A digital pathology ecosystem for education and research

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Financial disclosure

• I’m a co-founder and shareholder of Pathomation, one of the companies mentioned in this presentation
Who am I?

Education

• 2000: Hogeschool Gent (BE)
  – BS Computer Sciences

• 2001-2005: Troy State University (US)
  – Exchange program
  – MS Biological Sciences

• 2005-2010: Iowa State University
  – PhD Bioinformatics & Computational Biology

Professional

• 2000-2001: Becton Dickinson

• 2010-2013: HistoGeneX
  • Data Management
  • Bioinformatics
  • Section head

• 2014-now: VUB
  • Digital Pathology Manager
Presentation outline

• Introduction: Whole Slide Imaging (WSI)
• Current status of WSI at VUB
  – Educational tools medical school
  – Biobank: retrospective histopathology collections
  – Biobank: prospective histopathology collections
• Future plans
  – Slide / Data Exchange Research and Clinics
  – Image analysis
  – Scaling
What’s the difference?

- Whole Slide Imaging
  - A technique
  - Get a scanner
  - Generate LOTS of data
  - Easy

- Digital (histo)pathology
  - A method,
    - a way of thinking
  - Workflow management, integration
  - USE the data
    - valorization
  - Hard
What is Whole Slide Imaging (WSI)?

• The technique of converting glass-mounted microscopy material into a digital representation / image.
Why does it happen?

“The Translational Biology Toolbox”

Resolution Scale (~)

- Optical-
- PET-
- NMR Imaging-
- MRI-
- Ultrasound-
- CT-
- Mass Spec Imaging-
- Mass Spec Microscopy Imaging-
- Bright Field-
- Fluorescence-
- Super-resolution-
- Electron Microscopy-
- SIMS-
- NMR Spectroscopy-

Vrije Universiteit Brussel

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Where does it happen?
How does it happen? Going shopping!

Open API / file format
objective criterium
Image quality
subjective criterium
Technology evaluation
Once you’re happy...
VUB result (december 2014)
More infrastructure updates

I gave you slides; how do I get to see these?
So you want to see slides?

- You go to a website
- You download a .sis-file
- Which is not recognized by your browser
- Then you go to the scanner vendor’s website
- You download their free (but proprietary) viewer
- You install the viewer (do you have rights to do that?)
- You re-download the .sis-file
- You open the .sis-file in the locally installed viewer
- Sometimes the viewer is unstable and crashes
  - that’s normal; just start over
- Re-do this procedure on every device that you use
  - You just can’t do it on a Mac!
VUB result (January 2015)
More infrastructure updates

- Aperio CS/2 scanner
- Acquisition PC
- Enhanced network infrastructure
- Backup storage (approx. 50TB)
- Centralized mass storage (approx. 50TB)
- \histosrv slide management software and server

I gave you slides; how do I get to see these?

We’ll send you a link that you can open with your webbrowser

Cool!
Connecting people

Aperio CS/2 scanner \rightarrow Acquisition PC

Backup storage (approx. 50TB) \rightarrow Centralized mass storage (approx. 50TB)

\texttt{\backslash histosrv} slide management software and server

Enhanced network infrastructure

End-user workstation 1 (desktop) \rightarrow End-user workstation 2 (desktop) \rightarrow Development workstation (laptop)
Different imaging platforms

- **BD Pathway**
  - TIFF images, 12-or 16-bit per pixel, grayscale, non-pyramidal
  - Attovision software
- **Zeiss**
  - ZVI / CZI Images, multiple (fluorescent) channels
  - AxioVision Software / ZEN Studio
- **Nikon**
  - ND2 / TIFF images, multiple (fluorescent) channels
  - NIS Elements
- **Leica / Aperio**
  - SVS images, brightfield
  - Aperio eSlide Manager (formerly Spectrum)
  - Aperio ImageScope
- **3DHistech (UZBrussel)**
  - MRXS, brightfield
  - Pannoramic Viewer
Connecting equipment

Centralized mass storage (approx. 50TB)

Backup storage (approx. 50TB)

Enhanced network infrastructure

Becton Dickinson / BD Pathway IF

Zeiss IF

Leica / Aperio

Nikon IF
Developing the use cases:

- Education
- Biobanking
- Research
- QA
- Second opinion
- Primary diagnosis
• Taking our first steps
  – Trying it out on volunteers (aka students)
Use case 1: Education
Use case 1: The first course

- Histology education at [http://histology.vub.ac.be](http://histology.vub.ac.be) (GK, BMW)
Use case 1: Software architecture

- **Viewing software**: PMA.view Viewer
- **Slide hosting**: PMA.core Server
- **Student website**: Custom built

Whole slide image repository
Use case 1: Building on our success
Use case 1: Going mobile
Use case 1: Additional course

Pathology education at [http://pathology.vub.ac.be](http://pathology.vub.ac.be) (GK, BMW)
• Scaling up
  – Doing more than “just” education
Use case 2: Retrospective collections


Willy Gepts (1922-1991)
Use case 2: archival slides and clinical data
Use case 2: Retrospective collections

- Currently available: [http://gepts.vub.ac.be](http://gepts.vub.ac.be)
Use case 2: International Collaboration

- [http://foulis.vub.ac.be](http://foulis.vub.ac.be)

### Alan Foulis Collection

**Welcome**

**The collection**

**The research**

**Contact us**

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What is this site about?

Over the last 30 years Alan Foulis has conducted research into the pathogenesis of type 1 diabetes. He established a unique biobank of autopsy pancreases of children who died shortly after developing the disease. In conjunction with the group of Prof Noel Morgan at Exeter University, evidence of enterooviral infection of the insulin secreting cells in the pancreas has been found in these children. This observation has raised the possibility that the disease could be prevented by vaccinating infants against diabetogenic viruses. Prof Morgan’s group is one of 14 partners who have been awarded 8 million Euros by the European Union to study this association.

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Alan Foulis

Insulitis in the human endocrine pancreas
Use case 2: slide organization
Use case 2: meta-data capturing
Demo

- http://gepts.vub.ac.be
- http://foulis.vub.ac.be
• Putting our experience to good use
  – Digital pathology for the valorisation of a “live” biobank
Use case 3: Biobank

- Show-case for patients and samples.
- Facilitates patient selection for studies.
- Permanent record of cases allows retrospective validation of studies.

**Human Biospecimens**

- Clinical data

**Acquisition**

- Processing
- Storage
- Distribution

**Translational Biomedical Research**
Vlaamse Biobank (CMI – BBMRI. vl)

- Minimal clinical data (OECD)
- Extended epidemiological dataset
- HLA, auto-immune data
- Images
Biobank problems

- Without digital histopathology:
  - I’m looking for breast tumor tissue: Sure; glad to help
  - Does the sample contain cancer cells: Just trust us
  - Is it in situ or invasive?: Just trust us
  - Is it hormone-responsive?: We don’t have that information

- With digital histopathology:
  - I’m looking for breast tumor tissue: Sure; glad to help
  - Does the sample contain cancer cells: Have a look at the HE
  - Is it in situ or invasive?: Have a look at the HE and the immunostains (p63 – calponine)
  - Is it hormone-responsive?: Have a look at the immunostains and the fluo data (FISH)

Fidelity increases, confident about requests, investments pay off
Use case 3: Biobank (valorization)

- Sample
- Clinical Data
- Whole Slide Images
- Quantification of morphology
- Next Generation Sequencing Data
- Data generated during experiments
Use case 3: Biobank (inspiration)

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Use case 3: Our own biobank site

http://histosrv.vub.ac.be/dbb
Use case 3: Biobank “behind the scenes”

Custom ASP.net website http://histosrv.vub.ac.be/fielt

ADO.Net Data Abstraction Layer (DAL) --> Pathomation PMA.zui WS| visualization component

SLIMS database (meta-data) --> GenOhm Biobank

Leica eSM database meta-data) --> Aperio eSlide Manager

Leica Slide Repository --> Pathomation PMA.core slide hosting

MRX5 Slide Repository --> 3DHistech Pannoramic
• The VUB digital histopathology ecosystem
  – Multiple imaging platforms, multiple users, multiple applications, multiple portal websites

Central portal
http://www.diabetesbiobank.org

Diabetes Biobank
http://histosrvvub.ac.be/dbb

Historic curation
http://gepts.vub.ac.be
http://foulis.vub.ac.be

Education
http://histology.vub.ac.be
http://pathology.vub.ac.be
The future: Hospital and clinical

• Ongoing evaluation of scanner equipment
  – Currently 3DHistech on site
• Case presentation
  – “Easy” cases for medical school students (rotations)
  – Special cases (multidisciplinary oncology consults)
  – Residents in the pathology department
• Collection hosting
  – Historical (restrospective) collections
    • Students, residents, hospital staff members (don’t need to be pathologists!)
  – Thesis support: collect data, evaluate
    • in a uniform, centralized manner
• Fielt study
  – 200 cases, to be evaluated by different pathologists for tumor infiltrating immune cells, tumor cell %, PDL1 IHC staining evaluation in tumor and micro-environment
The future: training residents (ASO)

33 jaar, vrouw, massa rechter borst


E-CAD: +
ER: +
PR: +
HER2: +
Ki67: +

Proliferatieve borstziekte zonder atypie.
The future: MOC discussions
The future: distance consults

- Second / First Opinion
- Online reviewing
- Molecular Advisory Boards
The future: a user-friendly platform (tool!)
The future: image analysis

Step 1: find tissue

Step 2: locate the islets

Step 3: quantitate insulin
The future: intelligent querying

I’m looking for pancreatic tissue from a patient with recent onset diabetes and a susceptible HLA-DQ genotype. At least y% of the islets still have to contain insulin-producing cells.

Here you go.
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