



Multimodal imaging, deep learning and visualization in clinical imaging research

<https://mmiv.no/machinelearning>

Mohn Medical Imaging and Visualization Centre

*AI in healthcare
Bodø June 18th 2019*

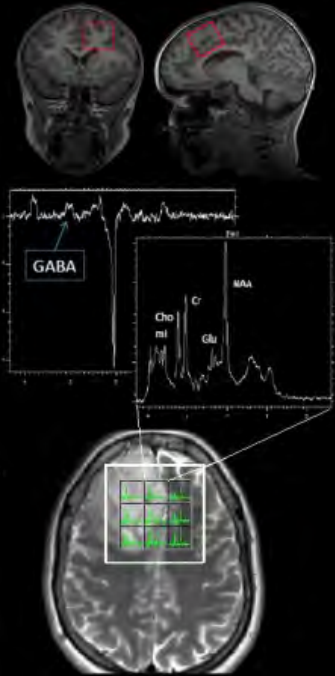
*Renate Grüner
m. +47 48110677
e. renate@fmri.no*

Mohn Medical Imaging and Visualization Centre

AIM: Research quantitative imaging and interactive visualization

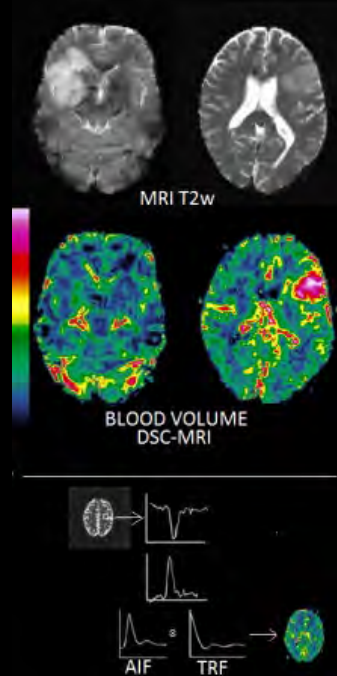
Core activities in machine learning/ artificial intelligence

Feature detection



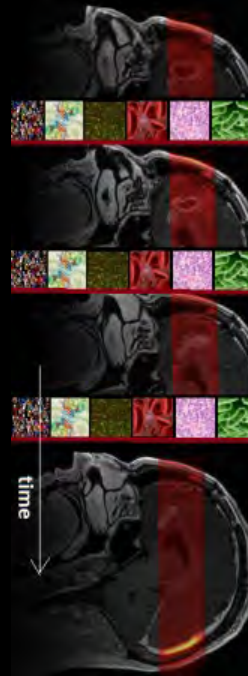
Novelty in data acquisition, reconstruction, visualization

Feature extraction



Novelty in data reduction, pattern recognition, vis.

Feature prediction

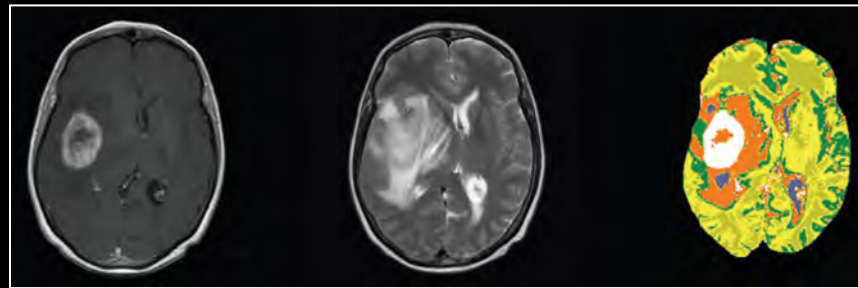
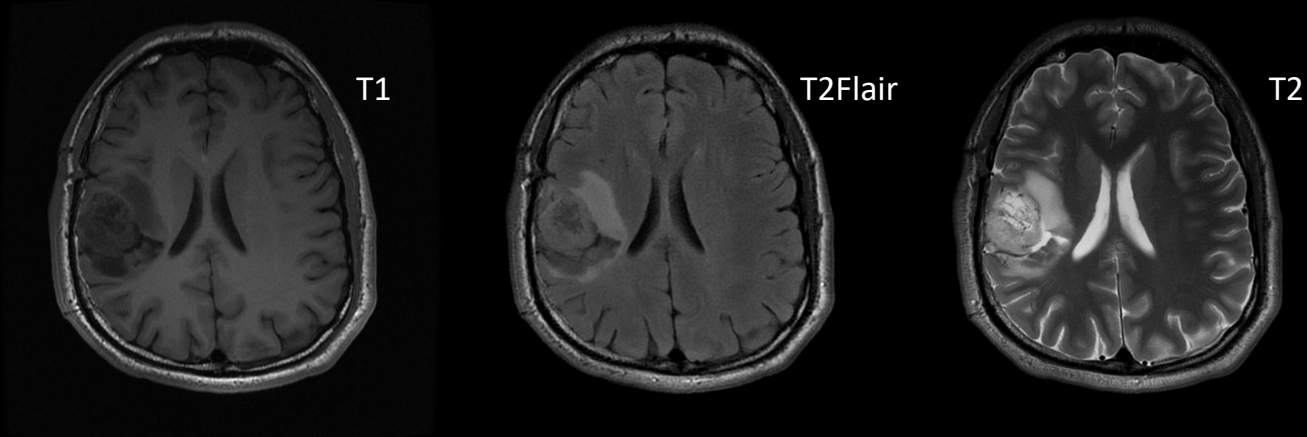


Novelty in linking features to prognosis/omics



Classical machine learning (SVM, KNN, ..)

...choosing appropriate features

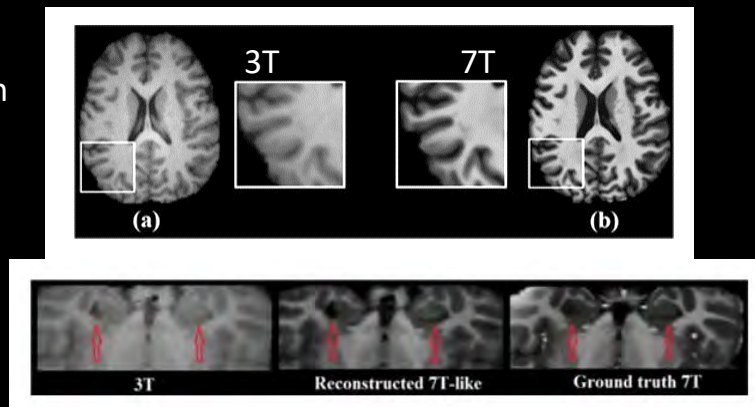


Feature extractions: Multispectral Imaging Analysis.
Kvinnslund, .., Grüner 2009

Deep Learning: Image reconstruction

- Information from high resolution images can be predicted from low resolution images using priors from paired dictionaries

Bahrami K et al. Reconstruction of 7T like images from 3T.
IEEE Trans Med Imaging 2016;
35:2085-2097



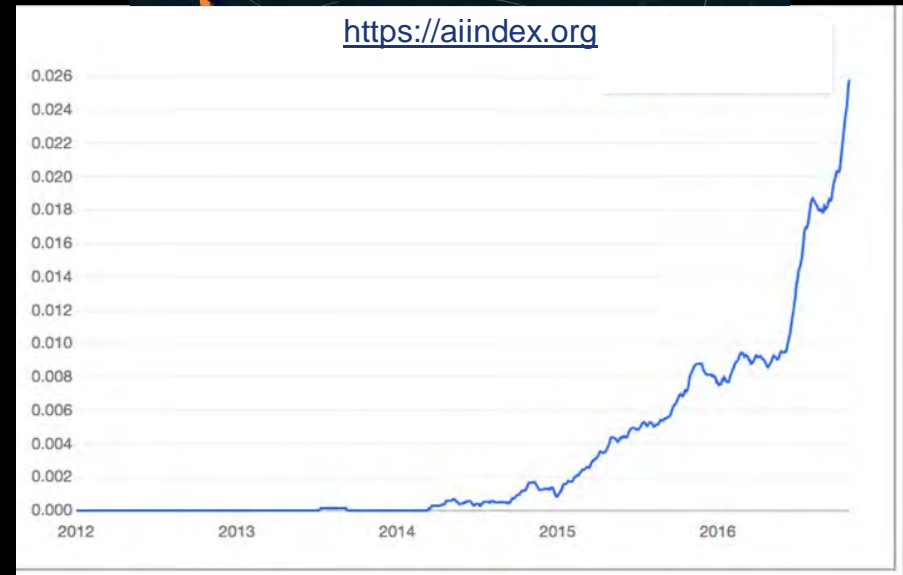
- Sparse sampling:



Schlemper et al. A Deep Cascade of CNN for dynamic MRI image reconstruction.
IEEE Trans Med Img. Vol 2; 2018

AI: An accelerating field

- «Human-level performance»
- Methods
- Companies (startups)
- Investments
- Universities (courses and publications)
- Media
- Governments



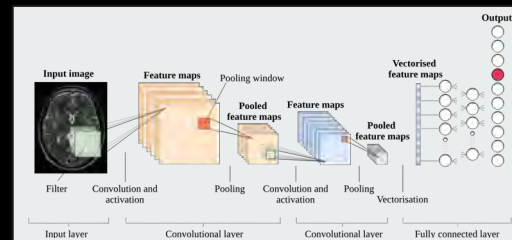
“Big data”



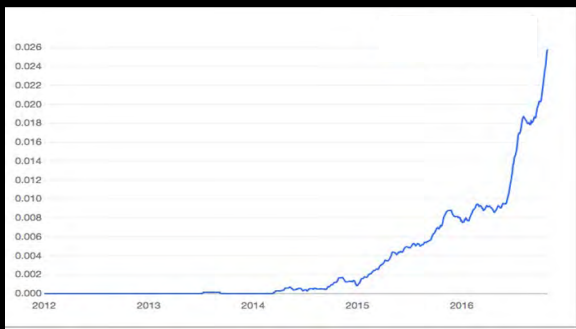
GPU



Old models, some new tricks



Investments



Open science

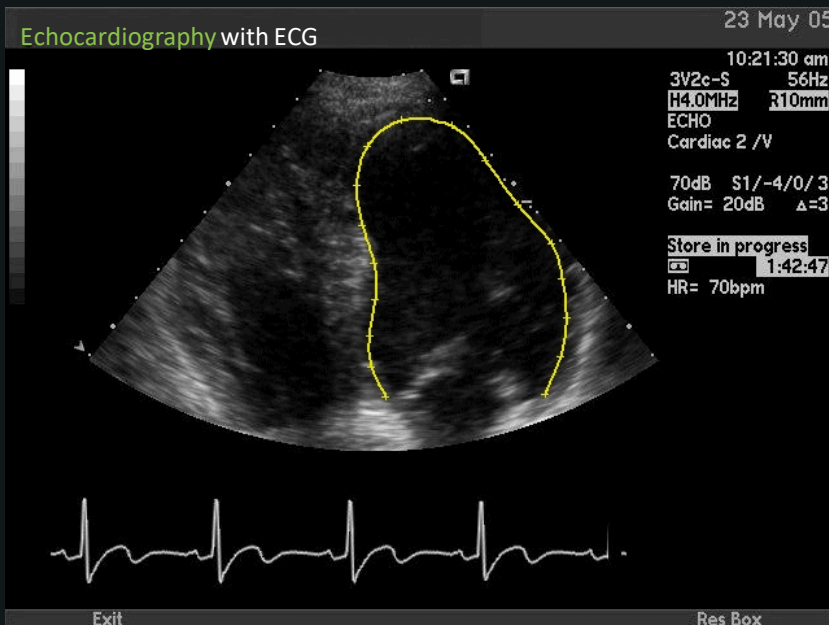


Frameworks

Open source
Open competitions
Open courses
Open data

Computational imaging & machine learning

... generic technologies



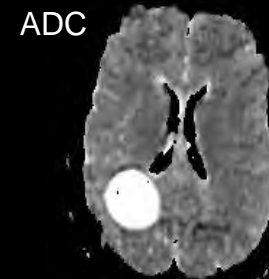
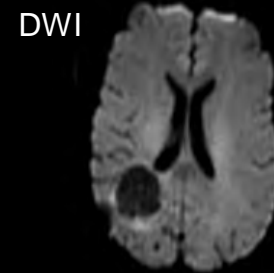
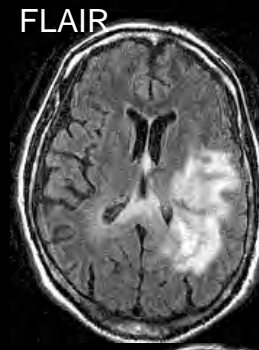
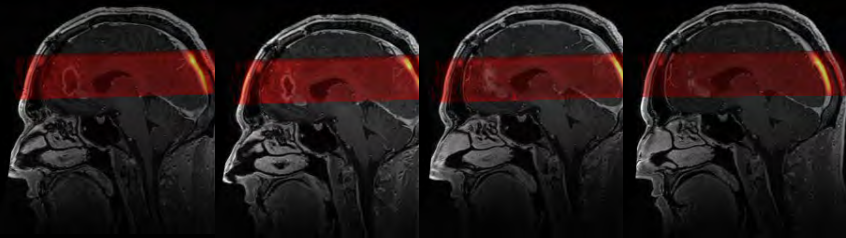
Contour detection + tracking + volume estimation
=> cardiac output [ml/min]



Object detection + tracking + number-plate recognition
=> electronic toll collection / vehicle speed [km/h]

Clinical imaging

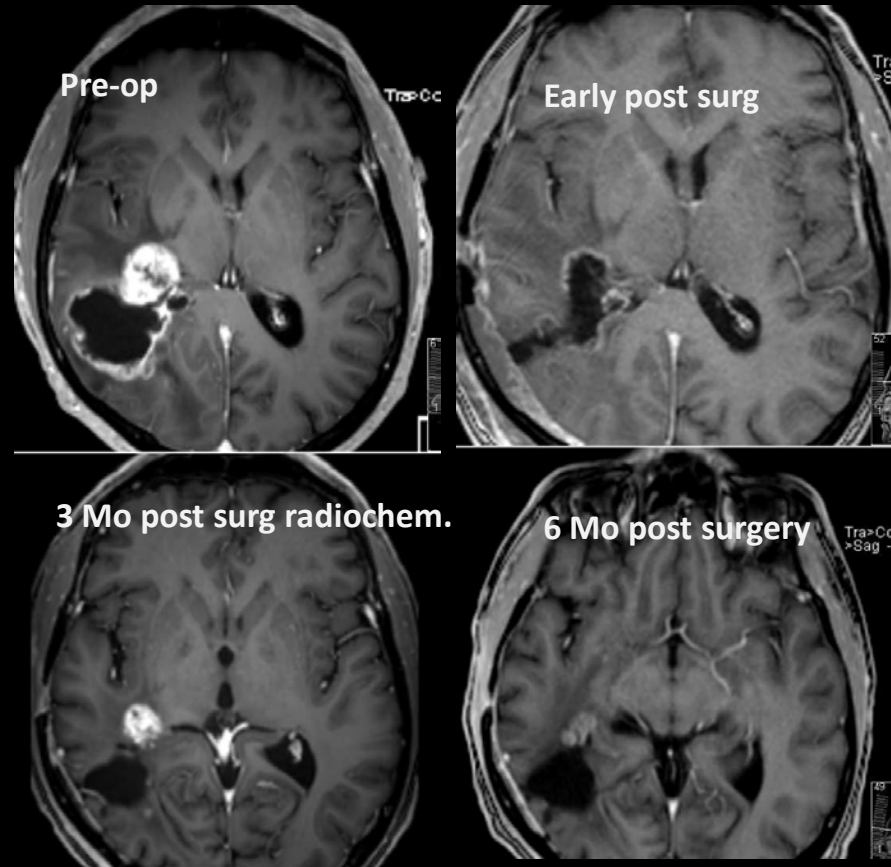
- Differential diagnostics:
Primarily morphology
including vessel mapping (MRI)
or glucose metabolism (PET)
("Surgical level")
- Qualitative assessments
- Individual, personalized
- Longitudinal information
- Patient history information



Astrocytoma

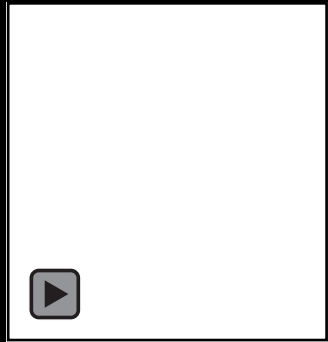
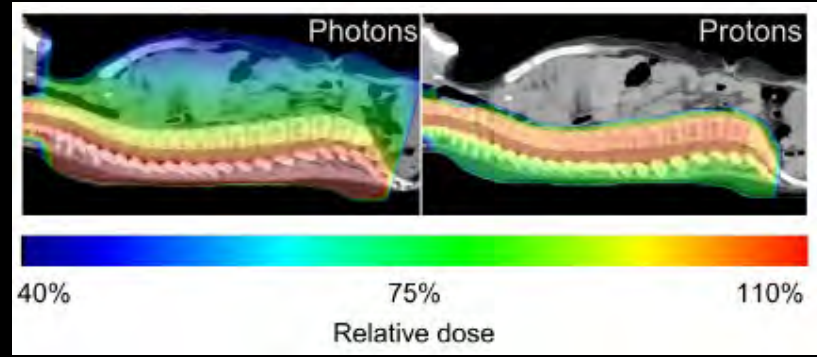
Cyst

Motivation: «*Every biopsy is an imaging failure*»

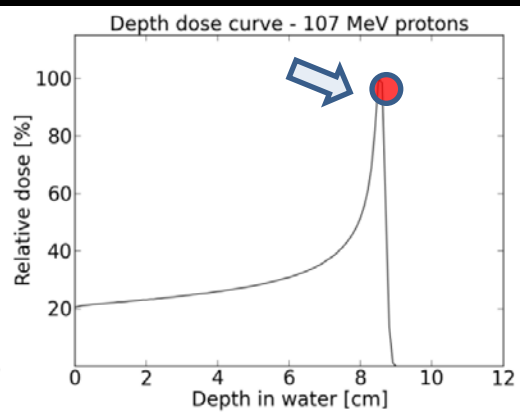
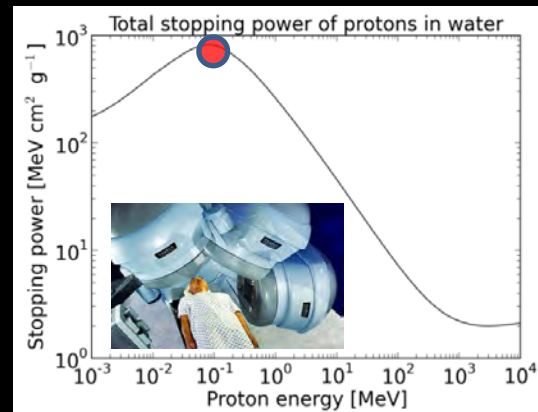


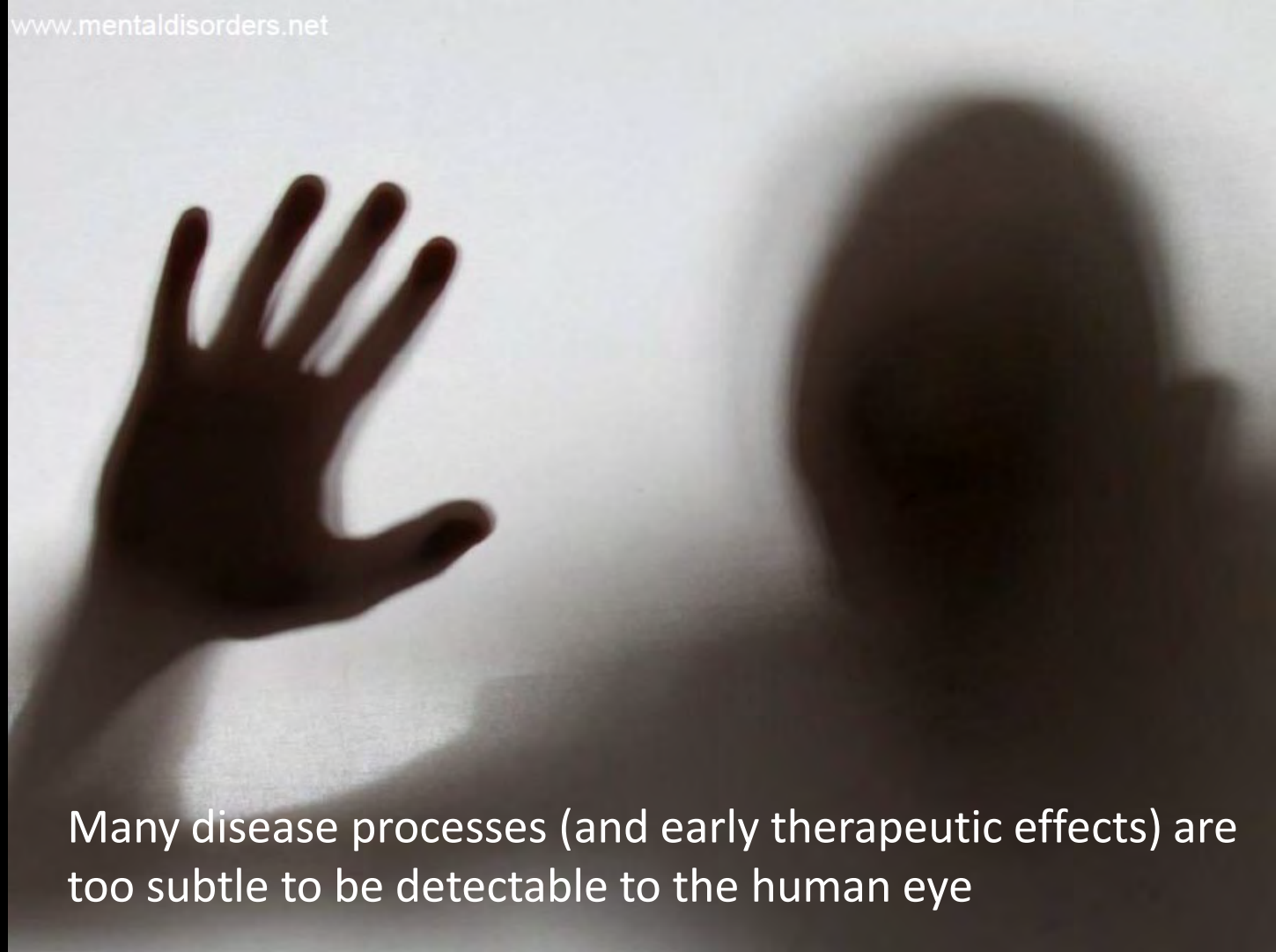
Motivation: Novel therapeutic interventions (larger variety/ more precise)

$$-\frac{dE}{dx} = 2\pi N_a r_e^2 m_e c^2 \rho \frac{Z}{A} \frac{z^2}{\beta^2} \left[\ln \left(\frac{2m_e \gamma^2 v^2 W_{max}}{I^2} \right) - 2\beta^2 - \delta - 2\frac{C}{Z} \right]$$



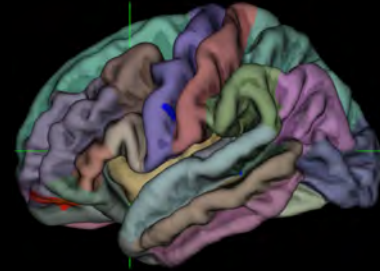
Anticancer drugs





Many disease processes (and early therapeutic effects) are too subtle to be detectable to the human eye

Research imaging



- Morphology (macrostructure)
- Physiology
 - Diffusion based imaging
 - Perfusion based imaging
 - fMRI (task/ rest)
 - Structural/functional connectivity (-> DCM)
- Metabolites (MRS) & metabolism and biochemistry (PET/ NM)
- New approaches

Traditional cross sectional:

- "Purity of diagnosis"*
- Sample size
- Control group (age, gender, ...)
- Medication (native vs washout)
-

Versus:

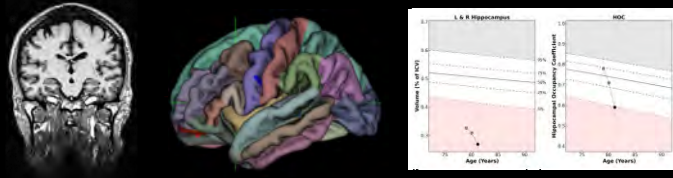
Big data, deep learning

- XXXomics/
Imaging genetics

-> personalized medicine

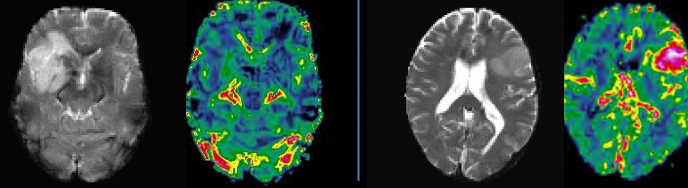
Imaging biomarkers

Structure



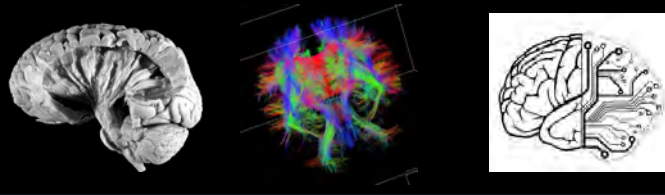
e.g. Volume

Microvasculature



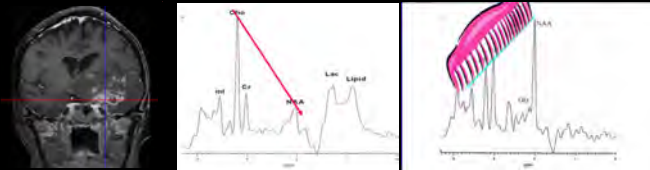
e.g. Blood flow

Microstructure



e.g. Orientation

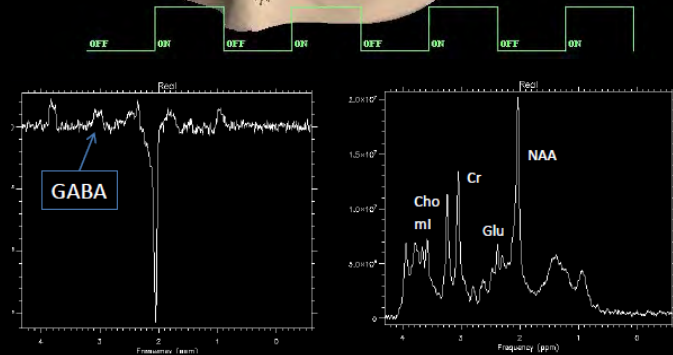
Biochemistry



e.g. Molecular concentrations

and more!!!

Auditory hallucinations: Perception of sounds that do not exist



DMN: Raichle et al 2001, 2010, 2015
EMN: Hugdahl, Raichle et al 2015

K. Kompus, R. Westerhausen, N = 103
K. Hugdahl *Neuropsychologia* (2011)

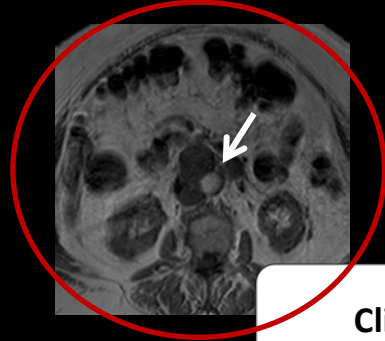


Courtesy Prof Kenneth Hugdahl, Faculty of Psychology, UIB

Precision Imaging in Gynecologic Cancer



Imaging is an important part of the diagnostic work up, *guides therapy* and is an important *research tool*



Gynecologic cancer patient

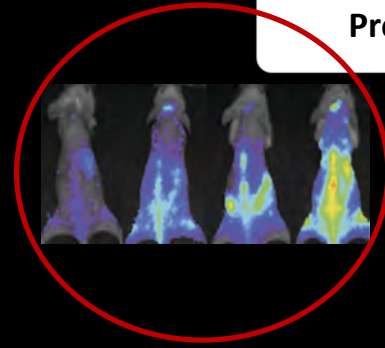


Clinical trials

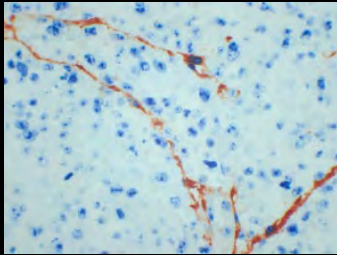
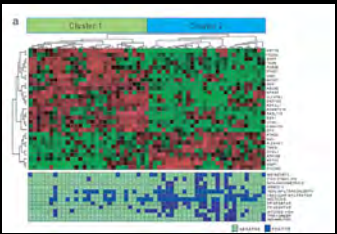
Preoperative imaging

Preclinical trials

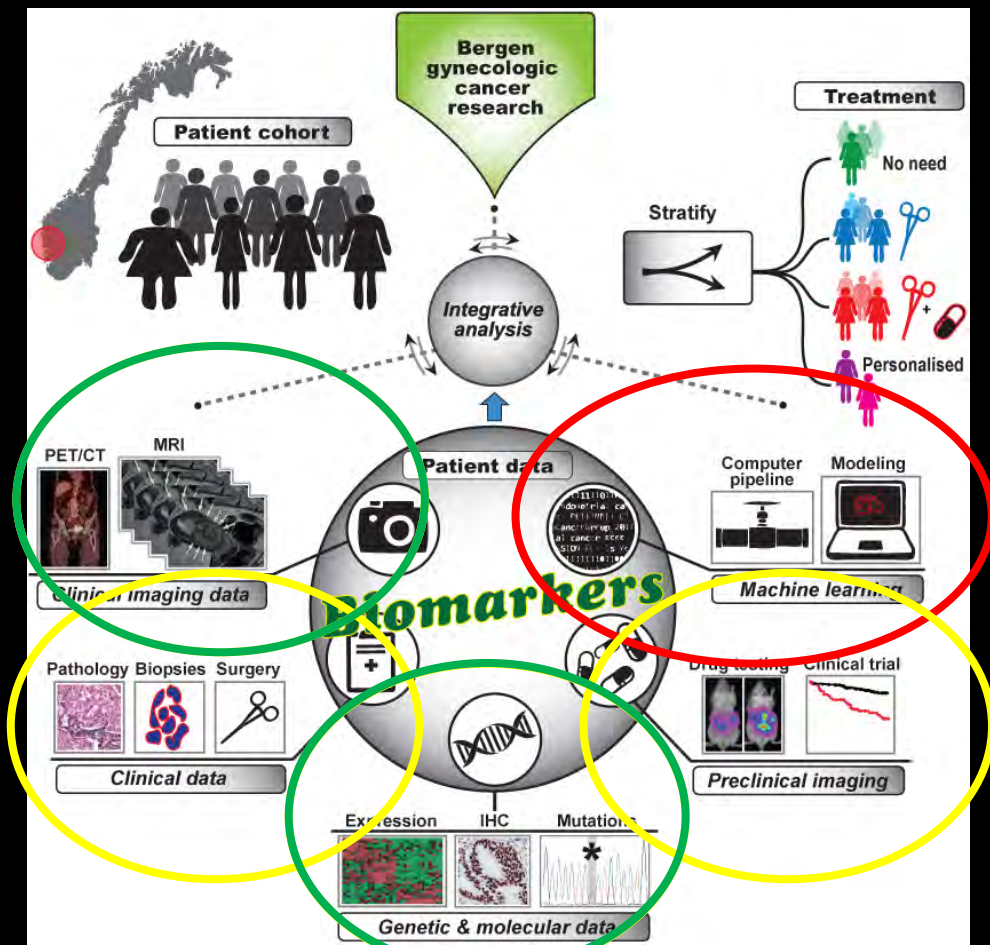
Biopsy and surgery
Tissue biobank



Molecular and genetic testing



Core MMIV project: Precision Imaging in Gynecologic Cancer



PI: Prof MD/ PhD I Haldorsen/
CR: PhD E. Hodneland (Norse)

WP 1.) Biomarker- and
preclinical/clinical studies
(MR~800, PETCT~500)

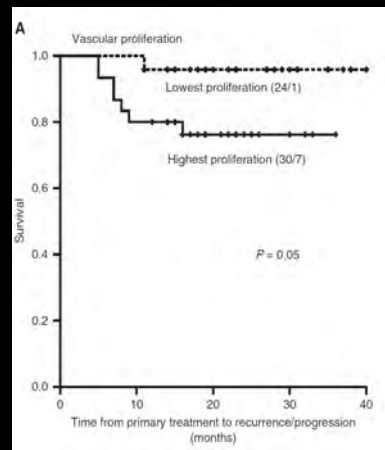
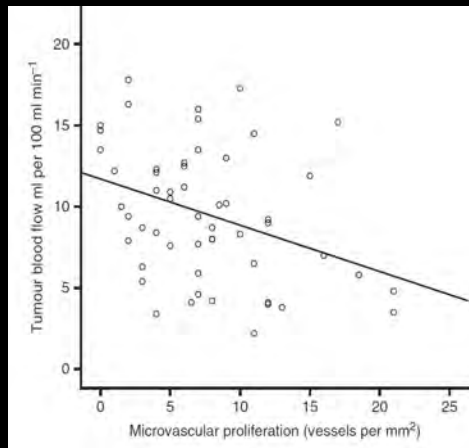
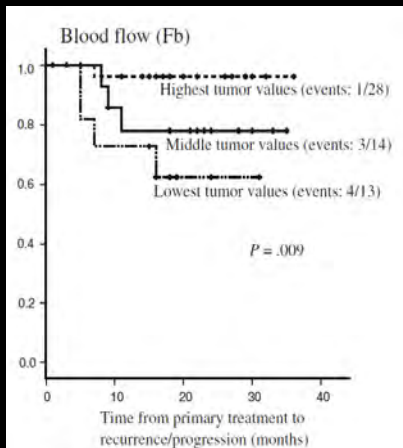
WP 2.) Radiogenomics

WP 3.) Machine learning

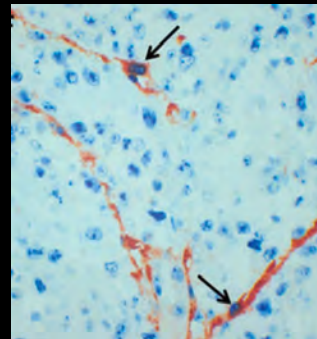
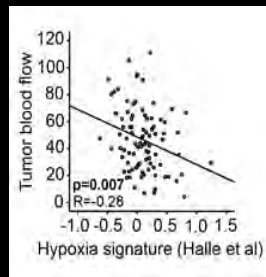


Jan'18

DCE- MRI in endometrial cancer identifies patients at increased risk of recurrence and links low tumor blood flow to increased vascular proliferation and hypoxia



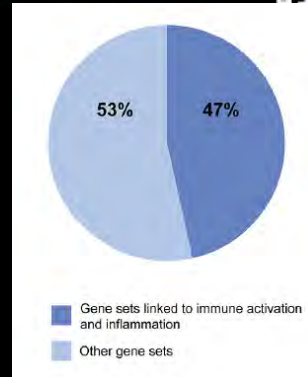
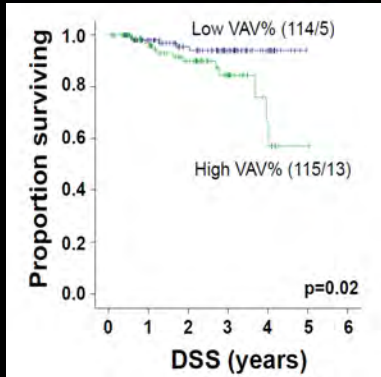
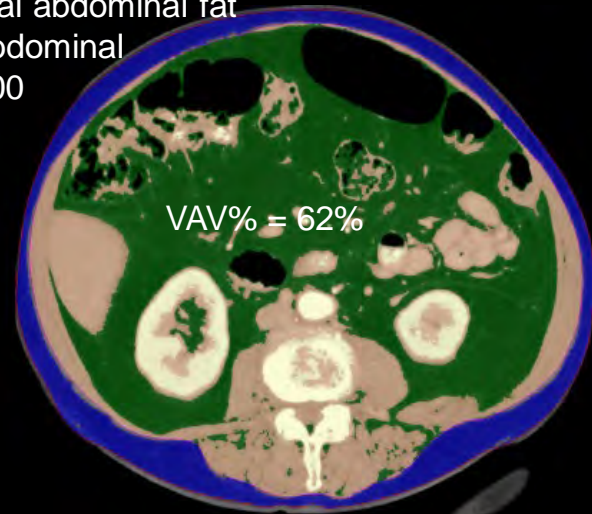
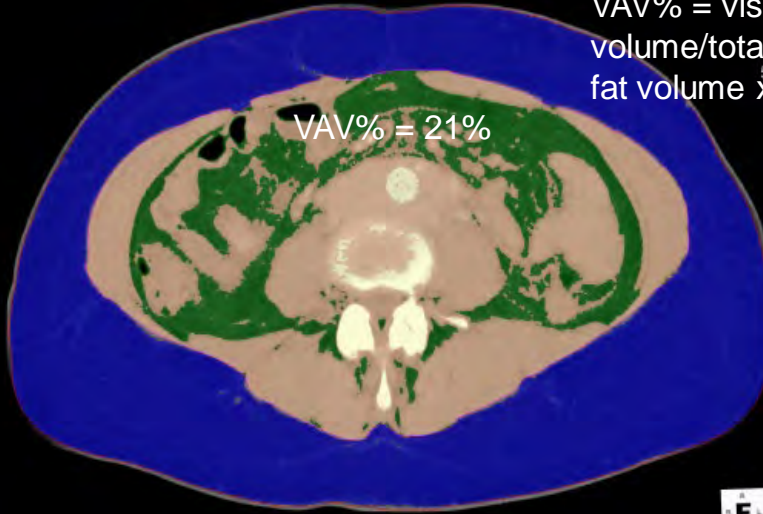
- Aggressive tumors are characterized by ↓ blood flow and ↑ microvascular proliferation.
- Low tumor blood flow is linked to upregulated hypoxia gene signature



Ki67/factor VIII

Visceral fat percentage in EC:

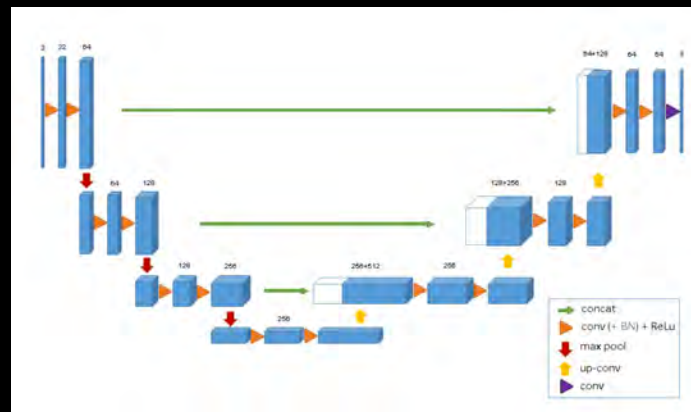
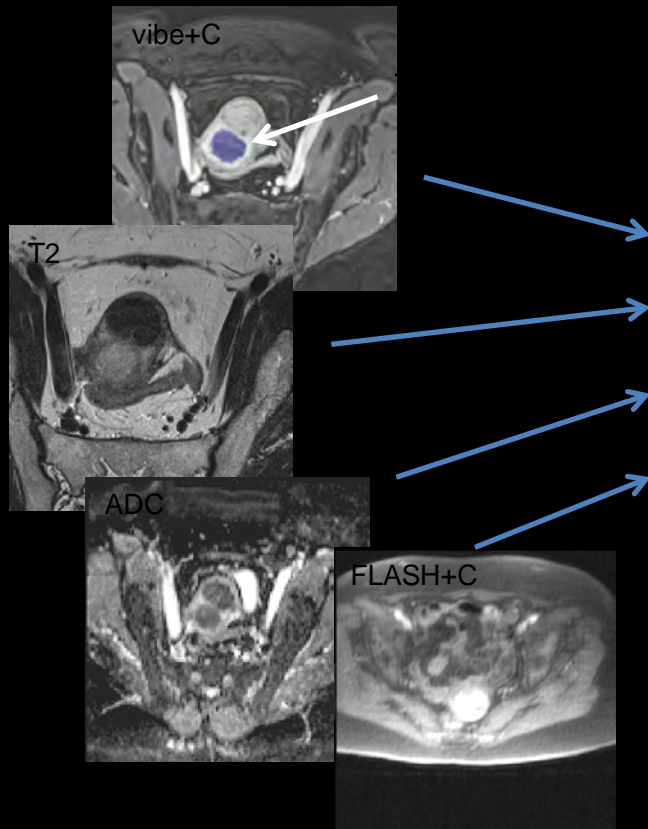
VAV% = visceral abdominal fat volume/total abdominal fat volume $\times 100$



predicts aggressive disease
is linked to activation of
gene sets linked to immune
activation and
inflammation

WP3 (MACHINE LEARNING)

STEP 1: Training of a deep learning segmentation network



Training of a deep learning segmentation network

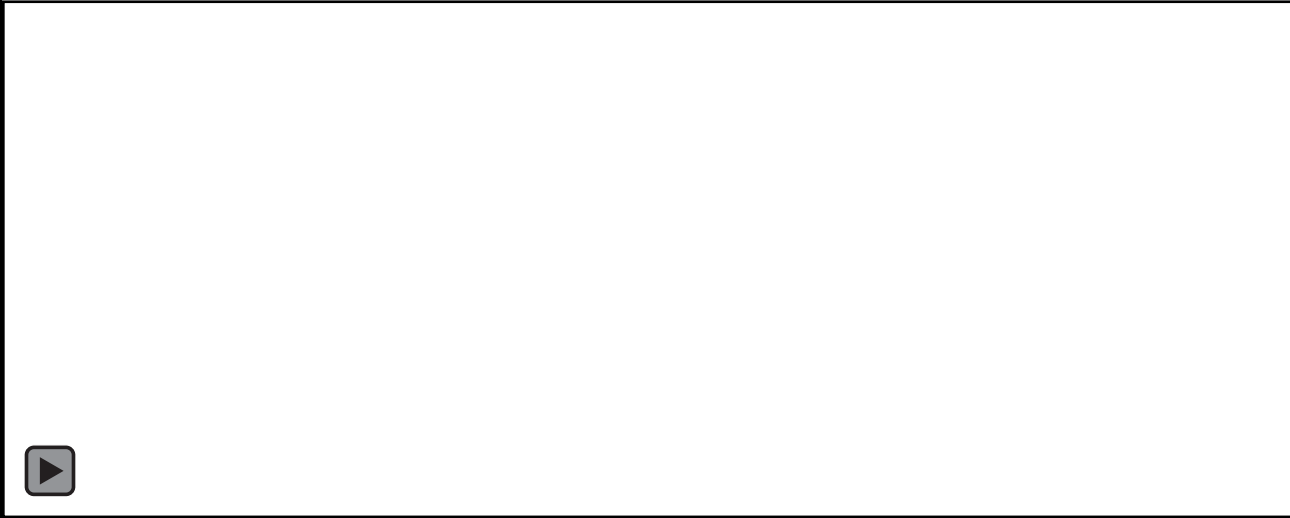
Manual segmentation of tumor



Automatic segmentation of tumor using machine learning

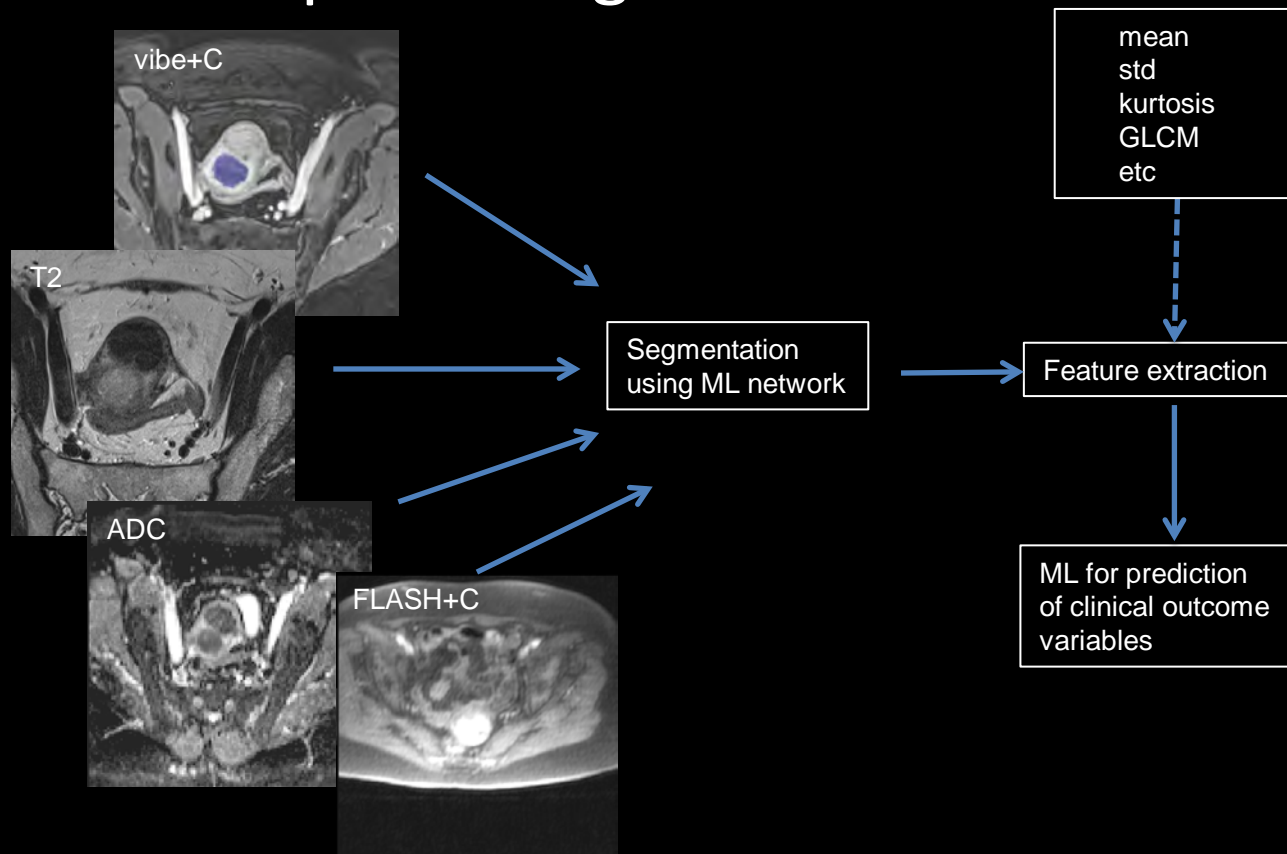


Automatic tumor segmentation using machine learning

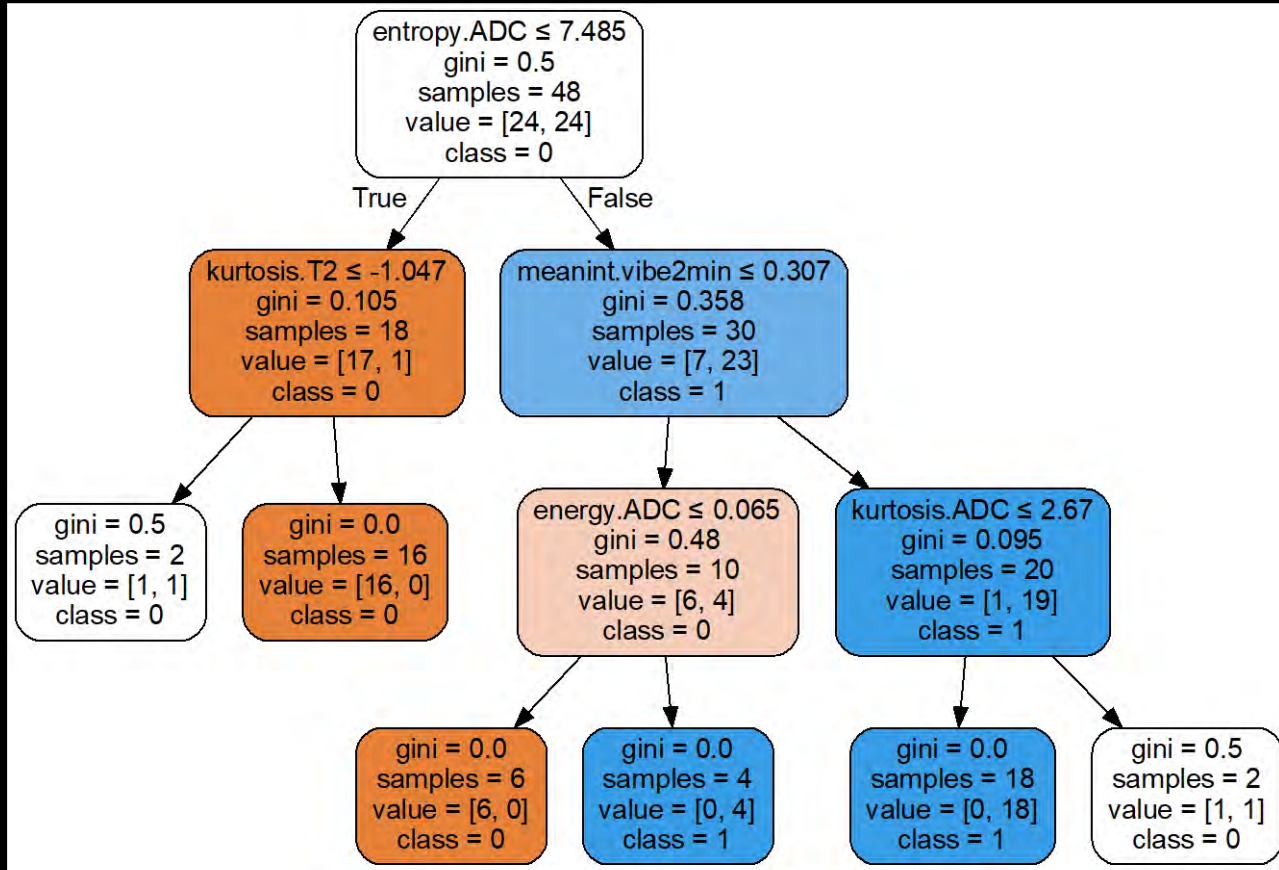


blue: true positive,
yellow: false positive,
orange: false negative

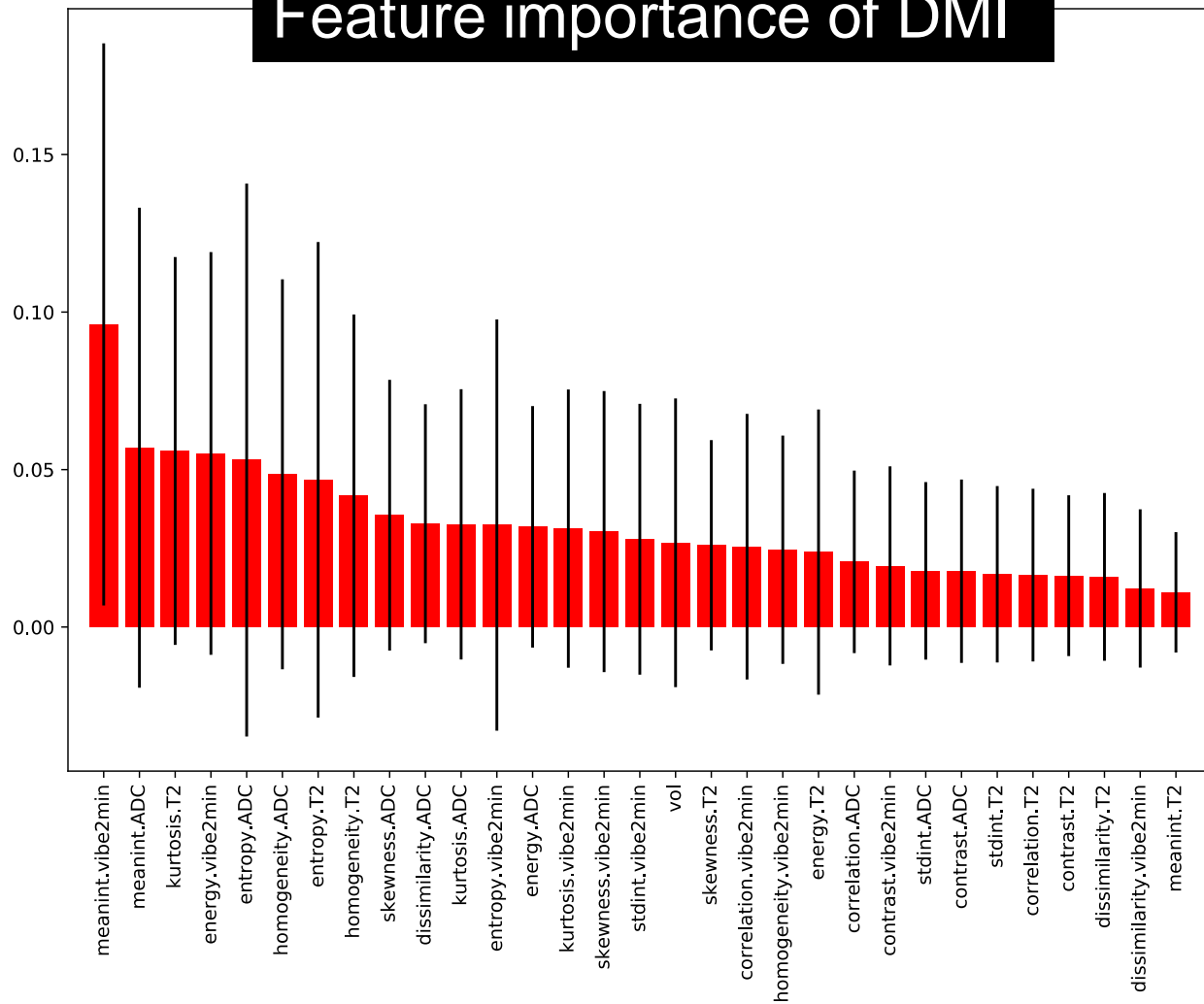
STEP2: Applying the MR data and segmented masks for predicting clinical outcome



Prediction of the staging parameter deep myometrial invasion (DMI)



Feature importance of DMI



Longitudinal followup:

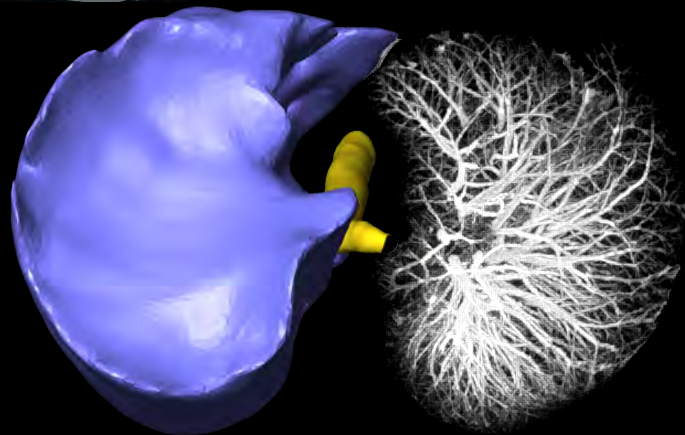
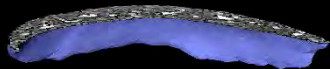
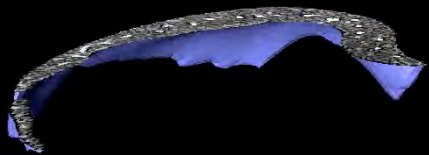
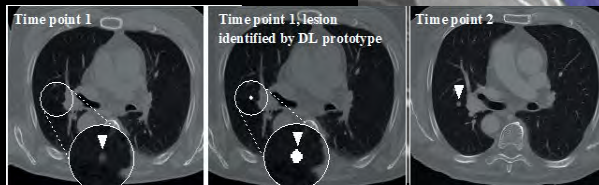
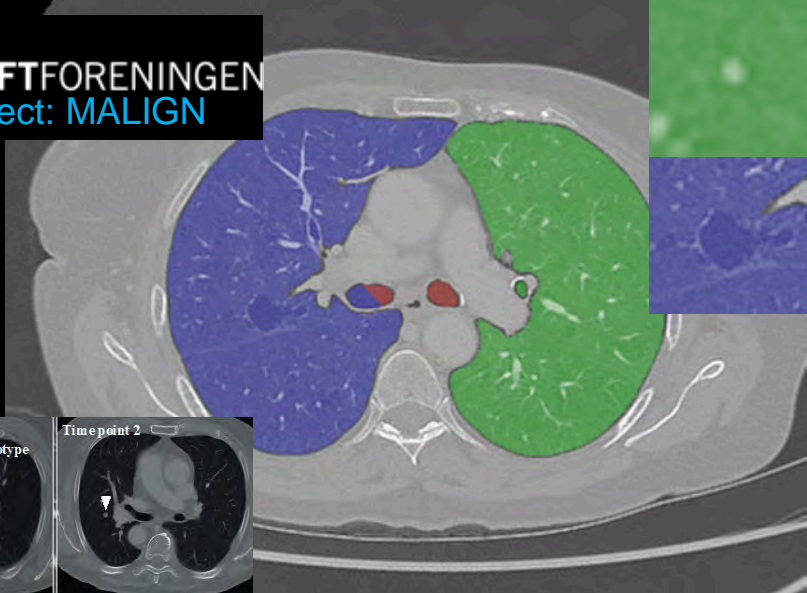


KREFTFORENINGEN
Project: MALIGN

CT Airway and Lung Segmentation for
Lung Nodule Detection and
Longitudinal Change Analysis



Hauke
Bartsch,
UCSD

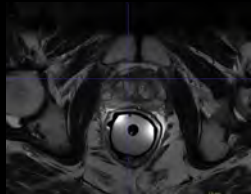
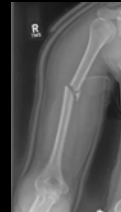
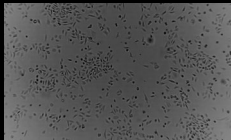
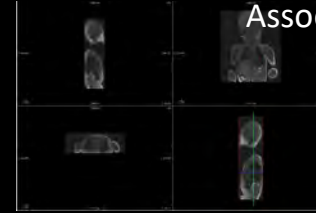
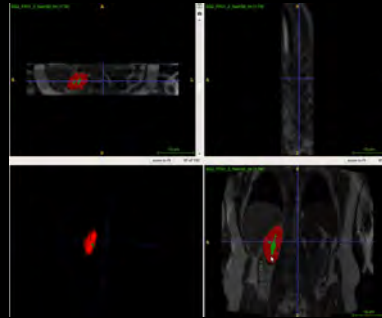
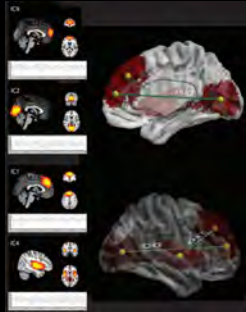
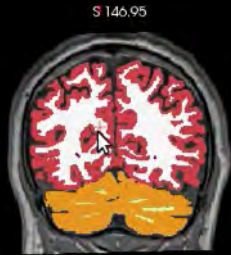


Core MMIV project: Machine learning

«Computational medical imaging and machine learning
– methods, infrastructure and applications»



PI: Prof PhD/MD A Lundervold,
Assoc Prof. PhD AS Lundervold



display episode

Hours	Capillary MRI rate	Glucose MRI rate	Protein MRI rate	Optical MRI rate	Glucose MRI rate	Protein MRI rate	Optical MRI rate	Glucose MRI rate	Protein MRI rate	Optical MRI rate	Mean Rate	Weight	Mean Rate	Protein MRI rate	Optical MRI rate	Respiratory rate	g
0	0.300000	NaN	48.0	NaN	NaN	NaN	NaN	NaN	NaN	NaN	33.0	NaN	68.000000	NaN	NaN	24.0	
1	0.718667	NaN	48.0	NaN	NaN	NaN	NaN	NaN	NaN	NaN	33.0	NaN	67.000000	NaN	NaN	24.0	
2	0.718667	NaN	48.0	NaN	NaN	NaN	NaN	NaN	NaN	NaN	33.0	NaN	67.000000	NaN	NaN	24.0	
3	0.000000	NaN	42.0	NaN	NaN	NaN	NaN	NaN	NaN	NaN	33.0	NaN	55.000000	NaN	NaN	24.0	
4	0.718667	NaN	54.0	NaN	NaN	NaN	NaN	NaN	NaN	NaN	48.0	NaN	74.000000	330.0	24.0		
5	0.718667	NaN	54.0	NaN	NaN	NaN	NaN	NaN	NaN	NaN	48.0	NaN	74.000000	330.0	24.0		
6	0.000000	NaN	NaN	NaN	NaN	NaN	NaN	NaN	NaN	NaN	NaN	NaN	NaN	NaN	NaN	24.0	
7	0.000000	NaN	NaN	NaN	NaN	NaN	NaN	NaN	NaN	NaN	NaN	NaN	NaN	NaN	NaN	24.0	



inputs of d-gen

Recent publications in machine learning and computational medicine



Zeitschrift für Medizinische Physik
Volume 29, Issue 2, May 2019, Pages 102-127

ELSEVIER


Review

An overview of deep learning in medical imaging focusing on MRI

Alexander Selvikvåg Lundervold^{1,2,3,4,5}, Arvid Lundervold^{1,2,3,4,5}

Show more

<https://doi.org/10.1016/j.zemedi.2018.11.002>
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Computerized Medical Imaging and Graphics
Volume 63, January 2018, Pages 24-30

ELSEVIER

Intensity-based volumetric registration of magnetic resonance images and whole-mount sections of the prostate

Are Losnegård^{1,2,3}, Lars Reisater⁴, Ole J. Halvorsen^{5,6}, Christian Beisland^{1,2,3}, Aurea Castillo⁷, Ludvig P. Muren⁸, Jarle Ravvik^{1,2,3}, Arvid Lundervold^{1,2,3,4,5}

Show more

Journals & Magazines > IEEE Transactions on Biomed... > Volume: 66 Issue: 6

In Vivo Detection of Chronic Kidney Disease Using Tissue Deformation Fields From Dynamic MR Imaging

11 Author(s) Erlend Hodneland¹; Eirik Keilegavlen²; Erik A. Hanson³; Erling Andersen⁴; Jan Ankar Monssen⁵; ... View All Authors



Hodneland et al.

A new framework for assessing subject-specific whole brain circulation and perfusion using MRI-based measurements and a multi-scale continuous flow model

1 Norwegian Biometric Centre, Bergen, Norway;
2 Department of Mathematics, University of Bergen, Bergen, Norway;
3 State Medical Imaging and Visualization Center, Department of Biomedicine, University of Bergen, Bergen, Norway;
4 Medical Physics Group, Institute of Diagnostic Interventional Radiology, Oslo University Hospital;
5 Biomedicine Department, Oslo University Hospital;
6 Medical Biomechanics Research Center, Department of Biomedical Engineering, University of Illinois, Urbana, Illinois;
7 Department of Biomedical Engineering, University of Illinois, Urbana, Illinois;
8 Department of Radiology, Karolinska University Hospital, Stockholm, Sweden



Original Research | Full Access

Preoperative tumor texture analysis on MRI predicts high-risk disease and reduced survival in endometrial cancer

Sigmund Ytre-Hauge MD, Julie A. Dyvik MD, Arvid Lundervold BSc, MD, PhD, Øyvind PhD, Camilla Krakstad PhD, Kristine E. Fasmer MSc, Henrica M. Werner MD, PhD ... See

First published: 13 August 2018 | <https://doi.org/10.1002/jmri.26184> | Cited by: 5



PUBLISH ABOUT BROWSE

Estimating the discretization dependent accuracy of coupled capillary flow measurements

Alexander Malykh, Arvid Lundervold, Jan Ankar Monssen, Erlend Hodneland



PUBLISH ABOUT BROWSE

OPEN ACCESS PEER-REVIEWED

RESEARCH ARTICLE

Inattention in primary school is not good for your future school achievement—A pattern classification study

Astri J. Lundervold, Torodd Bae, Arvid Lundervold

Published: November 28, 2017 • <https://doi.org/10.1371/journal.pone.0189310>



PUBLISH ABOUT BROWSE

OPEN ACCESS PEER-REVIEWED

RESEARCH ARTICLE

Lateral ventricle volume trajectories predict response inhibition in older age—A longitudinal brain imaging and machine learning approach

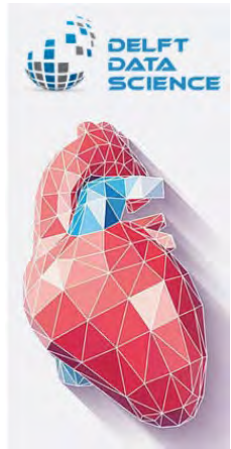
Astri J. Lundervold, Aleksandra Vrå, Arvid Lundervold

Published: April 2, 2019 • <https://doi.org/10.1371/journal.pone.0207967>

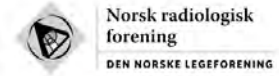
Dissemination



EUREKA!



Den Norske Dataforening
Ditt kompetansenettverk i et digitalt Norge



19. oktober 2018

Norsk radiologisk Foreningsstandpunkt om «Bruk av kunstig intelligens i radiologi».

(NoRafo ønsker å takke Alexander Lundervold ved Mohn Medical Imaging and Visualization Centre for nyttige innspill).



Courses



Summer school 2019 in Computational Biomedicine – Imaging, machine learning and precision medicine

ERASMUS+
Enriching lives, opening minds

OPEN EDUCATIONAL RESOURCES IN COMPUTATIONAL BIOMEDICINE

4 Participating countries:

MASTEREMNE ELMED223

Innovasjon og entreprenørskap

Kurset tilhører [Institutt for biomedisin](#) og er assosiert med [Mohn Medical Imaging and Visualization Centre](#).



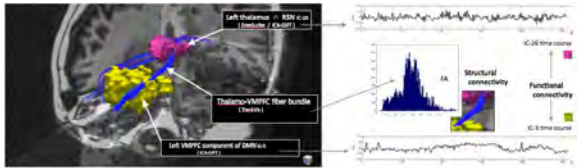
DAT253 Practical deep learning

ETTER- OG VIDEREUTDANNING

HELIKT620

Helseinformatikk

BMED360



Courses



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ELMED219



Summer school 2019 in Computational Biomedicine – Imaging, machine learning and precision medicine

ERASMUS+
Enriching lives, opening minds

OPEN EDUCATIONAL RESOURCES IN COMPUTATIONAL BIOMEDICINE

4 Participating countries:

MASTEREMNE

ELMED223

Innovasjon og entrepriser

STORTINGET Computational Medicine

Objectives and

Det medisinske fakultet

KUNSTIG INTELLIGENS – MULIGHETER, UTFORDRINGER OG EN PLAN FOR NORGE

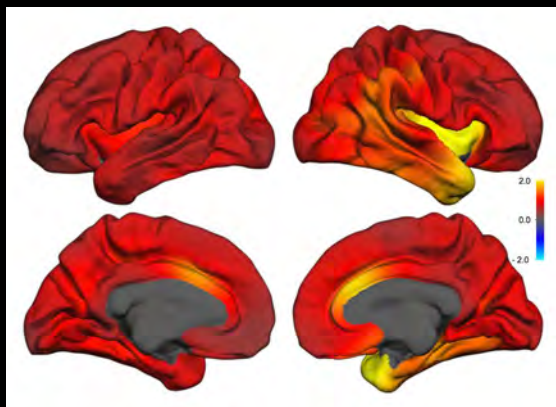
Rapporten argumenterer for at Norge trenger en strategi for kunstig intelligens, og kommer med 14 forslag som bl.a. går på hvilken kompetanse vi trenger, hvordan data om oss skal brukes og hvilken utvikling vi ønsker for samfunnet.

Nå kan studenter lære om kunstig intelligens og medisin

- The concepts and importance of "open science", "data sharing", and "reproducible research"



Core MMIV project: Advanced neuroimaging



Data from Bergen
sample, n = 19

Oltedal et al. (2017)
Neuroimage: Clinical

Oct 2018



LETET ETTER SVAR: Renate Gruner og Leif Oltedal ved Haukeland universitetssjukehus sammenligner MR-bilder tatt for og etter elektroshjokk-behandling. Foto: Silje Robinson

FORSKNING

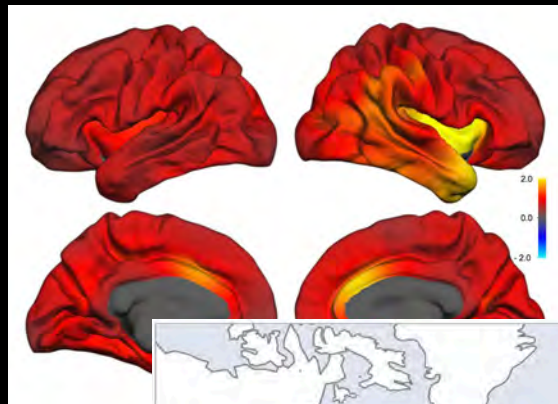
Bruker MR på jakt etter elektrosjokk-svar

Fra Bergen leder overlege Leif Oltedal verdens største MR-studie på elektroshjokk-

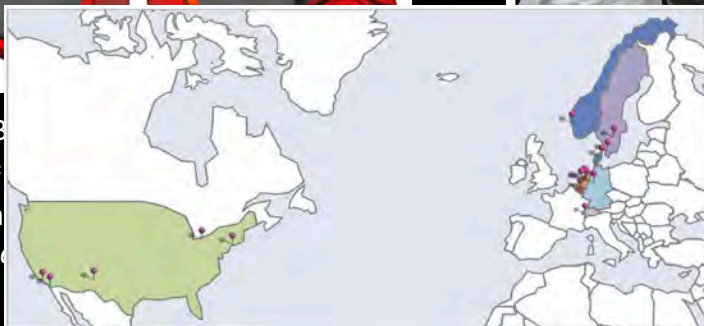
Core MMIV project: Advanced neuroimaging



te Grüner og Leif Olteidal ved Haukeland universitetssjukehus sammenligner MR-bilder tatt for og
ling. Foto: Silje Robinson



Data from B
sample, n =
Olteidal et al
Neuroimag



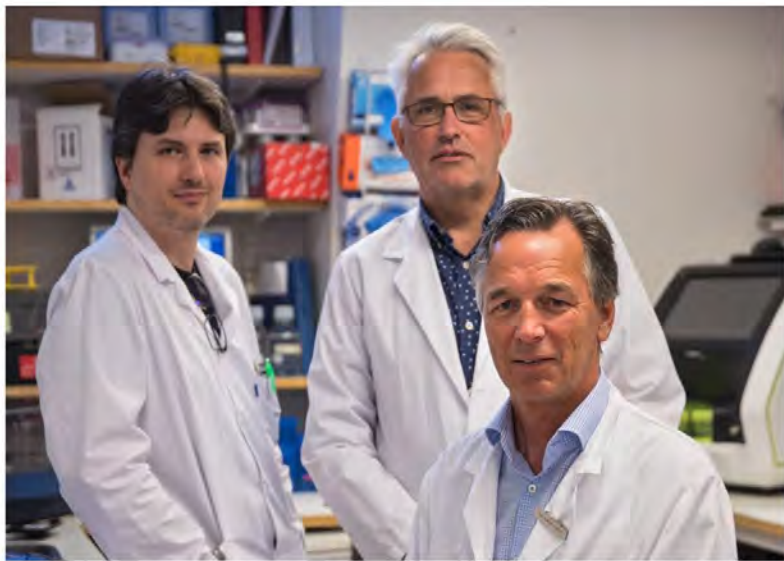
European Sites (10)
Norway: University of Bergen (coordinator), Belgium: KU Leuven,
Denmark: Copenhagen University, Sweden: Linköping and Lund University,
The Netherlands: VUmc Amsterdam, Radboudumc Nijmegen, UMC Utrecht,
Germany: University of Münster, Switzerland: University of Lausanne

North American Sites (5)
Cleveland Clinic, UCLA Los Angeles, University of New Mexico,
The Feinstein Institute for Medical Research New York,
UC San Diego (Imaging Core)

Current data (n = 550)

- 341 patients (15 sites)
- 100+ healthy controls
- 50+ other controls
- MRI and clinical data; before and after ECT

-> aiming at increasing to N= 2000



NYTT HÅP: Et nytt forskingssenter i Bergen skal forske på sykdommer som ALS. Forsker og professor Charalampos Tzoulis, nevrolog og overlege Kjell-Morten Myhr og professor og overlege Ole-Bjørn Tysnes skal lede forskningen. Foto: Gisle Oddstad

Åpner nytt forskingssenter i Bergen: Slik skal de løse ALS-gåten

Computational medicine in the clinic

worms



fish

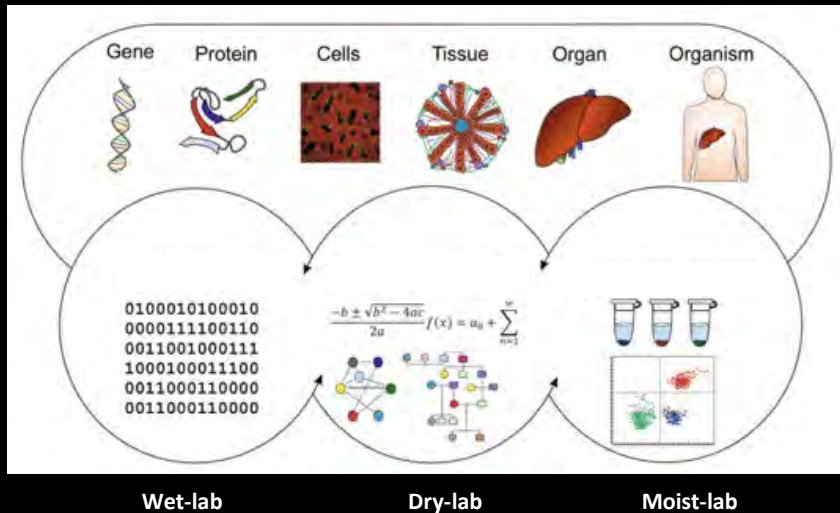


flies

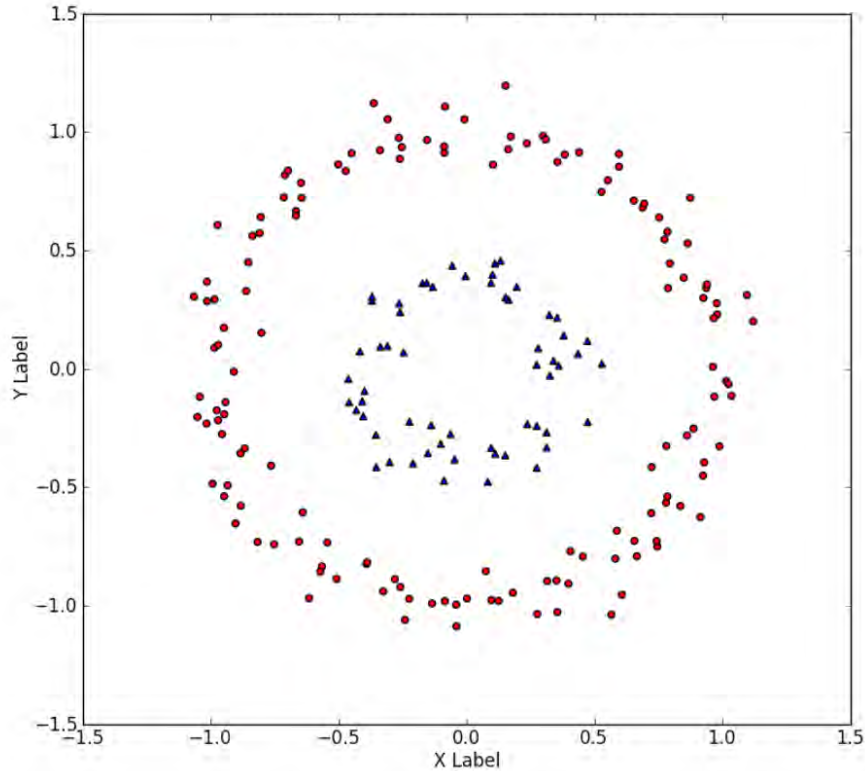


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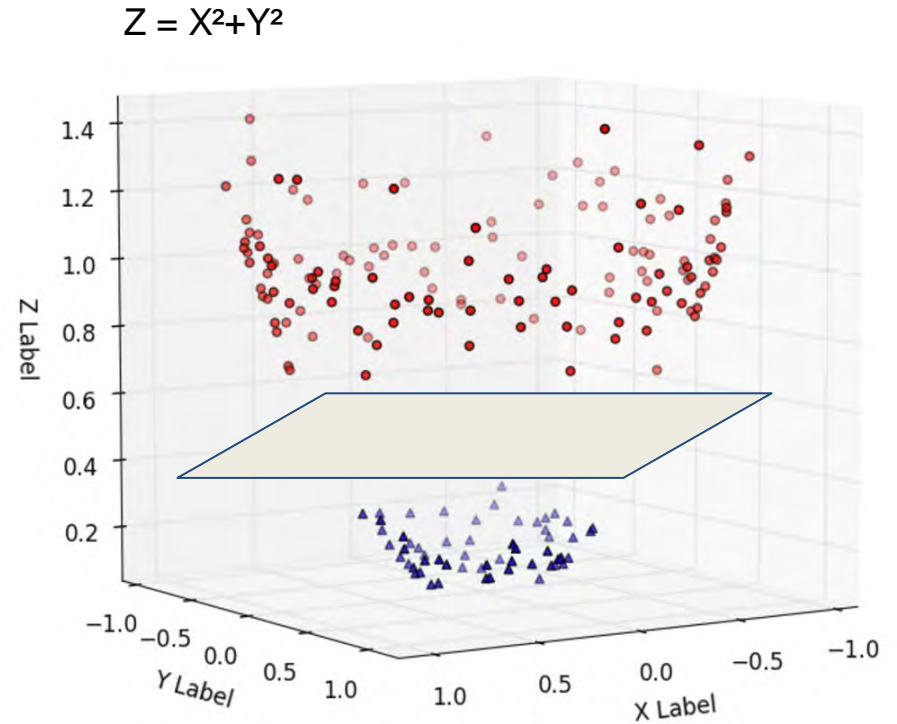
man



Data   in \mathbb{R}^2 linear separable ?



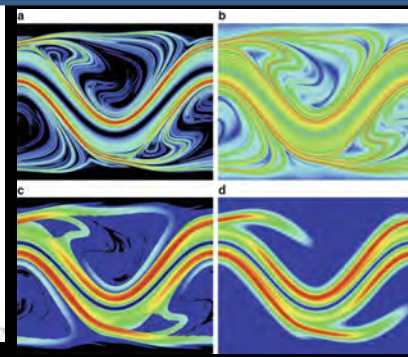
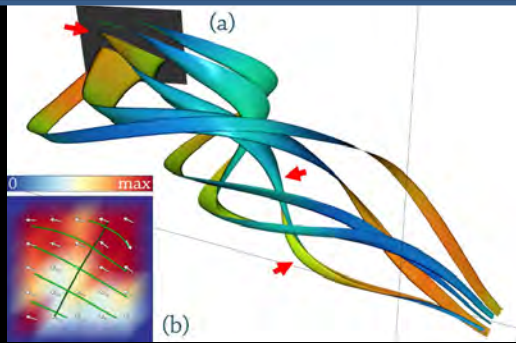
Data linear separable \mathbb{R}^3 !



Flow visualization



PI: Prof. H. Hauser

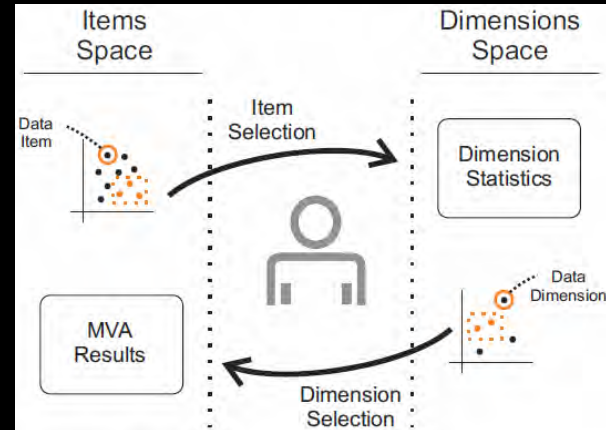


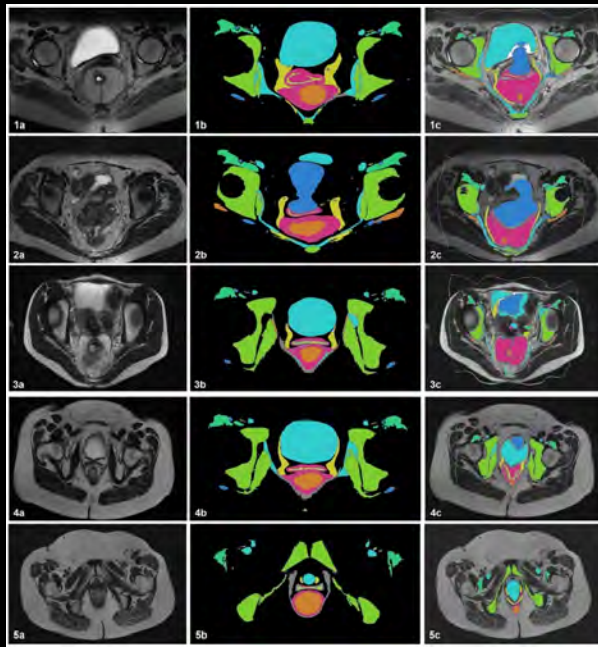
Core MMIV project: Medical Visualization

Research directions:

- Interactive visual analysis
- Visual parameter space analysis
- Visual integration and comparison
- Quantitative visualization
- Smart visual interface

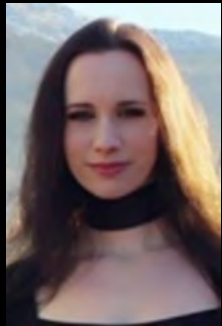
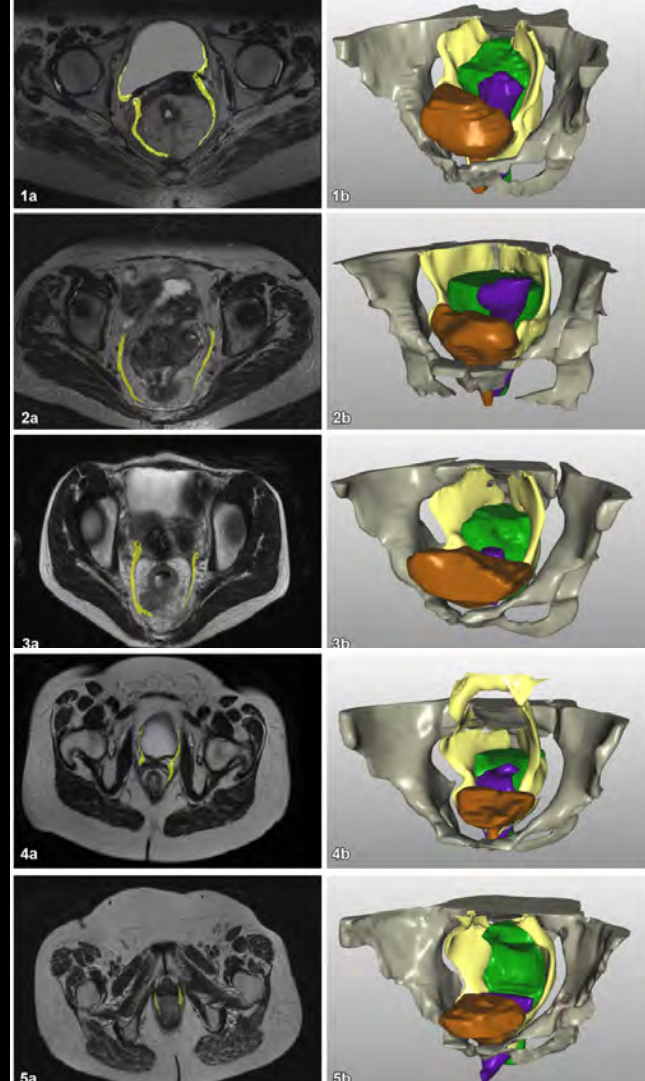
Higher dimensional data visualization





Presurgical:
patient specific 2D/3Dmodels

Medical education:
The online anatomical human
18000users worldwide

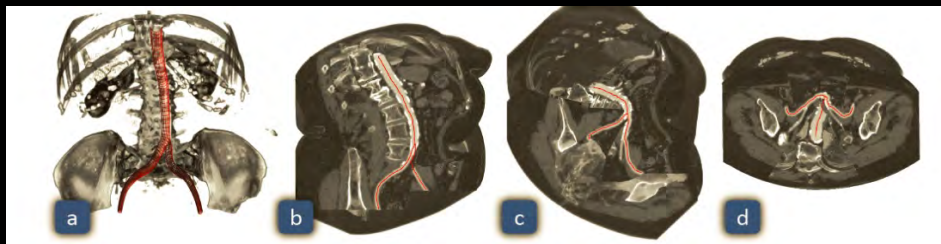


Core MMIV project: Medical Visualization

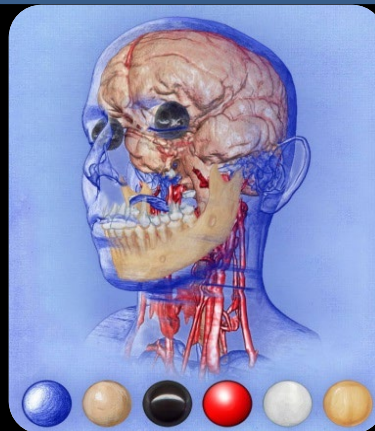
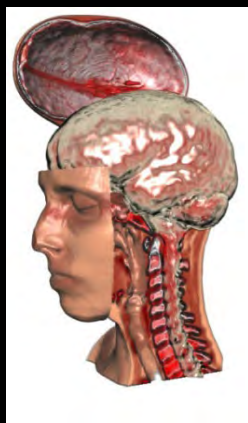
Medical visualization



PI: Prof S Bruckner



Illustrative
visualization





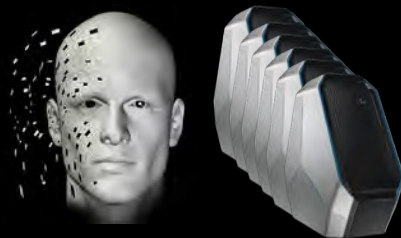
«The amount of change in 20 years is unimaginable, and we need to keep our finger on the pulse of this.»

Bradley Erickson, Mayo Clinic



Summary/ comments

- There is a gap between clinical imaging and research imaging
- Combination of imaging, advanced visualization and machine learning approaches may help bridge this gap. Requires and interdisciplinary agenda
- Infrastructure limitations (data integration, system integration, HPC). Information from registries, clinical information, extractions from EPJ.
- Limitations in regulatory framework (ethical and social risk/benefit assessment). Optimize solution for deidentification/ Safe handling of data. Share technical solutions (eg training in machine learning) rather than data?





URL: <http://www.mmiv.no>

Thank you for your attention!

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