Initial Clinical Validation of Clearing Histology with Multiphoton Microscopy (CHiMP) for Prostate Biopsy Diagnosis

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Ownership interest: Applikate Technologies, a startup company developing technology for direct-to-digital histology
CHiMP – Clearing Histology with MultiPhoton Microscopy

CHiMP is a tissue processing and imaging method that uses ex vivo multiphoton microscopy imaging generating optical rather than physical slices for primary diagnosis without the need for wax-embedding or microtome cutting.
CHiMP process

1. Tissue Cassette

2. Processor

3. Multiphoton Microscope

Web-based viewing software
CHiMP biopsy process for this prostate study

Delivery and formalin fixation: 
- ≥ 0.5 hrs

Tissue processing:
- 2.1 hrs
  - Dehydrant + dyes
  - Clearing

Imaging:
- 0.1 hrs

Image processing:
- 0.1 hrs

Total time: ~ 3 hrs
The CHiMPscope

Fastest multiphoton scope at this quality
Study design – patients undergoing prostate biopsy

Specimen source:
- Consented patient for single additional core biopsy
- Selection - intermediate to high likelihood carcinoma (based on imaging)
- 20 patients

Specimen prep:
- Standard formalin biopsy bottle
- Delivered to lab within 1 hr
- Processed for 2 hours

Imaging:
- 6-10 slices @ 300nm pixel size with 100 μm step size (~5 mins)

Post-imaging:
- Direct to dehydration for wax embedding
- 3 slides with 2 ribbons each = 6 slices
- IHC

Diagnostic comparison:
- 3 GU pathologists
- Physical Slide/CHiMP comparison
- > 4 week washout period
- Dx, grading, major and minor criteria, PIN, perineural invasion, IHC need
Intact full cores could be imaged using CHiMP

Human prostate biopsy imaged through full thickness with CHiMP. Slice spacing 100µm, scale bar 1mm. Scale bar 100µm.
Stackstreamer software was a practical interface
Interpretation comparison (preliminary)

- Every case evaluated by all 3 pathologists (60 evaluations)
- Final diagnosis based on all data: physical slides, digital slides, and IHC
Interpretation comparison summary

Correlation with final diagnosis

Number of interpretations

CHiMP Digital | Physical Slide

- Different
- IHC requested
- Grade +/- 1
- Exact
IHC worked well post CHiMP imaging

Ten cases were evaluated by PIN4 after CHiMP imaging

NO significant interpretation difficulties

PIN4 – Negative for carcinoma

PIN4 – Positive for invasive carcinoma

NKX3.1 – Dedifferentiated prostate carcinoma
Fewer artifacts are produced, likely better for machine learning

- No tears or folds
- No dirt or dust
- No hesitation marks

- No focus problems
- Thinner sections – clearer nuclei
- No fatty tissue issues
Current quality – 250 nm pixel size
Conclusions – CHiMP can replace physical slides

- Accurate primary diagnosis from unembedded clinical samples is possible
- Faster than physical slide scanning
- Less work (less expensive) than physical slide scanning
- Better quality than scanned physical slides
- Compatible with IHC
- Entire tissue preserved

Next

- Integrating Stackstreamer with Yale Path Portal
- Phase 2 - Integrate CHiMP principal diagnosis for routine clinical samples
- Kidney core biopsy Phase 1/2 validation
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See demo at:
demo.stackstreamer.com
demo/demo