Maastricht UMC+

Voorspellen van de uitkomst van longkankerbehandelingen

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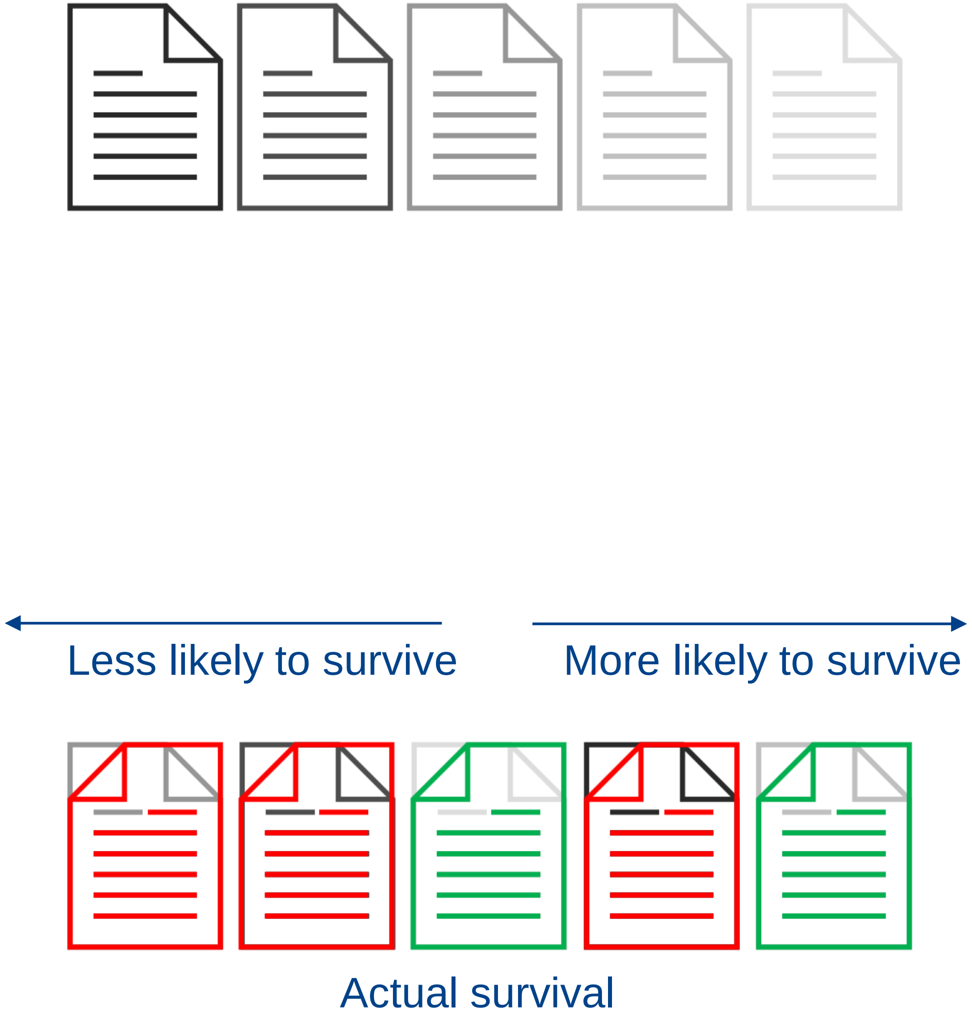
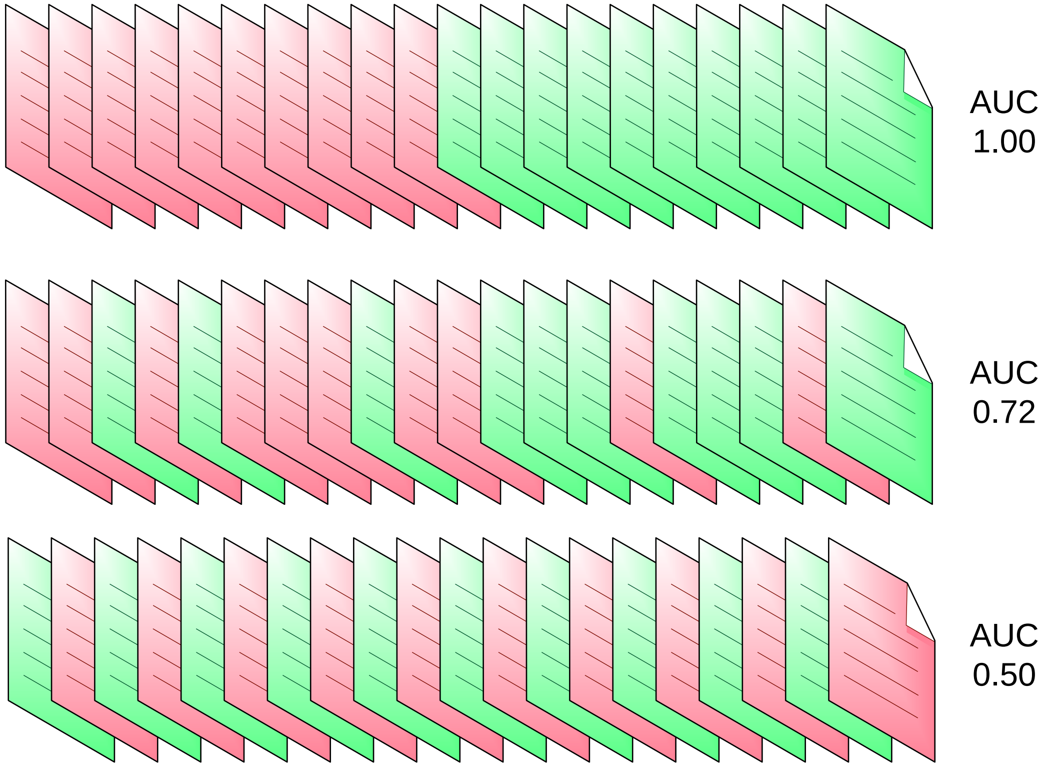
Themadag Radiotherapie | Catarharina Ziekenhuis Eindhoven | 14.00 - 14.25 (20 + 5)

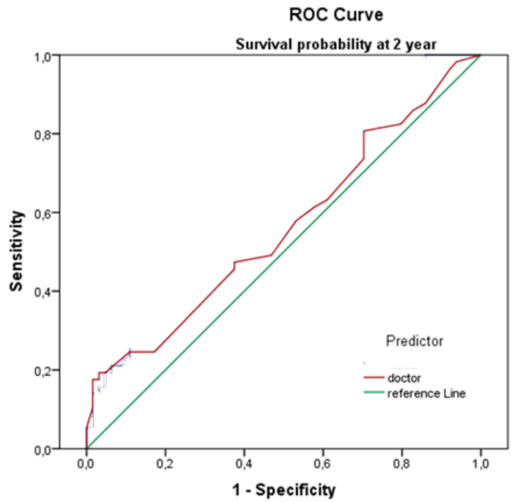
Maastricht UMC+ Maastro Maastricht University

Prediction of survival

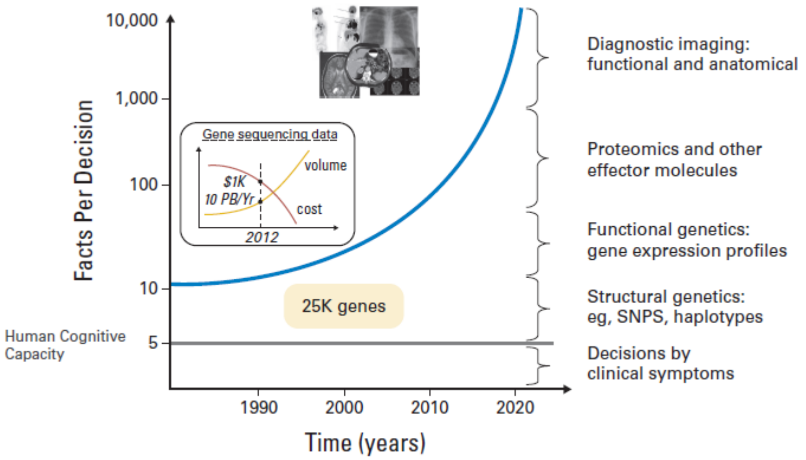




Prediction of individual outcomes is difficult

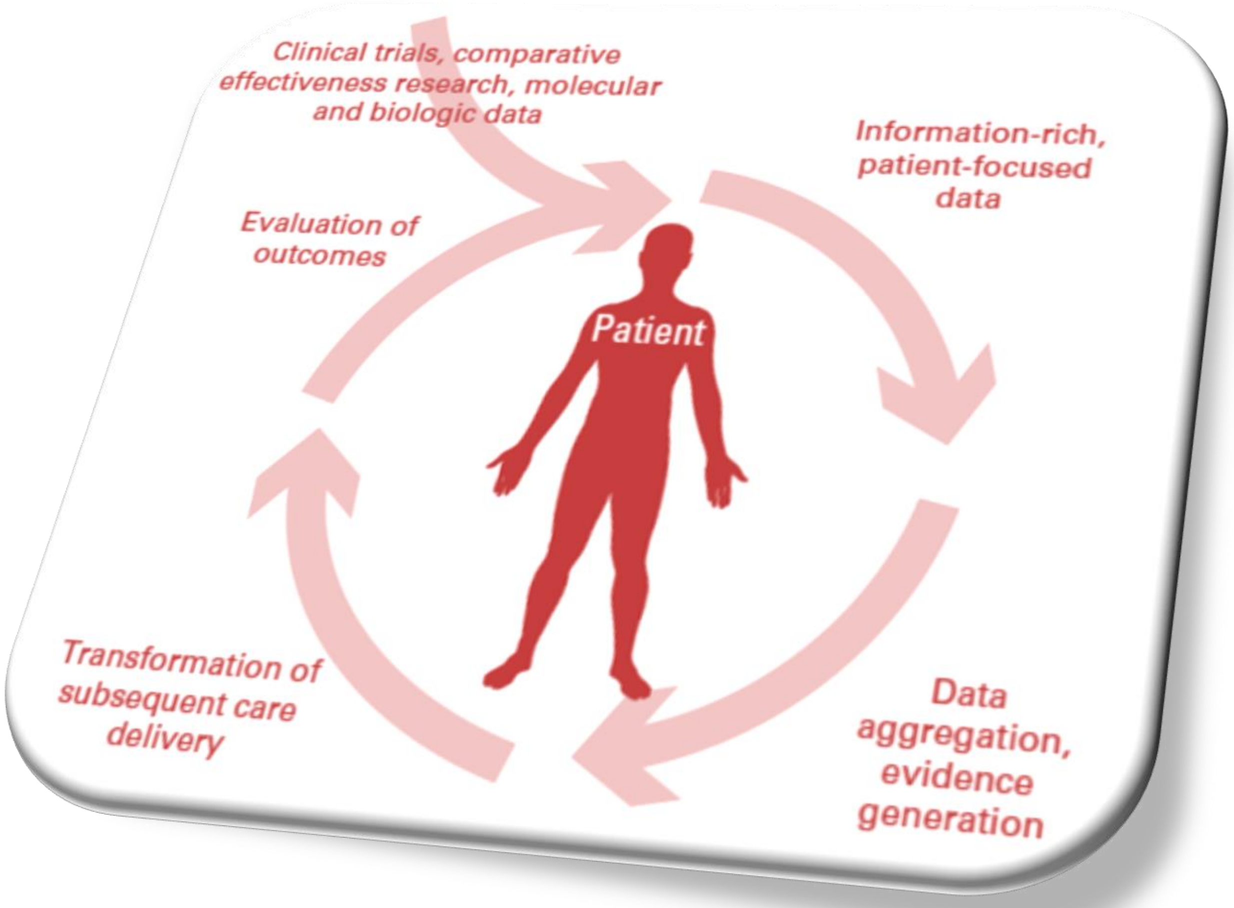


NSCLC (Lung Cancer)
2 year survival
158 patients
5 MDs
Prospective
AUC: 0.56

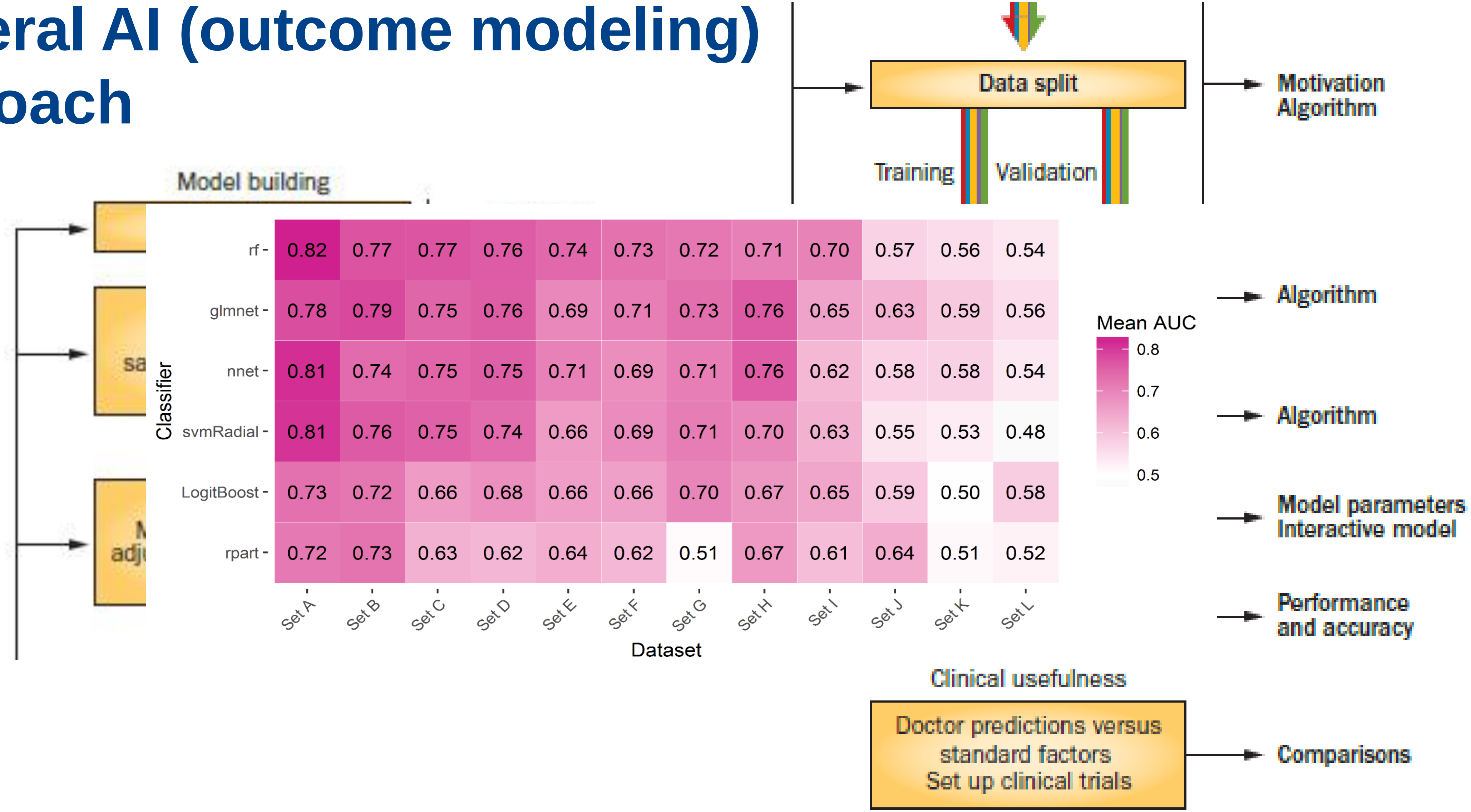


Oberije et al. , Radiother Oncol. 2014; 112: 37–43 / J Clin Oncol 2010;28:4268 / JMI 2012 Friedman, Rigby / BMJ Clinical Evidence

Potential of Real World Data & Artificial Intelligence Learning Health Care System – Faster Innovations & Better Outcomes



General AI (outcome modeling) approach



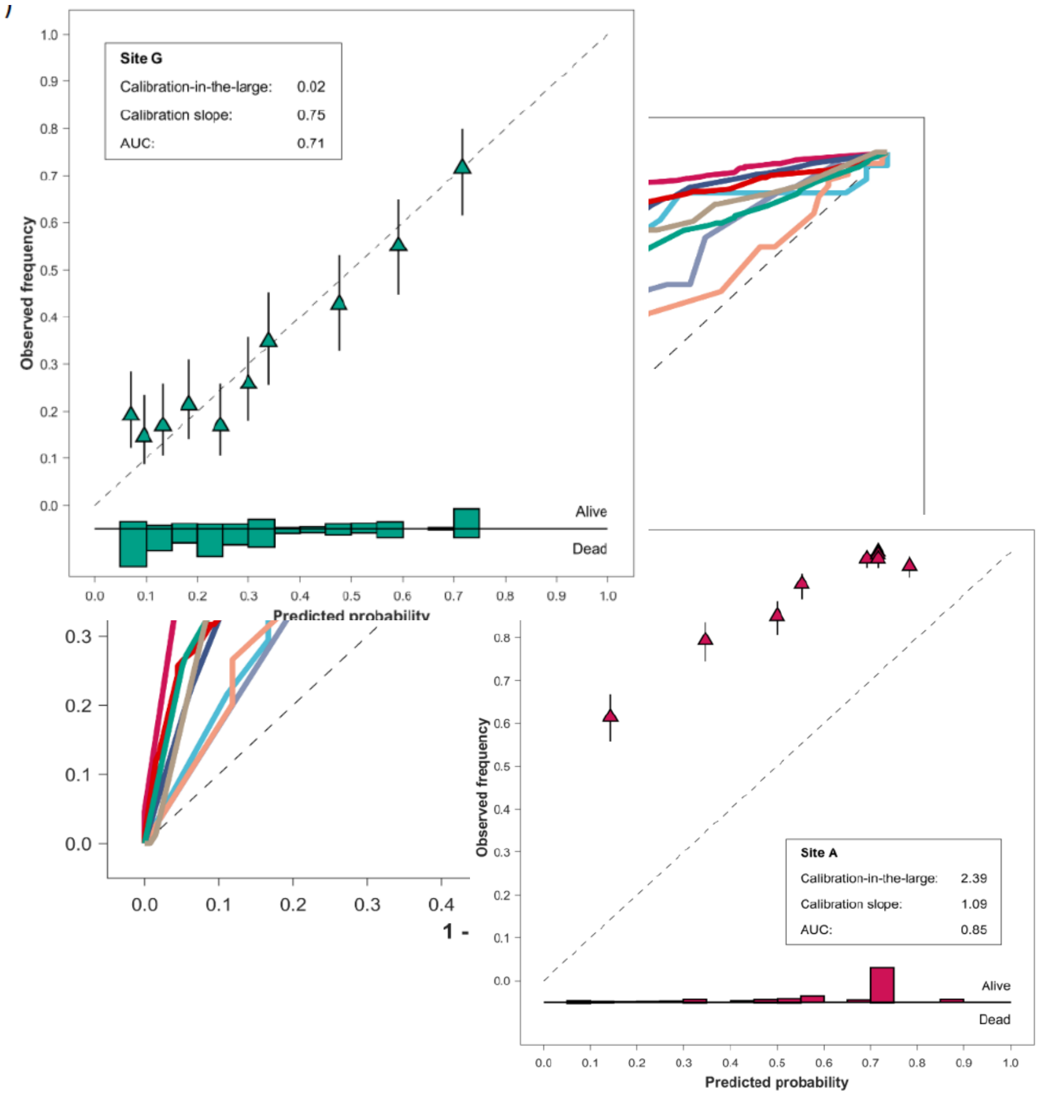
Lung cancer - Survival

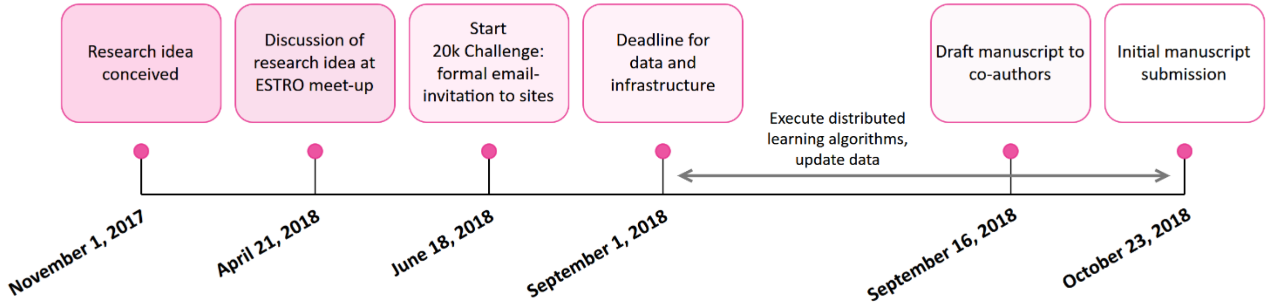
Table 1
Cohort information. NSCLC: non-small cell lung cancer. SBRT: stereotactic body radiotherapy. RT: radiotherapy. CHART: continuous, hyperfractionated, accelerated radiotherapy.

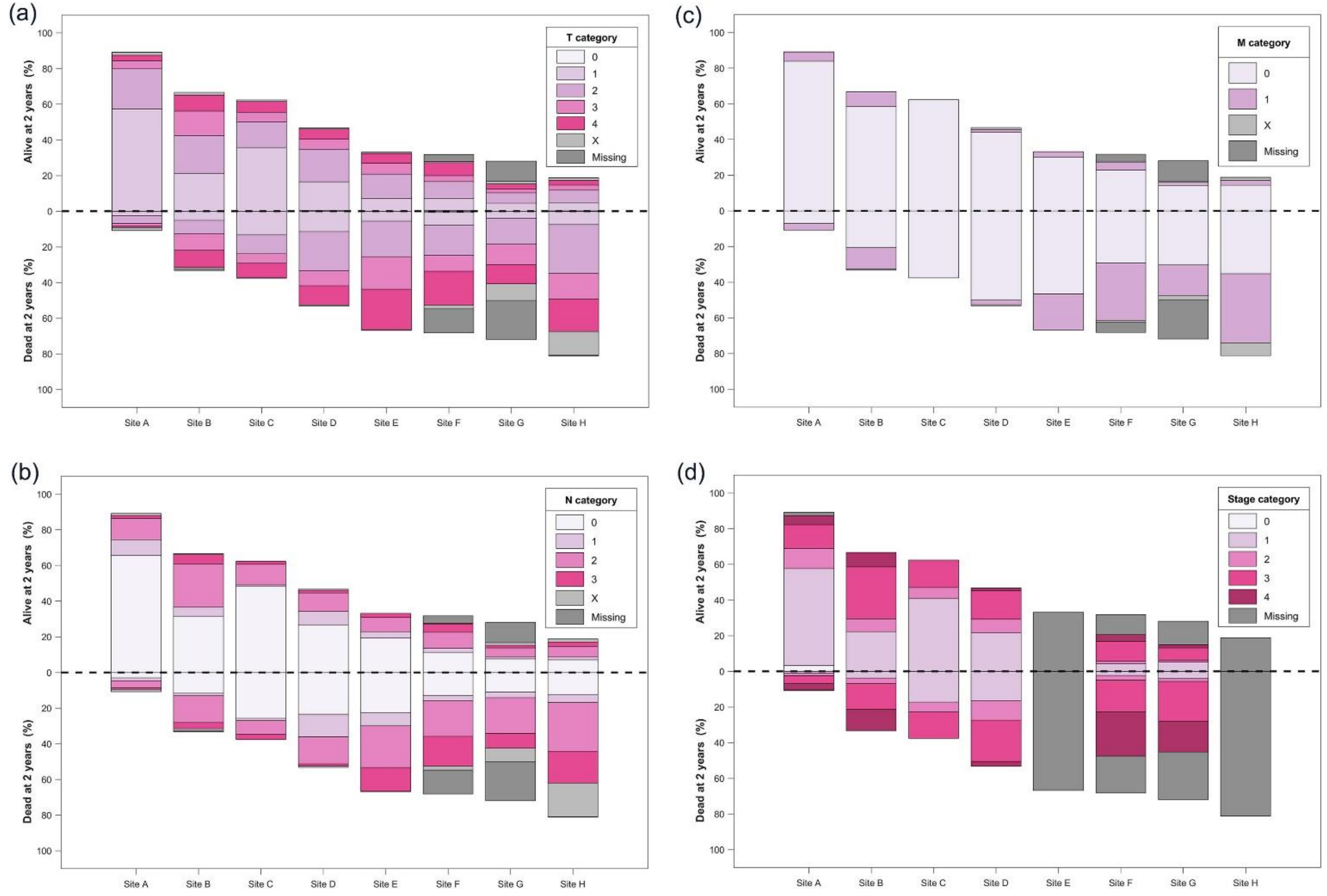
		Disease	Interval	Treatment
Shanghai	5214	-IV (histologically	January 2008-August 2016	(Chemo-)radiotherapy, surgery, chemotherapy. Filtered for having last follow-up records in 2018 or documented vital status.
Rome	706	I-IV, histo-cytologically	October 2004-May 2018	(Chemo-)radiotherapy, chemotherapy, surgery, multimodality treatment.
Rotterdam	829	ipheral stage I, 2) stage III	1) 2005–2016, 2) 2008–2013	1) SBRT only, 2) concurrent (chemo-)radiotherapy, surgery.
Cardiff	785	-IV (either clinical diagnosis lly confirmed)	2004–2017	Definitive radiotherapy (55 Gy in 20 fractions, CHART, concurrent or sequential chemo-radiotherapy or other standard/accepted radical radiotherapy schedules) excluding SBRT or post-surgery adjuvant RT.
Manchester	6211	I-IV (either clinical diagnosis lly confirmed)	1997–2018	First available T, N, and M staging information of lung cancer patients treated with curative and palliative RT. Includes post-surgery RT, (chemo-)radiotherapy, recurrences.
Maastricht	4110	I-IV	1982–2018	First available T, N, M, and overall staging information of lung cancer patients treated with curative and palliative RT. Includes post-surgery RT, (chemo-)radiotherapy, recurrences.
Amsterdam	16,260	I-IV	1955–2018	First available T, N, M, and overall staging information of lung cancer patients. Includes surgery, (chemo-)radiotherapy.
Nijmegen	2975	I-IV	1971–2018	First available T, N, M, and overall staging information of all lung cancer patients treated with curative and palliative RT. Includes post-surgery RT, (chemo-)radiotherapy, recurrences, SBRT.
	37,090			

Deist, T. M. *et al* *Radiotherapy and Oncology* **144**, 189–200 (2020).

Lung cancer - Survival



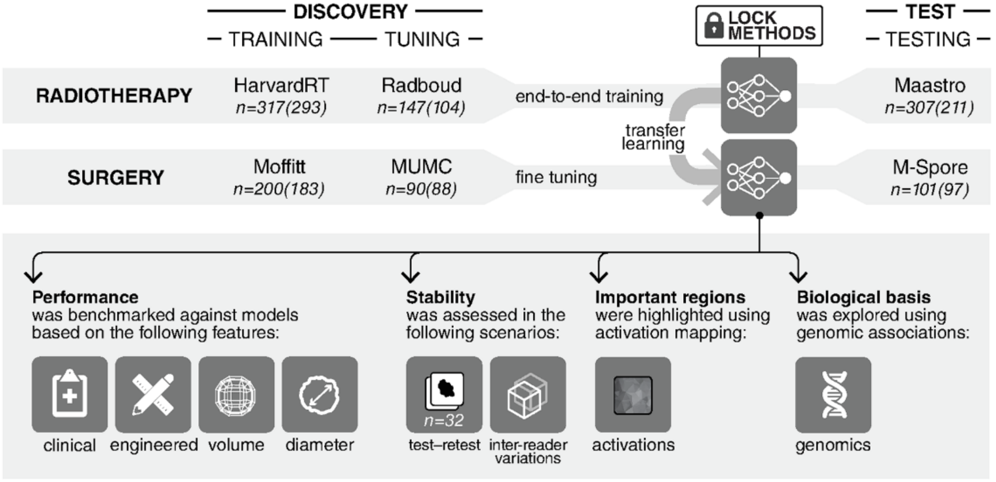


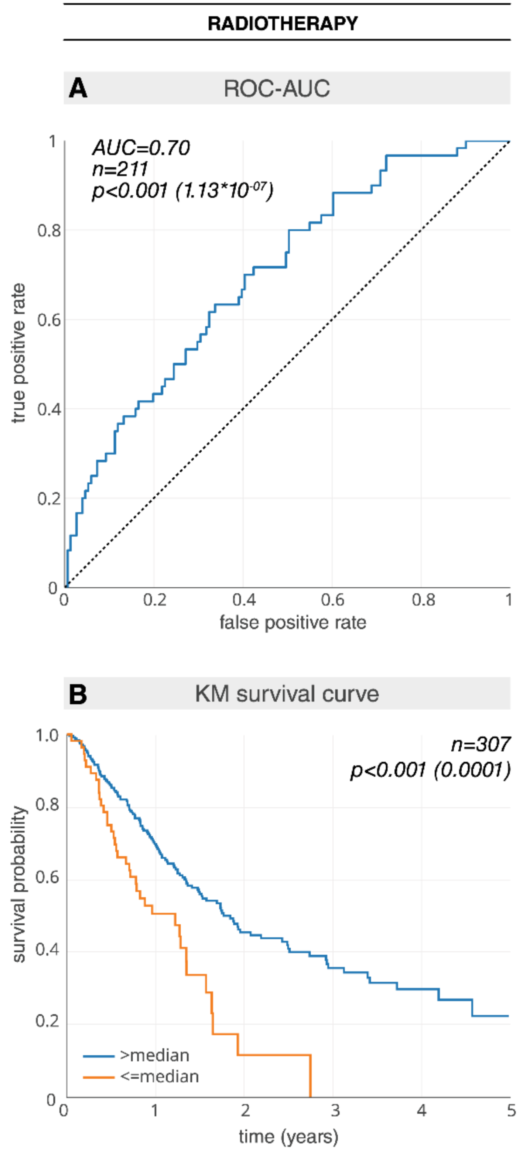


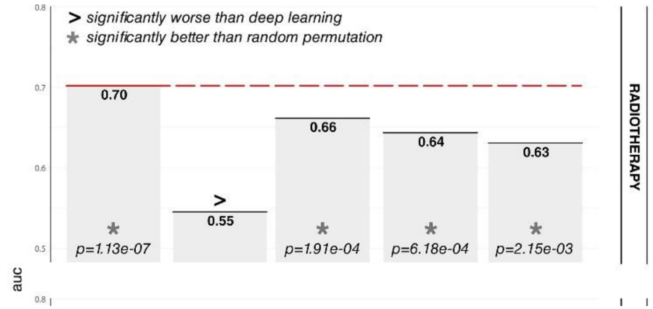
- Fully federated – no data sharing

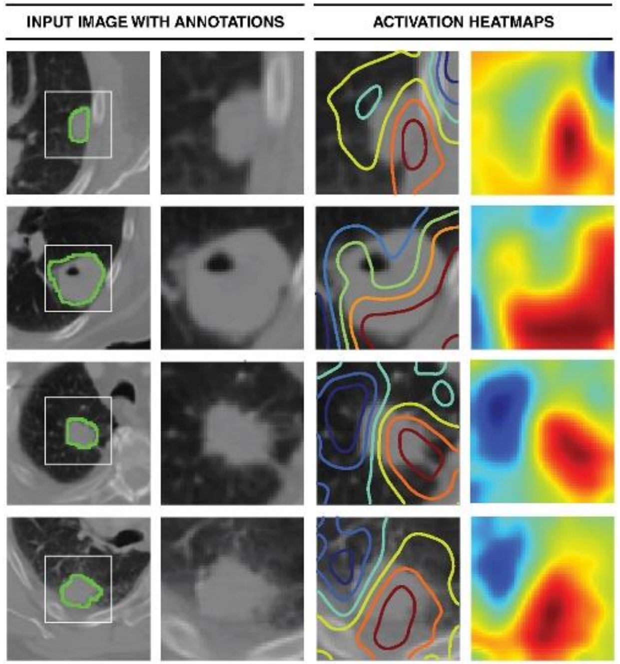
Deist, T. M. *et al* *Radiotherapy and Oncology* **144**, 189–200 (2020).

Lung cancer - Survival



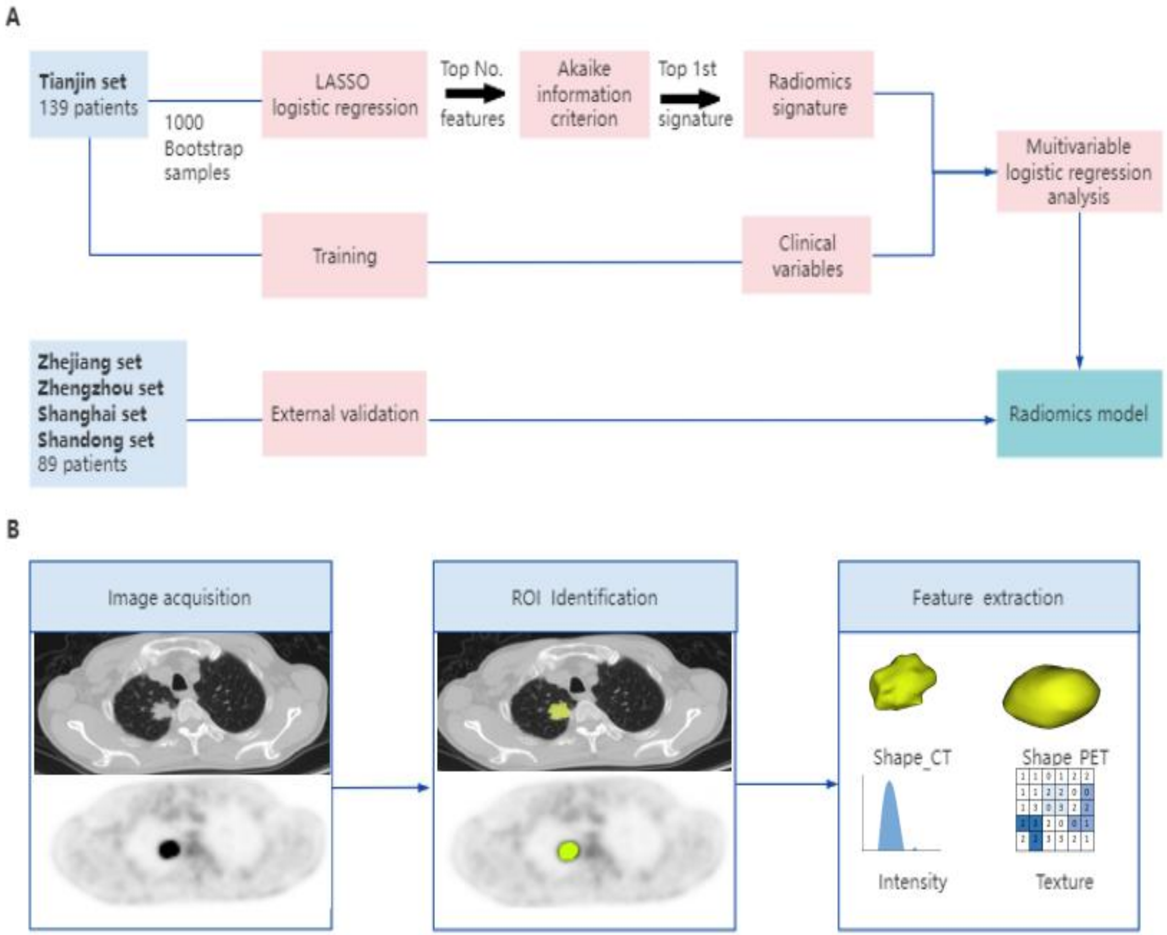


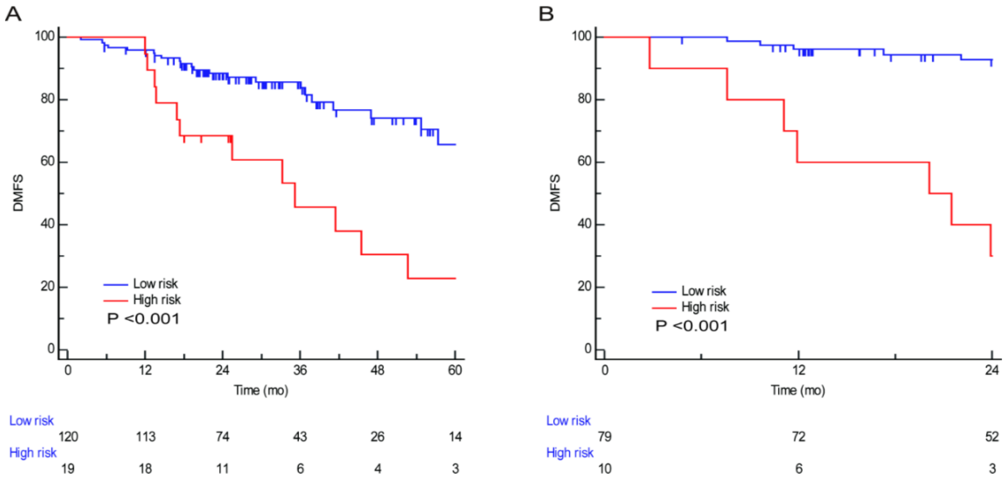




PLoS Med 2018 15(11): e1002711.

Lung cancer - Distant metastasis after SBRT



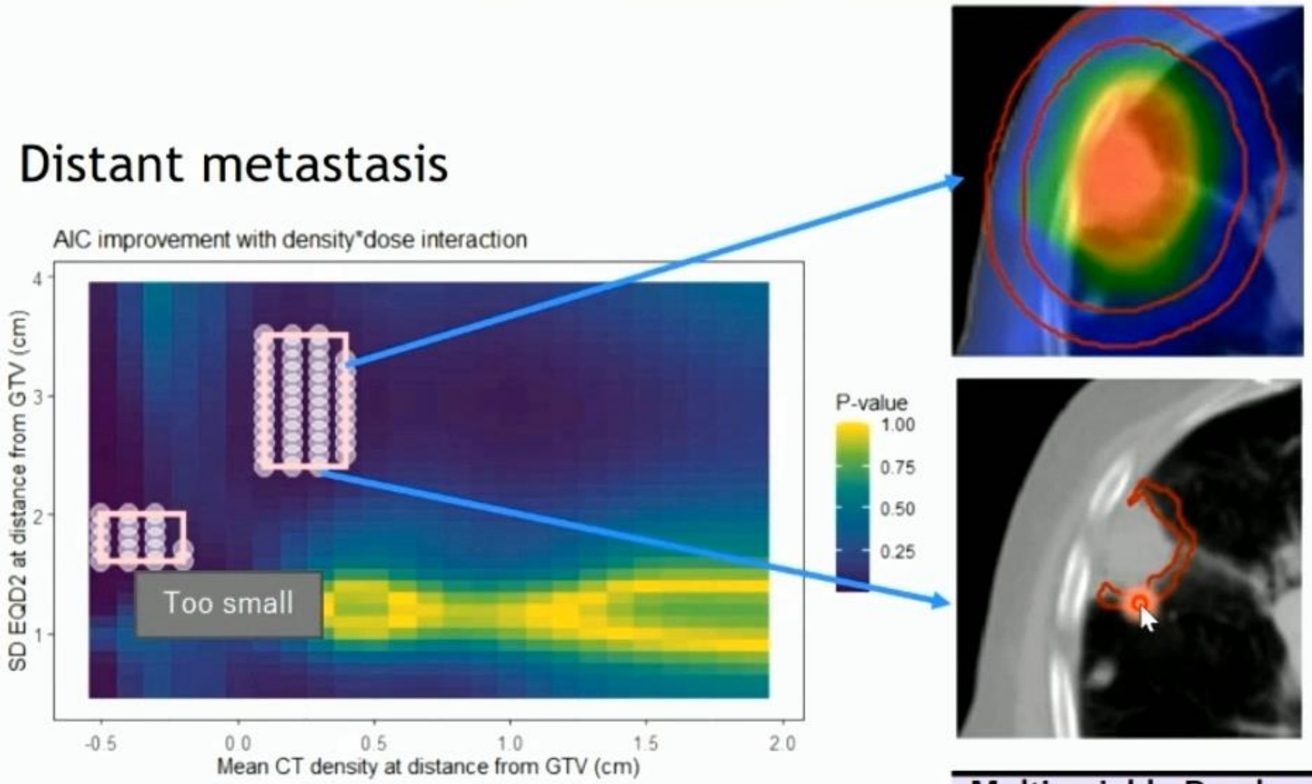


Model	Training set (95%CI)	Over-optimistic correction (95%CI)	External validation set (95%CI)
CT	0.819 (0.745-0.892)	0.804 (0.728-0.880)	0.786 (0.641-0.931)
PET	0.763 (0.678-0.848)	0.735 (0.646-0.824)	0.804 (0.681-0.927)
CT + PET	0.835 (0.780-0.891)	0.828 (0.757-0.898)	0.819 (0.692-0.947)

Lung cancer – Distant metastasis

ESTRO 2021

Distant metastasis



Link between peritumoural density and distant failure is modified by the dose variability outside the PTV

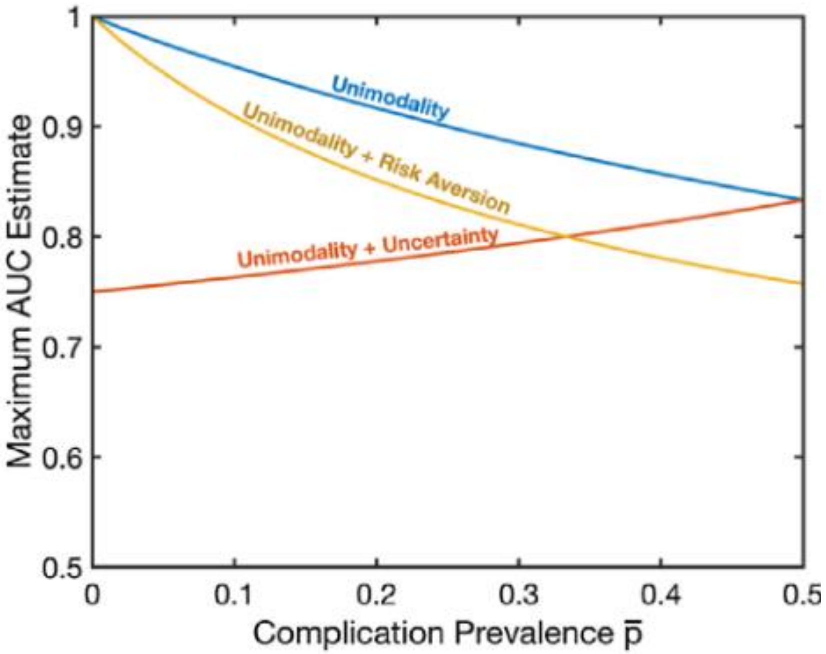
C-index: 0.69
Significantly improved model for **55%** of bootstrap resamples.

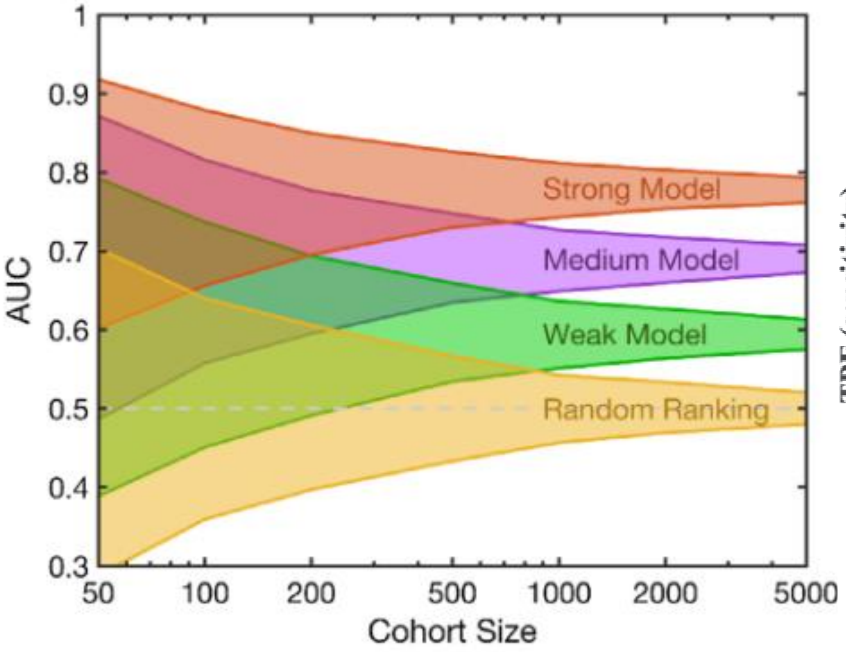
Multivariable P-value	With interaction	Without interaction
Density parameter	**0.042***	0.303
Dose parameter	**0.023***	0.703
Density*Dose	**0.025***	----

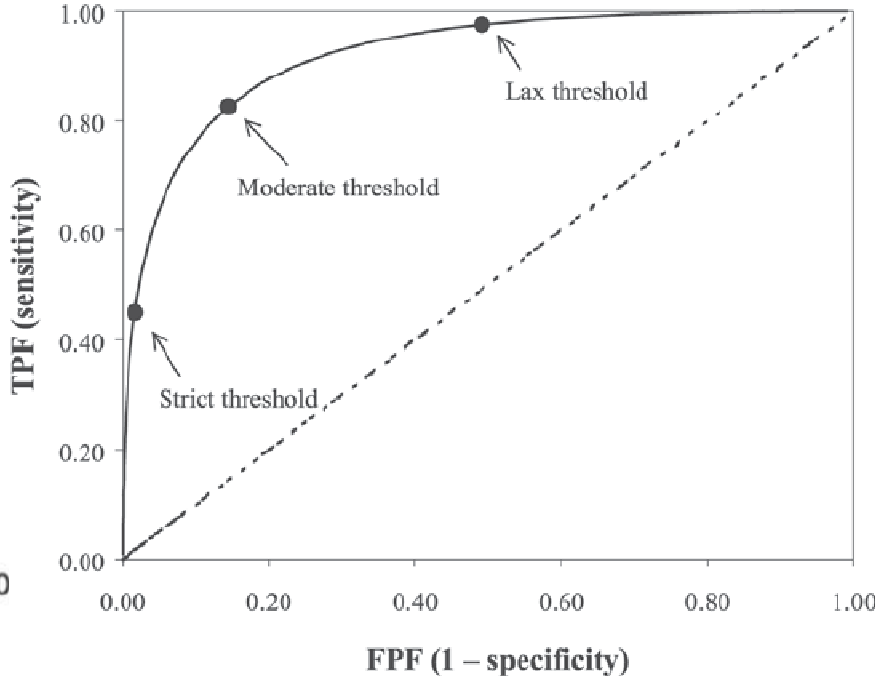
**correcting for age, sex, tumour location, tumour motion, tumour volume.

Davey et al. Front Oncol 2022

A note on AUC, determinism, prevalence, cohort size, operating point







Lung cancer – Model based indications for proton therapy

Radiatiepneumonitis graad ≥ 2

AUC 0.63

$$NTCP = \frac{1}{1+e^{-S}}$$

Waarbij:

$$S = -4.12 + 0.138 * MLD - 0.3711 * (\text{Roken: gestopt}) - 0.478 * (\text{Roken: actief}) + 0.8198 * (\text{Pulmonale comorbiditeit}) + 0.6259 * (\text{Tumor locatie}) + 0.5068 * \text{Leeftijd} + 0.47 * (\text{Sequentiële chemotherapie})$$

Variabelen:

MLD	Gemiddelde longdosis (Gy) op basis van intekening longen – GTV.
Roken: gestopt	Gestopt met roken = 1, nooit of actief roker = 0.
Roken: actief	Actief roker = 1, nooit gerookt of gestopt = 0.
Pulmonale co-morbiditeit	COPD of andere pre-existente longziekte = 1, Geen = 0.
Tumor locatie	Midden-/onderkwab = 1, bovenkwab = 0.
Leeftijd	≥63 jaar = 1, <63 jaar = 0.
Sequentiële chemotherapie	Ja = 1, nee = 0.

Slokdarm toxiciteit graad ≥ 2

AUC 0.73

$$NTCP = \frac{1}{1+e^{-S}}$$

Waarbij:

$$S = -3.634 + 1.496 * \ln(MED) - 0.0297 * (\text{Interval start-stop RT})$$

Variabelen:

MED	Gemiddelde oesophagus dosis (Gy).
Interval start-stop RT	Overall treatment time in dagen.

2-jaars mortaliteit

AUC 0.64

$$NTCP = \frac{1}{1+e^{-S}}$$

Waarbij:

$$S = -1.3409 + 0.0590 * SQRT(GTV) + 0.2635 * SQRT(MHD)$$

Variabelen:

GTV	Volume (cm^3) van GTV van tumor en klieren.
MHD	Gemiddelde hartdosis (Gy).

Performance vs Comprehensibility

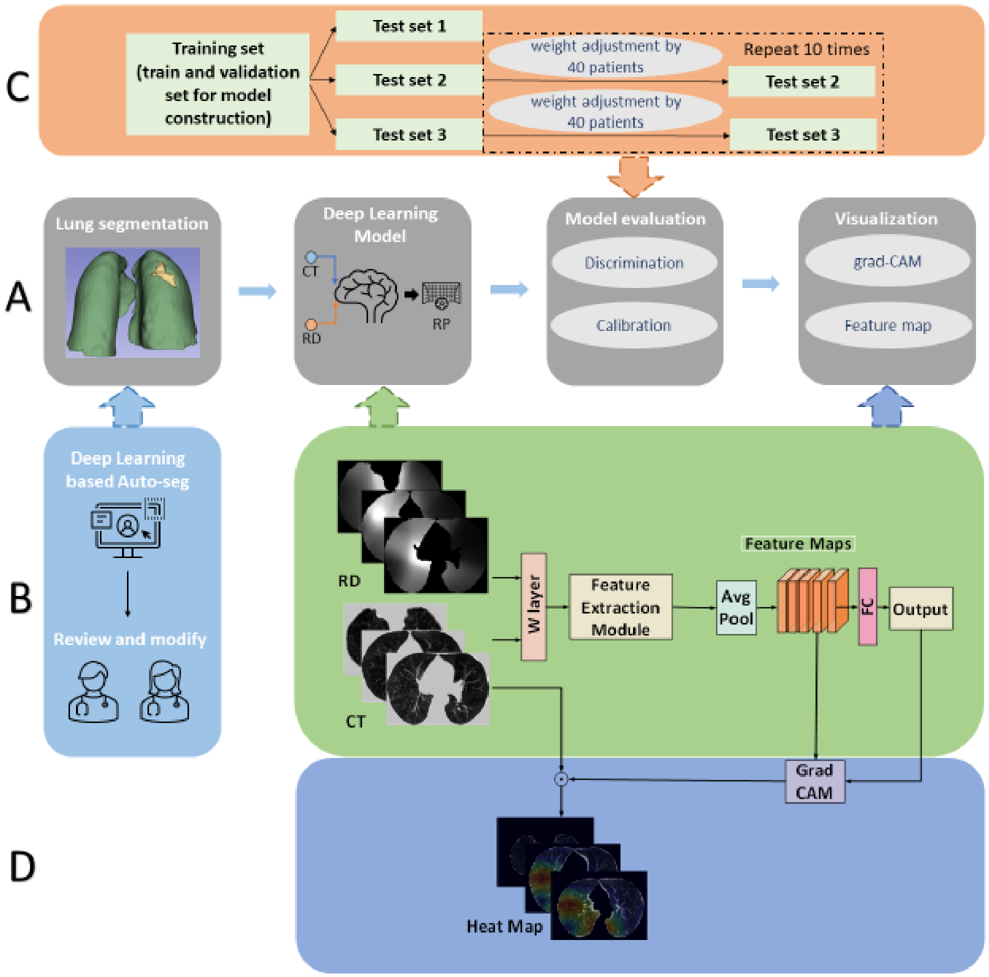
Table 3 | Comparisons between human evaluations and different types of AI approaches

Approaches	Model comprehensibility	Performance	Reproducibility	Dependency on prior knowledge	Development and training costs[a]	Running costs	Around-the-clock availability	Update costs
Human evaluation	High	Moderate or high	Moderate	High	High	High	Low	High
Rule-based algorithms	High	Moderate or high	High	High	Moderate or high	Low	High	High
Feature-based machine-learning methods	Moderate or high	Moderate or high	High	Moderate[b]	Moderate	Low	High	Moderate[c]
Deep artificial neural networks	Low or moderate	High	High	Low	Moderate	Low	High	Low

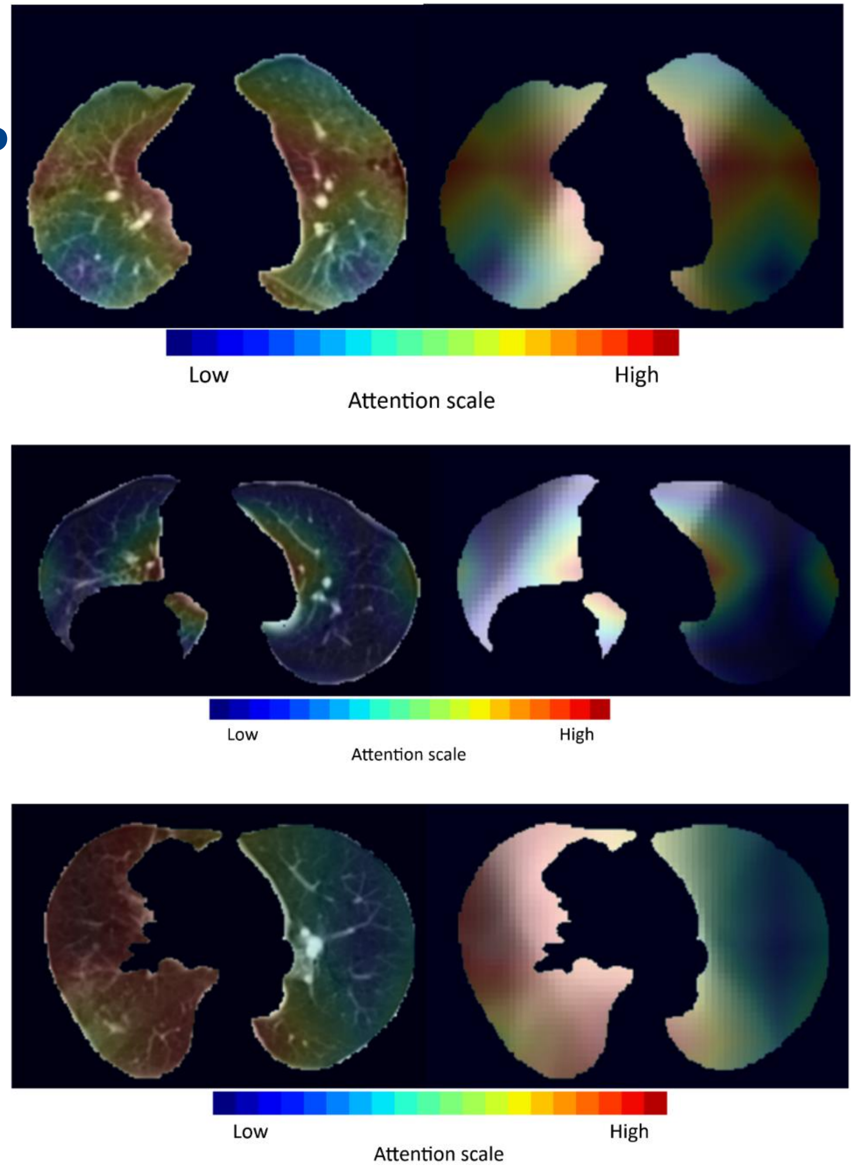
Yu et al, Nat Biomed Eng 2018;2:719

Lung cancer - Radiation pneumonitis

Tianjin (n=314+35, RP~21%), RTOG0617 (n=184 + 198, RP

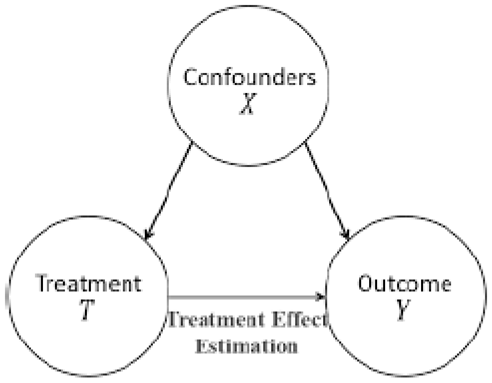


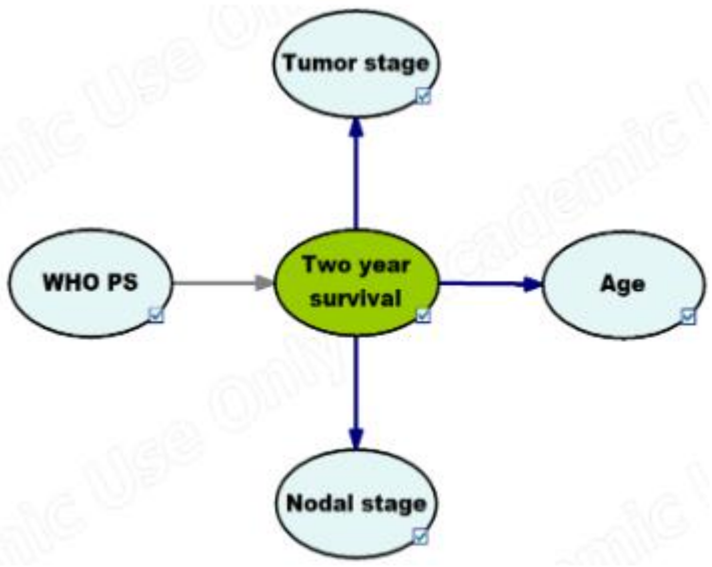
AUC
0.83
0.65
0.70

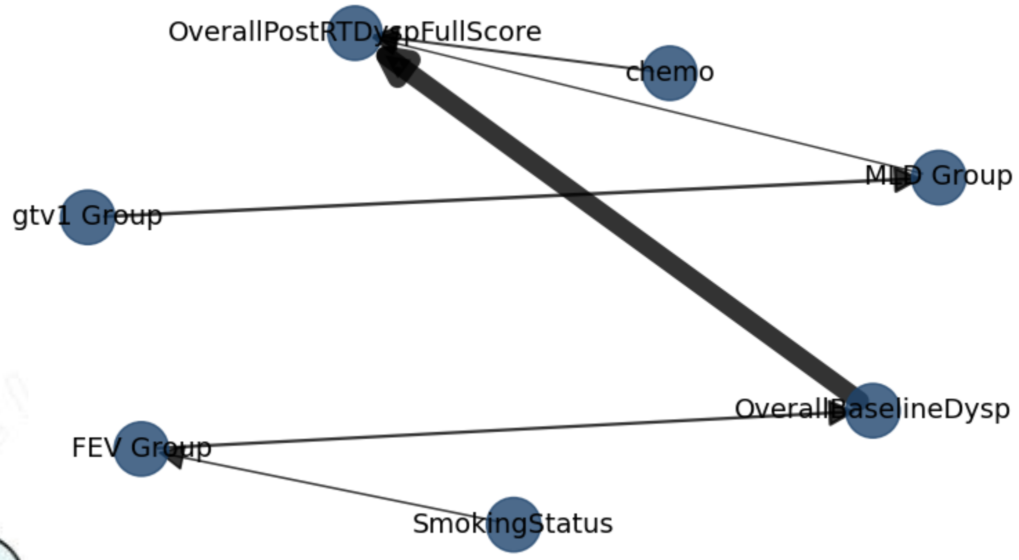


Correlation ≠ Causation

- Proton vs. Photon, Surgery vs. SBRT
- Explainable, unbiased AI needed
- Causal models -> human input needed







Key Messages

- Humans are not very good at predicting multifactorial outcomes
- AI can predict outcome better than humans, but when modeling consider
  - Training and Validation Data, Biases, Quality
  - Discrimination AND Calibration
  - Actionable insights
  - New insights
  - Interpretability
  - Causality

Who is this?

Pressure-Volume Loops in Cardiac Surgery

Proefschrift

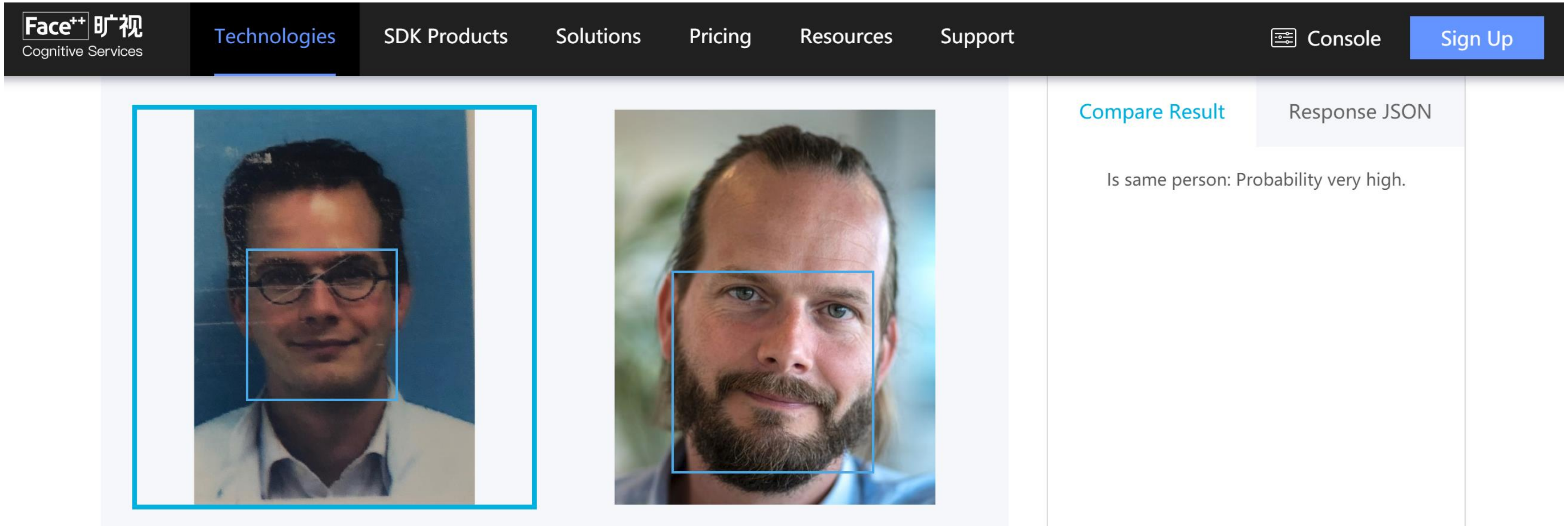
ter verkrijging van de graad van doctor
aan de Universiteit Maastricht,
op gezag van de Rector Magnificus,
Prof.dr. A.C. Nieuwenhuijzen Kruseman,
volgens het besluit van het College van Decanen,
in het openbaar te verdedigen,
op vrijdag 12 september 2003 om 14:00 uur

door

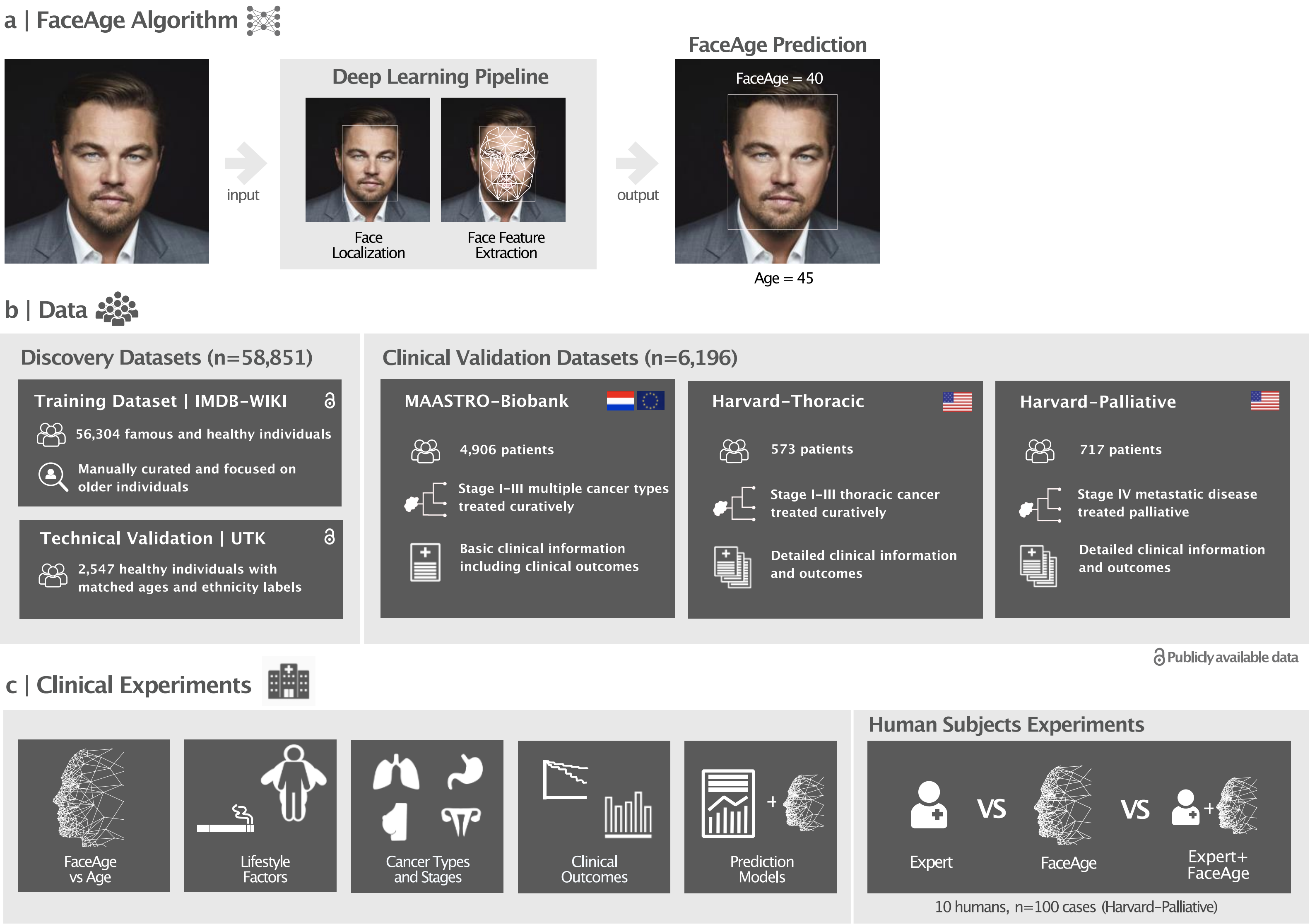
André Dekker

UNIVERSITAIRE PERS MAASTRICHT

And then this…FaceAge project

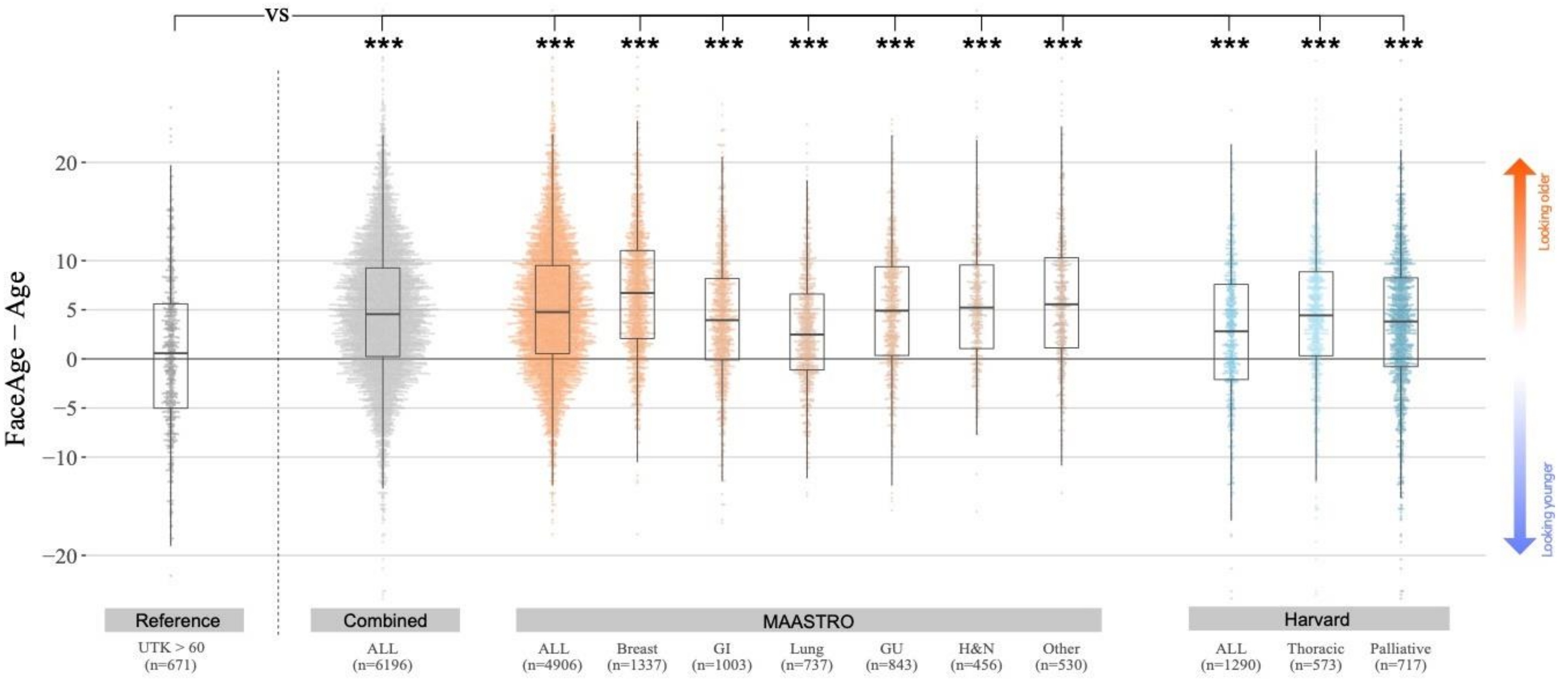


FaceAge



Zalay, Bontempi et al. Submitted

FaceAge



Zalay, Bontempi et al. Submitted

Acknowledgements

Netherlands
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UH Ghent, Belgium
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Asia
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Tata Memorial, Mumbai, India
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Princess Margaret CC, Canada
Ottawa Hospital Research Institute, Ottawa, Canada

South America
Albert Einstein, Sao Paulo, Brazil

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ICCC, Wollongong Australia
Calvary Mater, Newcastle, Australia
North Coast Cancer Institute, Coffs Harbour, Australia

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Philips, Bangalore, India
Sohard GmbH, Fuerth, Germany
Microsoft, Hyderabad, India
Mirada Medical, Oxford, UK
CZ Health Insurance, Tilburg, NL
Siemens, Malvern, PA, USA
Roche, Woerden, NL

Clinical Data Science research aims

1. Get access to all data of all people in the world
2. Learn personalized health prediction models from data
3. Apply prediction models to improve health

Cancer, Alzheimer's, Cardiovascular disease, Diabetes, Heart Failure, Parkinson's, Irritable Bowel Disease, Orthopedic Surgery, Rheumatoid Arthritis, Pediatric Surgery, Balance disorders, Hip dysplasia

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Thank you for your attention