

**Erasmus MC**

University Medical Center Rotterdam



# **Biomedical Imaging and Genetic (BIG) data analytics for precision medicine**

Wiro Niessen

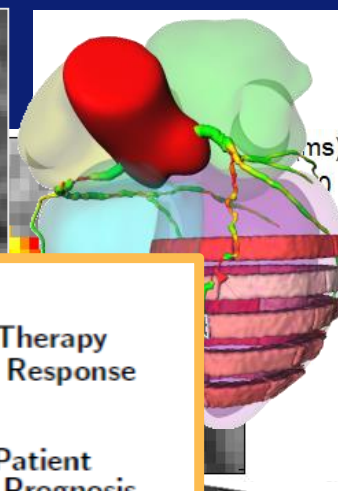
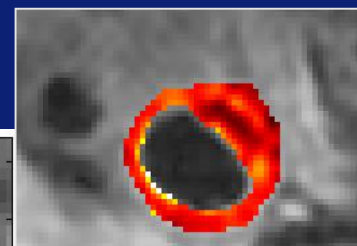
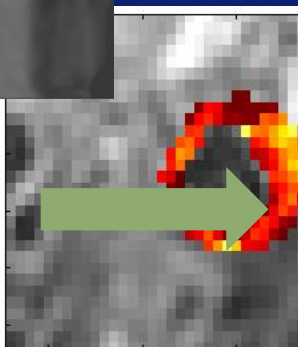
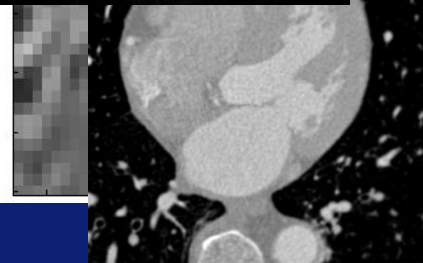
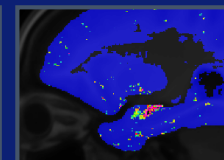
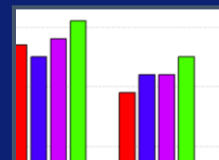
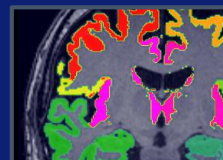
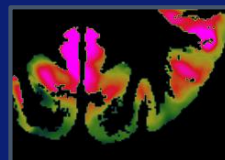
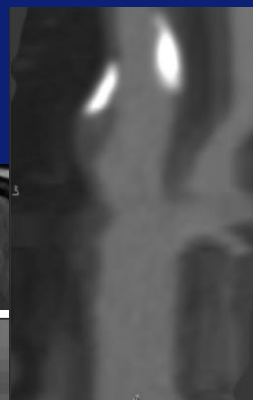
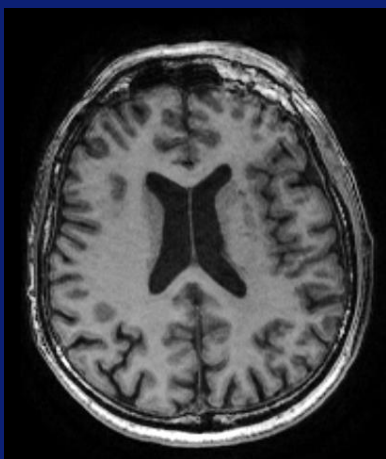
*Radiology & Medical Informatics / Imaging Physics*







*Erasmus MC / TU Delft*

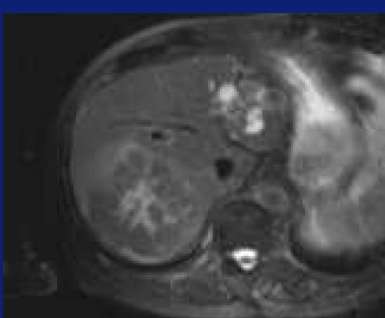
*Quantib (disclosure)*

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	Genetic Mutations		Therapy Response
	Tumor Phenotype		Patient Prognosis
	Dementia Diagnosis		Surgery Success

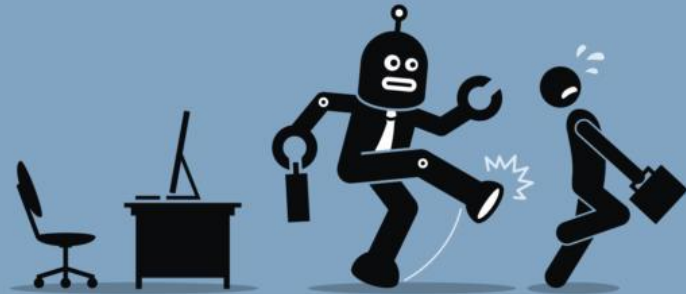


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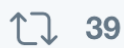
Anything  
you can do,  
AI can do  
better





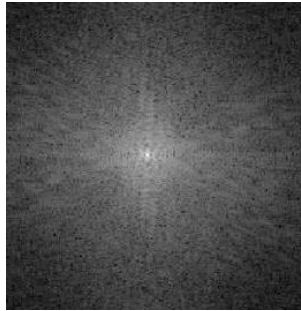
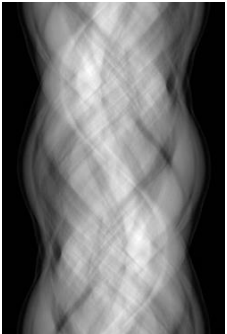
**Olaf Ronneberger** @ORonneberger · Nov 6

As of today the U-net [arxiv.org/abs/1505.04597](https://arxiv.org/abs/1505.04597) is the most-cited paper in the 21 years history of the #miccai conference (3201 citations according to google scholar [scholar.google.co.uk/scholar?hl=en&...](https://scholar.google.co.uk/scholar?hl=en&...)). It just overtook the Frangi-filter from 1998 ([scholar.google.co.uk/scholar?hl=en&...](https://scholar.google.co.uk/scholar?hl=en&...)).



# End to end approaches?

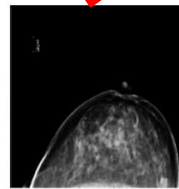
- Raw data



- Image reconstruction and analysis



Brain T1-Weighted MR



Mammogram

## Predictions



Genetic Mutations



Tumor Phenotype



Therapy Response



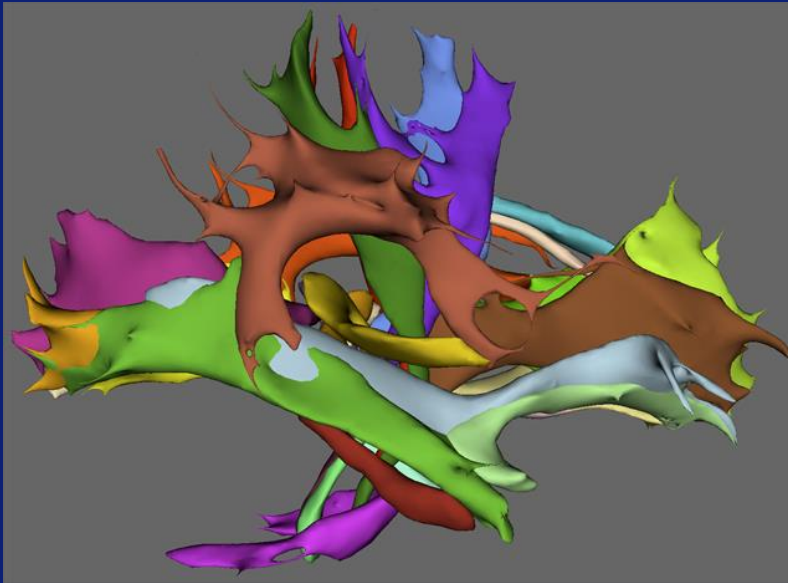
Patient Prognosis



Dementia Diagnosis



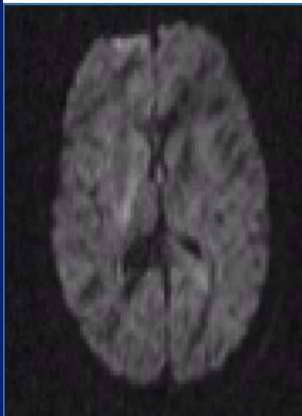
# White matter tract segmentation



Tractography and atlas-based segmentation

Minutes to multiple hours

Diffusion tensor



Reconstruction  
Step 1



Streamlines

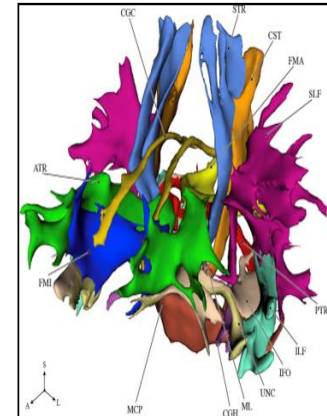


Clustering/Atlas  
Step 2



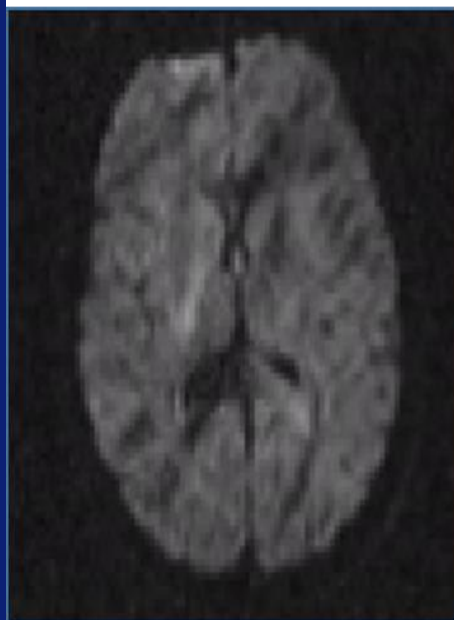
Step 3  
Post-processing

Segmentation

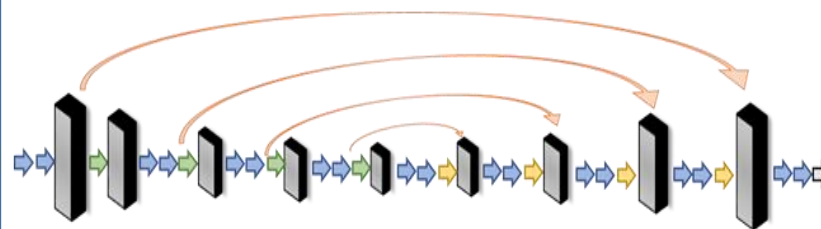


# White matter tract is now segmented in 0.5 sec

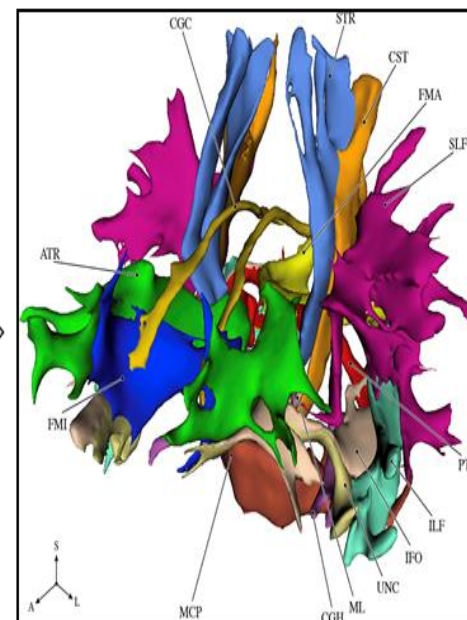
## Diffusion tensor



## Neuro4Neuro



## WM neural tract



Deep learning network trained and evaluated on more than 9.000 dMRI scans

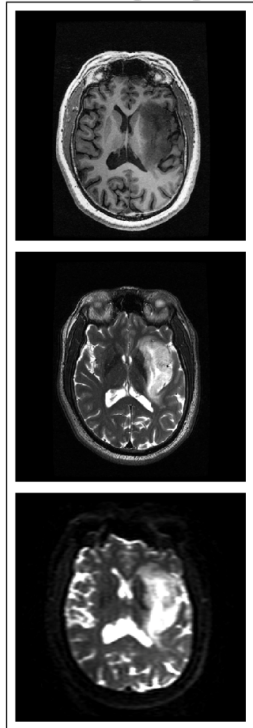
Bo Li, Esther Bron

**Who will be automated?**

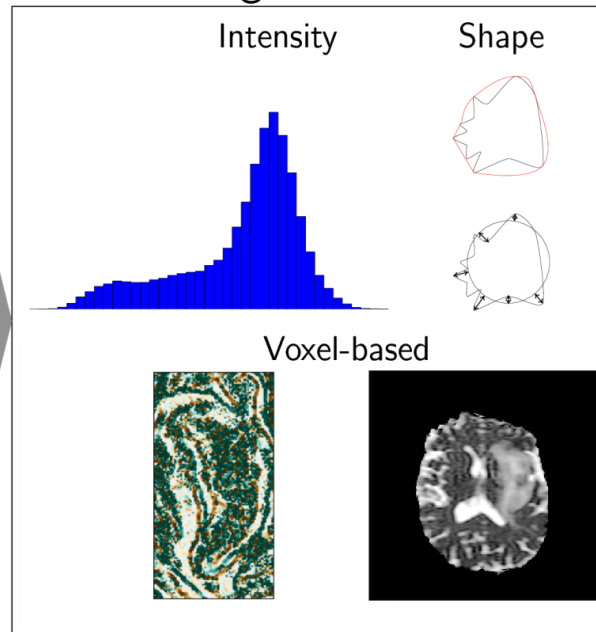


- Radiogenomics: predicting genetic mutation status from non-invasive imaging data

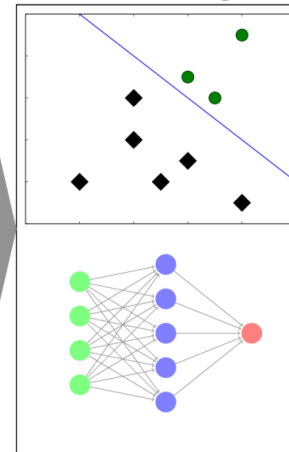
## Multiparametric Imaging



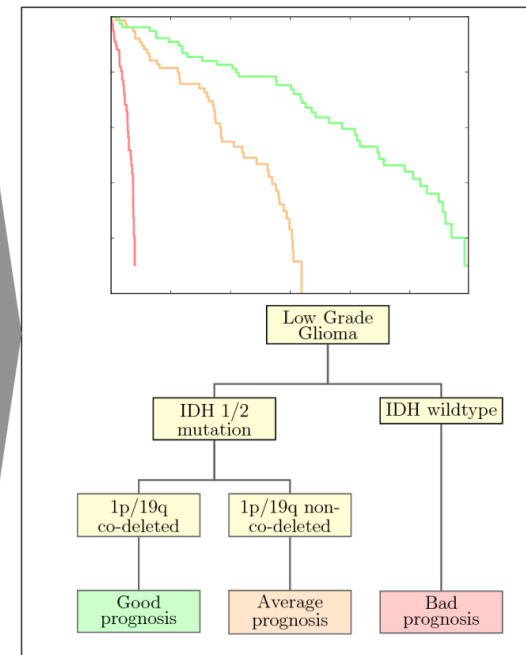
## Image features

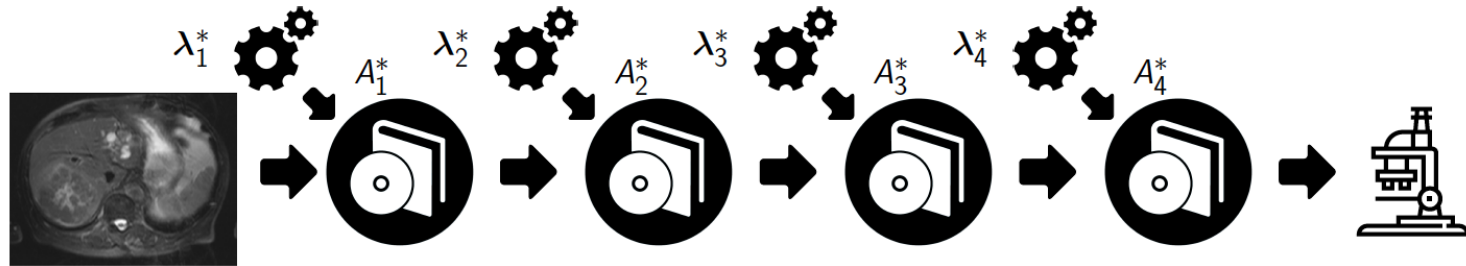


## Machine learning



## Prediction





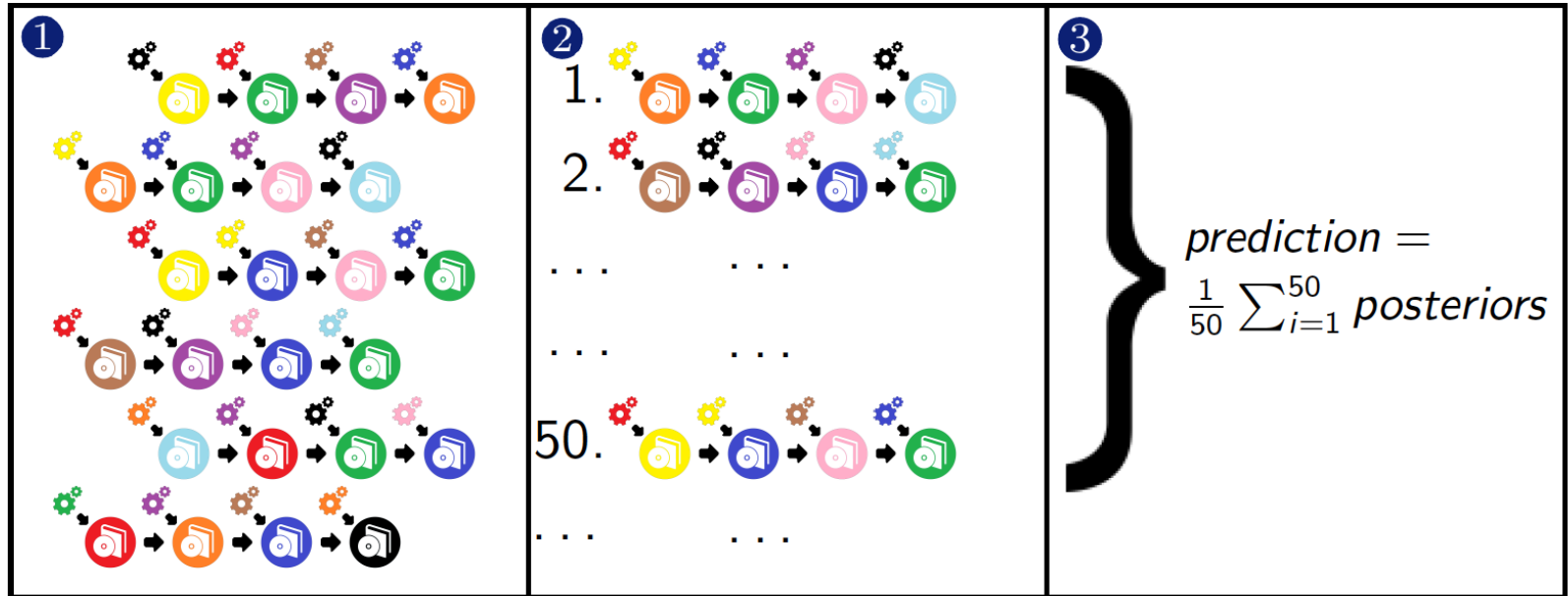
How to find optimal workflow for each application?

- Best algorithm(s)  $A^* \in \{A^{(1)}, \dots, A^{(k)}\}$  for each step?
- Best (hyper)parameters  $\lambda^* \in \{\Delta^{(1)}, \dots, \Delta^{(k)}\}$  for each step?

**Solution:** Combined Algorithm Selection and Hyperparameter optimization problem (CASH).<sup>1</sup>

$$A^*, \lambda^* \in \underset{A^{(j)} \in \mathcal{A}, \lambda \in \Delta^{(j)}}{\operatorname{argmin}} \frac{1}{k} \sum_{i=1}^k \mathcal{L} \left( A_{\lambda}^{(j)}, \mathcal{D}_{\text{train}}^{(i)}, \mathcal{D}_{\text{valid}}^{(i)} \right)$$

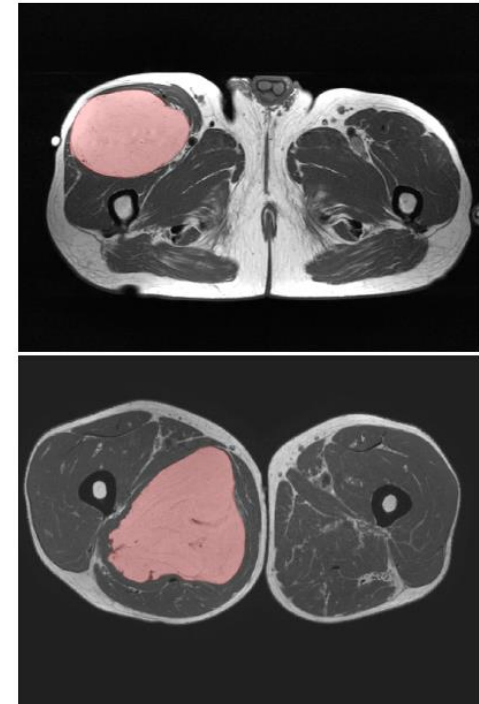
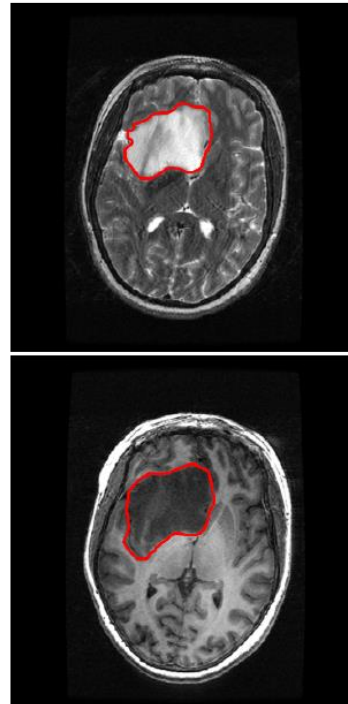
# Automatic radiomic signature optimization



WORC: extension of CASH to radiomics. Solver:

- ① Pseudo-randomly generate 100.000 different radiomics workflows.
- ② Evaluate and rank the workflows.
- ③ Create model from ensemble of top 50 workflows.

# Experiments

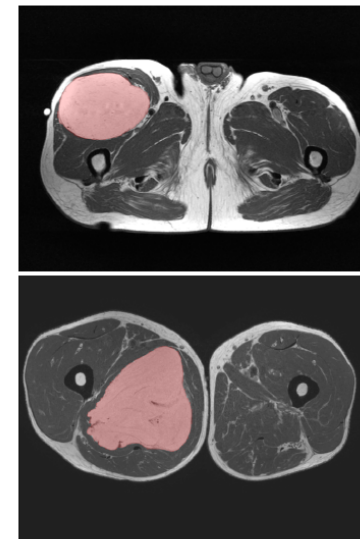
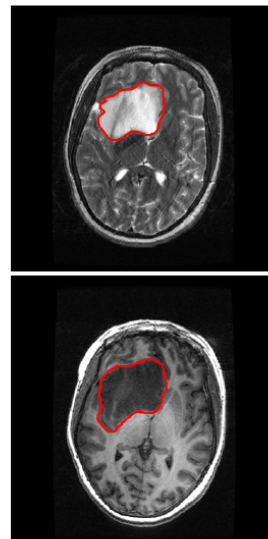
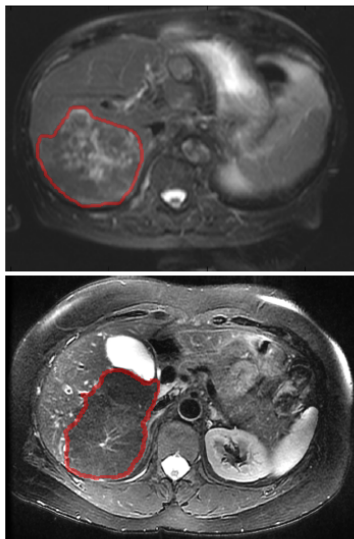


	Liver	Brain	Lipo
Label	Malignant/ Benign	1p19q co-deletion/ no co-deletion	Liposarcoma/ Lipoma
Modality	T2w (FatSat) MR	T2w + T1w MR	T1w MR

# Results

Reported as **mean** [95% confidence interval]

	Liver	Brain	Lipo
AUC	<b>0.93</b> [ 0.86, 0.99 ]	<b>0.80</b> [ 0.74, 0.85 ]	<b>0.84</b> [ 0.74, 0.93 ]
F1-score	<b>0.82</b> [ 0.76; 0.91 ]	<b>0.76</b> [ 0.71, 0.80 ]	<b>0.76</b> [ 0.66, 0.85 ]
Sensitivity	<b>0.74</b> [ 0.58, 0.89 ]	<b>0.67</b> [ 0.58, 0.76 ]	<b>0.73</b> [ 0.59, 0.86 ]
Specificity	<b>0.92</b> [ 0.85, 0.98 ]	<b>0.79</b> [ 0.72, 0.86 ]	<b>0.80</b> [ 0.67, 0.92 ]



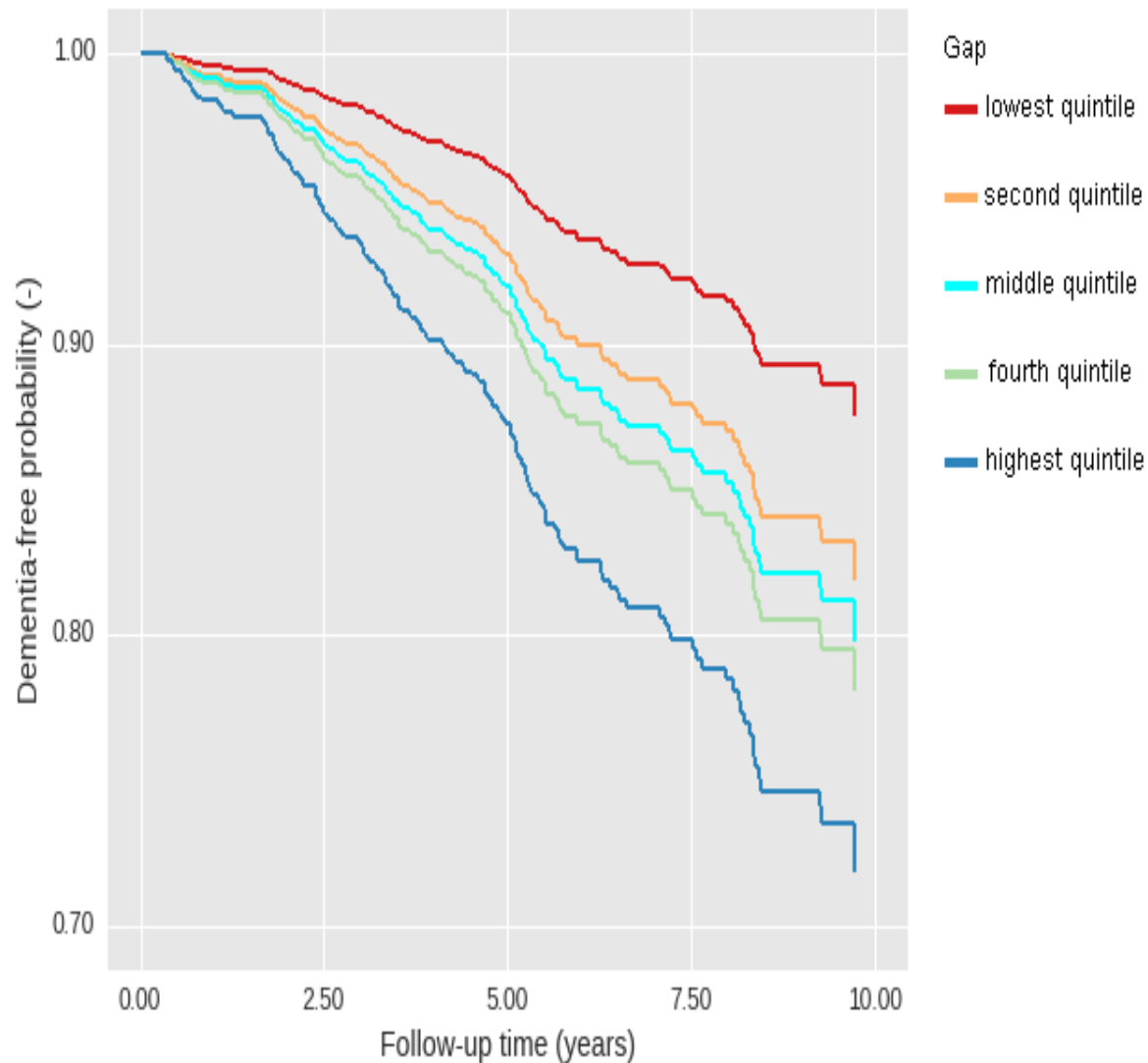
# Totally new imaging biomarkers



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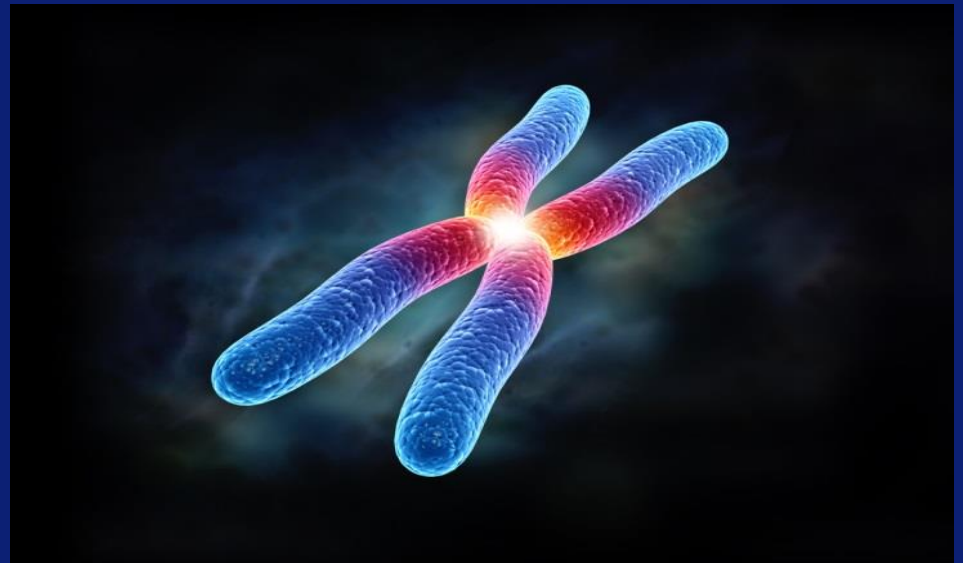
# Kaplan-Meier curves for new biomarker (delta brain / calendar age)





MRI

Genetics



# Population Imaging Genetics

**Risk factors:**

**Genetic**

**Blood pressure  
Smoking**

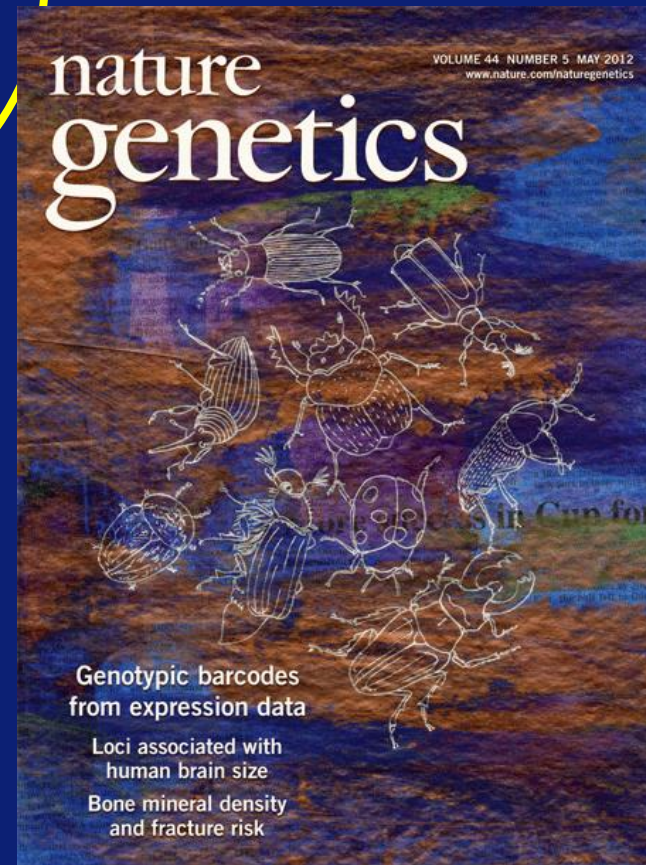
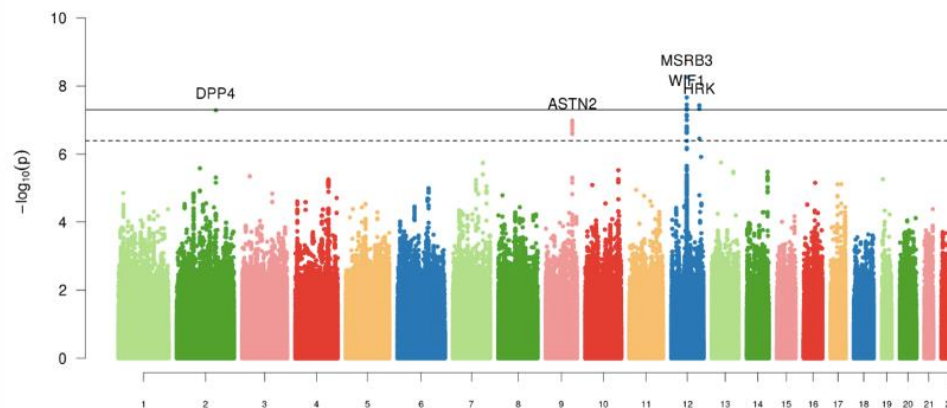
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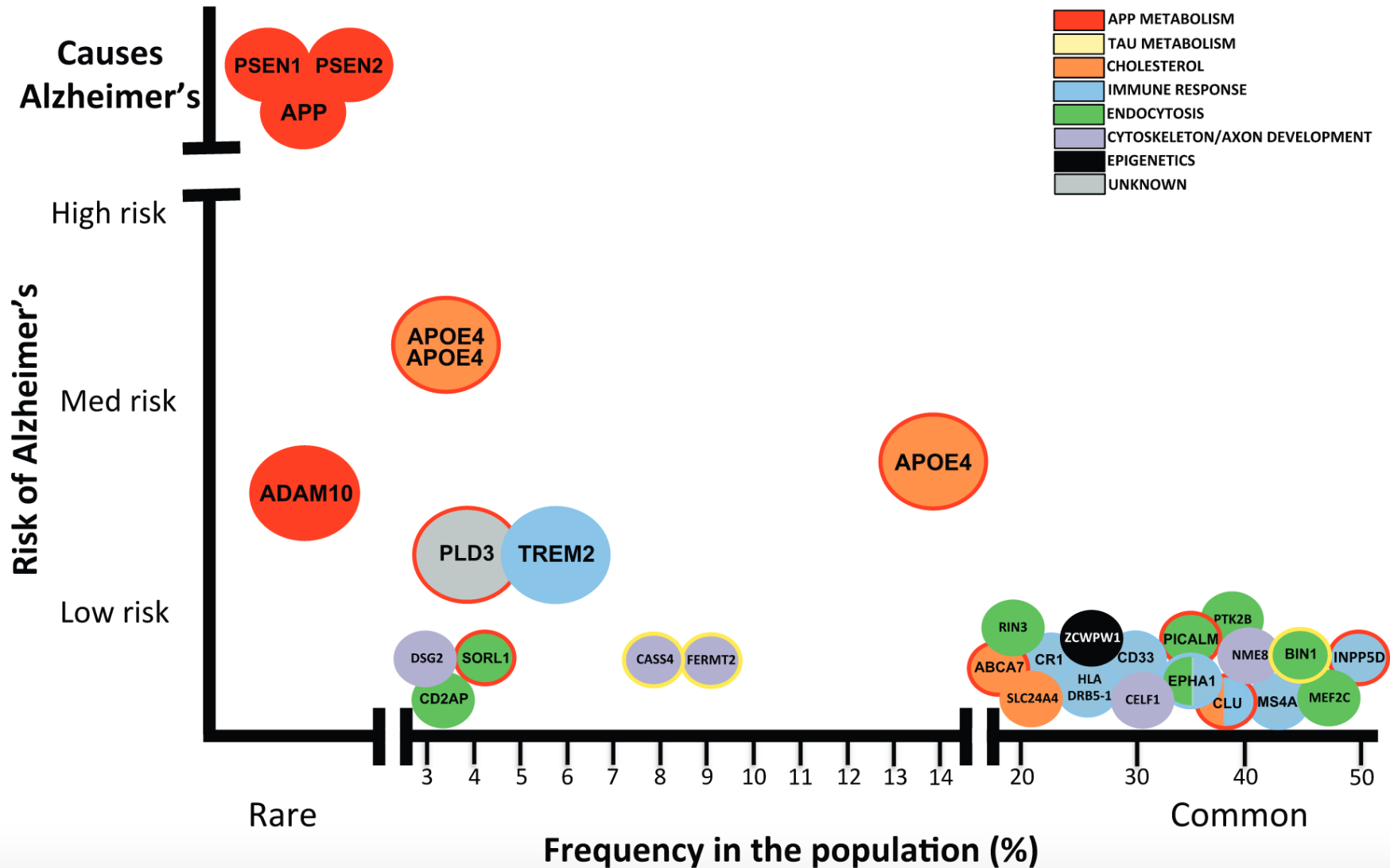
**Brain changes:**

**Hippocampal  
volume**

Figure 1: Genome-wide Manhattan plot for hippocampal volume



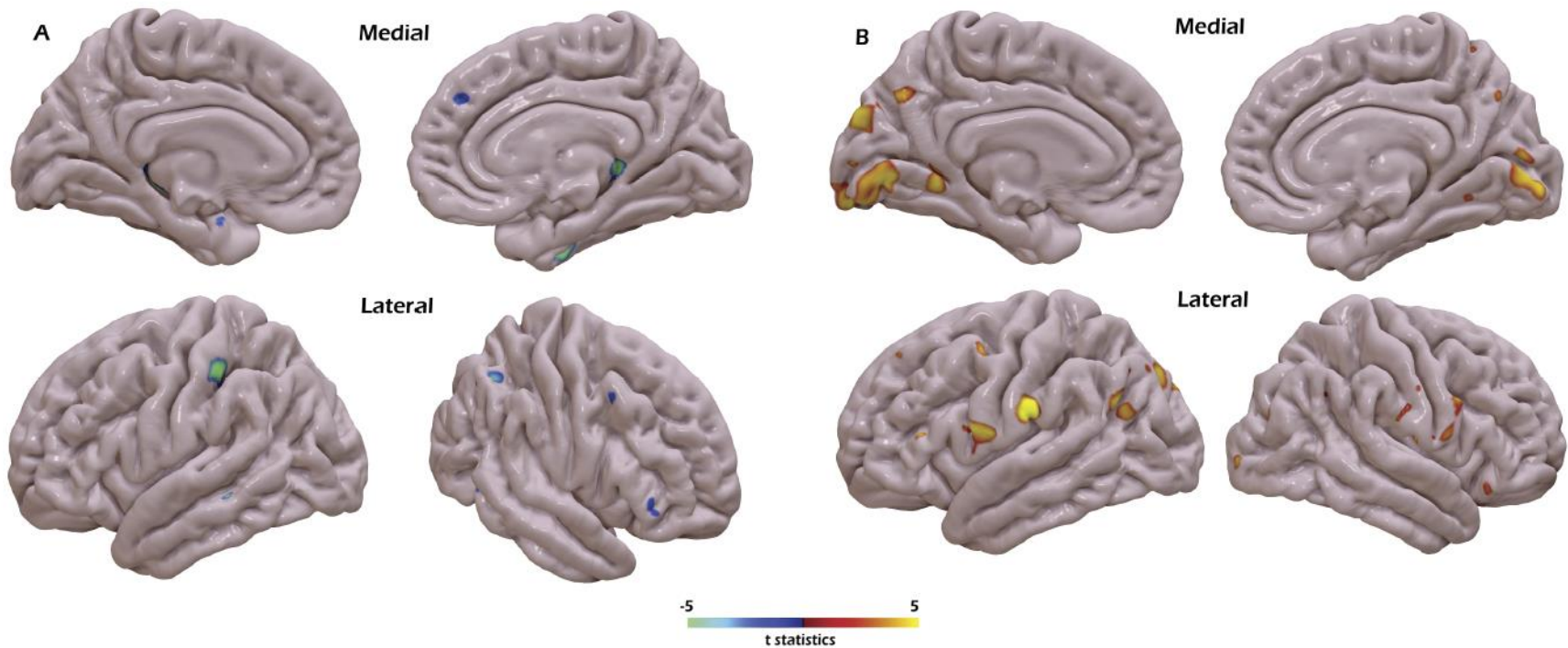
# Predicting is not easy ... AD risk genes





# Imaging genetics: gaining insight

VBM analysis consisted of 4071 nondemented persons with information available on both genome-wide genotyping and MRI data from the population-based Rotterdam Study. The mean age was 64.7 ( $\pm 10.7$ ) years and 2251 (55%) subjects were women.





# Some observations

- The current hype in AI in radiology is mostly about image perception
- Potential data driven science is much larger
  - diagnostic and prognostic workflow
  - modeling complex relations between imaging, omics & genetic data
- \*\* Holy grail questions:
  - Find phenotype =  $f(\text{genotype}, \text{environmental factors})$
  - Predict phenotype (T+1) =  $f(\text{genotype}, \text{environmental factors}, \text{phenotype (T)})$
- Access to good data and clinical knowledge about these data is key
  - we need to adopt FAIR data principles, and
  - build co-creation environments (clinicians, machine learning)
- Still large challenges to address!

# MICCAI – ACR / RSNA / ESR collaboration



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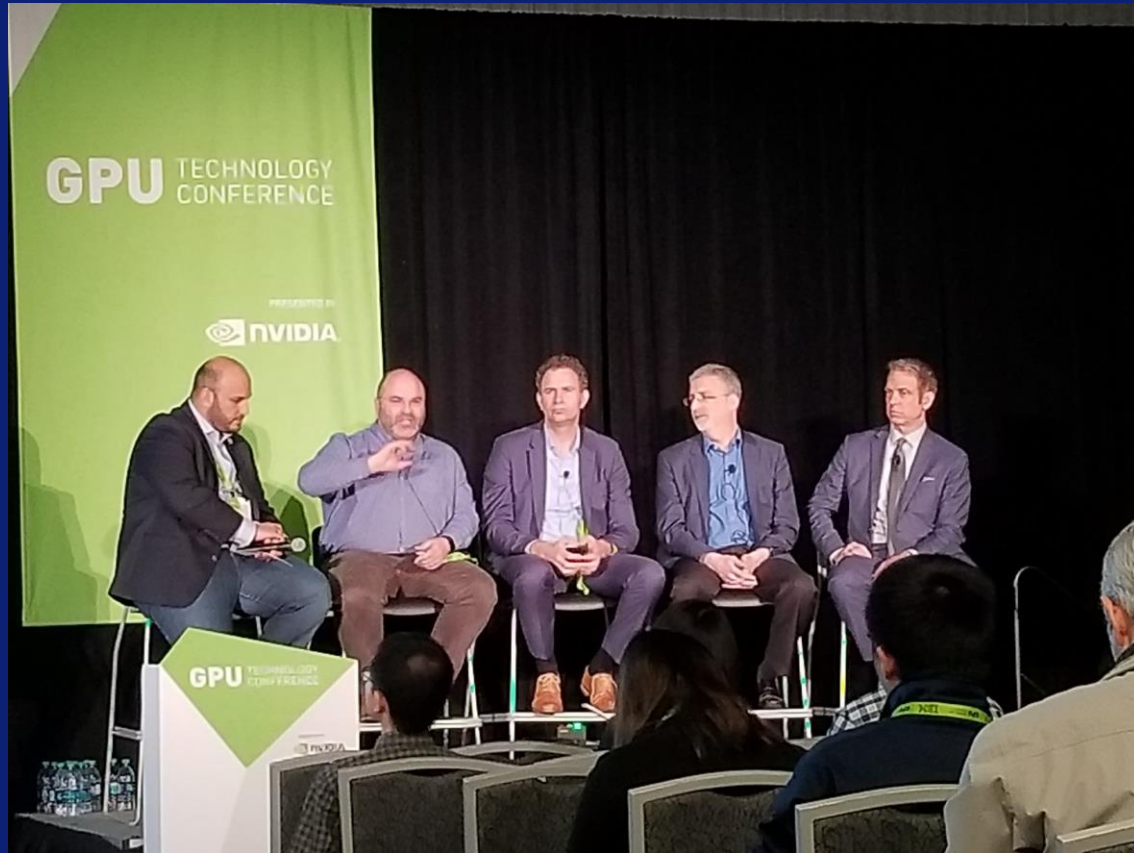
TOUCH-AI Directory

Our TOUCH-AI use cases are scenarios where use of artificial intelligence (AI) may help improve medical imaging care.

They were created to empower AI developers to produce algorithms that are clinically relevant, ethical, and effective. Each use case provides narrative descriptions and flow charts which specify the health care goal of the algorithm, the required clinical input, how it should integrate into the clinical workflow and how it will interface with users and tools.

# ACR – MICCAI MoU

“The ACR is creating use cases for imaging AI and will work with MICCAI to leverage this knowledge base in MICCAI's imaging AI competitions.”



# Acknowledgements

## Department of Radiology

- Marion Smits, Aad van der Lugt, Meike Vernooij, Maarten Thomeer, Gabriel Krestin

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## Department of Radiology & Medical Informatics

- Hakim Achterberg, Esther Bron, Marleen de Bruijne, Marius de Groot, Stefan Klein, Marcel Koek, Genady Roshchupkin, Martijn Starmans, Sebastian van der Voort