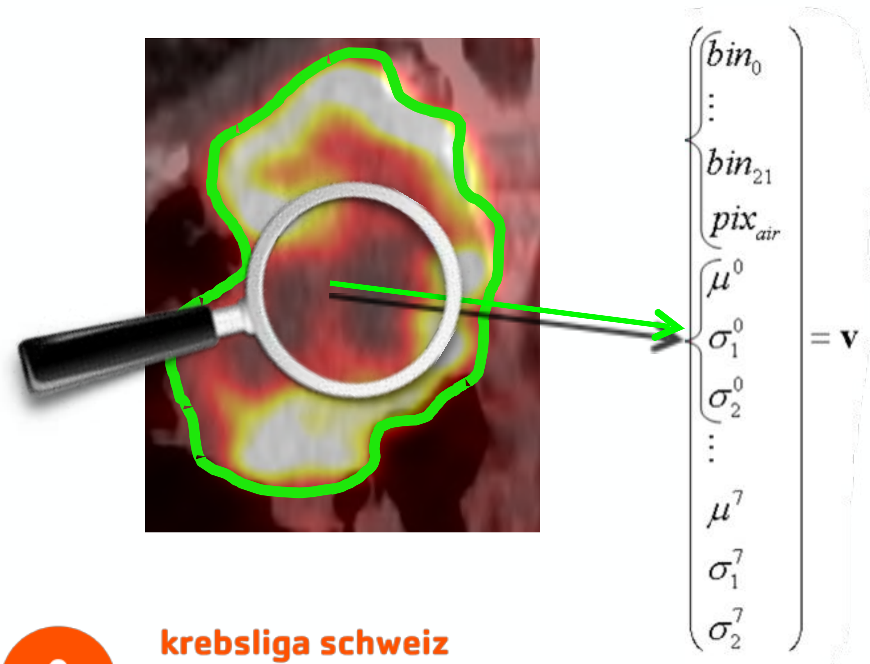
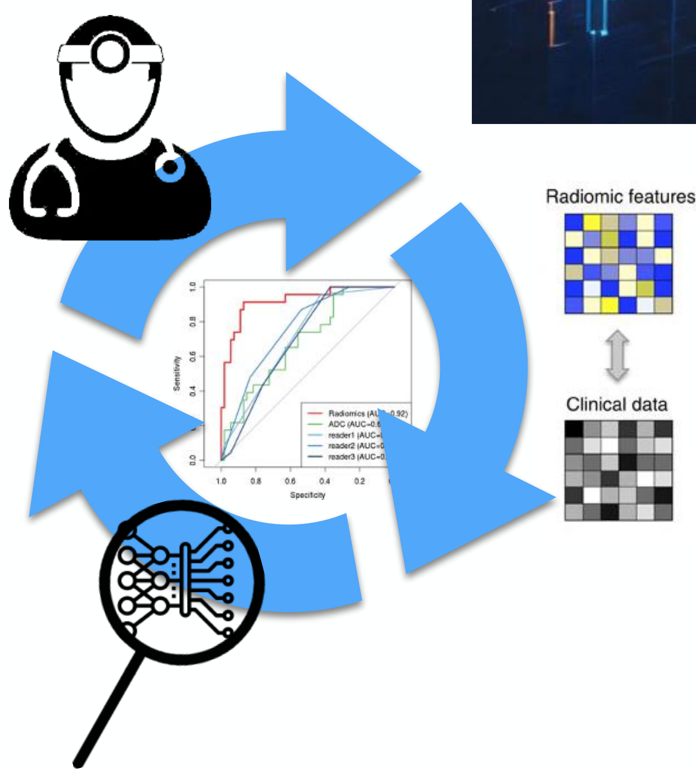
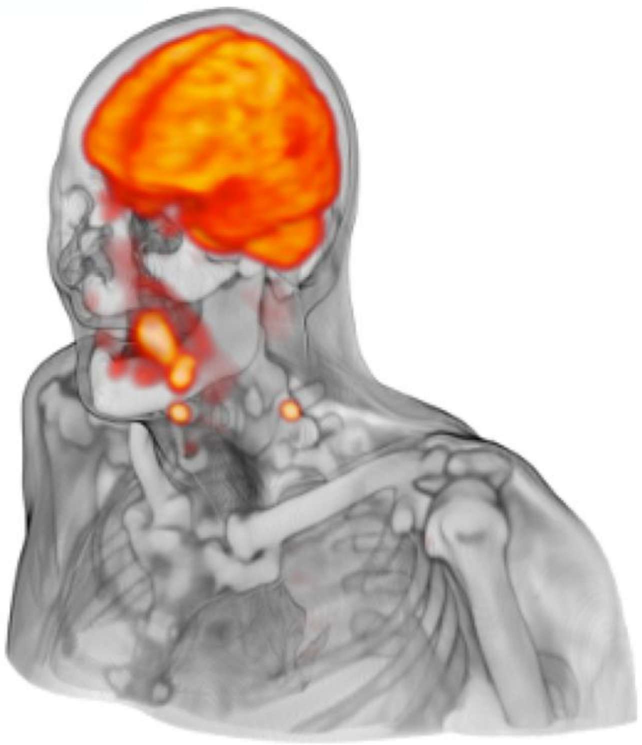
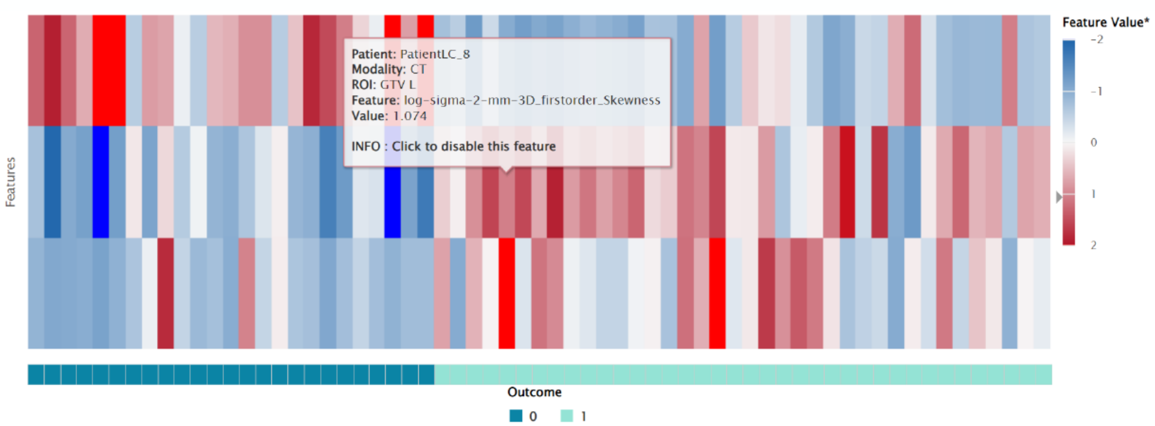
TRUSTWORTHY IMAGE-BASED AI FOR PERSONALIZED MEDICINE AND CLINICAL RESEARCH

Adrien Depeursinge
adrien.depeursinge@hevs.ch









krebsliga schweiz
ligue suisse contre le cancer
lega svizzera contro il cancro

HASLERSTIFTUNG

SNSF

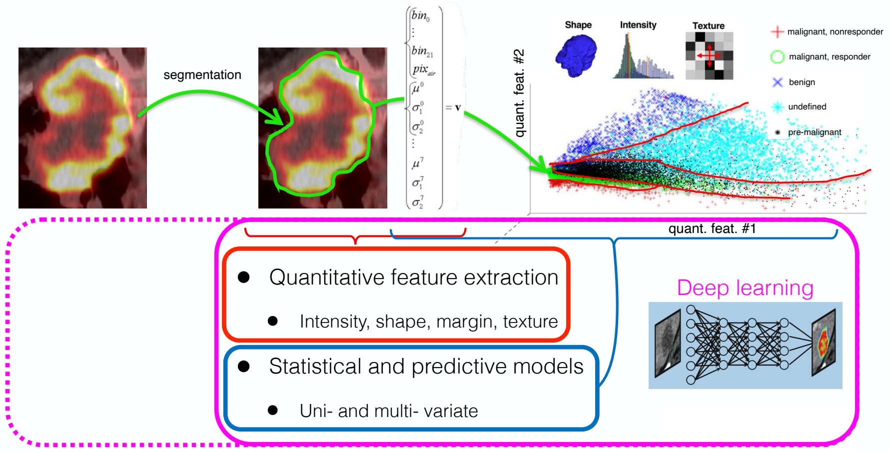
CHUV

SPHN

Hes·so VALAIS WALLIS

AGENDA

- Personalized medicine
- Artificial Intelligence (AI) for medical image analysis
  - Deep learning and Radiomics
    - Fundamentals
    - Addressed tasks
    - Clinical certification status



- Selected contributions from the CHUV/HES-SO ecosystem
  - The QuantImage v2 platform
  - The HECKTOR challenge
  - Explainable models for multiple sclerosis: MSxplain
- Conclusions

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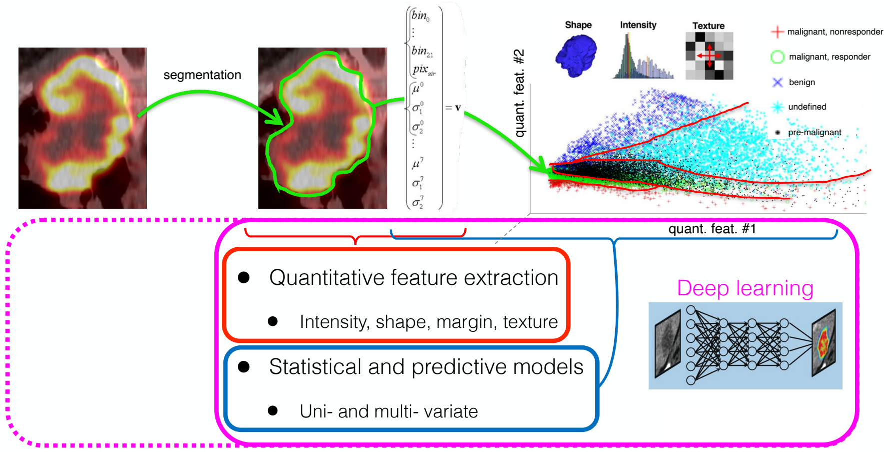

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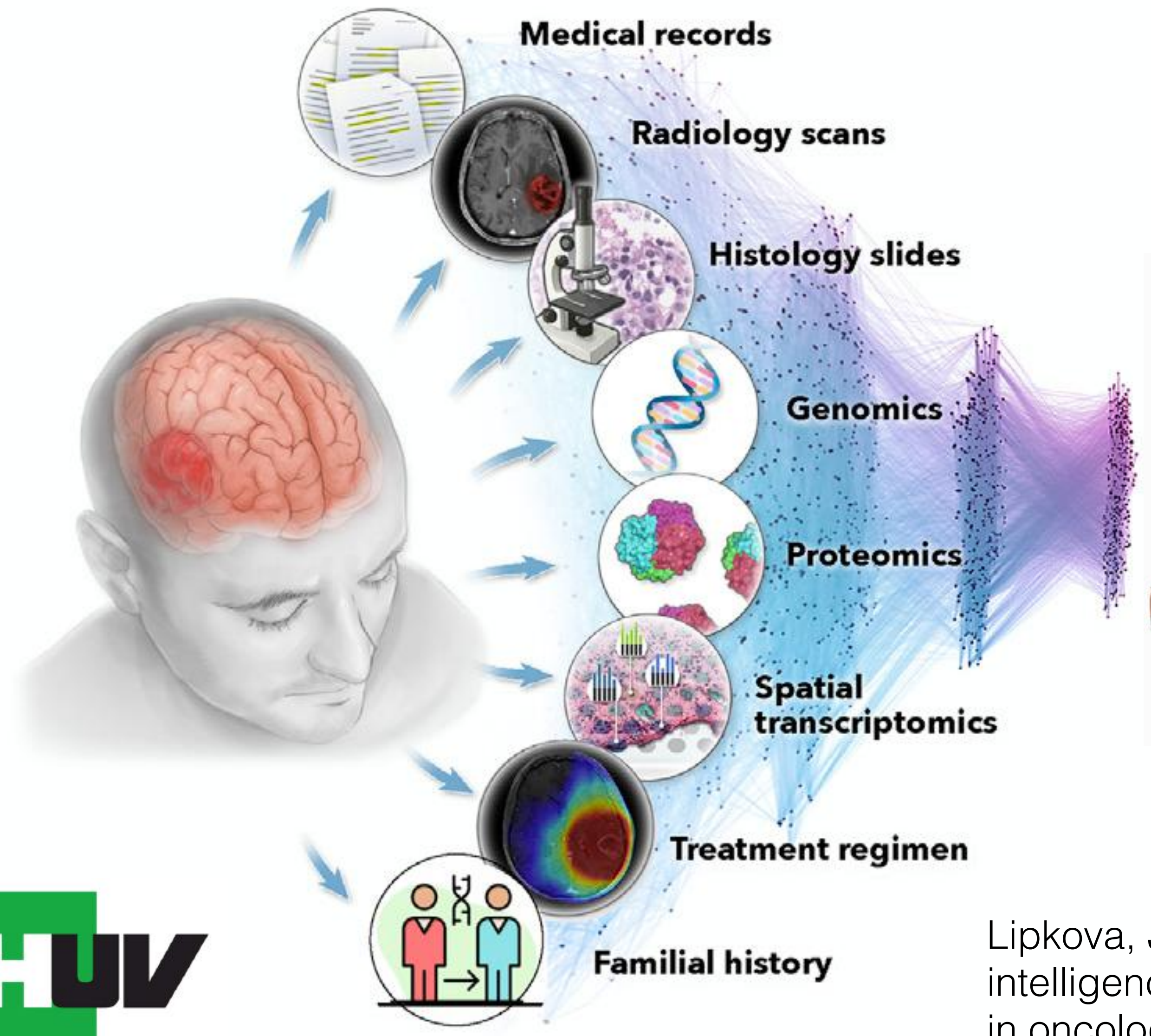
Personalized Medicine

- Goals: (A) Identify the state of a patient-disease pair and (B) Establish optimal treatment plan
- Method: Compare to previously documented cases/guidelines in terms of multimodal data

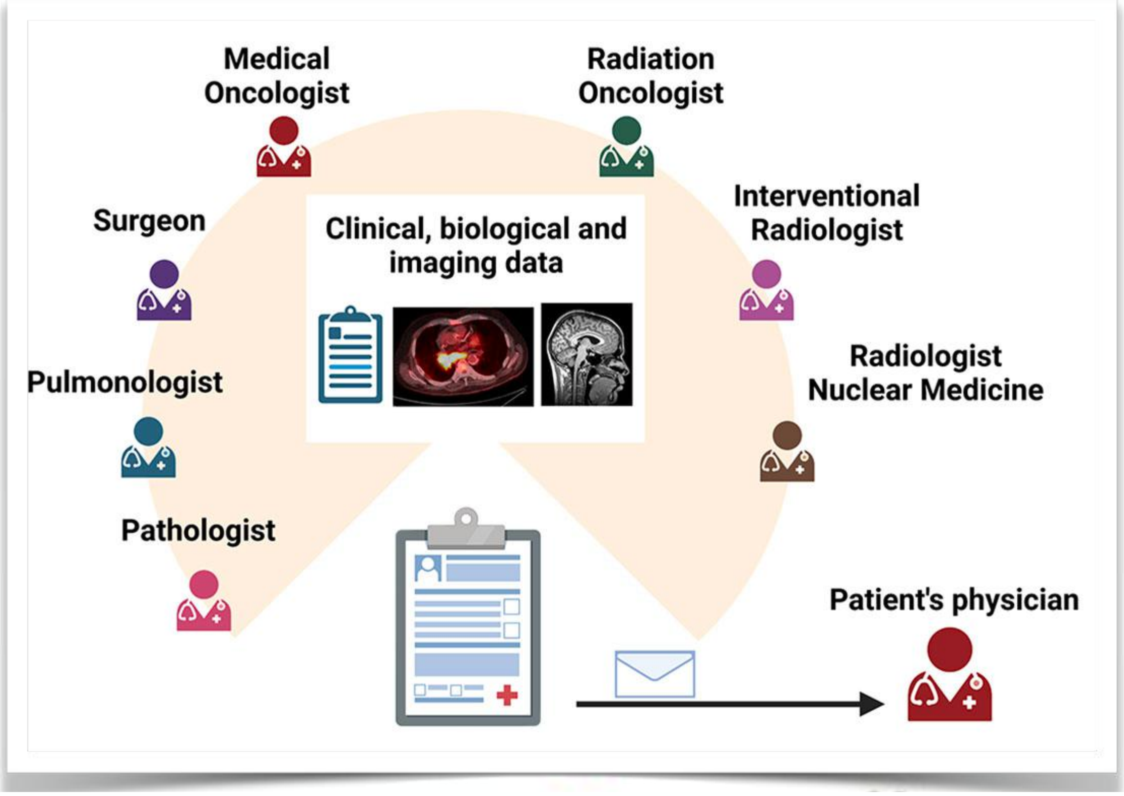


- Diagnosis
- Prognosis
- Survival
- Treatment response
- Treatment toxicity
- Recurrence
- Risk stratification
- Side effects
- ...

Lipkova, J et al. (2022) Artificial intelligence for multimodal data integration in oncology. Cancer Cell,10(40).

Personalized Medicine

- Goals: (A) Identify the state of a patient-disease pair and (B) Establish optimal treatment plan
- Method: Compare to previously documented cases/guidelines in terms of multimodal data
  - E.g. Multidisciplinary Tumor Boards (MTB)
    - Currently mostly based on guidelines and experience, confronted across medical/technical specialties
    - Since ~1995



https://www.ilcn.org/multidisciplinary-tumor-boards-six-eyes-see-more-than-two/, Feb 2024

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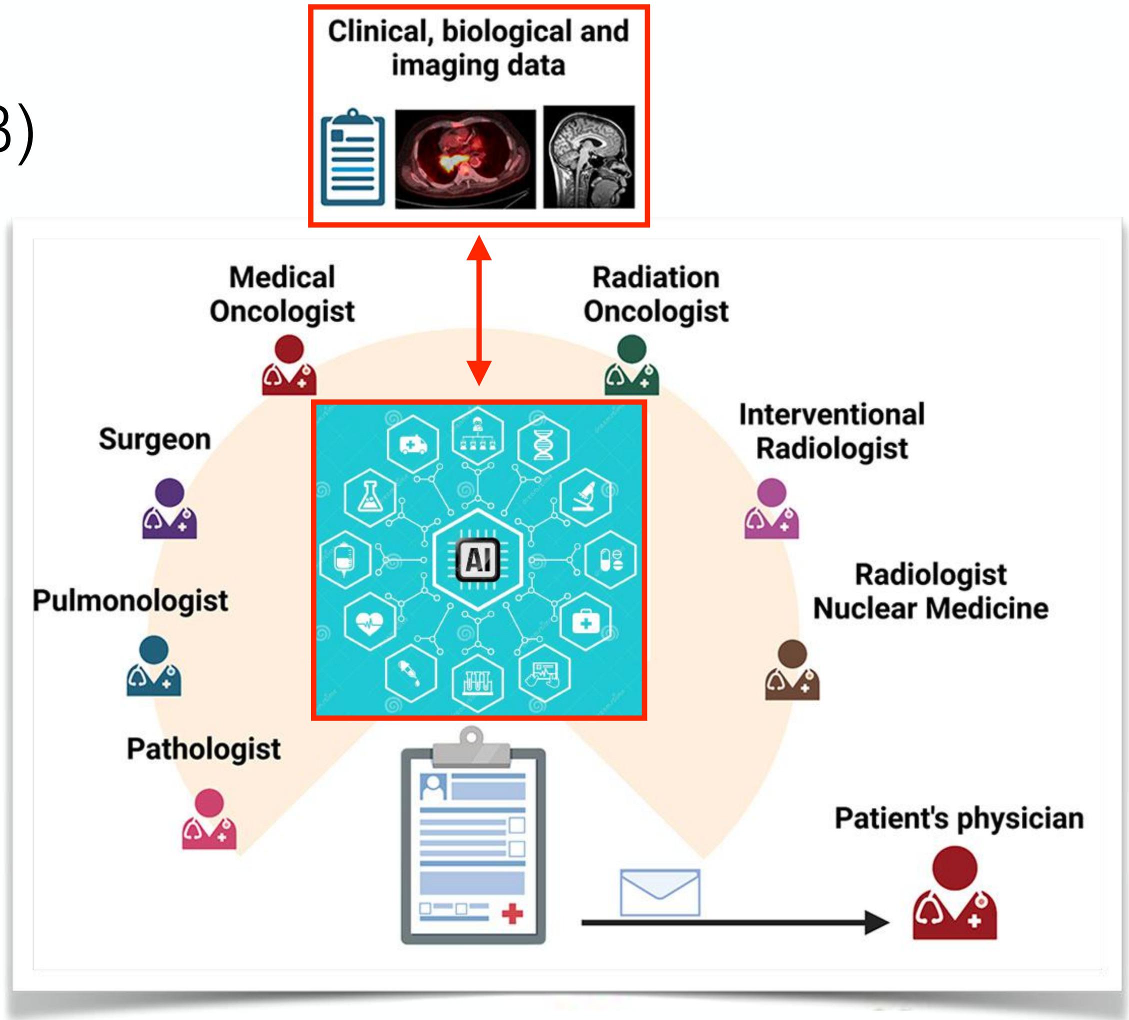
- Method: Compare to previously documented cases/guidelines in terms of multimodal data
  - E.g. Multidisciplinary Tumor Boards (MTB)
    - Currently mostly based on guidelines and experience, confronted across medical/technical specialties
    - Tomorrow: AI-augmented medical information systems for multimodal information aggregation



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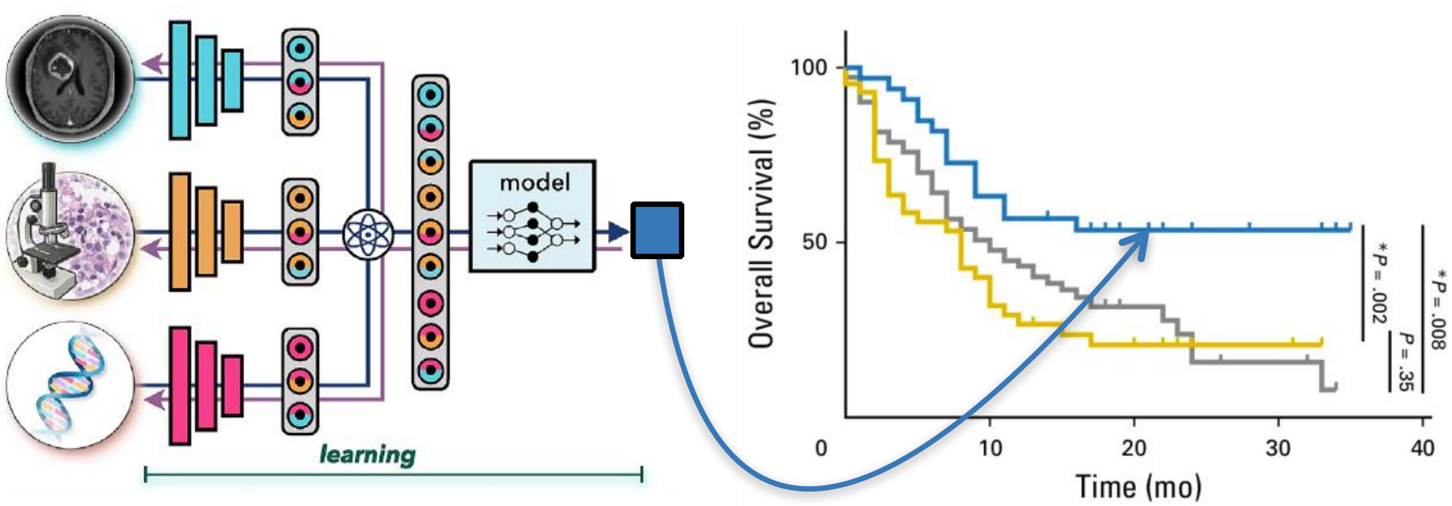
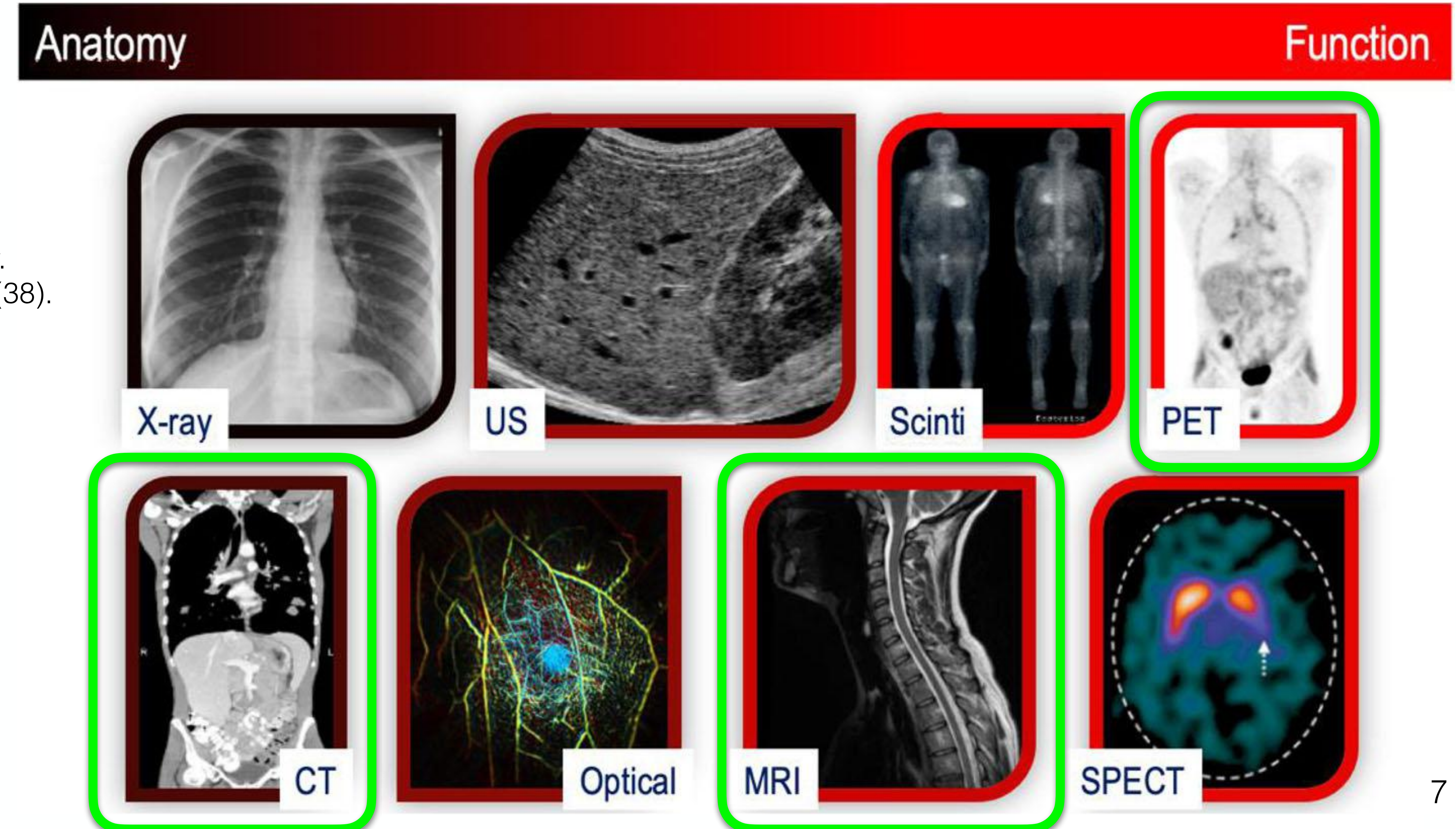


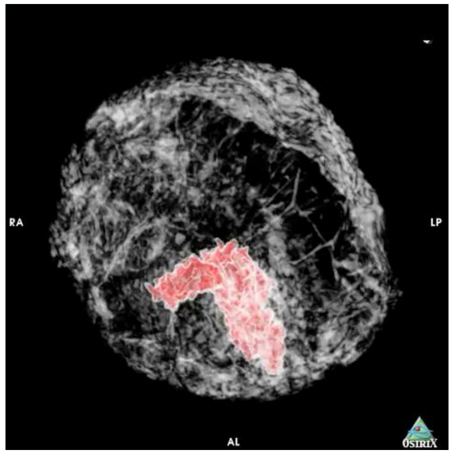
Clinical Imaging

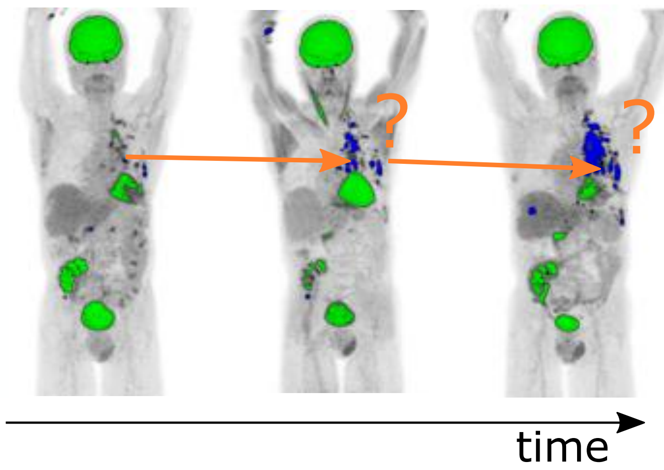
- Medical imaging has a central role for diagnosis, staging and to assess treatment response
- Observing anatomical, morphological and functional characteristics of organs and lesions in many dimensions

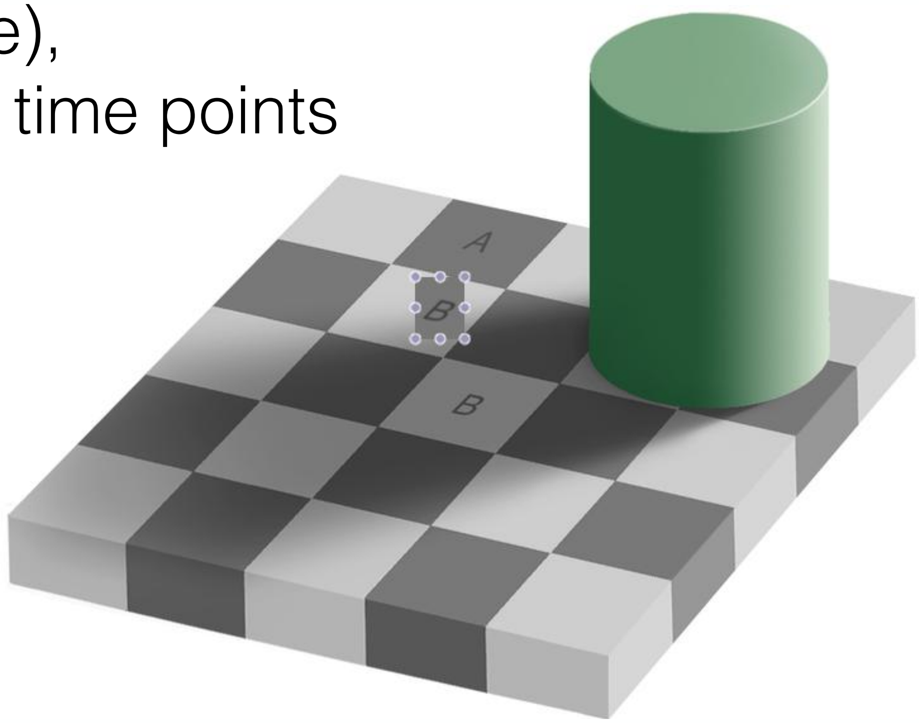
Beyer, T et al. (2020) What scans we will read: imaging instrumentation trends in clinical oncology. BMC Cancer Imaging, 20(38).



- Medical imaging has a central role for diagnosis, staging and to assess treatment response
- "Images Are More than Pictures, They Are Data"
  Gillies RJ et al. (2016) Radiomics: Images Are More than Pictures, They Are Data. Radiology, 278(2).
  - Multi-dimensional, quantitative (relative or absolute), complex tissue architectures, multiple lesions and time points







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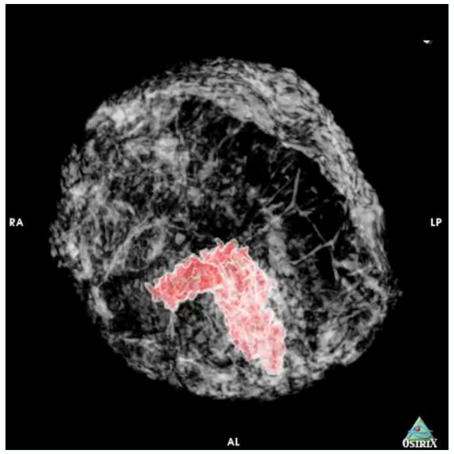
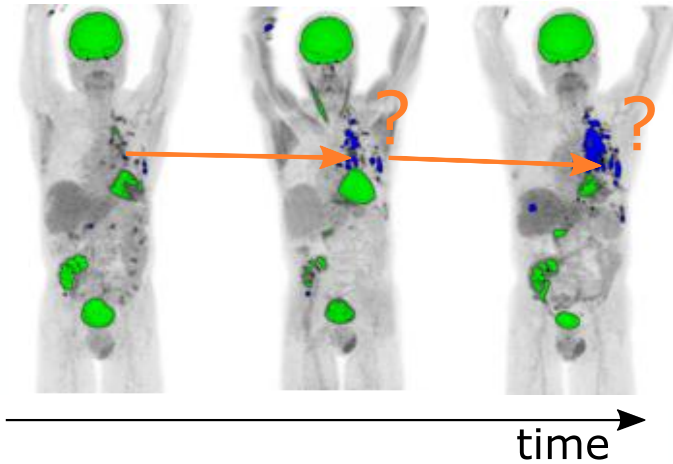
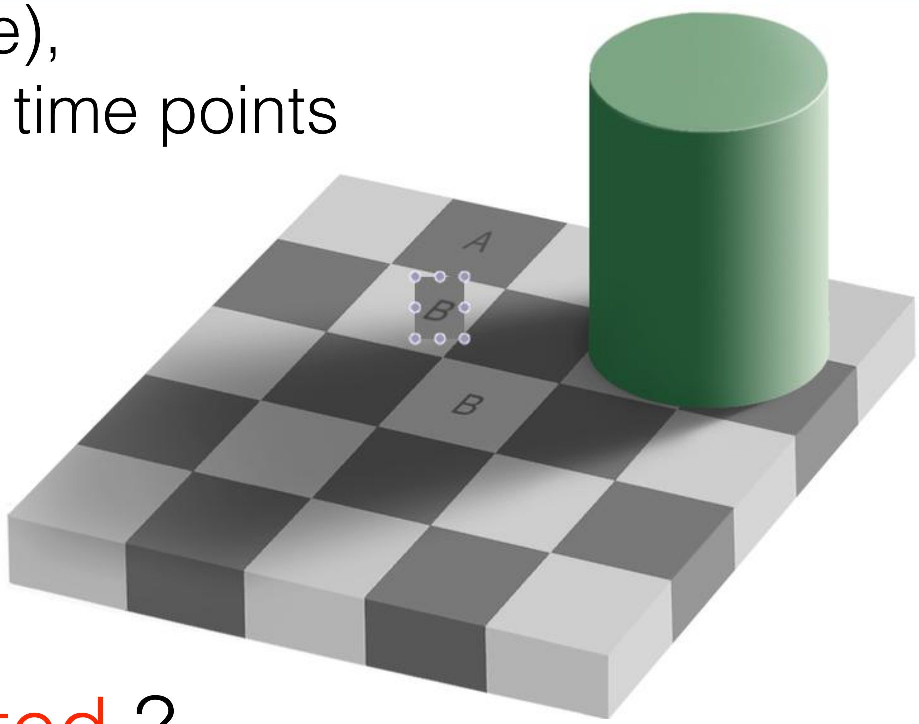
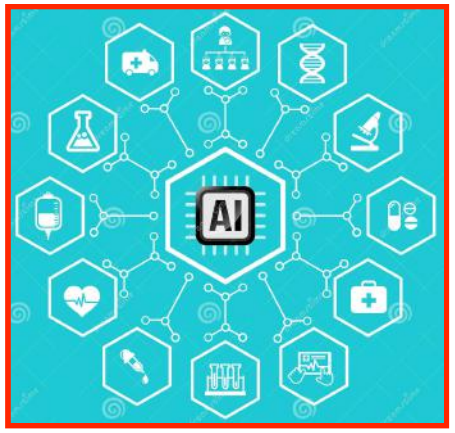






- Are clinical images currently underexploited ?
- Can AI help digesting multimodal, multidimensional, and multilesional quantitative imaging (in time series) and link them with other omics ?



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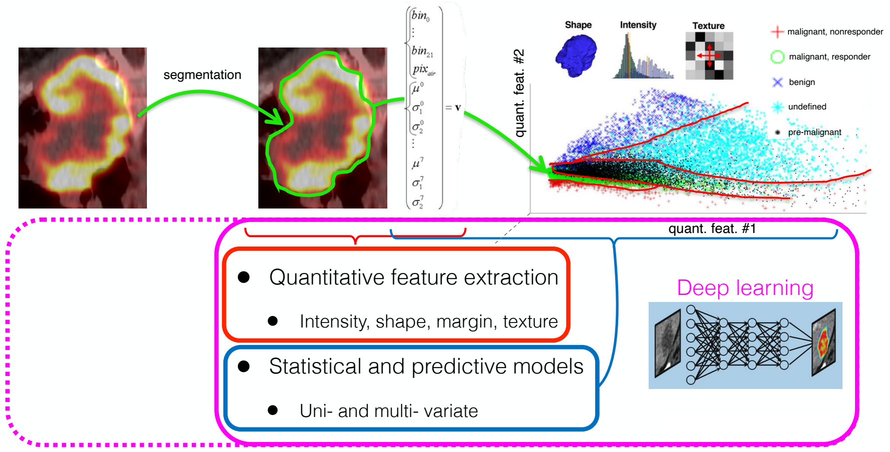

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IMAGE-BASED AI FOR PRECISION MEDICINE

- AI/ML-enabled medical software in Radiology and Nuc. Med.
  - Tasks

"Radiomics" for precision medicine:

(Huang et al. 2022)

- survival analysis
- outcome prediction
- diagnosis
- toxicity
- monitoring ("delta radiomics")

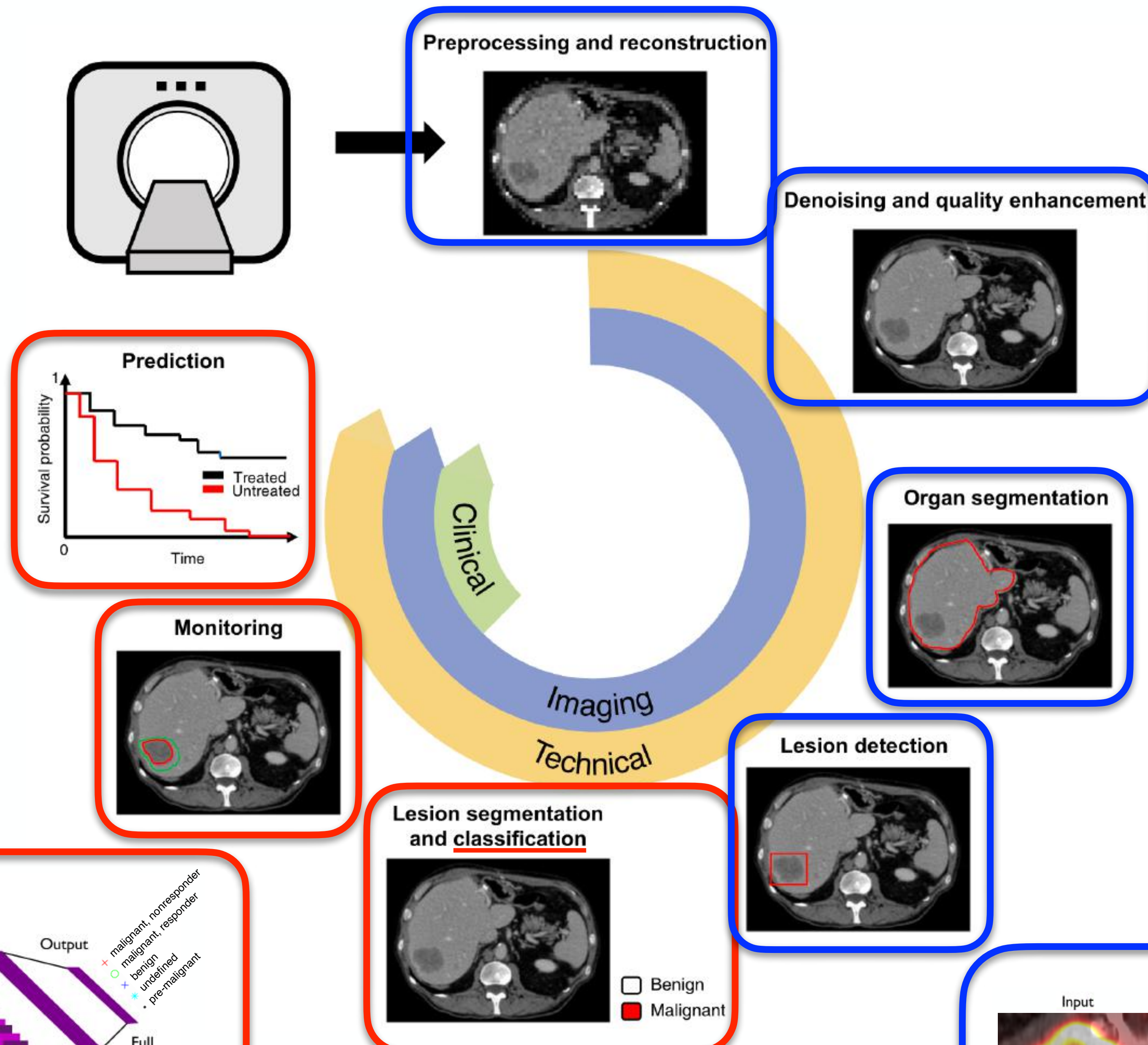
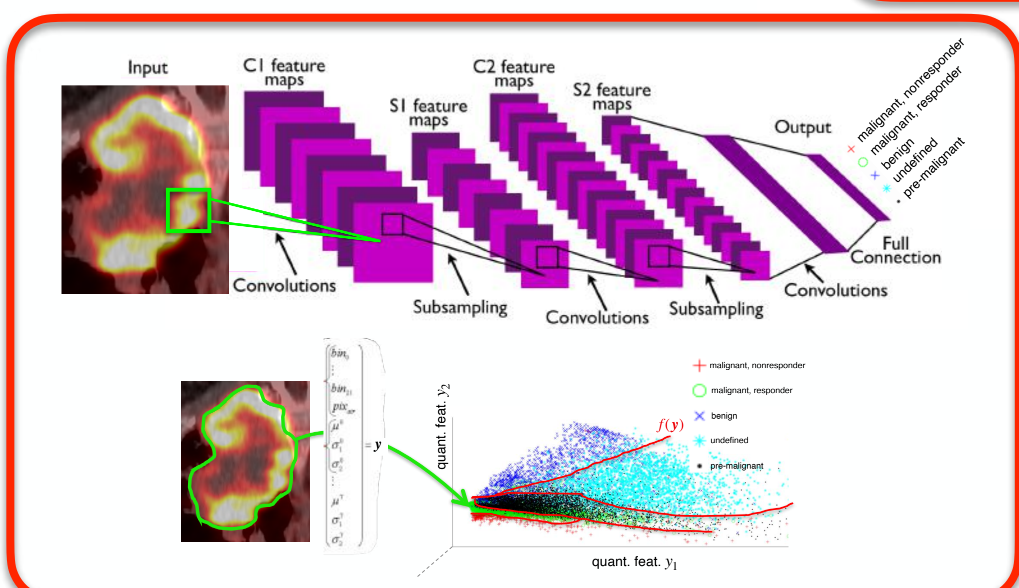


Image to prediction



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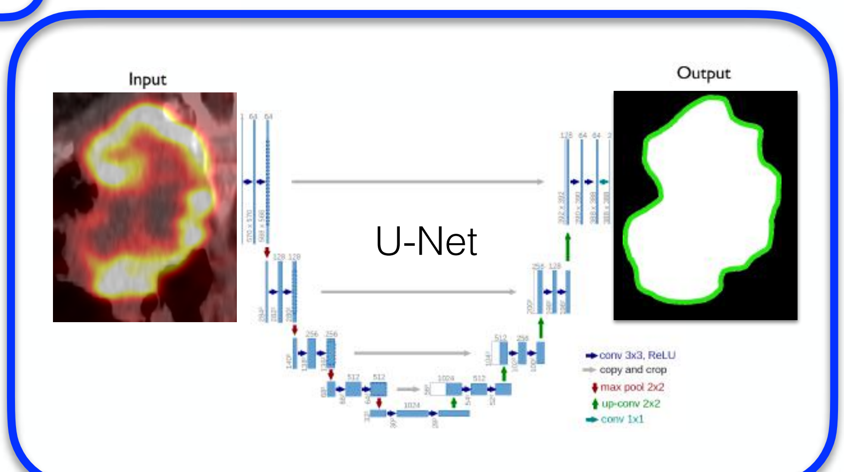

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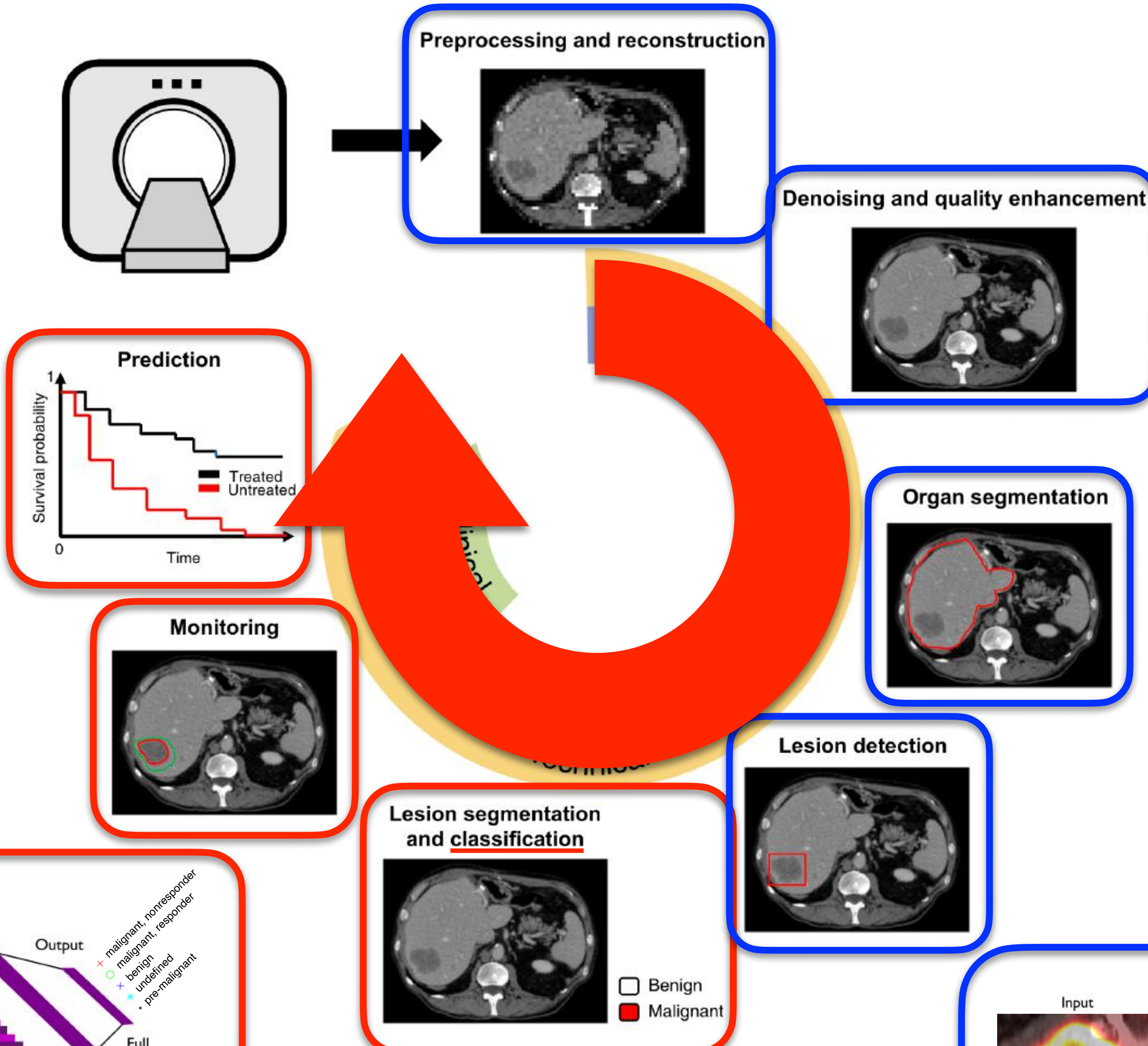

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Increasingly difficult tasks:

increasingly less observations when computing training losses

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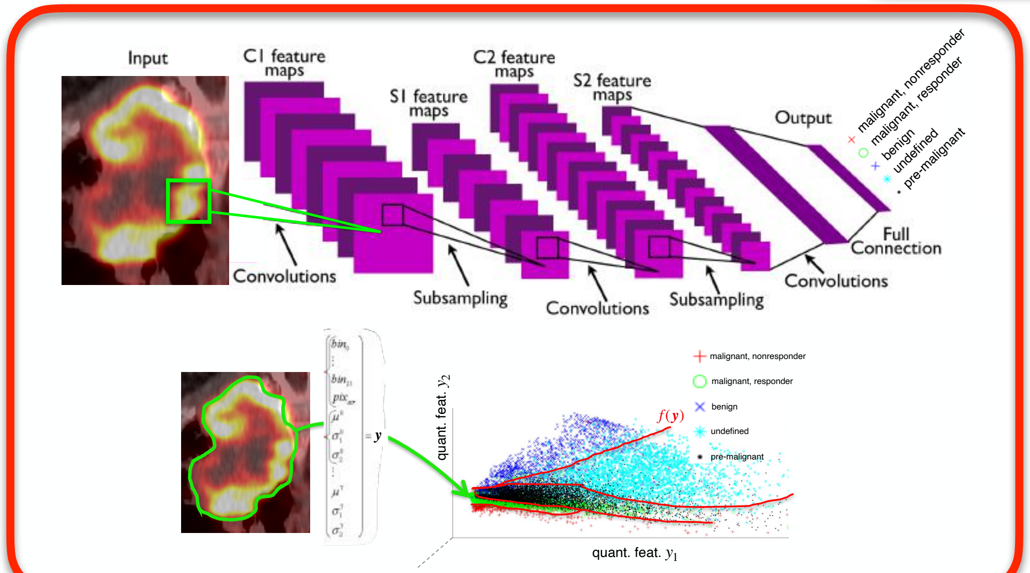

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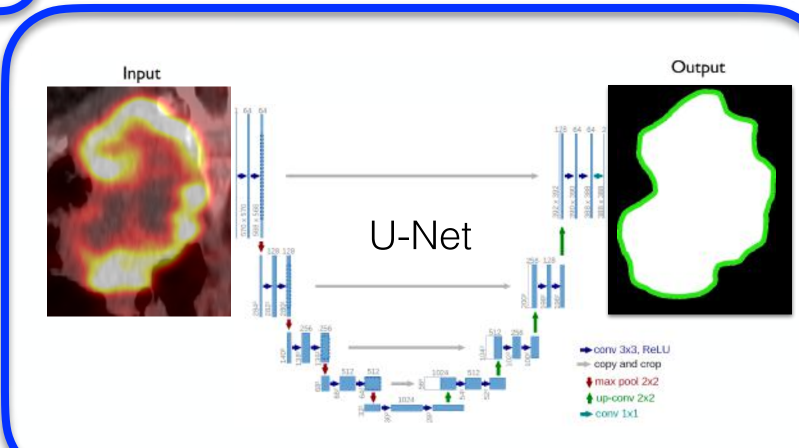

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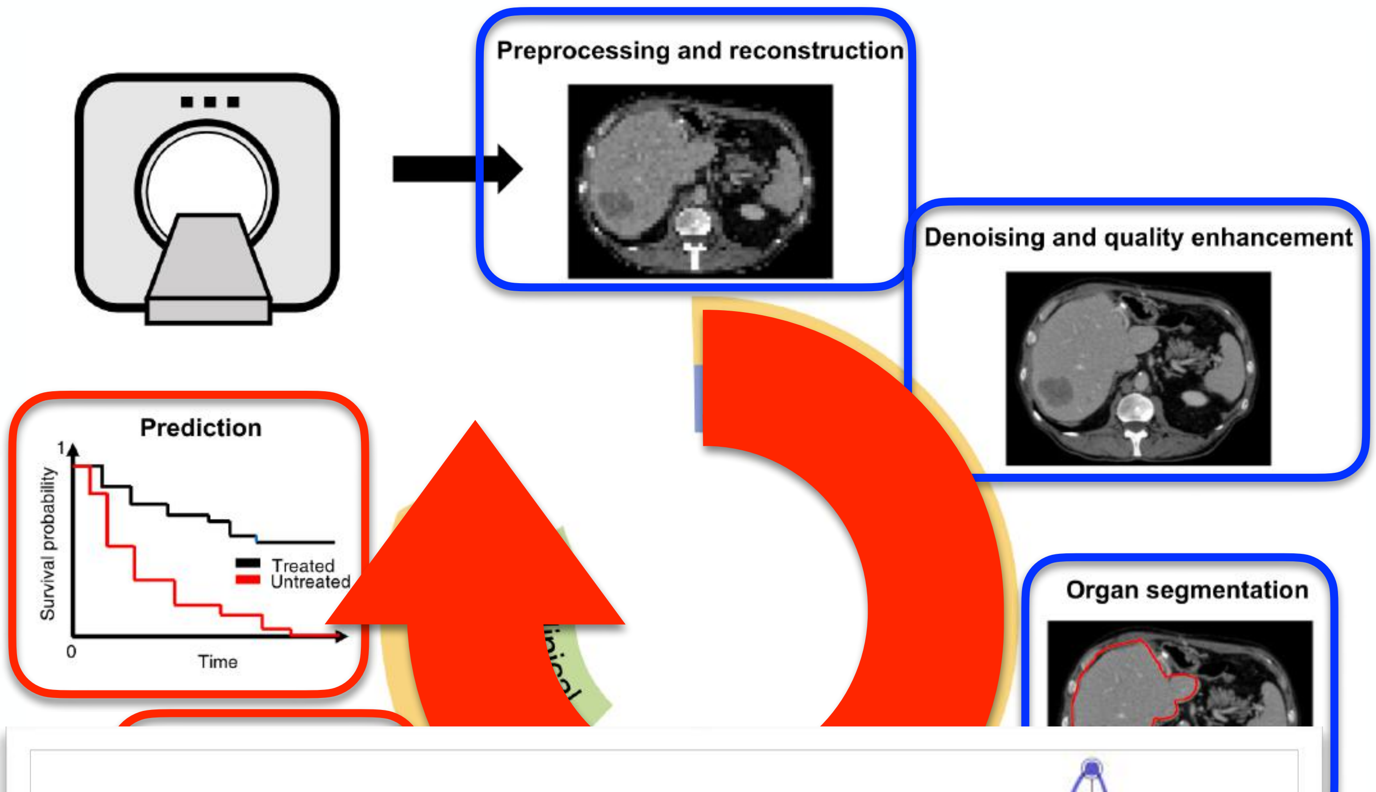

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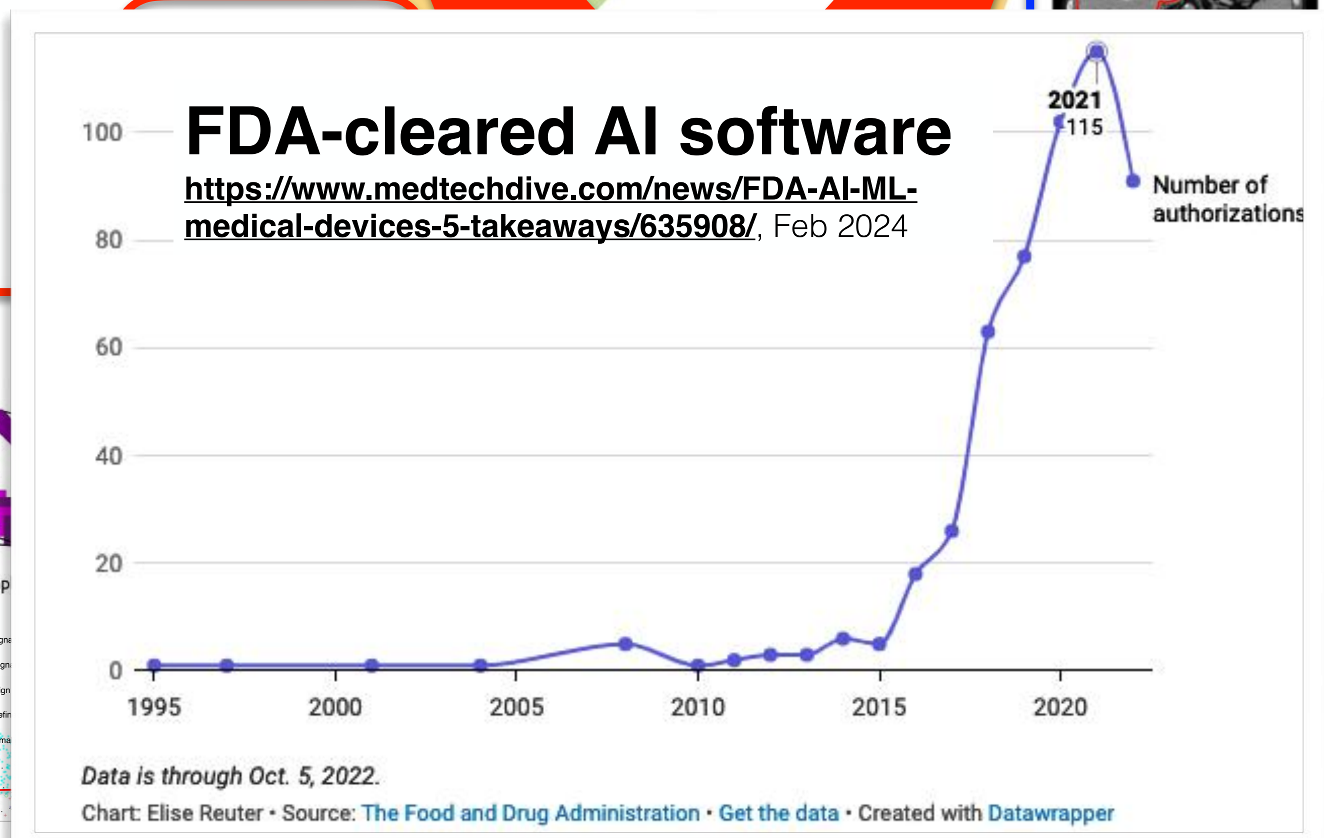

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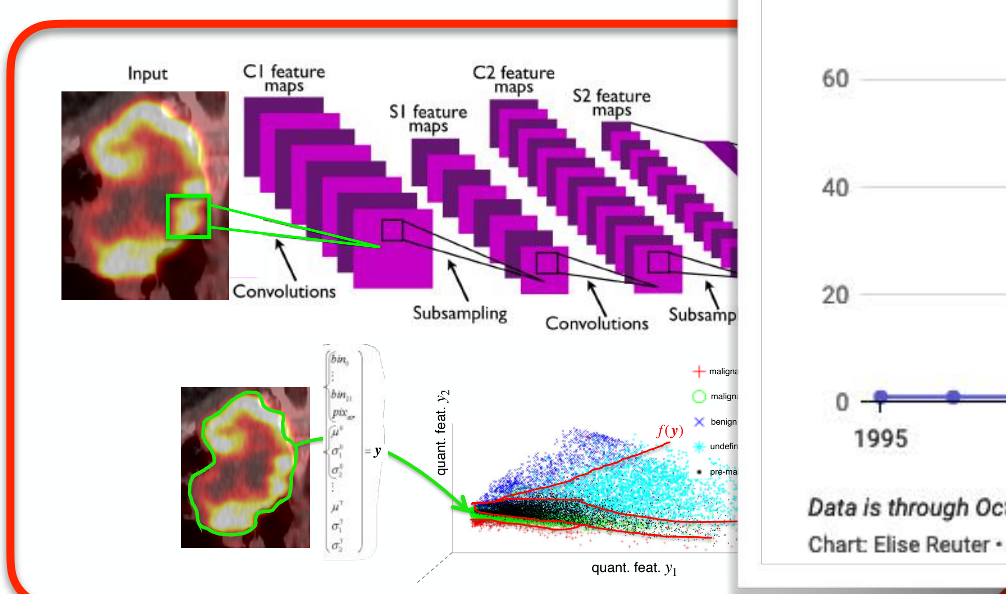

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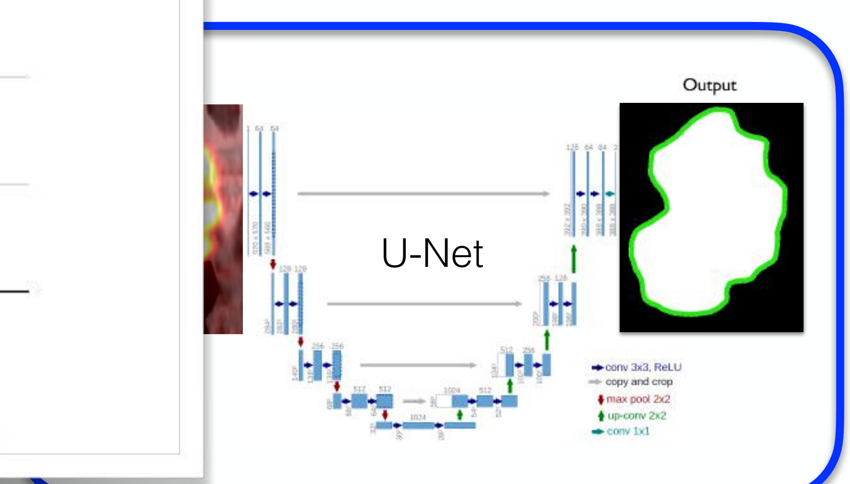
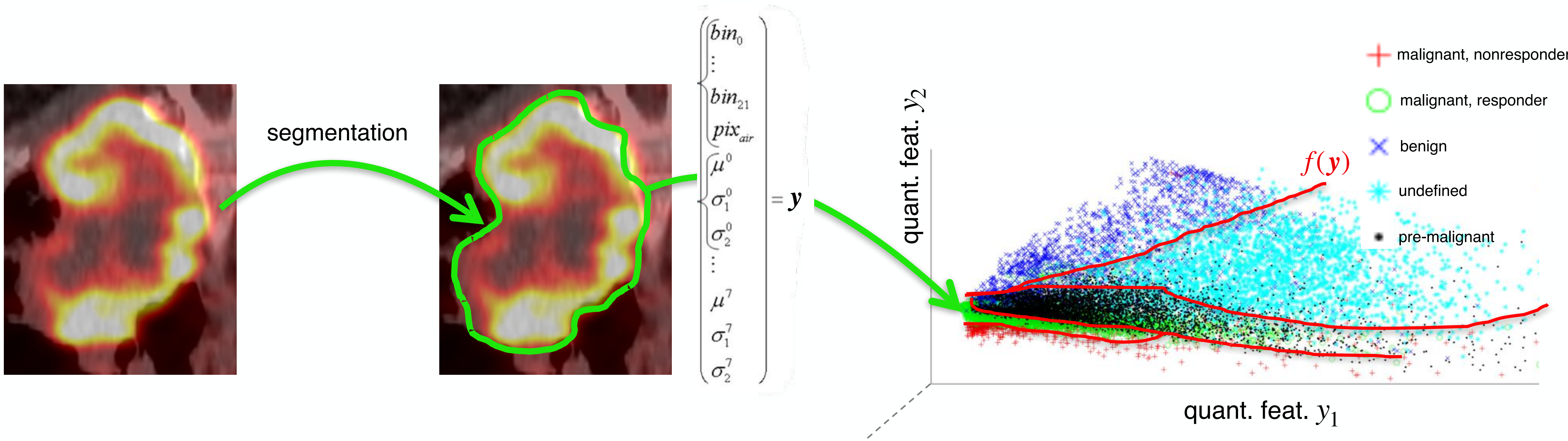


- Segmentation and outcome prediction

Kumar et al. (2012) Radiomics: the process and the challenges. Magn Res Imag, 30(9)

  - Quantitative approach to explore and reveal tissue structures related to relevant clinical endpoints …. in a non-invasive fashion !



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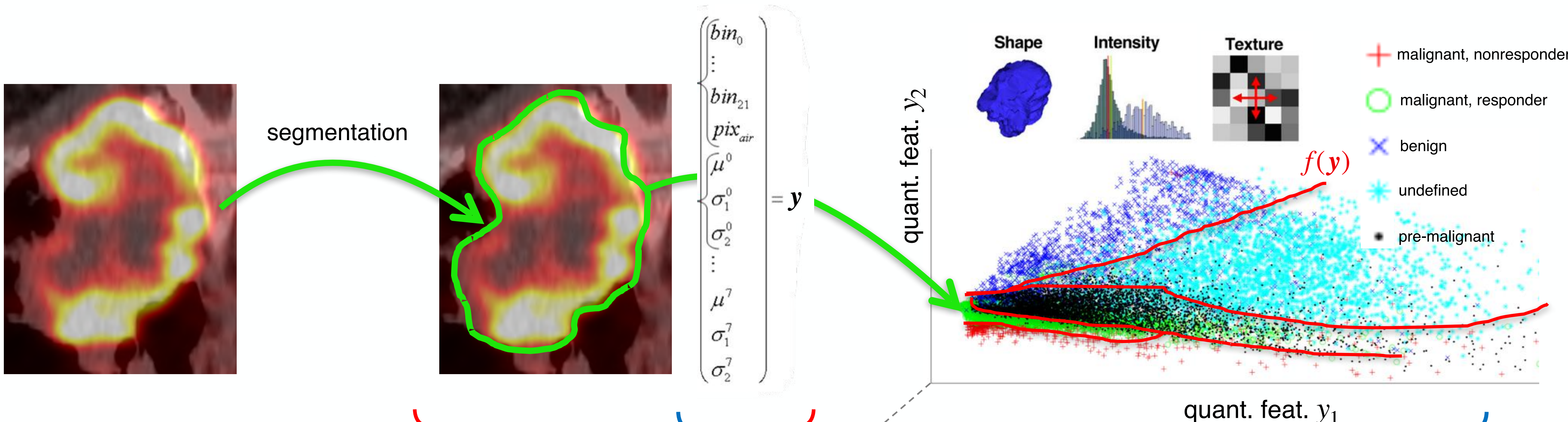

- Quantitative feature extraction
  - Intensity, shape, texture

- Statistical and predictive models
  - Uni- and multi- variate

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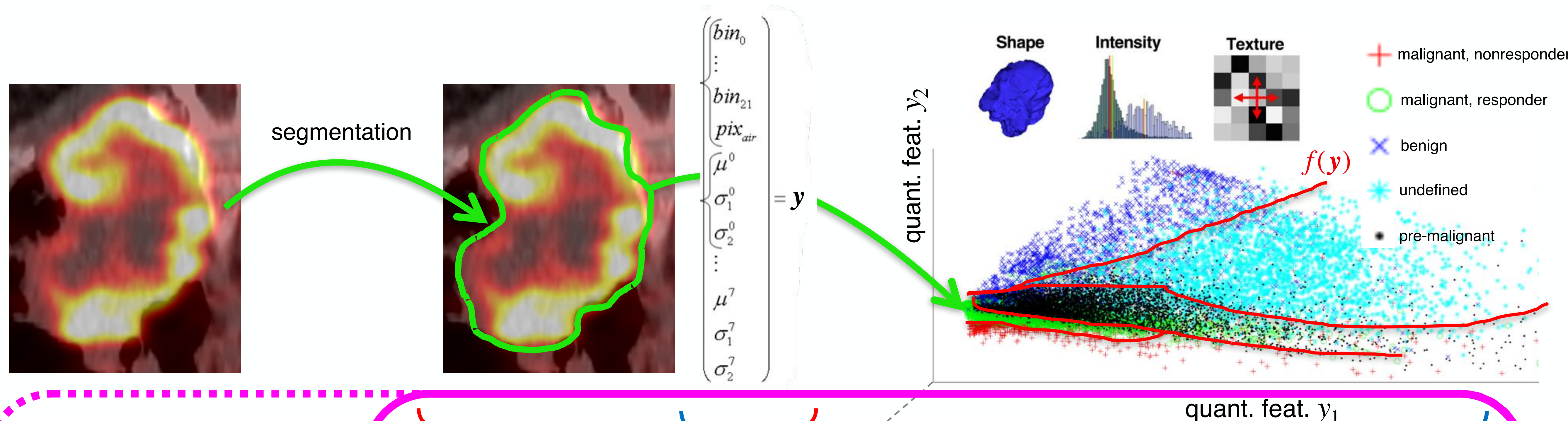

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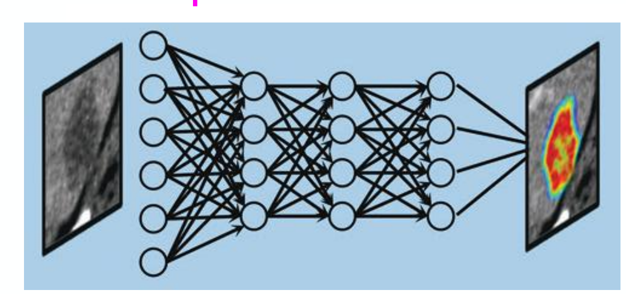
"deep radiomics"



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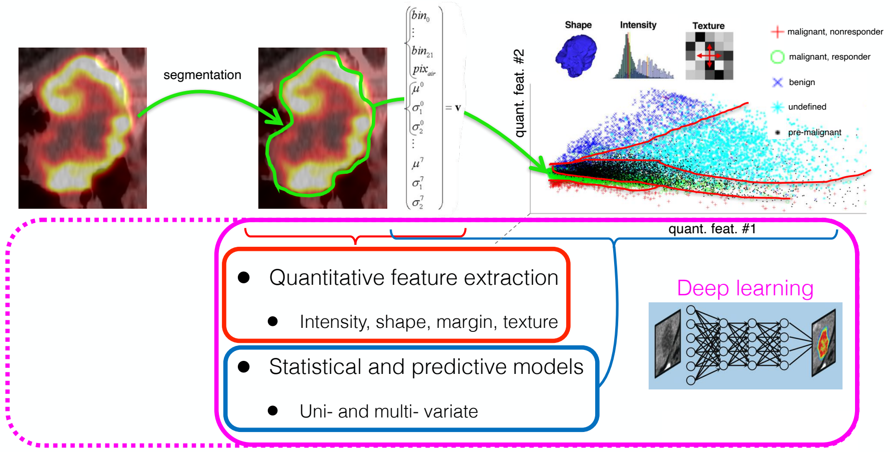

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Radiomics @ CHUV/HES-SO

Principal investigators:

- Prof. John O. Prior
- Prof. Niklaus Schaefer
- Prof. Clarisse Dromain
- Prof. Adrien Depeursinge
- Dr. Jonas Richiardi
- Dr. Mario Jreige
- Dr. Michel Cuendet
- Dr. Naïk Vietti-Violi
- Dr. Vincent Dunet
- Dr. Vincent Andrearczyk
- Dr. Daniel Abler
- Dr. Luis Schiappacasse
- Dr. Meritxell Bach Cuadra
- ~ 25 people, since 2018

Objectives:

- Investigate and validate links between quantitative imaging (deep/handcrafted) and clinical endpoints
- Optimize cost-effectiveness and value of clinical imaging
- Research infrastructure development (DICOM management, segmentation, image analysis, model building and validation)

Studies:

- Onco: Head & Neck, Brain Melanoma, Lung, Liver, …
- Other: Myocardial Perf., Mult. Sclerosis, Pancreatitis, …

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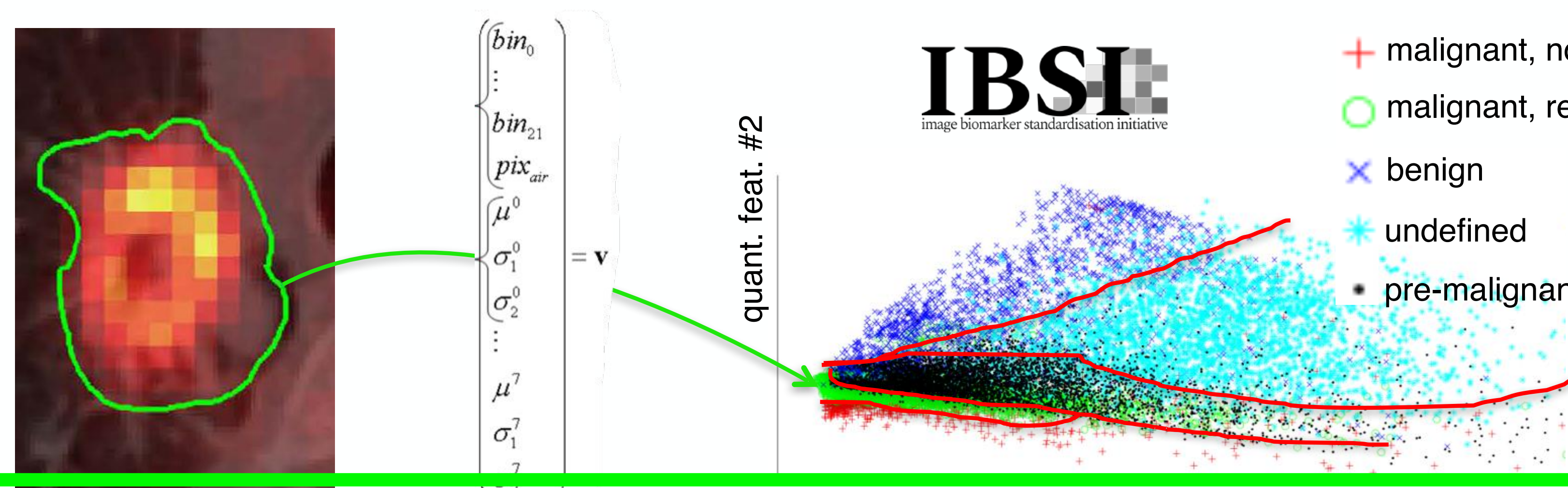
IBSI
image biomarker standardisation initiative



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Quantitative features: intensity, shape, texture

Predictive modeling: statistical, machine learning

Deep learning

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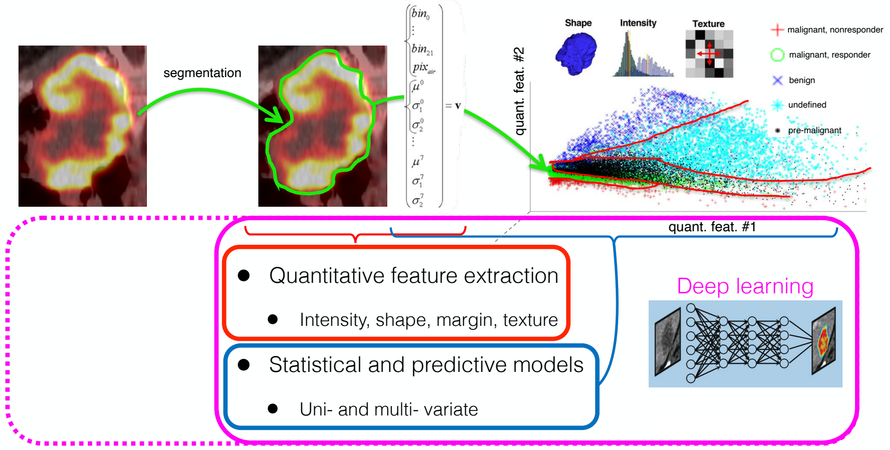

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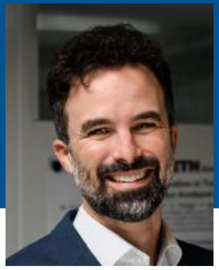
QUANTIMAGE V2


D. Abler

R. Schaer

V. Oreiller

J. Młynar

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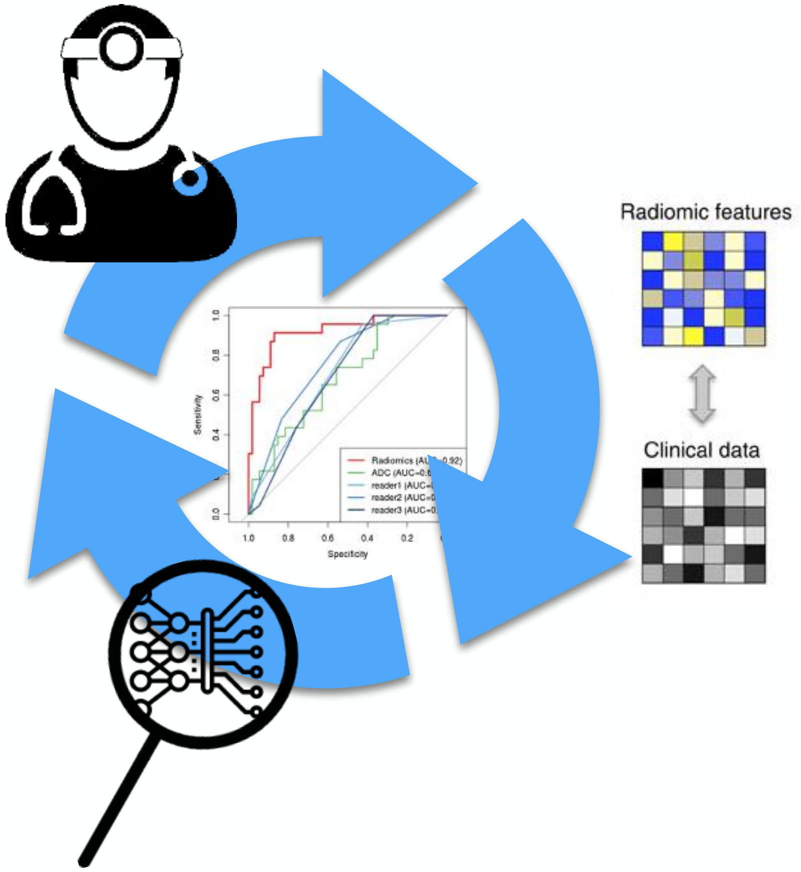
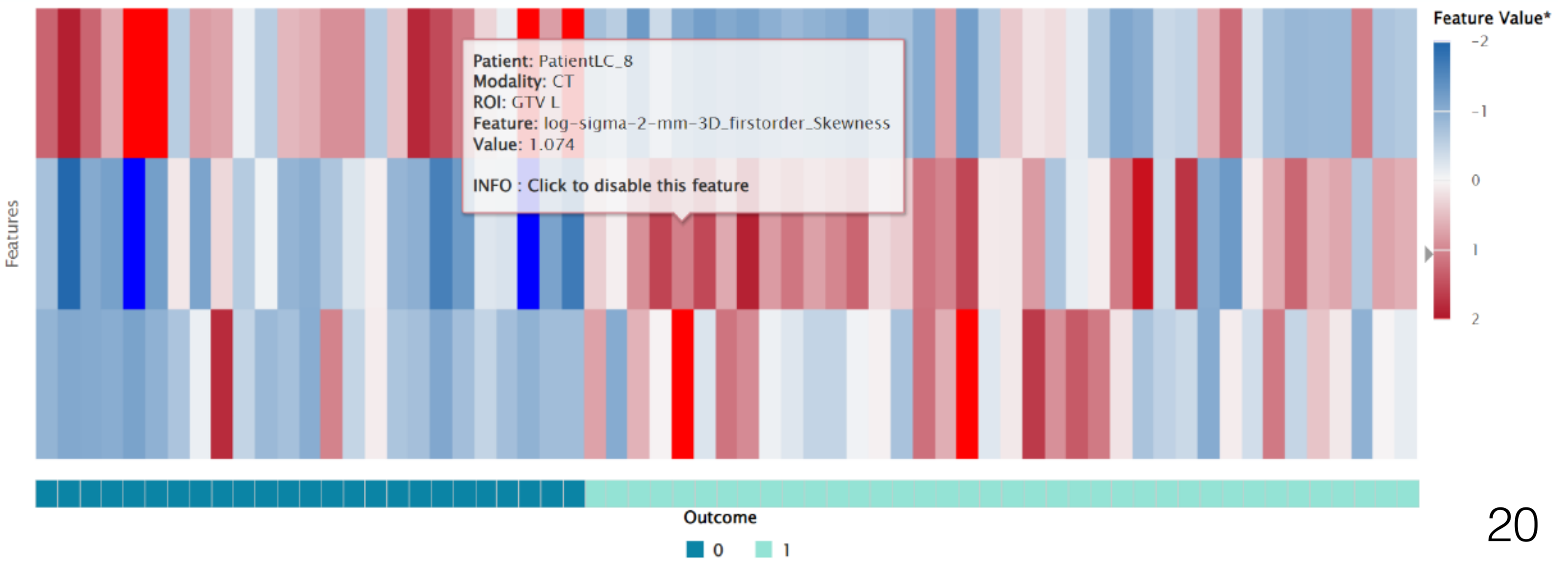
- QuantImage v2: A one-stop tool for clinical radiomics research[1]
  Abler D et al. (2023) QuantImage v2: a comprehensive and integrated physician-centered cloud platform for radiomics and machine learning research. Eur. Rad. Exp., 16(7).
  - Code-free access to state-of-the-art radiomics methods and machine learning
  - An integrated and collaborative cloud environment
    - Advanced cohort manager with Kheops online[2]
  - Feature extractor covering all feature families
  - A clinician-in-the-loop feature explorer to enable
    - Advanced data understanding (group homogeneity, outlier identification, feature meaning)
    - Development and validation of machine learning models
    - Model interpretability via feature exploration





[1]https://medgift.github.io/quantimage-v2-info/, Feb 2024
[2]https://kheops.online/, Feb 2024

QuantImage v2

D. Abler R. Schaer V. Oreiller J. Młynar F. Evéquoz M. Jreige J. O. Prior B. Spahr

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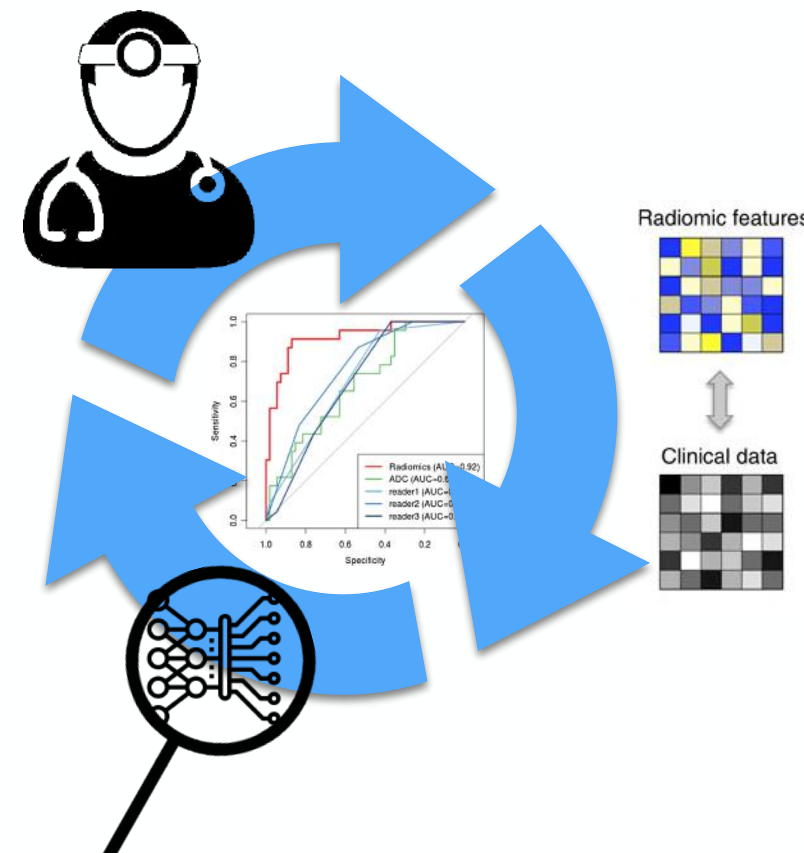
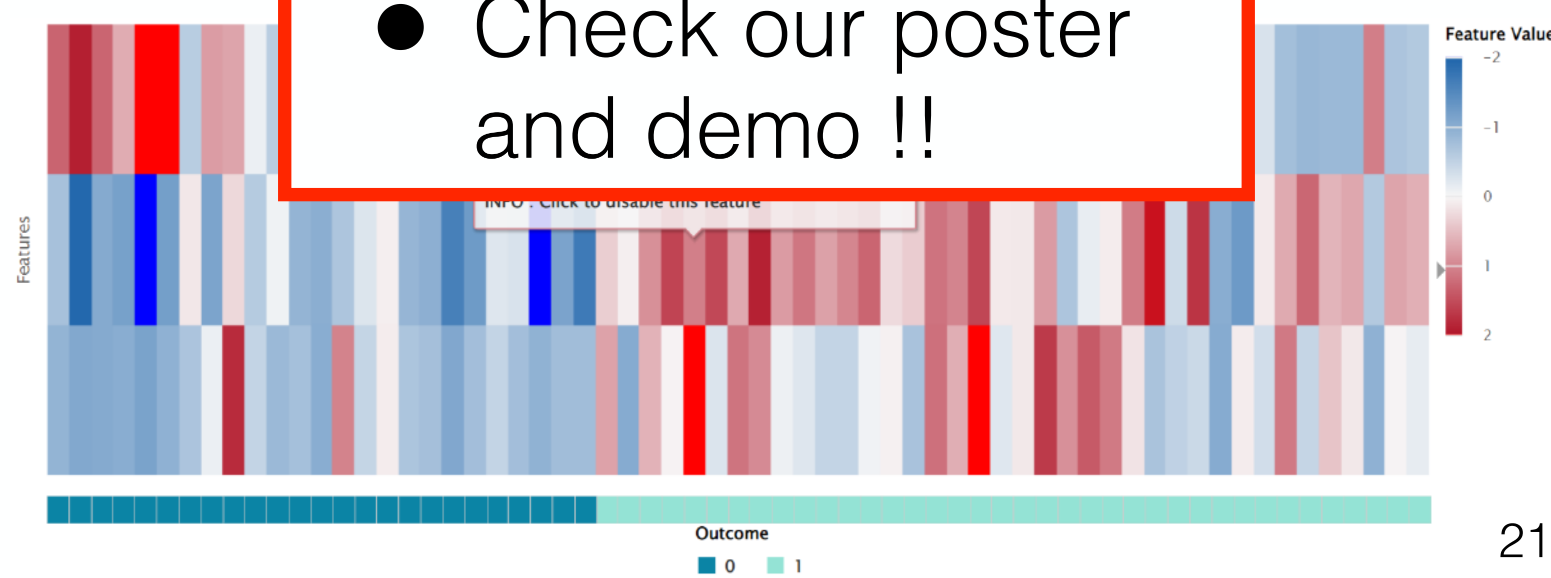


- Check our poster and demo !!



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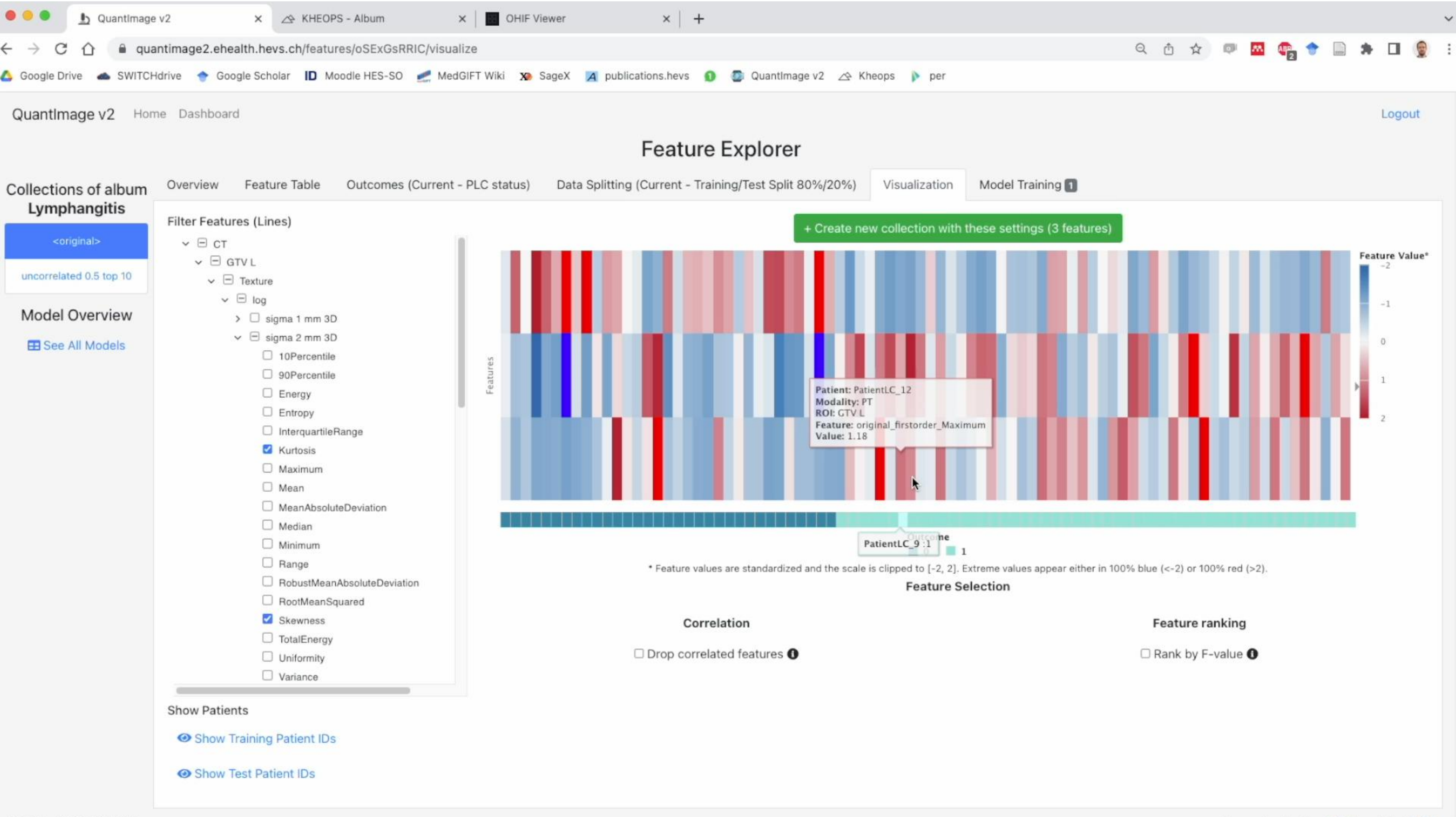

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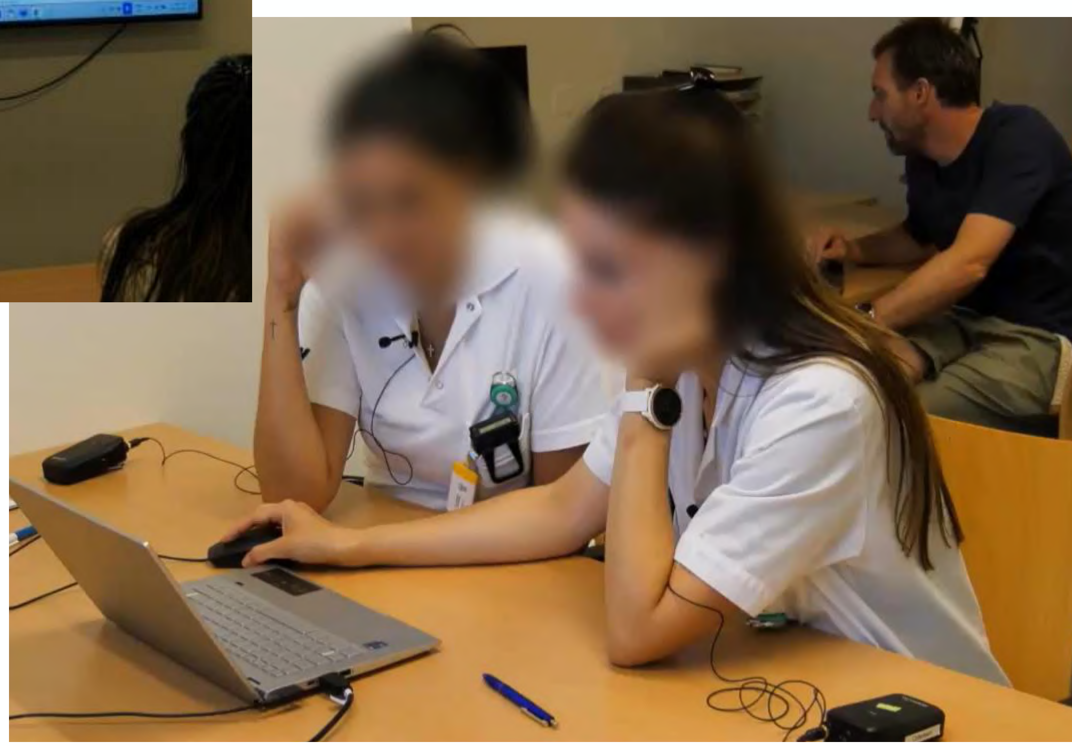
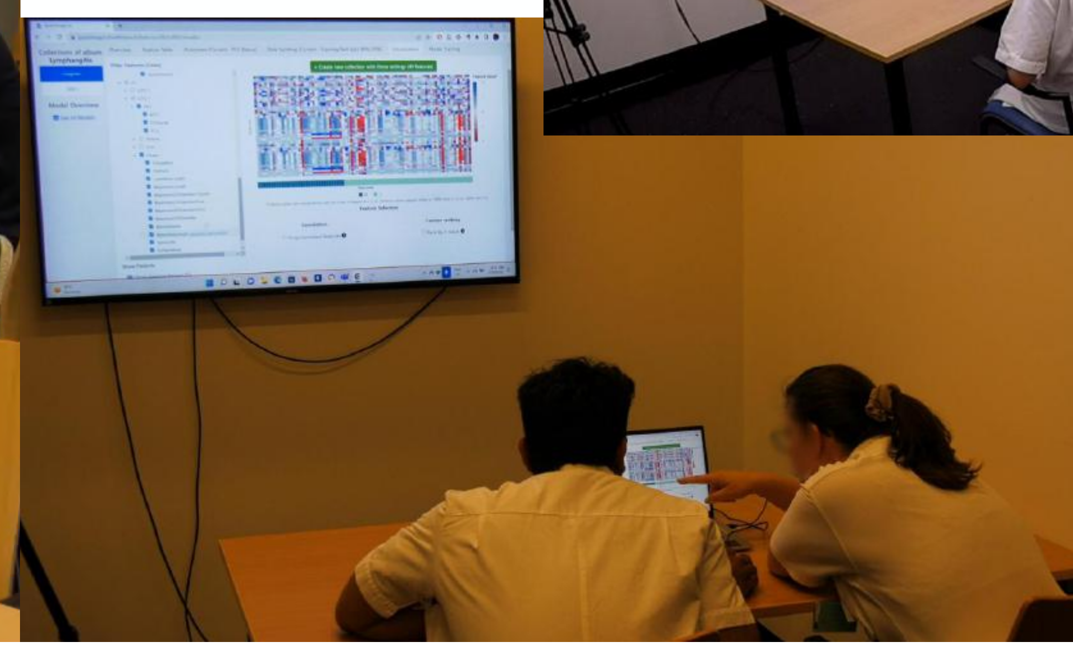
  - As an educational tool for medical students and professionals
    - Hands-on experience with the development of AI models for image-based personalized medicine

Młynar J et al. (2024) Making sense of radiomics: Insights on human-AI collaboration in medical interaction from an observational user study. Frontiers in Communication, In press.





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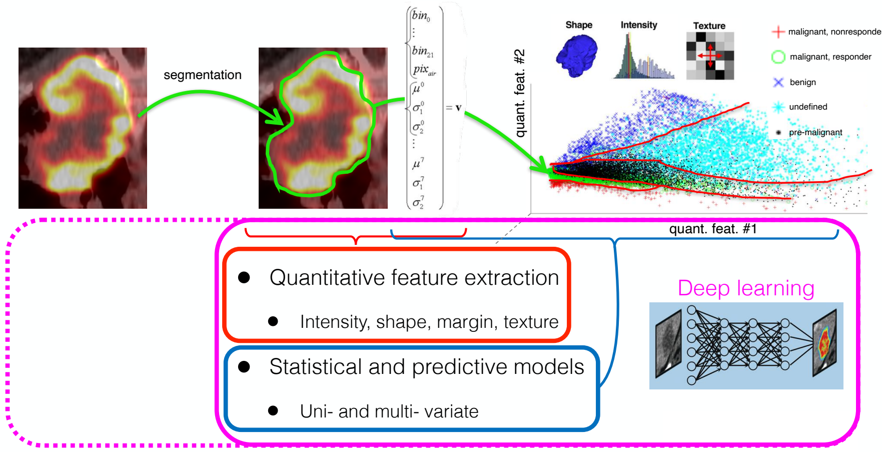

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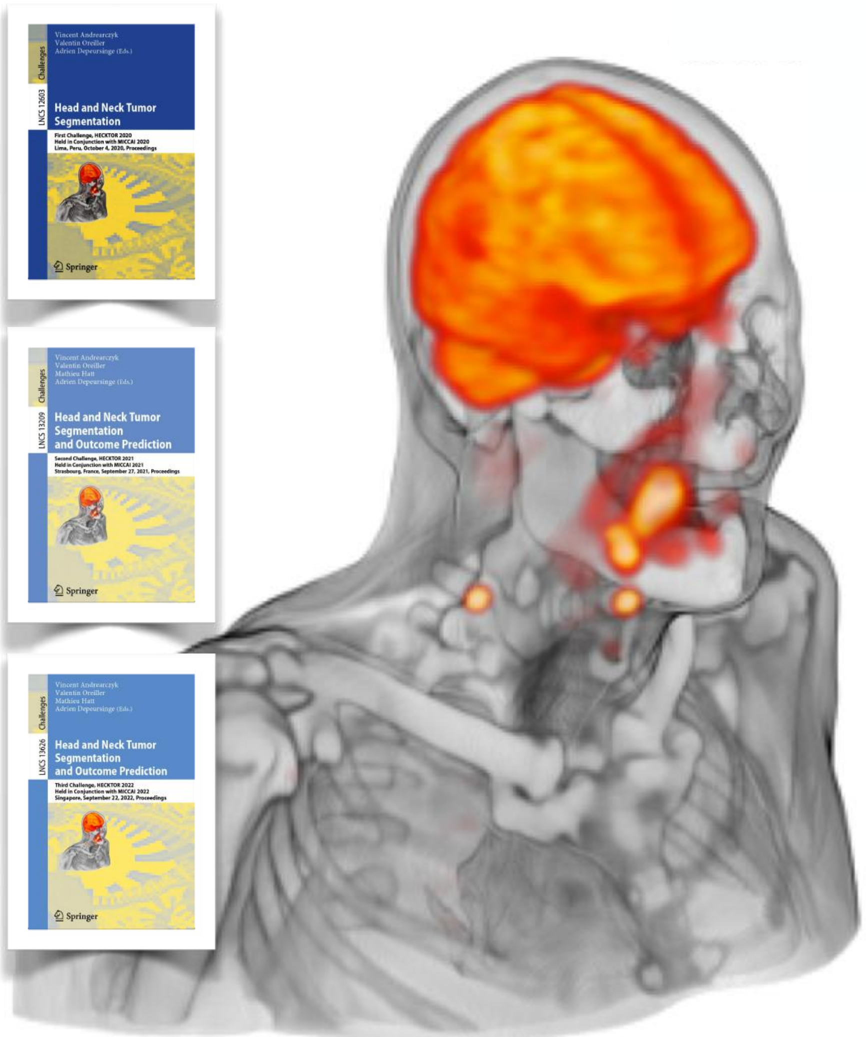
  - Explainable models for multiple sclerosis: MSxplain
- Conclusions

THE HECKTOR CHALLENGE

Vincent Andrearczyk Valentin Oreiller Mathieu Hatt Mario Jreige John O. Prior

- HECKTOR[1] 2020-2022: HEad and neCK TumOR segmentation and outcome prediction in PET/CT images
  Oreiller V et al. (2022) Head and neck tumor segmentation in PET/CT: The HECKTOR challenge. Medical Image Analysis, 77(1).



[1] https://hecktor.grand-challenge.org/, Feb 2024

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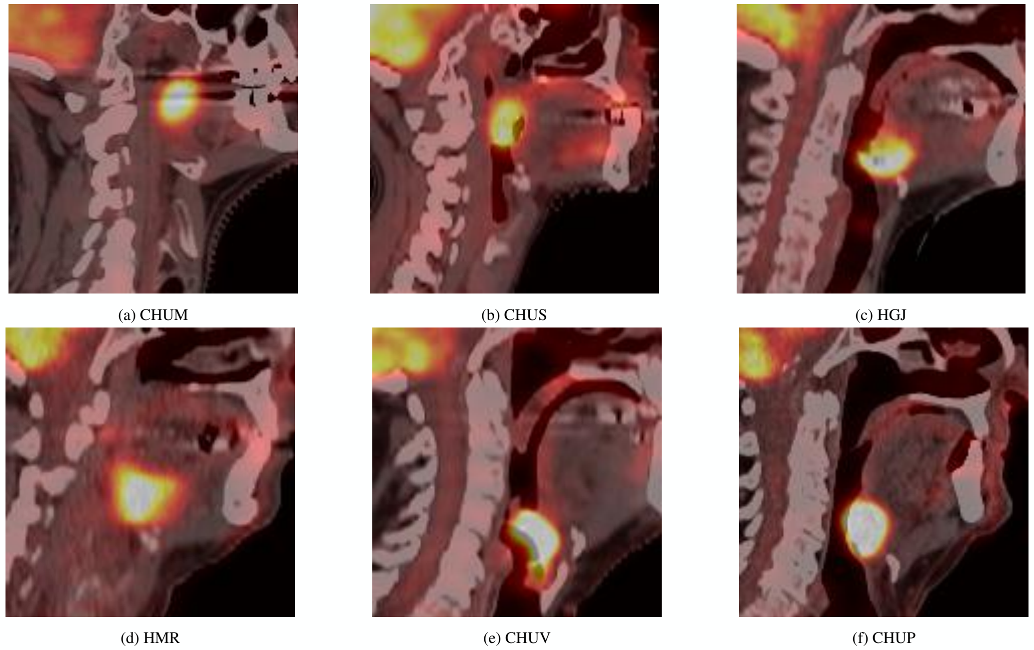
  - H&N cancer 5th leading cancer by incidence (Parkin et al. 2005)
  - High local failure: 40% in first 2 years after treatment (Chajon et al. 2013)
  - Precision oncology: finding optimal treatment for each patient, crucial for patient outcome AND well-being
  - FDG-PET/CT standard for staging and treatment planning
  - AI can help predict the best treatment based on PET/CT images and clinical data (Vallières et al. 2017, Bogowicz et al. 2017)



  - Correlate visual (lesion size, location and texture) and clinical (age, HPV status, smoking) features with response to treatment
  - **Performance is promising but not (yet?) clinically satisfactory**

Parkin DM, et al. (2005) Global cancer statistics, 2002. CA 55(2).
Chajon E, et al. (2013) Salivary gland-sparing other than parotid-sparing in definitive head-and-neck intensity-modulated radiotherapy does not seem to jeopardize local control. Rad. Onc. 8(1).
Vallières M, et al. (2017) Radiomics strategies for risk assessment of tumour failure in head-and-neck cancer. Nat. Sci. Rep. 7(1).
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Let's organize a challenge to solicit worldwide experts on medical image analysis !

(c) HGJ

(d) HMR (e) CHUV (f) CHUP

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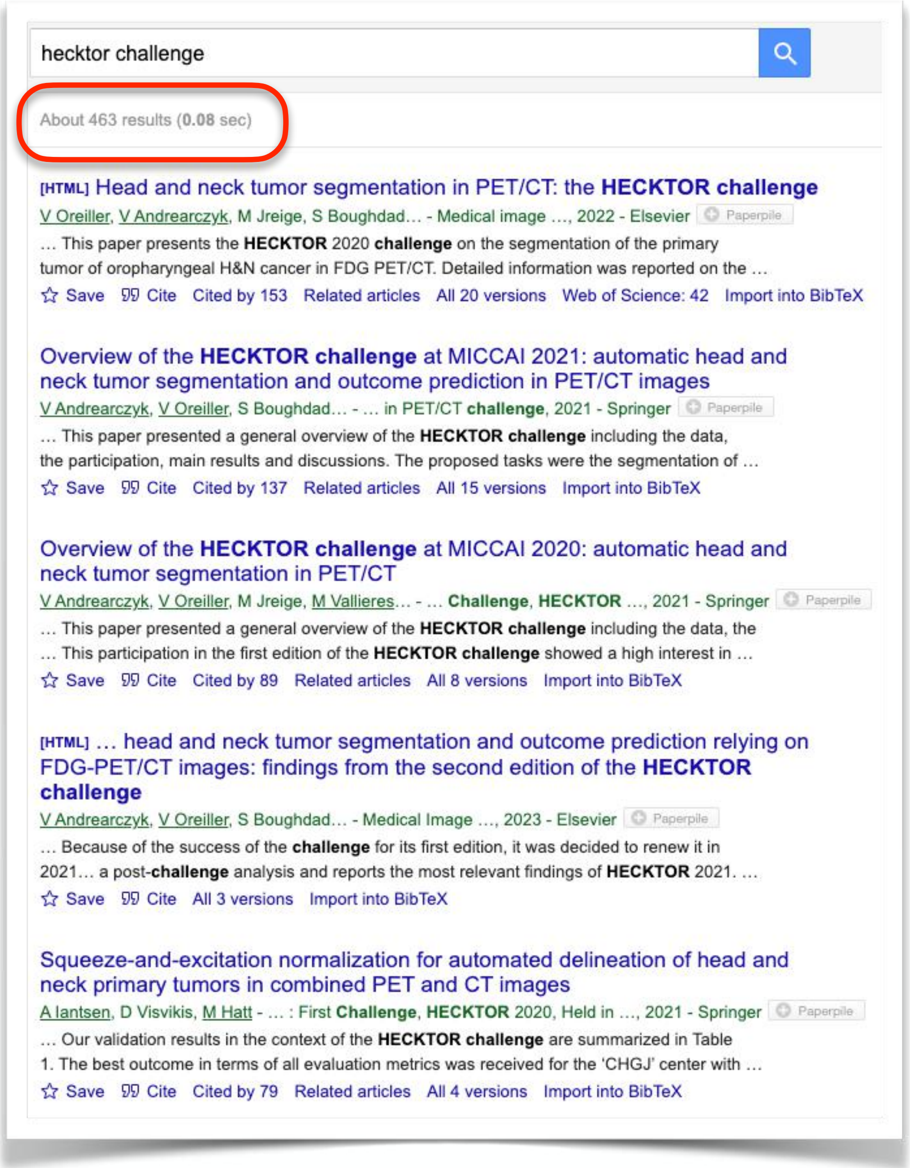
THE HECKTOR CHALLENGE

- HECKTOR 2020-2022 challenges comparison



		HECKTOR 2020	HECKTOR 2021	HECKTOR 2022
Data	# Training subjects	201	224	524
	# Test subjects	53	101	362
	# centers	5	6	9
	Inputs	FDG PET/CT extended oropharyngeal bounding box	FDG PET/CT extended oropharyngeal bounding box	FDG PET/CT full images
	Clinical data	✅	✅	✅
Tasks	GTVp segmentation	✅	✅	✅
	Outcome prediction		✅ PFS	✅ RFS
	GTVn segmentation			✅
	HPV status prediction			
	Federated learning			
	Participant papers	10	31	22

- Strong bibliometric impact
  - 3 proceeding volumes
  - ~11 papers from us with ~400 citations as of Feb 2024

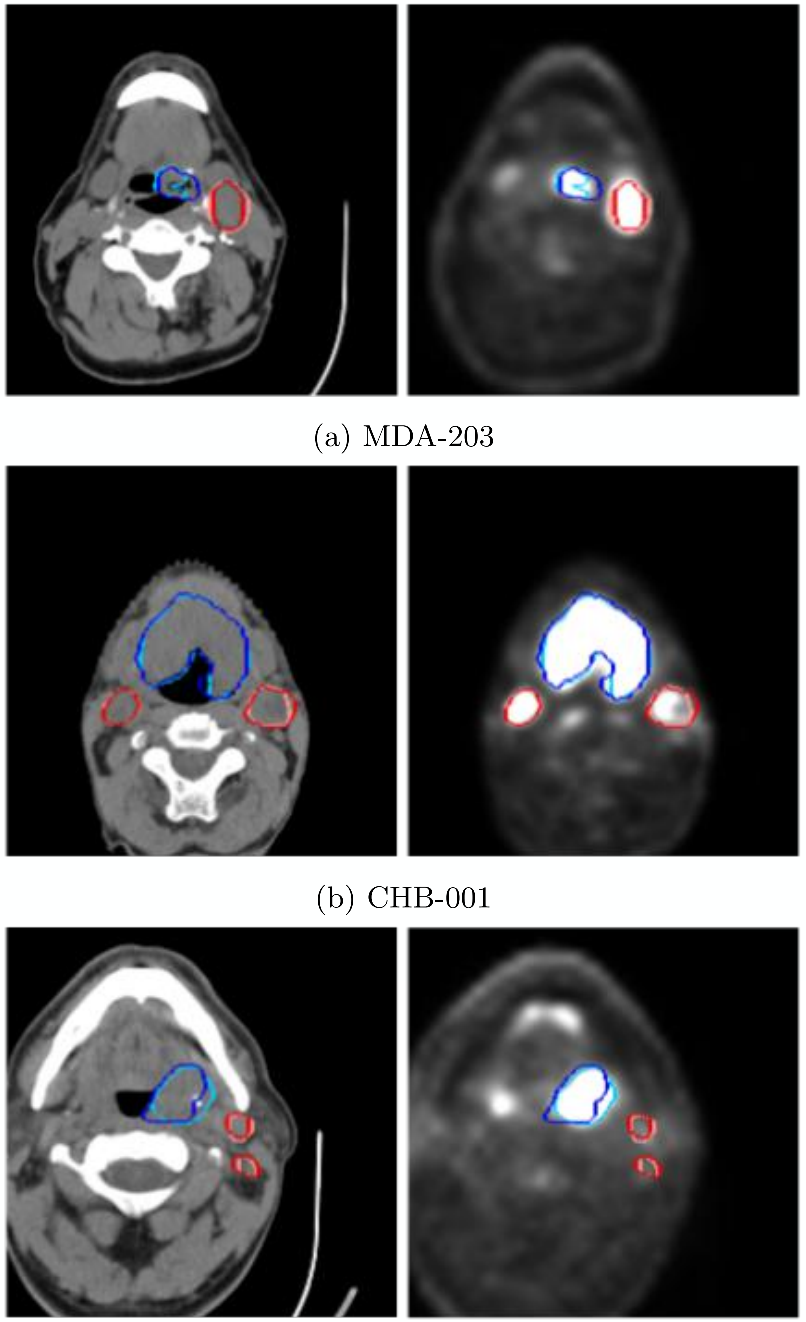
THE HECKTOR CHALLENGE

- HECKTOR 2020-2022: lessons learned
  - Segmentation of the primary tumor **GTVp** and lymph nodes **GTVn**

Team	DSC_{agg} GTVp	DSC_{agg} GTVn	mean DSC_{agg}	rank
NVAUTO [32]	**0.80066**	0.77539	**0.78802**	1
SJTU426 [41]	0.77960	**0.77604**	0.77782	2
NeuralRad [22]	0.77485	0.76938	0.77212	3
LITO [34]	0.77700	0.76269	0.76984	4
TheDLab [35]	0.77447	0.75865	0.76656	5
MAIA [45]	0.75738	0.77114	0.76426	6
AIRT [46]	0.76689	0.73392	0.75040	8
AIMers [21]	0.73738	0.73431	0.73584	9
RT_UMCG [10]	0.73741	0.65059	0.69400	17
HPCAS [38]	0.69786	0.66730	0.68258	18
ALaGreca [24]	0.72329	0.61341	0.66835	19
Qurit [1]	0.69553	0.57343	0.63448	20
VokCow [30]	0.59424	0.54988	0.57206	21
MLC [43]	0.46587	0.53574	0.50080	22
M&H_lab_NU [40]	0.51342	0.46557	0.48949	23
Average	0.72351	0.68682	0.70517	

- On par with expert performance
- Simple methods work well
  - 3D U-Net always in top three

Table: Leaderboard segmentation 2022



(a) MDA-203

(b) CHB-001

(c) USZ-010

- HECKTOR 2020-2022: lessons learned
  - Outcome prediction: Recurrence Free Survival (RFS)

Team	C-index	rank
LITO [34]	**0.68152**	1
BDAV_USYD [29]	0.68084	2
AIRT [46]	0.67257	3
RT_UMCG [26]	0.66834	4
RokieLab [49]	0.65817	5
MLC [43]	0.65598	6
VokCow [30]	0.64081	7
junma [25]	0.63896	8
LMU [47]	0.63536	9
TheDLab [35]	0.6305	10
SMIAL [9]	0.61877	11
TECVICO Corp [36]	0.59042	12
Average	0.64769	

Table: Leaderboard RFS prediction 2022

- RFS prediction not (yet?) ready for clinical use
  - More data needed to better represent (and focus) on subpopulations, e.g. HPV positive only, specific image acquisition protocols, …
- While 4/5 deep learning in top five, the winning team used a very simple radiomics approach

THE HECKTOR CHALLENGE

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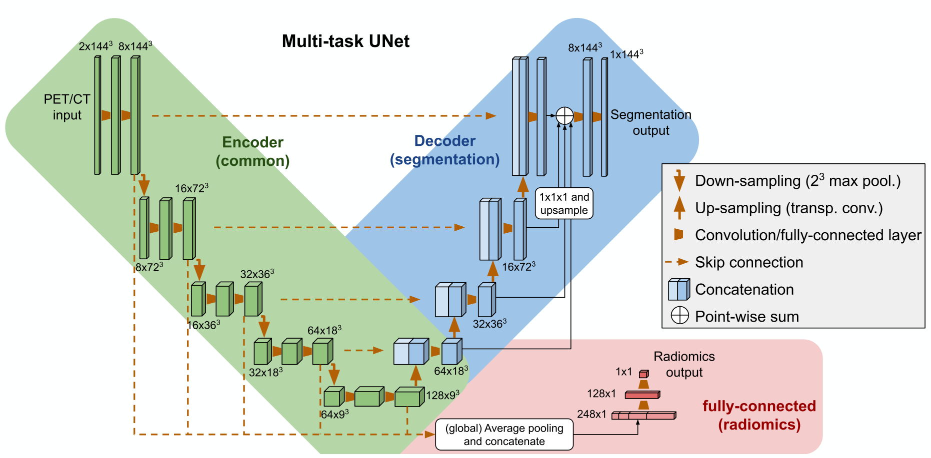
- Segmentation and outcome prediction tasks are synergistic
  - Learning to segment helps improving outcome prediction (Andrearczyk et al. 2021)



Andrearczyk V et al. (2021) Multi-Task Deep Segmentation and Radiomics for Automatic Prognosis in Head and Neck Cancer. PRIME.

The HECKTOR Challenge

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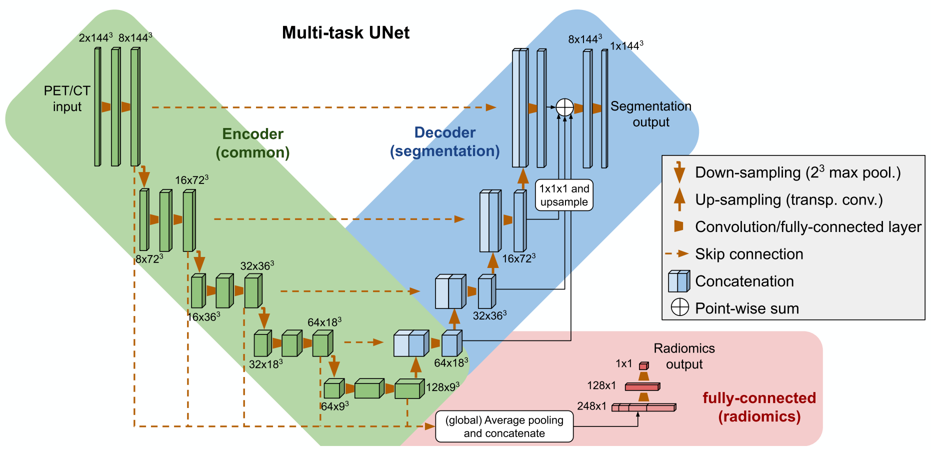
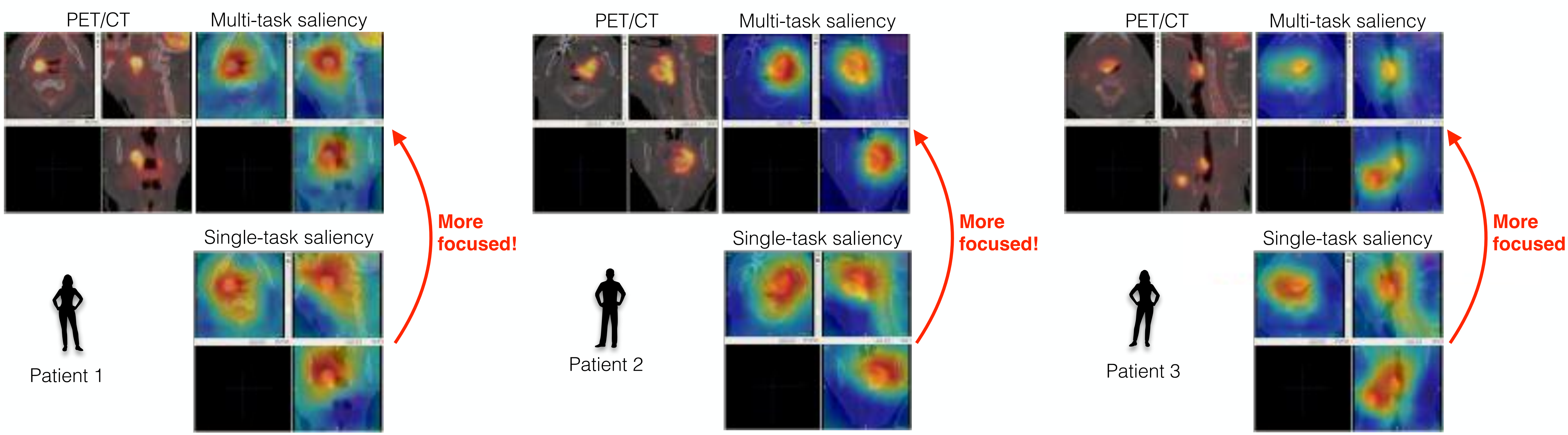


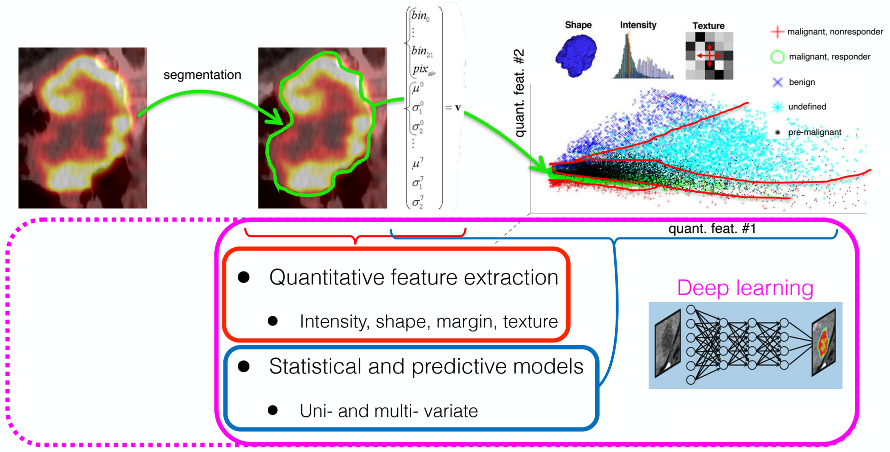
Andrearczyk V et al. (2021) Multi-Task Deep Segmentation and Radiomics for Automatic Prognosis in Head and Neck Cancer. PRIME.

- Saliency maps (Grad-CAM) show that the multi-task network focuses more on areas relevant to outcome prediction: the primary tumor and lymph nodes



Agenda

- Personalized medicine
- Artificial Intelligence (AI) for medical image analysis
  - Deep learning and Radiomics
    - Fundamentals
    - Addressed tasks
    - Clinical certification status



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HASLERSTIFTUNG

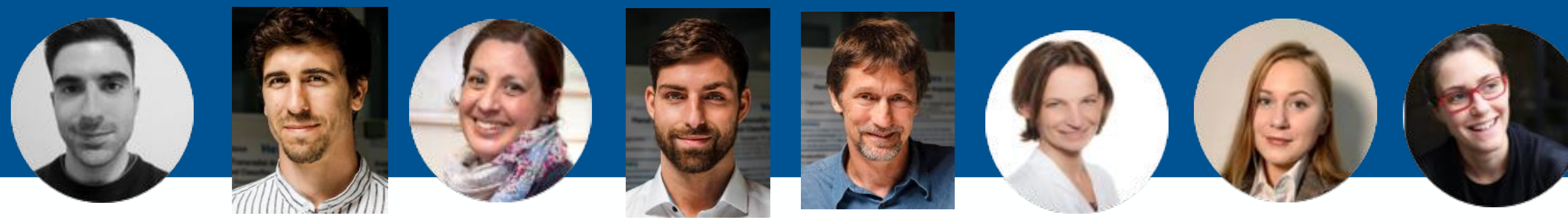
SPHN

SNSF

CHUV

Hes·so// VALAIS WALLIS

Explainable AI



F. Spagnolo V. Andrearczyk M. Bach Cuadra B. Spahr H. Müller C. Granziera N. Molchanova D. Ribes

- XAI: Opening the black box to reveal the internal mechanisms of complex deep models
  - Importance of XAI for safe clinical use (Lekadir et al. 2023)
    - For engineers (development)
    - For domain experts (development)
    - For end-users (production)
  - XAI still in its infancy (de Vries et al. 2023)
  - The MSxplain project[1]
    - Explainability
    - Interpretability
    - Uncertainty
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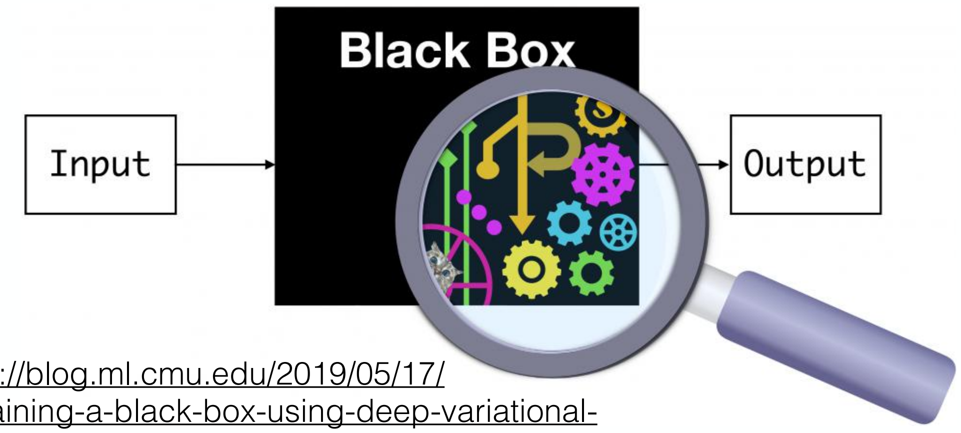
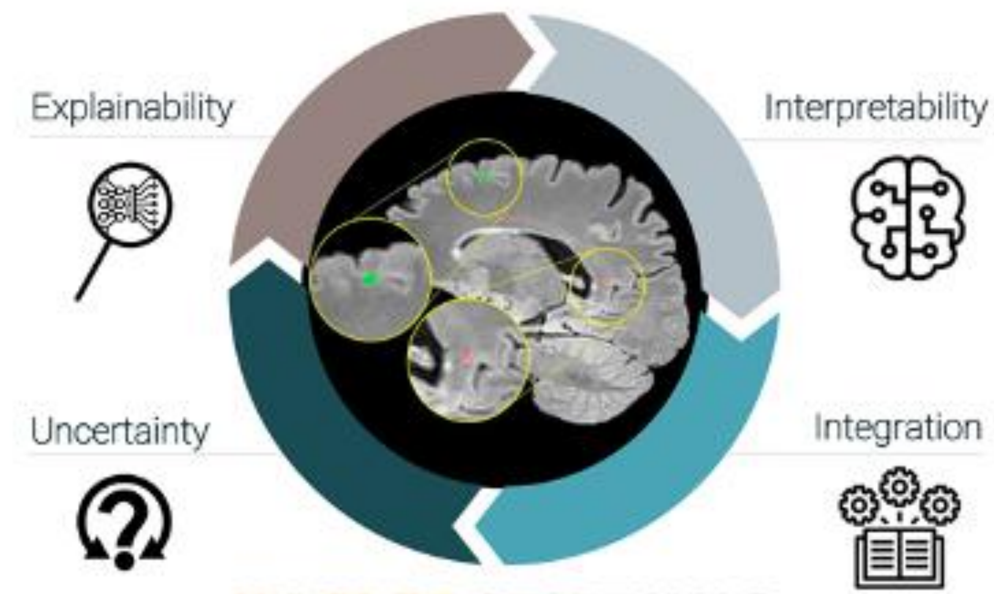


https://blog.ml.cmu.edu/2019/05/17/explaining-a-black-box-using-deep-variational-information-bottleneck-approach/, Feb 2024

MSxplain
Responsible AI in Multiple Sclerosis



HASLERSTIFTUNG

CIBM Center for Biomedical Imaging
THINK Translational Imaging in Neurology
medGIFT

Lekadir K et al.(2023). FUTURE-AI: International consensus guideline for trustworthy and deployable artificial intelligence in healthcare. 1. https://arxiv.org/abs/2309.12325v1
de Vries BM et al. (2023). Explainable artificial intelligence (XAI) in radiology and nuclear medicine: a literature review. Frontiers in Medicine, 10, 1180773.
[1]https://wp.unil.ch/mial/research/projects/msxplain/, Feb 2024

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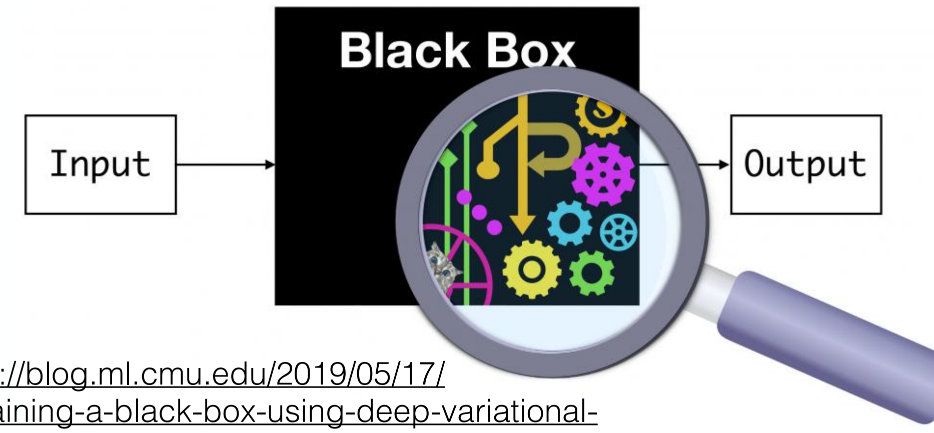

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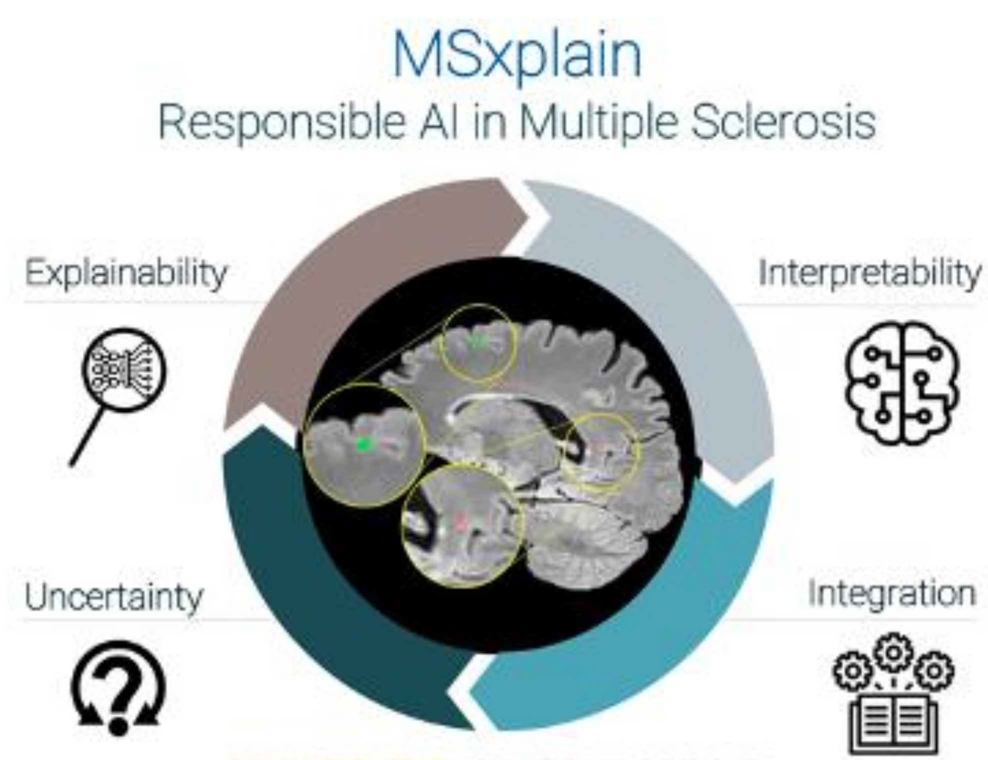

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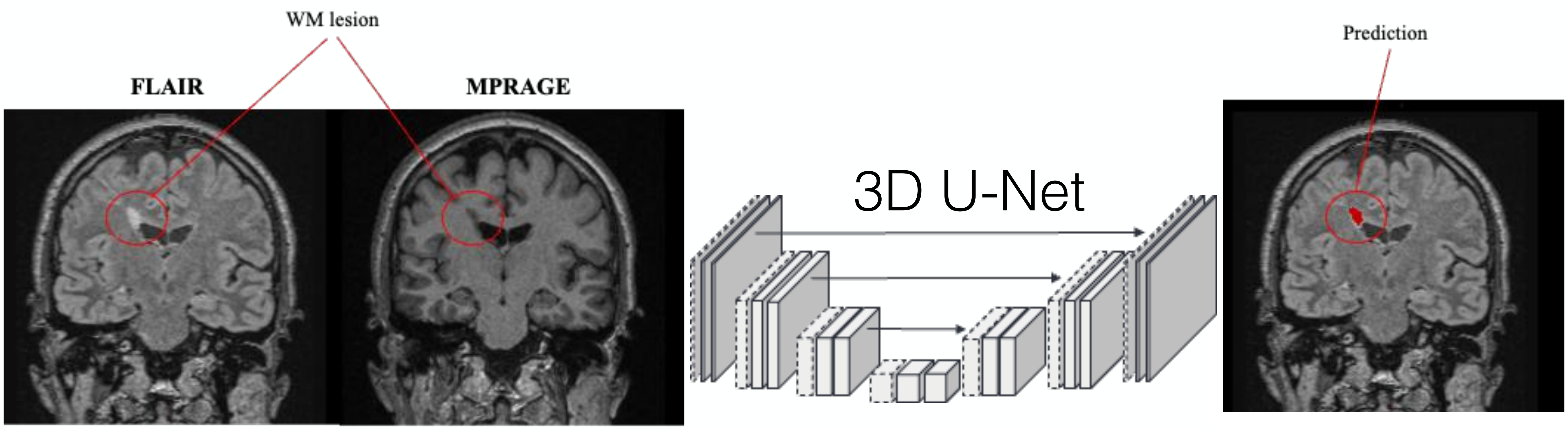
Explainable AI (XAI)

- XAI: Opening the black box to reveal the internal mechanisms of complex deep models
- Multiple Sclerosis (MS): automatic segmentation of White Matter Lesions (WML) as biomarkers of diagnosis and progression
  - Data: 687 patients with multiple timepoints, MRI (FLAIR and MPRAGE)
  - 3D U-Net with normalized dice and blob loss
    - Normalized Dice of 0.71 on the test set (~350 lesions)



la Rosa F et al. (2020). Multiple sclerosis cortical and WM lesion segmentation at 3T MRI: a deep learning method based on FLAIR and MP2RAGE. NeuroImage: Clinical, 27, 102335.

Explainable AI (XAI)

- XAI: Opening the black box to reveal the internal mechanisms of complex deep models
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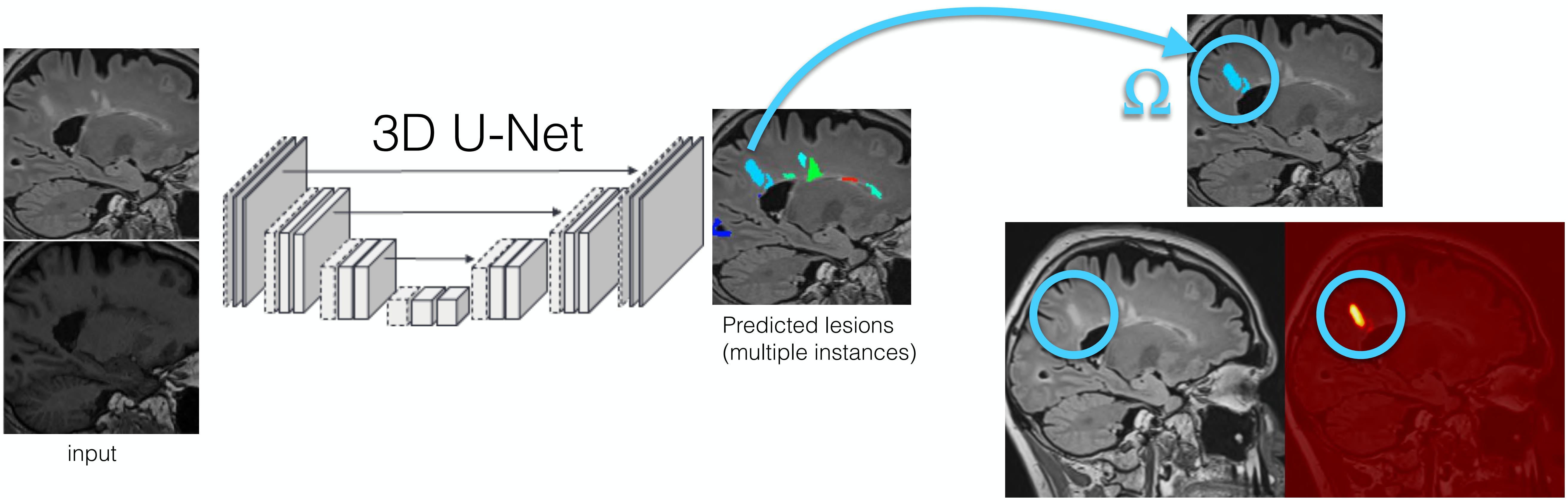
- XAI: understanding the model
  - What triggers a WML detection ?
    - What information does the model use for a specific WML instance Ω ?
      Spagnolo F. et al. (2024). Instance-level explanations in multiple sclerosis lesion segmentation, in preparation



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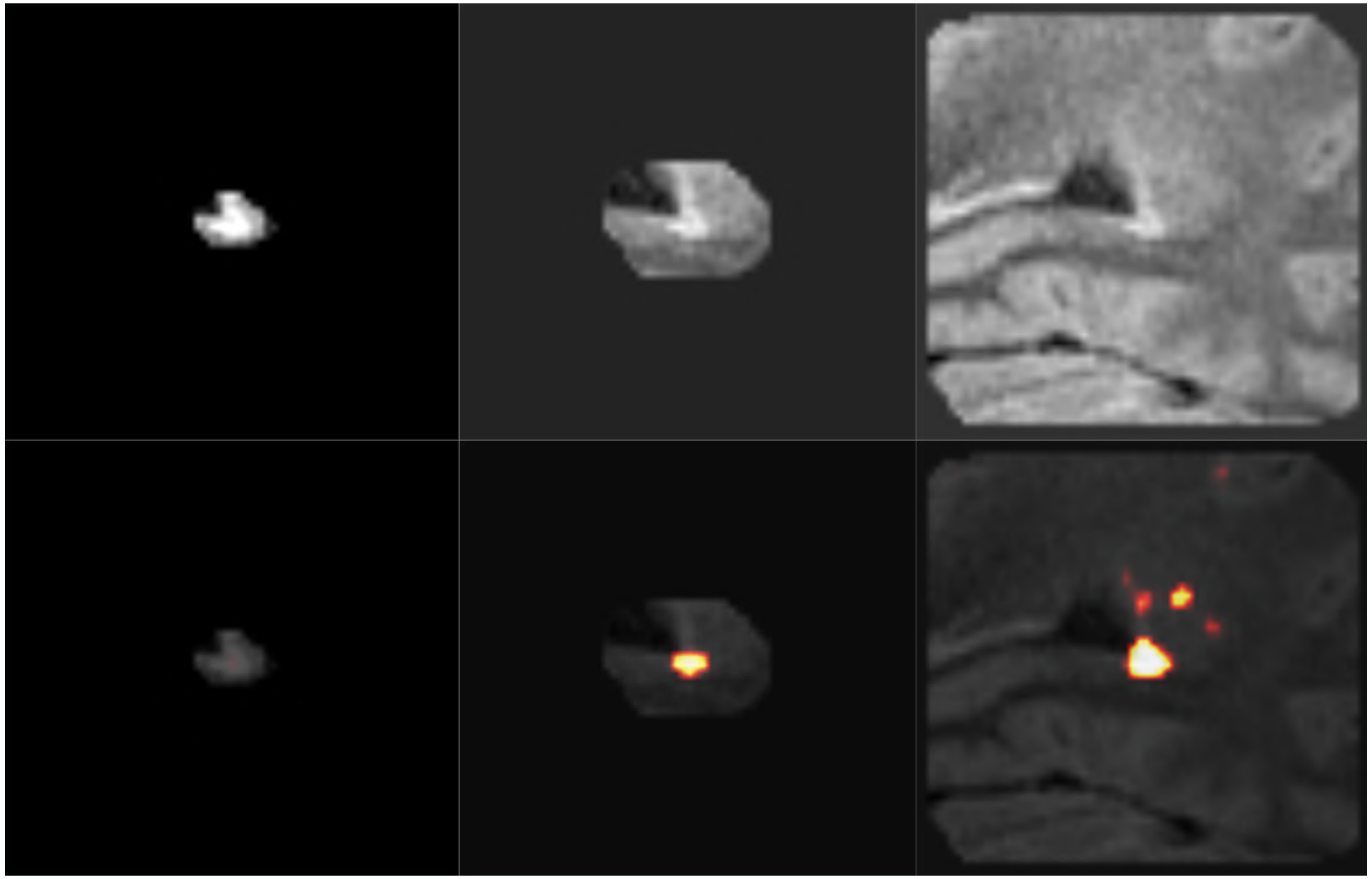
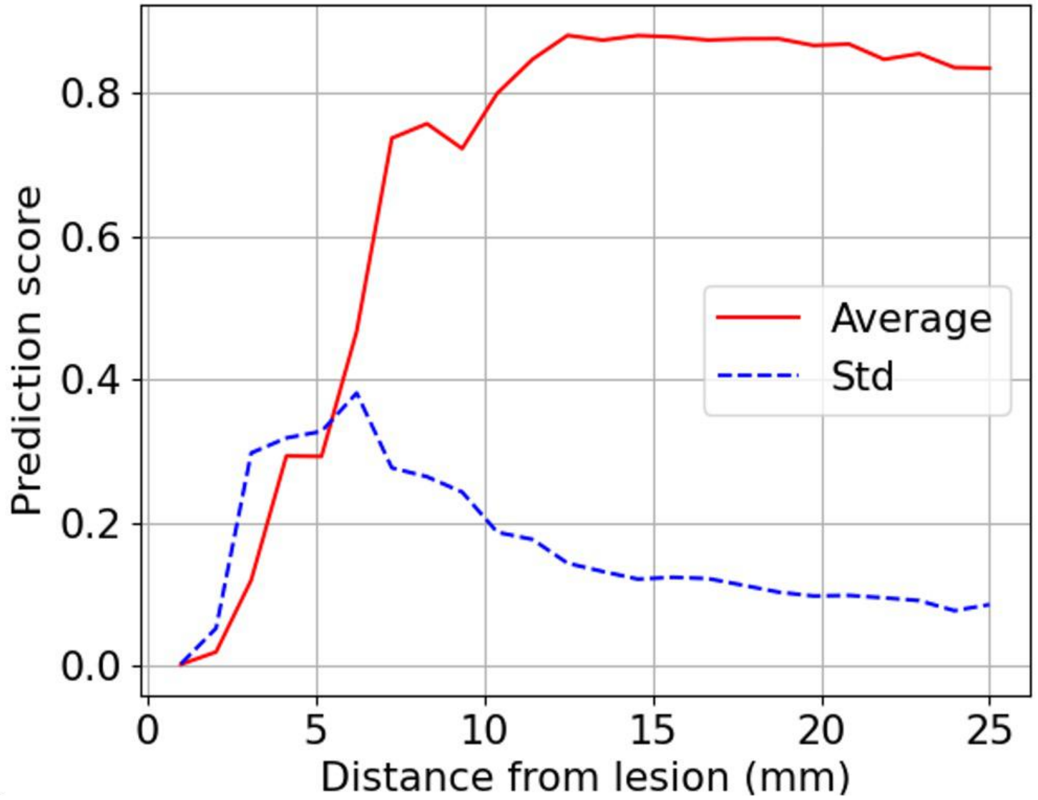
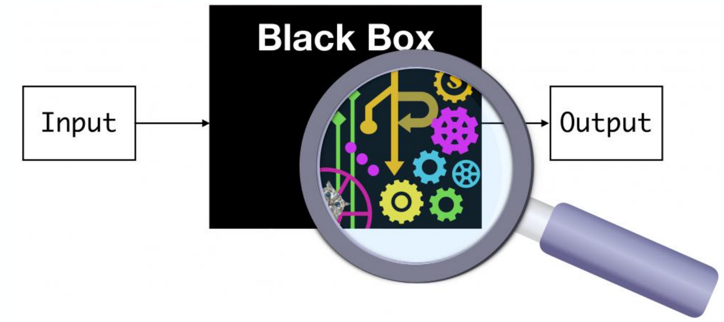




- Detection triggered if
  - Hyperintense signal in FLAIR
  - Surrounded by ~10-15mm of healthy WM
- Yields insights on which lesions will be missed by the model
- Can be used to optimize network design
  - E.g. patch size



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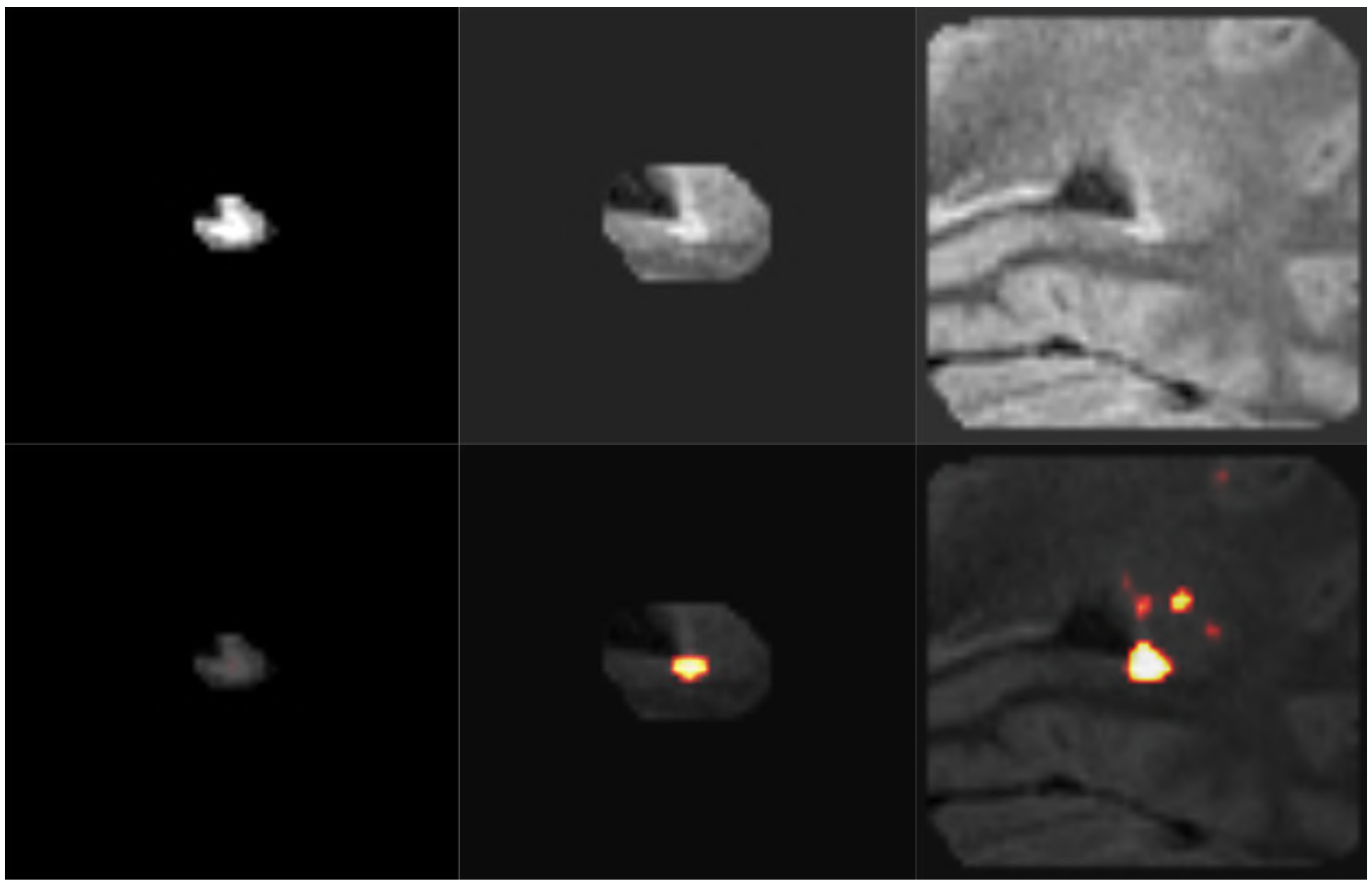

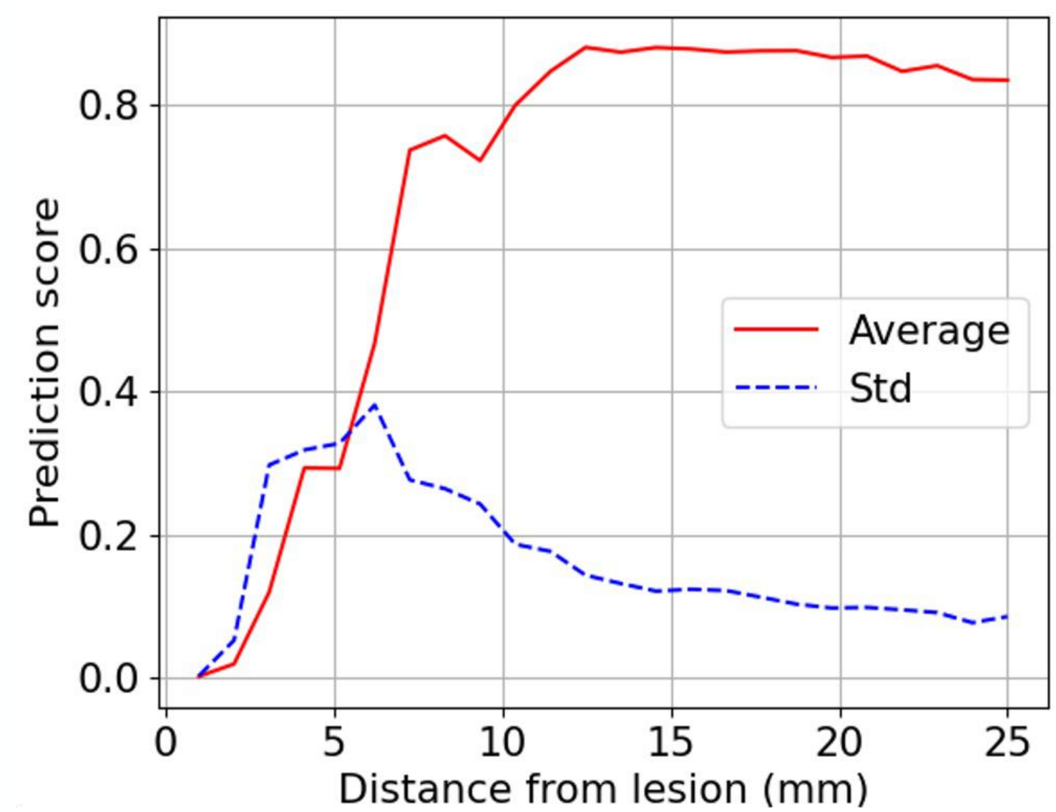

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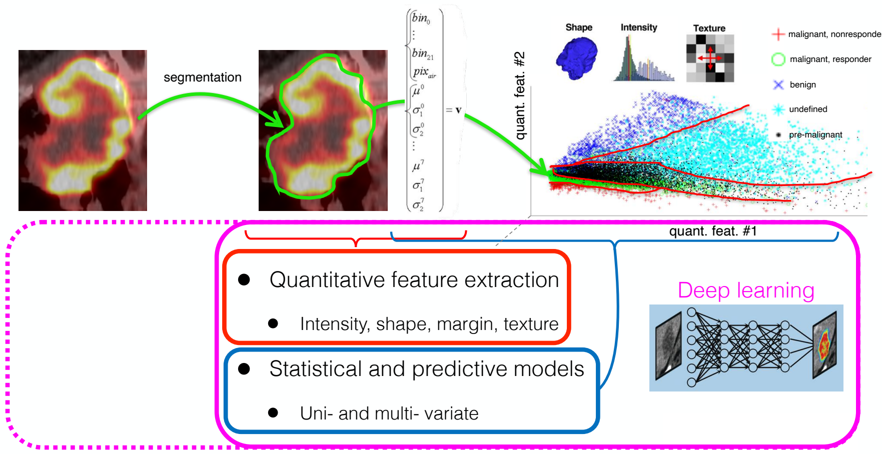

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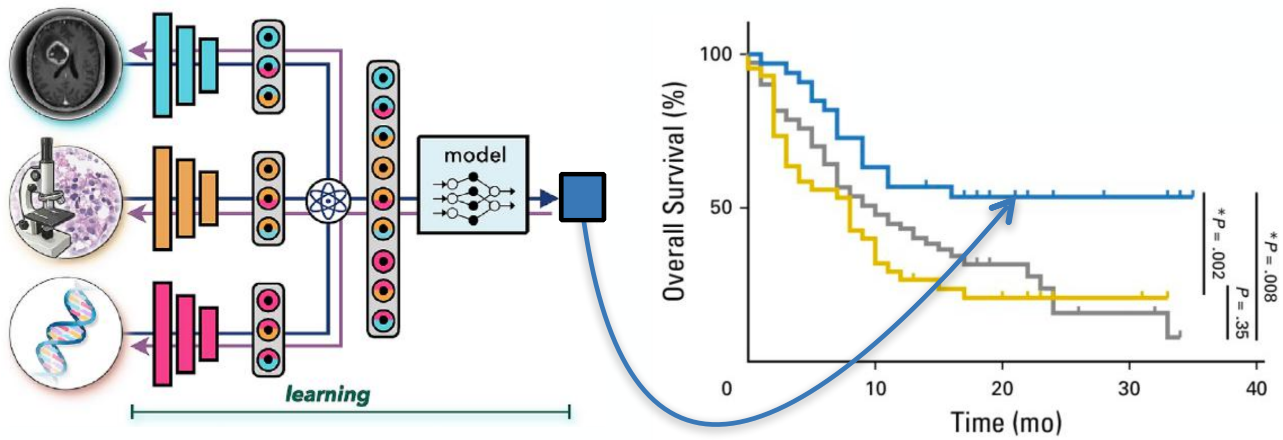
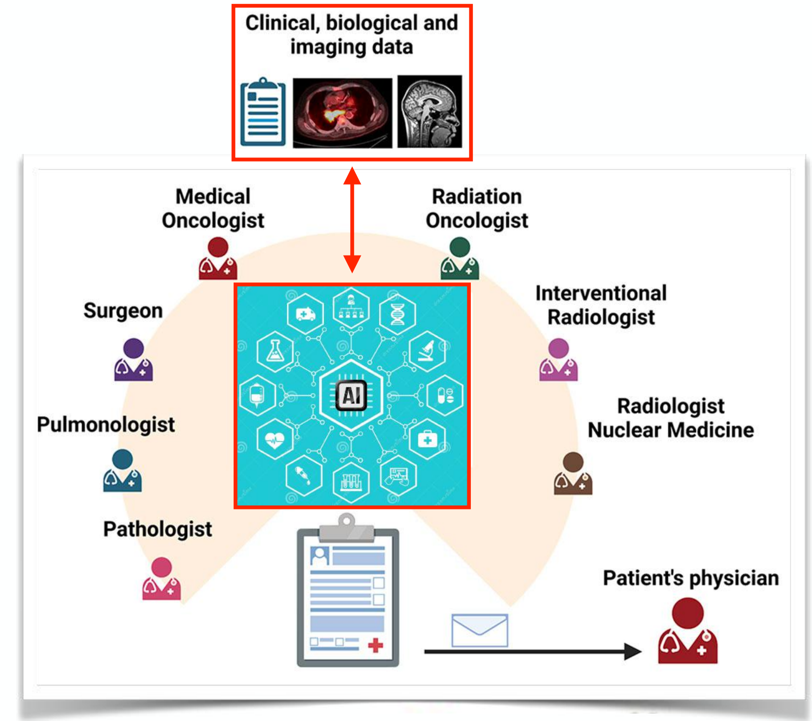
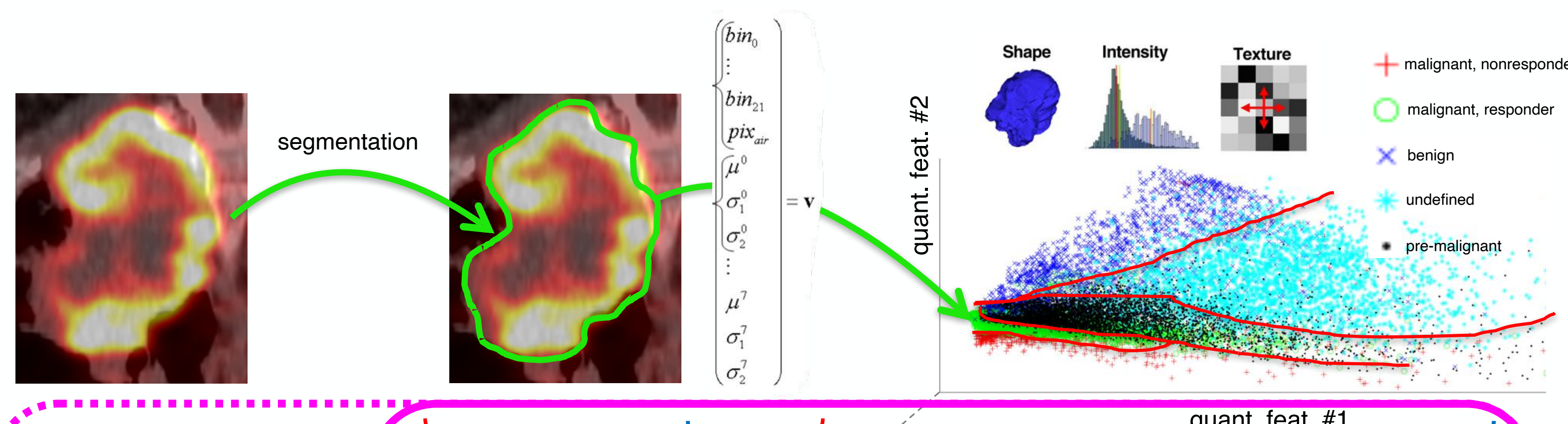
CONCLUSIONS

- AI-augmented medical information systems have tremendous potential for personalized medicine



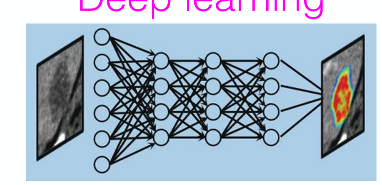


- AI is a perfect match to mine complex multimodal imaging
  - Segmentation is more mature than outcome prediction
  - Task synergy and large models arriving in radiology



- Quantitative feature extraction
  - Intensity, shape, margin, texture
- Statistical and predictive models
  - Uni- and multi- variate

Deep learning



CONCLUSIONS

- Automation of time-consuming and error-prone tasks to free human time for more interesting/challenging tasks
  - E.g. longitudinal lesion segmentation and volumetric response assessment: the TARGET project for brain metastases

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ligue suisse contre le cancer
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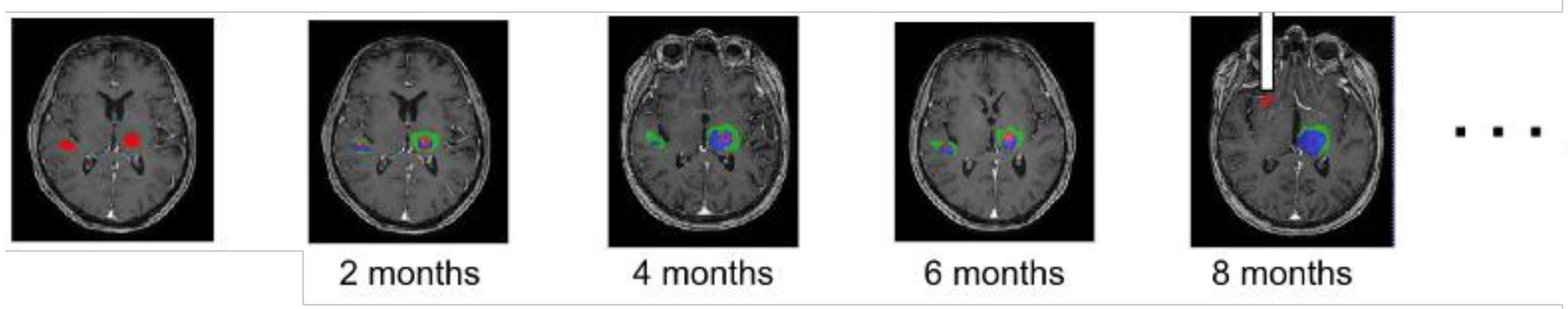
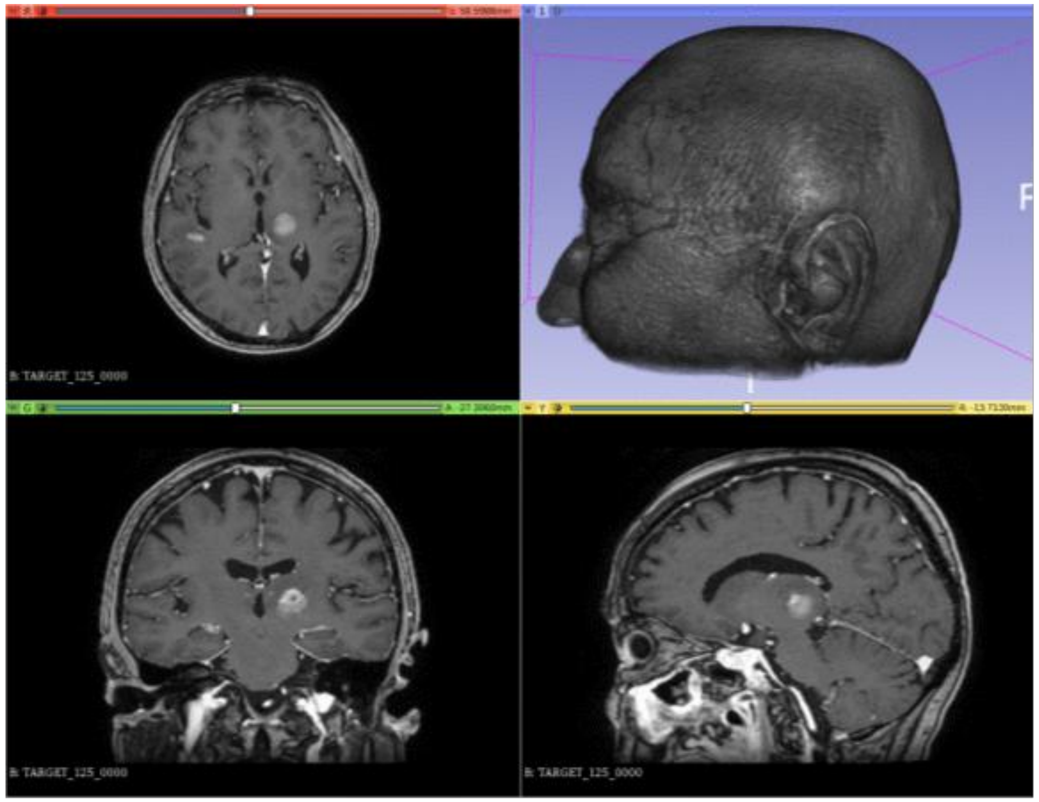
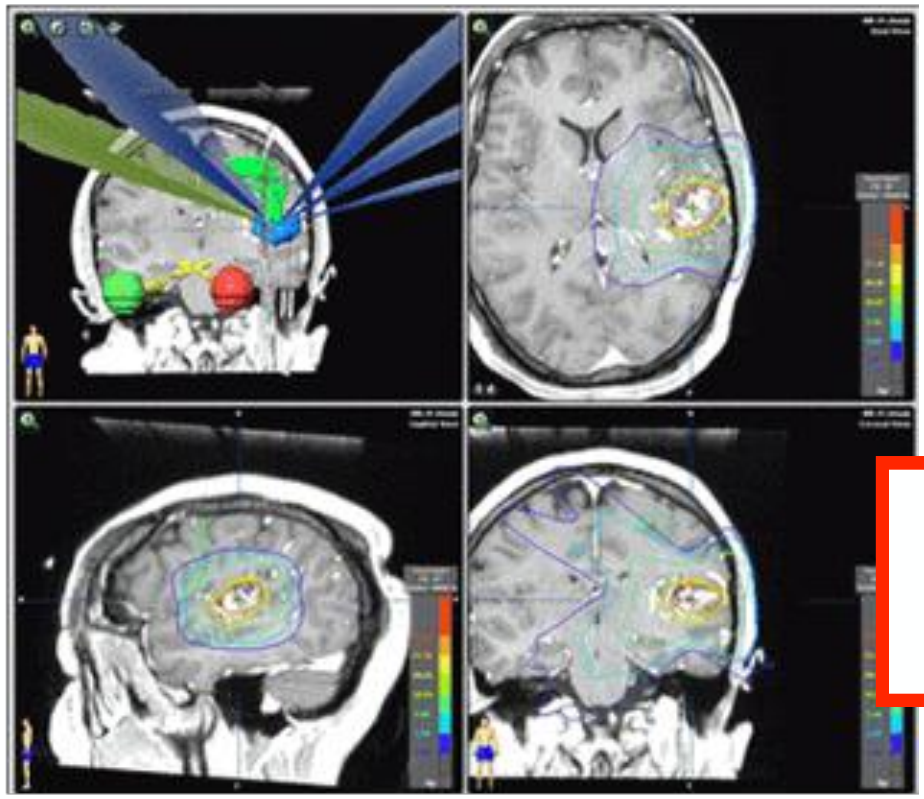
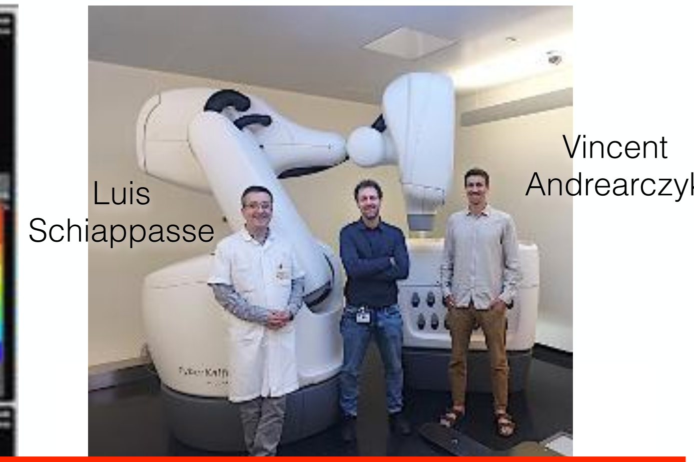




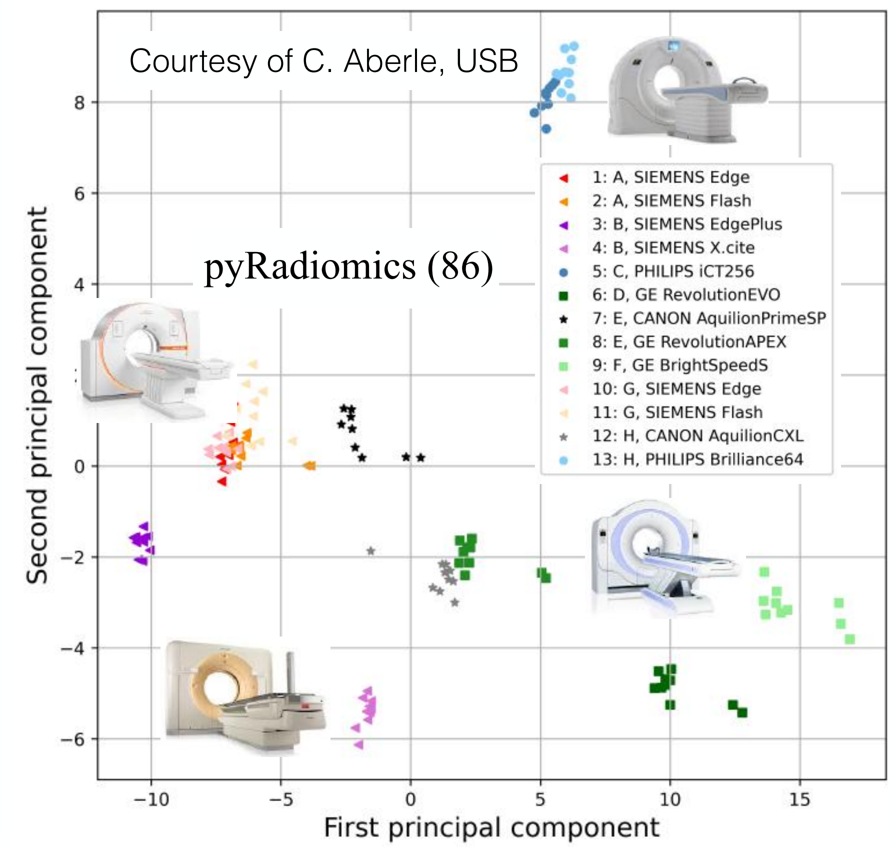


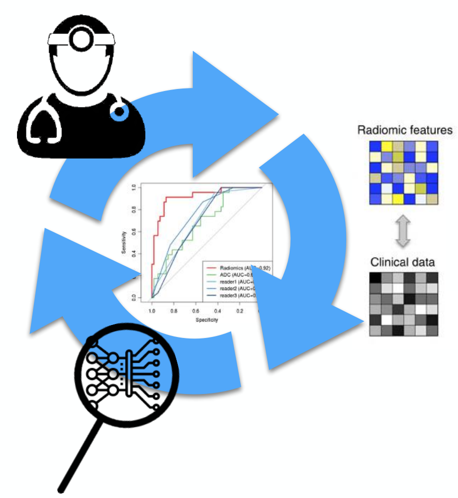


- Check out our poster !!

Conclusions

- Achieving trustworthy AI is a multifaceted challenge (1/2)
  - Generalization
    (Petzschner et al. 2024, Jimenez-Del-Toro et al. 2021, Temple et al. 2024, Oumoumi et al. 2024, Buvat et al. 2019)
    - Define the targeted population (disease, treatment, imaging equipment[1])
    - Data quality: not underestimate data curation
    - Importance of reporting/publishing negative results
  - Allow domain experts to formulate and test their hypotheses themselves
    - Importance of “no-code” and domain-specific AI platforms and education





Petzschner FH et al. (2024). Practical challenges for precision medicine. Science (New York, N.Y.), 383(6679), 149–150.
Jimenez-Del-Toro O et al. (2021). The Discriminative Power and Stability of Radiomics Features With Computed Tomography Variations Task-Based Analysis in an Anthropomorphic 3D-Printed CT Phantom. Invest Radiol, 56(12), 820–825.
Temple SWP et al. (2024). Gross failure rates and failure modes for a commercial AI-based auto-segmentation algorithm in head and neck cancer patients. Journal of Applied Clinical Medical Physics, e14273.
Omoumi P et al. (2024). Independent Evaluation of Commercial Diagnostic AI Solutions: A Necessary Step toward Increased Transparency. Rad., 310(1).
Buvat I et al. (2019). The Dark Side of Radiomics: On the Paramount Importance of Publishing Negative Results. J. Nuc. Med., 60(11).
[1] https://github.com/QA4IQI/qa4iqi.github.io, Feb 2024

Conclusions

- Achieving trustworthy AI is a multifaceted challenge (2/2)
  - Involve the international community
    - Open data and scientific challenges
    - Discuss process definition, software implementation and good practices: standardization[2] (Zwanenburg et al. 2020)
  - Integration and ergonomy: do not disrupt existing workflows
  - Tailor XAI to gain insights about the internal rules of complex deep models
    - Reveal how “stupid” is the model (Kaufman et al. 2023)
  - Create a core group with interdisciplinary skills and passion!
    - Know each other’s strengths and motivation

Zwanenburg A et al. (2020). The Image Biomarker Standardization Initiative: Standardized Quantitative Radiomics for High-Throughput Image-based Phenotyping. Radiology, 295(2), 328–338.
Kaufman RA et al.. (2023). Explainable AI And Visual Reasoning: Insights From Radiology. 23. https://arxiv.org/abs/2304.03318v1

[2] https://theibsi.github.io/, Feb 2024

Thank you

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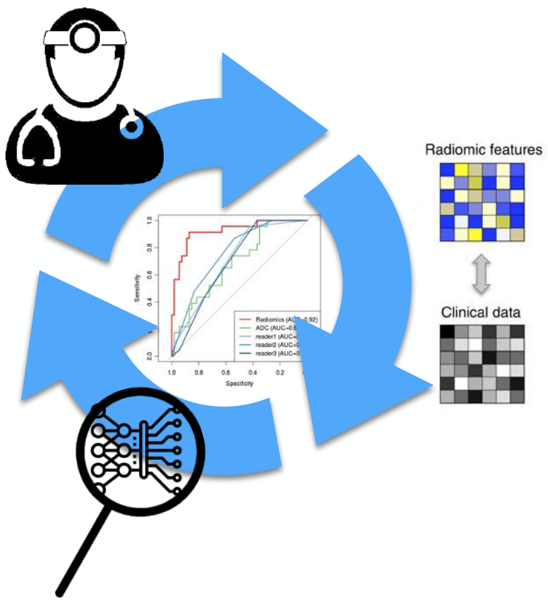
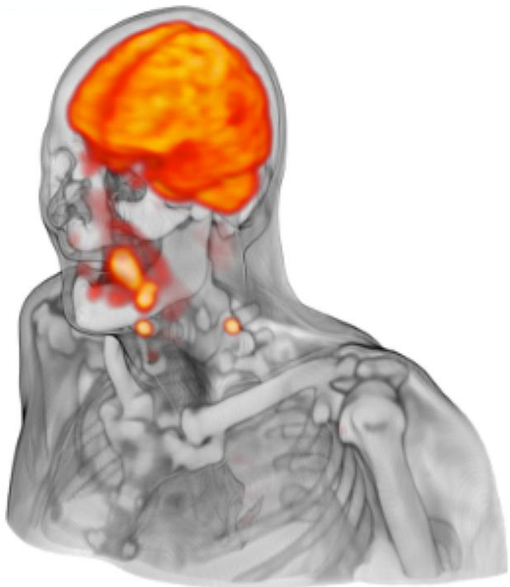
- Links & info
  - QuantImage v2
    https://medgift.github.io/quantimage-v2-info/
  - HECKTOR challenge
    https://hecktor.grand-challenge.org/
  - MedGIFT group
    https://medgift.hevs.ch/
  - Image Biomarker Standardisation Initiative (IBSI)
    https://theibsi.github.io/
  - MSxplain
    https://wp.unil.ch/mial/research/projects/msxplain/
  - QA4IQI
    https://github.com/QA4IQI/qa4iqi.github.io





IBSI image biomarker standardisation initiative

krebsliga schweiz
ligue suisse contre le cancer
lega svizzera contro il cancro

HASLERSTIFTUNG

SNSF

SPHN

Hes·so// VALAIS WALLIS

CHUV