

Building a Nonclinical Pathology Lab of the Future

Feature

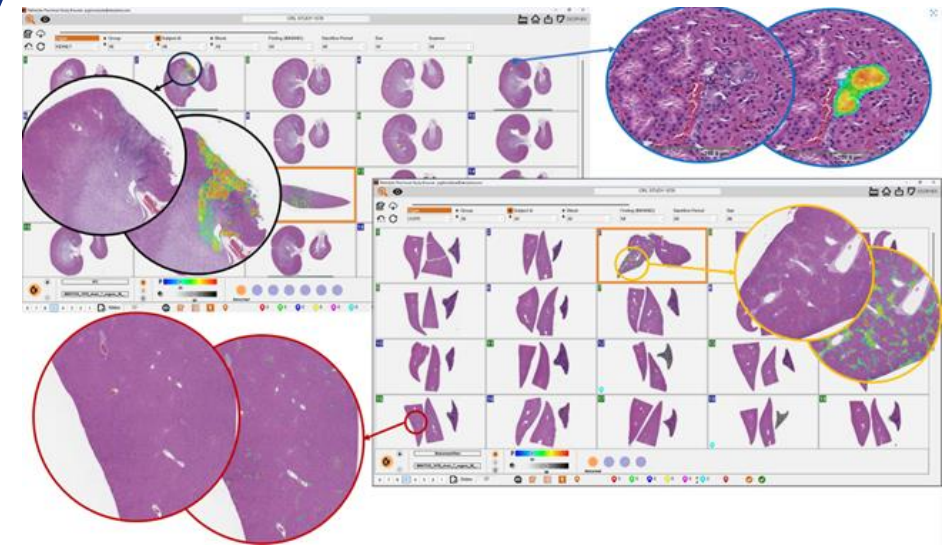
Building a nonclinical pathology laboratory of the future for pharmaceutical research excellence

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Disclosures

- Lead a research and development partnership with Deciphex, Ltd



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Digital Toxicologic Pathology

Introduction

Digital toxicologic pathology

- **Objective:** Support pathologist quality, efficiency, training, recruitment and retention
 - Enable a **GLP validated digital ecosystem** that is fit for purpose for the toxicologic pathologist
 - Facilitate an **automated and integrated workflow** from the laboratory to the pathologist
 - Provide the opportunity for **advanced analytics and machine learning** AI approaches

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Rudmann, et al. Drug Discovery Today 28:1-7

Medical pathology

Value Proposition- Efficiency

Full microscopic vs digital work process is faster:

Overall normalised mean time to diagnosis was 85% on the digital pathology workstation compared with 115% on the microscope, **a relative reduction of 26%** (<https://doi.org/10.1136/jclinpath-2021-207961>)

Since implementation, Granada University Hospitals pathologists **have signed out 21% more cases per year on average**. (Arch Pathol Lab Med.2020 Feb;144(2):221-228. doi: 10.5858/arpa.2018-0541-OA)

But only the review of slide or image alone is comparable or slower:

Microscope review was **1 min 13 s** compared to **1 min 32 s** per whole slide image

Our nonclinical pathology data

Value Proposition- Efficiency

TABLE 2

Proof-of-concept study demonstrating the increased efficiency of using a fit-for-purpose digital slide viewer versus a traditional light microscope for a simulated nonclinical review.

Pathologist activity	Time savings (vs microscope)
Find/sort slides and replace in box	1279%
Find a specific animal in boxes	4322%
Find one tissue for all animals in a group	72–241%
Locating substructures in tissues	23–46%
Overall	42%

<https://doi.org/10.1016/j.drudis.2023.103747>

>60% reduction in time for fully trained digitally enabled pathologist (see *slide 4* for breakout) using digitally enabled workflow with Patholytix vs glass slide and microscope for **remote** pathologist

For Non-Remote Pathologist:

	Glass Slide	Patholytix
Remove and replace control spleens and threshold against tx group spleens	80	40
1001	14	6.1
1002	20	6
1003	17.5	7.1
3001	25	6.1
3002	26	8.9
3003	23.5	8.5
Target organ pull and mix	10	0.1
	216 minutes	82.8 minutes

Includes all steps from locating and removing slides from box, blinding, and returning slides to box

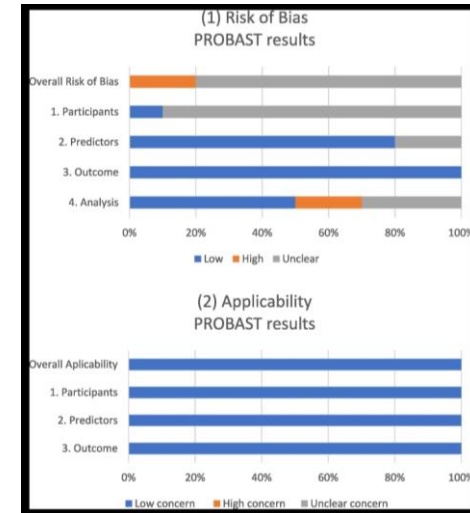
1001-1003 and 3001-3003= full tissue reads (includes all steps from locating and removing slide from box to replacing slide to box)

Includes all steps from locating and removing slides from box for each target organ, blinding, and returning slides to box

Decision support AI

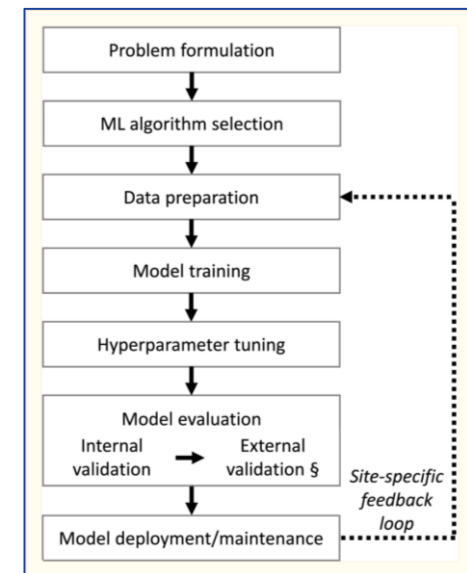
Value Proposition- Quality

- Systematic Review of literature (2001 manuscripts with search terms)
- 8 journal articles and 2 conference proceedings for analysis



3 models for diagnosis, 4 for classification (3 for prognosis, and 1 for both classification and prognosis)

- All models for cancer diagnostics
 - Ground truth= pathologist's opinion/diagnosis
 - Models were CNN based
 - Most diagnoses on WSI at 40x with H&E
 - Accuracy and area under the curve greater than 87% and 90% pathologist vs pathologist + AI



J Path Informatics 2023 Nov 5:15:100348. doi: 10.1016/j.jpi.2023.100348

Decision Support AI

Value Proposition-Quality

[New research may lead to use of AI in cancer diagnostics for dogs more affordable, available - Augusta Free Press](#)

[How AI-powered handheld devices are boosting disease diagnostics - from cancer to dermatology \(nature.com\)](#)

[Computer-assisted mitotic count using a deep learning-based algorithm improves interobserver reproducibility and accuracy - PubMed \(nih.gov\)](#)

[Deep learning algorithms out-perform veterinary pathologists in detecting the mitotically most active tumor region - PubMed \(nih.gov\)](#)



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Digital Toxicologic Pathology

Workflow



The digital workflow



Pathology/Histology LIMS

Necropsy to Dig Path bar coding
Automated metadata workflow
Post life operational automation
Study reporting automation



Image Management System

Support CRL scanning for full digital
Cloud based for image and data storage
Client transfer of digital images + metadata
Interface with AI systems (Visiopharm)



Digital Microscope

Fit for purpose for pathologist
Client web-based access
Leader for industry adoption
AI integration potential

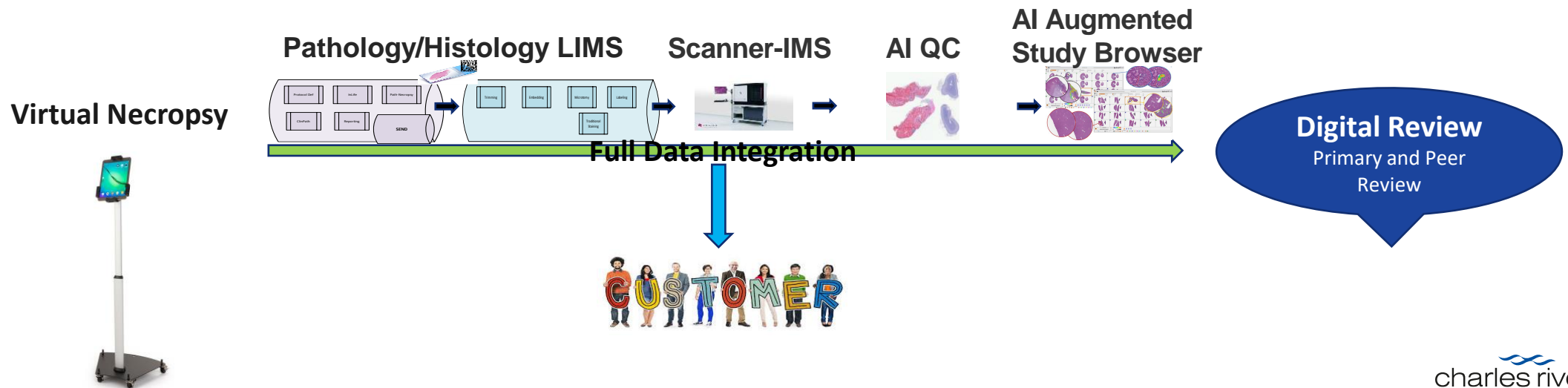


Image quality control

- In line AI classifiers to identify common scanning artifacts

Manual QC Review

- 100 slides QC'd
- 1hr 42min to review
- Crash 6 times
- 10 slides failed
 - 9 slides failed for scratch
 - 1 slide failed for out of focus

AI Supported QC Review

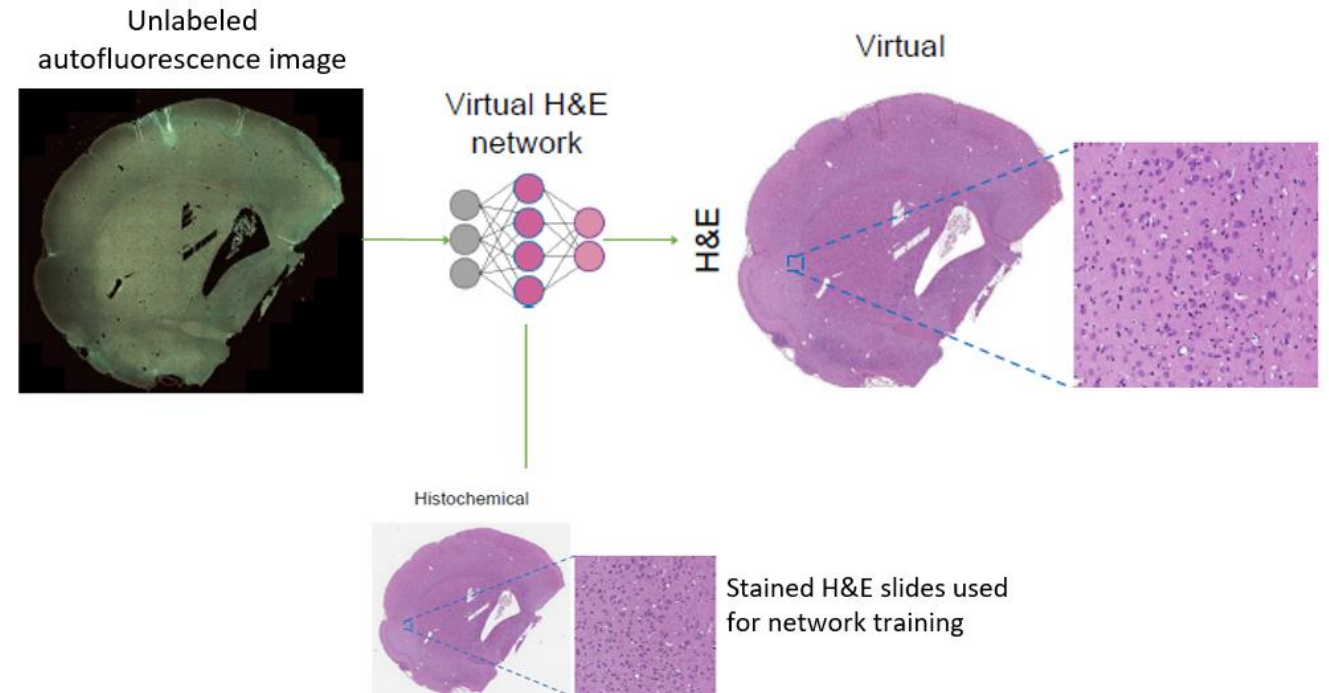
- 5 slides flagged for QC by AI during upload process
- 58 seconds to review
- 2 slides failed for out of focus
- 5 scratches identified through eSM thumbnails



Virtual staining

<https://pictorlabs.ai/technologies>

- Deep learning AI tool
- Autofluorescence image
- Trained using CRL H&E slides
- Opportunities for multiplexing with other virtual stains:
 - + Special stains: Fluoro-Jade B, Trichrome, PAS, Jones
 - + IHC: GFAP, Iba1



Esther Crouch and Dan Rudmann (Global), Mary Olanich (CRL-DUR)

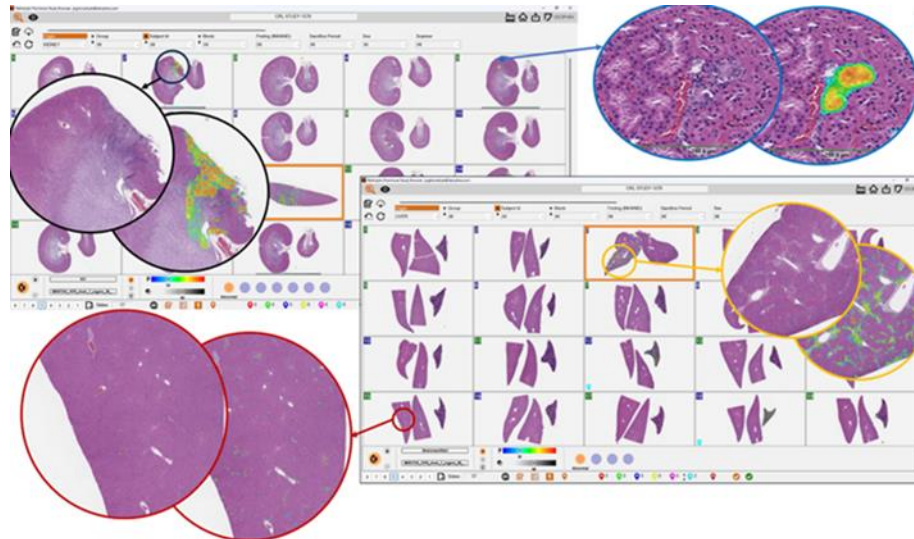
Decision Support for Toxicologic Pathologists

Opportunities

- Efficiency and quality bump
- Validated quantification tools
- Refinement of evaluation (no controls)
- Multimodal models (OW, CP, and AP)

Challenges

- Generalization of models
- Object detection/rare events
- Investment to develop- data and time
- Training/change management



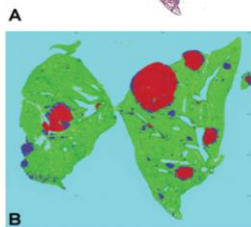
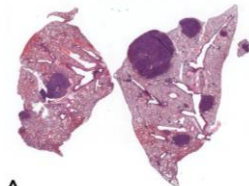
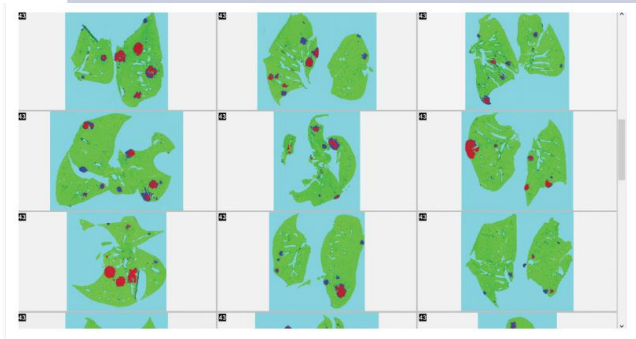
Screening workflow example

TgRasH2 Positive Control Confirmation

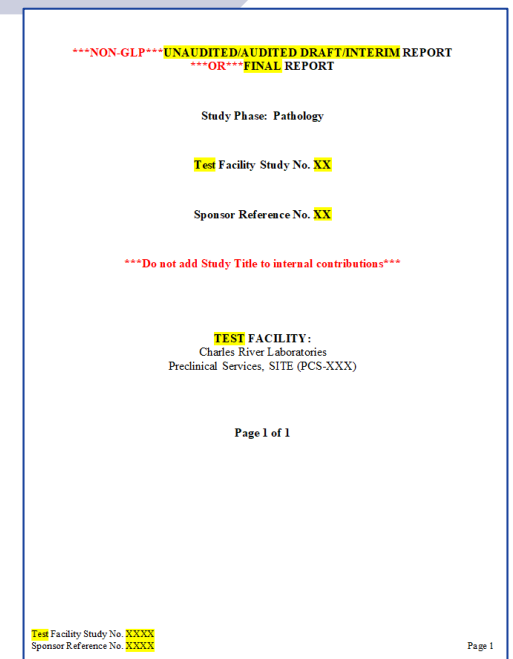
Scanning and AI

Automated Analysis

Pathologist's Reporting



Group	Males	Females
Urethane	10/10	10/10



Rudmann, et al. Toxicol. Pathol. 2021 49:938-949

Decision support workflow example

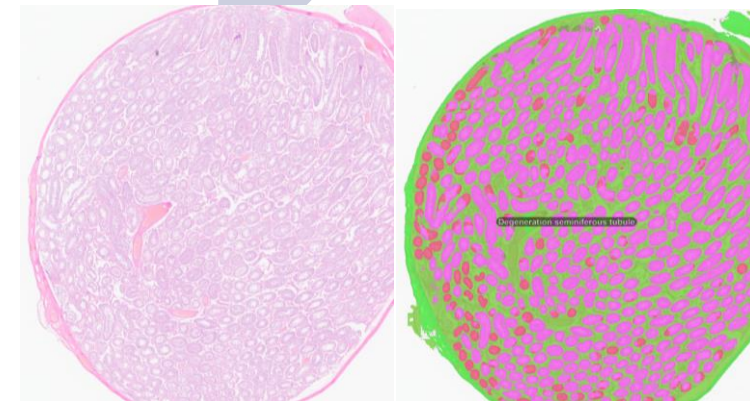
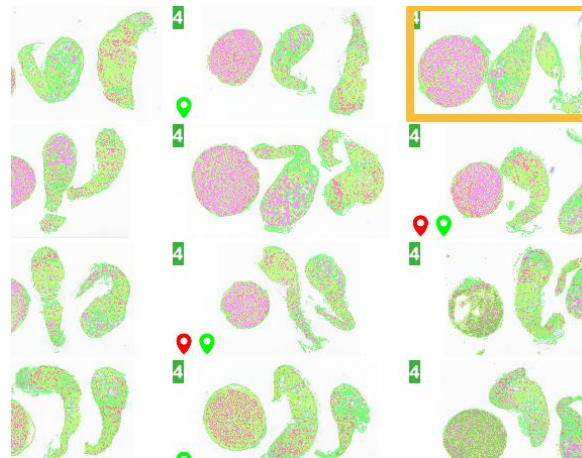
Rat Testes Diagnostics

Organ Weight Review

Automated Deep Machine Learning

Standard Histology Augmented with AI

	Testis Weight (g) [G]			
Mean	3.5896	3.2948	3.0588 *	1.5785 **
SD	0.3367	0.2334	0.7963	0.1342
N	10	10	10	10
%Diff	-	-8.2126	-14.7872	-56.0257



Summary

- Digital pathology innovation starts with the development of the GLP validated digital ecosystem
- Digitized whole slide images enable advanced analytics and AI-based machine learning approaches
- The AI augmented digital pathology workflow must be qualified and validated for the intended use of the toxicologic pathologist

Acknowledgement: CRL-Deciphex Research and Development team