CENTRE DE LUTTE CONTRE LE CANCER LEON BERARD

Omics and AI driven radiotherapy approaches in H&N cancers

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The Truth is rarely pure and never simple …

Oscar Wilde

The challenges for 2022 and beyond

- Automatic primary tumor GTV and nodal CTV delineation
- Omics profile as prognostic factor
- Omics profile to change the treatment intensity

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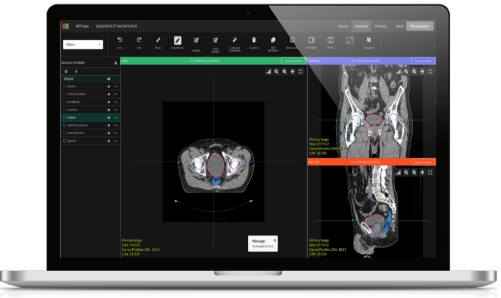
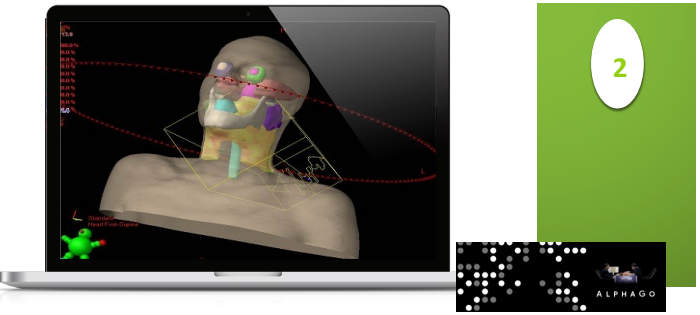
AI-based software to improve target and OAR volume delineation?





1

Plan preparation

Multi-modal, multi-organ organ segmentation through Unique combination of Deep and transfer learning

Auto-identify organs at risks and tumors in patients anatomy in a few minutes with medical accuracy

2

Dose Optimization:

Unique combination of parallel multi-objective Master-Slave optimization & reinforcement learning

Produce the best possible treatment plan in minutes instead of hours /days, protecting 30% more organs at risk

"A system's ability to correctly interpret external data, to learn from such data, and to use those learnings to achieve specific goals and tasks through flexible adaptation"

Courtesy of N. Paragios, 2021

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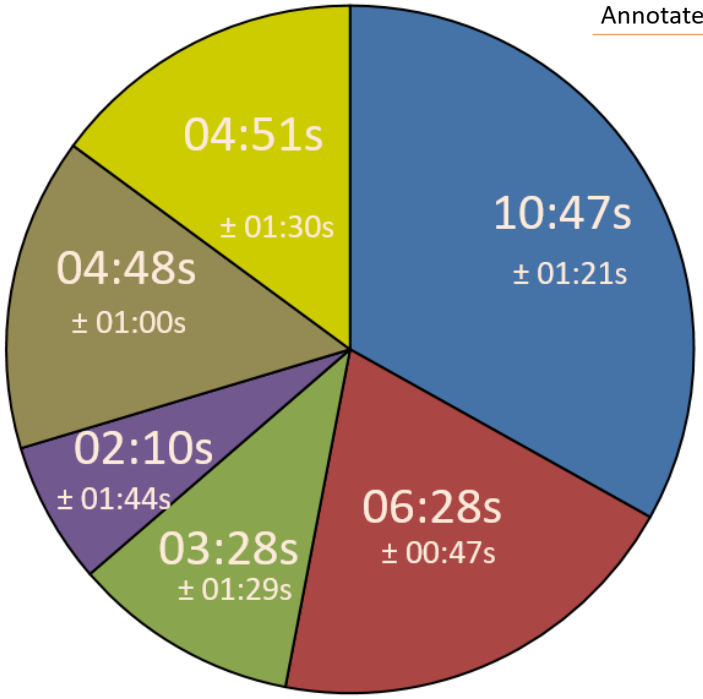
Courtesy of N. Paragios, Oct 2022

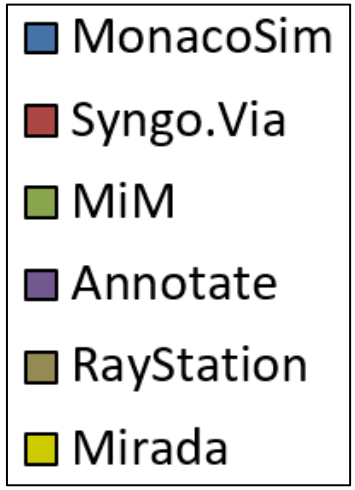
AI for OAR delineation

Mean saved time in comparison to MonacoSim

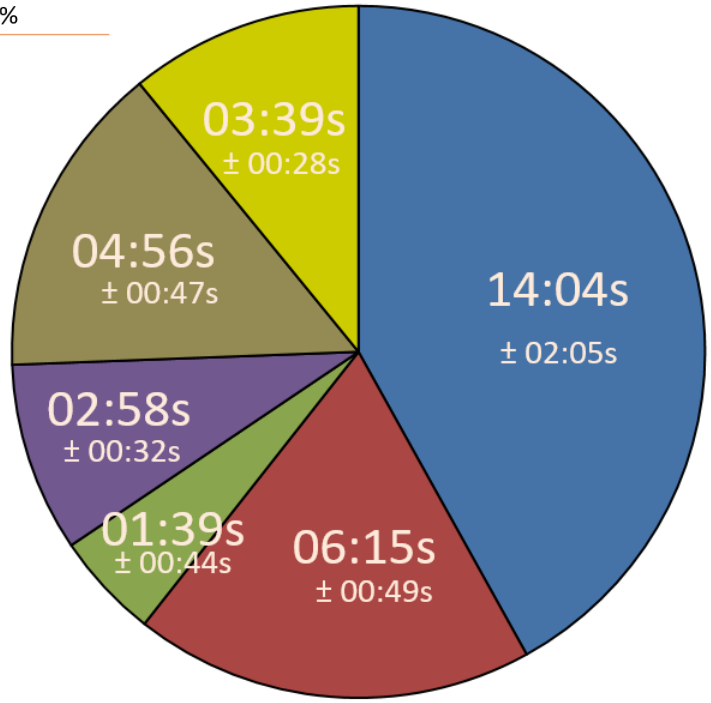
	PELVIS	THORAX
Syngo.Via	40 %	56 %
Raystation	55 %	65 %
Mirada	55 %	74 %
MiM	68 %	88 %
Annotate	80 %	79 %

PELVIS





THORAX



Automatic AI-based GTV delineation

Comparing different CT, PET and MRI multi-modality image combinations for deep learning-based head and neck tumor segmentation

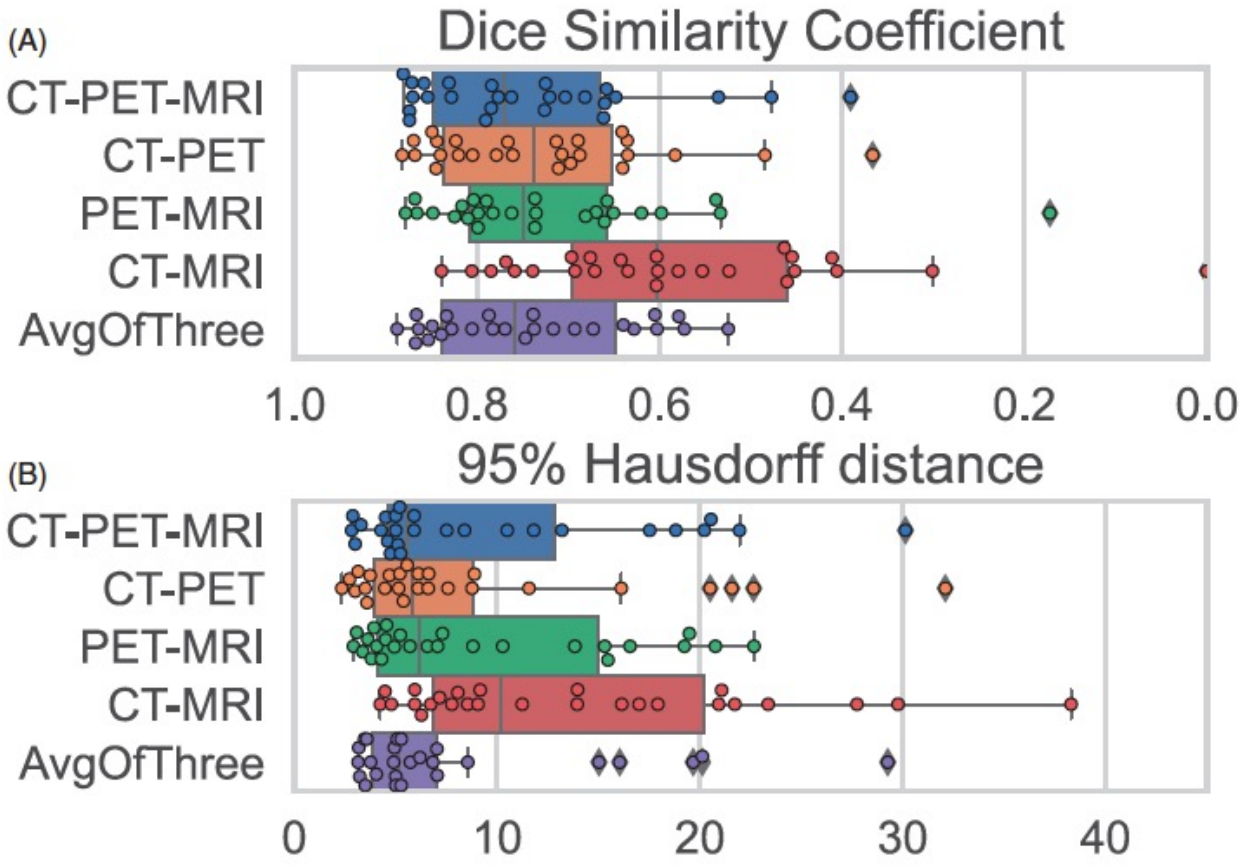
Jintao Ren[a,b,c], Jesper Grau Eriksen[a,d], Jasper Nijkamp[a,b*] and Stine Sofia Korreman[a,b,c*]

[a]Department of Clinical Medicine, Aarhus University, Aarhus, Denmark; [b]Danish Centre for Particle Therapy, Aarhus University Hospital, Aarhus, Denmark; [c]Department of Oncology, Aarhus University Hospital, Aarhus, Denmark; [d]Department of Experimental Clinical Oncology, Aarhus University Hospital, Aarhus, Denmark

- 153 patients with pharyngo-laryngeal SCC
- 60% T1-T2; 75% N^+
- CT, coronal MRI-T1, axial MRI-T2, mDixon MRI, FDG-PET acquired with an immobilization mask

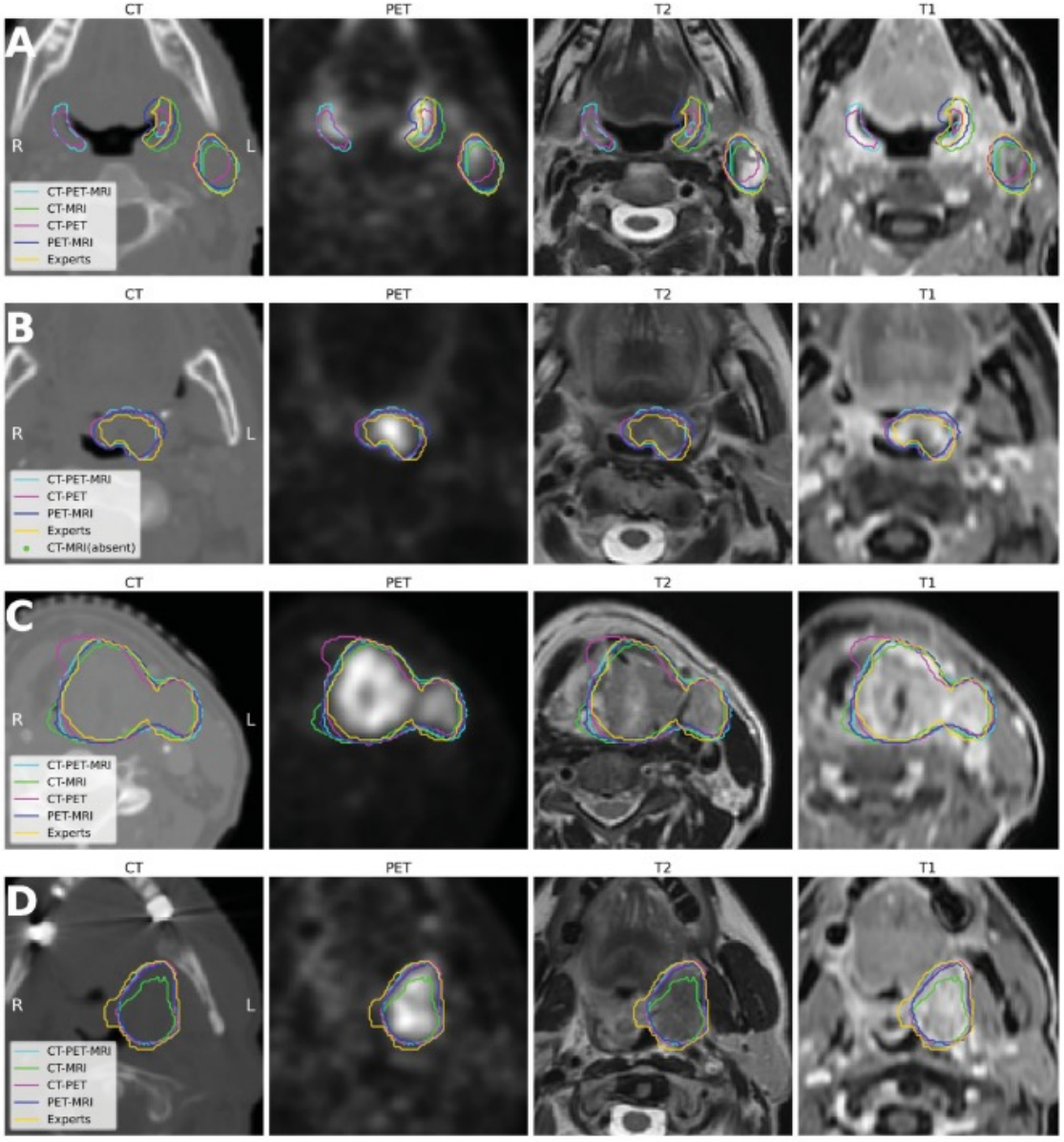
Ren et al, Acta Oncol, 2021

Automatic AI-based GTV delineation



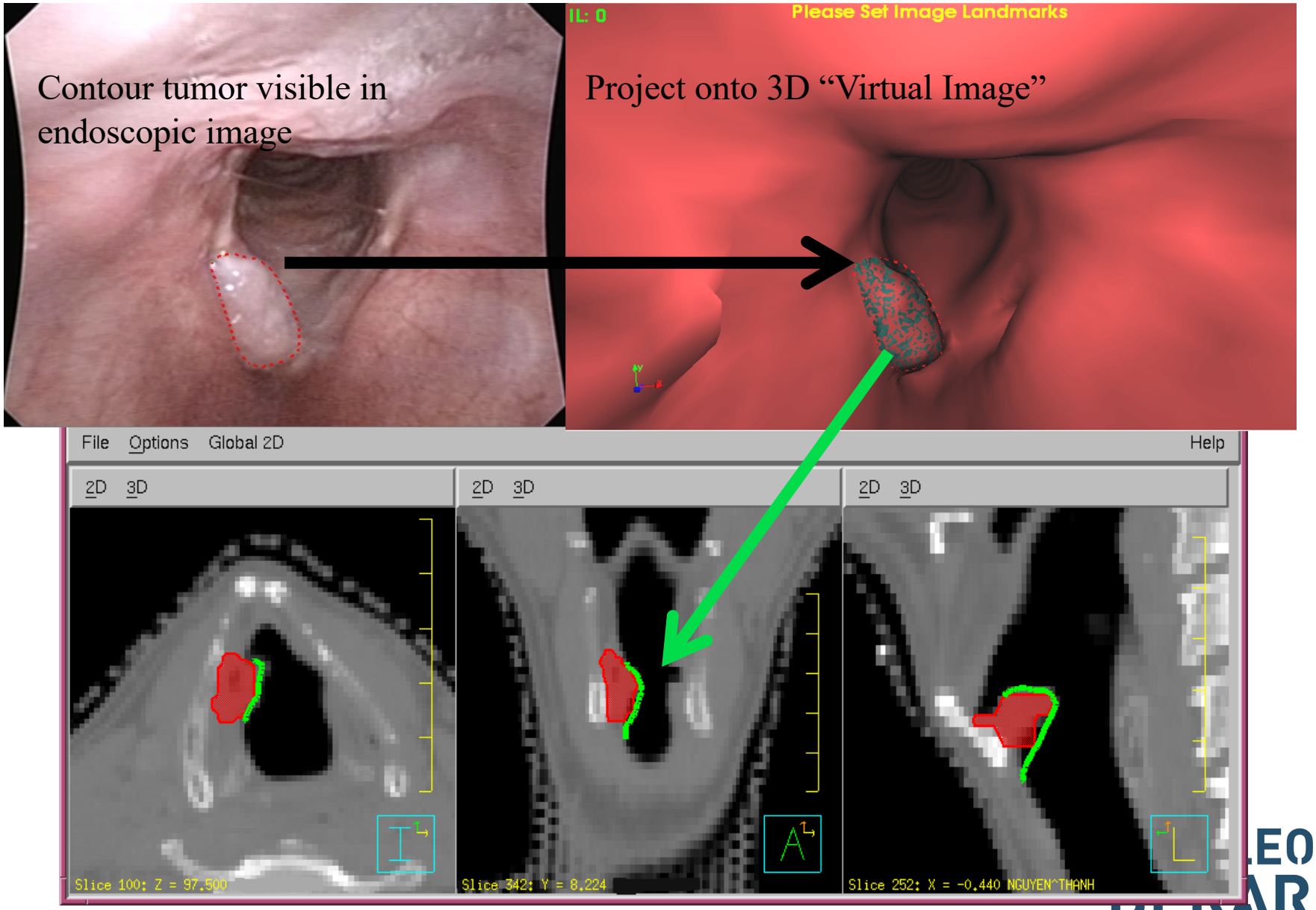
Ren et al, Acta Oncol, 2021

Automatic AI-based GTV delineation



Ren et al, Acta Oncol, 2021

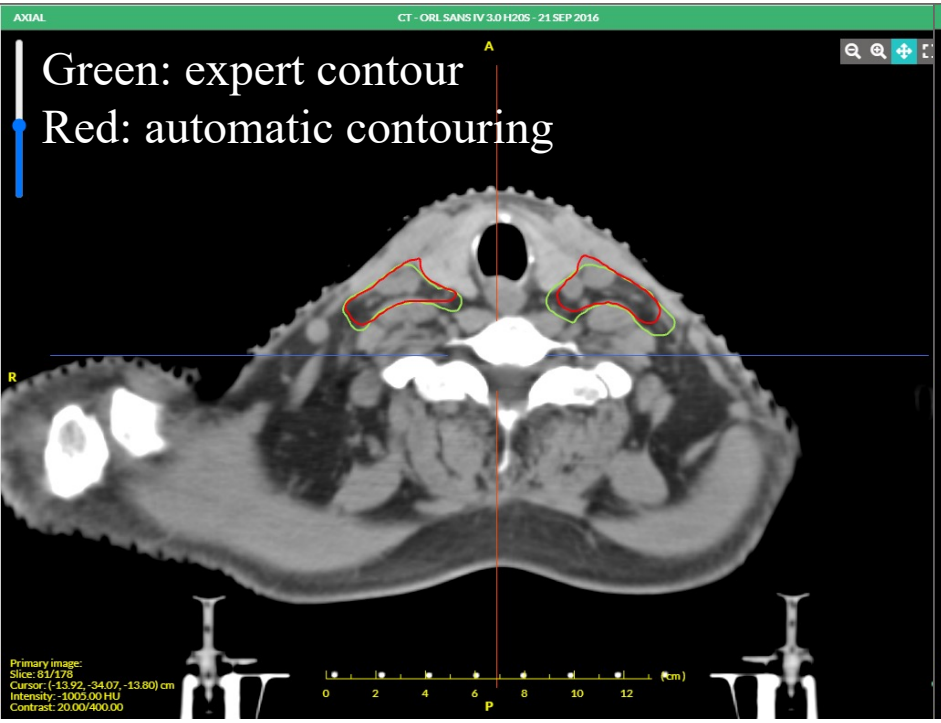
Endoscopic Contouring

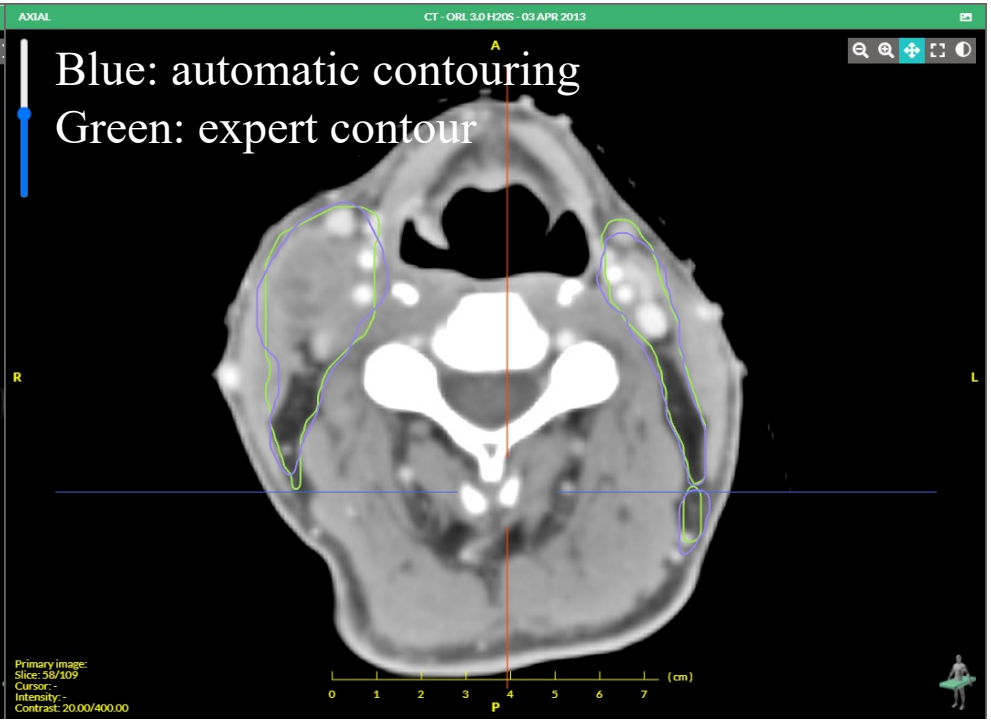


Weersink et al Med. Phys 38 6458, 2011

Weersink, US Patent: 9,138,597

Automatic nodal target volume delineation





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Courtesy of N. Paragios, Oct 2022

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Genomics profile as prognostic factor: the HPV status

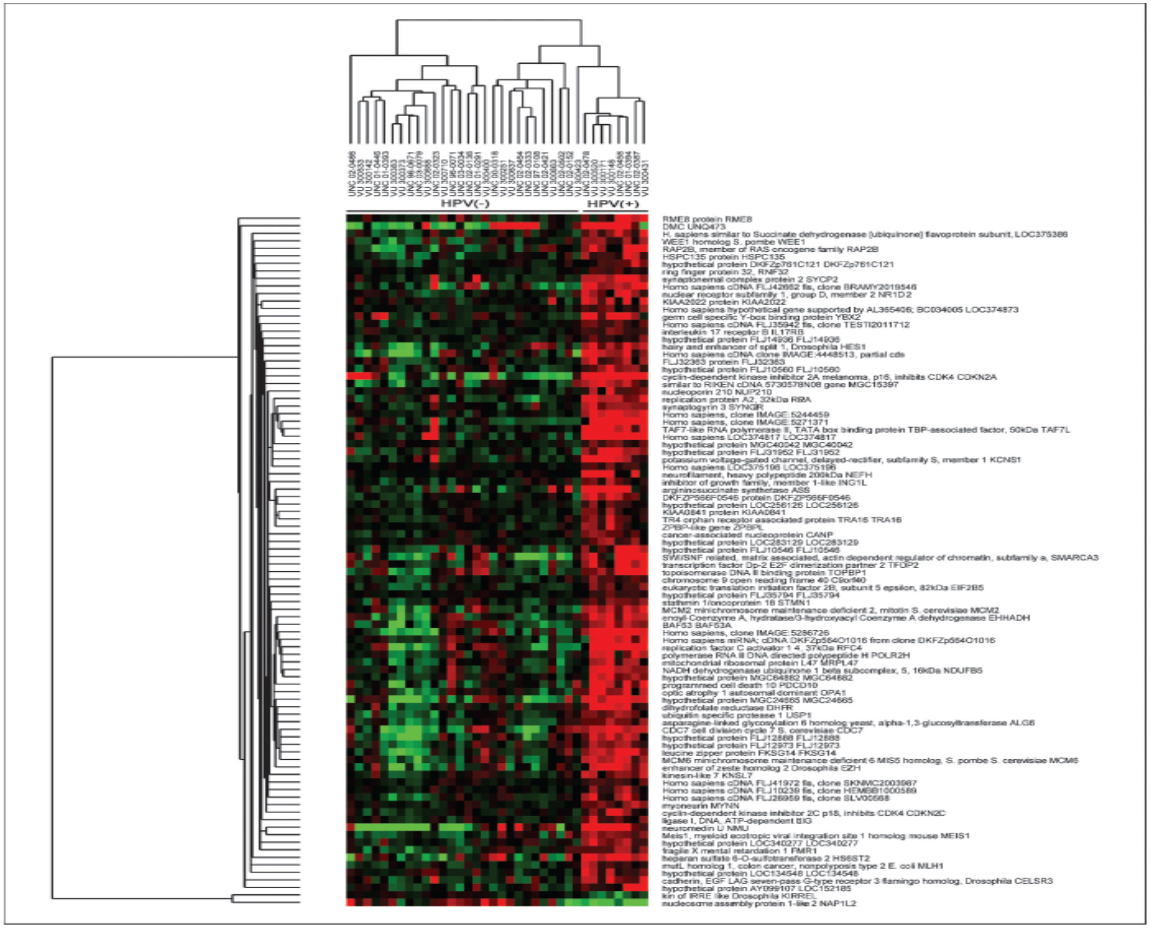
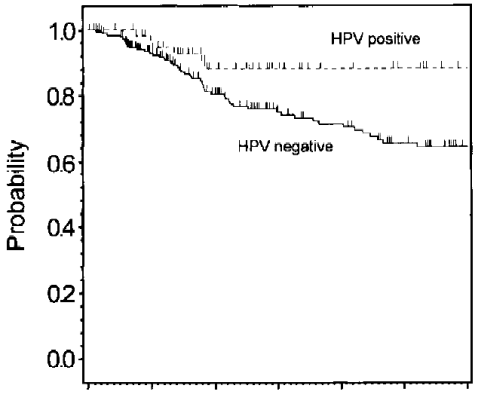


Fig. 2. Cluster diagram of 91 genes that are differentially expressed between HPV$^+$ and HPV$^-$ HNSCC tumors. HPV$^+$ tumors form a separate cluster (*right*).

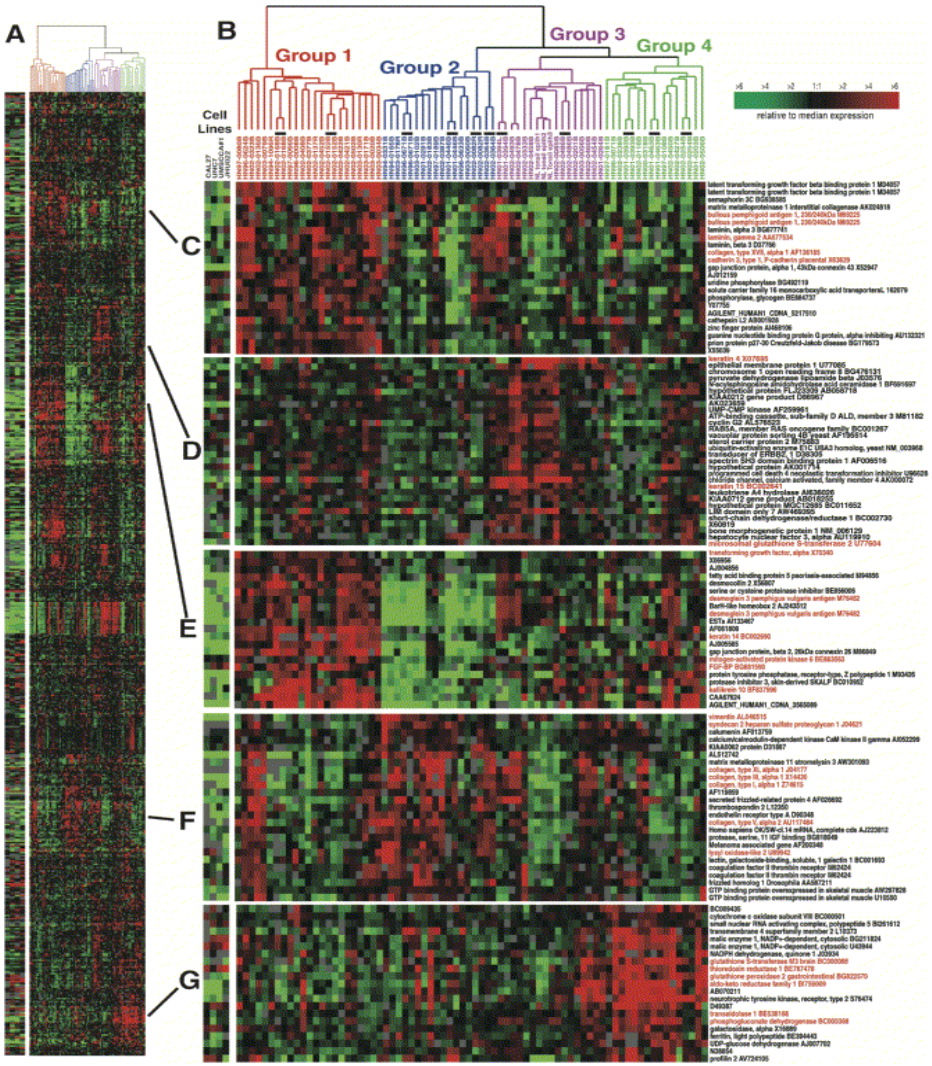


Time in Months	0	10	20	30	40	50	60
Number at risk:							
HPV positive	61		37		18		10
HPV negative	191		116		75		48

Gemelli October 2022

Slebos JR Clin Cancer Res 2006

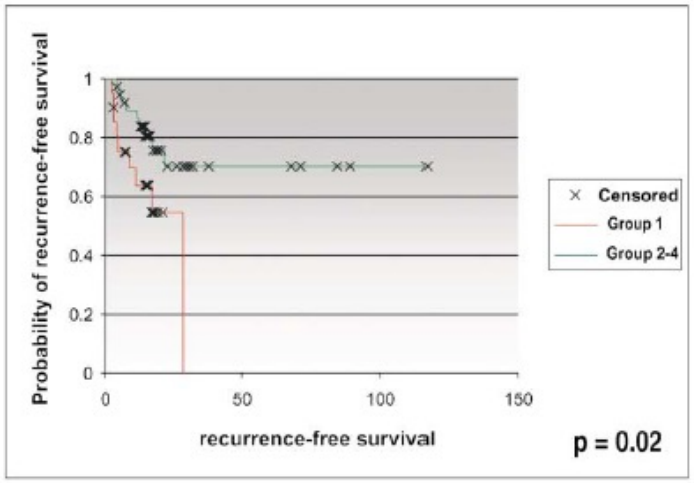
Genomics profile as prognostic factor: HNSCC gene expression

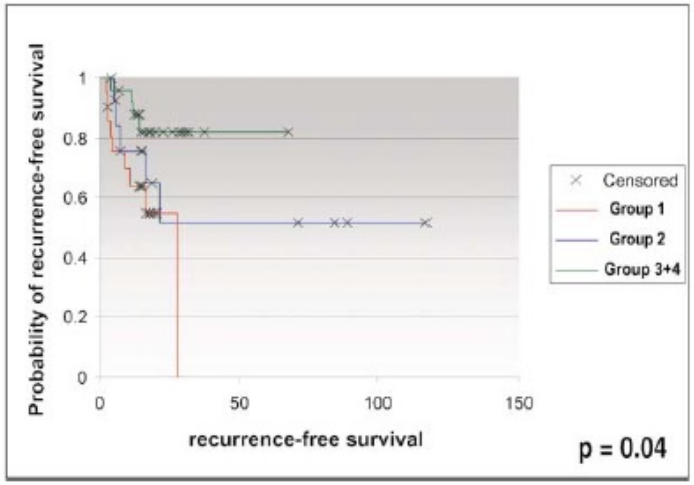


- Group 1: EGFR-pathway signature
- Group2: mesenchymal-enriched signature
- Group 3: normal epithelium-like subtype
- Group 4: high level of antioxidant subtype

Chung Cancer Cell 2004

Genomics profile as prognostic factor: HNSCC gene expression





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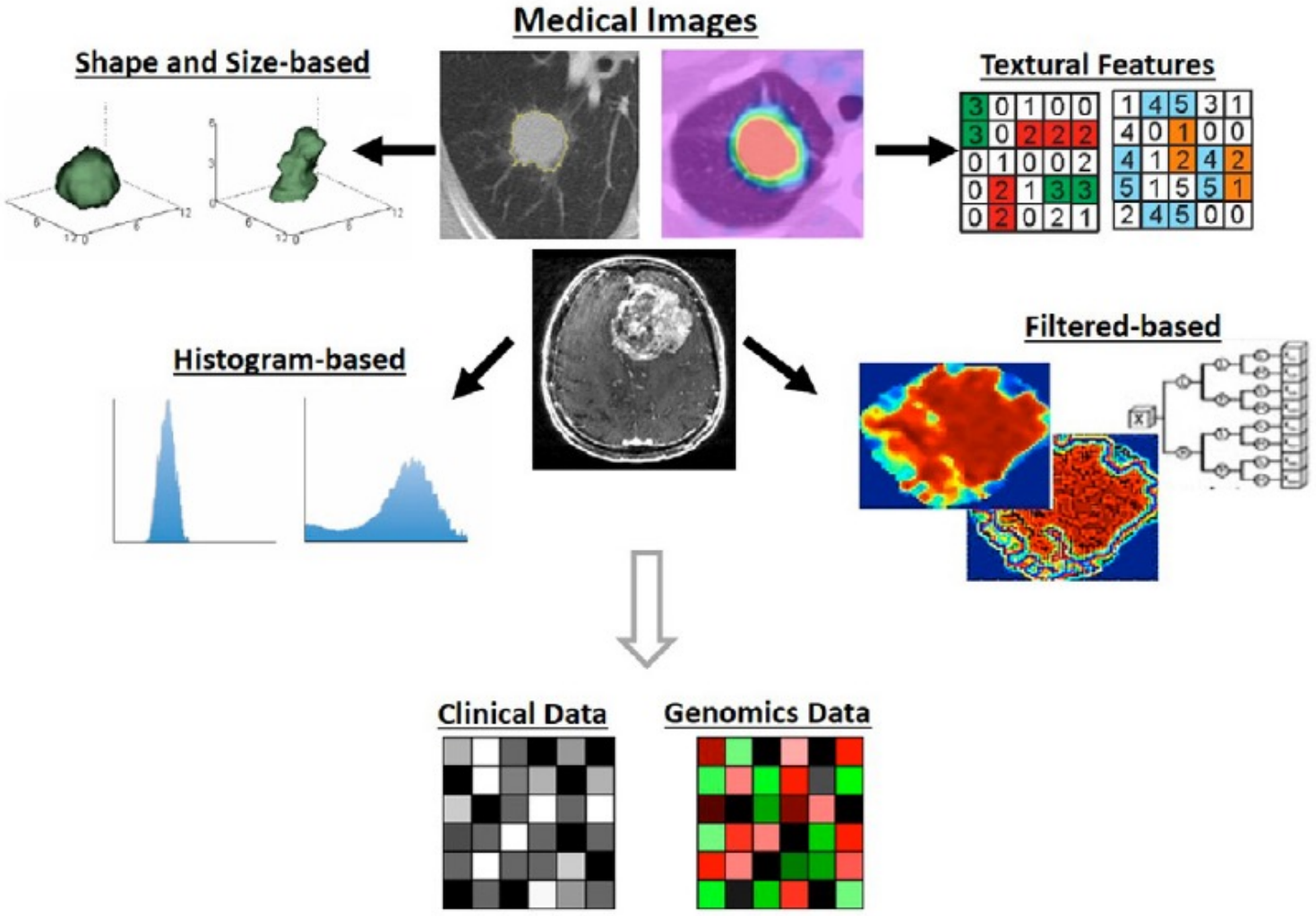
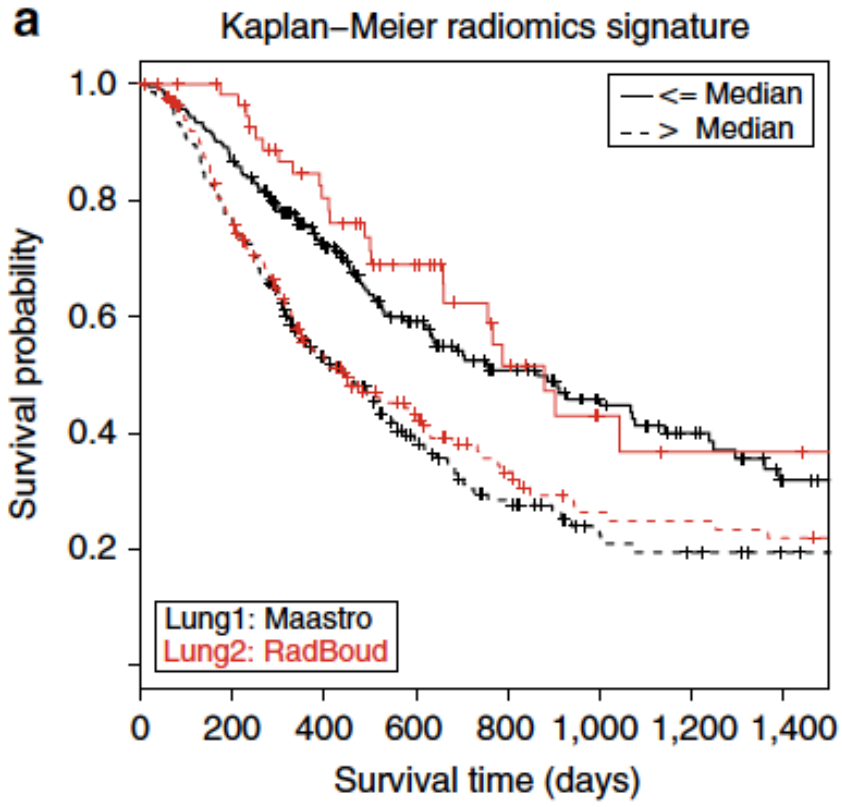
Chung Cancer Cell 2004

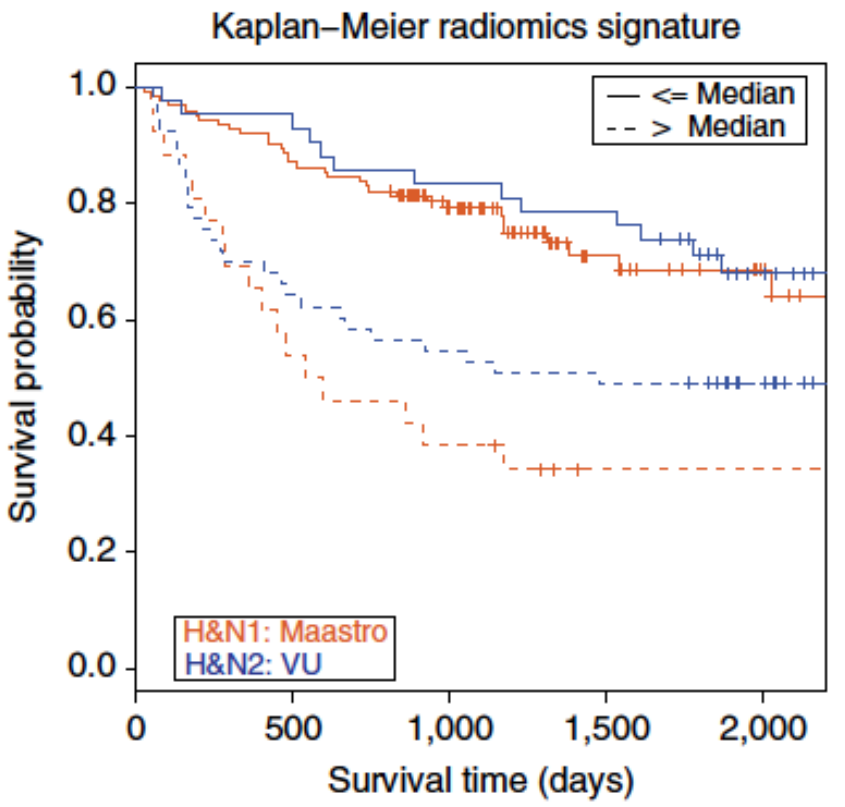
Radiomics for treatment individualization



Yip, PMB, 2016

Radiomics for treatment individualization

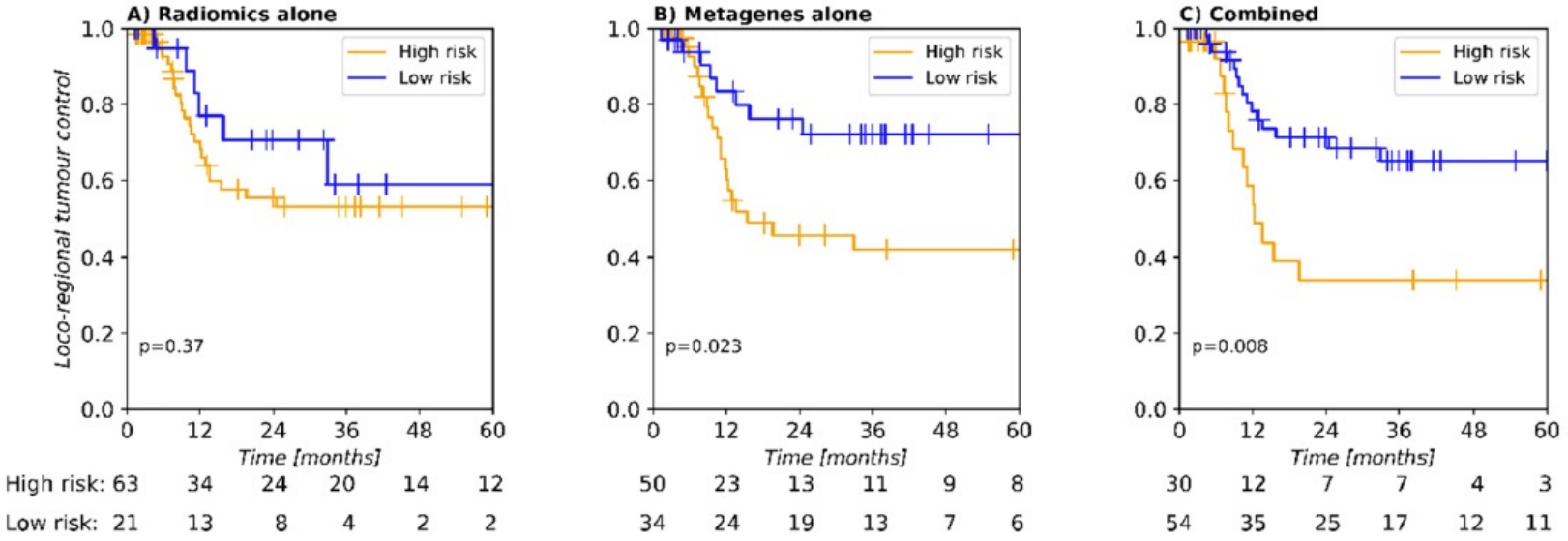




- 1019 patients
- ≈ 100 stable imaging features

Aerts et al, Nature Com, 2014

RadioGenomics for treatment individualization



- 206 HNSCC patients treated by chemo-radiotherapy
- ≈ 446 imaging features (e.g. intensity, texture, morphology)
- Four molecular subtypes

Meneghetti et al, Nature comm, 2022

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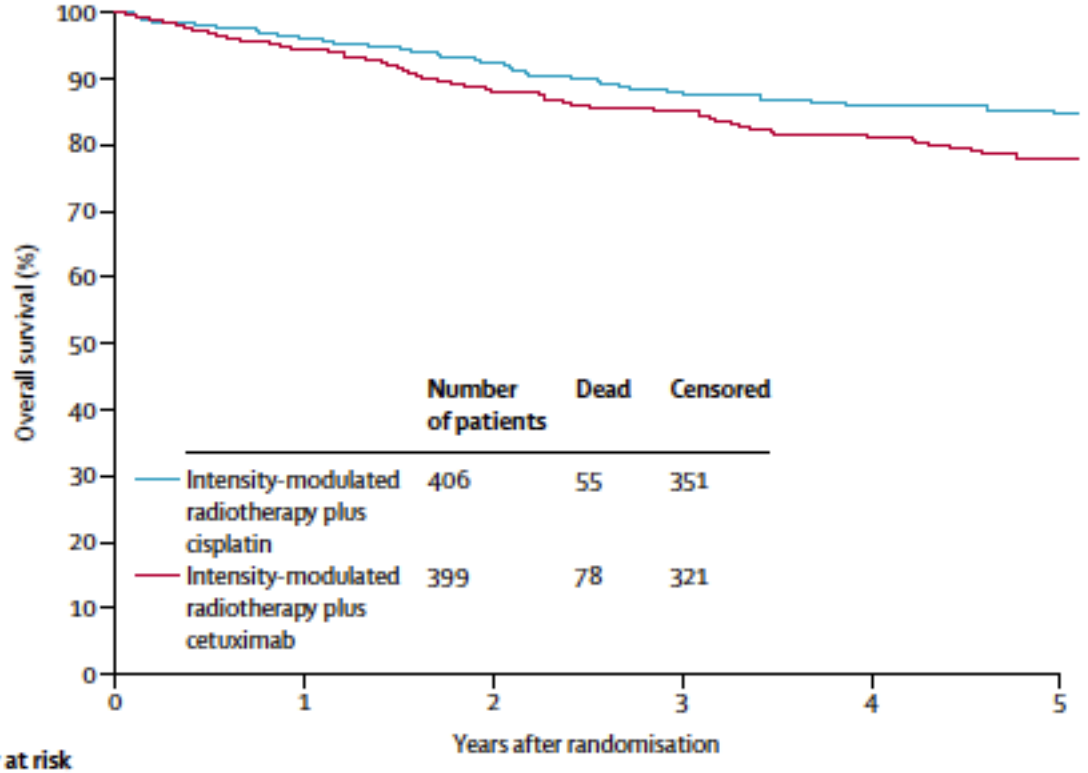
Treatment de-intensification in HPV^{+} H&N SCC

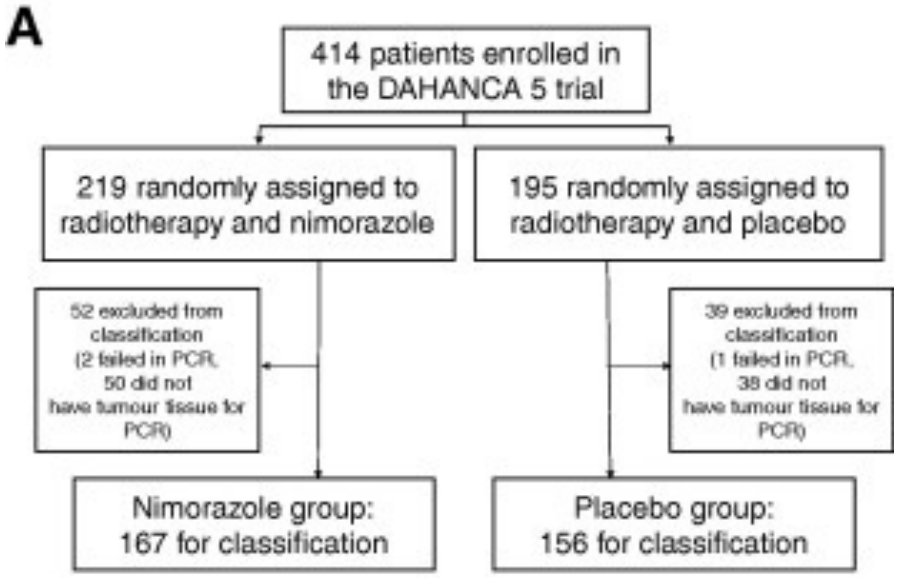
RTOG 1016: p16^{+} stage III-IV oropharyngeal SCC

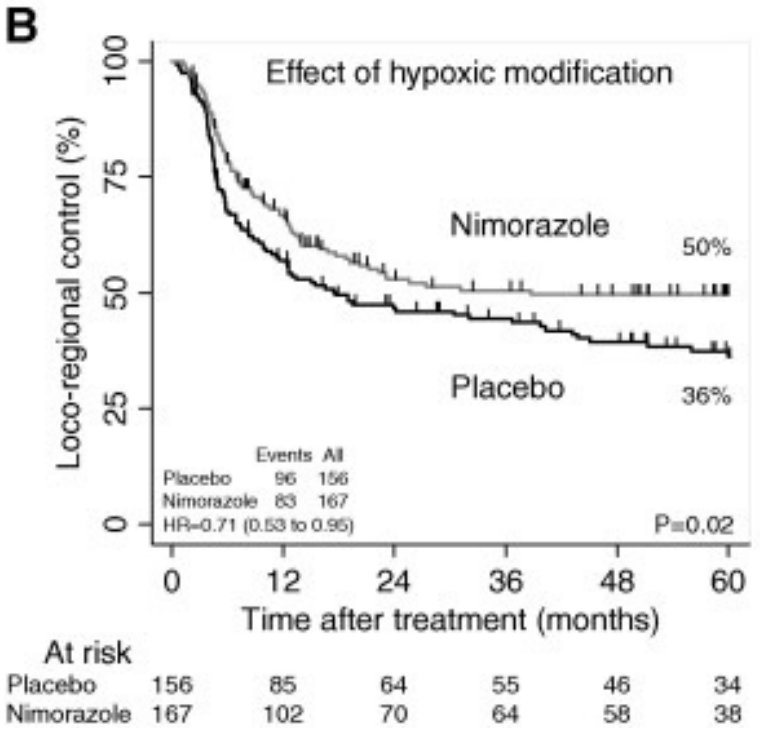
RT-cddp >< RT-cetuximab



Gillison, Lancet Oncol 2018

Nimorazole as hypoxic sensitizer





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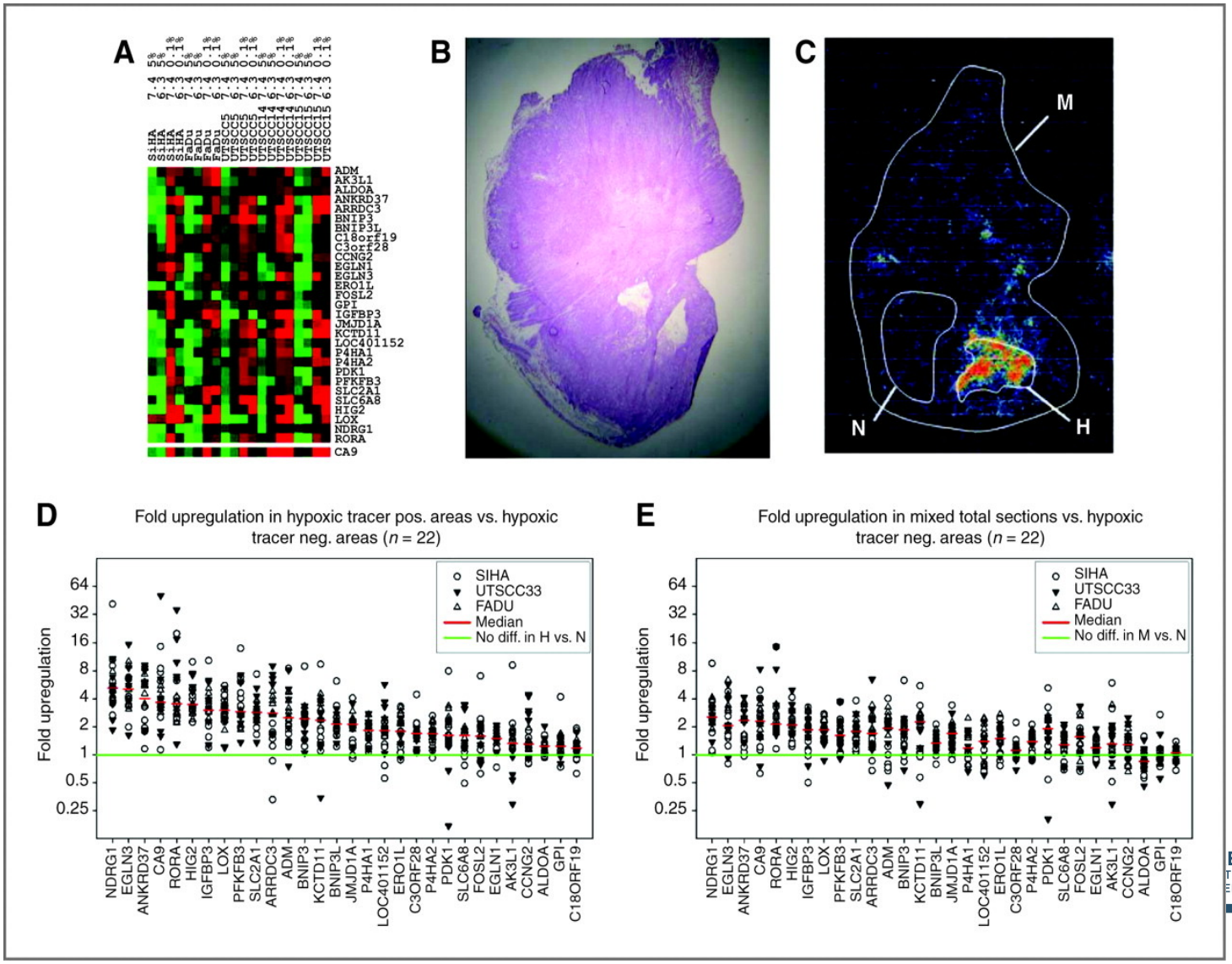
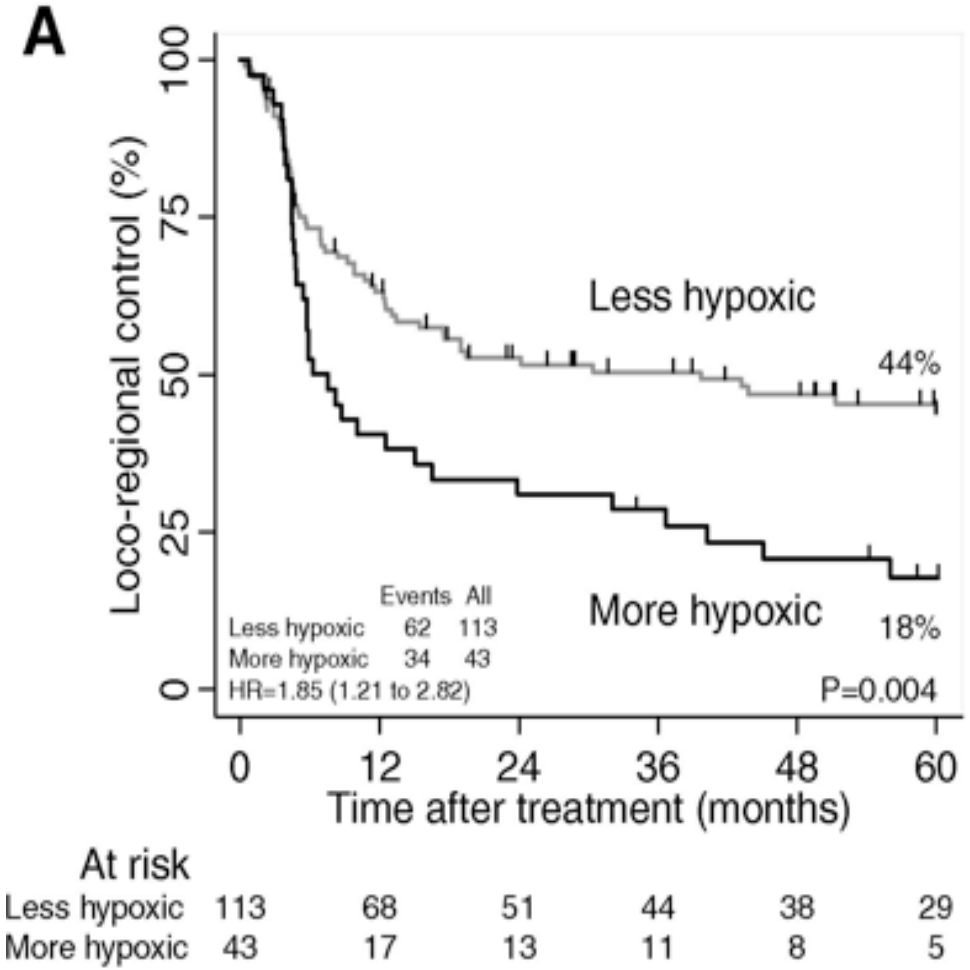
Hypoxic gene signature



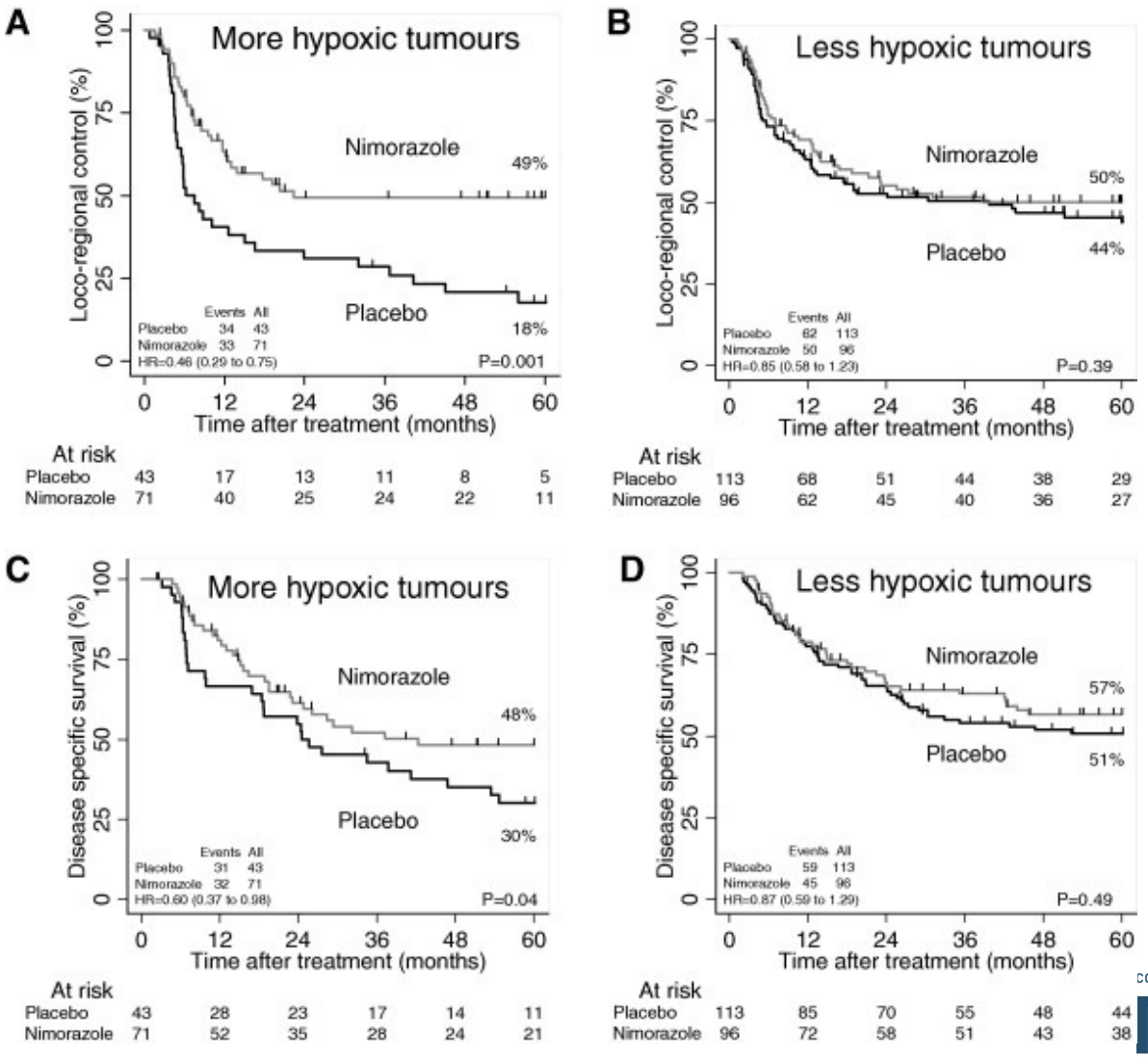
Toustrup K et al. Cancer Res 2011

Fifteen hypoxic gene signature in HNSCC



Toustrup K, Radiother Oncol, 2012

Hypoxic gene signature and nimorazole in HNSCC



Toustrup K, Radiother Oncol, 2012

Accelerated chemo-radiotherapy with or without nimorazole for p16-negative HNSCC: the randomized DAHANCA 29 - EORTC 1219 study.

V. Grégoire, Y. Tao, J. Kaanders, J.P. Machiels, N. Vulquin, S. Nuyts, C. Fortpied, H. Lmalem S. Marréaud, J. Overgaard

Radiation Oncology Dept., Centre Léon Bérard, Lyon, France

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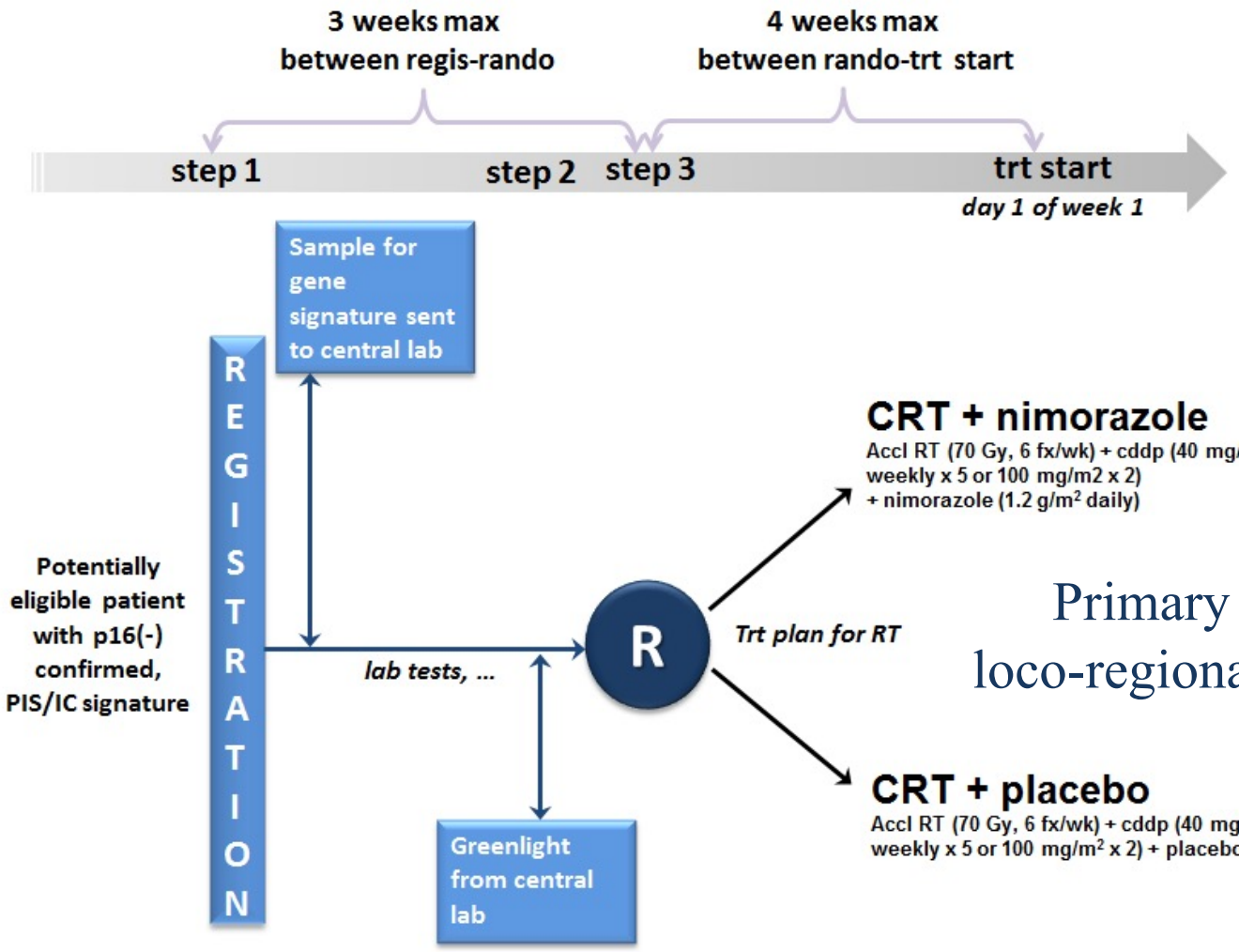
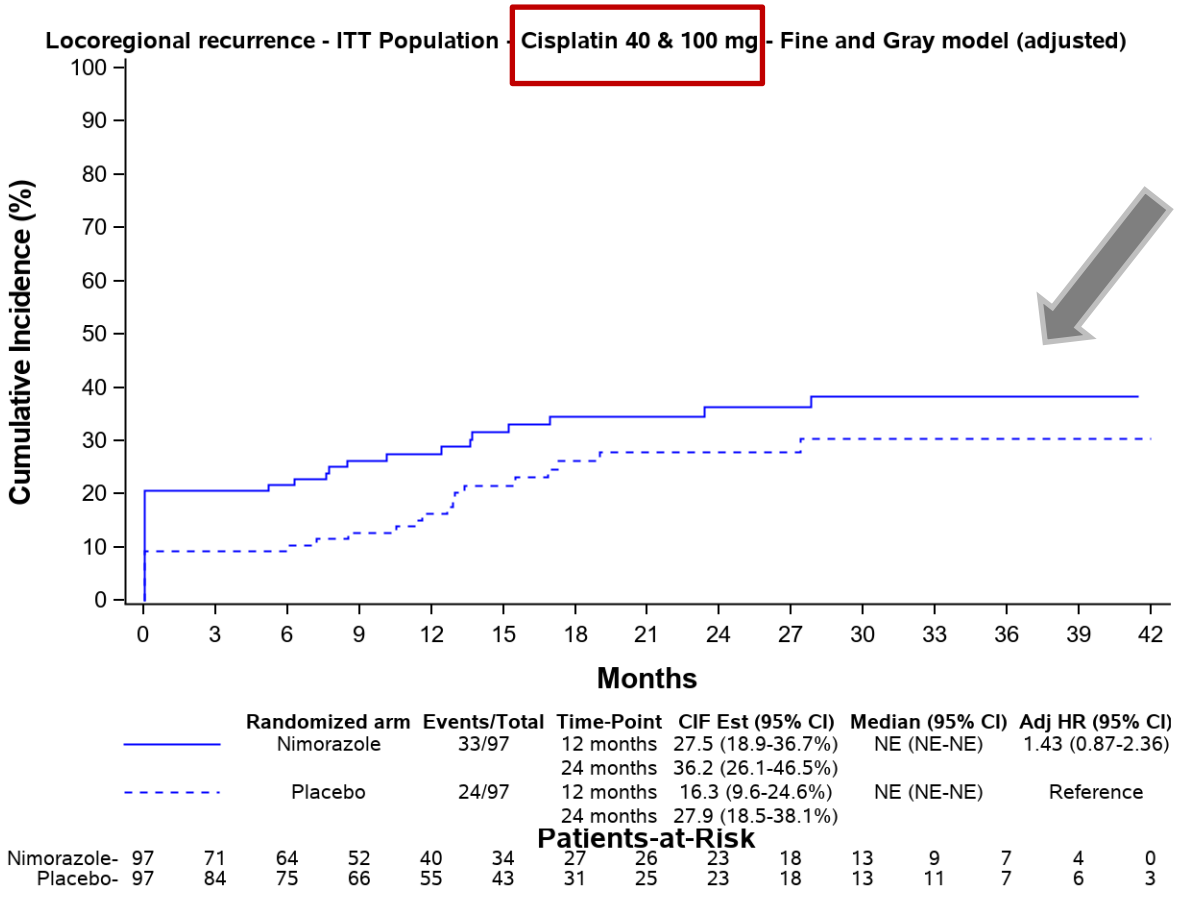
EORTC-1219 Dahanca: study design

Blinded & randomized trial; 640 patients (200 patients in the positive hypoxic gene profile)



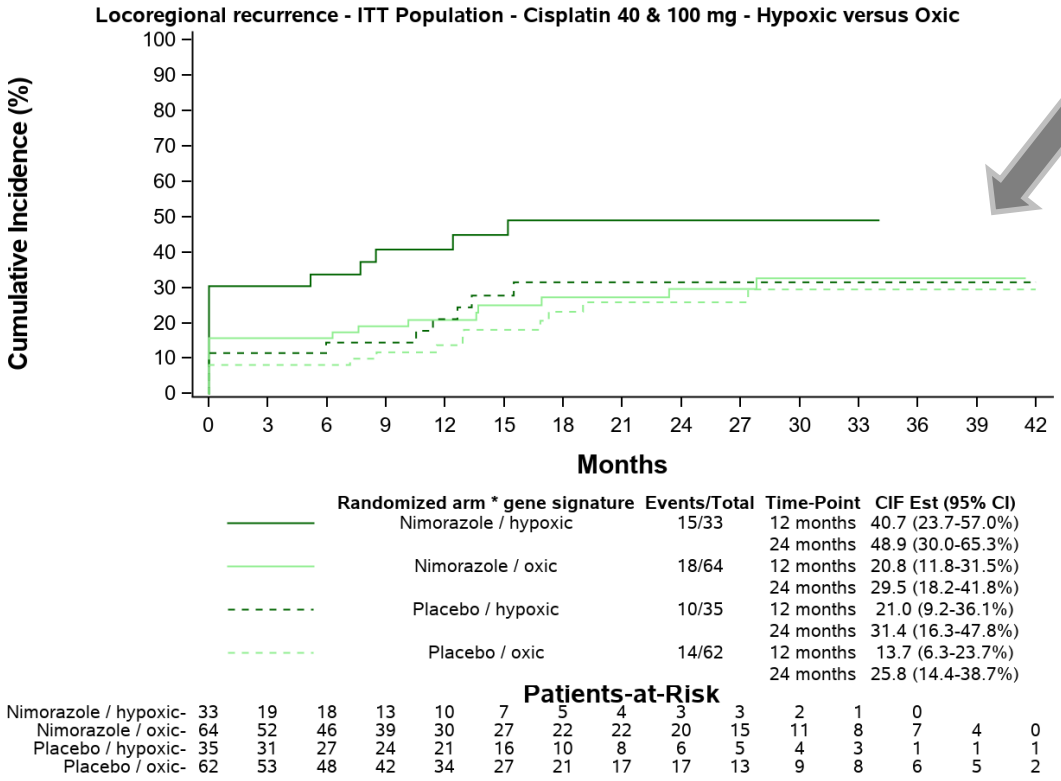
Primary endpoint:
loco-regional control rate

Primary endpoint: loco-regional control



Tail of curves driven by cisplatin 100 mg/m² only

Loco-regional control & hypoxic gene signature effect



Tail of curves driven by cisplatin 100 mg/m² only

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Summary

- AI-based automation and homogenization of OAR and TV selection and delineation
- Need of redefining the role of the Radiation Oncologist…
- Various prognostic omics signature
- No demonstration yet of omics-based treatment intensity modification

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Experience is simply the name we give to our mistakes.

Oscar Wilde

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