
aiforia®
AI for image analysis
Translate images into
discoveries, decisions, and diagnoses

Content

- Introduction to Aiforia
- Introduction to AI and image analysis
- How to train AI with Aiforia
- Applications
- Case studies (neuroscience, cancer, liver, other diseases)

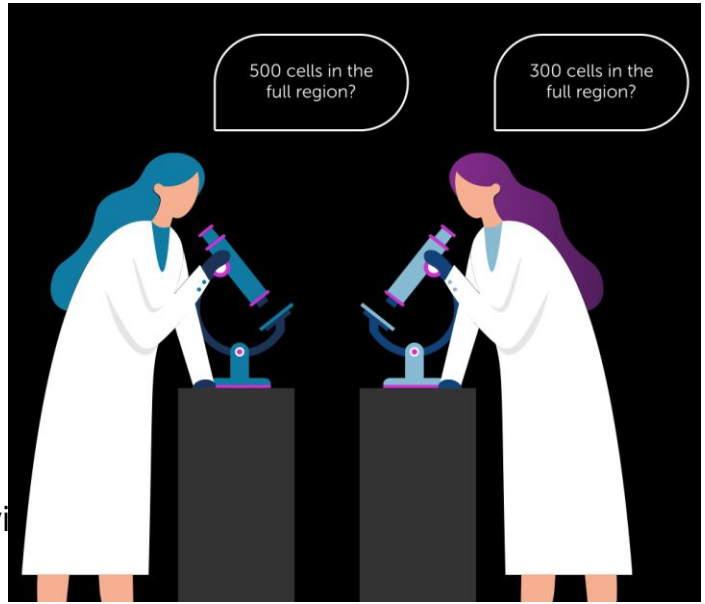
The challenge

Pathologist are facing a growing burden

- Rising rates of diseases, rising sample numbers
- While workloads are increasing, the number of pathologists are not
- Less are specializing in the field

Current tools have severe limitations:

- Manual
- Time consuming
- Prone to inter- and intra- observer subjectivi
- Not standardized



The solution: AI-assisted analysis

Digitizing pathology

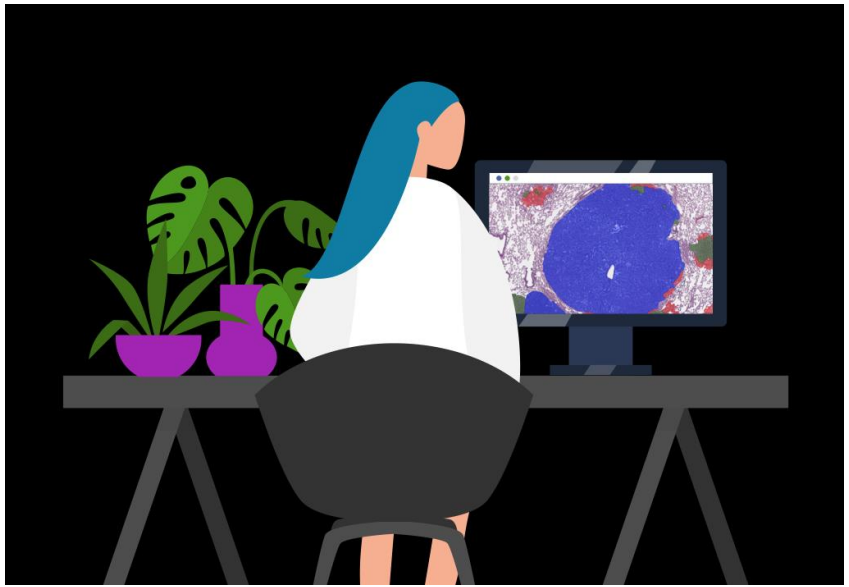
Digital pathology is the process of digitizing glass slides using a whole slide imaging scanner and analyzing these with an image viewer. It has changed the paradigm of microscope-based pathology.

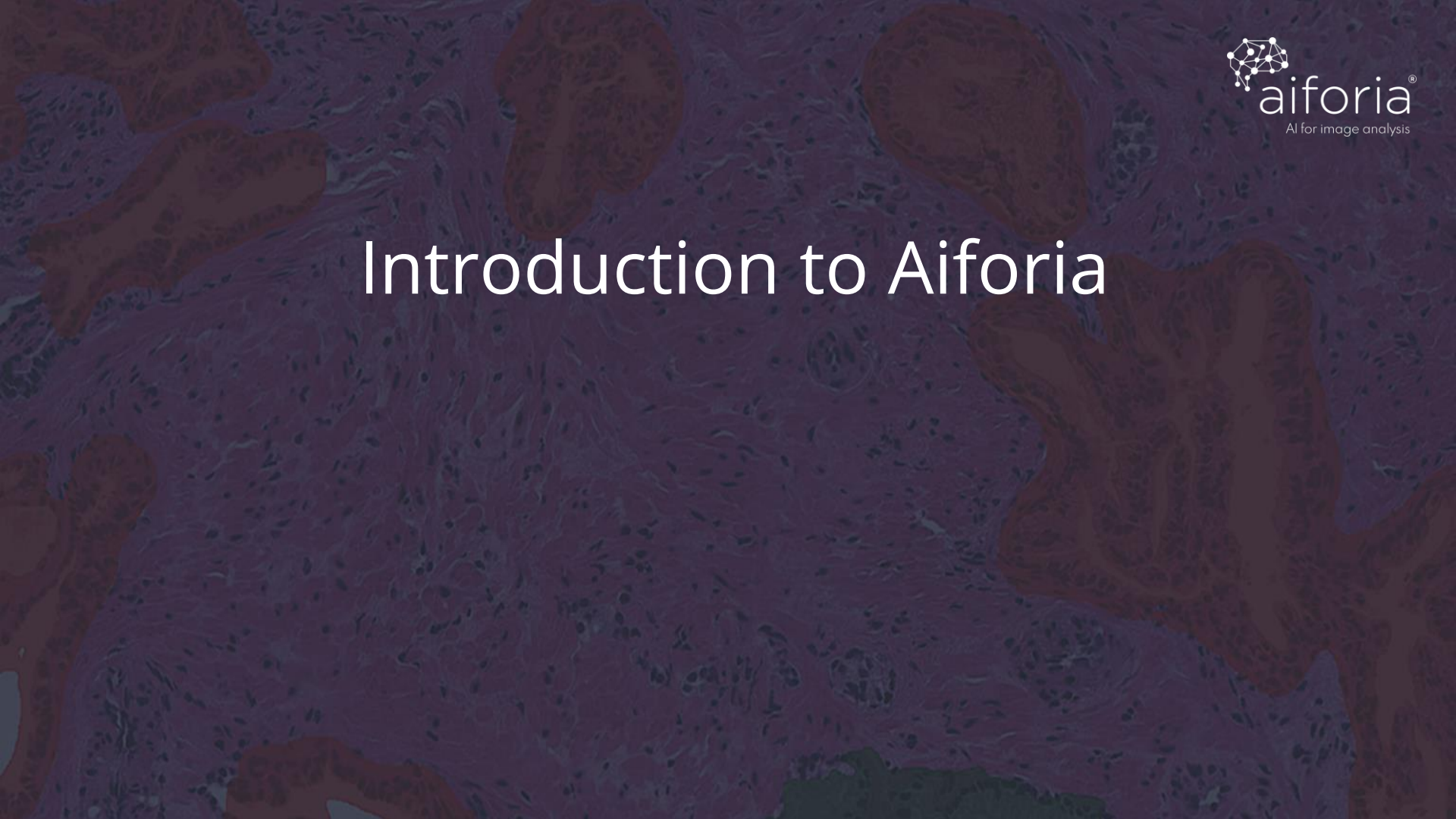
Digital pathology benefits include: enhancing lab workflows, collaborating more efficiently, improving patient care, and enabling the use of new technologies like AI.

Benefits of AI-assisted analysis:

- Accurate, quantitative data, compared to visual estimates
- Consistent results, removes human error and bias
- Significant time savings, even 90% less hands-on time

Aiforia provides a first-in-class AI development and analysis tool for medical experts.





Introduction to Aiforia

aiforia®
AI for image analysis

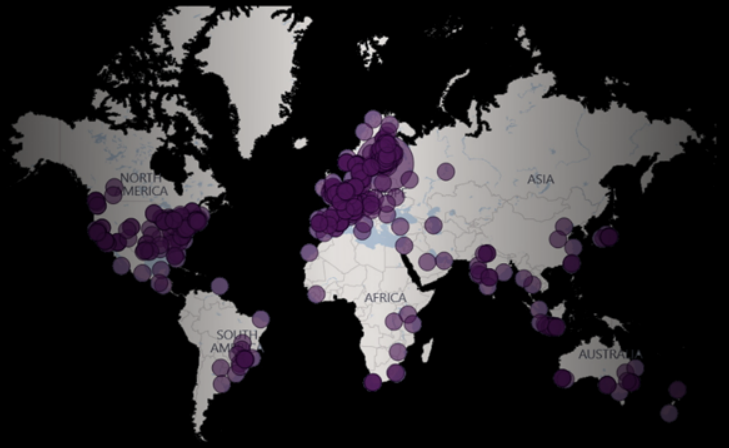
Our mission

Aiforia's mission is to provide the highest quality solutions for AI-assisted analysis to enhance the translation of medical images into data and discoveries in all realms of healthcare. From medical research to clinical diagnostics, Aiforia aims to elevate the work of healthcare professionals to new heights.

Aiforia Technologies

- **Locations:** Helsinki, Finland & Boston, US & the Netherlands
- **Our team:** We are a comprehensive mix of experienced scientists and entrepreneurs. Our team brings together expertise in medical sciences, artificial intelligence and life sciences industries:
  - **Science team:** medical scientists and pathologists specialized in translational cancer research, in vitro diagnostics, and more and supported by an in-house annotation team
  - **Software team:** together hold over 100 years experience in AI and software development
  - **Commercial team:** experience spanning pharmaceutical, biotechnology sectors and B2B software sales and BD

Aiforia® Create is intended for research use only.
Aiforia® Clinical is CE marked for in vitro diagnostic use in EU & EEA. In other countries Aiforia® Clinical is for research use only.



AIFORIA USERS AROUND THE WORLD

• AIFORIA'S CLOUD PLATFORM IS USED GLOBALLY •

3,000+ users

Pathologists, medical scientists, and researchers use Aiforia's AI and image analysis tools worldwide.

50+ countries

Aiforia's cloud-based software and services are used in over 50 countries across the world.

1 million+ images

Over 1 million images have been analyzed with Aiforia and 400+ AI models developed.

Who are our customers?

Aiforia's solutions are created for pathologists and healthcare professionals in pharmaceutical, biotechnology, contract research organizations (CROs), and academic institutions.

Massachusetts Institute of Technology

Bristol-Myers Squibb

AstraZeneca

UNIVERSITY OF OXFORD

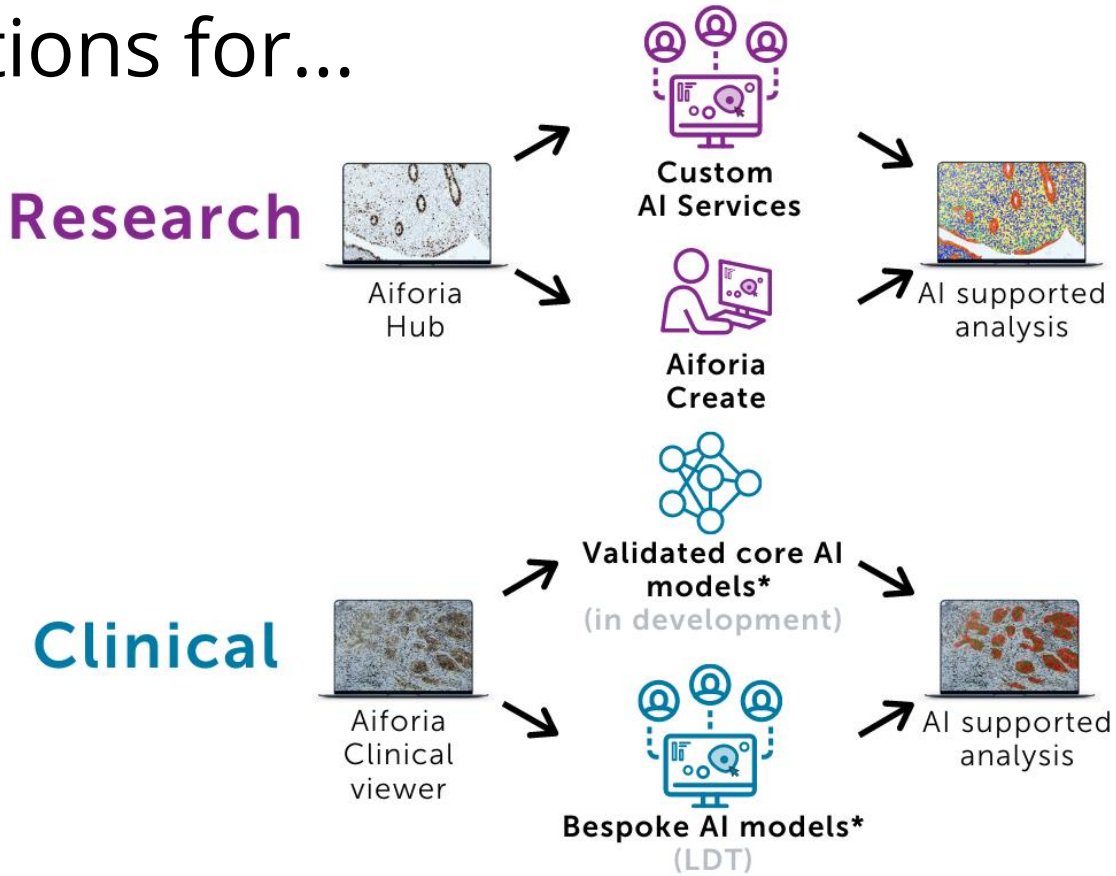
charles river

ORION

SANOFI

Karolinska Institutet

Aiforia’s solutions for…



*Aiforia’s AI models and AI platform Aiforia Create ® are sold for research use only (RUO).
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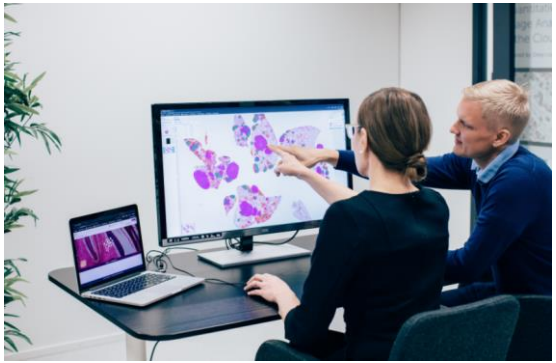
Aiforia’s AI solutions for research

Aiforia Custom AI Services

AI models developed by scientists, for scientists.

Whether you are looking to accelerate your preclinical analysis or scale your pathology services, you can now enhance your image analysis workflow with Aiforia.

With our Custom AI Services Aiforia scientists build AI models for your specific needs.

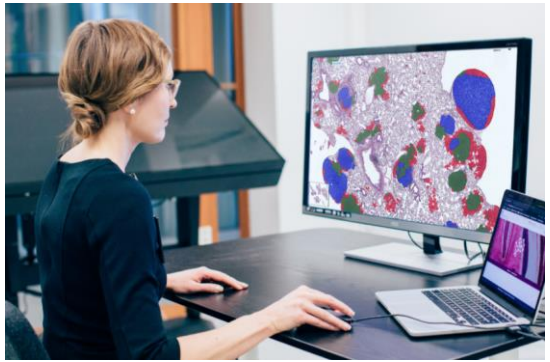


Aiforia Create

Your cloud-based tool to develop AI models.

Using our cloud-based tool, Aiforia Create, develop AI models for any image analysis task. Simply annotate to train our neural networks to identify, quantify, or measure (the possibilities are limitless!) your features of interest.

To use Aiforia Create you do not need to code or invest in any dedicated hardware.



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How to use AI for image analysis with Aiforia

You can analyze any 2D image (i.e. WSI, IF, etc.).

All major scanner and file formats supported.

Image uploaded to cloud-based Aiforia platform which enables remote access validation, and sharing.

Develop your own AI model with Aiforia Create

Use our Aiforia Custom AI Services

End result:

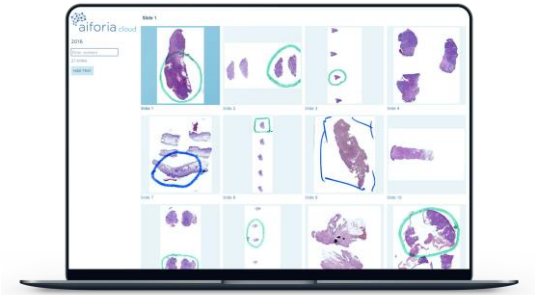
- Automate manual tasks
- Produce highly accurate data
- Collaborate remotely
- Standardize image analysis

Aiforia’s AI solutions for clinical diagnostics

Aiforia Clinical viewer

Enhance your diagnostic workflow with the CE-IVD marked Aiforia Clinical viewer.

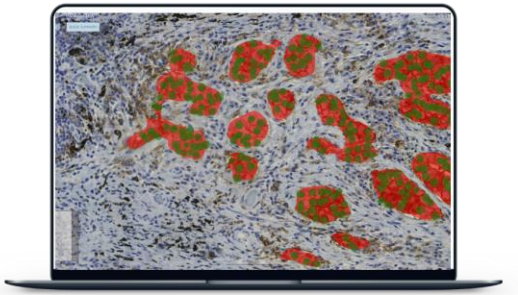
The viewer tool is made for the clinical pathology workflow to enhance the analysis of images from tissue samples, especially in remote viewing and collaboration. The browser-based viewer can be integrated into any hospital IT infrastructure and its installation can be matched to your specific needs.



Aiforia’s AI model pipeline

Deep learning AI models for image analysis (AI-assisted diagnostics are RUO).

AI is a powerful tool ready to replace manual, inconsistent, and error-prone methods in clinical labs and to provide assistance to pathologists in their case review. Aiforia is currently developing AI models for a range of different diseases from cancer to liver diseases.



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What makes Aiforia’s solutions unique?

The combination of…

Our cloud-based platform

- Easily scalable
- Integrate without restrictions
- Work and collaborate remotely
- Store images & data securely
- Automatically access latest updates & features
- Any 2D image can be analyzed

Our deep learning AI in your hands

- Label input data with easy to-use UI
- Train neural net (NN)
- Deploy AI for IA
- Update and combine NNs easily
- Industry-leading tools: Image match, the patented Annotation Assistant, and more!

Our people

- Science team with wide range of expertise (i.e. oncology, pathology, neuroscience, and more!)
- Software team together have 100+ years' professional experience in developing AI solutions
- In-house annotation team

Our scientific support

- Science team offers customer support and on-demand projects for bespoke solutions
- Dedicated on-boarding specialist
- Additional on-going single point of contact support
- Cloud platform makes support seamless

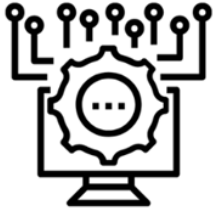
Our cloud-based platform

Scale easily with unparalleled computing power

Work and collaborate flexibly with remote access

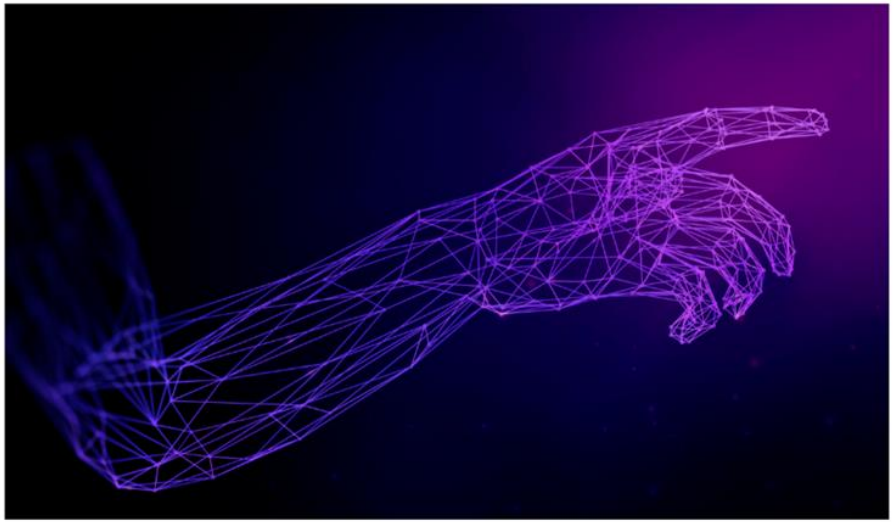
Automatically access the latest updates and features

Store your images and data securely



Integrate without any restrictions

Our deep learning AI in your hands



- Label input data by annotating
- Train convolutional neural net (NN)
- Deploy AI for IA
- Update NN easily
- Combine NNs easily
- Industry-leading tools: Image match, the patented Annotation Assistant, instance segmentation, and more!

Our people and scientific support: the Aiforia Science Team

Thomas Westerling-Bui PhD
Director of Scientific Strategy

- PhD in cancer biology
- Post-doctoral fellowship at Dana Farber Cancer Institute researching the genomics of breast and prostate cancer

Anna Knuuttila DVM, PhD
Senior Scientist

- Board certified veterinary pathologist
- PhD in viral epidemiology
- Specialization degree in infectious animal diseases

Sami Blom PhD
Director of Application Development

- PhD in cancer biology
- Specializing in the fields of translational cancer research and in vitro diagnostics

Hanna-Kaisa Sihvo DVM PhD Dipl ECVP
Senior Scientist

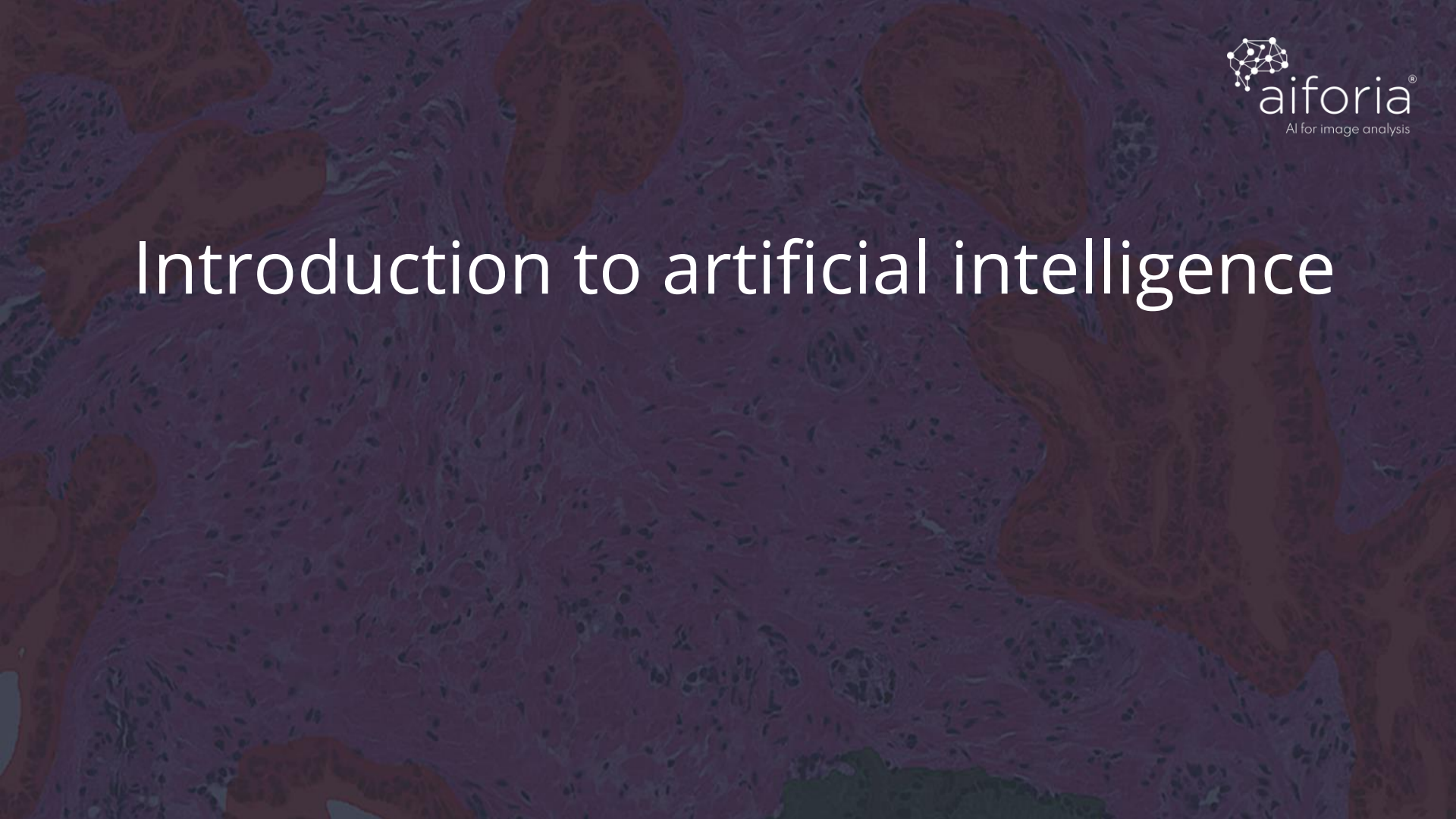
- ECVP certified veterinary pathologist
- 10+ years experience in diagnostics and research pathology

Lindsey Smith PhD
Field Application Scientist

- PhD in neuroscience
- Experienced in electrophysiology and a wide variety of neuropathologies

Darshan Kumar PhD
Customer Success Scientist

- PhD in cell and molecular biology
- Experienced in virology, immunology and microscopy



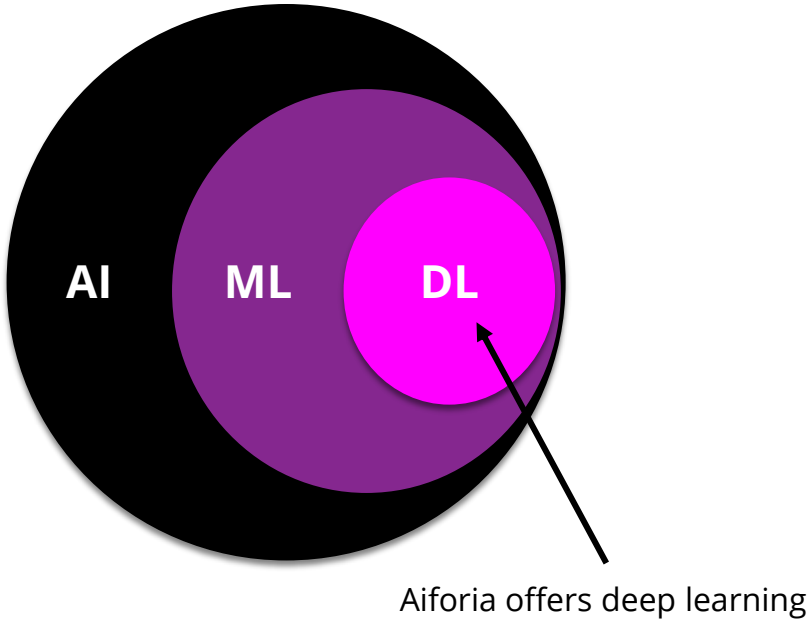
Introduction to artificial intelligence

Artificial intelligence

Artificial intelligence (AI)
Techniques that enables computers to mimic human intelligence

Machine learning (ML)
Use of statistical methods to enable machines to learn from data rather than through explicit programming

Deep learning (DL)
A subset of ML, often referred to as the next-generation of machine learning as DL is more autonomous and powerful in its learning and capabilities.



DL vs ML

Deep learning

- Always made of artificial neural networks, arranged in up to **hundreds of layers**
- Learns more **autonomously**: independently constructs an idea of features
- Allows us to solve even **more challenging problems** than machine learning can
- Surpasses human capability in tasks like image recognition

Machine learning

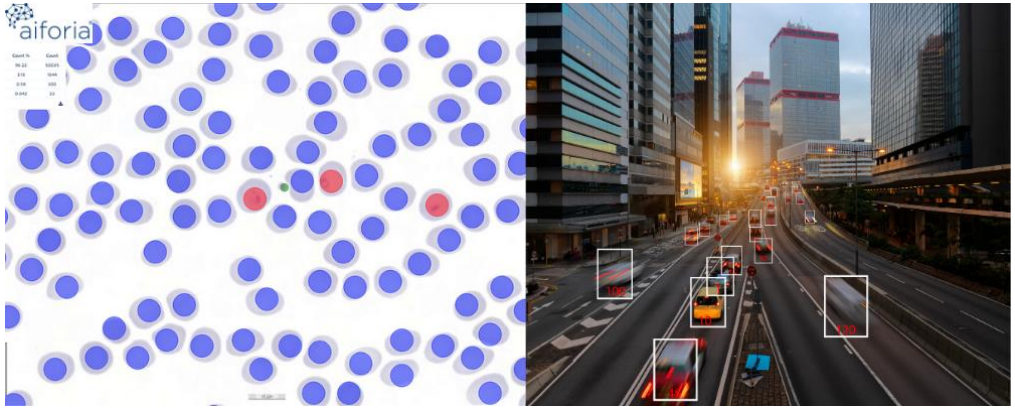
- Different models of ML, some formed of neural networks, arranged in just a **few layers**
- To learn, it **requires user** to identify and create features

Deep dive into deep learning

One of the most powerful applications of DL is image recognition and analysis. It is already surpassing human capability in image analysis.

Deep learning is built from artificial neural networks, they are computing systems designed to find patterns that are too complex to be manually taught to machines to recognize.

Neural networks see images as a grid of numbers, represented by the pixels in an image. In order to use DL for image recognition, the networks must first be trained, with for example images of a specific types of cells.



Neural networks

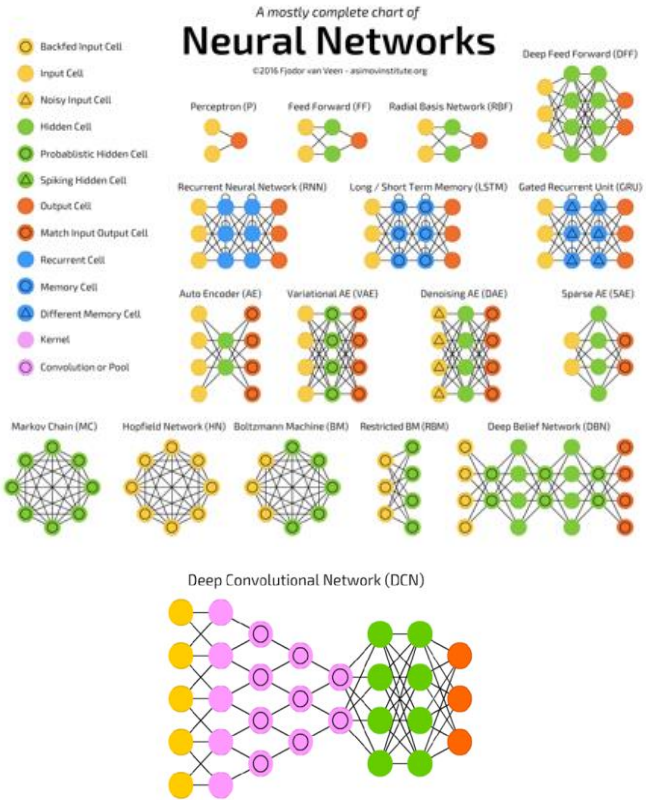
Artificial neural networks (ANNs) are what form and drive deep learning.

ANNs are made up of a collection of connected units of mathematical functions, referred to as artificial neurons.

In deep learning models the neurons can range in amount from dozens to millions of units always arranged in a series of layers.

Aiforia's AI is made of convolutional neural networks (CNNs).

CNNs are incredibly powerful, enabling image recognition and analysis to reach new heights.

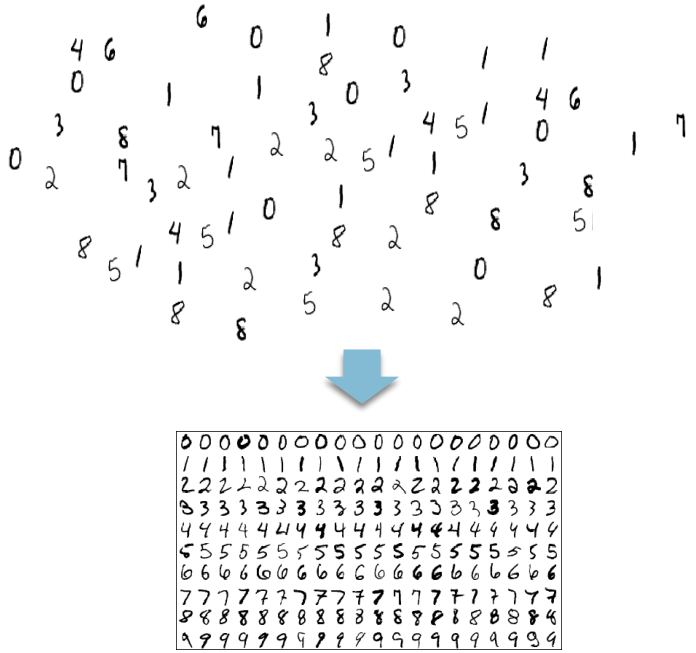


How do neural networks analyze images?

CNNs decipher sensory data, such as images, through a sort of machine perception by recognizing patterns as numerical. This basically means that sensory information is translated into numbers.

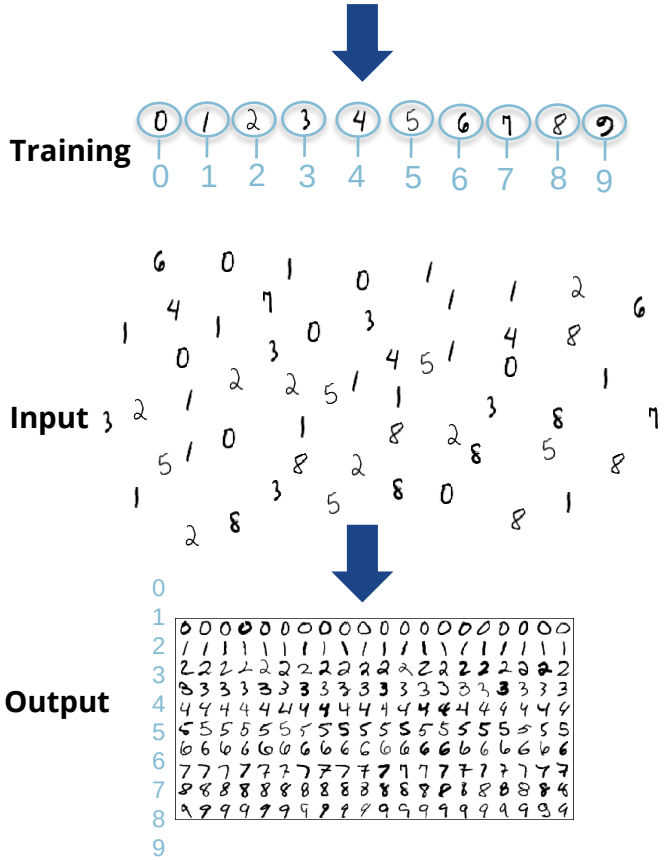
There are different methods by which they learn to recognize these patterns: supervised, semi-supervised, or unsupervised learning.

Aiforia uses supervised learning.



Supervised learning

- Labeled data
- You need a lot of data = myth
- Establishing a ground truth is essential
- Algorithm attempts to learn a general rule that maps input to output
- Categorical outputs (classification) and continuous data (regression)
- Quantifiable data: No, area mm2, area%, metrics, etc.



Supervised learning

Semantic segmentation

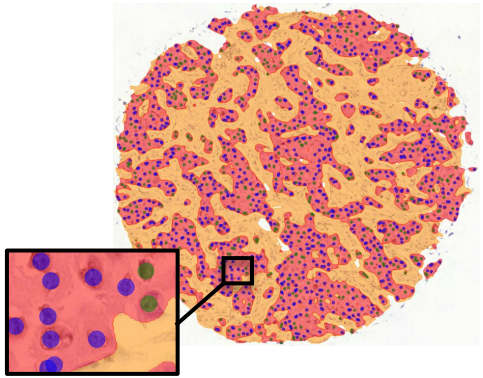
- Tissue
- Cells
- Artefacts

Object detection

- Cells
- Pathogens

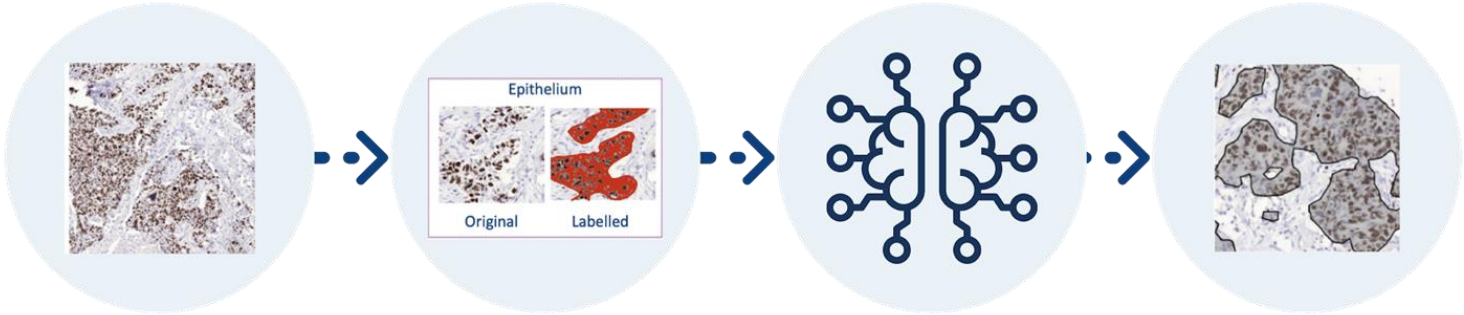
Regression

- Continuous value



How to create AI models with Aiforia

Training workflow



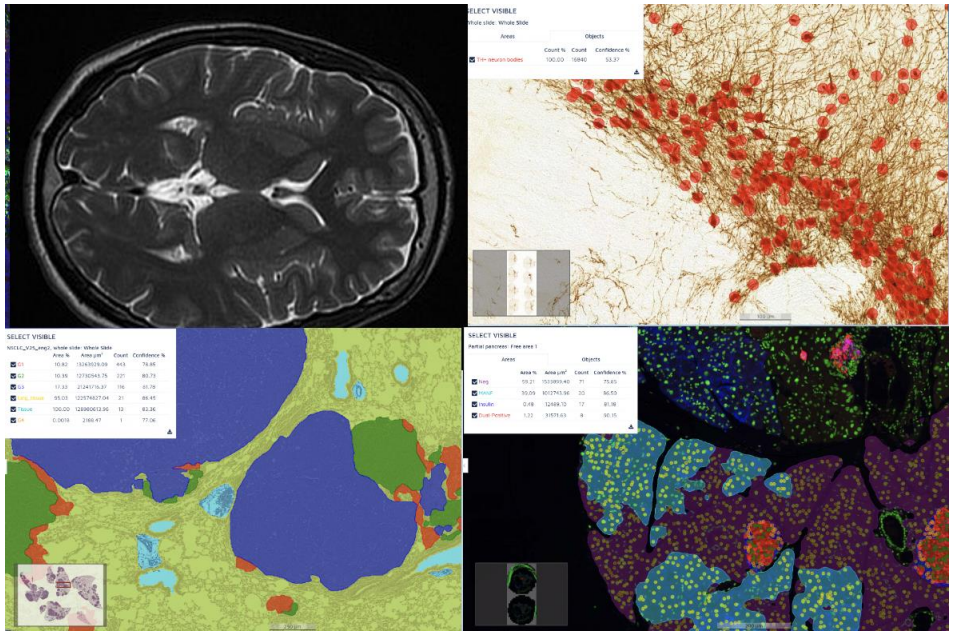
Applications

Any feature in any image

Any 2D image from any field can be analyzed

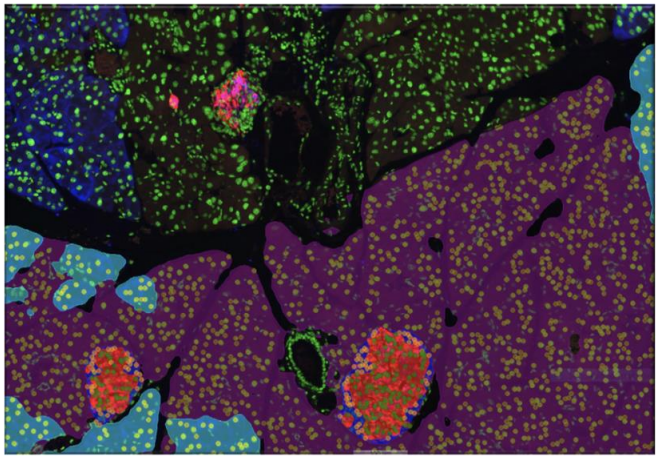
So far over 400+ AI models have been developed with Aiforia across a huge number of medical fields:

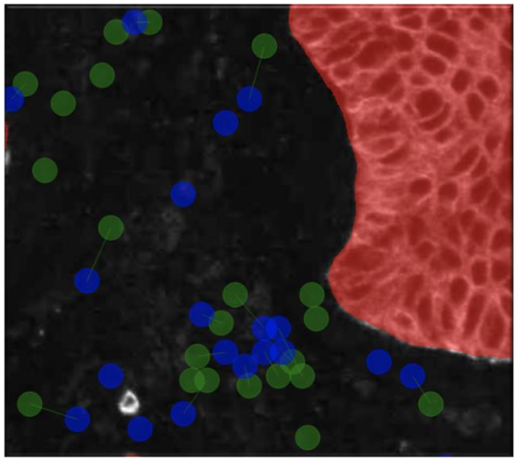
- **GI tract**
  - Irritable bowel disease
  - Inflammation, etc.
- **Liver diseases**
  - NAFLD/NASH
  - PSC, etc.
- **Cancer**
  - Breast cancer grading
  - PD-L1 scoring, etc.
- **Neurological diseases**
  - Neuron quantification
  - Parkinson's, etc.
- **Microbiology**
  - Tuberculosis
  - Malaria, etc.
- The list goes on!



Fluorescence

BioMarker Quantification (area µm², area% / No, %)

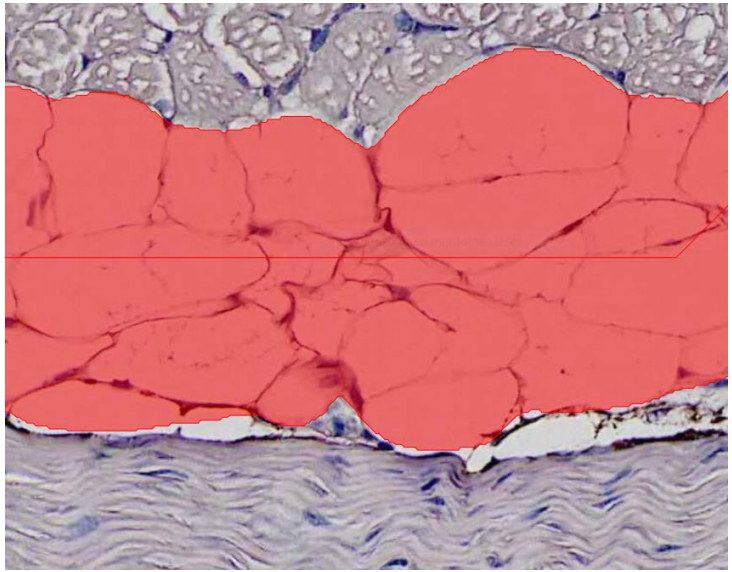




Pancreas, IF: Courtesy of Lindahl, University of Helsinki, Finland

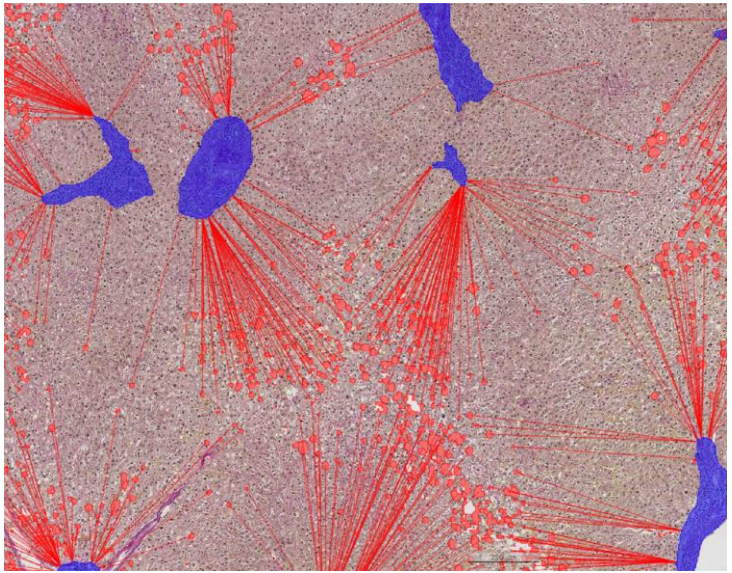
Quantification and metrics

Length, width, perimeter (µm)



Courtesy of Nofima, Norway

Spatial distribution (distance µm, No)



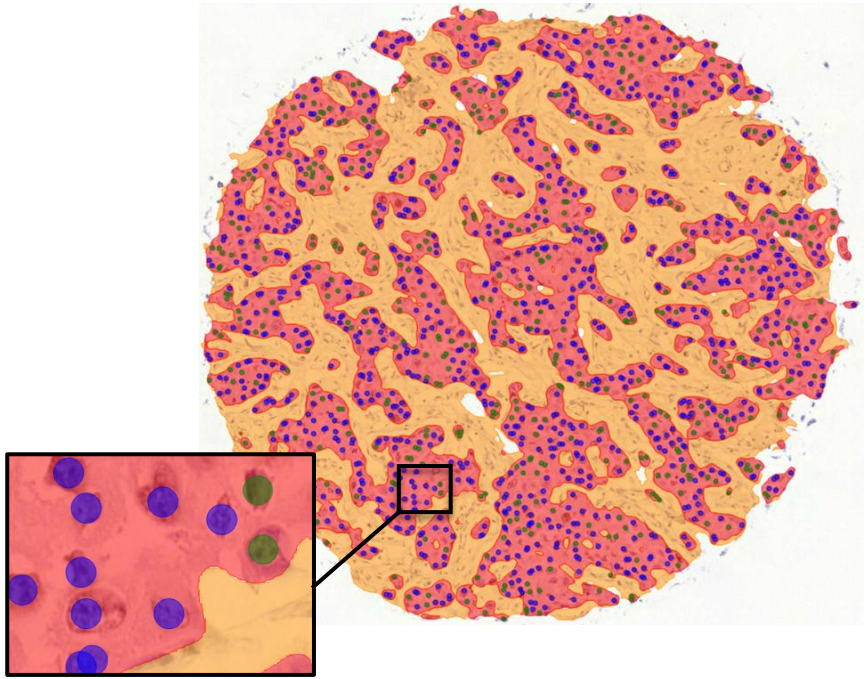
Courtesy of H. Yki-Järvinen, University of Helsinki, Finland

Segmentation and object detection

Unique:

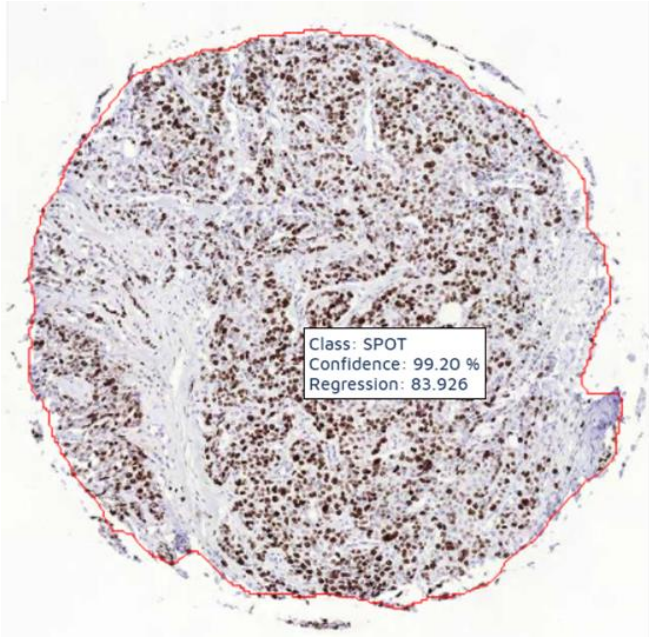
Multi-class capability

Combination of segmentation and object detection



Regression models

- IHC staining
- Positivity/intensity
- Reactivity
- Cell/nuclear size
- Disease-free survival
- Other end points



Ki67-IHC staining intensity in breast tumor epithelium

Case studies

Neuroscience case study

Neuron quantification in Parkinson’s disease study

Received: 16 March 2018 | Revised: 24 July 2018 | Accepted: 10 August 2018
DOI: 10.1111/ejn.14129

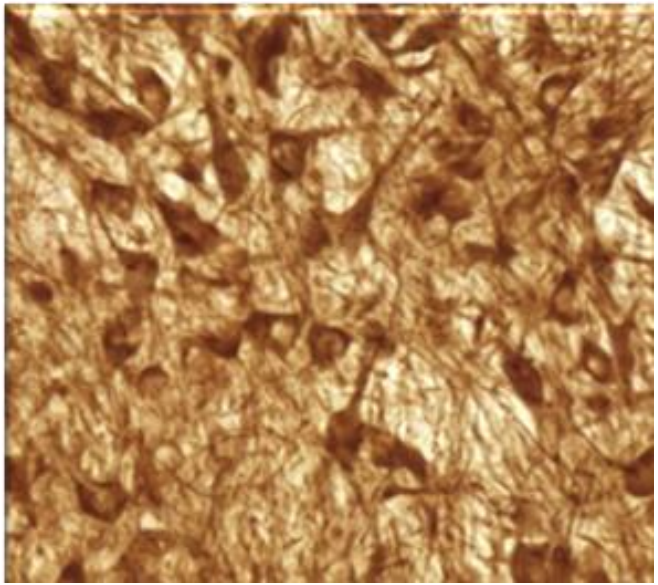
TECHNICAL SPOTLIGHT

WILEY EJN European Journal of Neuroscience FENS

Implementation of deep neural networks to count dopamine neurons in substantia nigra

Anna-Maija Penttinen[1*] | Ilmari Parkkinen[1*] | Sami Blom[2] | Jaakko Kopra[3] | Jaan-Olle Andressoo[1] | Kari Pitkänen[2] | Merja H. Voutilainen[1] | Mart Saarma[1] | Mikko Airavaara[1]

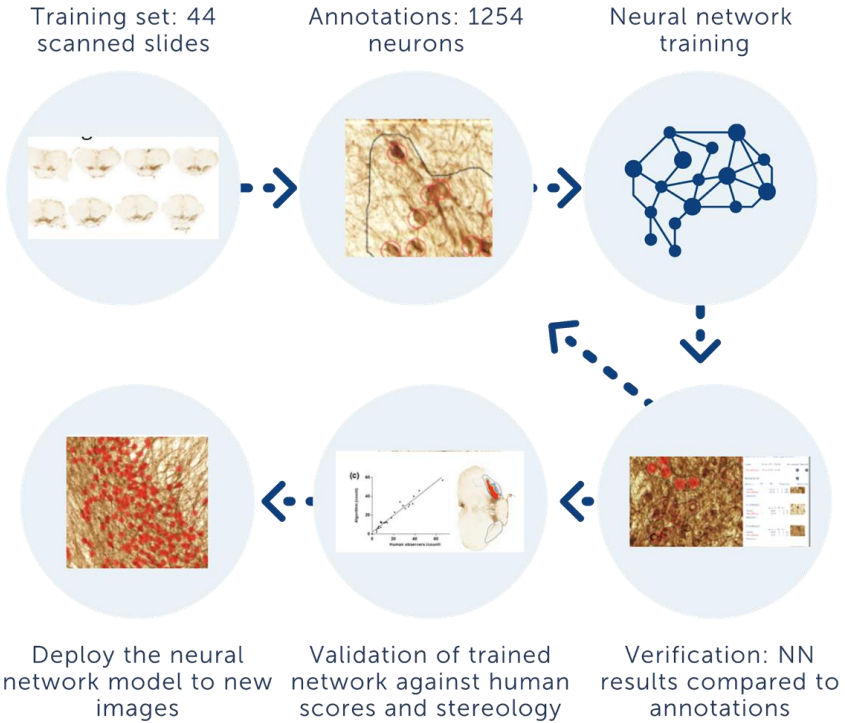
- Dopamine neuron counting in rodent models is an important and widely used research method in PD
- Stereology is the gold standard
- Neurons are counted by eye-balling on random regions-of-interest



Materials and methods

- 37 male Wistar rats, 5 male glial cell line-derived neurotropic factor (GDNF) hypermorphic mice in triple mixed background
- 6-OHDA injection
- Brain fixed in 4% paraformaldehyde
- Coronal sections: 3/mouse; 6/rat
- Anti-tyrosine hydroxylase antibody visualized with 3´,3´-diaminobenzidine. No counterstain.
- Section thickness 40 µm
- Scanning: Extended focus with five focal layers and 2 µm intervals, a total depth of 10 µm, rendered in a single focal plane. Resolution 0.22 µm/pixel. Pannoramic P250 Flash II whole slide scanner.

Training the neural networks: workflow



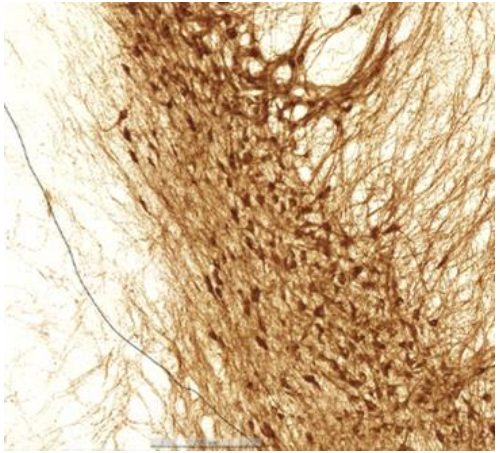
Results

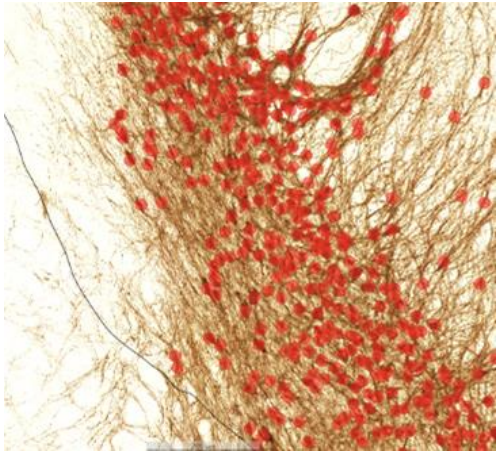
Omits the problem of random sampling

- No counting rules
- Uneven Th+ cell density not a problem
- Counts all ROIs at once

The analysis of a section takes about 45 mins with full hands-on time if using the current gold standard method, stereology.

By using the Aiforia Platform, the analysis was reduced to 20 seconds making the analysis 100x faster with full automation.



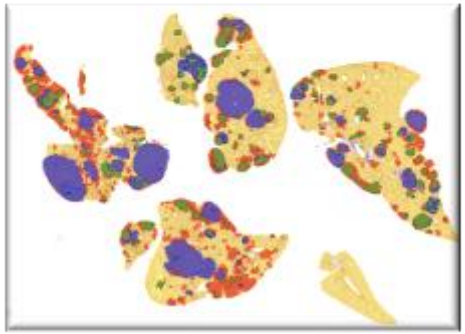


Cancer case study

Automatic histopathologic analysis of murine lung tumors

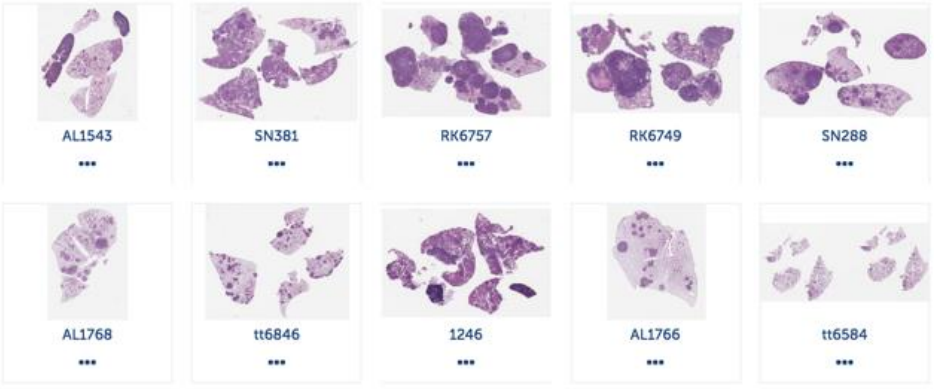
KOCH INSTITUTE for Integrative Cancer Research at MIT

The Jacks Lab



Materials and methods

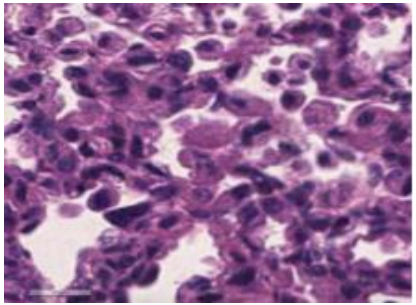
- Digital whole-slide images (WSI): Training set 93 slides; validation set 34 slides
- Grade 1 - 4 *Kras; P53* mutant mouse lung tumors
- HE staining
- Aperio scanner (Leica) with 0.504 µm/px resolution
- Images uploaded to Aiforia Hub



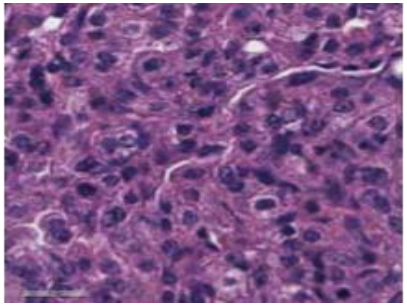
Training the neural networks

Deep Neural Network model trained to:

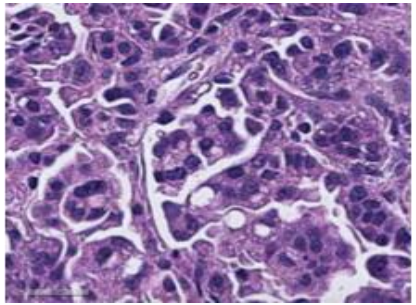
- Detect lung parenchyma and tumors
- Classify tumors according to histopathologic grade (1-4)



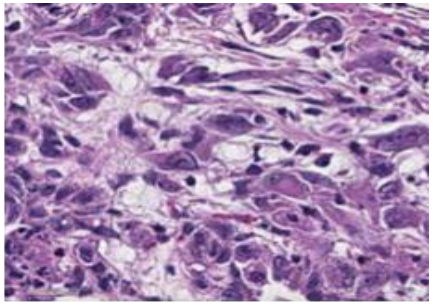
Grade 1



Grade 2



Grade 3



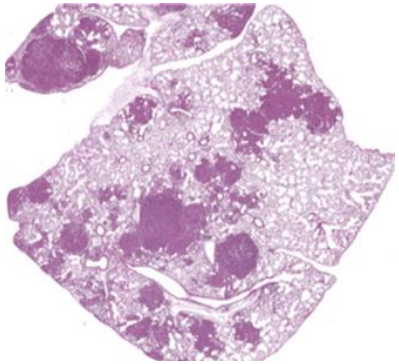
Grade 4

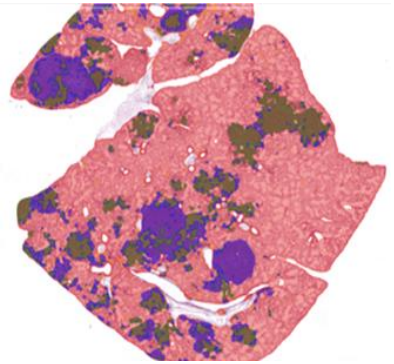
Results

Neural network model performance against training data (total training area):

Lung parenchyma and tumor detection 99.7% (error 0.3%)

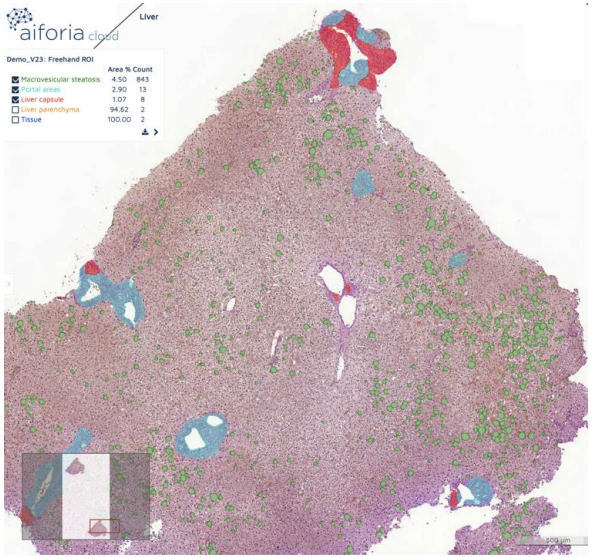
Average analysis time for validation slides: **3min 30sec** per WSI

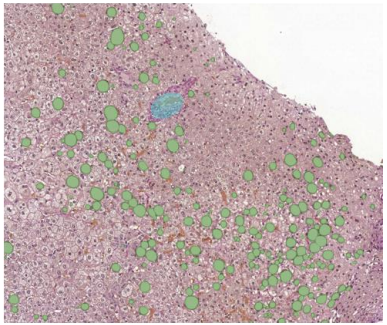




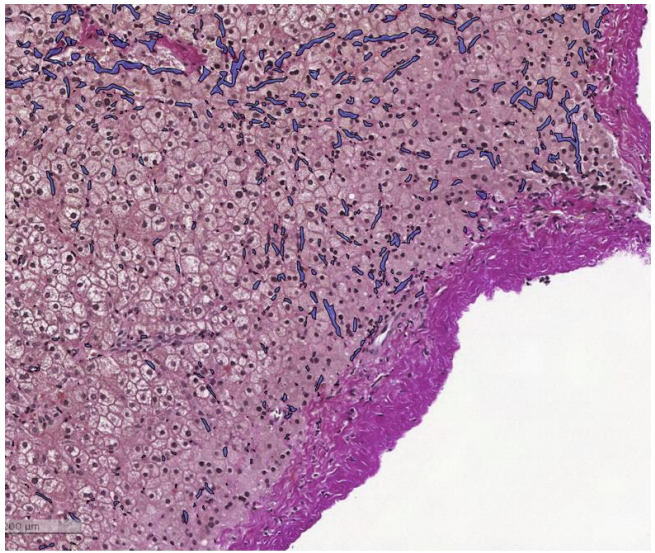
Liver case study

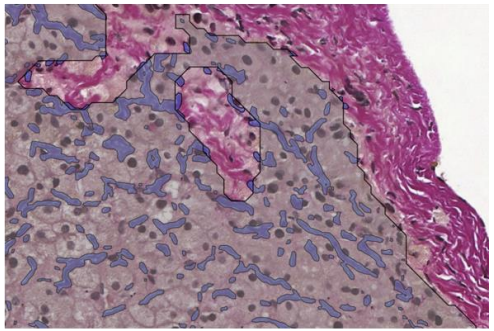
NASH - Quantification of fat accumulation in liver





Quantification of fibrosis in liver tissue



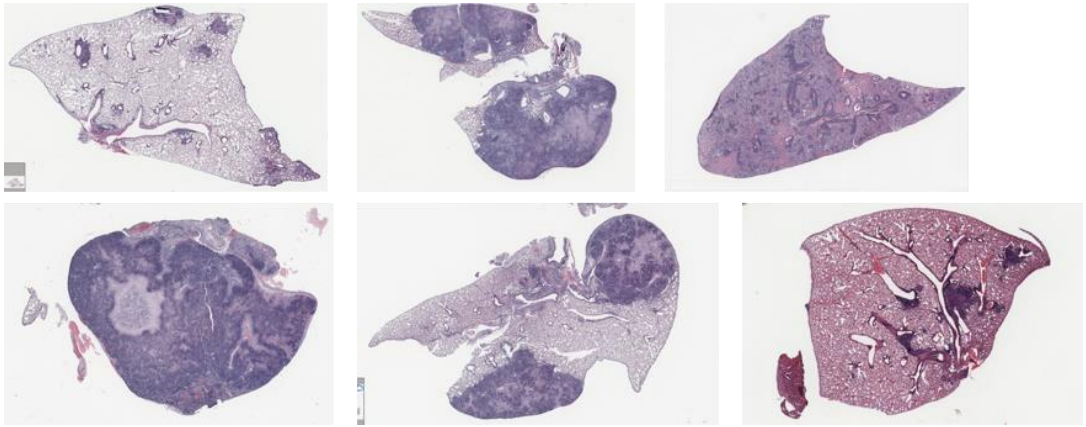


Courtesy of H. Yki-Järvinen, Univerity of Helsinki, Finland

TB case study

- Digital **whole-slide images** (WSI) of TB infected mouse lung sections (H&E) acquired using digital scanner and uploaded to Aiforia®. **Image resolution 0.244 µm/px**
- **3 mouse models:** sensitive, supersensitive, resistant
- **Training set:** 57 animals
- **Validation set:** 54 animals
- Deep Convolutional Neural Network trained to detect lung parencyma, granulomas and necrosis

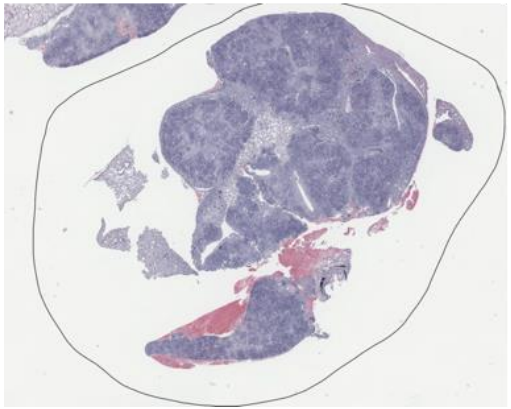
The TB mouse models shows considerable lesion heterogeneity

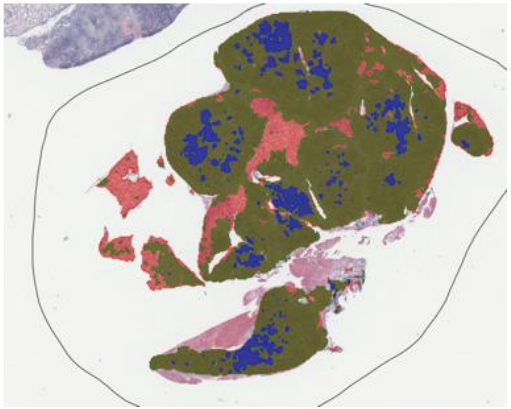


Results

Analysis time for slides: **3–11 min** per WSI

	Area %	Count	Area mm²
necrosis	9.62	252	2.35
granuloma	83.56	71	24.41
exclude_lumens_veins_fat	100.00	35	29.21





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