMA sections were produced, stained and digitally scanned.
- TMAlab (Aperio) and ImageScope/AnalyzTMA software were used to facilitate image evaluation and to share results with collaborators.
- Quality of immunostaining, FISH, ISH and DNA and accuracy of pathology diagnosis or categorization were assessed.

**Results**

- The ACSR has produced 8 TMA blocks using 259 source blocks with a total of 728 0.6 and 1.0 mm cores from various lymphomas collected from global collaborators.
- Tissue cores for DNA isolation and characterization were also collected at the time of construction.
- RNA, DNA, IHC, and ISH were used to assess samples for immunophenotyping and molecular genotyping.
- DNA was isolated from samples but was not of quality for molecular testing and signals from FISH probes were limited to a few samples.

**Significance**

- QA expedites research, particularly with global collaborators.
- Tissue quality varies as does correctness of pathology designation.
- Support follow-up correlative studies by investigational samples.
- Collaborative digital image review can be a cost/time-effective evaluation when coupled with digital imaging analysis.

**Conclusions**

- Digital imaging and AnalyzeTMA software facilitated evaluation of stained TMA based tissue sections.
- Samples from resource poor sites were generally troubled by delayed fixation, poor quality formalin fixation, suboptimal tissue processing (particularly temperature control), and poor tissue section H&E stained slide preparation.
- Collected tissues also reflected the difficulty of consistent quality pathology interpretation in resource constrained sites. Lymphomas are particularly troubled because of confusion of lymphomas with other small malignant tumor types and by interpretations attempted from poorly produced H&E stained diagnostic slides.
- Quality performance of globally-gathered FFPET for RNA, DNA, IHC, ISH and FISH excludes some tissues from the research tissue biorepository.