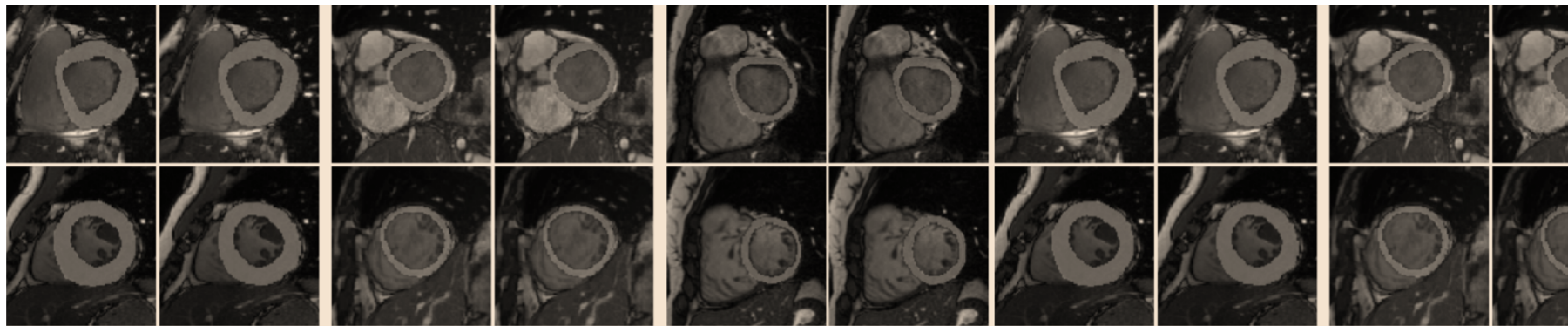
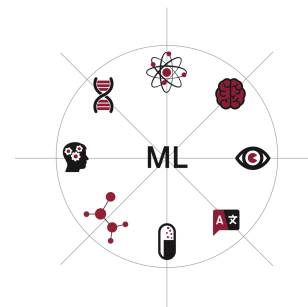




Cluster of Excellence: Machine Learning – New Perspectives for Science



Machine learning for medical image analysis and why clinicians are not using it





Quick Personal Introduction

- **Master of Science, ETH Zürich (2012)**
- **Doctoral Studies, King's College London @ St. Thomas Hospital (2016)**
Title: "Manifold alignment for imaging and modelling respiratory motion" Advisors: Prof. Andrew King, Prof. Daniel Rueckert
- **Post-doc, Imperial College London (2016-2017)**
Biomedical Image Analysis Group (BioMedIA)
Advisor: Prof. Daniel Rueckert
- **Postdoctoral Fellow - ETH Fellowship, ETH Zürich (2017-2019)**
Biomedical Image Computing Group
Advisor: Prof. Ender Konukoglu
- **Senior Research and Development Engineer, PTC Vuforia (2020-2021)**
Guest Researcher at ETH Zürich (2020-2021)

ETHzürich

KING'S
College
LONDON

Imperial College
London

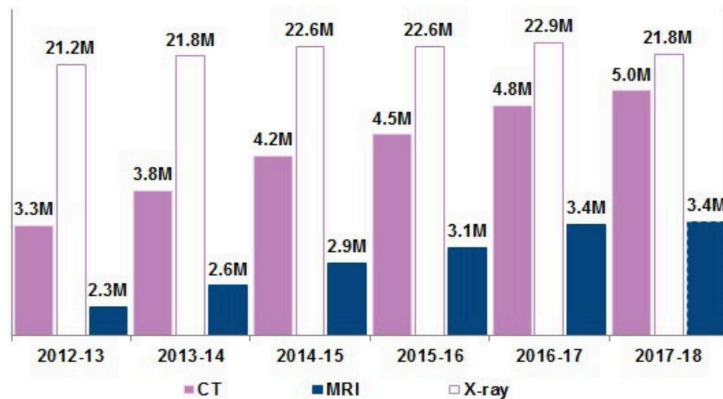
ETHzürich

 **ptc** / **ETH**zürich

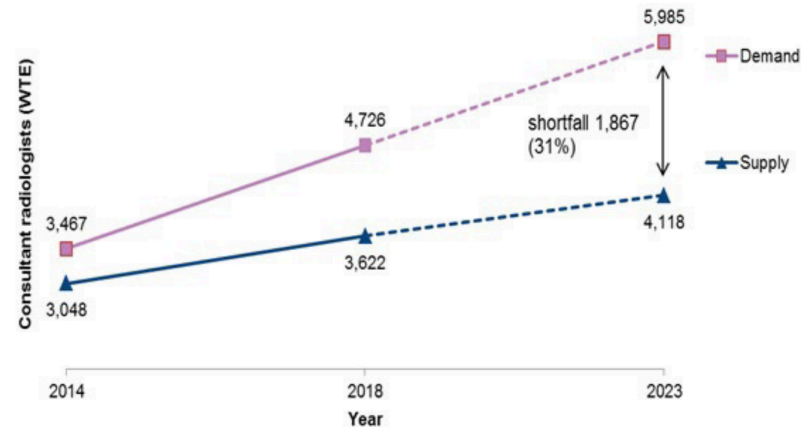


Why do we need machine learning in medical image analysis?

→ **More efficient** processing of medical data



~31% increase in MR and CT images



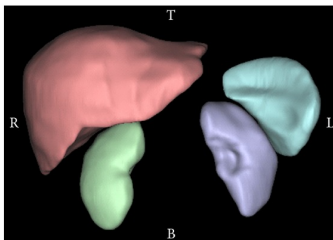
Only ~18% increase in radiologists

Why do we need machine learning in medical image analysis?

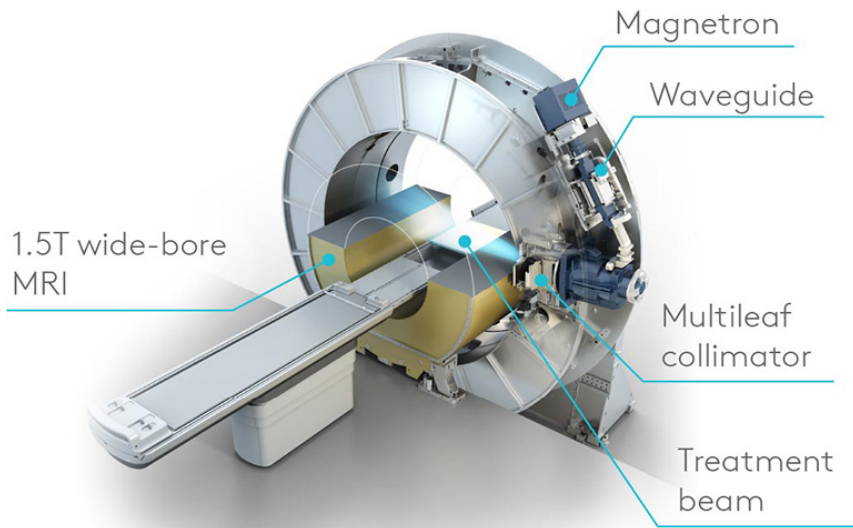
→ Personalisation of treatments, **novel workflows**



(a)

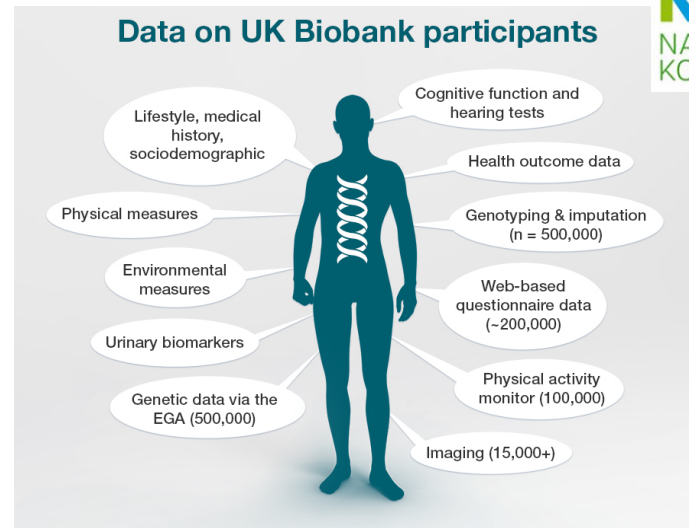
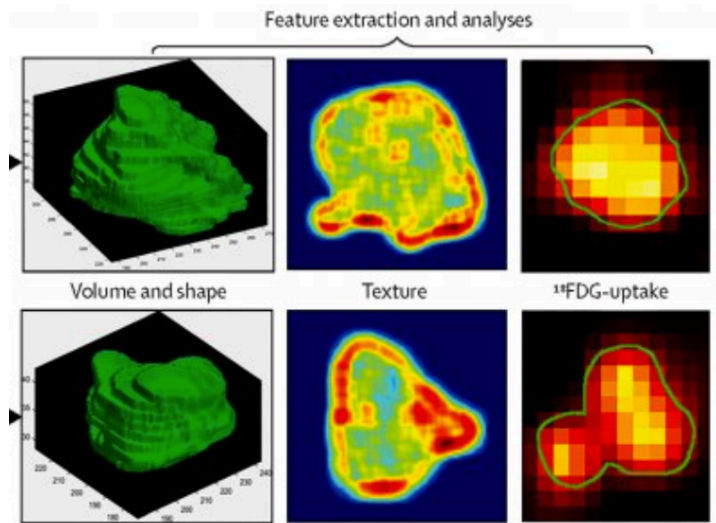


(b)



Why do we need machine learning in medical image analysis?

→ Discovery of **novel clinical biomarkers** from big medical data





Why do we need machine learning in medical image analysis?

→ **Safer** medicine

- Large amount of misdiagnosis and unnecessary treatments
- In the US most people experience at least one diagnostic error in their life-time
- Physicians
 - are often overworked
 - use intuitive reasoning and “often cannot fully explain how a diagnostic hypothesis occurs to them”¹
 - Are subject to biases (e.g. confirmation bias, self-serving bias, prejudice, ...)



TOM SIMONITE BUSINESS 01.25.2021 07:00 AM

New Algorithms Could Reduce Racial Disparities in Health Care

Machine learning programs trained with patients' own reports find problems that doctors miss—especially in Black people.

¹Brush, J. E., & Brophy, J. M. (2017). Sharing the Process of Diagnostic Decision Making. JAMA Internal Medicine, 177(9), 1245



Deep Learning on Medical Images

Human-level CMR image analysis with deep fully convolutional networks

Wenjia Bai^{1*} Matthew Sinclair¹ Giacomo Tarroni¹ Ozan Oktay¹ Martin Rajchl¹
Ghislain Vaillant¹ Aaron M. Lee² Nay Aung² Elena Lukaschuk³ Mihir M. Sanghvi²
Filip Zemrak² Kenneth Fung² Jose Miguel Paiva² Valentina Carapella³
Young Jin Kim³ Hideaki Suzuki⁴ Bernhard Kainz¹ Paul M. Matthews⁴
Steffen E. Petersen² Stefan K. Piechnik³ Stefan Neubauer³ Ben Glocker¹
Daniel Rueckert¹

Published: 25 January 2017

Dermatologist-level classification of skin cancer with deep neural networks

Andre Esteva , Brett Kuperl , Roberto A. Novoa , [Justin Ko](#), Susan M. Swetter, Helen M. Blau & Sebastian Thrun 

Attaining human-level performance with atlas location autocontext for anatomical landmark detection in 3D CT data

Alison Q. O'Neil¹, Antanas Kascenas¹, Joseph Henry¹, Daniel Wyeth¹, Matthew Shepherd¹, Erin Beveridge¹, Lauren Clunie¹, Carrie Sansom¹, Evelina Šeduikytė¹ Keith Muir², and Ian Poole¹

Human-level Performance On Automatic Head Biometrics In Fetal Ultrasound Using Fully Convolutional Neural Networks

Matthew Sinclair, Christian F. Baumgartner, Jacqueline Matthew, Wenjia Bai, Juan Cerrolaza Martinez, Yuanwei Li, Sandra Smith, Caroline L. Knight, Bernhard Kainz, *Senior Member, IEEE*, Jo Hajnal, Andrew P. King, Daniel Rueckert, *Fellow, IEEE*



Is the problem solved?

Geoff Hinton in 2016:

“People should stop training radiologists now. It’s just completely obvious that within 5 years deep learning is going to do better than radiologists.”





Reality

As of October 2019 there are 28 medical AI solutions operating on image data that have been approved by the food and drug administration (FDA)

“The Lancet” meta-study

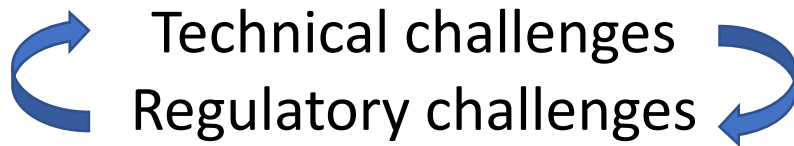
A comparison of deep learning performance against health-care professionals in detecting diseases from medical imaging: a systematic review and meta-analysis

[Xiaoxuan Liu, MBChB](#) [†] • [Livia Faes, MD](#) [†] • [Aditya U Kale, MBChB](#) • [Siegfried K Wagner, BMBCh](#) • [Dun Jack Fu, PhD](#) • [Alice Bruynseels, MBChB](#) • et al. [Show all authors](#) • [Show footnotes](#)

- Little evidence comparing performance of humans and machines
- Often not comparing performance in clinical environments
- **The true diagnostic power of AI remains uncertain**



Why isn't AI used more in clinical practice?



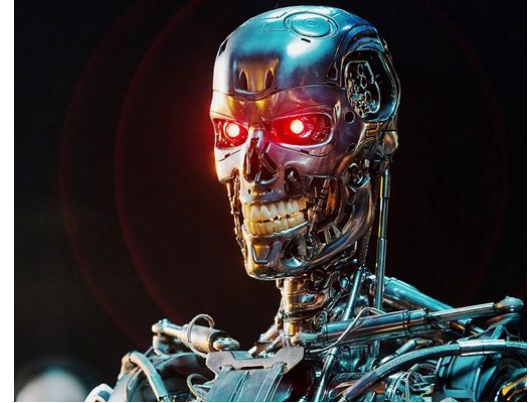
Human factors



Human factors

Physicians' fears about AI:

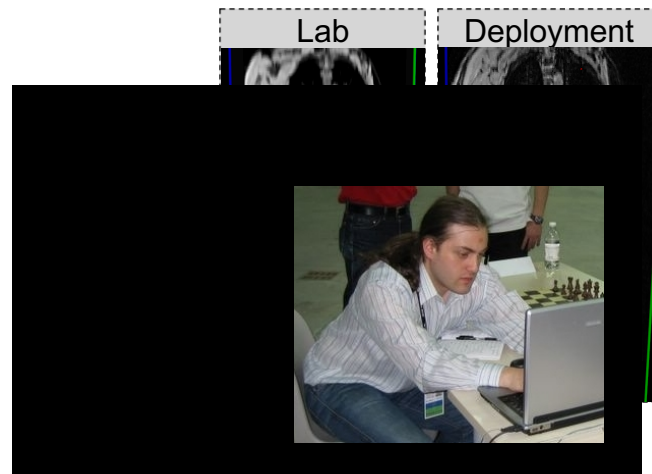
- Interferes with ability to make independent diagnoses
 - Hurts relationship with patients
 - It's a form of management control
-
- Med students who know the technology are less afraid of it
 - Less than one-third of med students knows AI basics
 - Med students get more AI information from media than lectures
-
- **Solution: Better education at student and professional level**
 - **Better involvement of medical community in AI research**



"AI won't replace radiologists, but radiologists who use AI will replace radiologists who don't", Curtis Langlotz

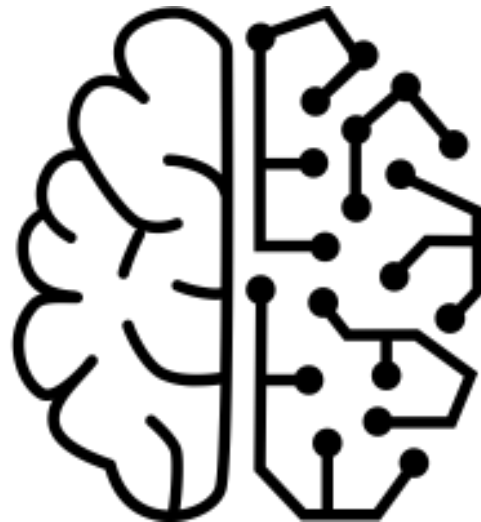
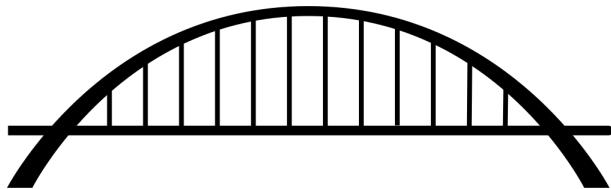
Technical challenges

- Deep networks lack robustness + non-standardised medical image acquisition
- Annotated data scarce and expensive
- Medical images are often 3D or even 3D+t
- Human vs. AI approach, rather than human **with** AI



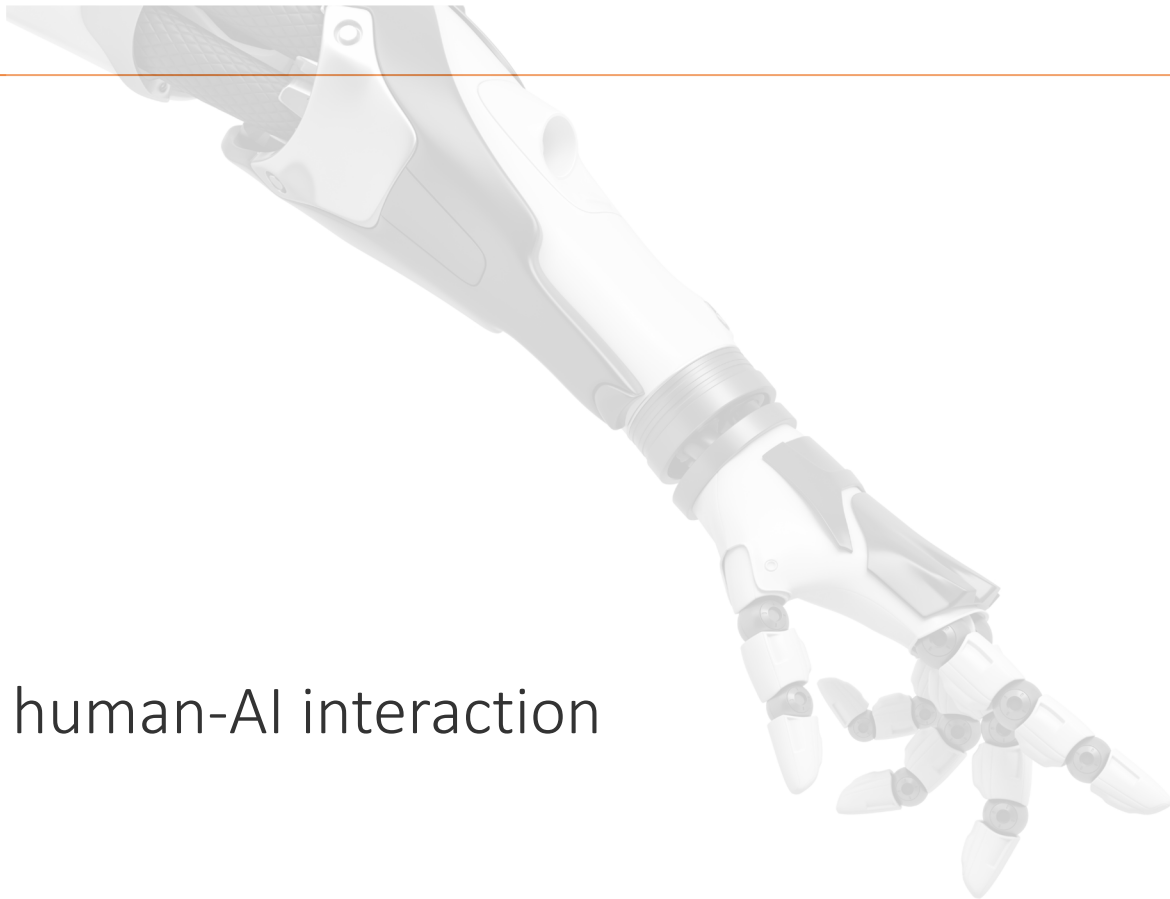


My Research





Technologies for better human-AI interaction

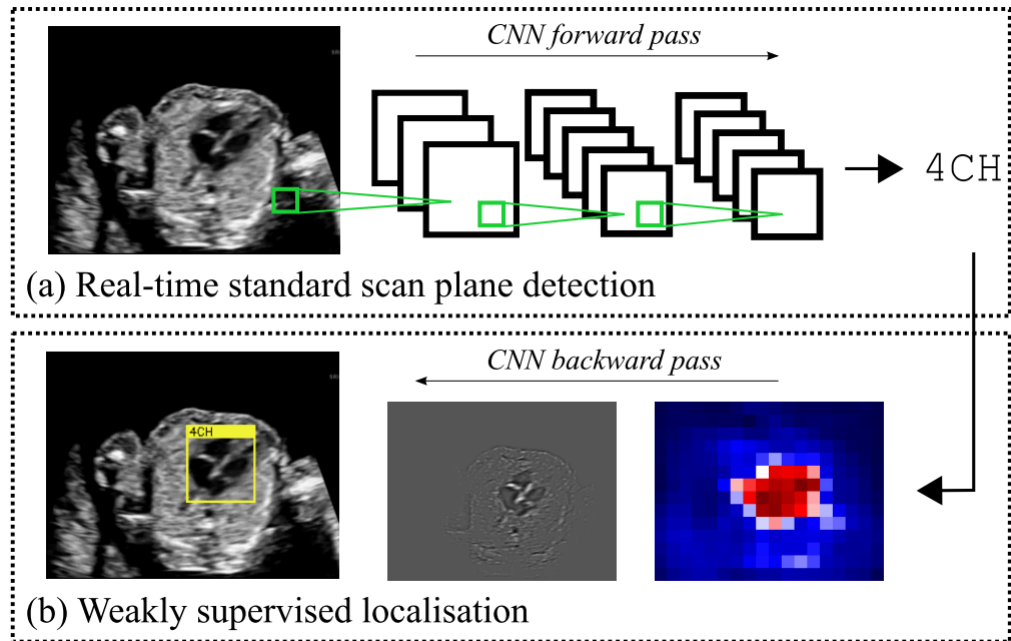


Interpretability of fetal scan plane detection network



Problem: Identify correct standard view planes in 20 weeks old fetus

Scan plane classification and associated saliency-map explanations



Real-Time Detection and Localisation of Fetal Standard Scan Planes in 2D Freehand Ultrasound

Christian F. Baumgartner, Konstantinos Kamnitsas, Jacqueline Matthew, Tara P. Fletcher, Sandra Smith, Lisa M. Koch, Bernhard Kainz and Daniel Rueckert

Video Demonstration

-

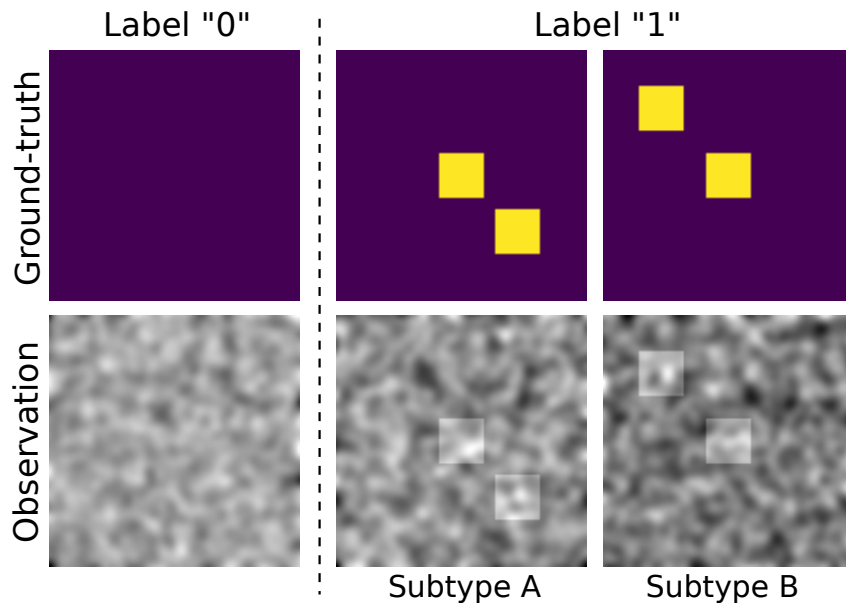
Overview of proposed method



Interpreting a classifier vs. understanding a class

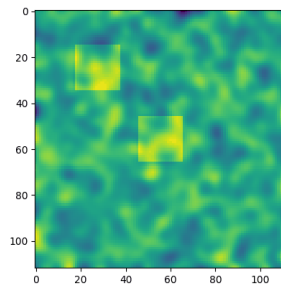
- Saliency maps show us which pixels a classifier is paying attention to
 - Saliency maps **do not** show us all pixels characterising a class
- **Take away:** We should not use saliency maps for weakly supervised localisation
- In this work we investigated an alternative way of identifying *all* pixels belonging to a class

Motivation: toy classification problem

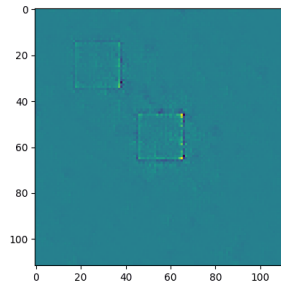


Result of Guided-Backpropagation

Input Image:



Saliency map:



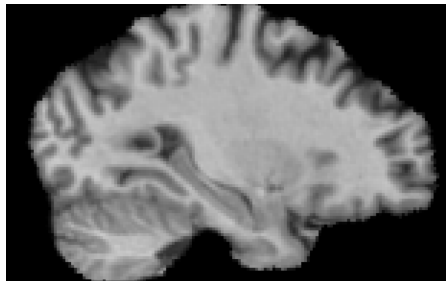
Classifier focuses on minimum features required for classification!



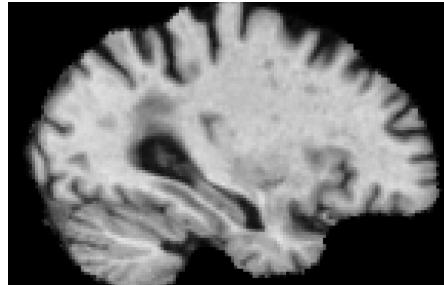
Alternative method for feature attribution not involving classifiers

Assume our image data are samples from two probability distributions:

$$p(x|c = 0)$$



$$p(x|c = 1)$$



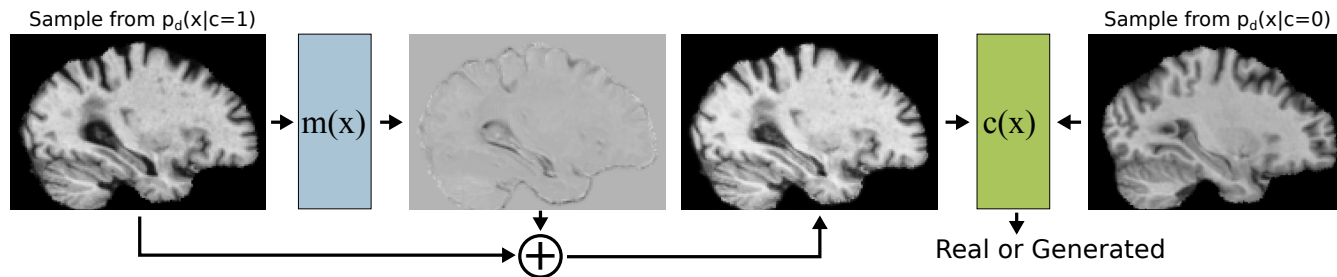
$c=0$ (mild cognitive impairment)

$c=1$ (Alzheimer's disease)

Can we find a function $m(x)$ that when added to a healthy image, will make it look like a diseased image?

Finding the class-related pixels using Wasserstein GANs

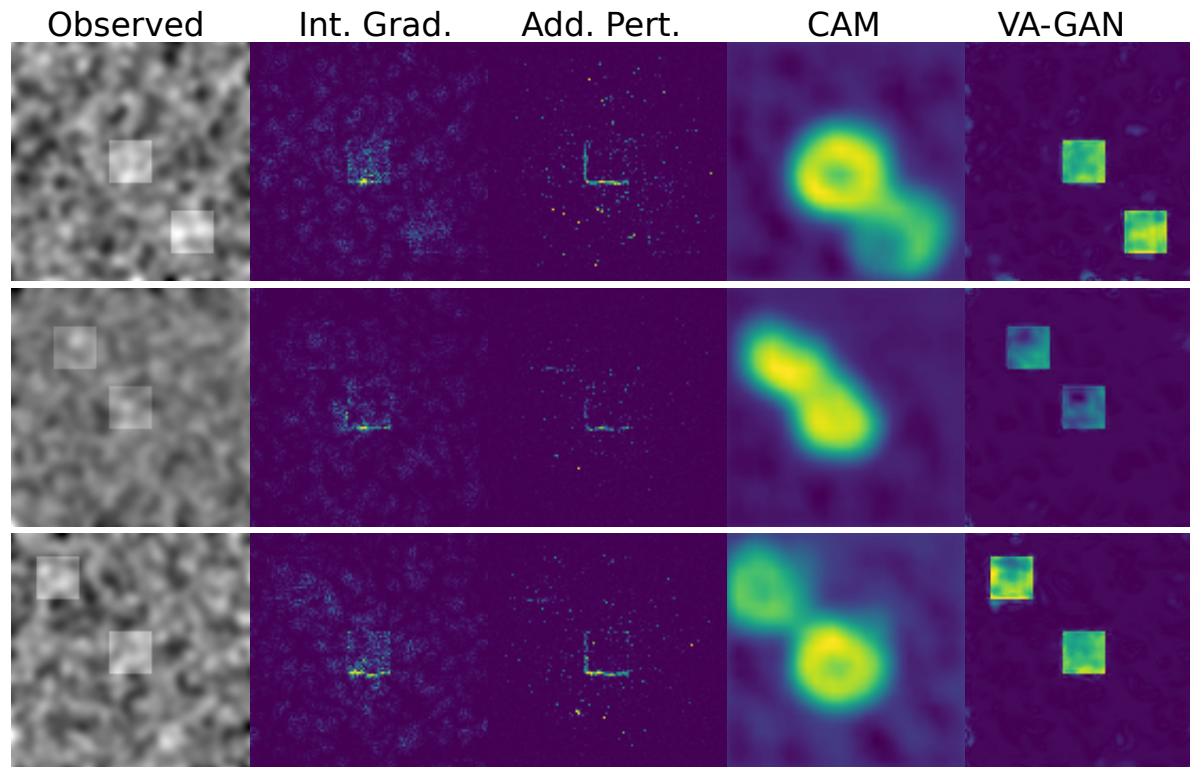
WGANs are a flavour of GANs that can be shown to minimize the Wasserstein-1 or Earth Movers Distance between the probability distributions.



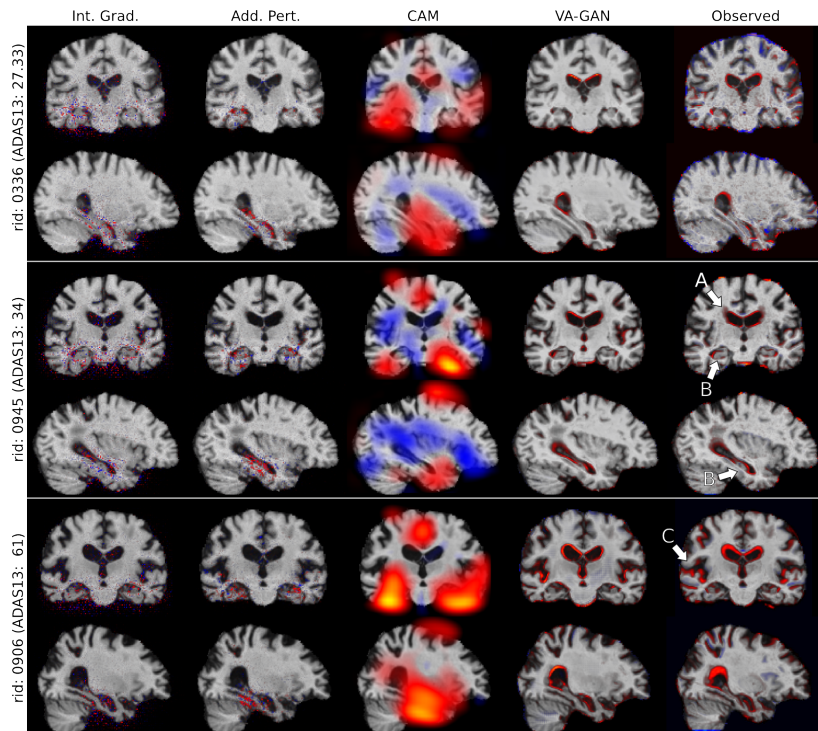
$$\begin{aligned}\mathcal{L}_{GAN}(\theta, \phi) &= \mathbb{E}_{x \sim p_d(x|c=0)}[c_\phi(x)] \\ &\quad - \mathbb{E}_{x \sim p_d(x|c=1)}[c_\phi(x + m_\theta(x))] \\ \theta^* &= \arg \min_{\theta} \max_{\phi} \mathcal{L}_{GAN}(\theta, \phi) + \lambda \mathcal{L}_{reg}(\phi),\end{aligned}$$



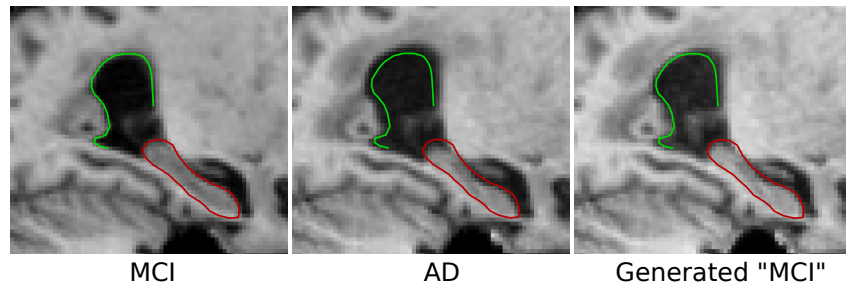
Experiments on toy data



Experiments on Alzheimer Brain Data

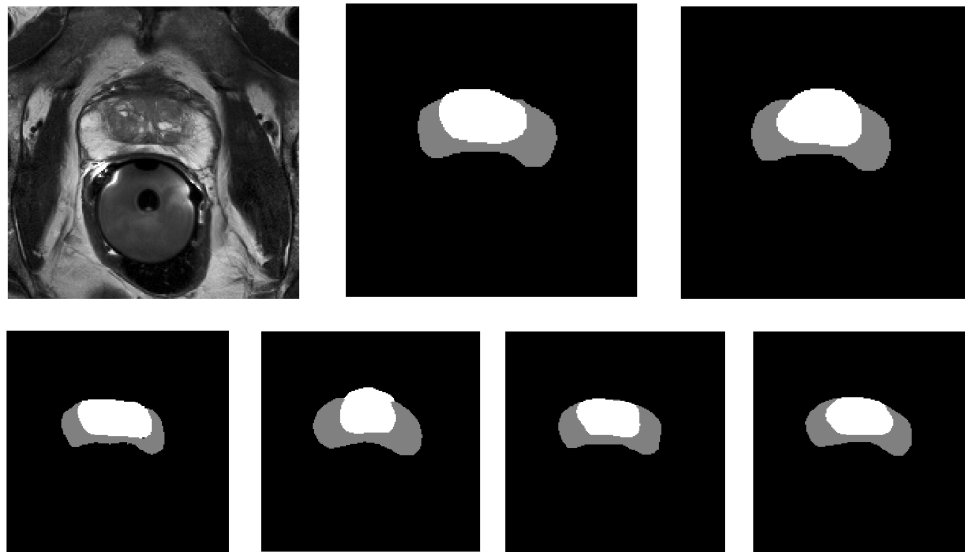


Close-up of Hippocampus




Inter-operator uncertainty quantification


Segmentation of prostate transitional and peripheral zones



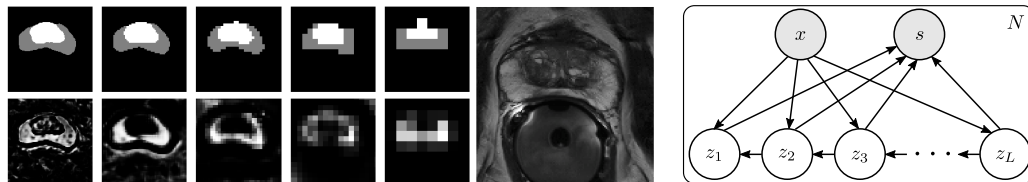
We would like to model the distribution

$$p(s|x)$$

x 

s 

We postulate a hierarchical generative process for the images



$$p(s|x) = \int p(s|z_1, \dots, z_L) p(z_1|z_2, x) \cdots p(z_{L-1}|z_L, x) p(z_L|x) dz_1 \cdots dz_L$$



Variational Inference in our conditional hierarchical model

$$p(s|x) = \int p(s|z_1, \dots, z_L) \underbrace{p(z_1|z_2, x) \cdots p(z_{L-1}|z_L, x)p(z_L|x)}_{\text{Use } q(z/s, x) \text{ to approximate } p(z/x)} dz_1 \cdots dz_L$$

Use $q(z/s, x)$ to approximate $p(z/x)$

$$\log p(\mathbf{s}|\mathbf{x}) = \mathcal{L}(\mathbf{s}|\mathbf{x}) + \text{KL}(q(\mathbf{z}|\mathbf{s}, \mathbf{x}) || p(\mathbf{z}|\mathbf{s}, \mathbf{x}))$$



Evidence lower bound (ELBO)



Variational Inference in our conditional hierarchical model

We can use a variational approximation $q(z/s, x)$ to approximate $p(z/x)$.

$$\ln p(s|x) \geq \mathcal{L}(s|x)$$

$$\begin{aligned} \mathcal{L} = & \mathbb{E}_{q(z_1, \dots, z_L | x, s)} [\log p(s | z_1, \dots, z_L)] - \alpha_L \text{KL} [q(z_L | s, x) || p(z_L | x)] \\ & - \sum_{\ell=1}^{L-1} \alpha_\ell \mathbb{E}_{q(z_{\ell+1} | s, x)} [\text{KL} [q(z_\ell | z_{\ell+1}, s, x) || p(z_\ell | z_{\ell+1}, x)]], \end{aligned}$$

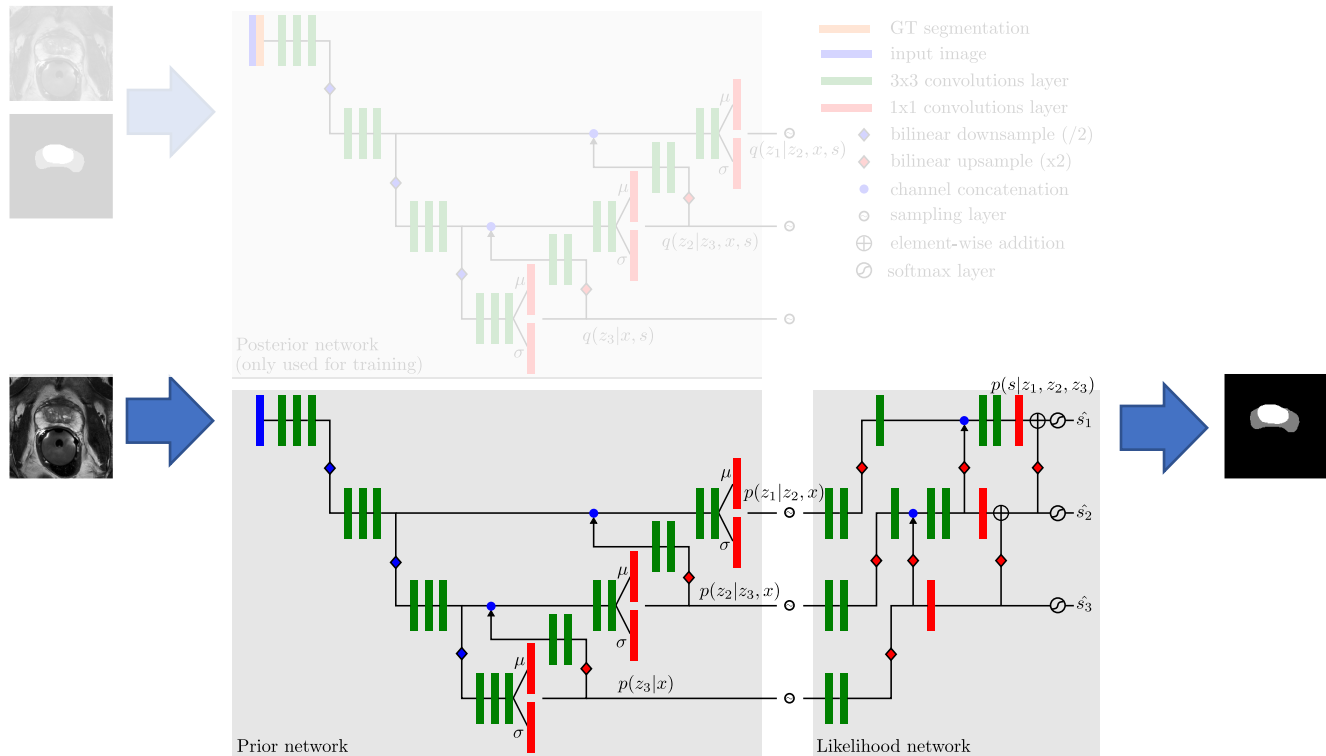
$$p(z_\ell | z_{\ell+1}, x) = \mathcal{N} \left(z_\ell | \phi_\ell^{(\mu)}(z_{\ell+1}, x), \phi_\ell^{(\sigma)}(z_{\ell+1}, x) \right)$$

$$q(z_\ell | z_{\ell+1}, x, s) = \mathcal{N} \left(z_\ell | \theta_\ell^{(\mu)}(z_{\ell+1}, s, x), \theta_\ell^{(\sigma)}(z_{\ell+1}, s, x) \right)$$

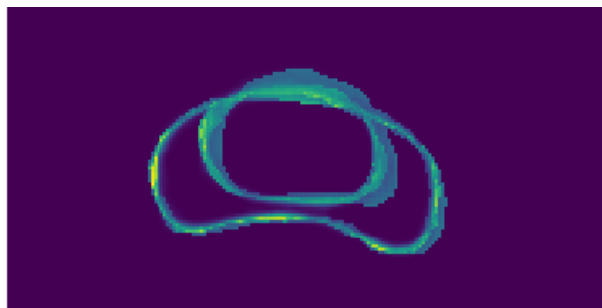
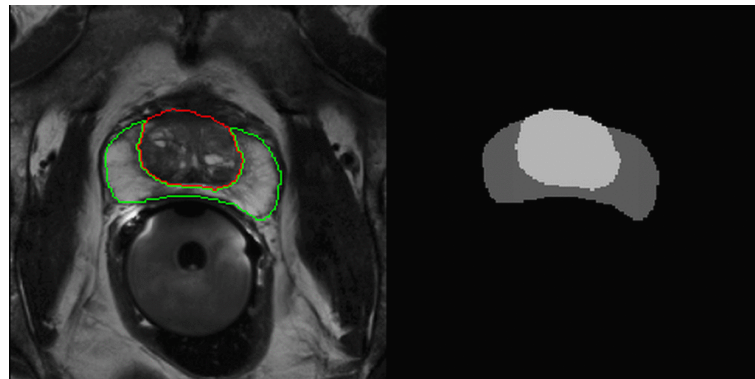
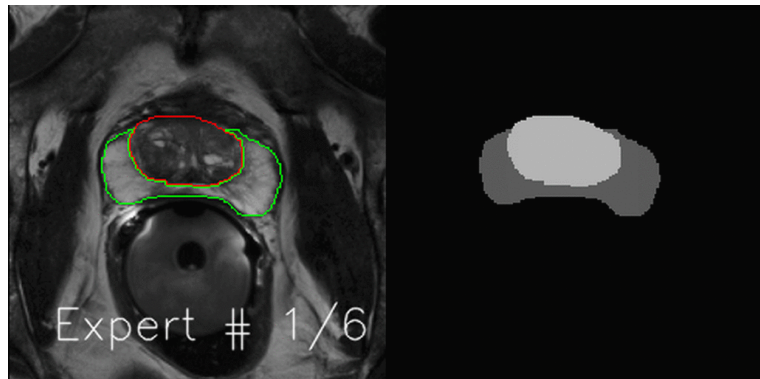
$$p(s|z) = \text{Cat}(s | \pi(z))$$



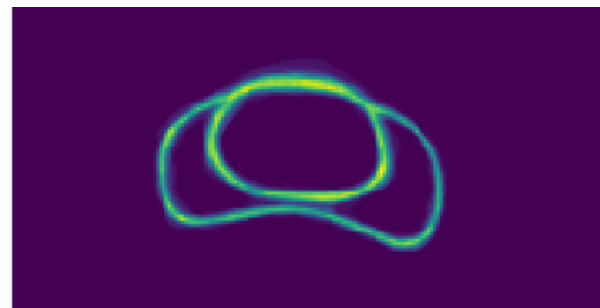
Implementing the hierarchical model with neural networks



Learned uncertainty can be displayed as samples or as uncertainty map

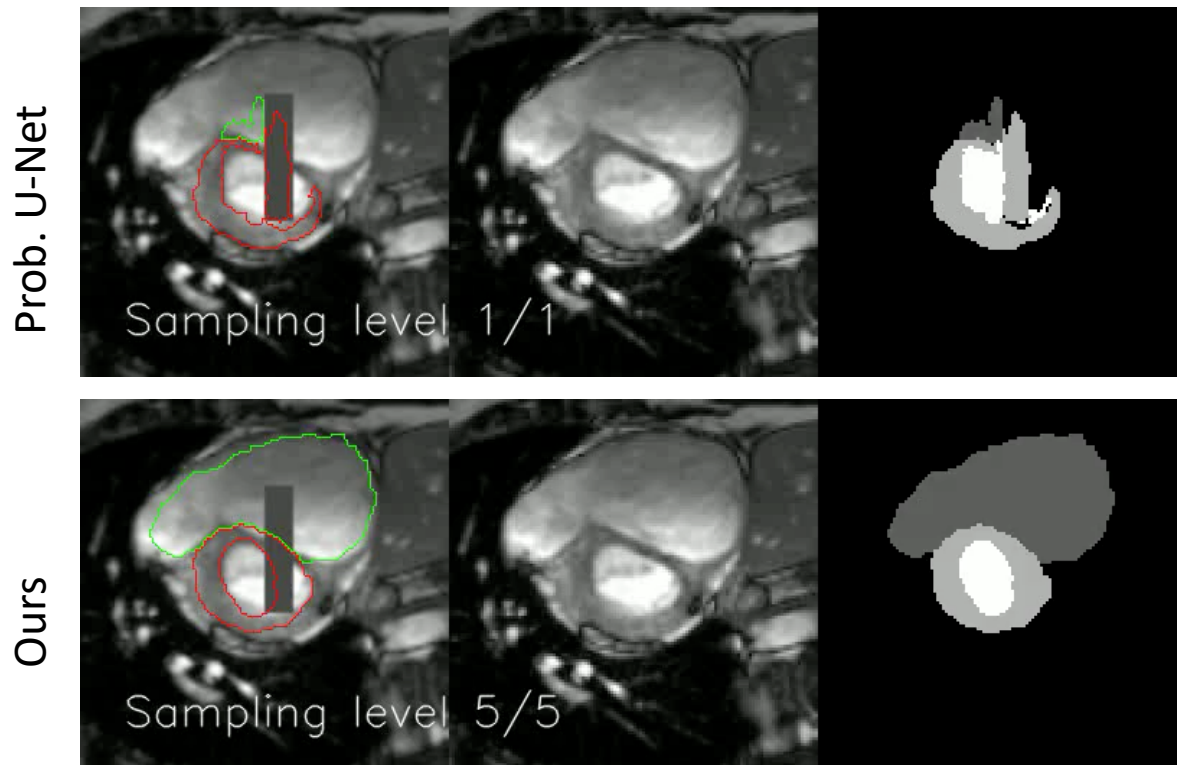


Annotator variance



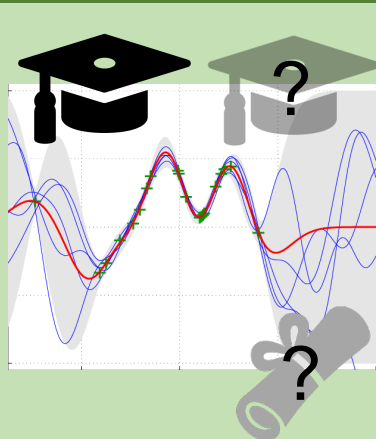
Predicted variance

Intriguing Robustness properties

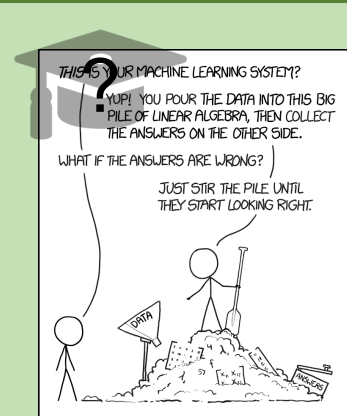


Future directions

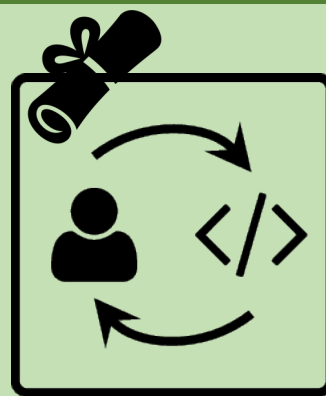
Methodological advances to enable human-AI collaboration



Uncertainty Estimation
Robustness

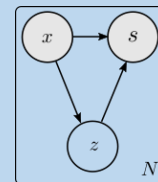


Interpretable
ML



Human-in-the-loop
Systems

Generative Modelling



Probabilistic
Inference



Summary

- We are seeing the beginning of an AI revolution in medical imaging
- This revolution will open many exciting avenues for improving patient outcomes
- However, the initial, superficial success of deep learning is misleading
- There remain challenging methodological problems to be solved, especially involving the human-AI interface
- Real research progress will happen in collaborations between clinicians and AI researchers



Thank you for your attention!



PhD in robust ML for Medical Image Analysis (joint with M. Hein)



PhD or Post-doc in interpretable ML for Medical Image Analysis



Master student uncertainty quantification in neuroimaging
(joint with **AIRAm**ed)
artificial intelligence in radiology



christian.baumgartner@uni-tuebingen.de