ML in Medical Imaging

with example applications to neurology

Jorge Cardoso

Reader, KCL

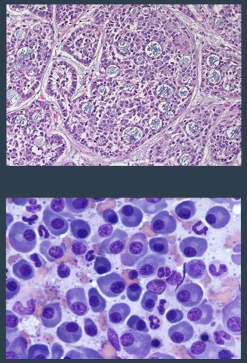
“Up to three-to-five years ago all that [medical] data was just sitting there. Now it is being analyzed and interpreted. It is the most radical change happening in healthcare.”

-- Eric Topol

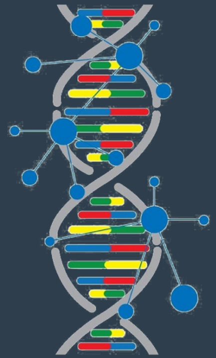
AI IN MEDICINE

27K Medical AI papers - ~30 FDA Approved products
~7 Billion USD investment by 2021

RADIOLOGY
CT, MR, US, X-RAY



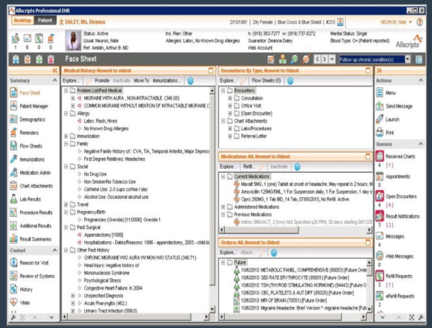
PATHOLOGY
TISSUE & CELL



GENETICS

DERMATOLOGY
OPHTHALMOLOGY

...



ELECTRONIC HEALTH
RECORDS

HOW FAR COULD WE GO?

No more human errors in medicine?

Best outcome for each patient?

Affordable care?

No bias due to small demographics?

Automated diagnosis for most diseases?

Instantaneous diagnoses and wide screenings?

Ability to deal with rare diseases?

Two worlds

Public-heath &
epidemiological Research

Observational studies

Clinical-quality data

Academic Research Studies

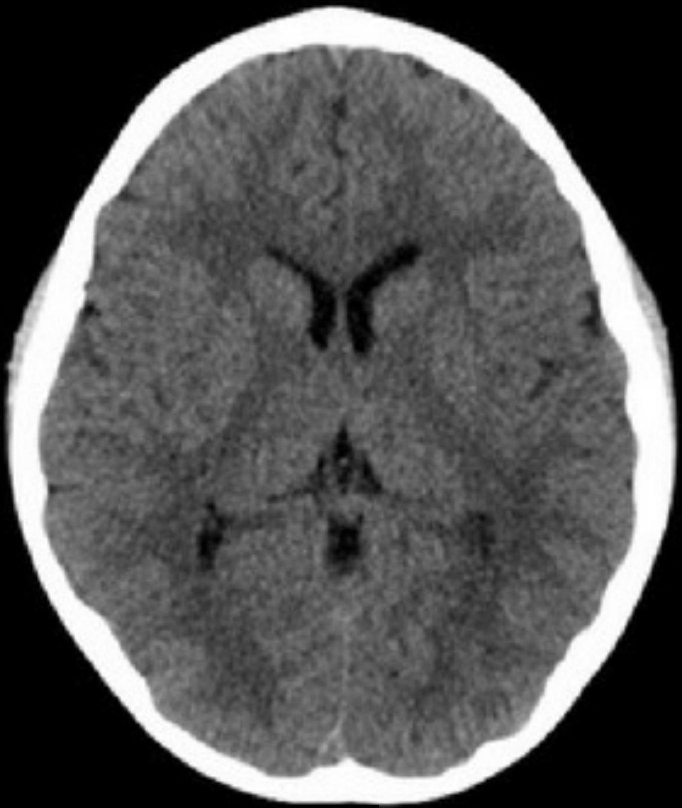
Randomised Clinical Trials

Research-quality data

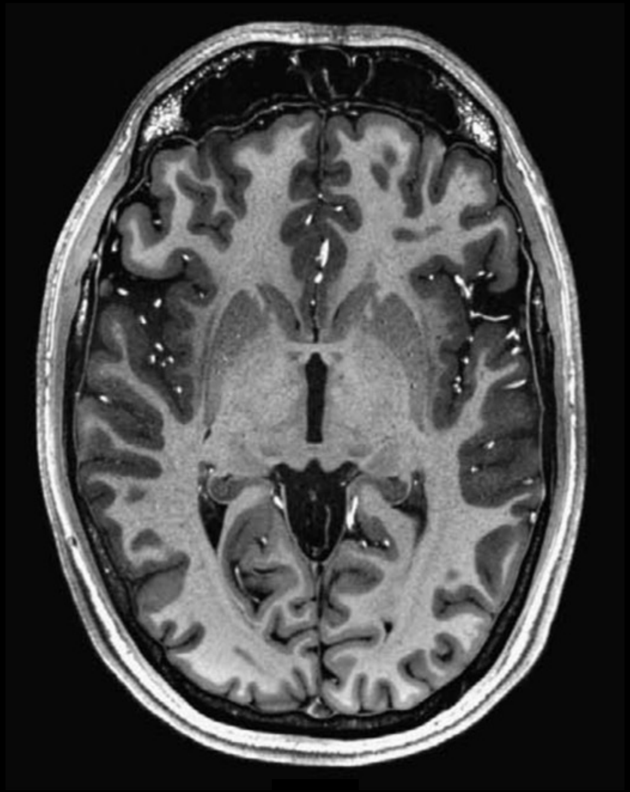
Neuroimaging for Research Data

Classic Methods

Imaging modalities

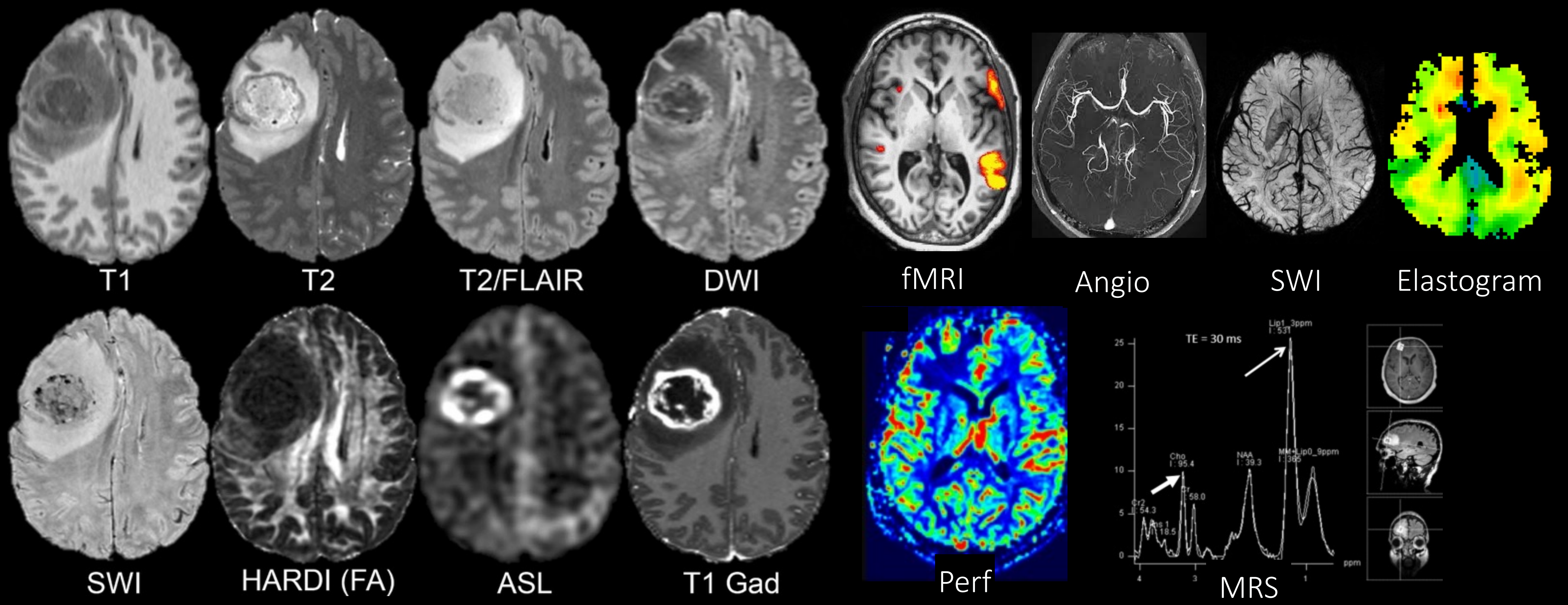


CT

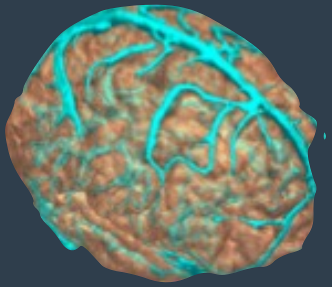


MRI

Imaging Sequences - MRI

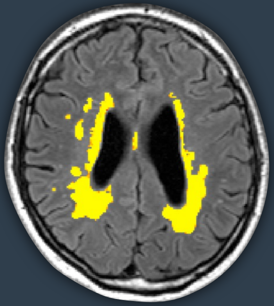


Quantifying the brain

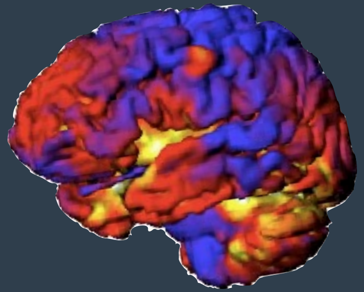


Vessel Extraction

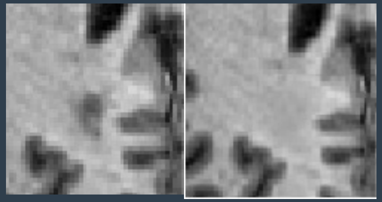
Atrophy
Estimation



Lesion Segmentation



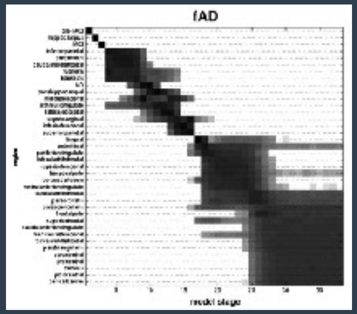
Cortical Thick.



Inpainting

Functional Connectivity

Disease Progression
Modelling



Tissue Segmentation
& Parcellation

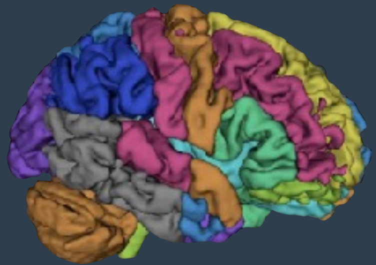
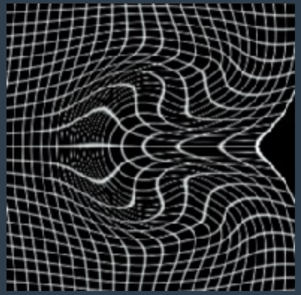


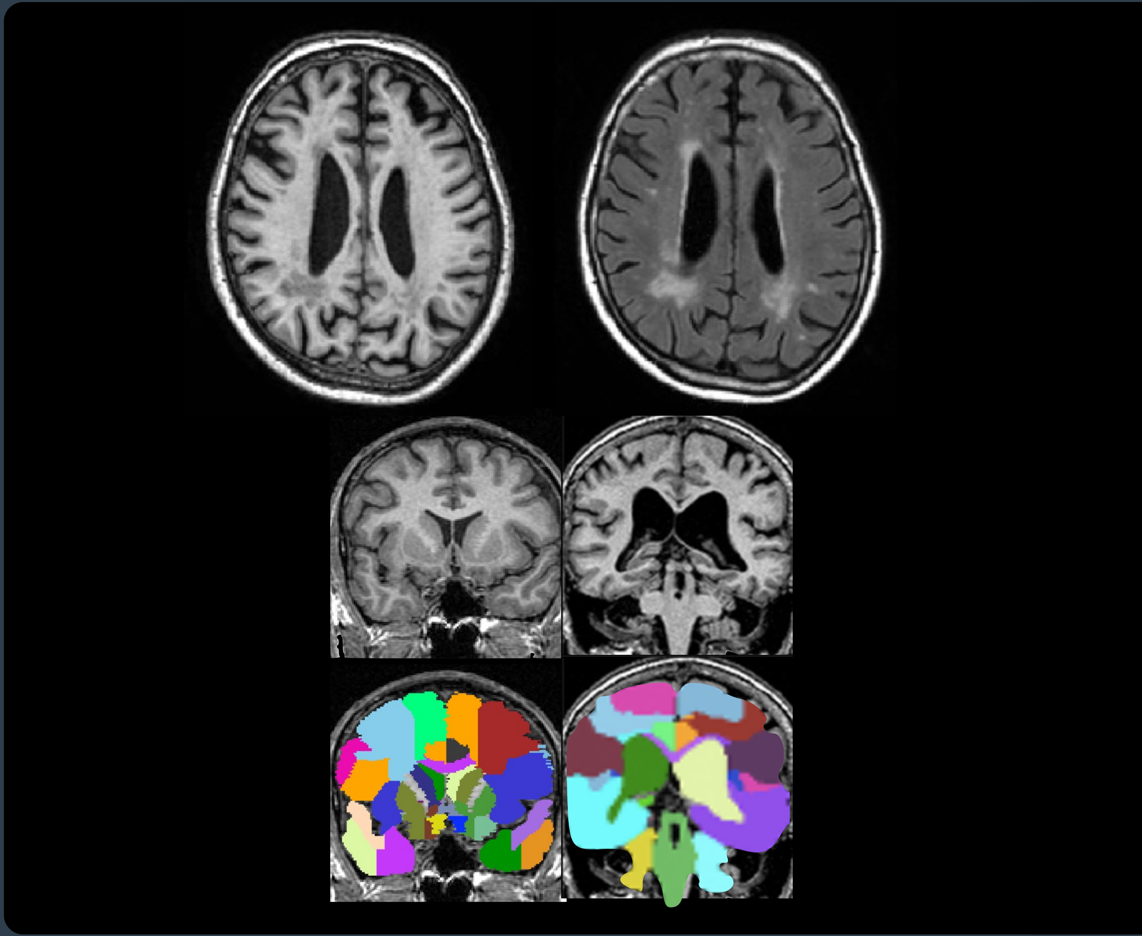
Image Registration



Network Analysis

Clinical Research - Challenges in Neuroimaging

- Small datasets (normally)
- Very variable input data
- Accuracy is paramount
- Speed is not important (with exceptions)
- Ability to extrapolate
- Problem specific solutions
- No ground truth

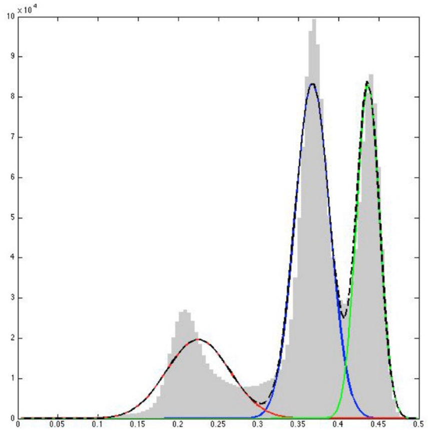


Classic strategies and aims

Quantify the brain

- Surrogate Biomarkers
  - Volume, Size, Shape, Thickness
  - Pathologies lesions (counts, locations, regions, etc)
  - Quantitative measures (flow, perfusion, R1/R2, diffusion)
  - Network graph (connectivity, functional)
- Group Analysis
  - Regions/Voxels (VBM, TBM)
  - Surfaces/skeleton (Freesurfer, TBSS)

Model based – Mixture of Gaussians

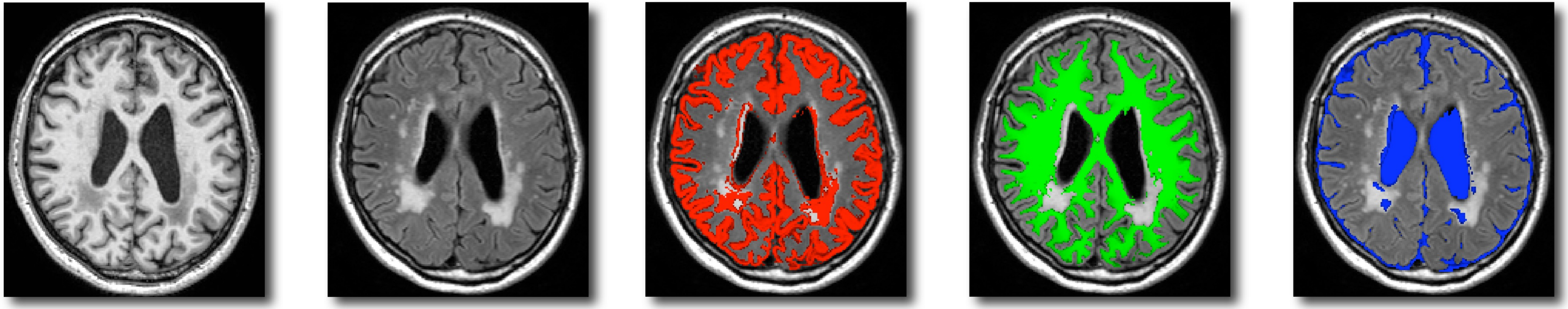


Number of components

Vector of intensities at voxel n

Gaussian density distribution

$$p\left(\boxed{\mathbf{y}_n}|\boldsymbol{\Theta}_K\right) = \sum_{k=1}^{\boxed{K}} w_k \boxed{\phi}\left(\mathbf{y}_n|\theta_k\right)$$



Ashburner et al. 2005 Neuroimage

Classic strategies and aims

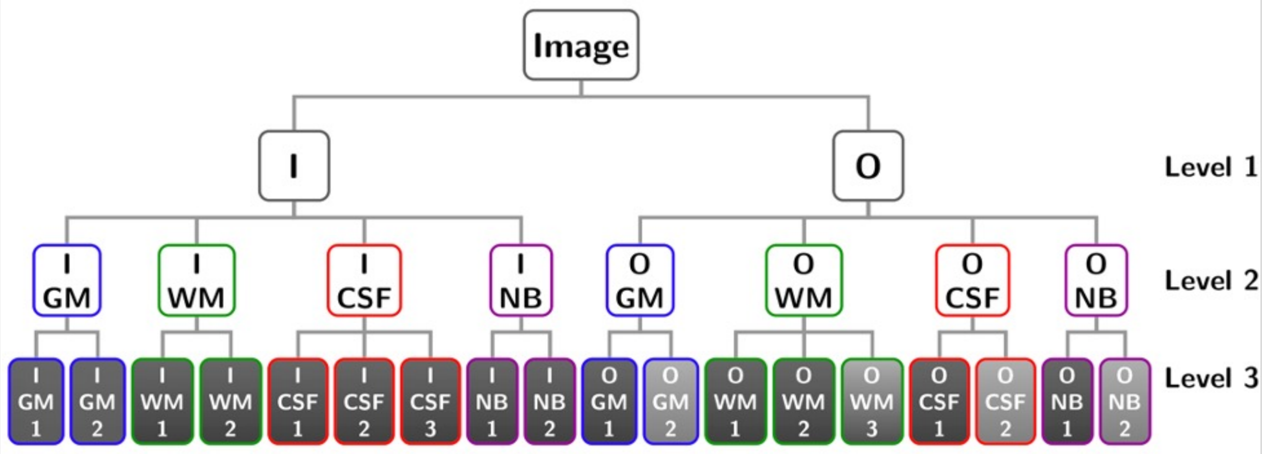
Quantify the brain

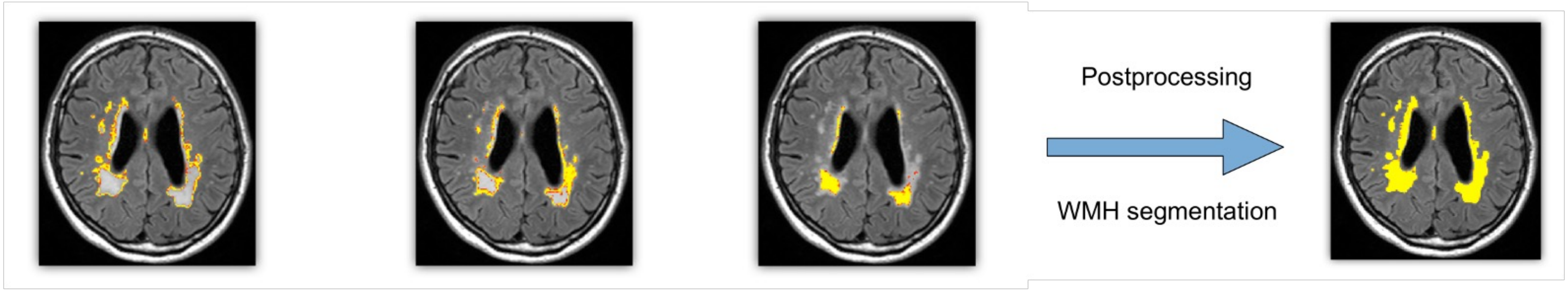
Surrogate Biomarkers

Volume
Size
Shape
Thickness

Pathologies
lesions
(counts, locations,
regions, etc)

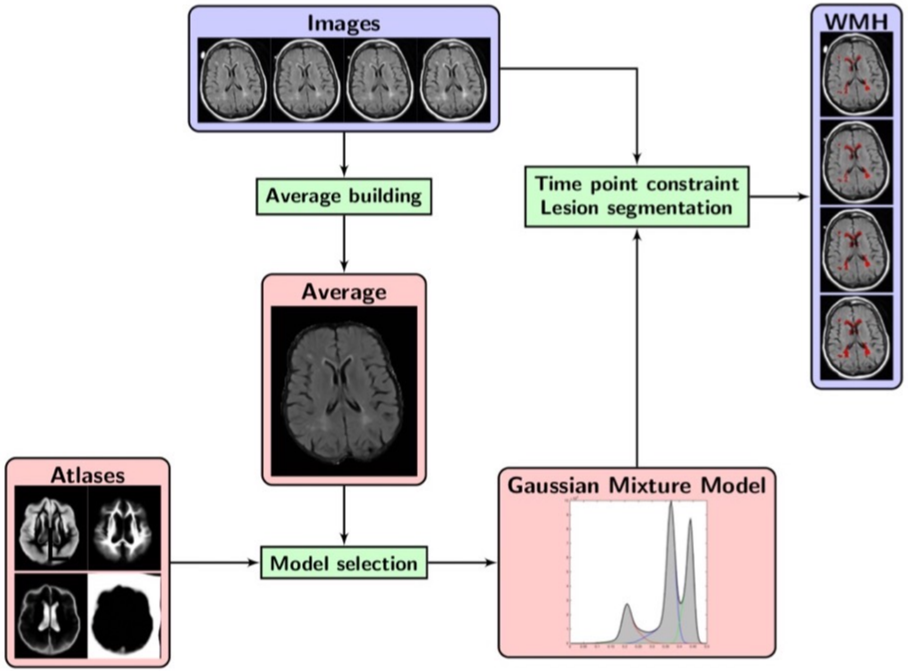
Model based – Modelling Outliers

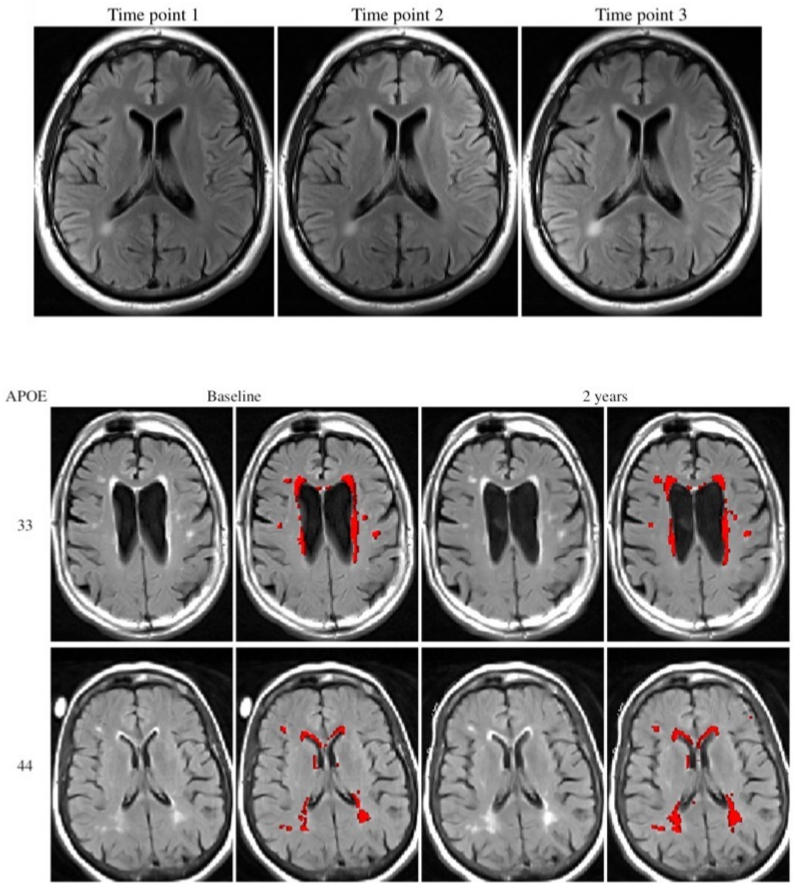




Sudre et al. 2015 IEEE TMI

Model based – Longitudinal Modelling





Classic strategies and aims

Quantify the brain

Surrogate Biomarkers

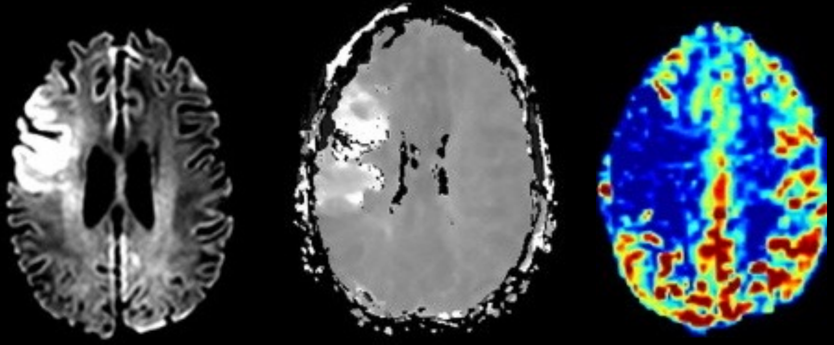
Volume
Size
Shape
Thickness

Pathologies
lesions
(counts, locations, regions, etc)

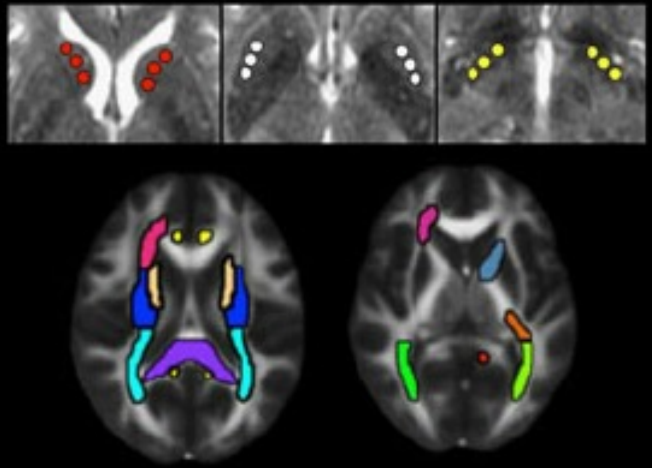
Quantitative
measures
(flow, perfusion, R1/R2, diffusion)

Quantitative parametric maps

DWI DSC ASL



DWI - FA



(Quantitative Value, Region of interest) => Regional measurement

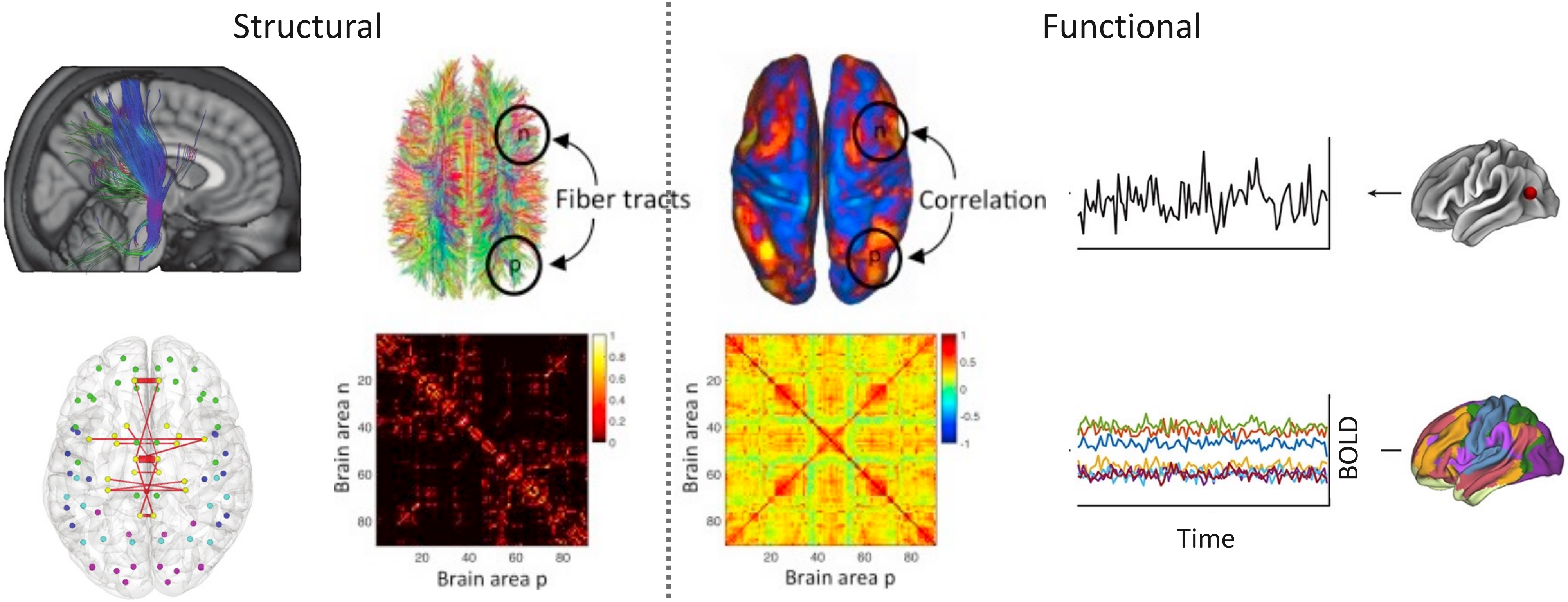
Classic strategies and aims

Quantify the brain

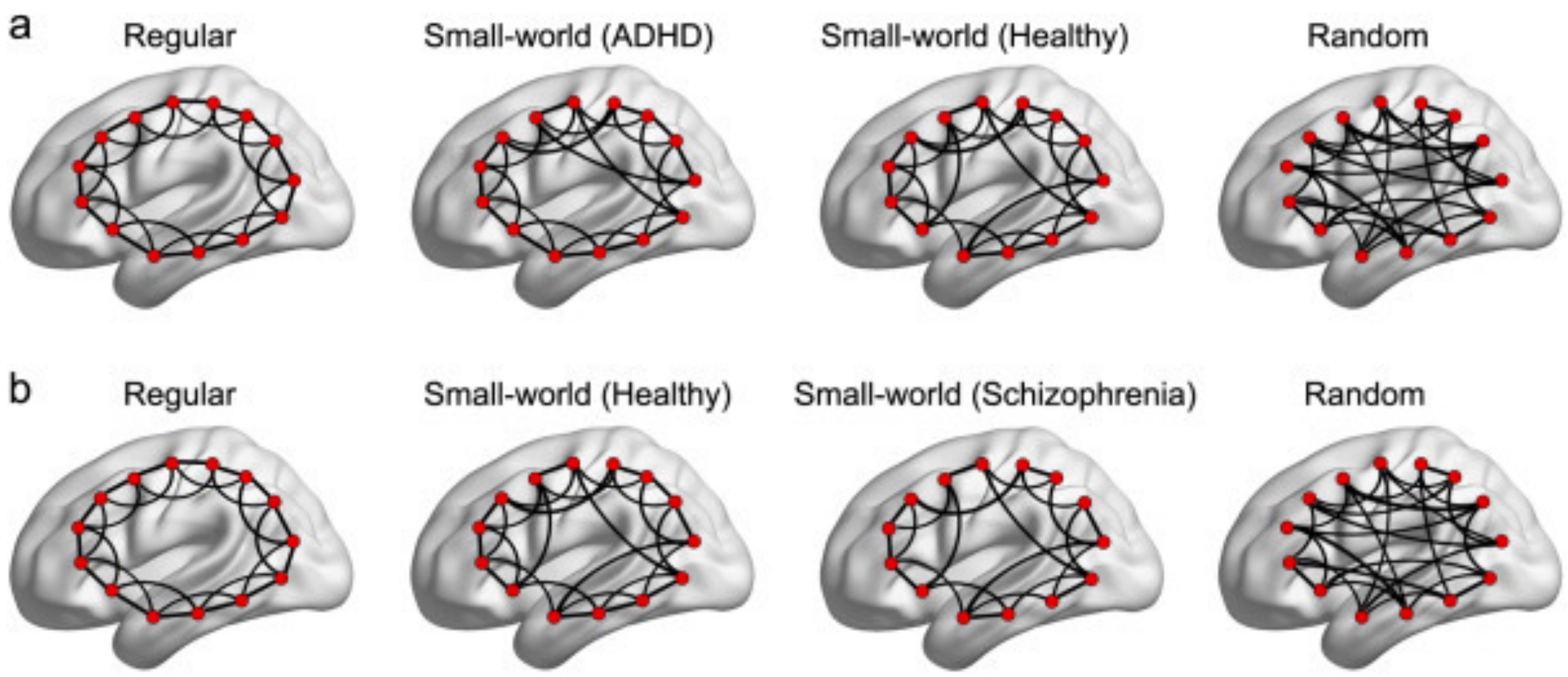
Surrogate Biomarkers

Volume Size Shape Thickness	Pathologies lesions (counts, locations, regions, etc)	Quantitative measures (flow, perfusion, R1/R2, diffusion)	Network graph (connectivity, functional)

Structural and functional connectivity



Understanding how the brain is organised



Classic strategies and aims

- Quantify the brain
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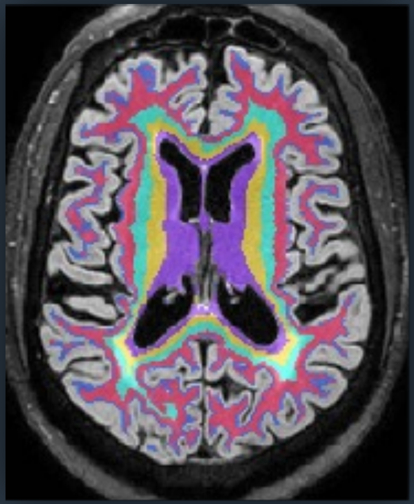
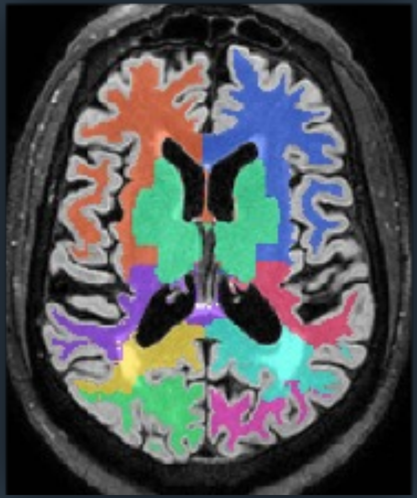
Regional Data Representation

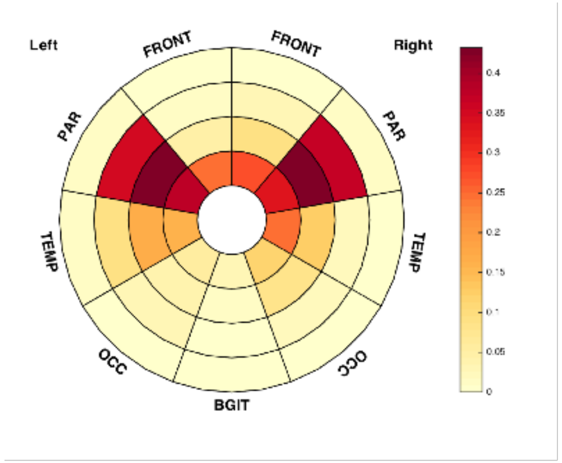
Layers
Laplace equation between ventricular and cortical surface
Normalised distance
Discretised = 4 layers



Lobes
Cortical parcellation
Aggregation of regions
Minimum Euclidean distance

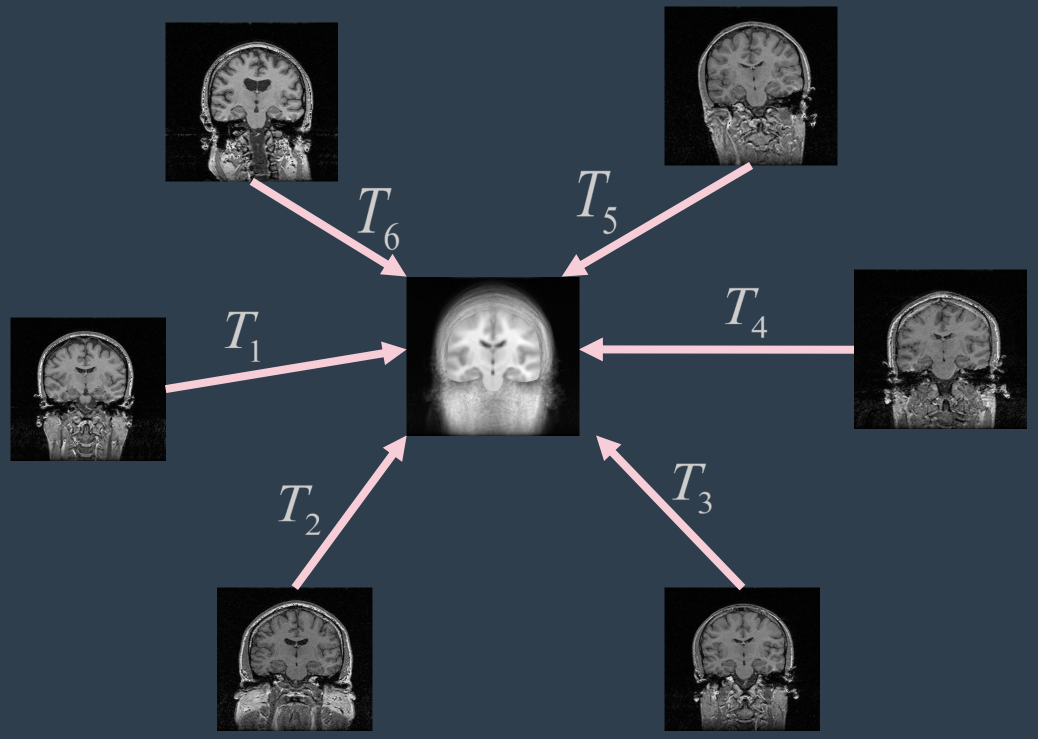


- **Lesion frequency:** Proportion of a region occupied by WMH
- **Lesion distribution:** Proportion of the WMH volume localised in a region



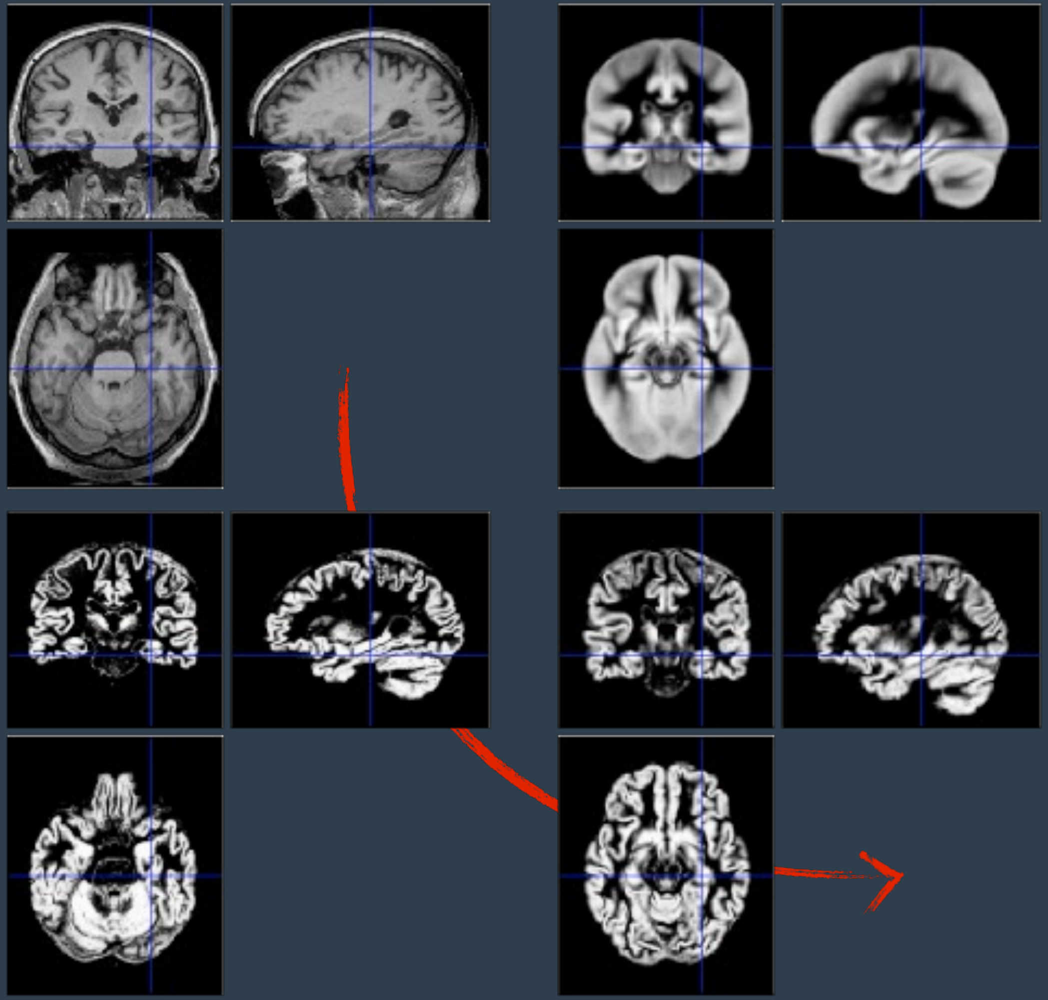
Group Alignment - Voxel-wise

- Non-Rigid Alignment + Congealing



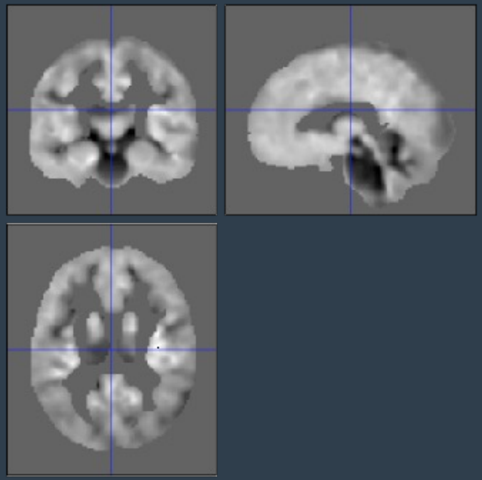
Group Alignment – VBM

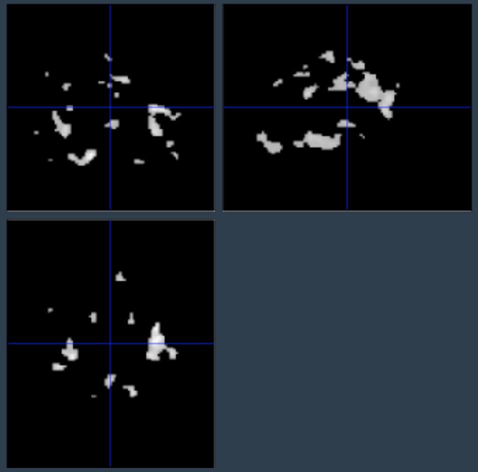
- Segment
- Normalise
- Modulate (?)
- Smooth

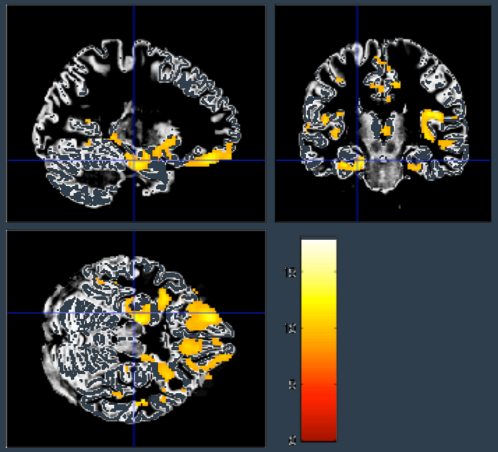


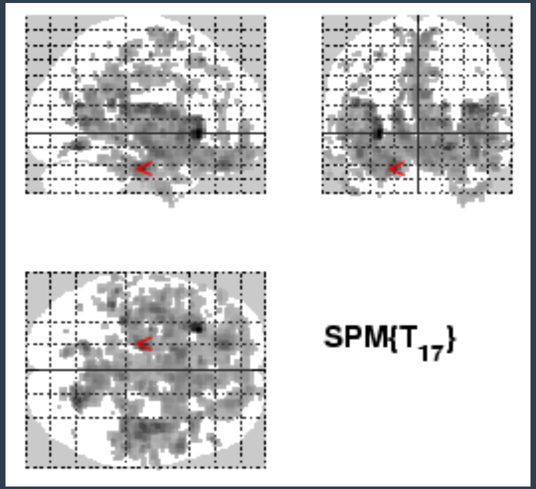
Group Alignment – VBM

- Segment
- Normalise
- Modulate (?)
- Smooth
- Voxel-wise statistics









Classic strategies and aims

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    - Surfaces/skeleton (Freesurfer, TBSS)

Classic strategies and aims

Quantify the brain

Predict/Infer targets

Surrogate Biomarkers

Group Analysis

Linear Models

Non-linear Models

Volume
Size
Shape
Thickness

Pathologies lesions (counts, locations, regions, etc)

Quantitative measures (flow, perfusion, R1/R2, diffusion)

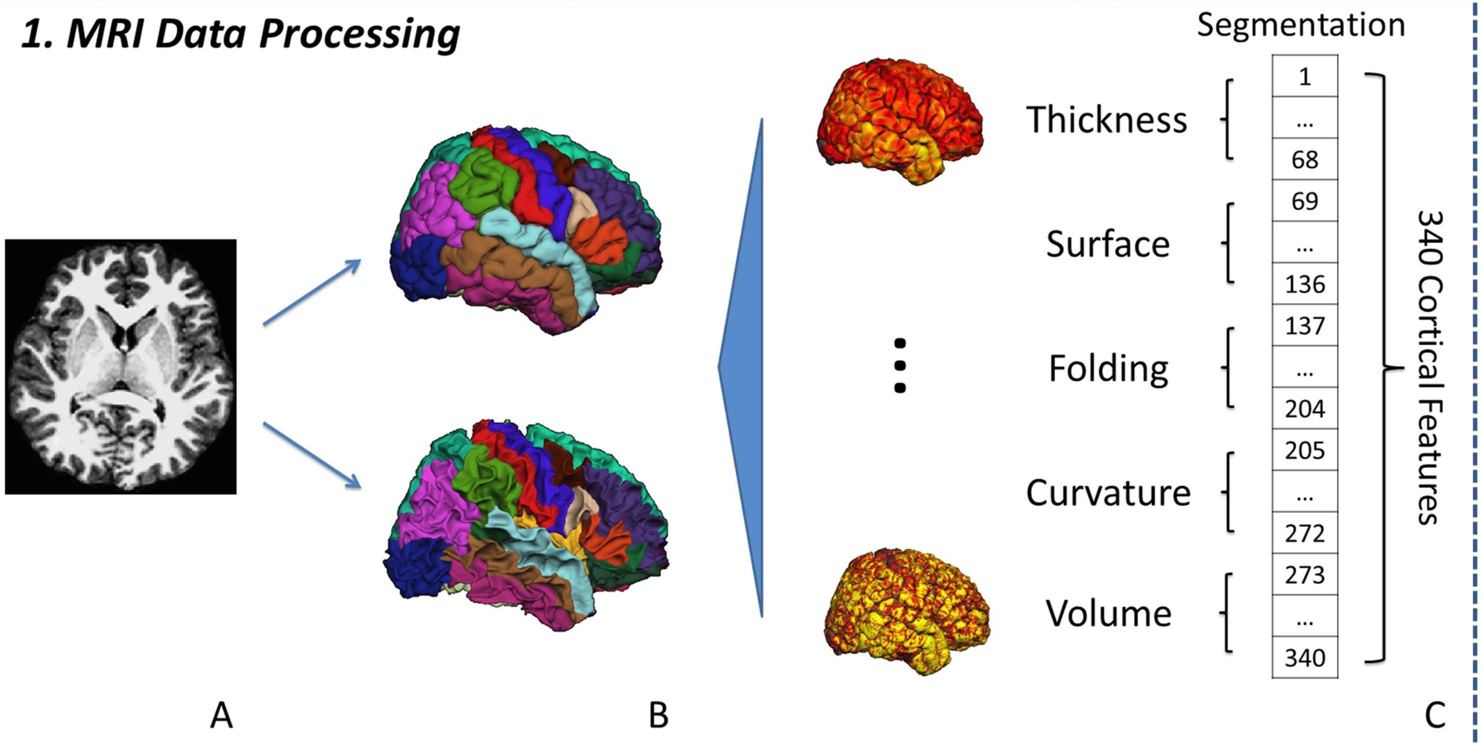
Network graph (connectivity, functional)

Regions/Voxels (VBM, TBM)

Surfaces/skeleton (Freesurfer, TBSS)

Classic ML classification “pipeline”

1. MRI Data Processing



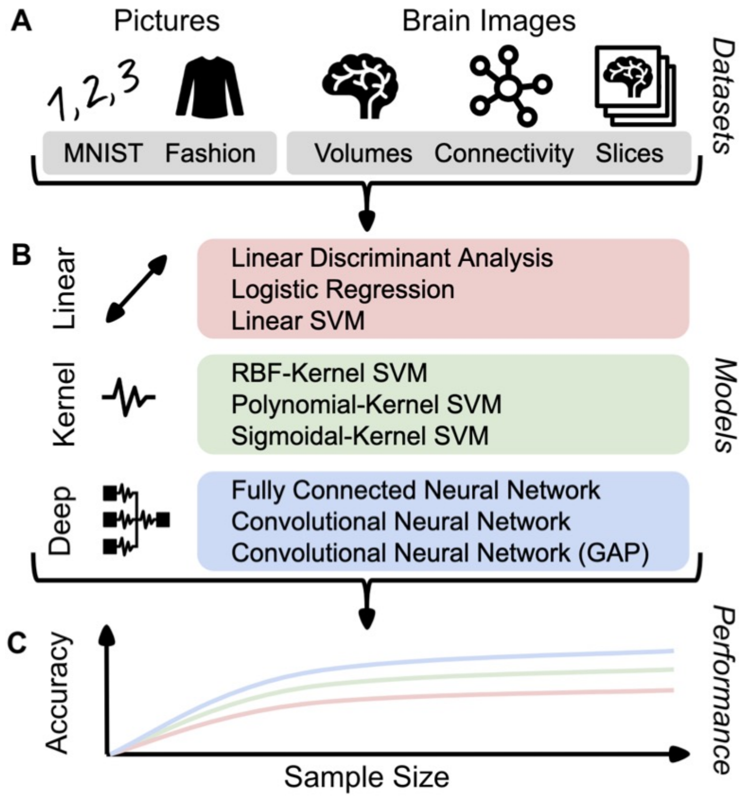
2. Feature Selection

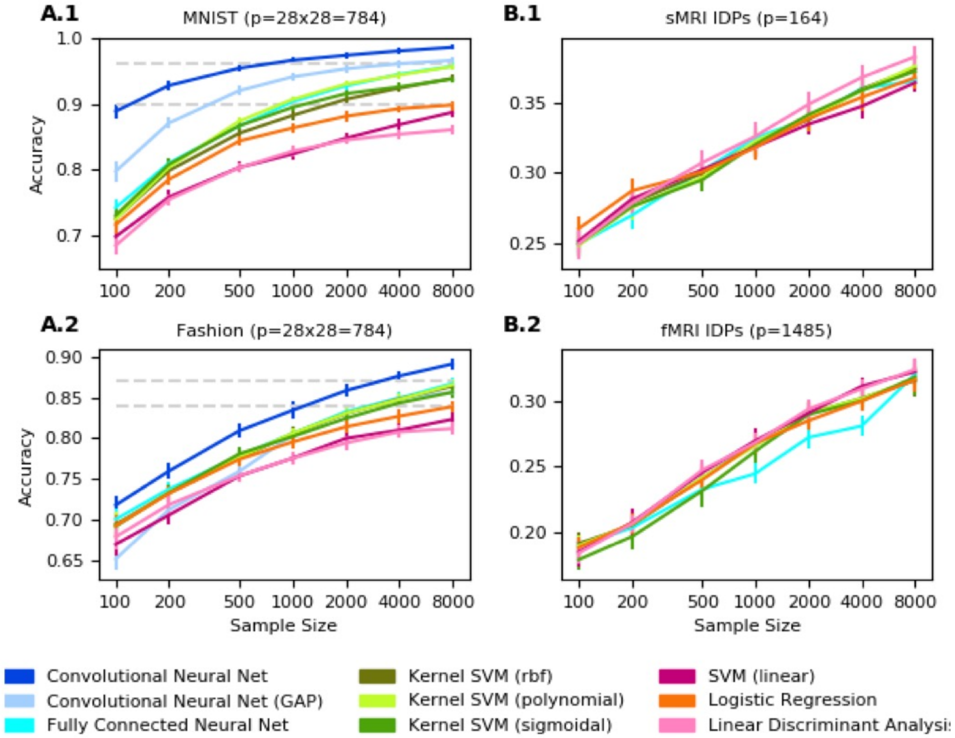
- **Normalisation**
- **F-Score**

3. Classification

- **Log Regression**
- **SVM**
- **Rand Forests**

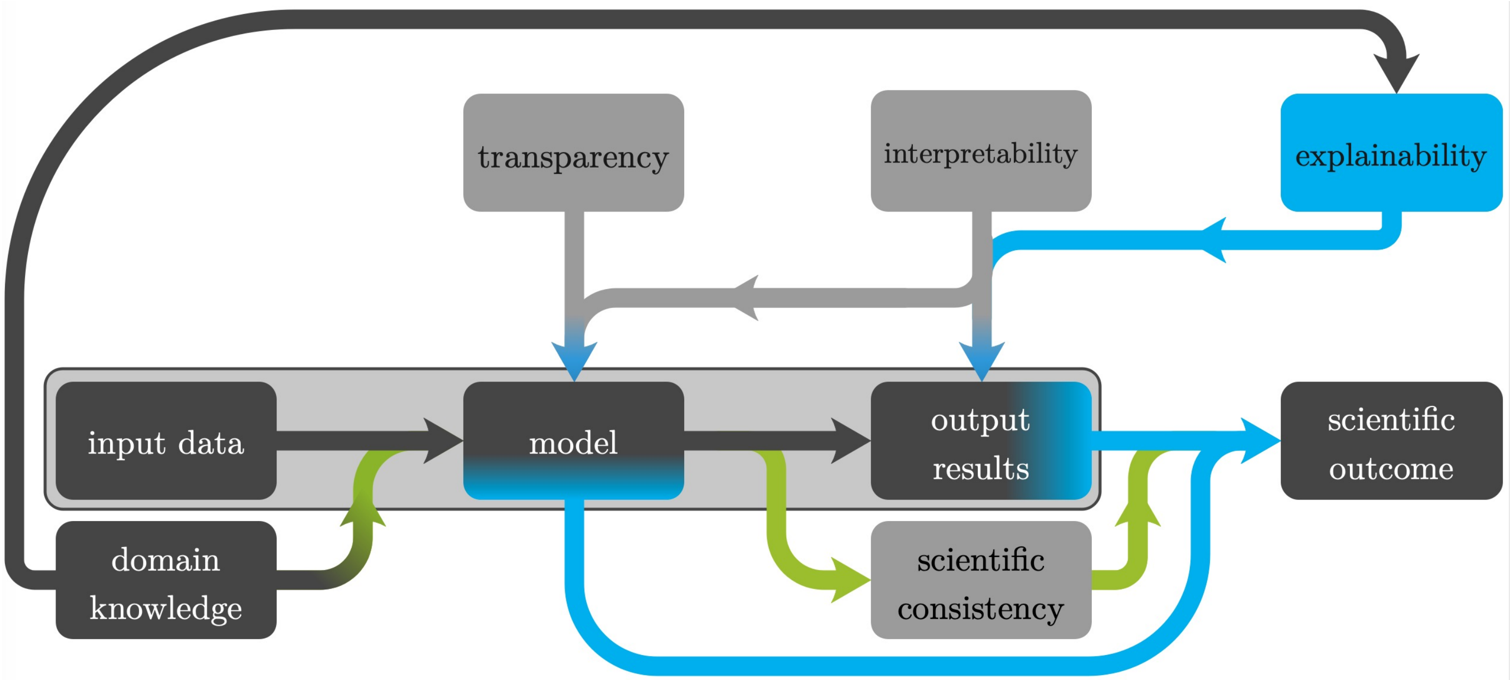
Linear vs Non-linear methods

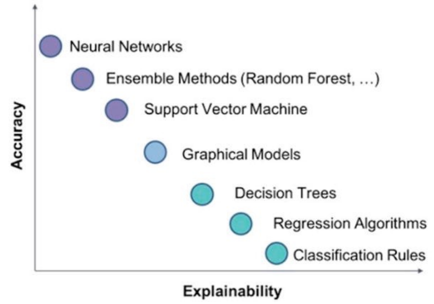




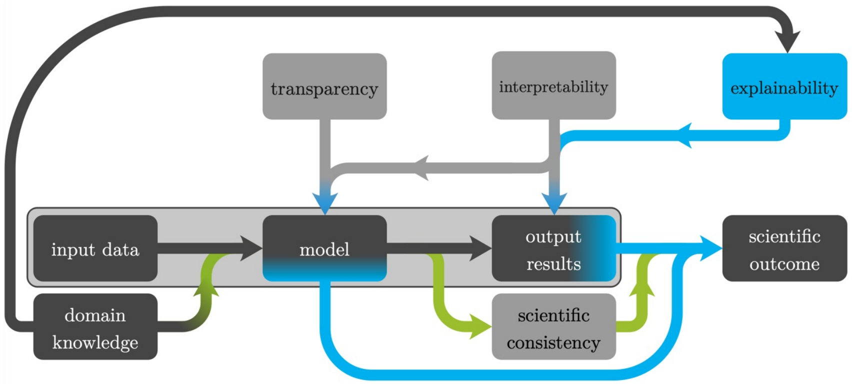
- Schulz et al. Nature Communications 2020

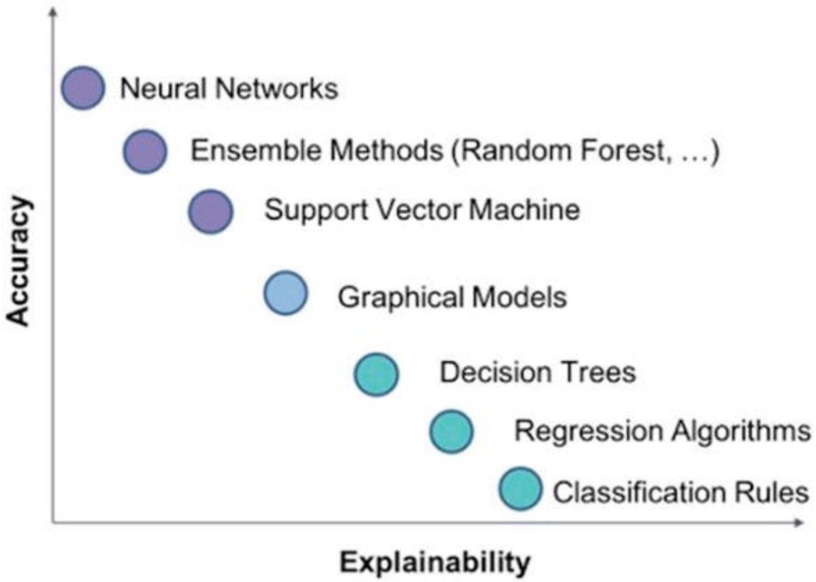
Explainability and discovery





Explainability and discovery





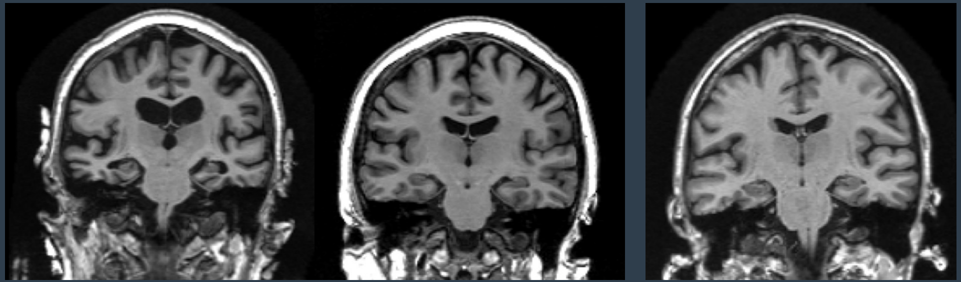
From Explicit Models to Deep Learning

"A computer program is said to learn from experience E with respect to some class of tasks T and performance measure P, if its performance at tasks in T, as measured by P, improves with experience E"

- *Classification: Map input to one of k classes* $f : \mathbb{R}^n \rightarrow \{1, ..., k\}$
- *Regression: Map input to a continuous value* $f : \mathbb{R}^n \rightarrow \mathbb{R}$
- *One-class Classification: Find a distance d from a compact distribution* $f : \mathbb{R}^n \rightarrow \{d\}$
- *Segmentation: Map input to to one of k classes per input element* $f : \mathbb{R}^n \rightarrow \mathbb{R}^{nk}$
- *Encoding-Decoding: Learning the structure of the data* $f : \mathbb{R}^n \rightarrow \mathbb{R}^z \rightarrow \mathbb{R}^n$

From Explicit Models to Deep Learning

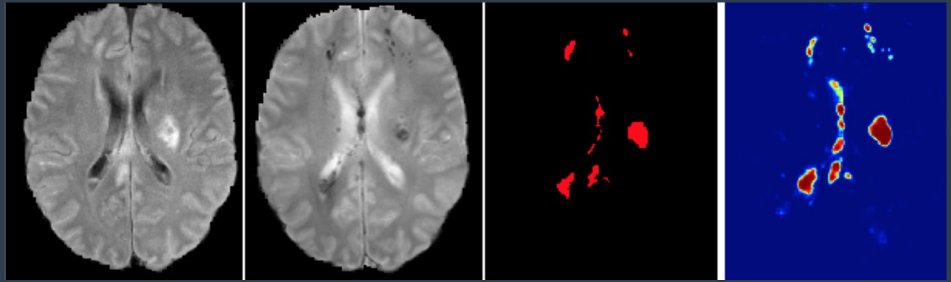
- Classification



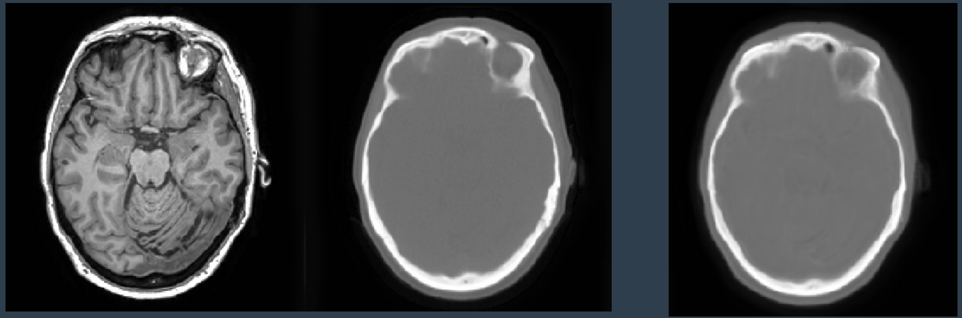
AD   Control   ?

- Dimensionality Reduction

- Segmentation



- Regression



MRI   CT   Predicted CT

Conclusions - Part 1

- Uses primarily advanced and good quality data
- Models with simplifying assumptions tend to work
- Classic models/methods/tools tend to be problem specific
- Historical focus on discovery and understanding the brain
- Classic models have slowly been replaced with ML models even for simple tasks
- Lack of translation
  - Models trained on research data tend to fail in real-world patient care

Scaling up

Two worlds

Public-heath &
epidemiological Research

Observational studies

Clinical-quality data

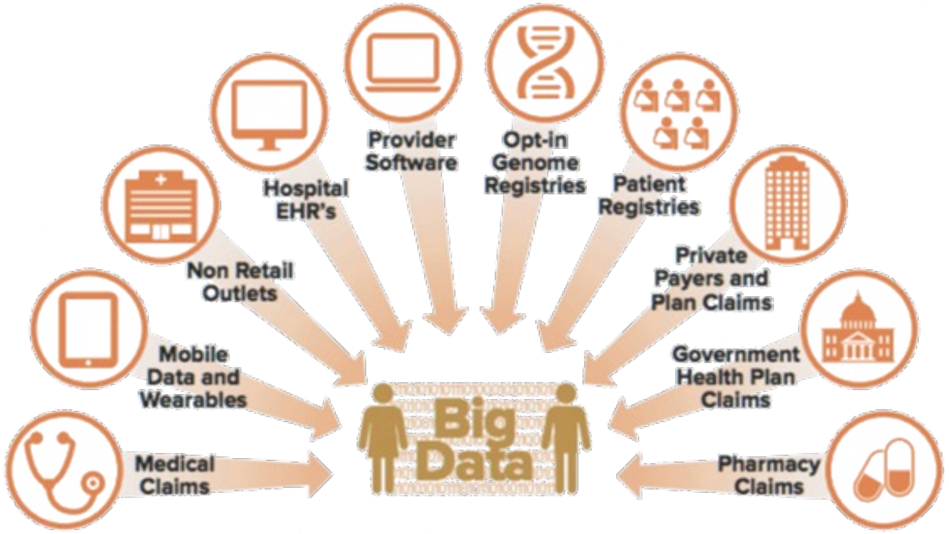
Academic Research Studies

Randomised Clinical Trials

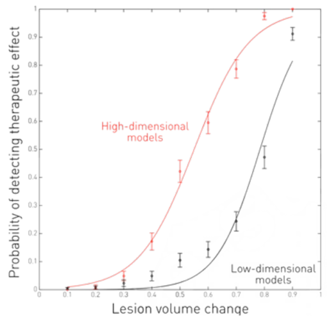
Research-quality data

The Big Data opportunity

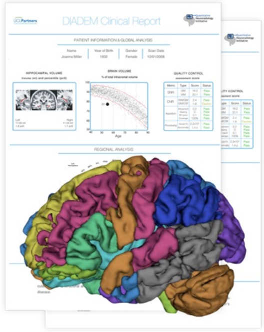
- Exploring & exploiting retrospective data
- Data-driven improvements of quality of care
- Improve patient happiness and outcomes
- Inform operational and administrative decisions



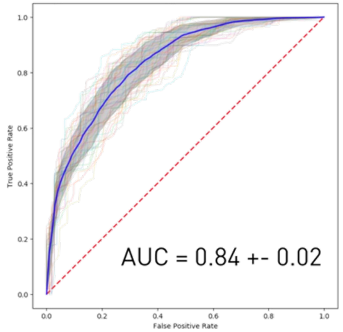
AI in Healthcare



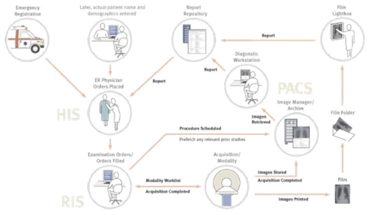
Patient Care



Clinical Efficiency



Live Auditing

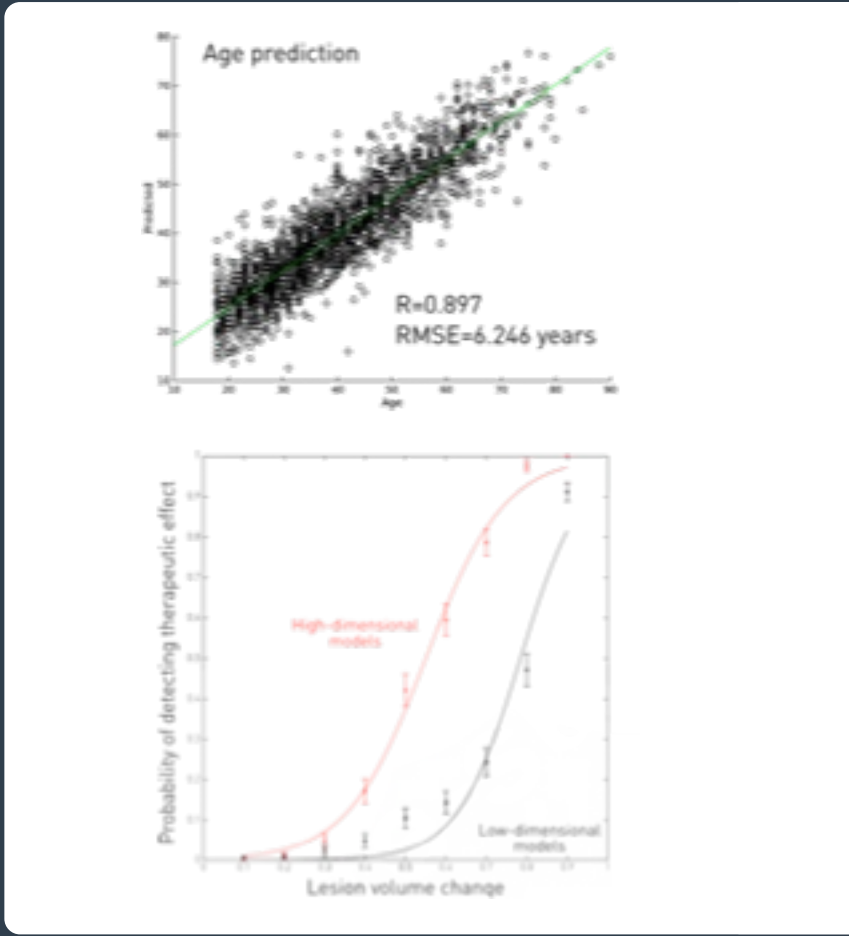


Operational Efficiency

Value Based Heathcare

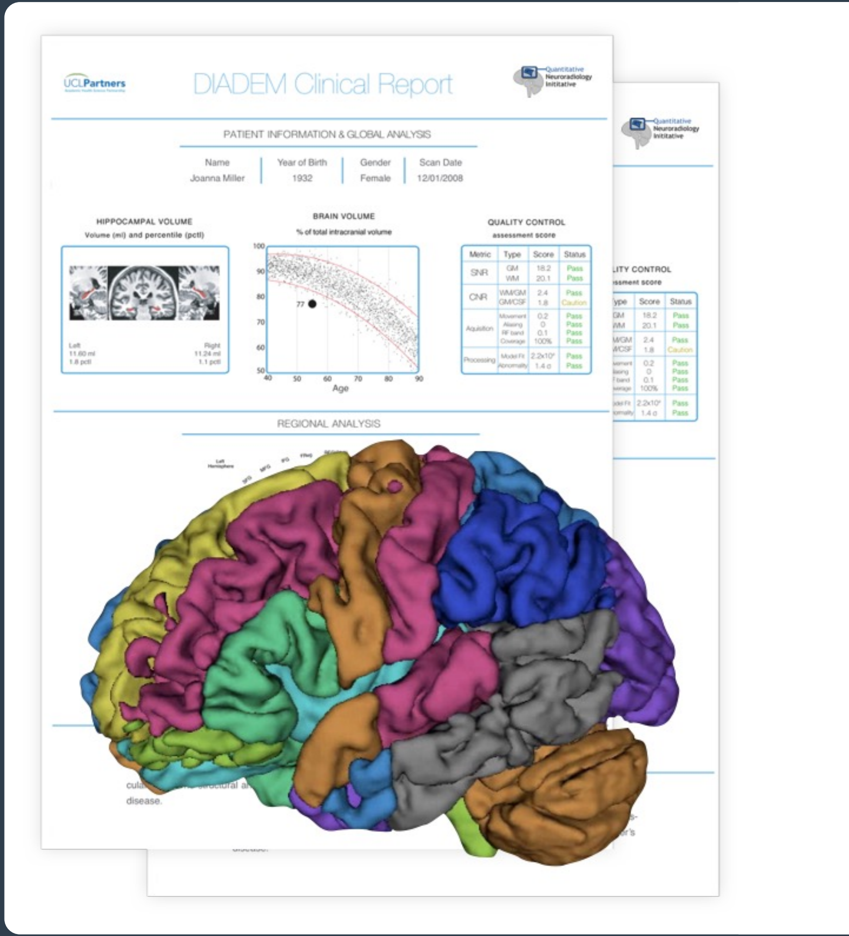
AI for Improving Patient Care

- Task:
  - Extract measurement or predict outcomes given some input data
- Data:
  - Radiological/Blood/Genetic Data
- Application examples:
  - Baseline Diagnosis
  - Prognosis
  - Drug response
  - Intervention Response



AI for Clinical Efficiency

- Task:
  - Automate labour-intensive tasks
- Data:
  - Radiological/Blood/Genetic/Clinical Data
- Application examples:
  - Data Preparation
  - Automated Quantification
  - Prioritisation
  - Software Integration

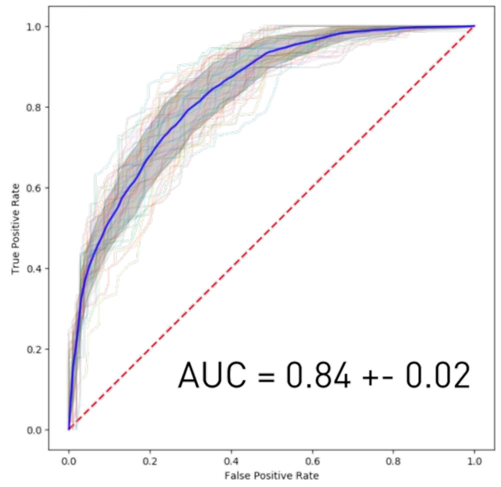


AI for Value Based Care

- Task:
  - Optimise the value (outcome/cost) of the full neurological care pipeline
- Data:
  - Medical events, clinical tasks, cognitive assessments, patient accessions, etc
- Application examples:
  - Optimise for outcomes
  - Maximise value of the full care pipeline
  - Optimise hospital-specific care pathways
  - Optimise for recovery or sustainability of health

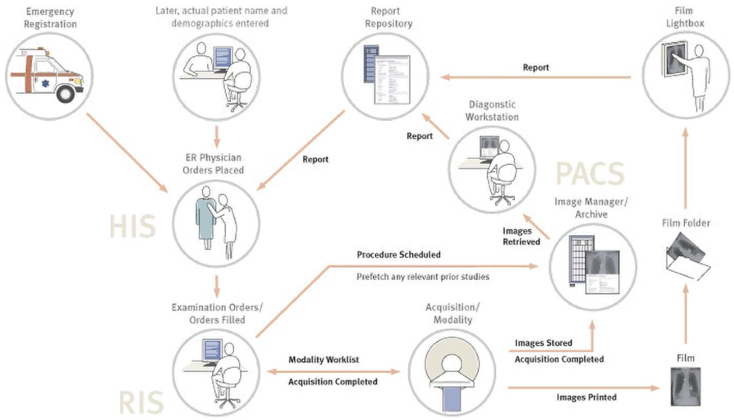
AI for Clinical Auditing

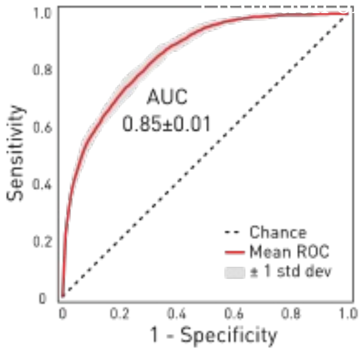
- Task:
  - Continuous assessment of quality of care
- Data:
  - Medical events, outcomes, costs, etc
- Application examples:
  - Live audit of clinical service delivery
  - Automated drug efficacy characterisation
  - Help achieve local CCG standards
  - Dashboarding of NHS performance targets



AI for Operational Efficiency

- Task:
  - Clinical data can inform administrative decisions
- Data:
  - Interventions, costs, bed usage, load, throughput, etc
- Application examples:
  - Predict hospital length of stay
  - Predict missed appointments
  - Balance staffing requirements given throughput
  - Optimise the cost/charge codes



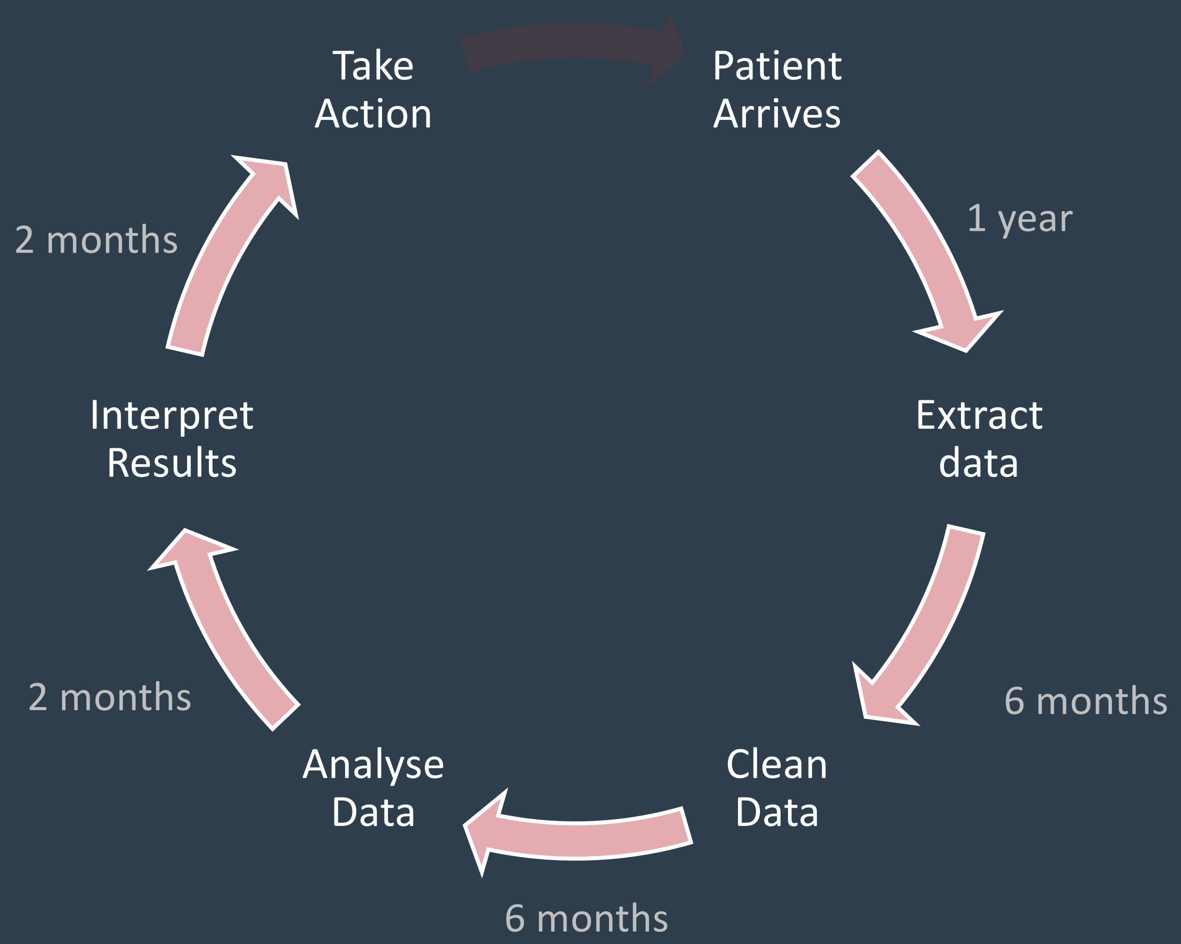


The London Medical Imaging & AI Centre for Value Based Healthcare

- UKRI + OLS funded
  - 5 years
  - £30+M funding
- Partnership
  - 5 Universities
  - 10 Hospitals
  - 20+ pathways
  - 10+ startups
  - 5 large industrial partners

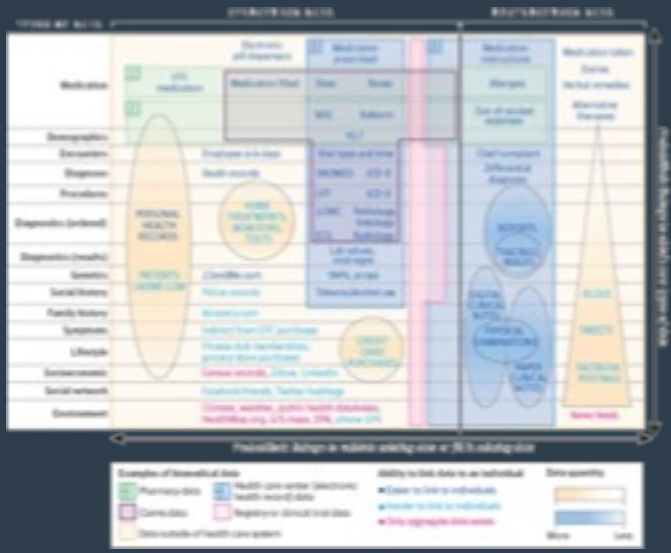
NHS Barts Health NHS Trust
NHS East Kent Hospitals University NHS Foundation Trust
NHS Guy's and St Thomas' NHS Foundation Trust
NHS Imperial College Healthcare NHS Trust
NHS King's College Hospital NHS Foundation Trust
NHS Lewisham and Greenwich NHS Trust
NHS Royal Brompton & Harefield NHS Foundation Trust
NHS South London and Maudsley NHS Foundation Trust
NHS University Hospitals Sussex NHS Foundation Trust
University College London Hospitals NHS Foundation Trust
Imperial College London
King's College London
UCL
Queen Mary University of London
Health Innovation Network South London
KiTEC

From static snapshots … to actionable analytics



The translational challenge

- Real world data
  - Missing, causal, dirty, unstructured, and encompassing
- Data Aggregation
  - Data collection from multiple databases and EHR/PACS/RIS systems
  - Utilisation of ontologies and standards compliance
- Data Search
  - Structured + Unstructured data, large volumes
- Informatics Infrastructure and governance
  - Computing, storage, deployment
- Computational/Technical Challenges
  - Model size vs labelled data, data complexity

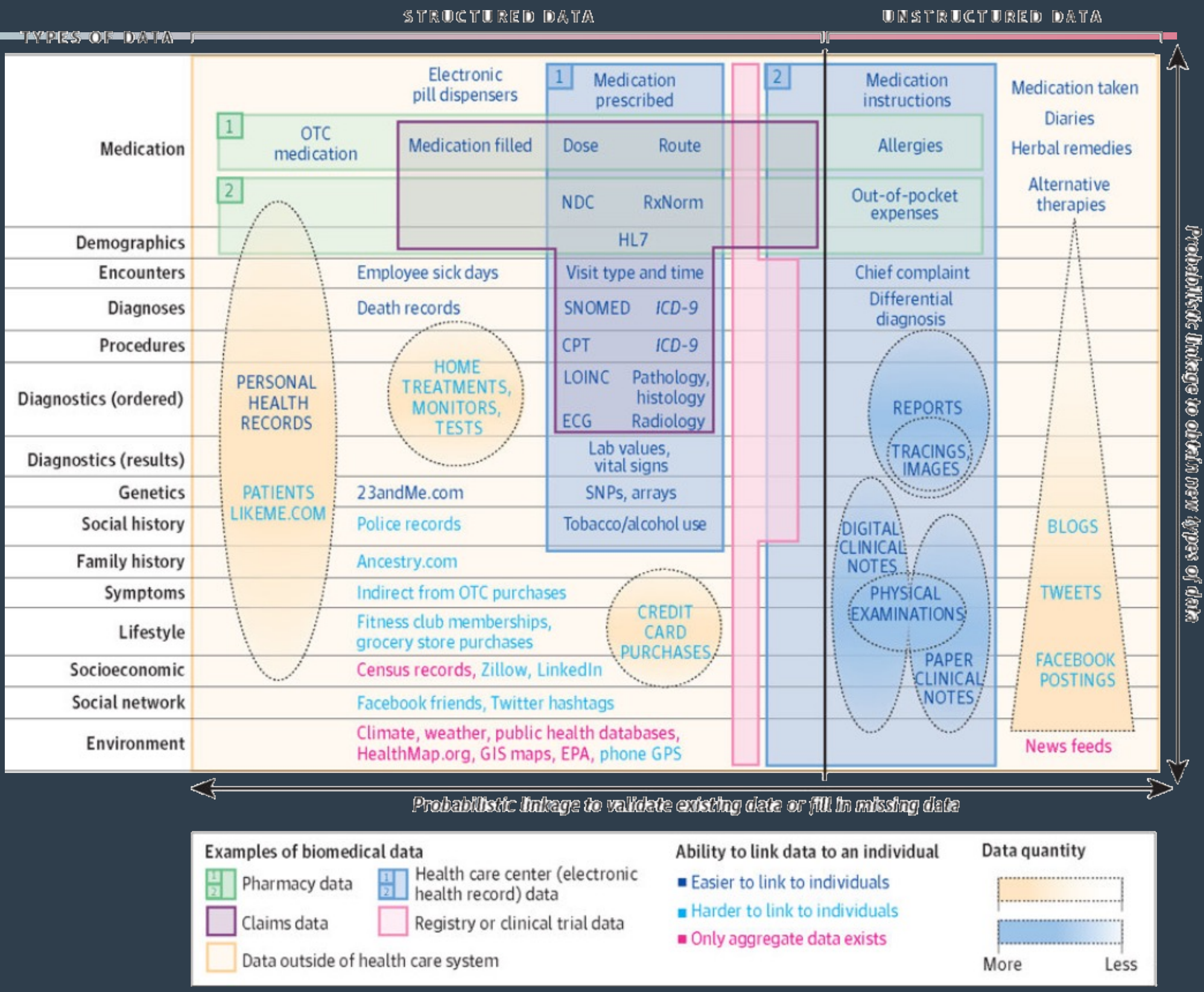


The width of clinical data

AI CENTRE for Value Based Healthcare

AMIGO Artificial Medical Intelligence Group

- Health records
  - Diagnosis, procedures, outcomes
- Images
  - MRI, CT, US, X-ray, Pathology
- Drugs
  - OTC medication
  - Hospital Pharmacy
- Costs
  - Income and costs per encounter/event
- Medical devices
- Genomic Data



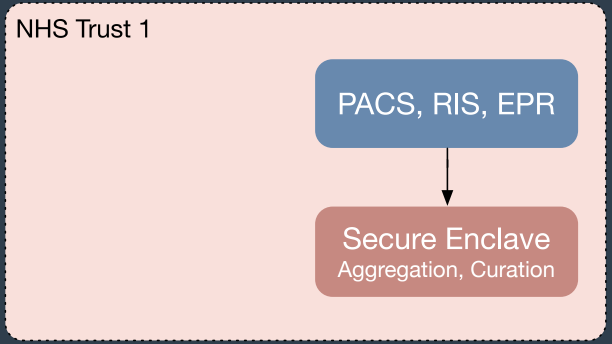
Informatics Infrastructure

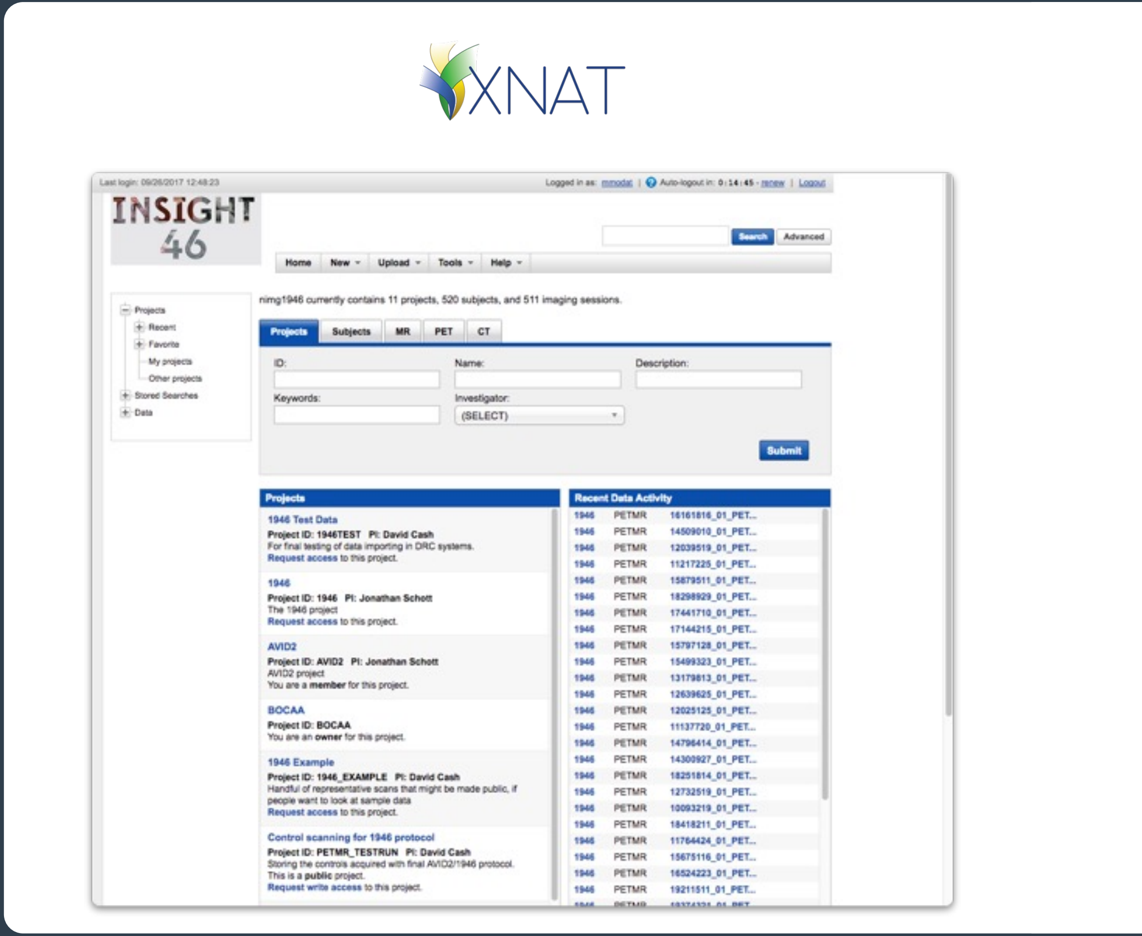
- Make data research ready
  - Develop data storage, curation and search
  - Aggregate data from multiple feeds
- Data governance and patient privacy
  - "Move models, not data"
  - Federated learning across hospitals
- Model/Data governance framework
  - AI model auditing to avoid data leaks
- Needs formalisation of infrastructure
  - Nvidia/IBM

Infrastructure – Imaging Data Storage

AI CENTRE for Value Based Healthcare

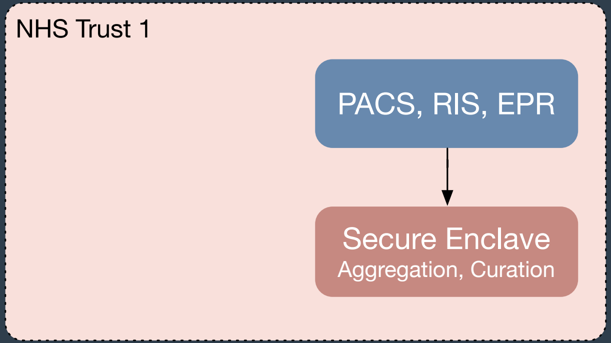
AMIGO Artificial Medical Intelligence Group



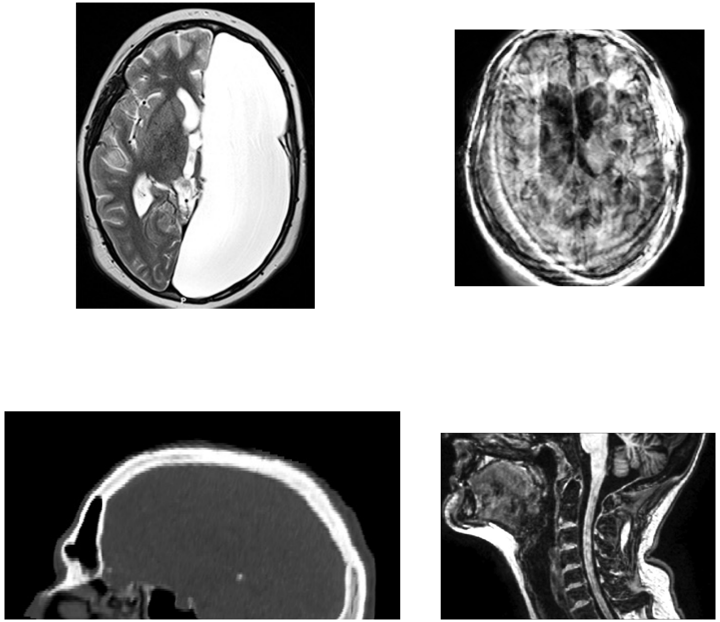


- eXtensible Neuroimaging Archive Toolkit
- Developed at WashU
- Manage, import, archive, process imaging data

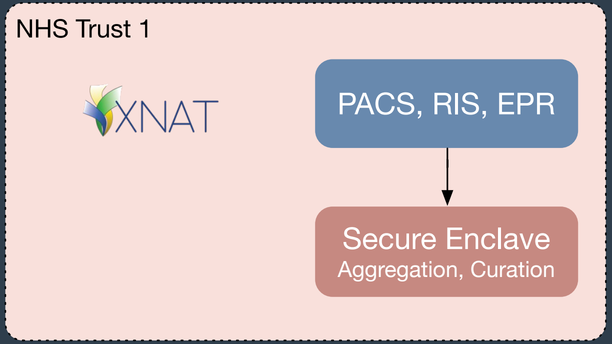
Imaging & real clinical data



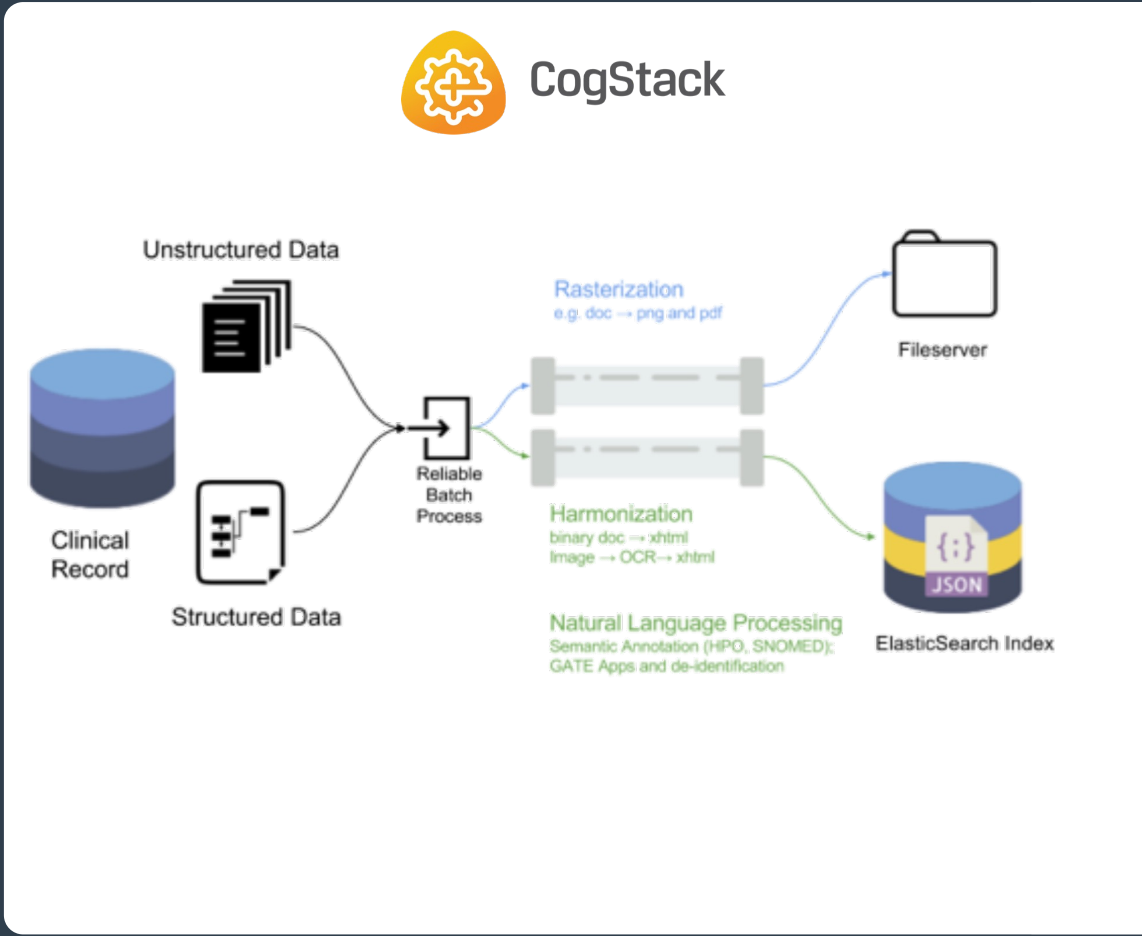
- What kinds of pathologies? General-purpose models
- Does it have an artefact and is in FOV? Need for QC tools
- Is the image of the right kind? Modality classifier
- Is all necessary data available? Deal with missing data
- How much do the models know? Uncertainty modelling



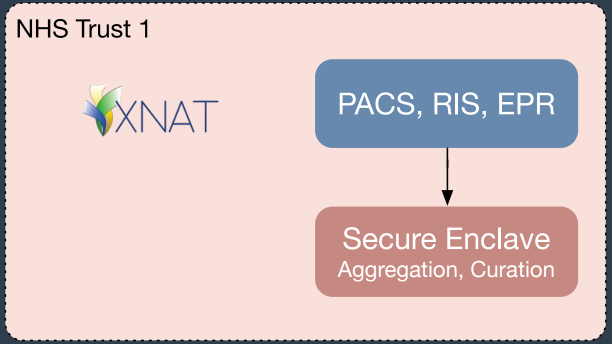
Infrastructure – EHR



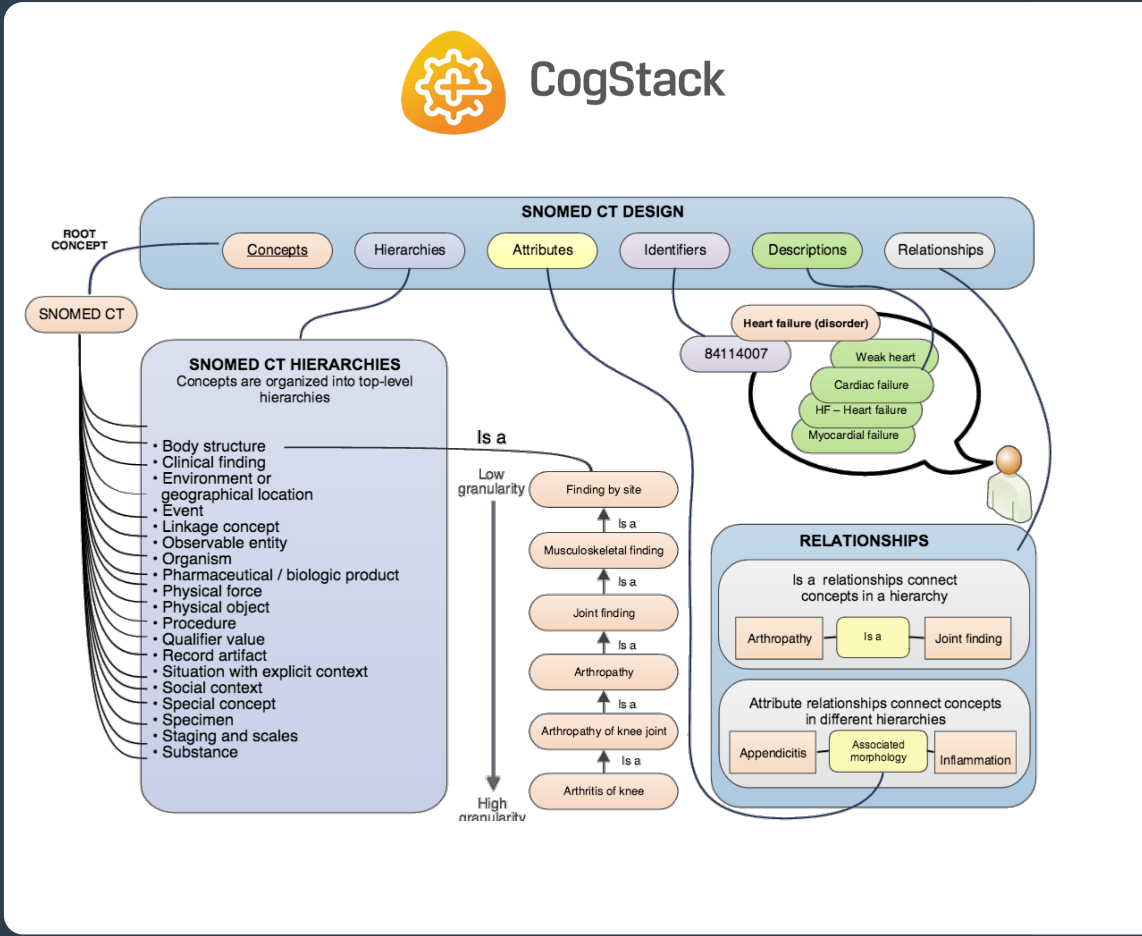
- Developed at KCL
- Manage, import, archive, process EHR data
- Convert documents (raster, pdf, word, etc) into standard XHTML files
- Harmonise data in JSON Elastic Search index



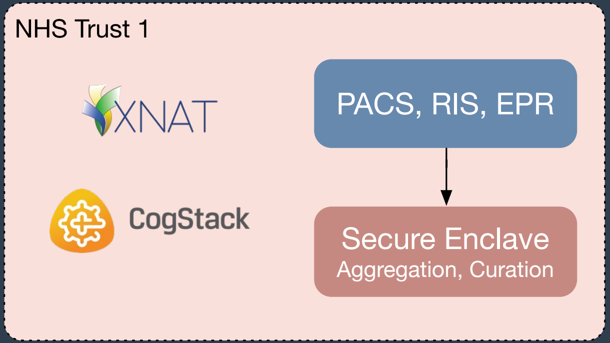
Infrastructure – EHR Storage



- Standards Compliance
  - HL7 FHIR
  - Data Feeds
- Ontologies
  - SNOMED CT concepts
  - LOINC codes

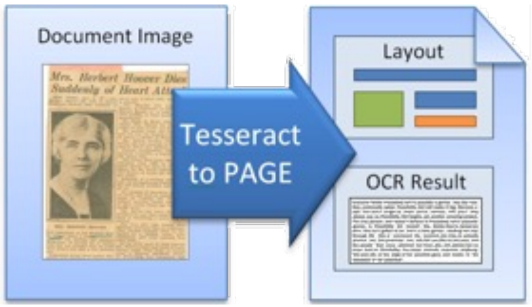


Infrastructure – Natural Language

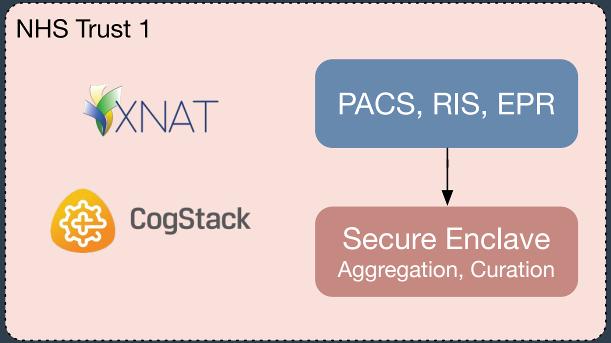


- Apache TIKA
  - Document Conversion
    - E.g. (word, pdf, etc) → (text, html)
  - Works out of the box on thousands of file types
- Tesseract (OCR)
  - Reading scanned documents
  - Performs well on scans with reasonable quality

Semantic EHR



Infrastructure – Natural Language

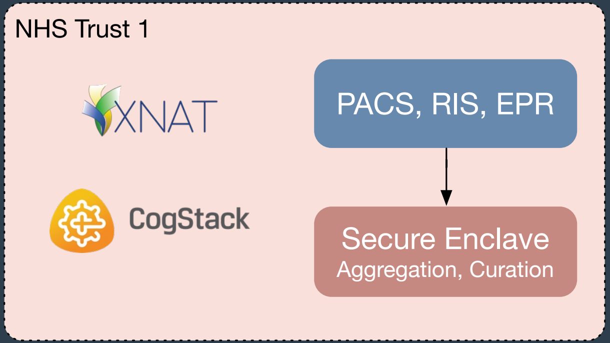


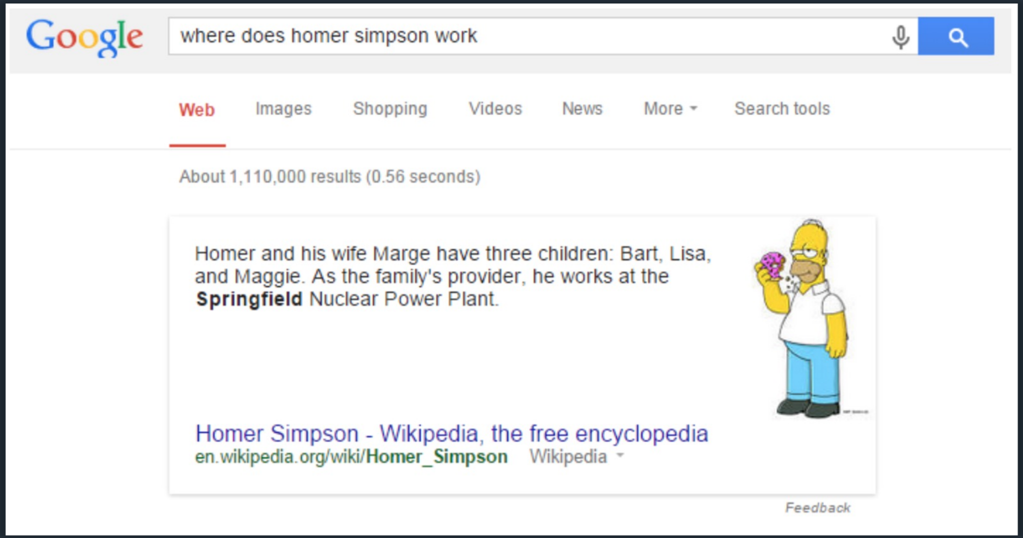
"Mrs Smith is a 65 year old woman with atrial fibrilation had a CVA in March. She had a past history of a #NOF and OA. She has a family history of breast cancer. She has been prescribed apixiban. She has no history of haemorrhage."

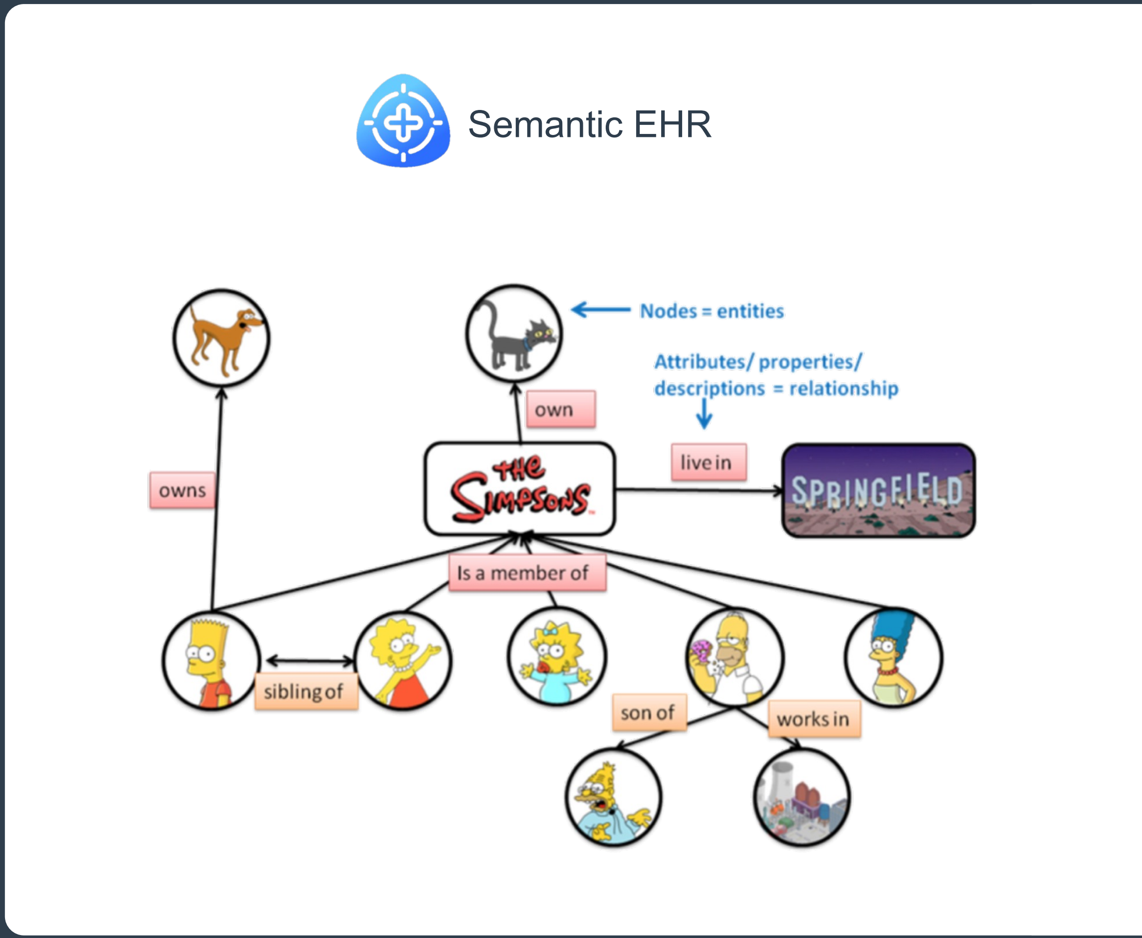
Semantic EHR

Spelling, typos , Nomenclature, Acronyms, Negations, Family history

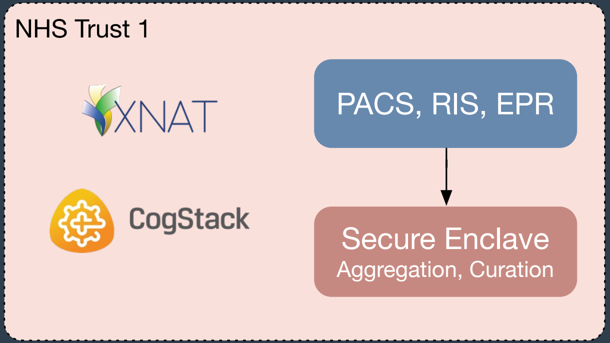
Infrastructure – Natural Language – Semantics



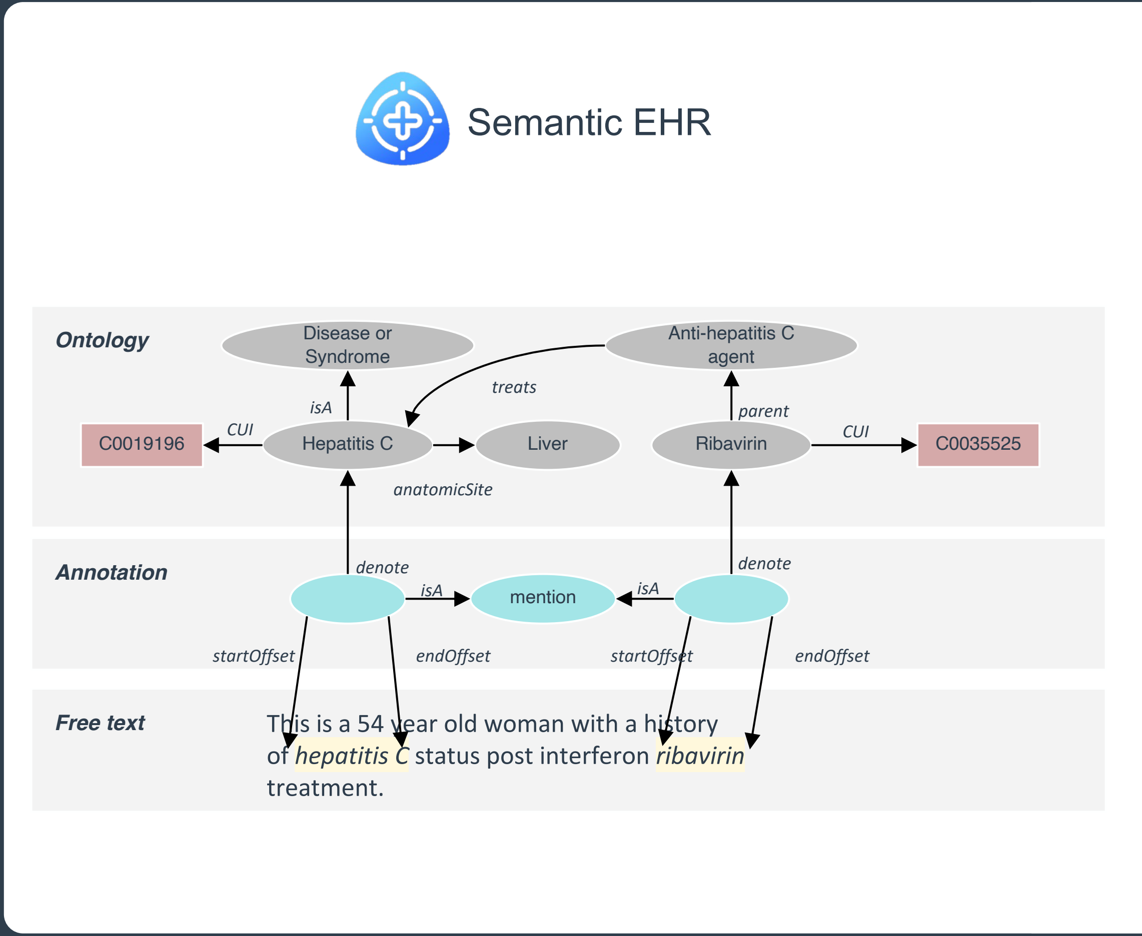




Infrastructure – Natural Language – Semantics



- Ontologies
  - SNOMED CT concepts
  - LOINC codes



Infrastructure – Natural Language – Semantics

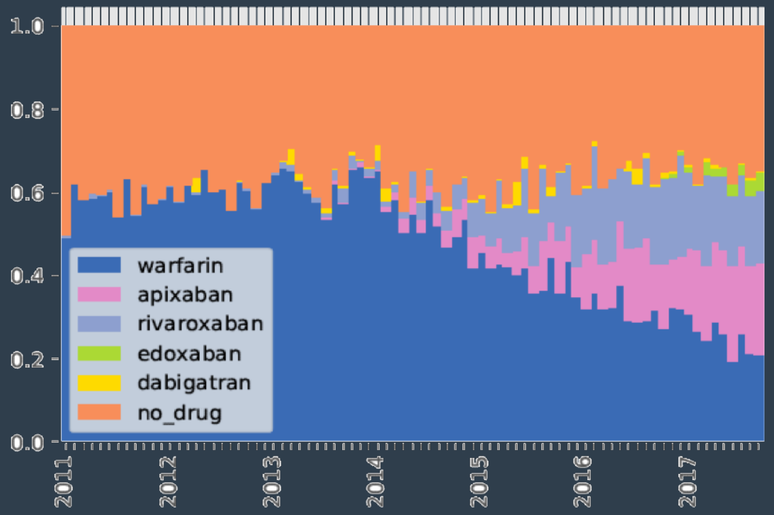
NHS Trust 1

XNAT

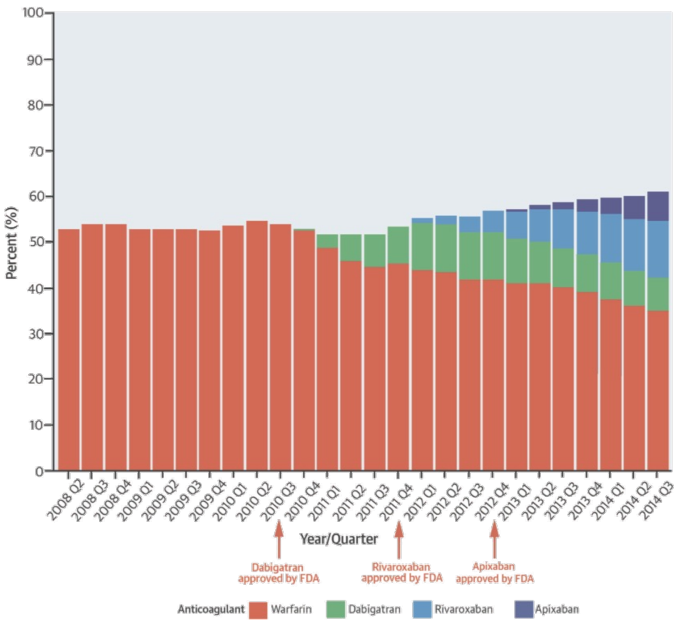
CogStack

PACS, RIS, EPR

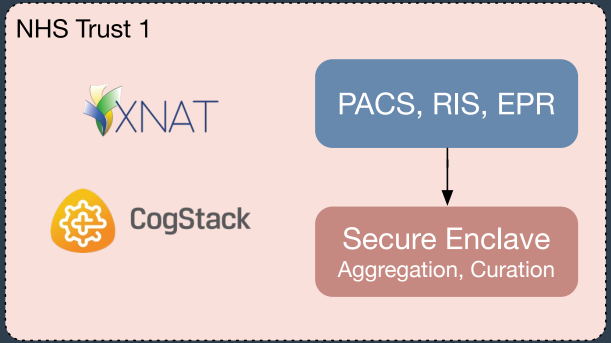
Secure Enclave
Aggregation, Curation

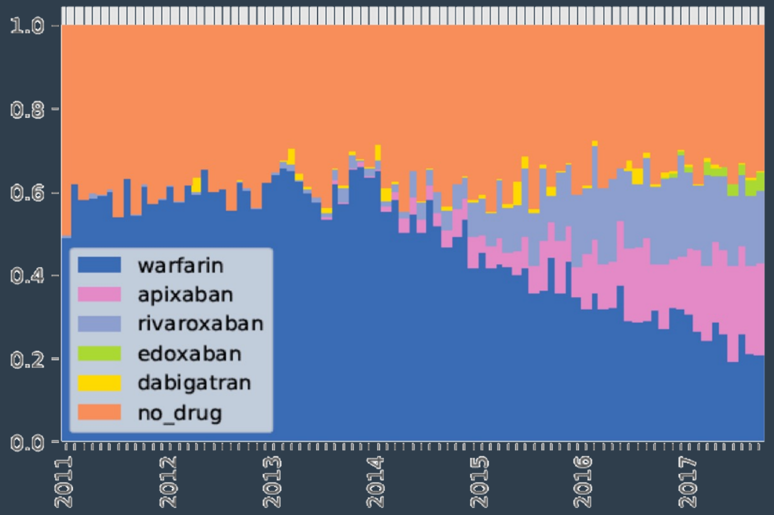


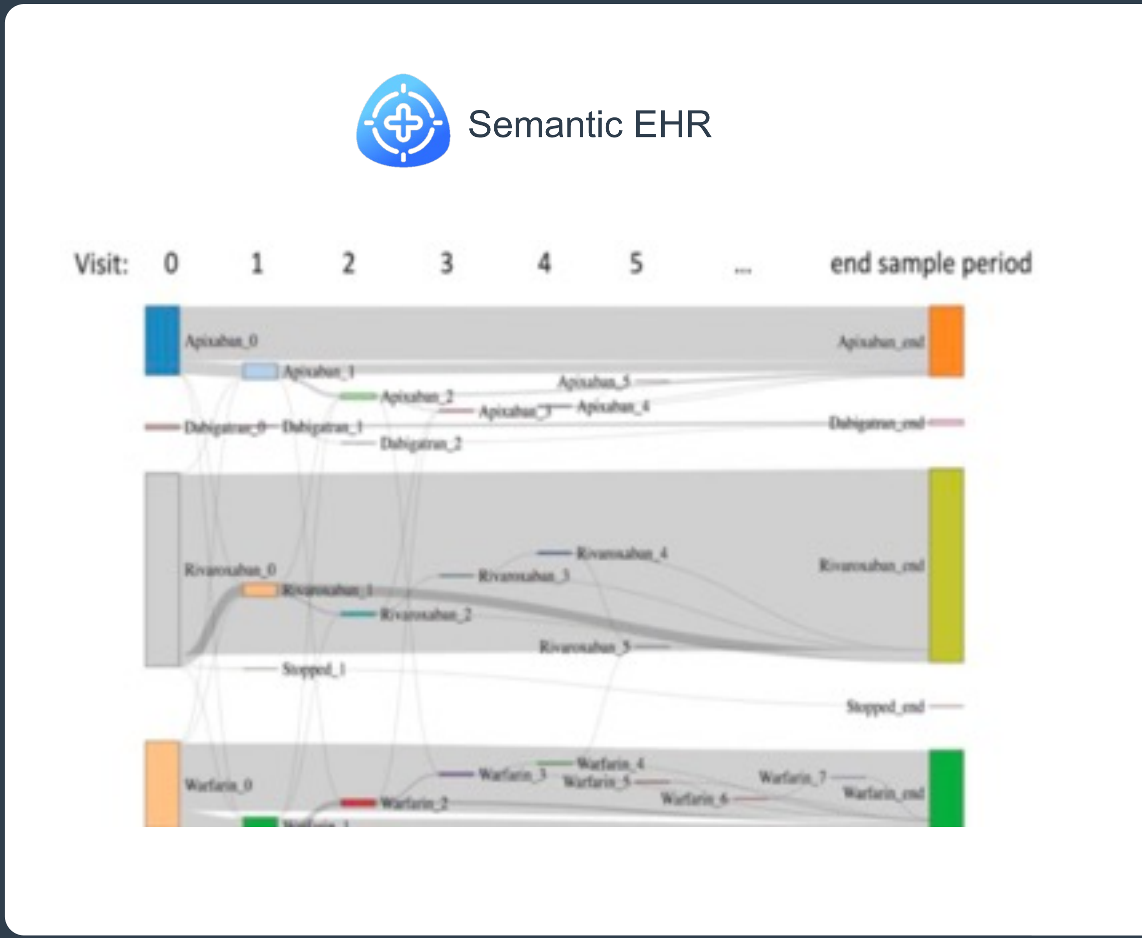
Semantic EHR



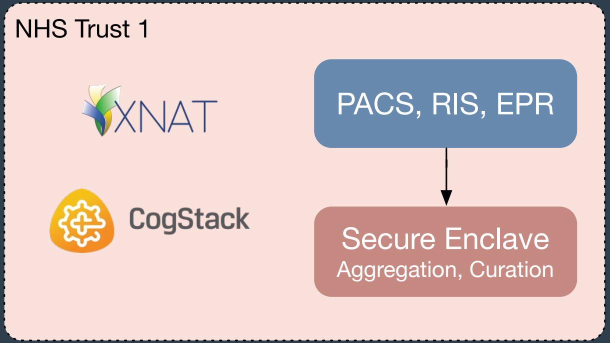
Infrastructure – Natural Language – Semantics



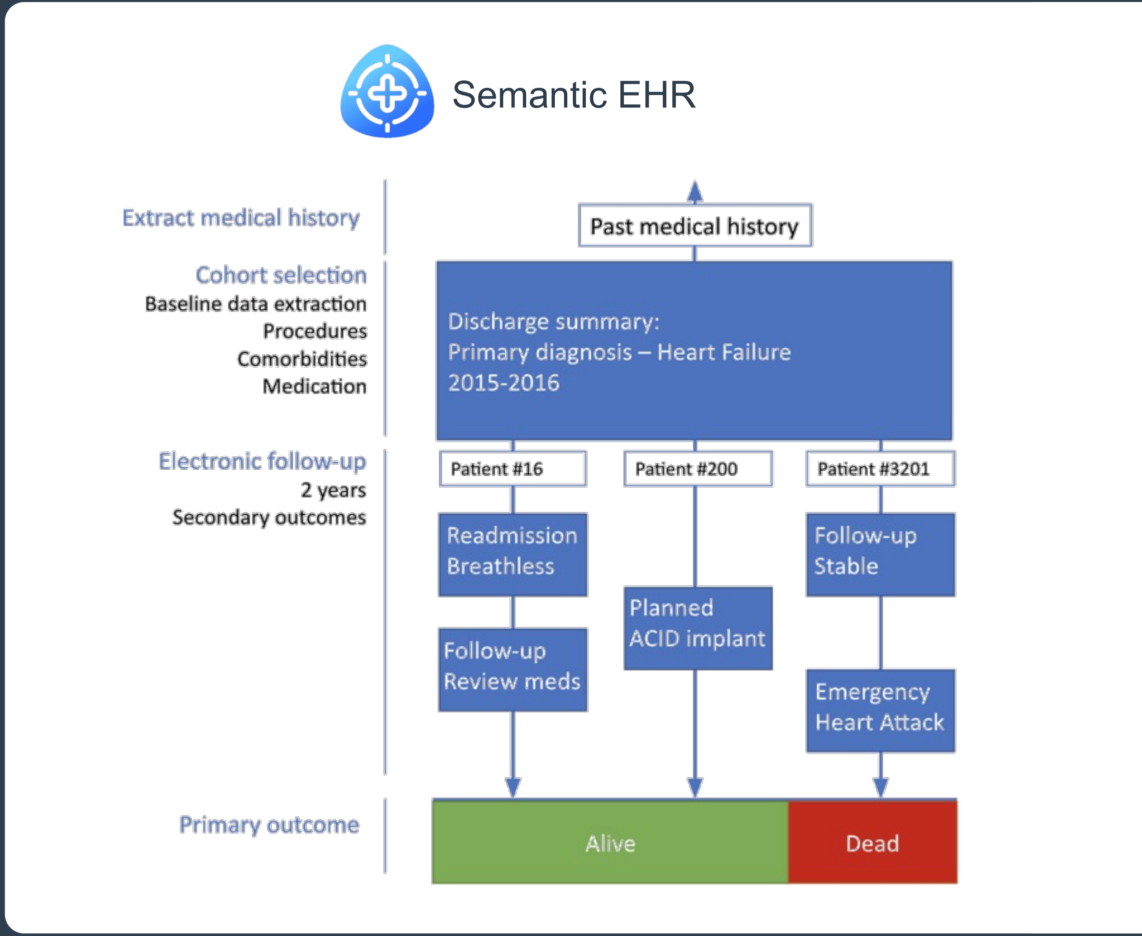




Infrastructure – Natural Language – Semantics



- 1st Step: Cohort Selection
- 2nd Step: Follow up
- 3rd Step: Primary Outcome



Infrastructure – Patient Flow at Scale

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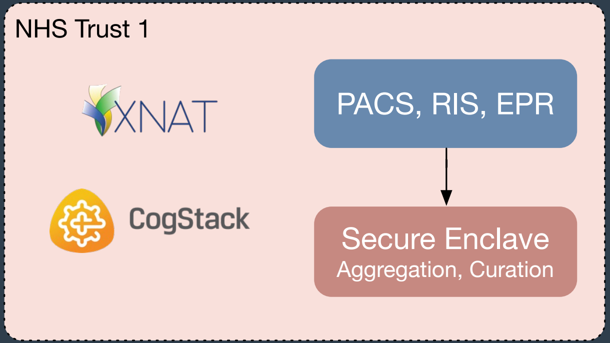
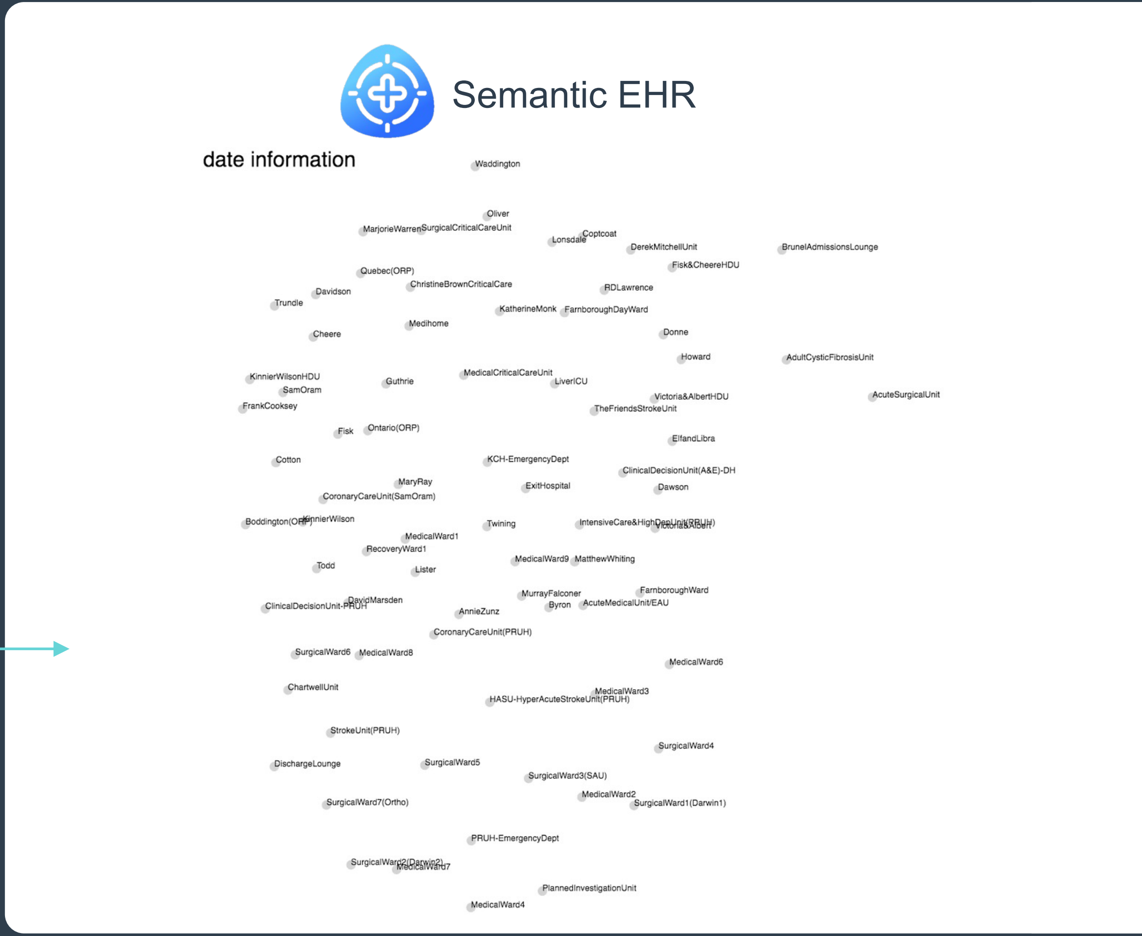
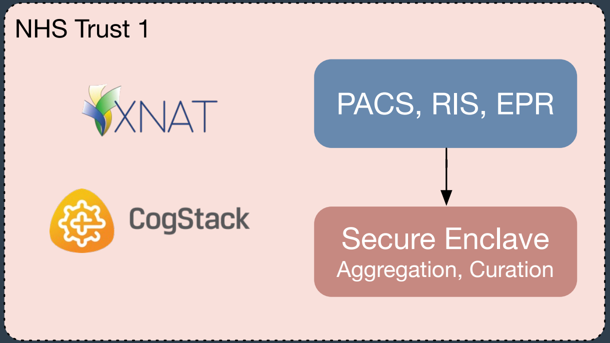


Patient id	From ward	To ward	Time
238492	A&E	Assessment	01/01/16 @10:23:04
238492	Assessment	Exit	01/01/16 @22:19:46
58204818	A&E	Stroke unit	01/01/16 @10:23:55



Infrastructure – Patient Flow at Scale



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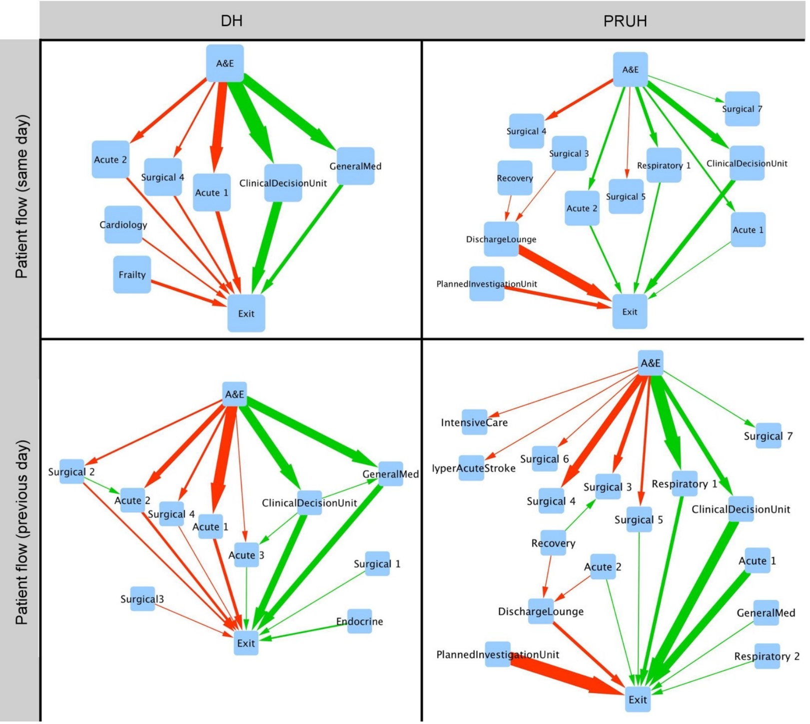
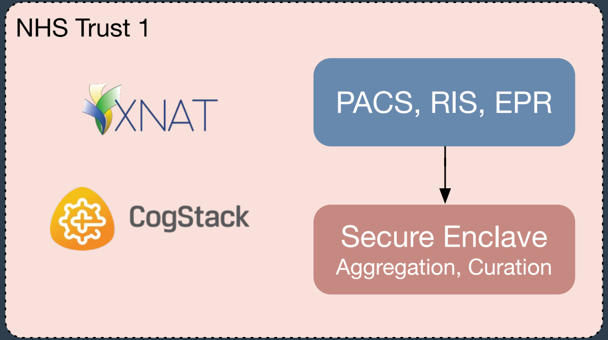
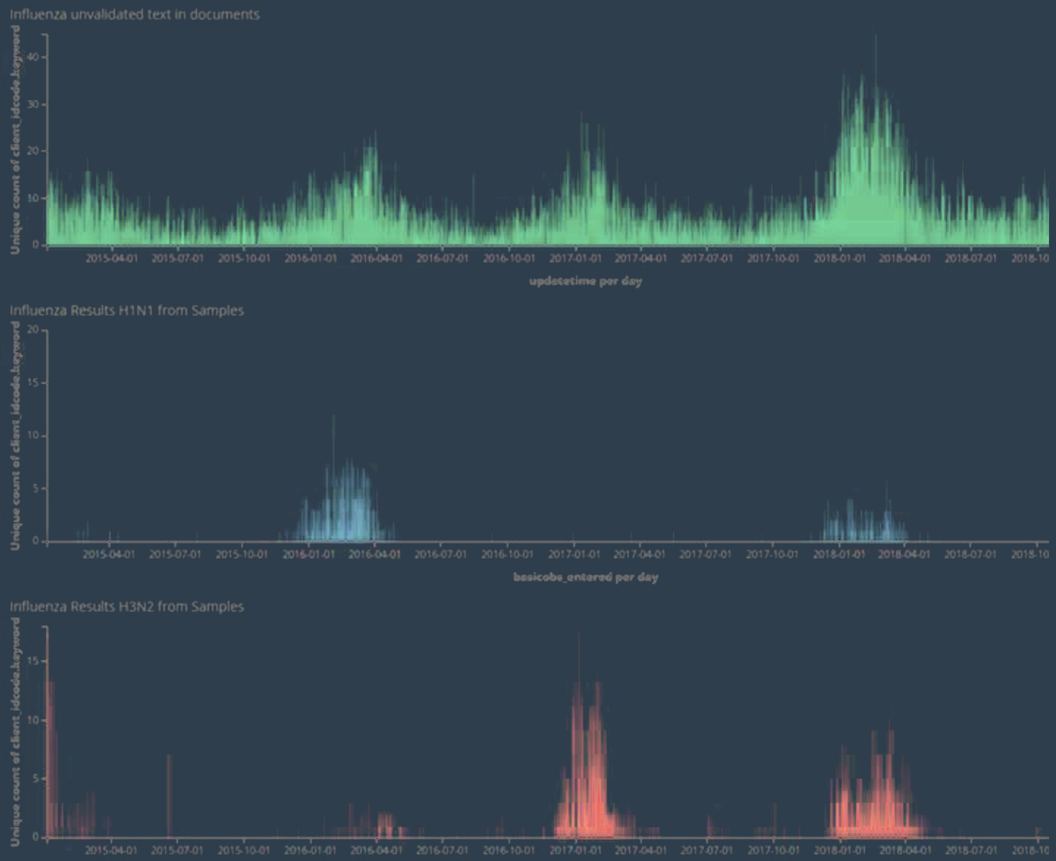
Semantic EHR



Infrastructure – Find previously unseen patterns



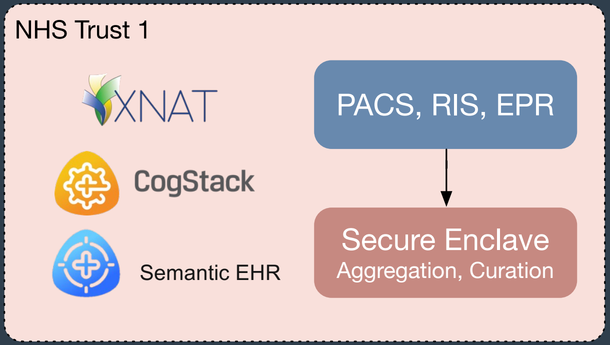
Semantic EHR



H1N1 Lab Sample

H3N2 Lab Sample

Infrastructure – AI Learning Platform

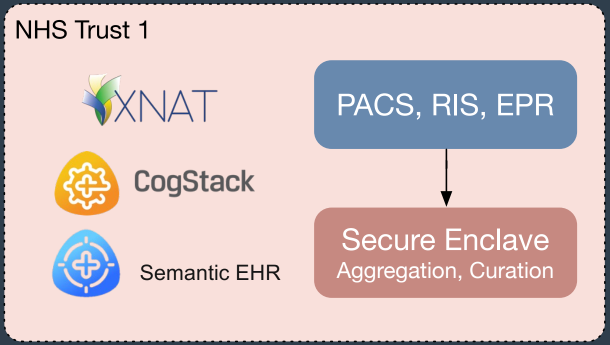


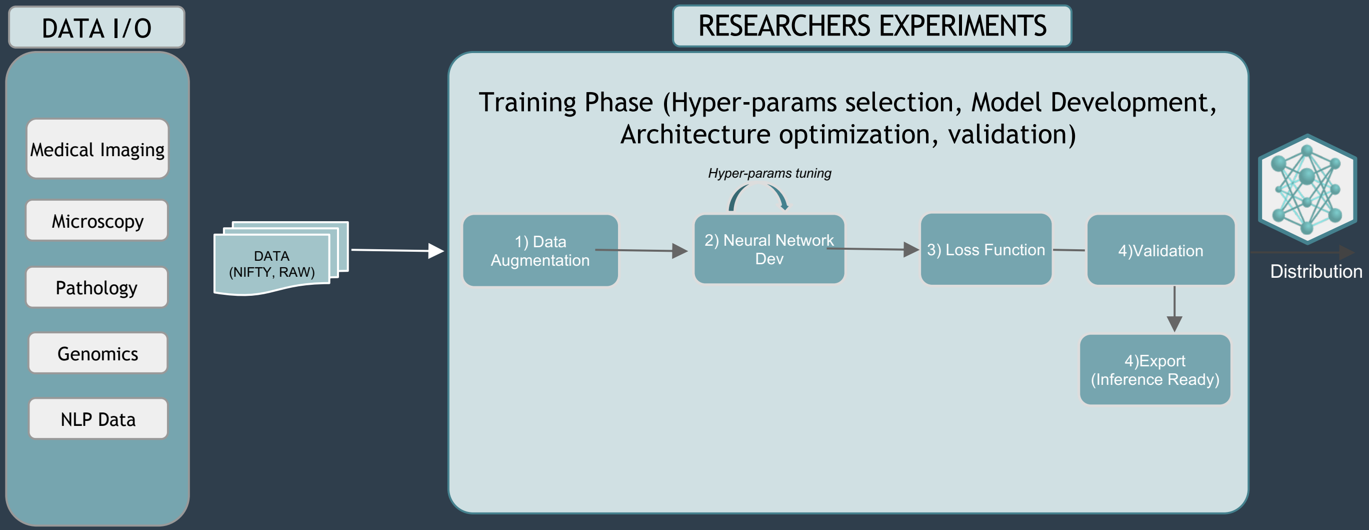
MONAI

"The MONAI framework is the open-source foundation being created by Project MONAI. MONAI is a freely available, community-supported, PyTorch-based framework for deep learning in healthcare imaging. It provides domain-optimized foundational capabilities for developing healthcare imaging training workflows in a native PyTorch paradigm." -

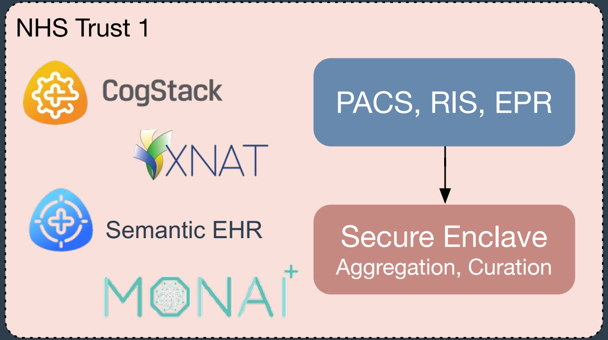
www.monai.io

Infrastructure – AI Learning Platform

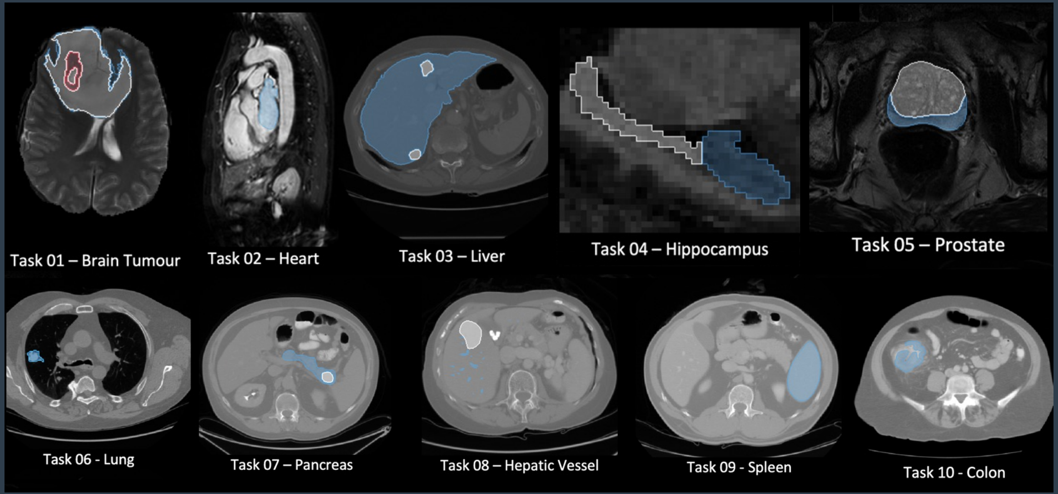




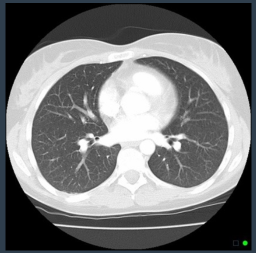
Infrastructure – Automate Expert/Expensive Tasks

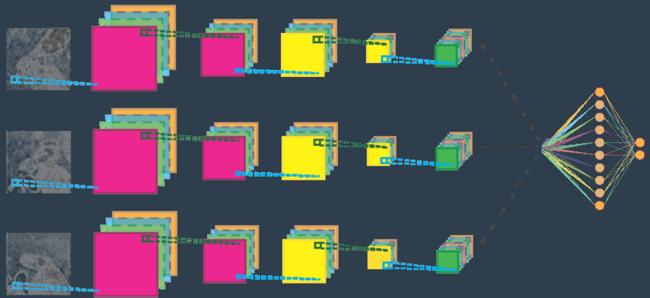


Localizing and contouring regions of interest

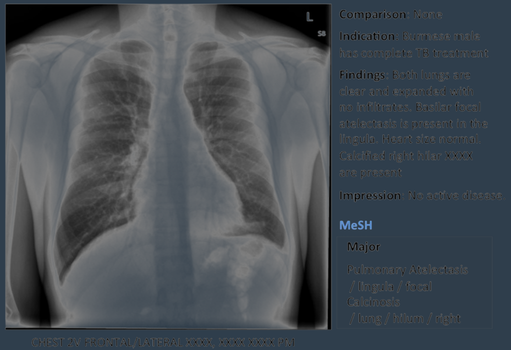


Diagnose patients from images





Automated reporting describing an image



End-to-end Computational Pathway

AI CENTRE for Value Based Healthcare

AMIGO Artificial Medical Intelligence Group

CogStack

XNAT

Near real-time
Data Harmonisation
Search Engine

Semantic
EHR

AI-based language
processing and
understanding

MONAI

AI-based modelling and
predictions

Heterogeneous data → **Inferred structure** → **Actionable Models**

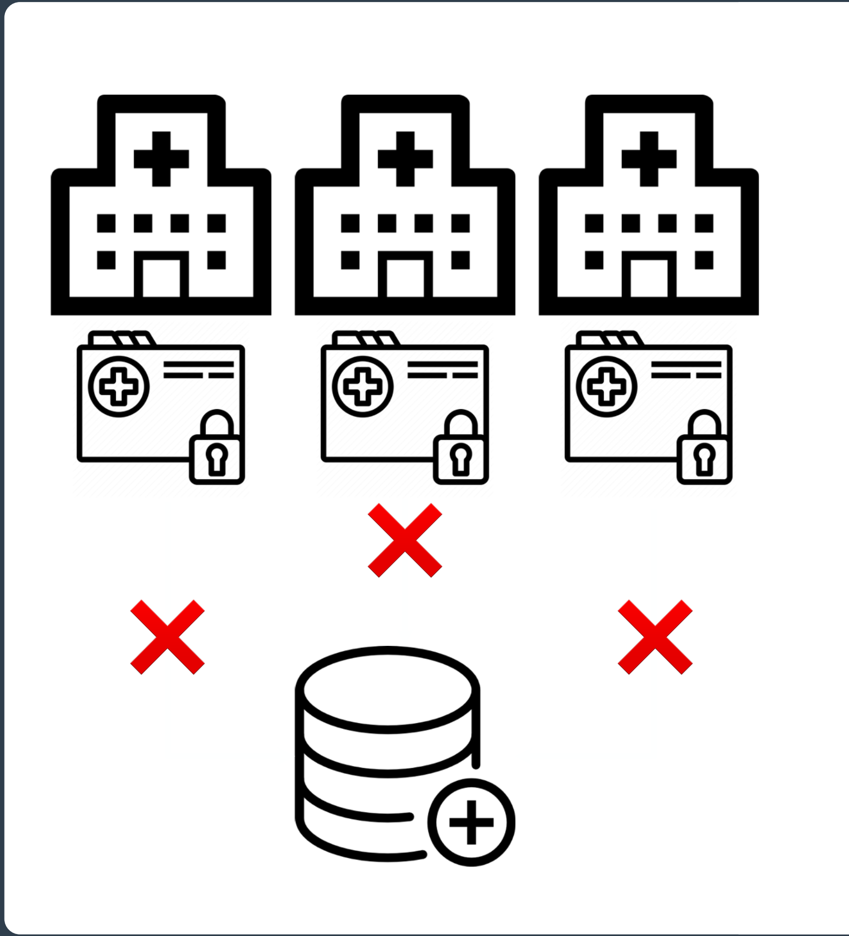
Apps Platform

- Enterprise Semantic Search
- Precision Medicine
- Business Intelligence and Analytics
- Live Alerting
- Patient Timeline

Scaling up data access

Creating large, centralized medical dataset is challenging

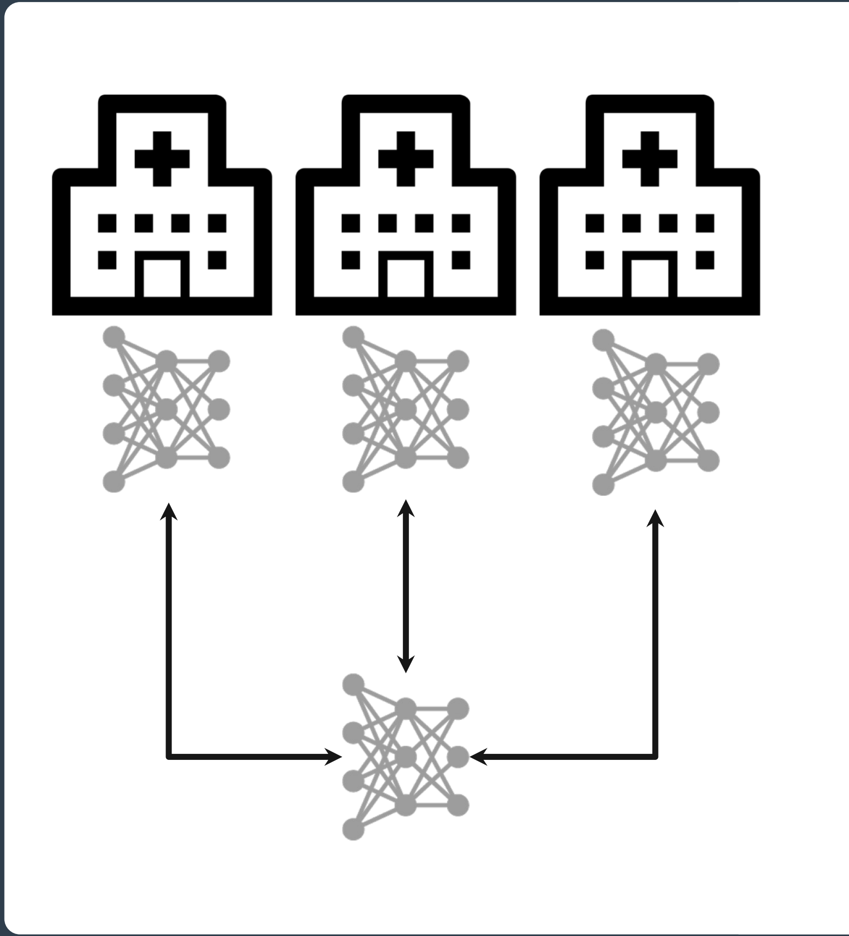
- Private data can’t be shared
- Anonymization is not truly effective
- Data annotation is costly. Data is an asset
- Bureaucracy of data sharing is complex



Scaling up data access

Collaborative learning solves crucial issues in healthcare

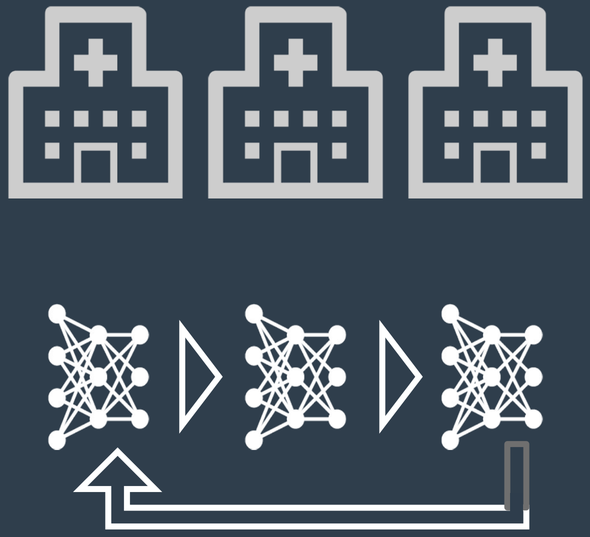
- Private data can’t be shared
- Anonymization is not truly effective
- Data annotation is costly. Data is an asset
- Bureaucracy of data sharing is complex
- Share models, not data!



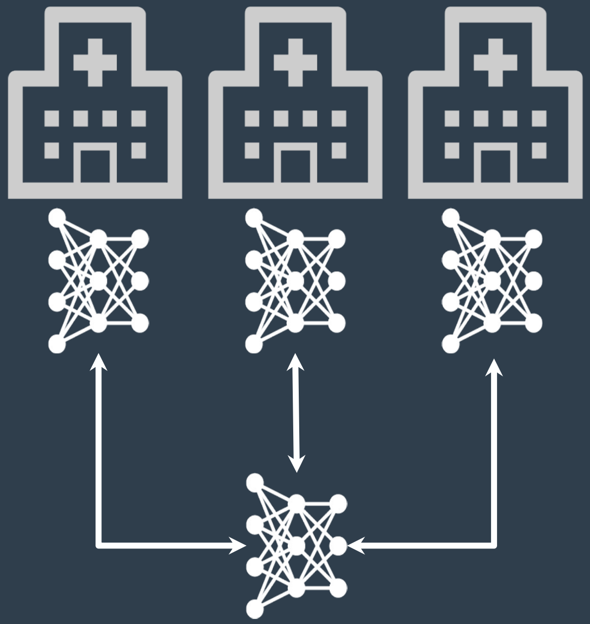
Collaborative learning methods

Obtaining strong models without pooling data

CYCLICAL LEARNING



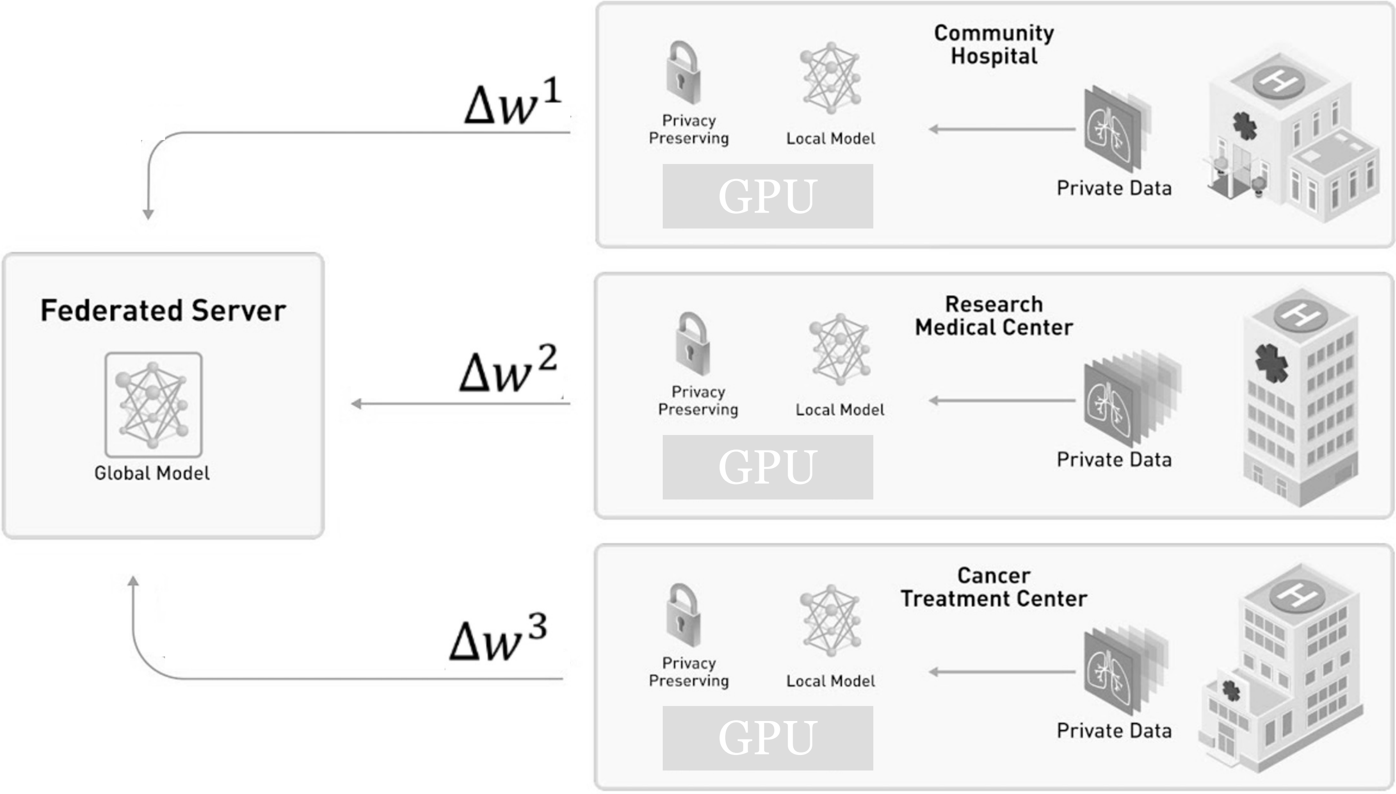
FEDERATED LEARNING



Server-client Federated Learning

Changing the way AI algorithms are trained

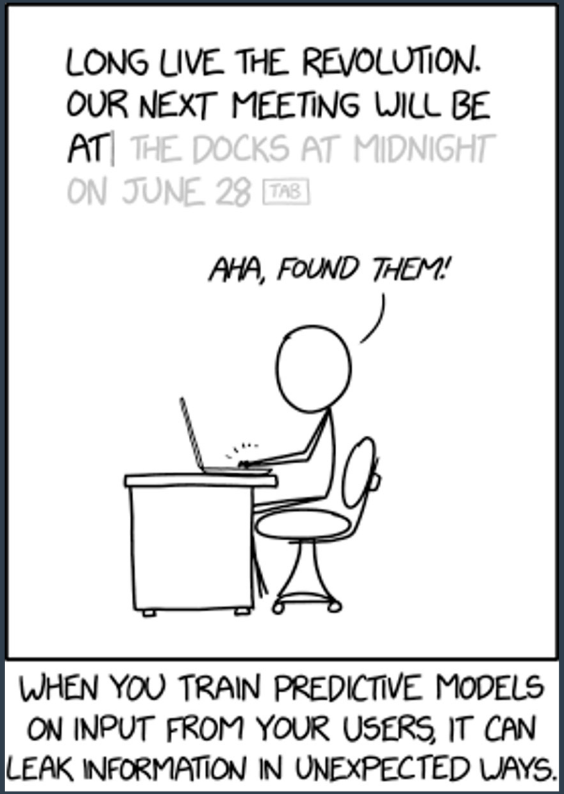
$$\sum_{k=1}^{K} \frac{n_k}{n} w_{t+1}^{k}$$



Privacy Preserving FL

Building differential privacy for collaborative training

- Federated privacy baseline
  - No direct data sharing
  - Authentication, authorisation, secure connection
- Private information can still leak out…
  - Network may memorize data in its parameters
  - Additional privacy mechanisms need to be enforced
  - Literature proposes various strategies for FL privacy



https://xkcd.com/2169/

Current Challenges

SYSTEM ARCHITECTURE

Local training in each institution requires computational infrastructure available on-site. Computational requirements for training shift from centralized data-centers attached to data lakes to single institutions or even edge devices.

TRACEABILITY & ACCOUNTABILITY

Data is the new oil! Due to the value and cost of data, it is necessary to trace how different participant to FL training contribute to the final model. A system to link back contributions to the model to participants is also needed.

INITIATIVES & CONSORTIA

Defining collaborations and initiatives leveraging federated learning requires rethinking current agreements between institution. Even though data governance issues are solved, institutions share models that might correspond to IP.

PRIVACY & SECURITY

Deep learning models have a large number of parameters, this may cause parts of the training set to be memorized in their parameters. In federated learning this mechanism determines a possible leakage of private information.

Conclusions - Part 2

- The real world is hard
- Data is complex and dirty
- Integration is a challenge
- Governance/privacy barriers
- Regulatory barriers
- If solved, impact can be massive

Neuroimaging at Scale

The real world vs Research data

Public-heath & epidemiological Research

Observational studies

Clinical-quality data

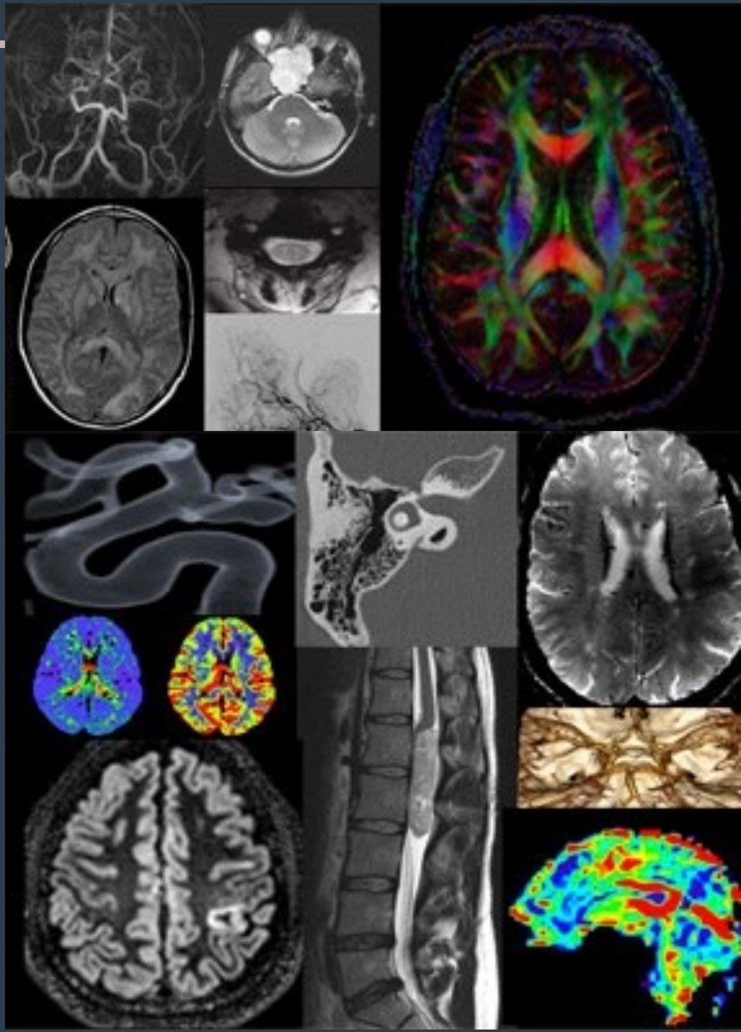
Research Studies

Randomised Clinical Trials

Research-quality data

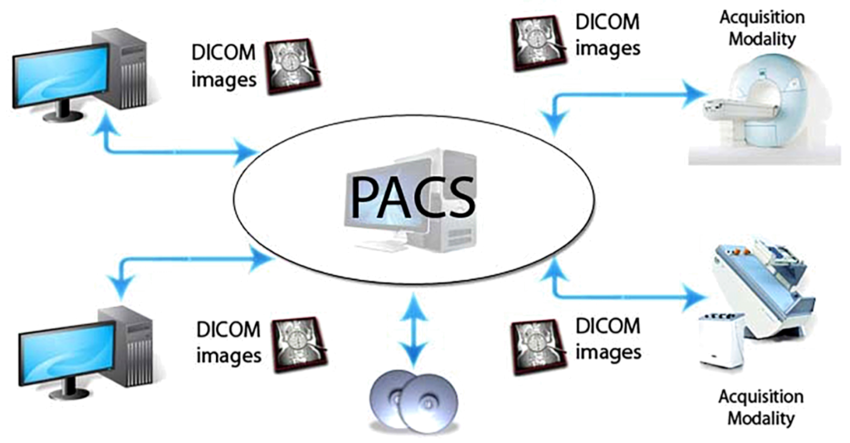
AI-enabled Neuroimaging

- Neurology is dependent on imaging for differential diagnosis
- (Neuro)radiology is in “trouble”
  - Imaging increases at 10-12%/y
  - But (neuro)radiologists increase at 1-3%/y
  - Limited health provider funding & training rates
- Improving neurological care requires predictive models
  - Data is not being properly utilised
  - Neurological and radiological care is not integrated
- Operations/admin is mostly non data driven



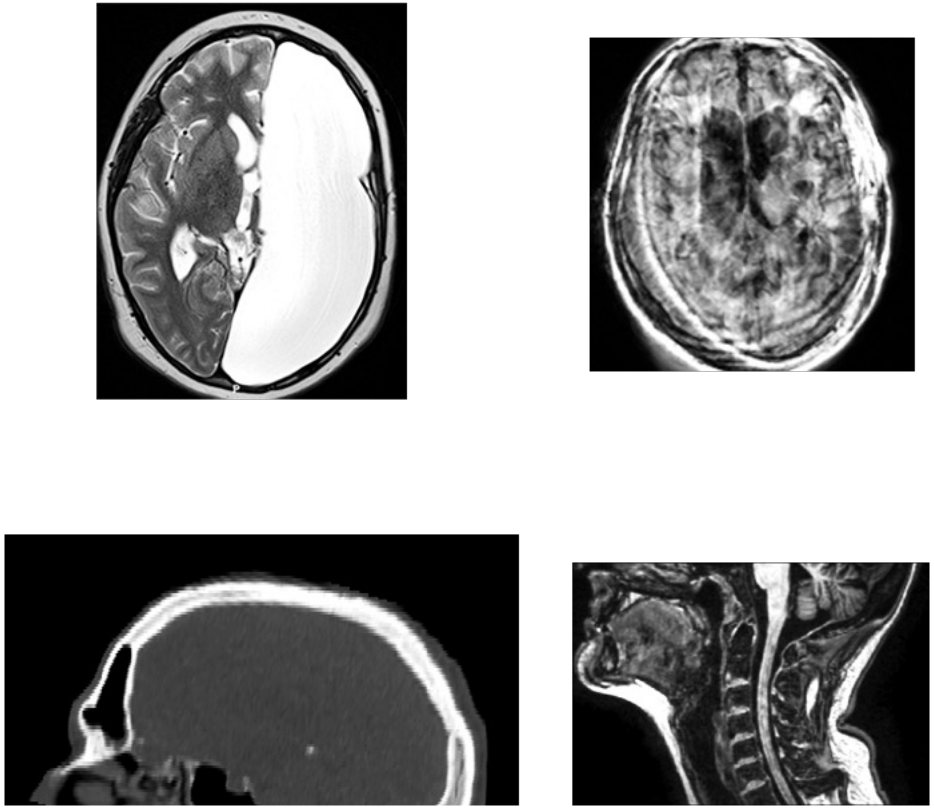
Imaging Big Data - The Raw Data

- +2Ms Volumes - ~150.000 sessions
  - Many images & follow-up data
  - 14k “different” sequences
  - 15+ different scanners
  - Mostly 1.5T and 3T
- RIS - Radiological reports
- CDR - ICD-10 codes
- Blood tests



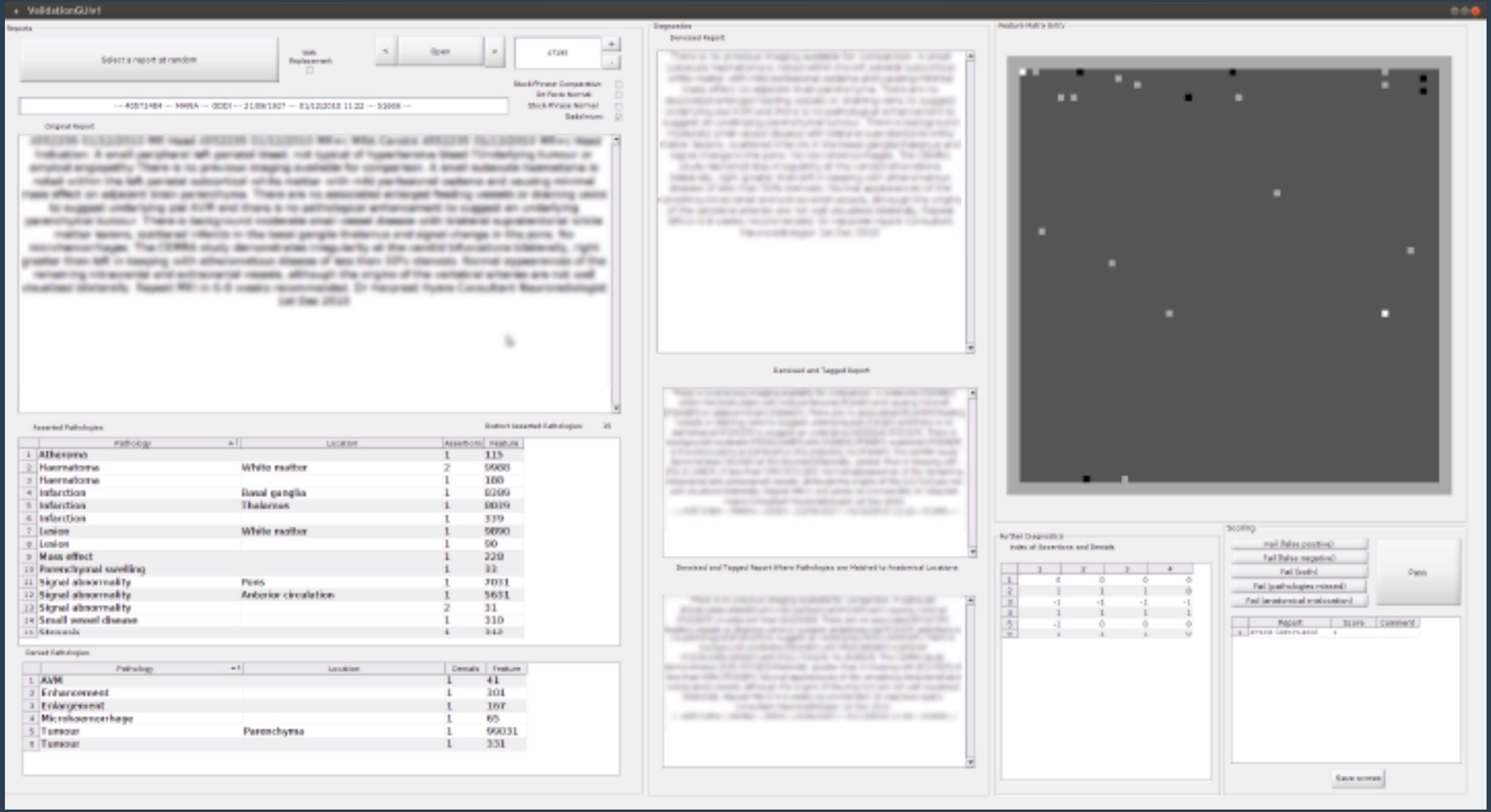
The challenges of the real world

- What kinds of pathologies?
  - Task-specific vs. general-purpose
- Does the image have an artefact? In FOV?
  - Need for QC tools and robust algorithms
- What are the acquisition differences?
  - Knowledge of acquisition physics
- Is all necessary data available?
  - Deal with missing data
- Is the image of the right kind?
  - Modality and body part classifier



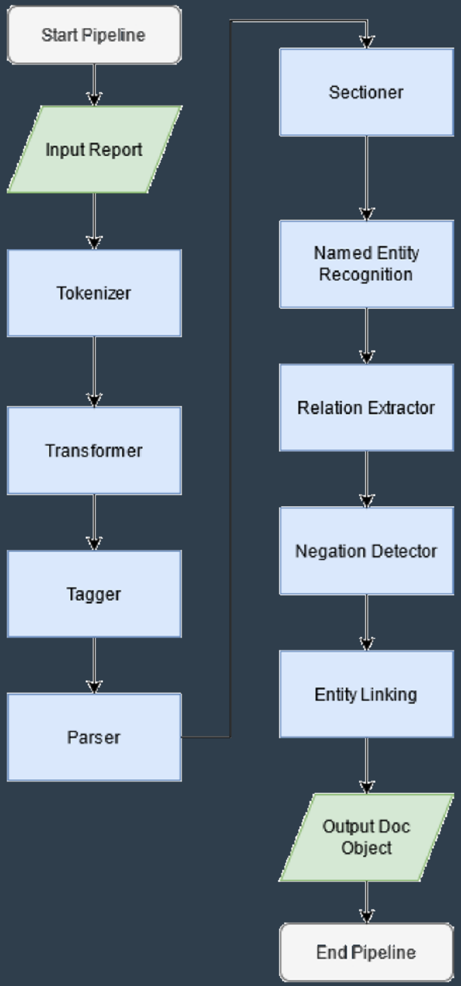
Where do we start?

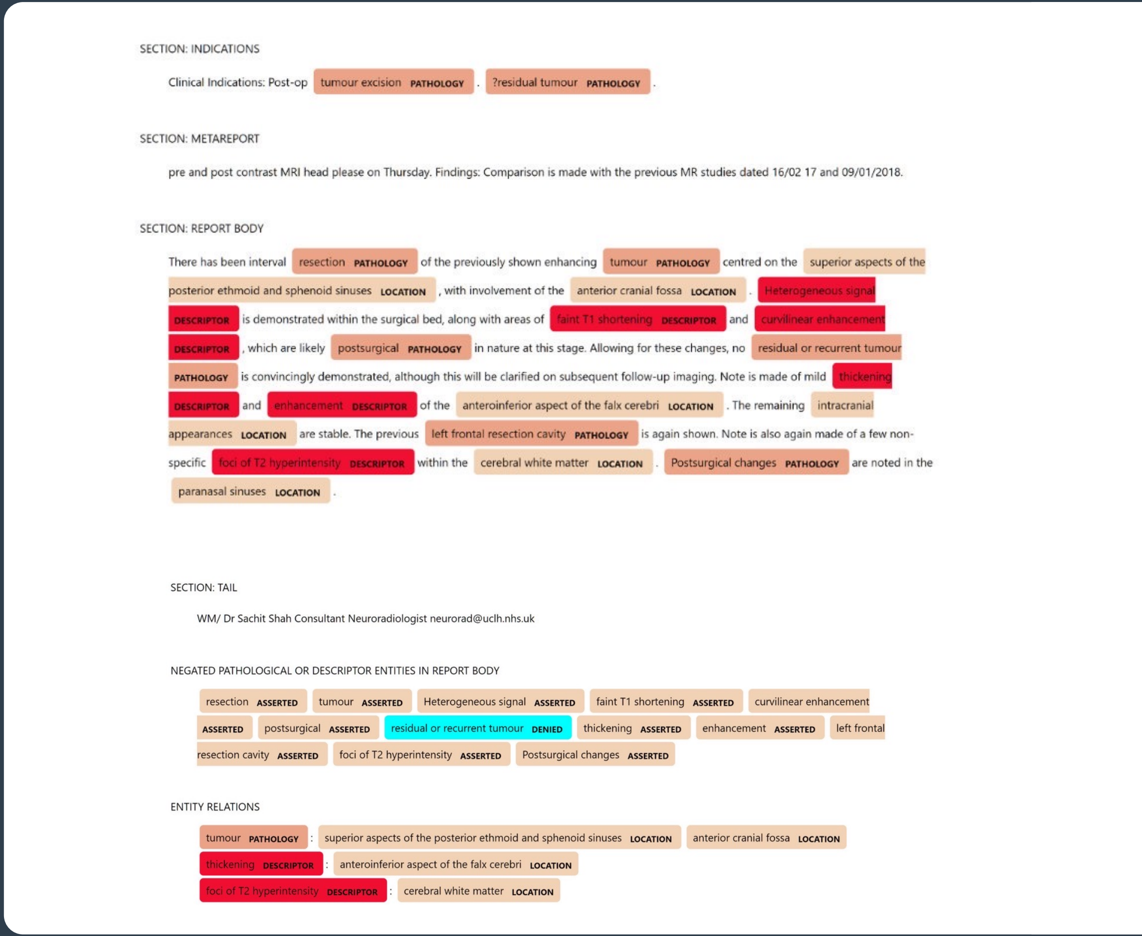
Problem: Where do we start?



Radiological report blurred for confidentiality purposes

NLP Pipelines applied to Radiological text





SECTION: INDICATIONS

Clinical Indications: Post-op tumour excision PATHOLOGY . ?residual tumour PATHOLOGY .

SECTION: METAREPORT

pre and post contrast MRI head please on Thursday. Findings: Comparison is made with the previous MR studies dated 16/02 17 and 09/01/2018.

SECTION: REPORT BODY

There has been interval resection PATHOLOGY of the previously shown enhancing tumour PATHOLOGY centred on the superior aspects of the posterior ethmoid and sphenoid sinuses LOCATION , with involvement of the anterior cranial fossa LOCATION . Heterogeneous signal DESCRIPTOR is demonstrated within the surgical bed, along with areas of faint T1 shortening DESCRIPTOR and curvilinear enhancement DESCRIPTOR , which are likely postsurgical PATHOLOGY in nature at this stage. Allowing for these changes, no residual or recurrent tumour PATHOLOGY is convincingly demonstrated, although this will be clarified on subsequent follow-up imaging. Note is made of mild thickening DESCRIPTOR and enhancement DESCRIPTOR of the anteroinferior aspect of the falx cerebri LOCATION . The remaining intracranial appearances LOCATION are stable. The previous left frontal resection cavity PATHOLOGY is again shown. Note is also again made of a few non-specific foci of T2 hyperintensity DESCRIPTOR within the cerebral white matter LOCATION . Postsurgical changes PATHOLOGY are noted in the paranasal sinuses LOCATION .

SECTION: TAIL

WM/ Dr Sachit Shah Consultant Neuroradiologist neurorad@uclh.nhs.uk

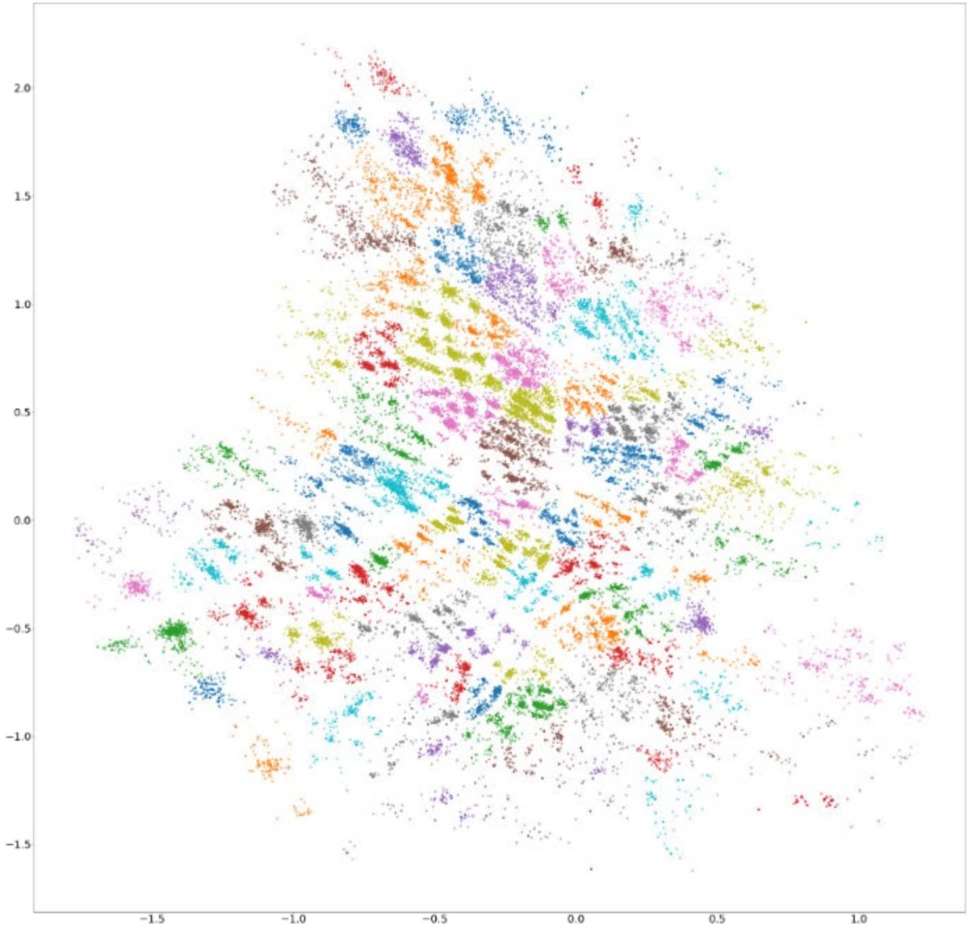
NEGATED PATHOLOGICAL OR DESCRIPTOR ENTITIES IN REPORT BODY

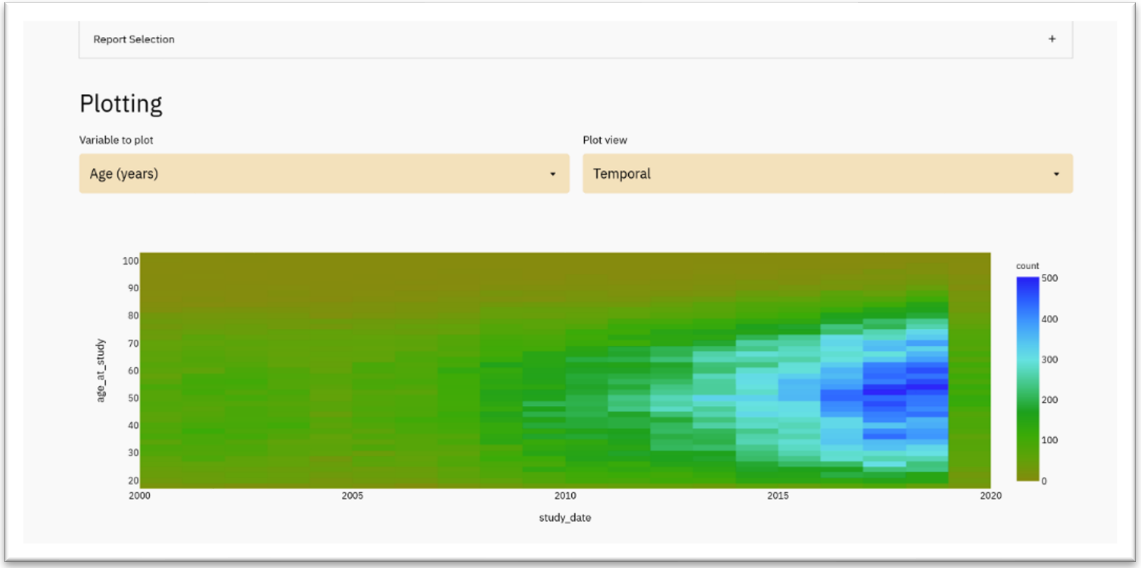
resection ASSERTED tumour ASSERTED Heterogeneous signal ASSERTED faint T1 shortening ASSERTED curvilinear enhancement ASSERTED postsurgical ASSERTED residual or recurrent tumour DENIED thickening ASSERTED enhancement ASSERTED left frontal resection cavity ASSERTED foci of T2 hyperintensity ASSERTED Postsurgical changes ASSERTED

ENTITY RELATIONS

tumour PATHOLOGY : superior aspects of the posterior ethmoid and sphenoid sinuses LOCATION anterior cranial fossa LOCATION
thickening DESCRIPTOR : anteroinferior aspect of the falx cerebri LOCATION
foci of T2 hyperintensity DESCRIPTOR : cerebral white matter LOCATION

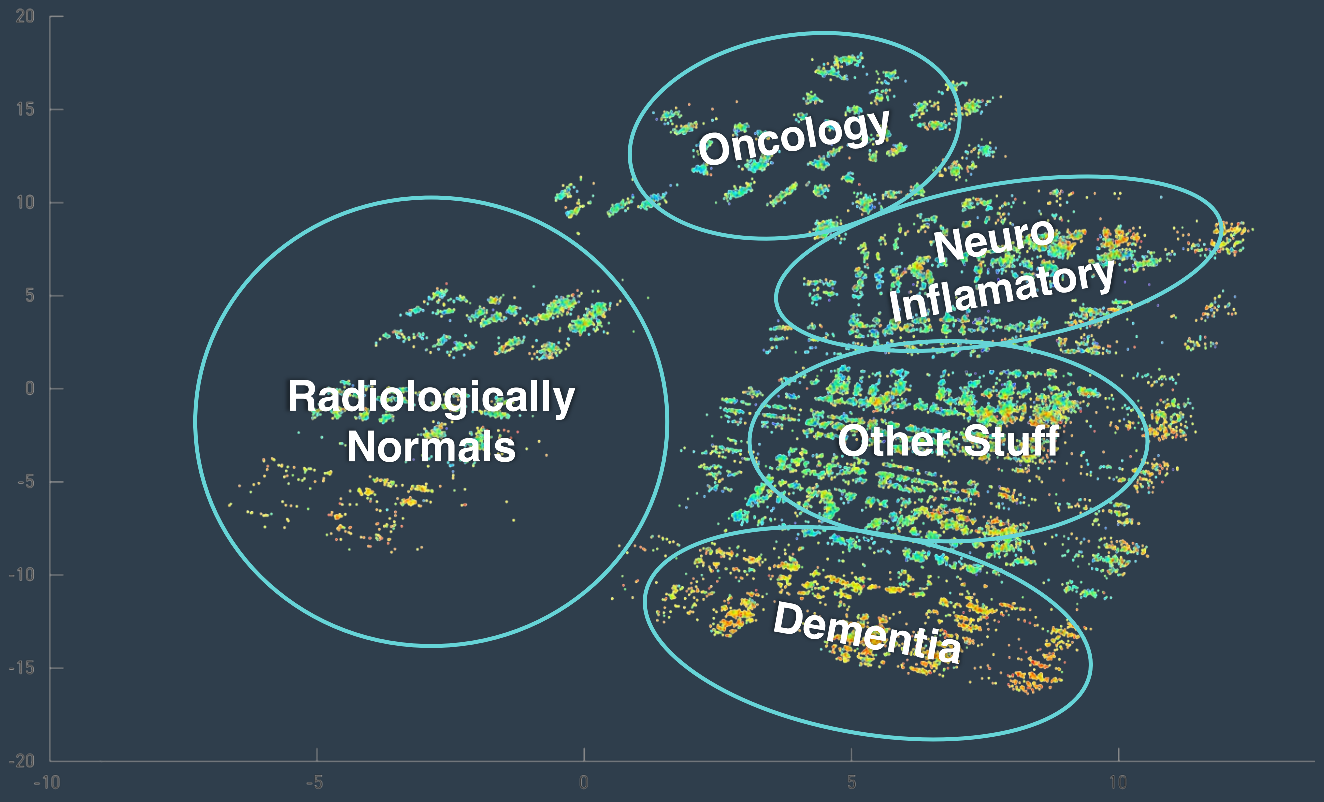
Clustering and Inspecting Reports



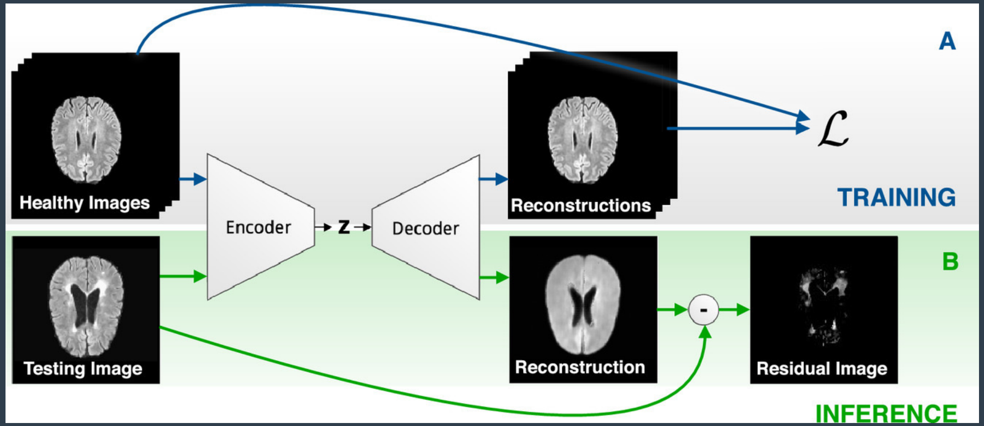


Clustered Reports

- 40k radiological normals, with 6k asserted normals



Variational autoencoders

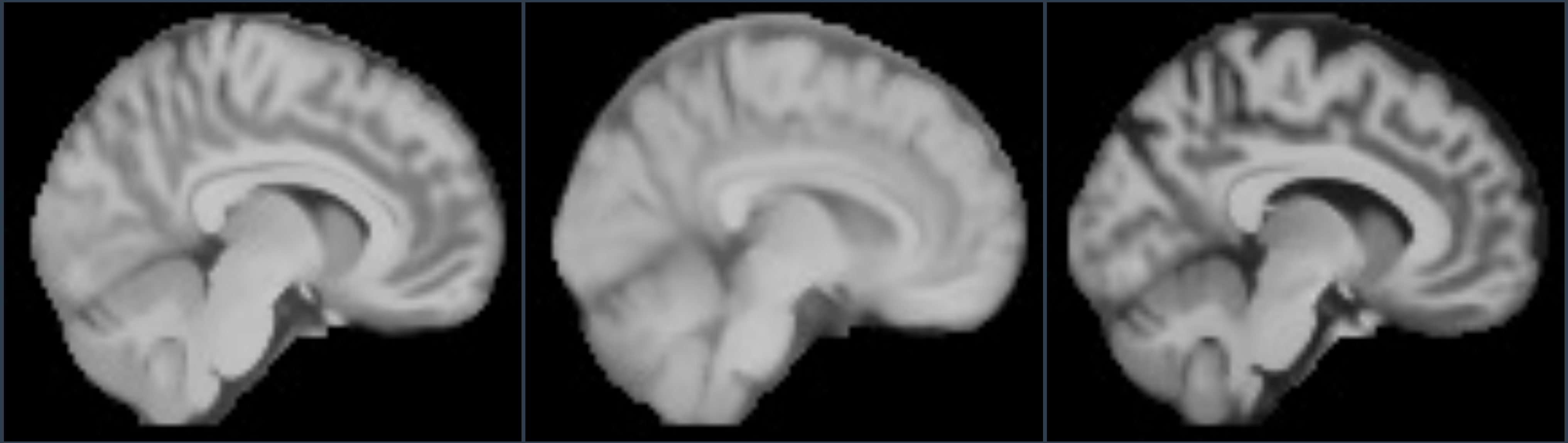


Baur, et al. (2020). ArXiv:2004.03271

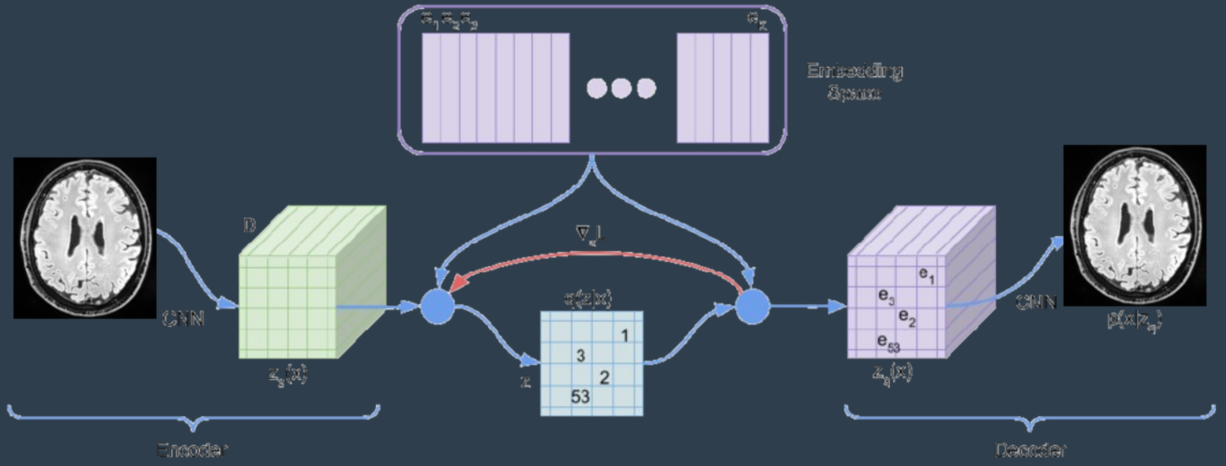
Anomaly quantified by test image location on learnt normal manifold

Limited by VAE expressivity

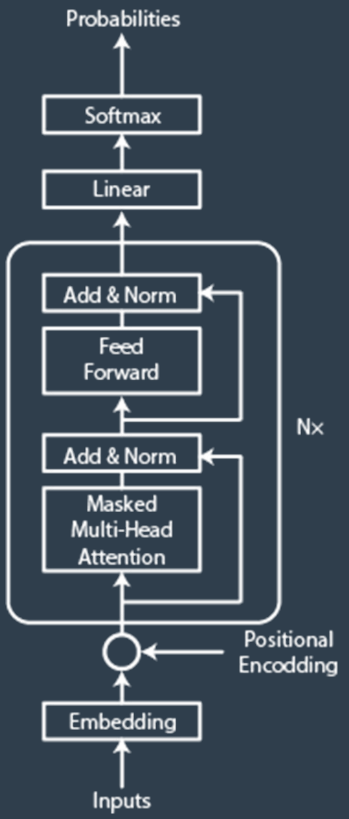
Unsupervised Learning



VQ-VAE + Transformers



+



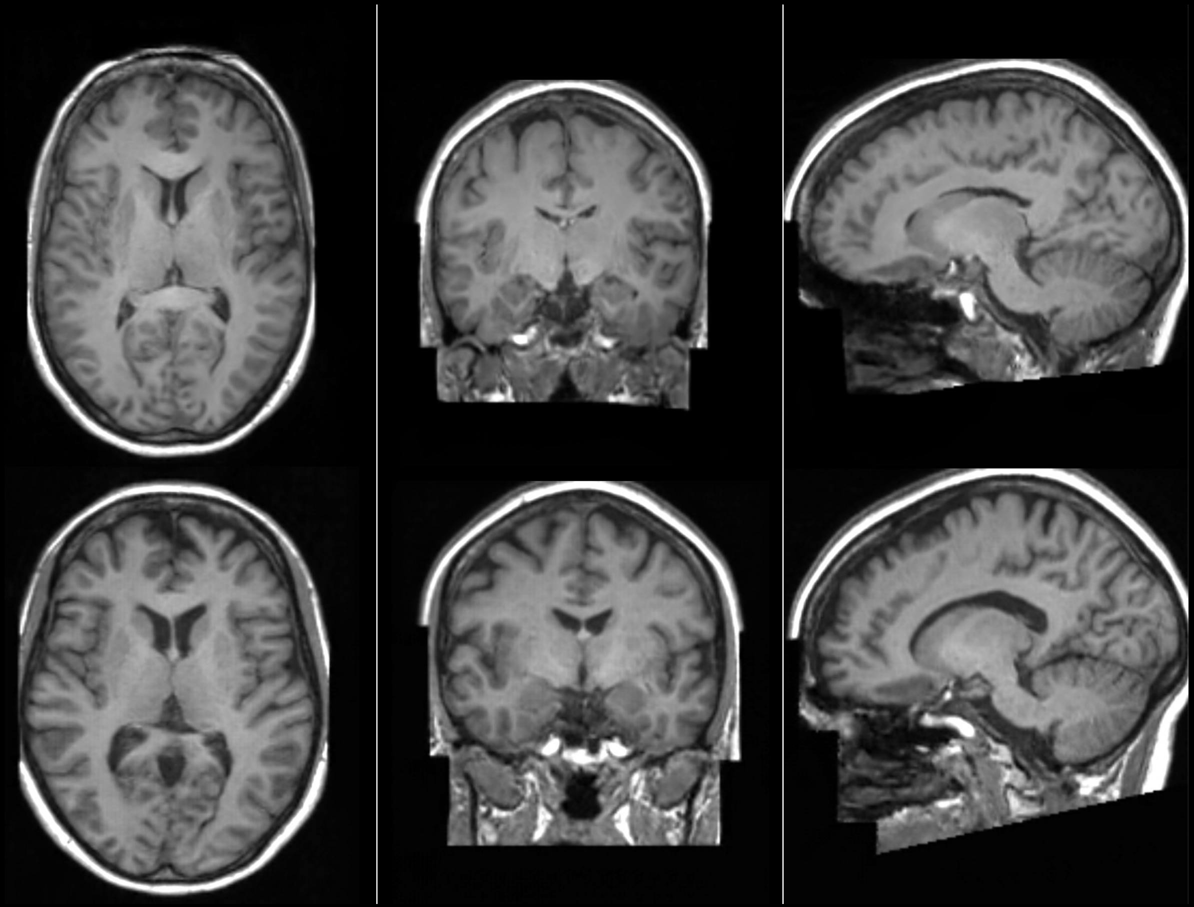
Combines expressivity with compactness

Scaling to 3D is hard

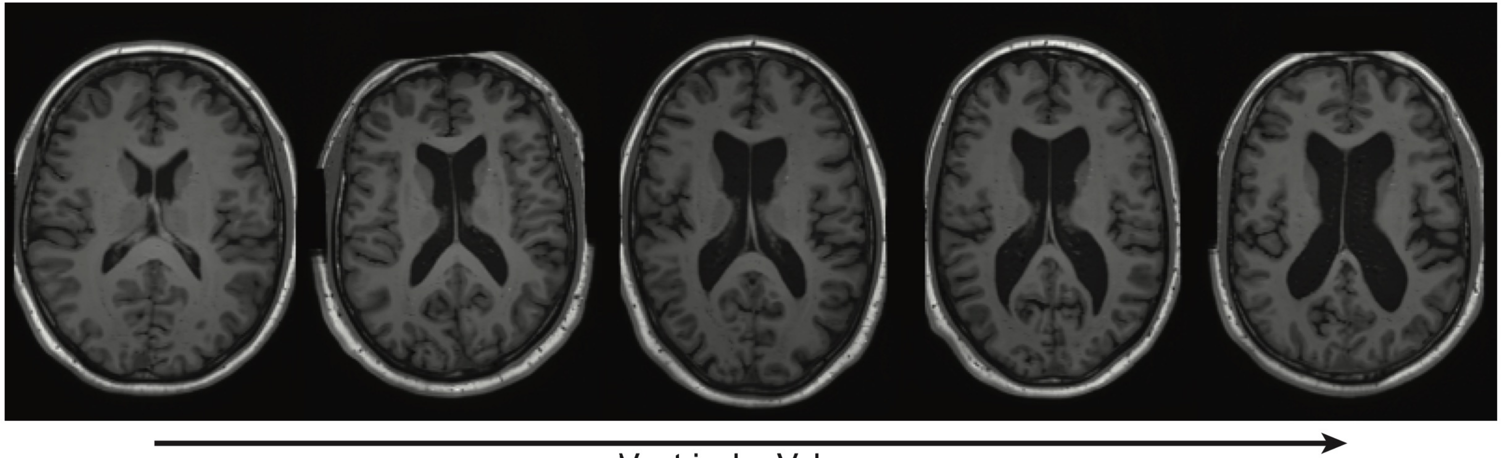
This Brain does not exist

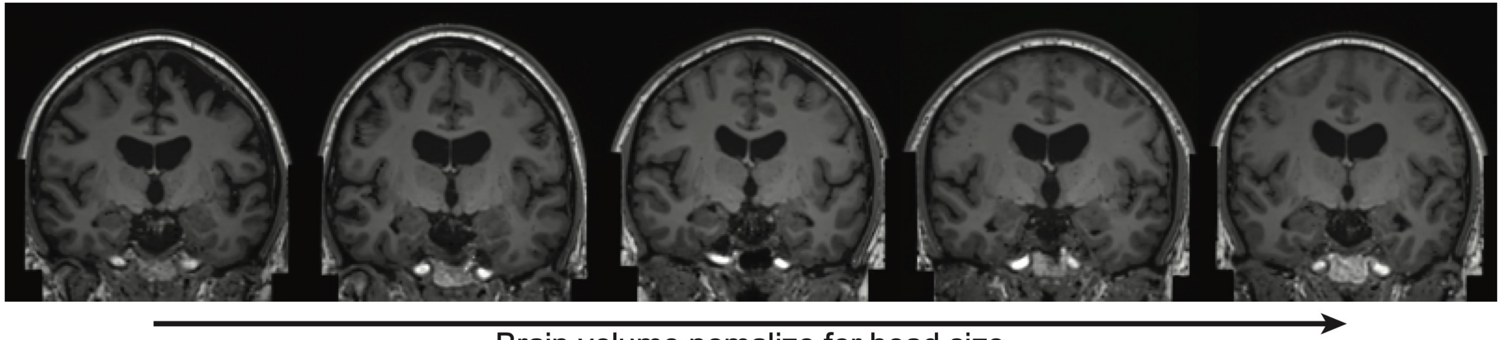
http://amigos.ai/thisbraindoesnotexist/

Real vs fake?

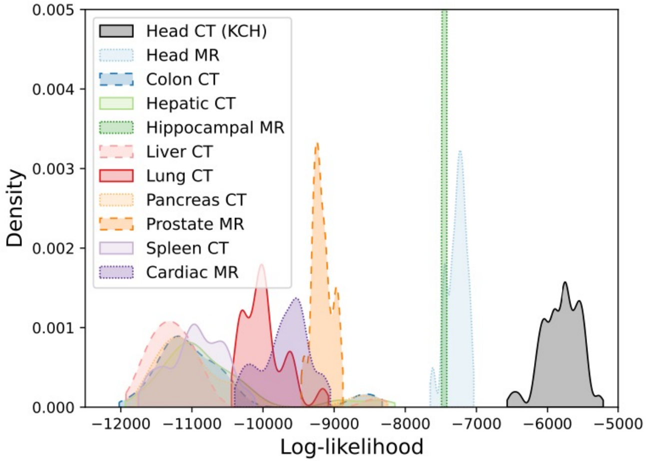


Conditional generative modelling.

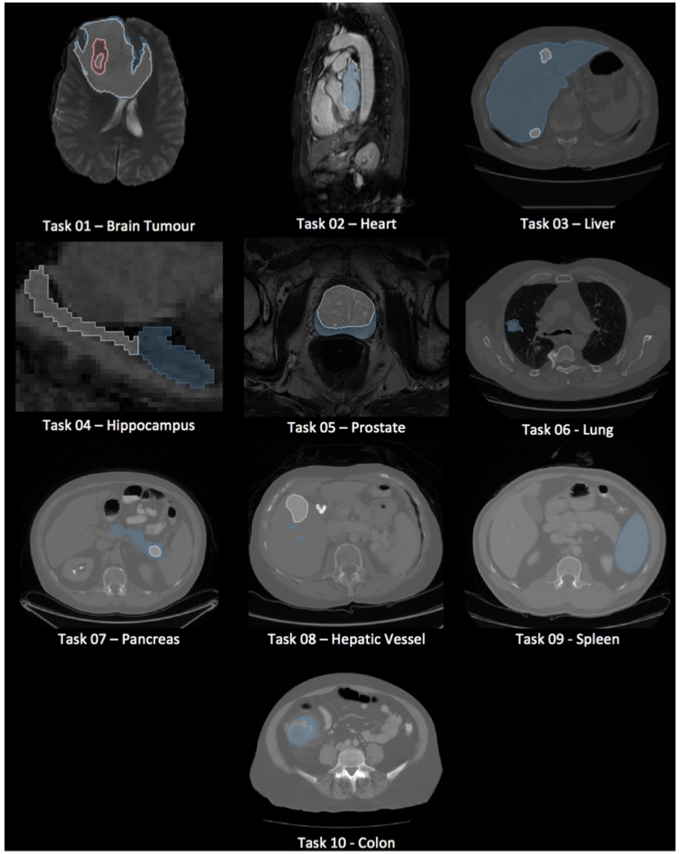




How do we detect wrong data?

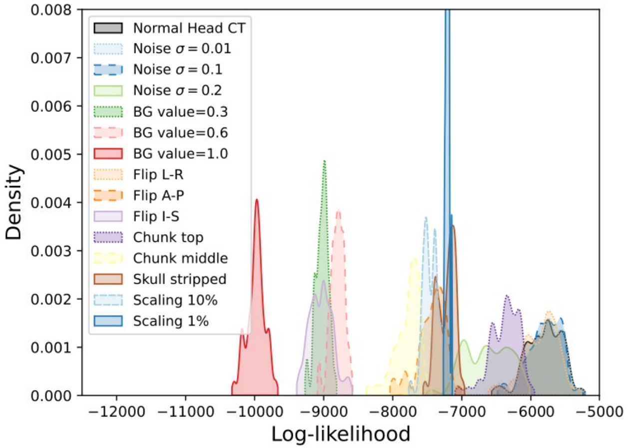


	Dataset	Likelihood	AUC
Non Head CT	Head MR	-7288 (134)	1.00
	Colon CT	-10809 (789)	1.00
	Hepatic CT	-10712 (763)	1.00
	Hippocampal MR	-7465 (20)	1.00
	Liver CT	-11116 (658)	1.00
	Lung CT	-9957 (289)	1.00
	Pancreas CT	-10798 (791)	1.00
	Prostate MR	-9140 (134)	1.00
	Spleen CT	-10895 (382)	1.00
	Cardiac MR	-9661 (318)	1.00

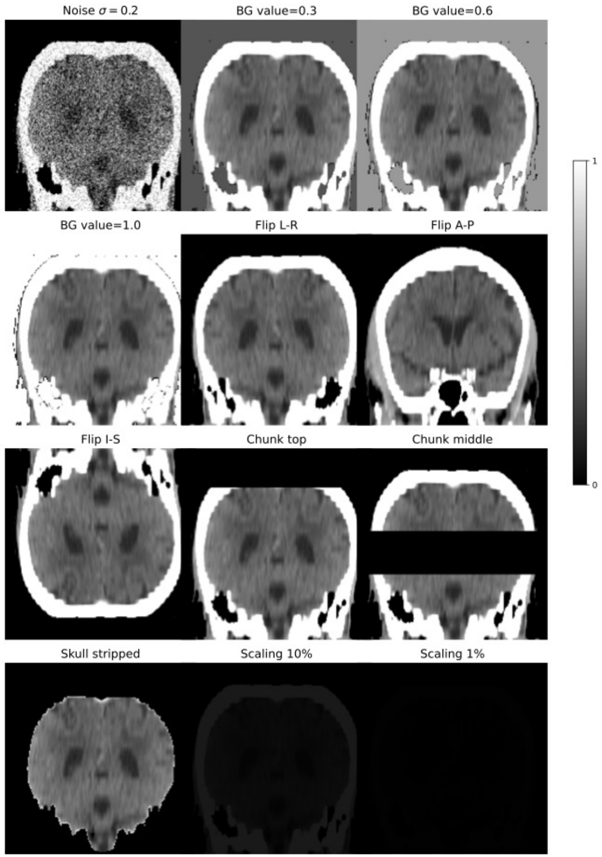


- Graham et al. MIDL 2022

How do we detect wrong data?

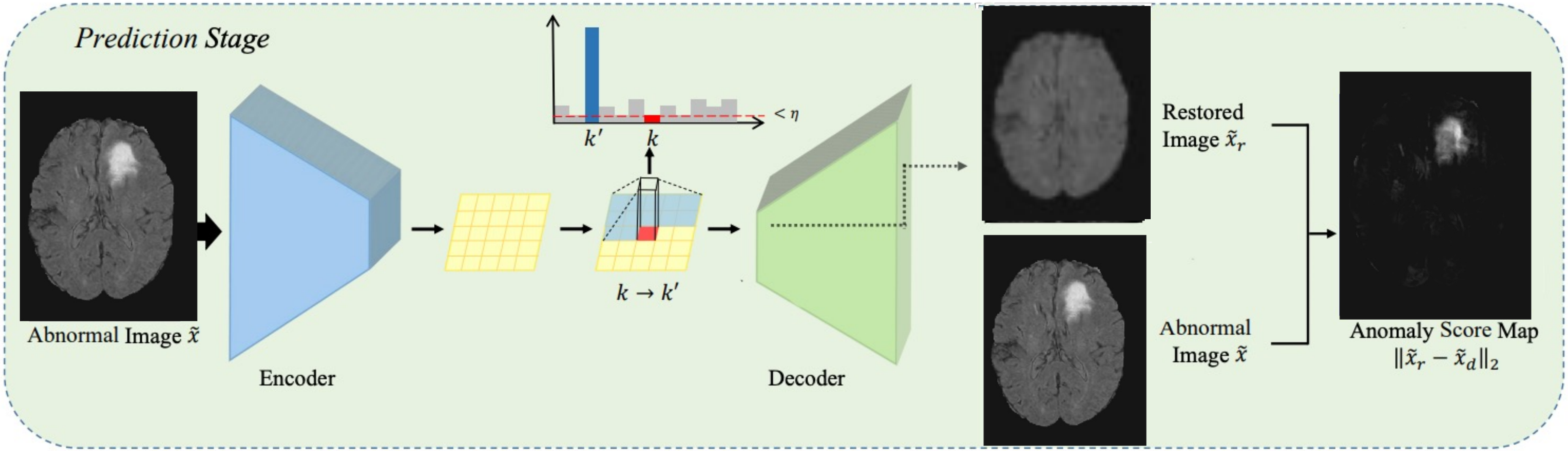


	Dataset	Likelihood	AUC
Corrupted Head CT	Noise $\sigma = 0.01$	-5796 (253)	0.49
	Noise $\sigma = 0.1$	-5793 (237)	0.49
	Noise $\sigma = 0.2$	-6637 (324)	0.98
	BG value=0.3	-9022 (89)	1.00
	BG value=0.6	-8803 (100)	1.00
	BG value=1.0	-9979 (127)	1.00
	Flip L-R	-5850 (253)	0.55
	Flip A-P	-7435 (205)	1.00
	Flip I-S	-9036 (165)	1.00
	Chunk top	-6382 (214)	0.96
	Chunk middle	-7784 (179)	1.00
	Skull stripped	-7226 (125)	1.00



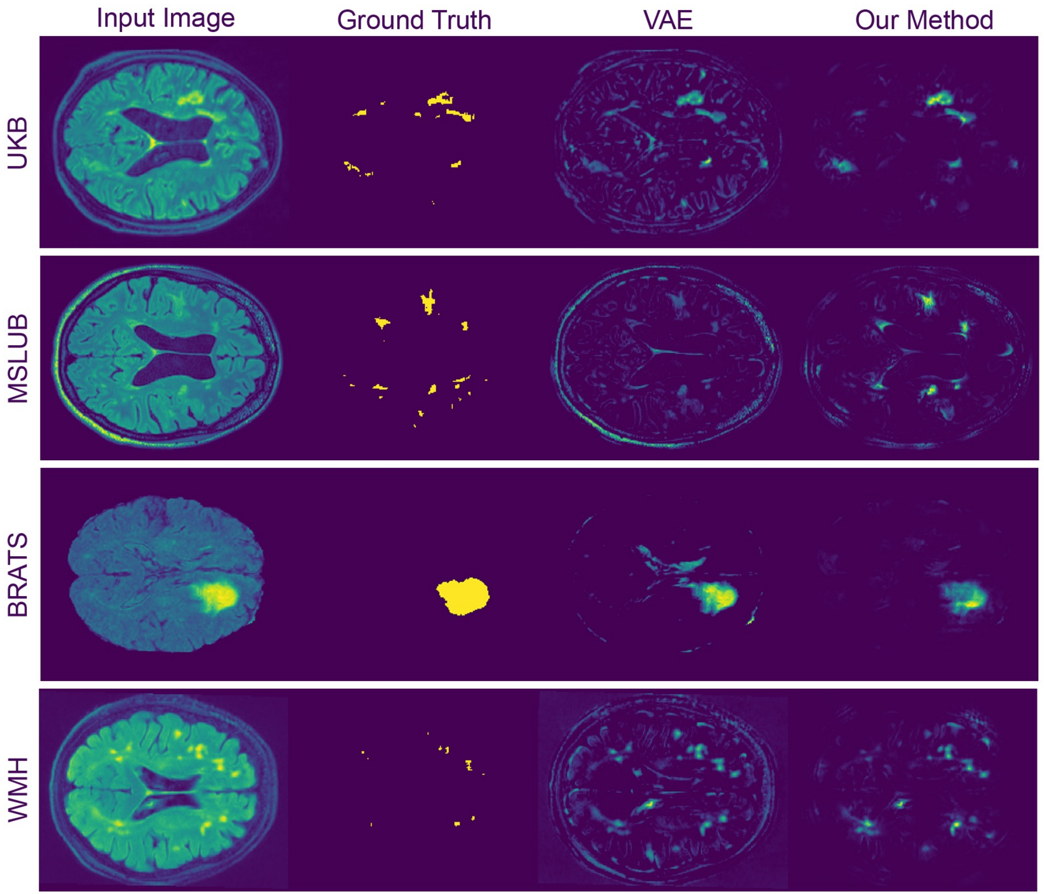
- Graham et al. MIDL 2022

Problem: How do we detect outliers?



- Lopez Pinaya et al. MIDL 2021

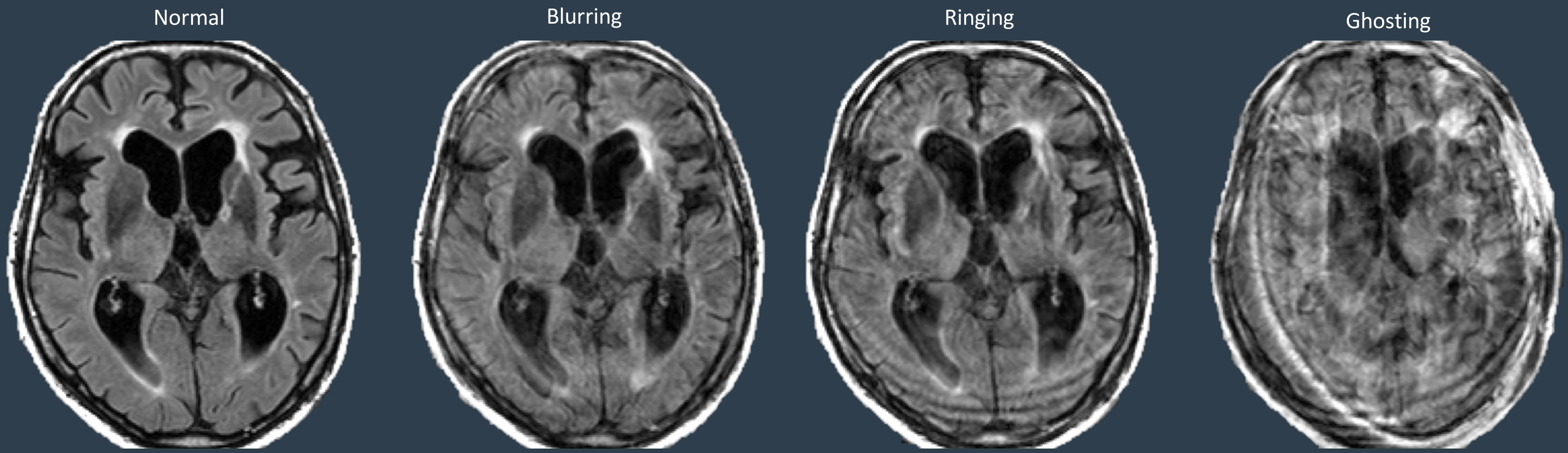
Problem: How do we detect outliers?



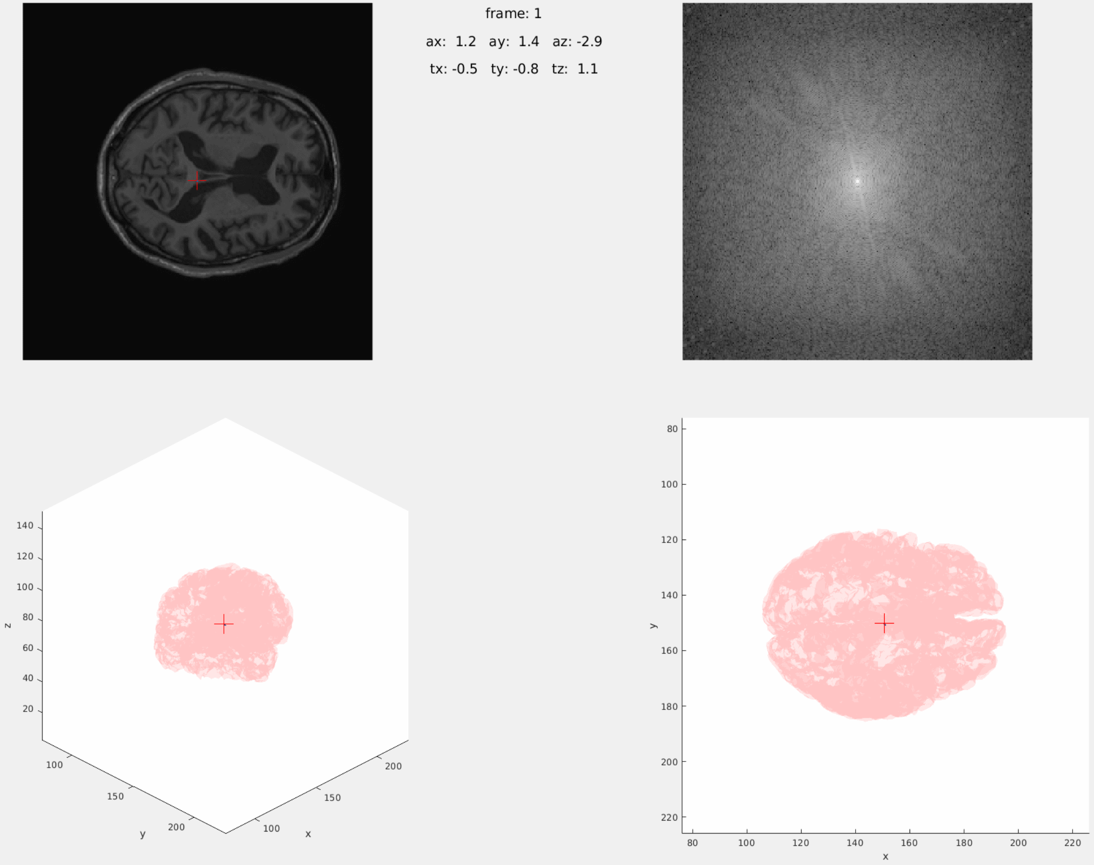
UKB Dataset	[DICE]
AE (Dense) (Baur et al., 2020a)	0.016
AE (Spatial) (Baur et al., 2020a)	0.054
VAE (Dense) (Baur et al., 2020a)	0.016
VQ-VAE (van den Oord et al., 2017)	0.028
VQ-VAE + Transformer + Masked Residuals + Different Orderings (Ours)	**0.232**
MSLUB Dataset	
AE (Dense) (Baur et al., 2020a)	0.041
AE (Spatial) (Baur et al., 2020a)	0.061
VAE (Dense) (Baur et al., 2020a)	0.039
VQ-VAE (van den Oord et al., 2017)	0.040
VQ-VAE + Transformer + Masked Residuals + Different Orderings (Ours)	**0.378**
BRATS Dataset	
AE (Dense) (Baur et al., 2020a)	0.276
AE (Spatial) (Baur et al., 2020a)	0.531
VAE (Dense) (Baur et al., 2020a)	0.294
VQ-VAE (van den Oord et al., 2017)	0.331
VQ-VAE + Transformer + Masked Residuals + Different Orderings (Ours)	**0.759**
WMH Dataset	
AE (Dense) (Baur et al., 2020a)	0.073
AE (Spatial) (Baur et al., 2020a)	0.150
VAE (Dense) (Baur et al., 2020a)	0.068
VQ-VAE (van den Oord et al., 2017)	0.100
VQ-VAE + Transformer + Masked Residuals + Different Orderings (Ours)	**0.429**

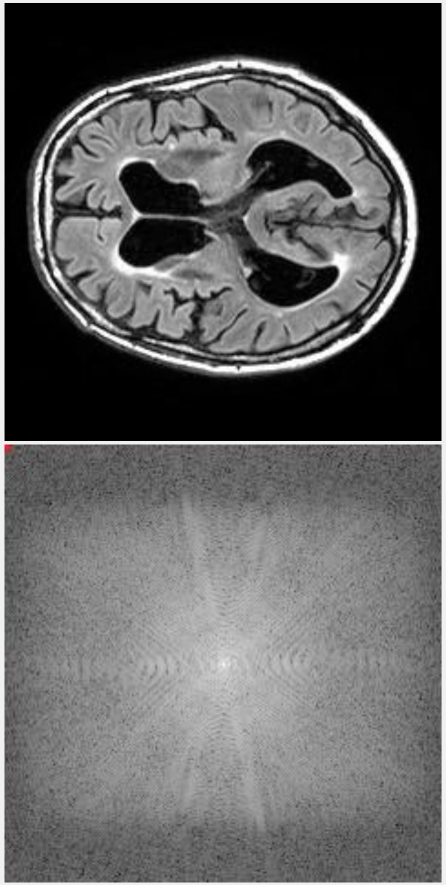
Problem: What to do when data has artifacts?

- Artefacted data is common
- Problematic data is normally not labelled
- Deep learning systems are bad at extrapolating
- Realistic augmentation can improve ability to deal with artefacts

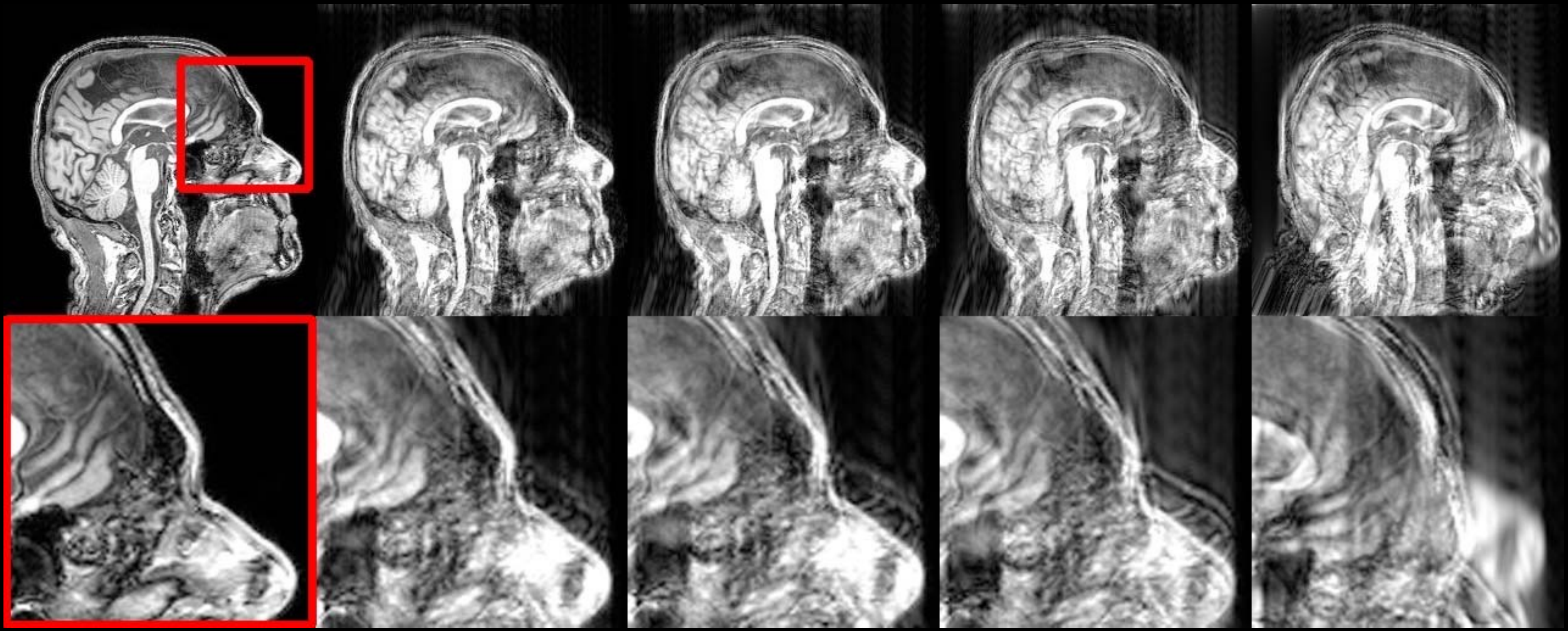


Movement model

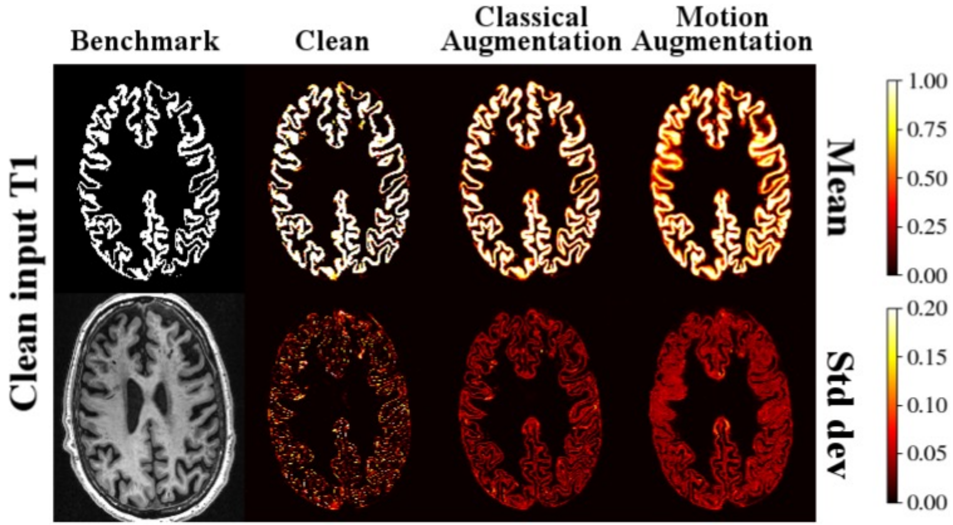


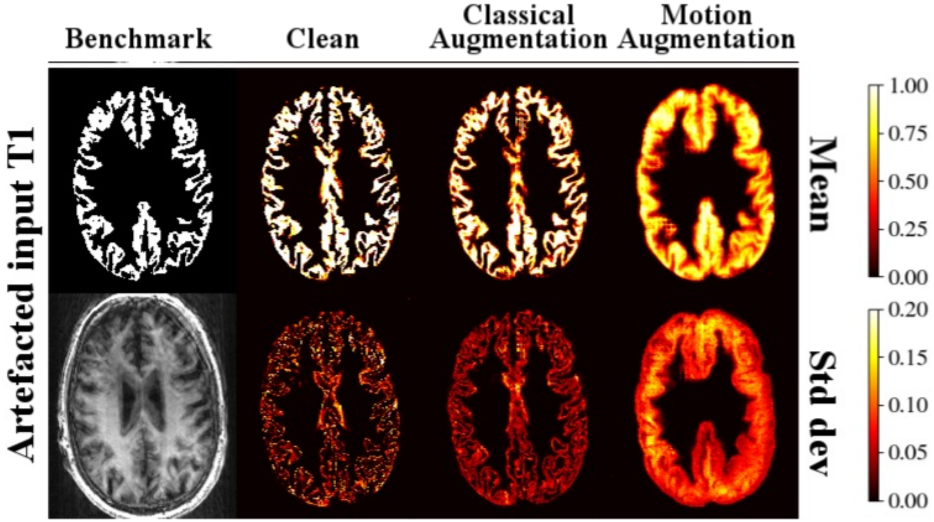


Simulated artefacts

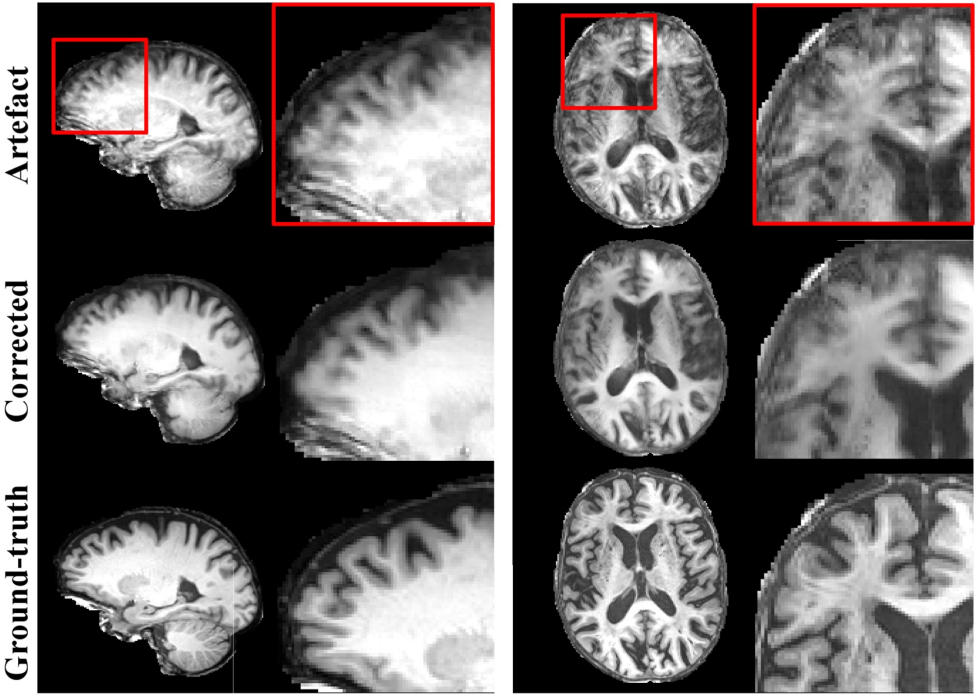


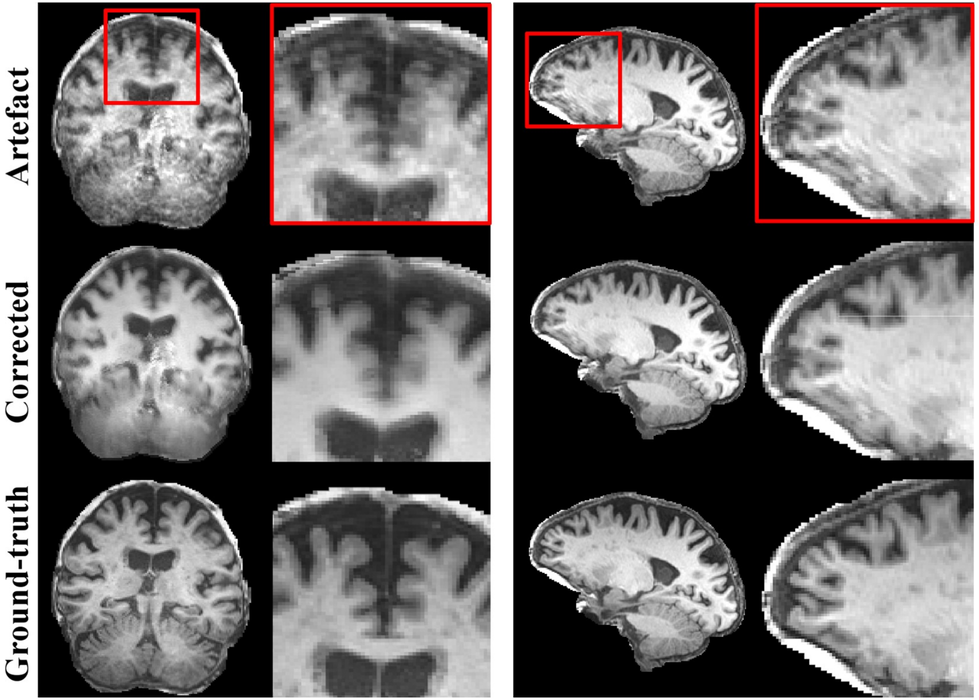
Robustness to artefacts





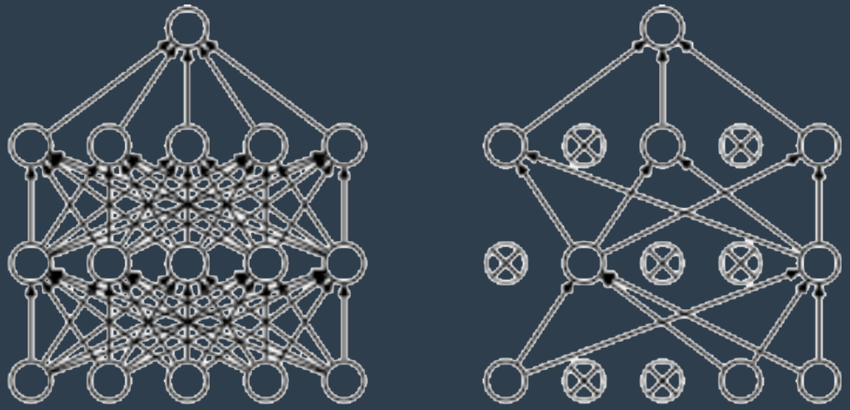
Removal of artefacts





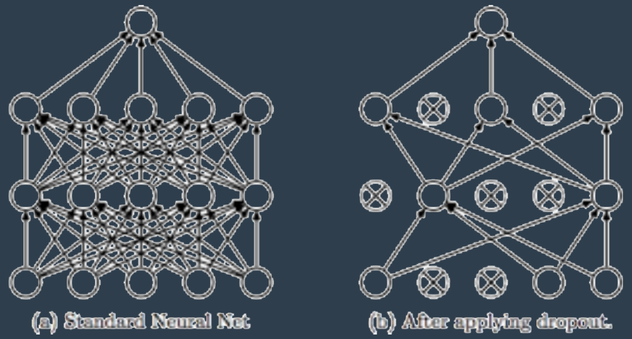
Problem: Can you trust your results?

- Solution: Don’t make one prediction, but predict a distribution
- Sampling sub-models of a network approximates the Epistemic uncertainty
- Dropout during inference can be used to sample from these sub-models and approximate the uncertainty

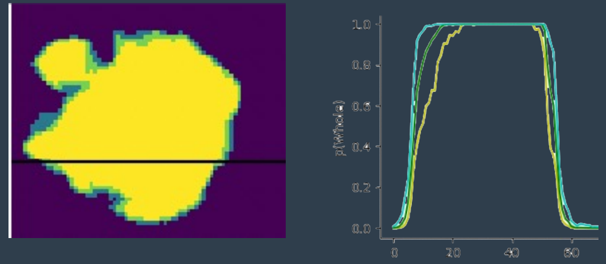


(a) Standard Neural Net (b) After applying dropout.

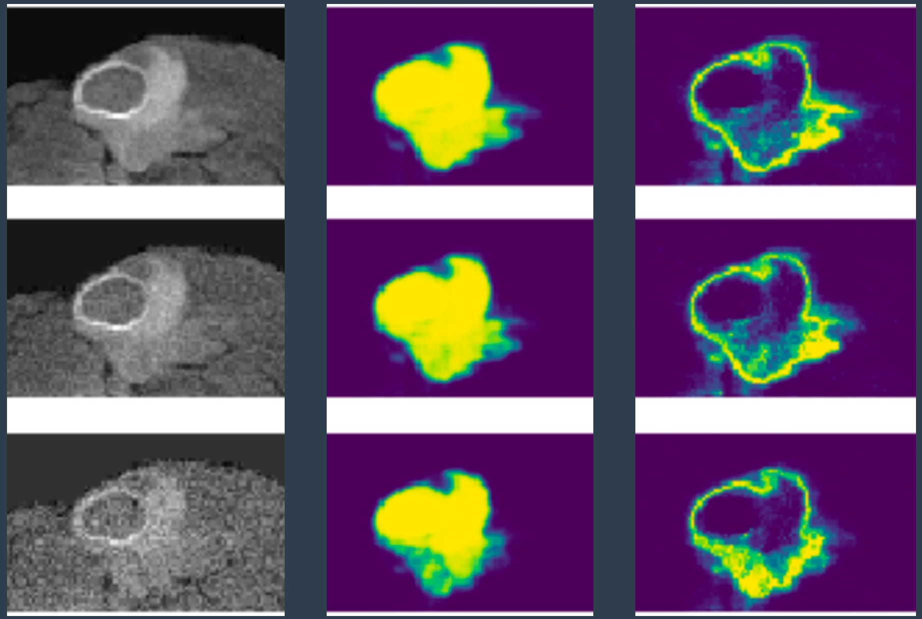
Uncertainty – Behaviour in the presence of noise



Distribution over contours

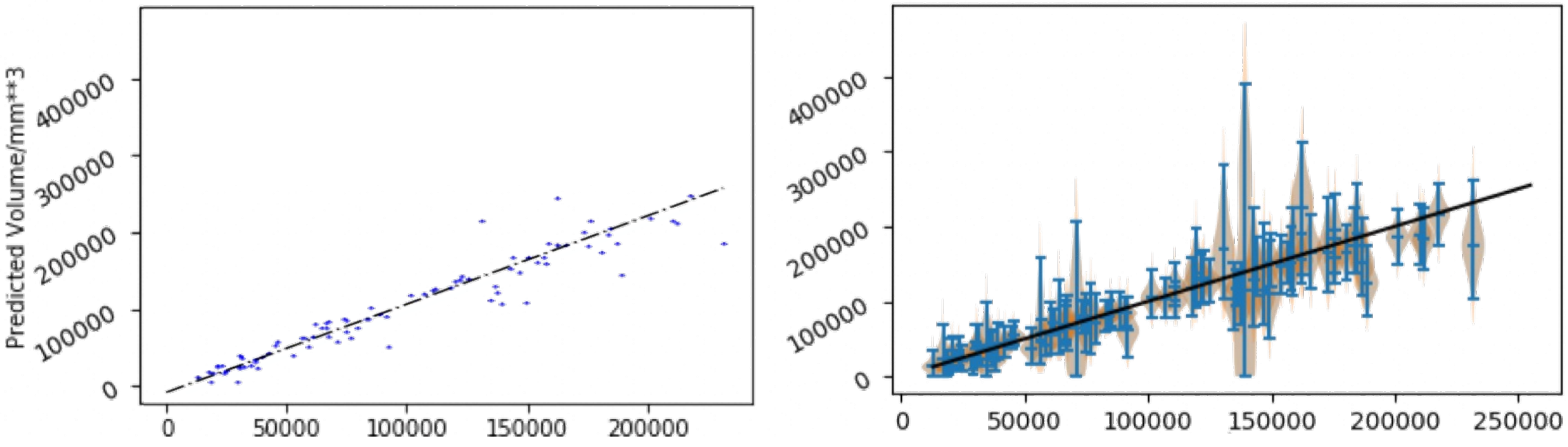


Relationship between uncertainty and image noise



Uncertainty – Safe Biomarkers

Calibrated whole tumour volume prediction uncertainty

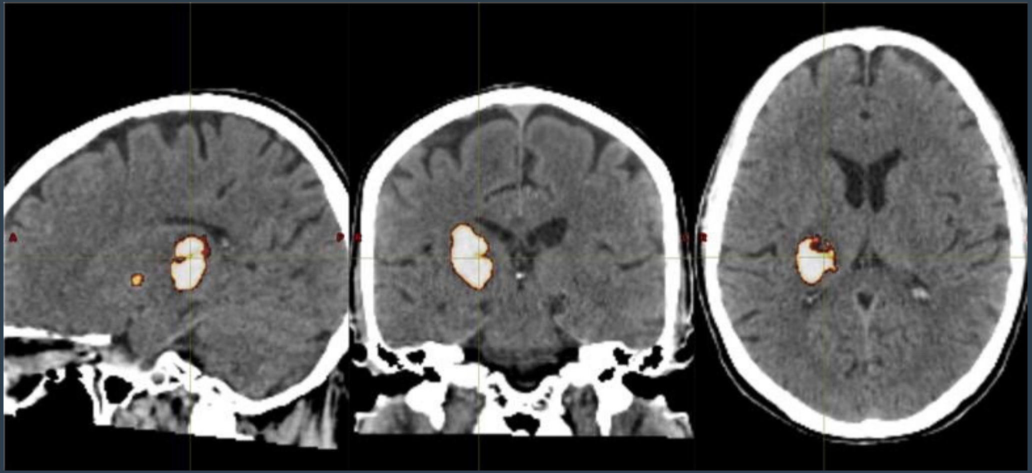


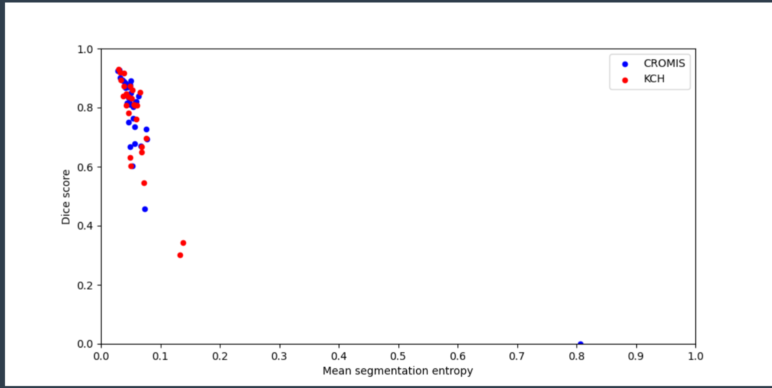
Uncertainty – Ensemble-based

- Can we combine task-specific uncertainty with OOD detection to provide a comprehensive, clinically useful measure of our ML model's uncertainty?
- Can calculate the per-voxel entropy for an ensemble of models, i=1…N

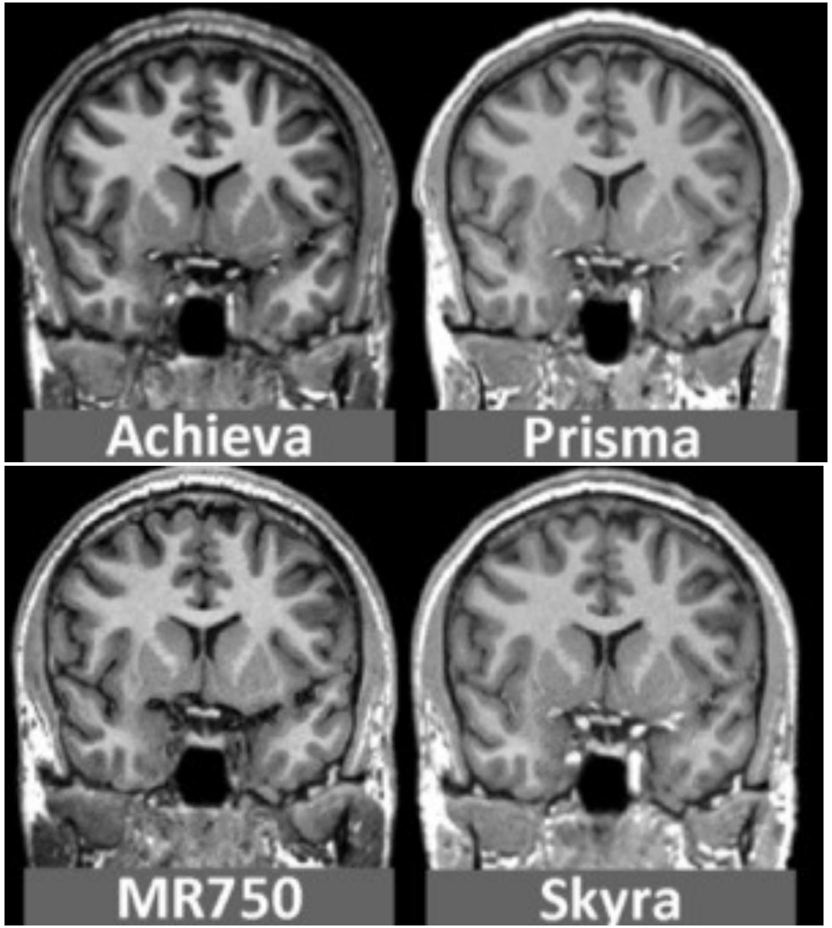
$$U_s(\mathbf{x}) = -\sum_{i=1}^{N} p_s^i(\mathbf{x}) \log(p_s^i(\mathbf{x})).$$

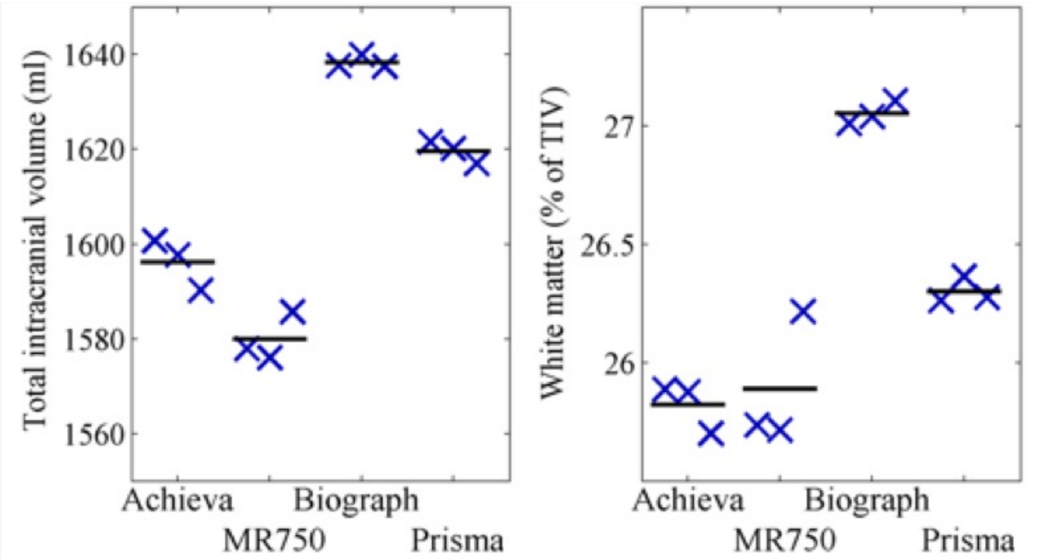
- Averaging this quantity over the structure of interest gives a structure-specific uncertainty metric



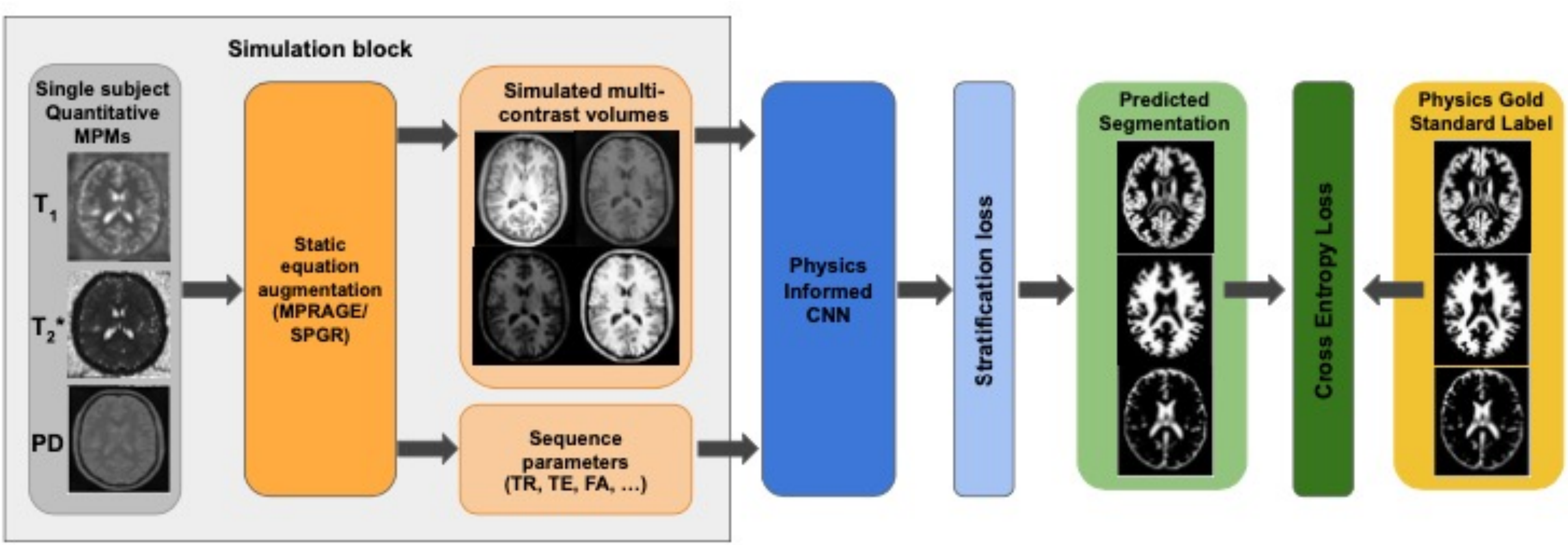


Problem: Different acquisitions → Different results

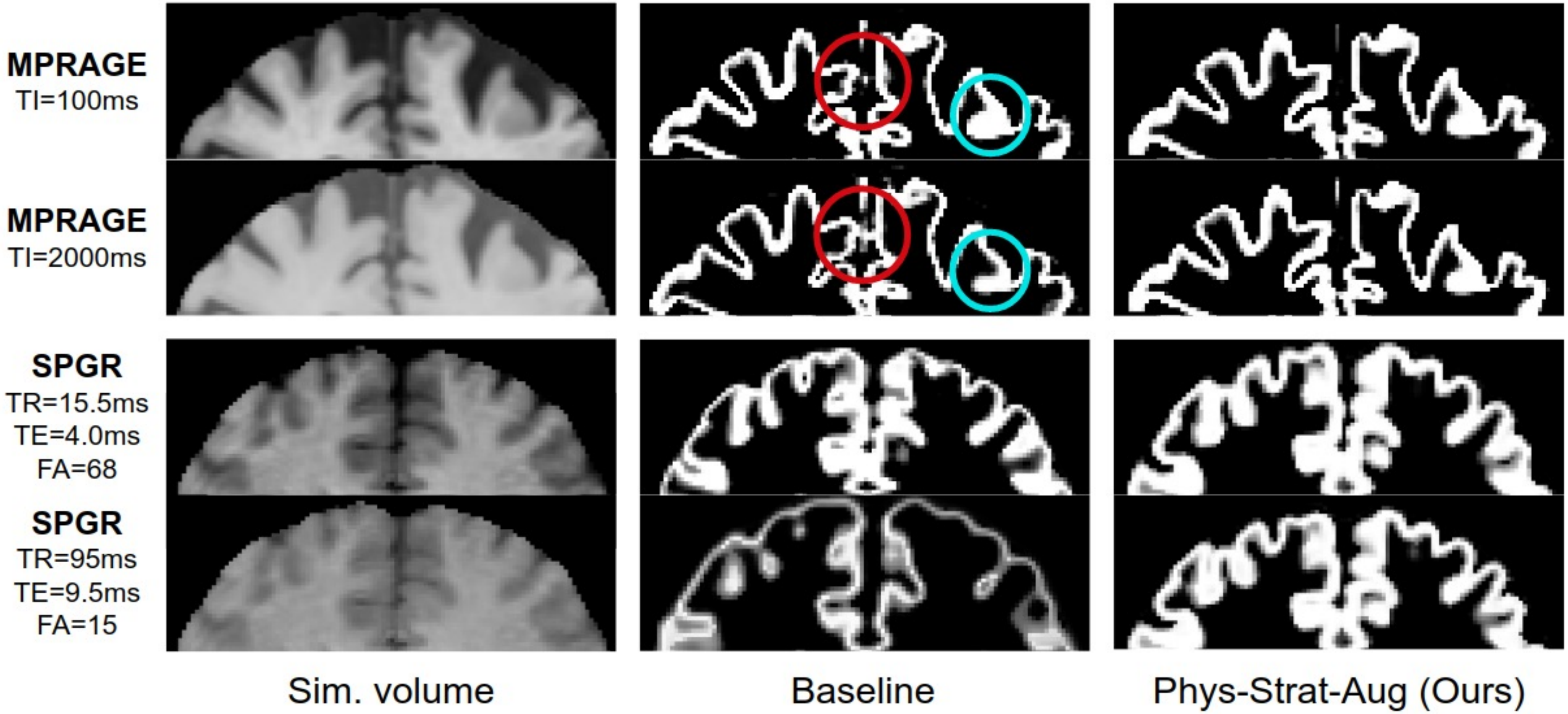




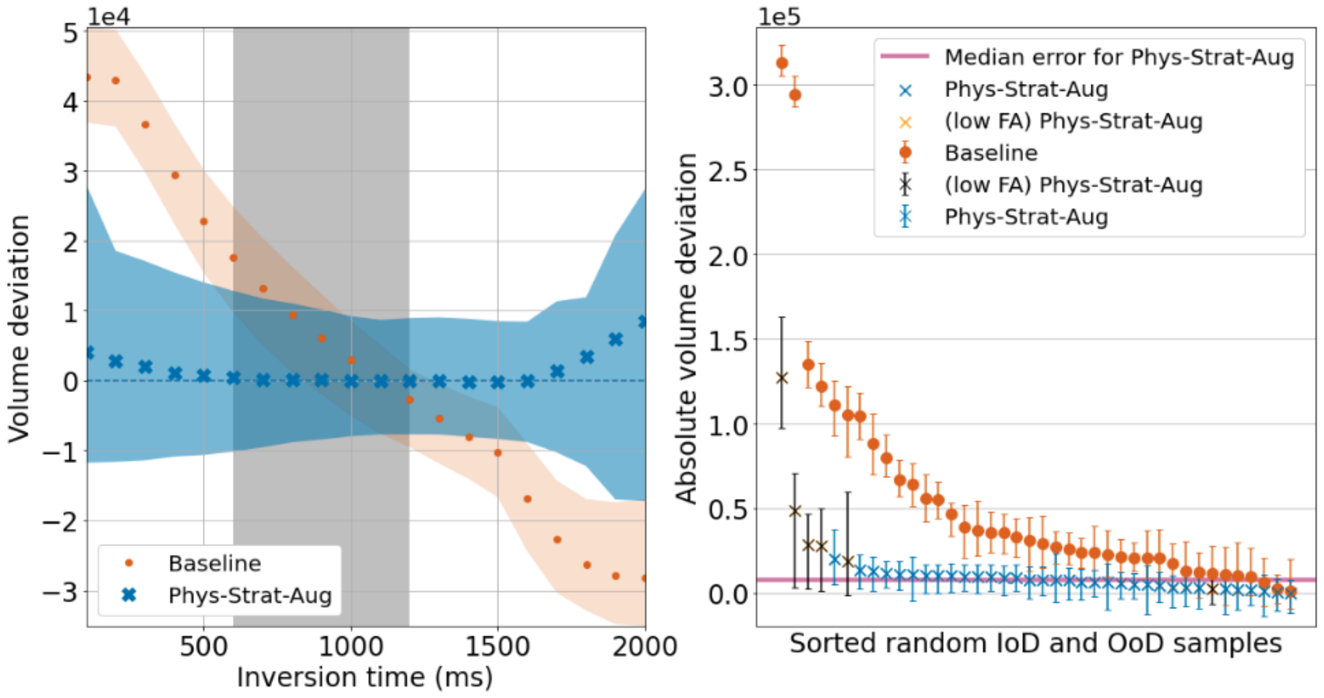
Physics Invariance



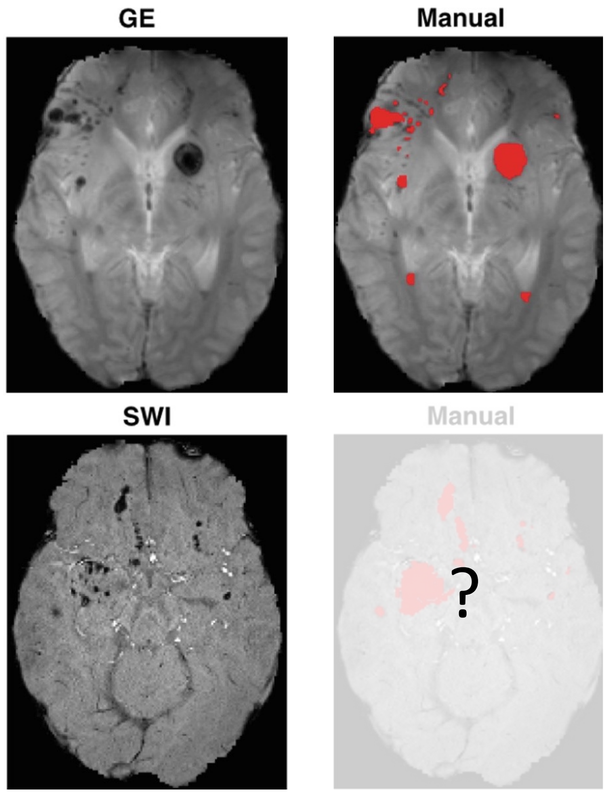
Physics Invariance

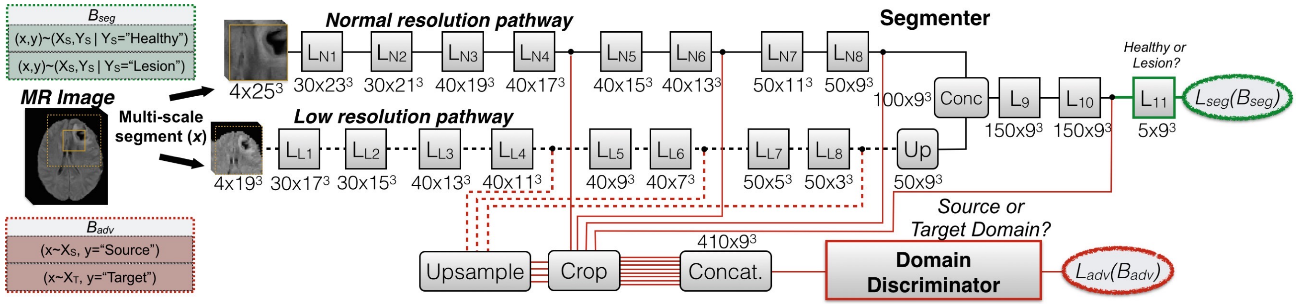


Physics Invariance

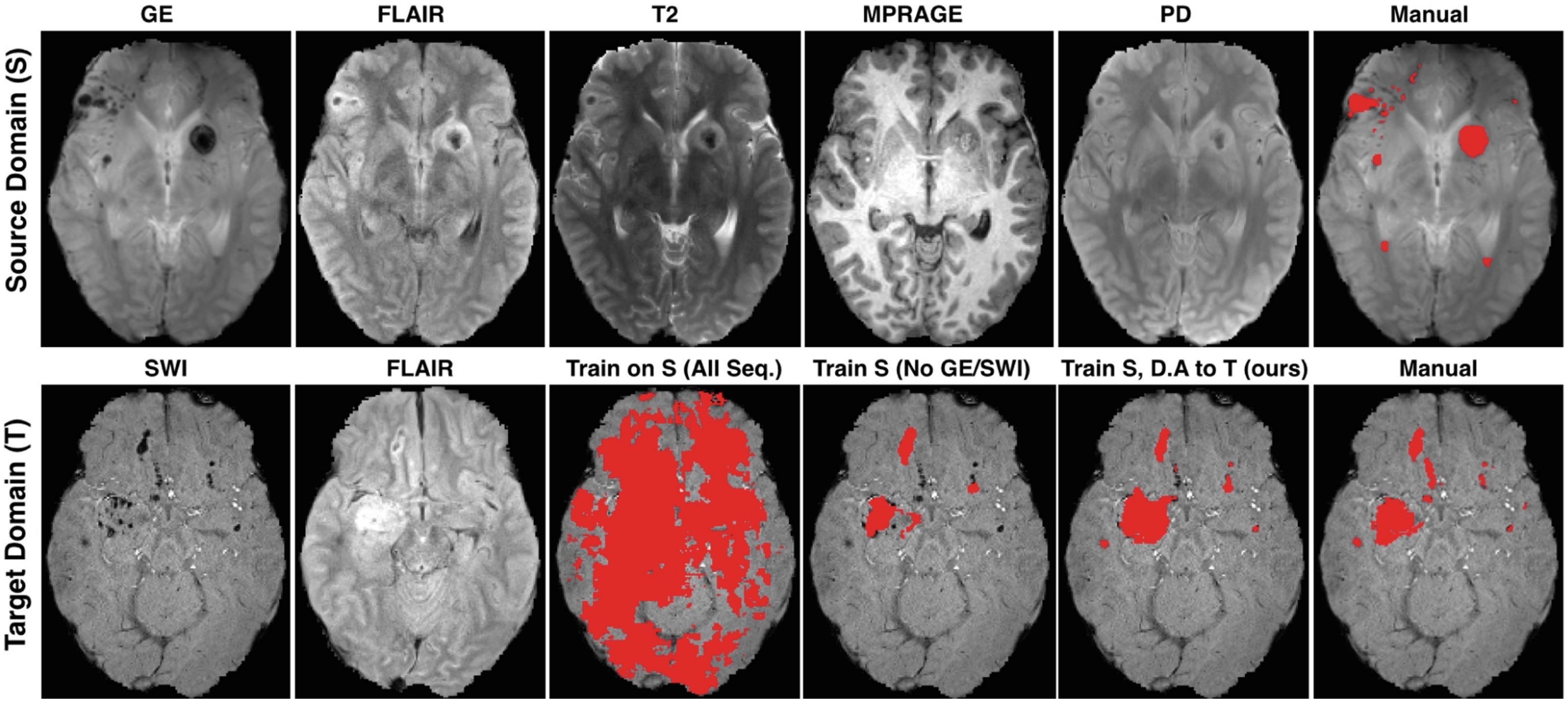


Problem: How to bridge large domain gaps?





Domain Adaptation GE->SWI



Problem:
How to learn from missing and unlabelled images?

AI CENTRE for Value Based Healthcare

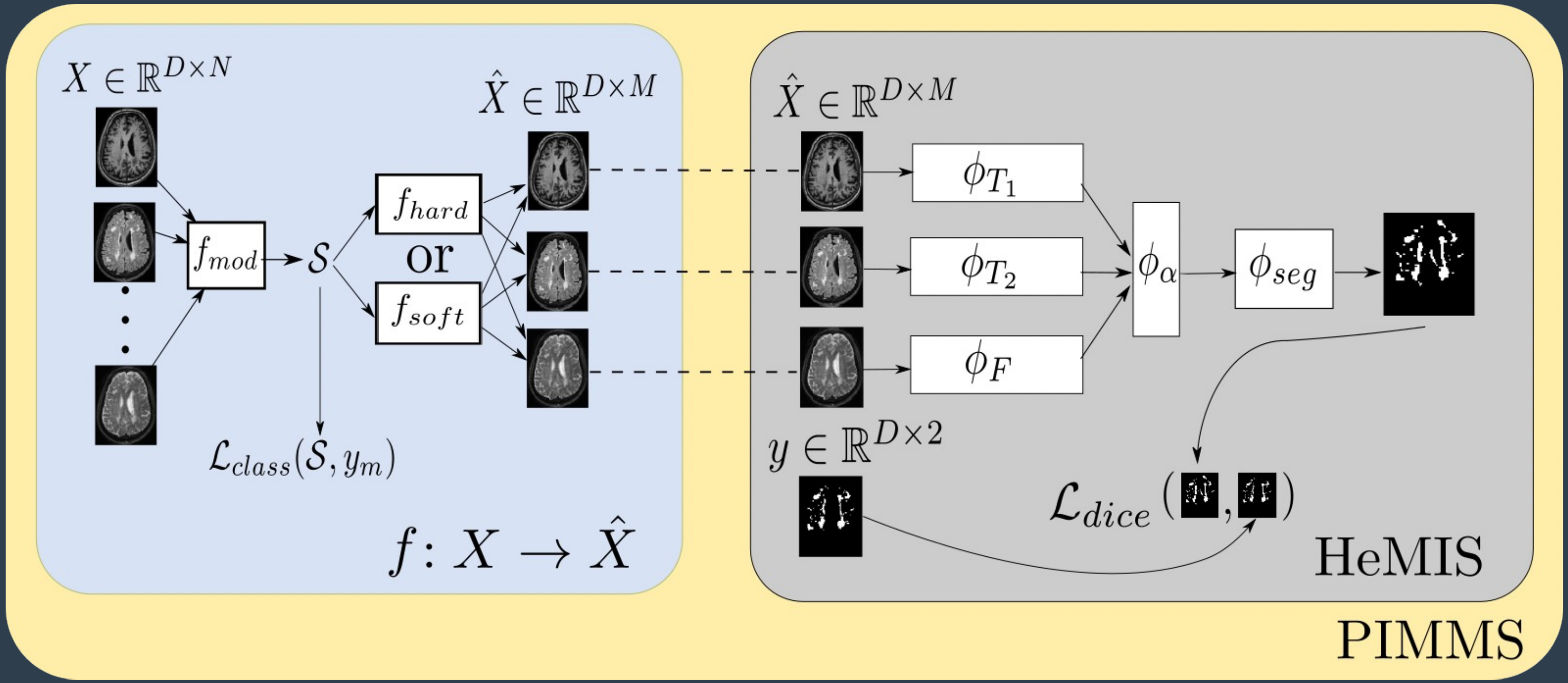
AMIGO Artificial Medical Intelligence Group

- Almost every patient has a unique set of sequences/parameters
- Humans can do their task with what they are given (and know when they likely can't)
- Algorithms should do too…

- MRI sequences are not standardized (no DICOM tag)
- When radiologists receive images from a MRI session, they don't know which image is which
- This does not affect humans, but does affect algorithms

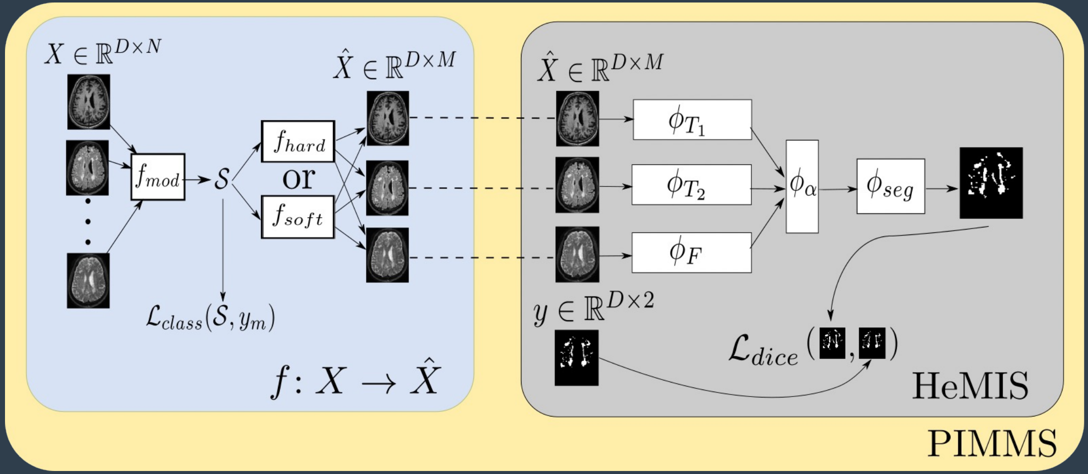
Problem:
How to learn from missing and unlabelled images?

- Solution: Make algorithms invariant to permutation and missing data



Permutation Invariant Segmentation

- Solution: Make algorithms invariant to permutation and missing data



Modalities			Mixed Holdout							
			Dice Score				Avg. Symmetric Distance			
T_1	T_2	F	HeMIS	Soft	Hard	Online	HeMIS	Soft	Hard	Online
●	●	●	0.47	**0.51**	0.48	**0.54**	0.71	0.65	0.71	1.9
●	●	○	0.3	**0.39**	0.3	0.24	2.32	**1.92**	2.36	4.21
○	●	●	0.26	**0.32**	**0.26**	**0.4**	0.77	0.82	0.76	3.32
●	○	●	0.44	**0.45**	**0.45**	**0.52**	0.61	0.63	0.62	2.06
●	○	○	0.1	**0.1**	0.1	**0.19**	3.42	3.76	3.51	4.48
○	●	○	0.08	**0.08**	0.07	**0.09**	4.07	4.13	4.53	7.48
○	○	●	0.16	**0.18**	**0.16**	**0.41**	0.56	0.61	**0.54**	3.31

Modalities			Dice Score				Avg. Symmetric Distance			
T_1	T_2	F	HeMIS	Soft	Hard	Online	HeMIS	Soft	Hard	Online
Silver Protocol Holdout										
●	○	●	0.48	0.46	0.46	0.44	0.68	0.72	1.12	3.52
●	○	○	0.11	0.11	0.08	**0.21**	0.79	0.79	1.63	5.17
○	○	●	0.25	0.16	0.24	**0.5**	0.69	**0.68**	0.8	2.77
Gold Protocol Holdout										
●	○	●	0.59	0.64	0.62	0.61	0.76	**0.57**	0.72	1.18
●	○	○	0.41	0.35	0.42	**0.47**	0.8	**0.44**	**0.77**	2.18
○	○	●	0.38	0.38	0.26	**0.45**	1.01	1.75	20.75	3.63

What have we discussed so far?

- Unsupervised learning of text allows the detection of normal vs abnormal
- Unsupervised learning of images allows the localization of abnormalities
- Corrupting data realistically (e.g. artefacts) increases robustness to these problems
- Uncertainty is a way to get around information limits and convey risk-calibrated predictions
- Models can be made robust to missing and unlabeled data

- We did not discuss
  - “Is it the right body part?”
  - “Is it in the field of view?”
  - “Does it have sufficient quality?”

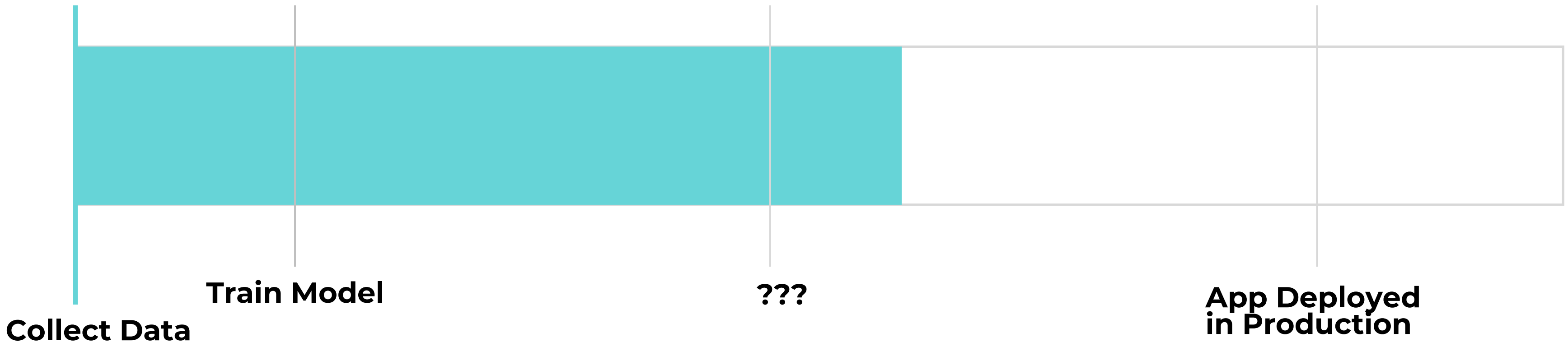
How to we reach patients?

Why is it hard?

More than 87% of data science projects never make it to production.

Selecting the right DICOM datasets
Loading DICOM Datasets
Pre / Post processing Input Images
Performing Inference
Exporting AI results to DICOM

Visualizing inference results
Performance Optimization
Resource Utilization
Monitoring

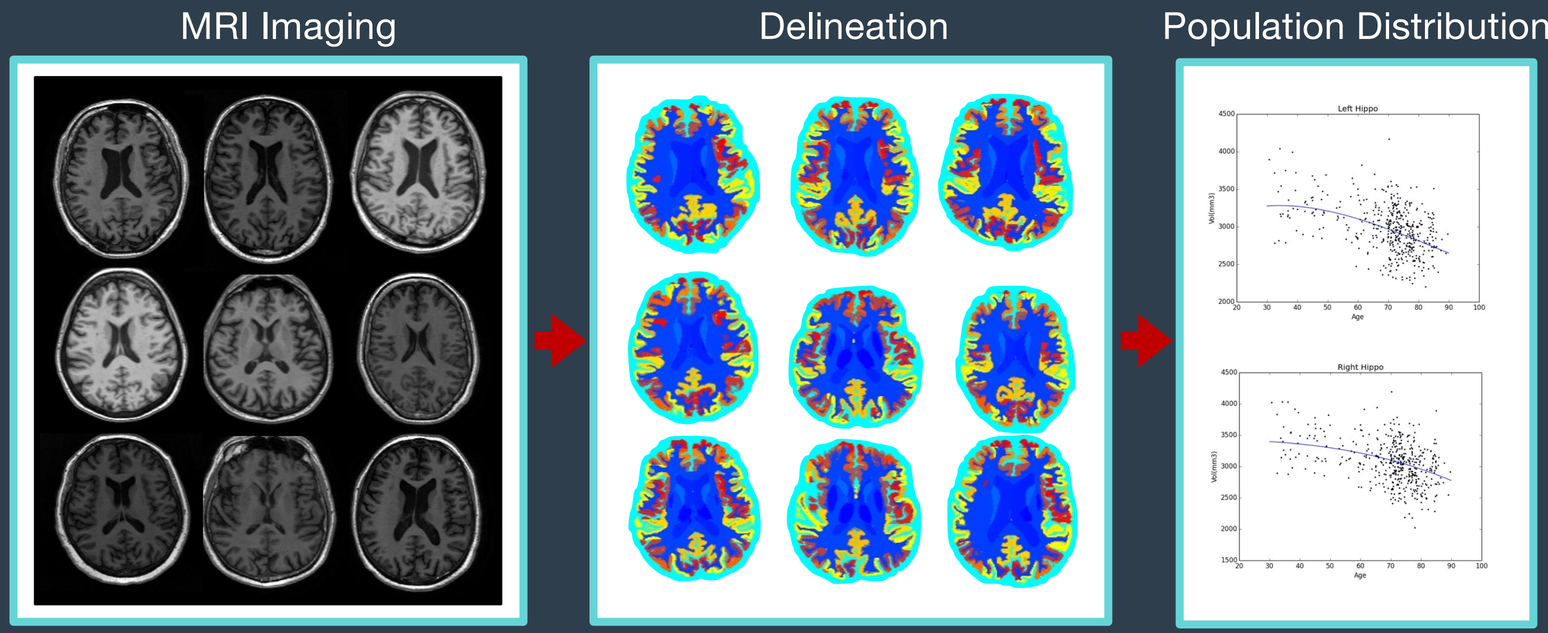


Detecting atrophy in the train

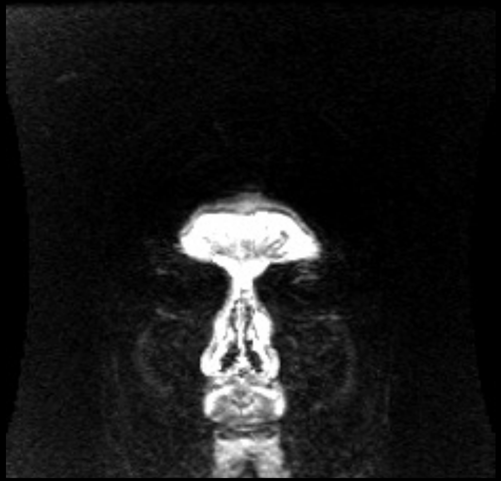
AI CENTRE for Value Based Healthcare

AMIGO Artificial Medical Intelligence Group

- Atrophy is a deviation from normality (volume wise)
- Select radiologically normal subjects – ~40k
- Estimate regional statistics per age, sex, etc



Detecting atrophy in the train

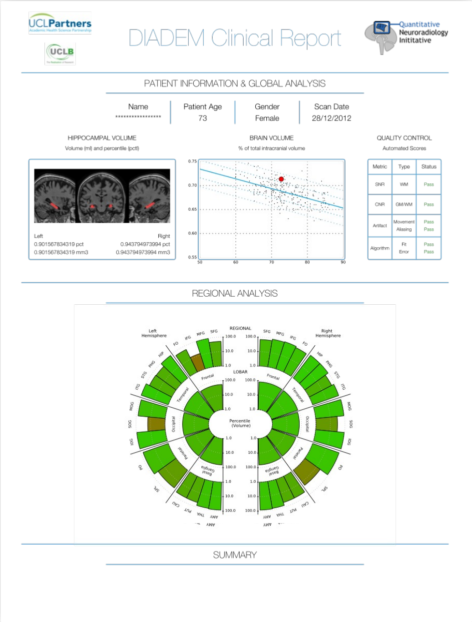


Healthy

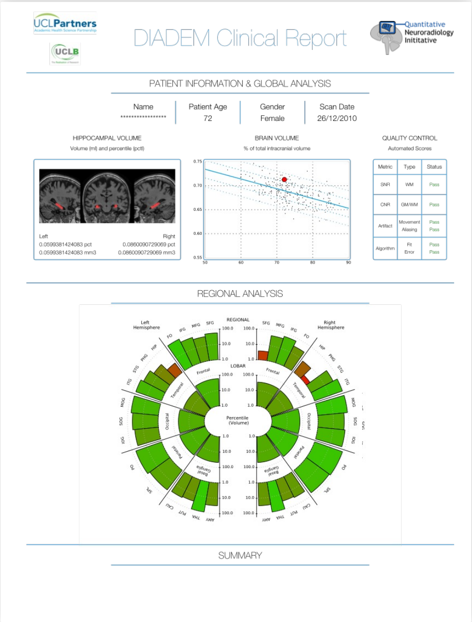
Early Alzheimer's Disease

Alzheimer's Disease

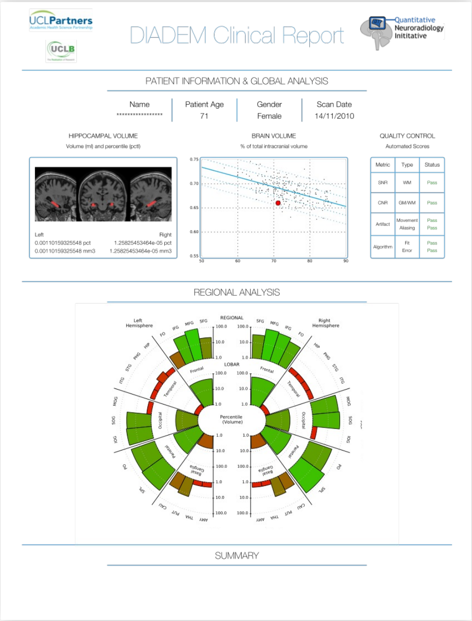
Detecting atrophy in the train



Healthy

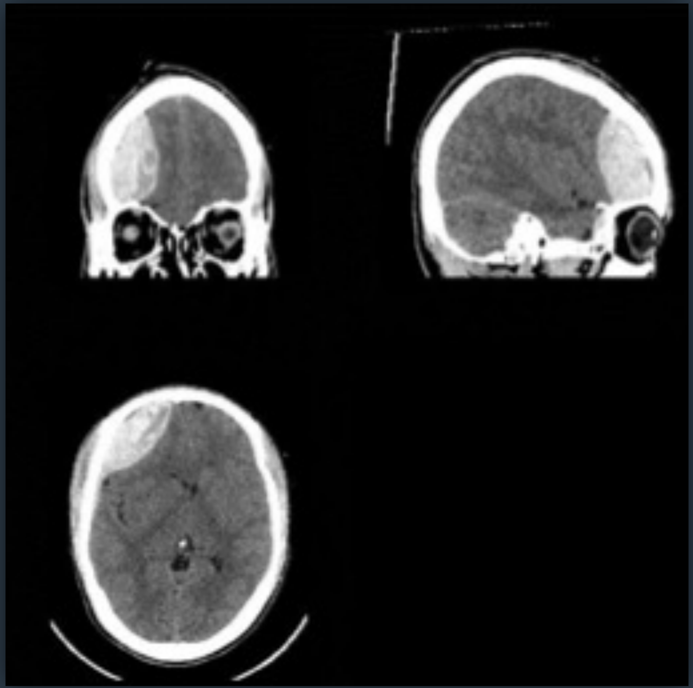


Early Alzheimer's Disease



Alzheimer's Disease

What will happen after a stroke?



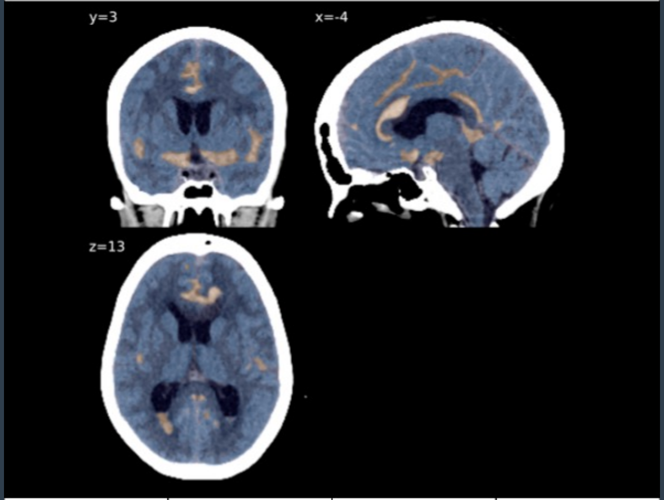
Receive Image → Is image in distribution? → Aling to standard space → Segment Lesion → Phenotype → Report

What will happen after a stroke?

Name: William Theiss
DOB: 16/11/1963
Hospital No.:
NHS No.: 2919427148

Exam date: 24/12/2003
Exam time: 09:04:45
Sequence: PLAIN THIN
Instrument: DISCOVERY MR750

Requestor: Nicole Mackie
Role:
Department: MRI Dept
Location: KCH Clinical Research



Global lesion parameters

Centre of mass: -4, 3, 14
Volume: 49.8±11.5 ml (50th)

Tissue distribution	*%*	*Cent*
Grey	38±12	38th
White	4±1	4th
CSF	56±10	56th

Global tissue parameters

Compartment	*ml*	*Cent*
Grey	500	100th
White	372	100th
CSF	204	100th
Bone	408	100th
Soft tissue	977	100th
Cranium	1084	100th

Focal grey involvement

Compartment	*Lat*	*% hit*	*Cent*
Anterior Cingulate Cortex	L	38±7	38th
Rolandic Operculum	L	32±14	32nd
Anterior Cingulate Cortex	R	32±8	32nd
Middle Cingulate Cortex	L	31±6	31st
Middle Cingulate Cortex	R	27±5	27th
Caudate	L	25±1	25th
Insula	R	20±5	20th
Superior Temporal Pole	L	20±2	20th
Supplementary Motor Area	L	17±7	17th
Supplementary Motor Area	R	15±5	15th
Calcarine Cortex	R	12±3	12th
Superior Temporal Gyrus	L	12±1	12th
Insula	L	11±2	11th
Medial Frontal Gyrus Superior	L	9±4	9th

Focal white involvement

Compartment	*Lat*	*% hit*	*Cent*
Cingulum Posterior	L	19±7	19th
Cingulum Anterior	L	13±3	13th
Cingulum Anterior	R	12±2	12th
Optic Radiations	L	9±2	9th
Superior Londgitudinal Fasciculus I	L	5±1	5th
Superior Londgitudinal Fasciculus III	L	5±2	5th
Corpus Callosum	-	4±1	4th
Anterior Thalamic Projections	L	3±0	3rd
Inferior Longitudinal Fasciculus	L	2±1	2nd

Focal CSF involvement

Compartment	*Lat*	*% hit*	*Cent*
Lateral Ventricle Superior	L	20±1	20th

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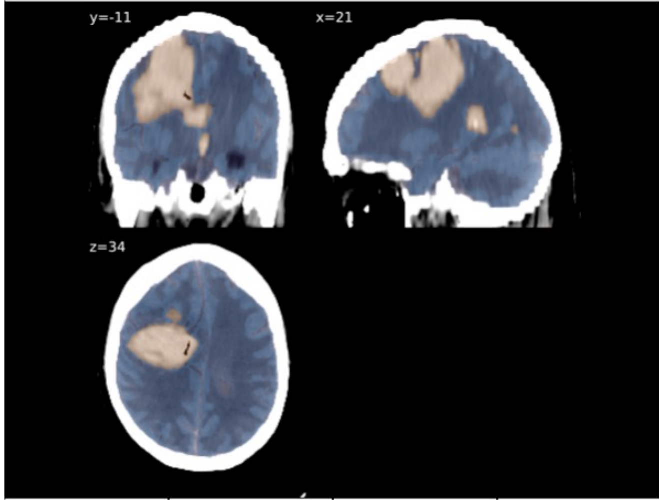
Name: Melissa White
DOB: 20/04/1950
Hospital No.:
NHS No.: 5316440595

Exam date: 22/12/2009
Exam time: 08:57:41
Sequence: 2.5/5mm
Instrument: DISCOVERY MR750

Requestor: Inger Monge
Role:
Department: MRI Dept
Location: KCH Clinical Research



Global lesion parameters

Centre of mass: 21, -11, 34
Volume: 130.4±10.2 ml (100th)

Tissue distribution	*%*	*Cent*
Grey	26±4	26th
White	9±1	9th
CSF	58±3	58th

Global tissue parameters

Compartment	*ml*	*Cent*
Grey	623	100th
White	490	100th
CSF	291	100th
Bone	577	100th
Soft tissue	1606	100th
Cranium	1411	100th

Focal grey involvement

Compartment	*Lat*	*% hit*	*Cent*
Supplementary Motor Area	R	78±2	78th
Paracentral Lobule	R	61±1	61st
Precentral Gyrus	R	47±1	47th
Middle Cingulate Cortex	R	39±0	39th
Superior Frontal Gyrus	R	37±2	37th
Rolandic Operculum	R	26±1	26th
Inferior Frontal Gyrus Pars Operularis	R	21±1	21st
Supplementary Motor Area	L	20±1	20th
Insula	R	20±2	20th
Cerebelum 9	R	19±1	19th
Hippocampus	R	18±3	18th
Thalamus	L	17±1	17th
Cerebelum 9	L	17±2	17th
Calcarine Cortex	L	15±2	15th
Middle Cingulate Cortex	L	14±0	14th
Paracentral Lobule	L	14±0	14th
Postcentral Gyrus	R	13±2	13th
Middle Frontal Gyrus	R	12±0	12th
Medial Frontal Gyrus Superior	R	10±1	10th
Lingual Gyrus	L	9±4	9th

Focal white involvement

Compartment	*Lat*	*% hit*	*Cent*
Superior Londgitudinal Fasciculus I	R	37±0	37th
Cortico Spinal Tract	R	36±1	36th
Fornix	-	24±2	24th
Superior Londgitudinal Fasciculus II	R	22±1	22nd
Anterior Thalamic Projections	R	21±1	21st
Optic Radiations	L	18±3	18th
Corpus Callosum	-	12±1	12th
Superior Londgitudinal Fasciculus III	R	9±0	9th
Inferior Longitudinal Fasciculus	L	6±2	6th
Cingulum Anterior	R	5±0	5th
Anterior Thalamic Projections	L	4±0	4th
Inferior Fronto Occipital Fasciculus	L	4±1	4th
Cortico Spinal Tract	L	2±0	2nd
Inferior Fronto Occipital Fasciculus	R	2±0	2nd
Inferior Longitudinal Fasciculus	R	2±0	2nd

Focal CSF involvement

Compartment	*Lat*	*% hit*	*Cent*
4th Ventricle	-	83±2	83rd
3rd Ventricle	-	76±2	76th
Lateral Ventricle Superior	R	67±1	67th
Lateral Ventricle Superior	L	42±9	42nd

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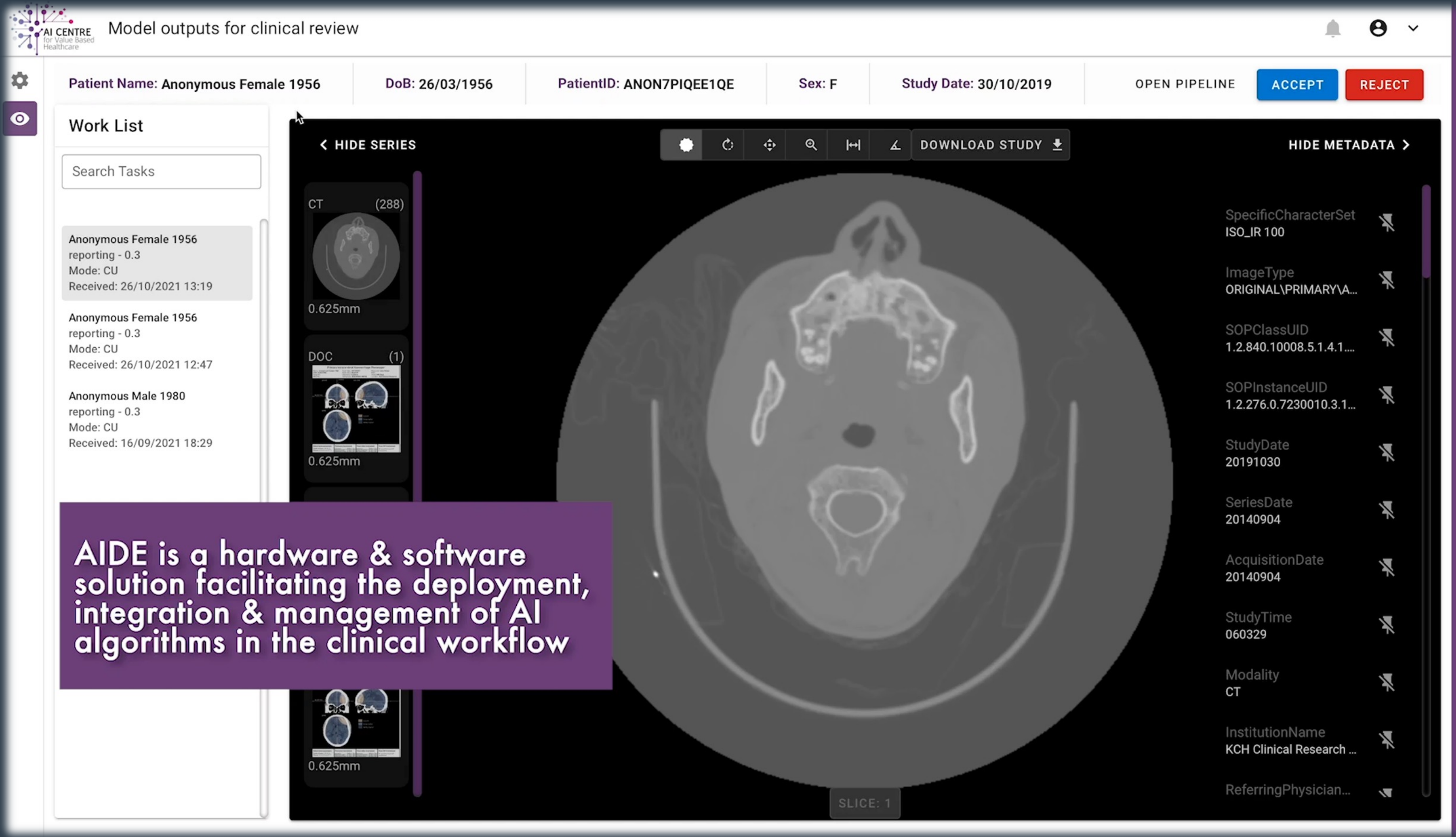
Let's see it in action...



AIDE is a hardware & software solution facilitating the deployment, integration & management of AI algorithms in the clinical workflow

Conclusions – Part 3

- Real world data is hard, and what can go wrong will go wrong
- We (rarely) can change how data is collected
- Many techniques are needed to handle the mess and make AI safe in clinical care
- Solving real world problems are be very rewarding
- AI in neurology/neuroimaging is now a reality

KING'S College LONDON

AI CENTRE for Value Based Healthcare

AMIGO Artificial Medical Intelligence Group

THANK YOU!

QUESTIONS?