Omics driven radiotherapy approaches

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What omics are relevant to radiotherapy

- Transcriptomics
- Radiomics
- Dosomics
- Epigenomics

Multiomics

- NOT: Proteomicsphenomics/cellomics, connectomics and interactomics, secretomics, matrisomics, exosomics, angiomics, chaperomics and epichaperomics, phosphoproteomics, ubiquitinomics, metalloproteomics, terminomics, degradomics and metadegradomics, adhesomics, stressomics, microbiomics, immunomics, salivaomics, materiomics and other biomics.
- n=27

What is the goal ……………..

- Identify subpopulations within any tumour group with different radiation response characteristics

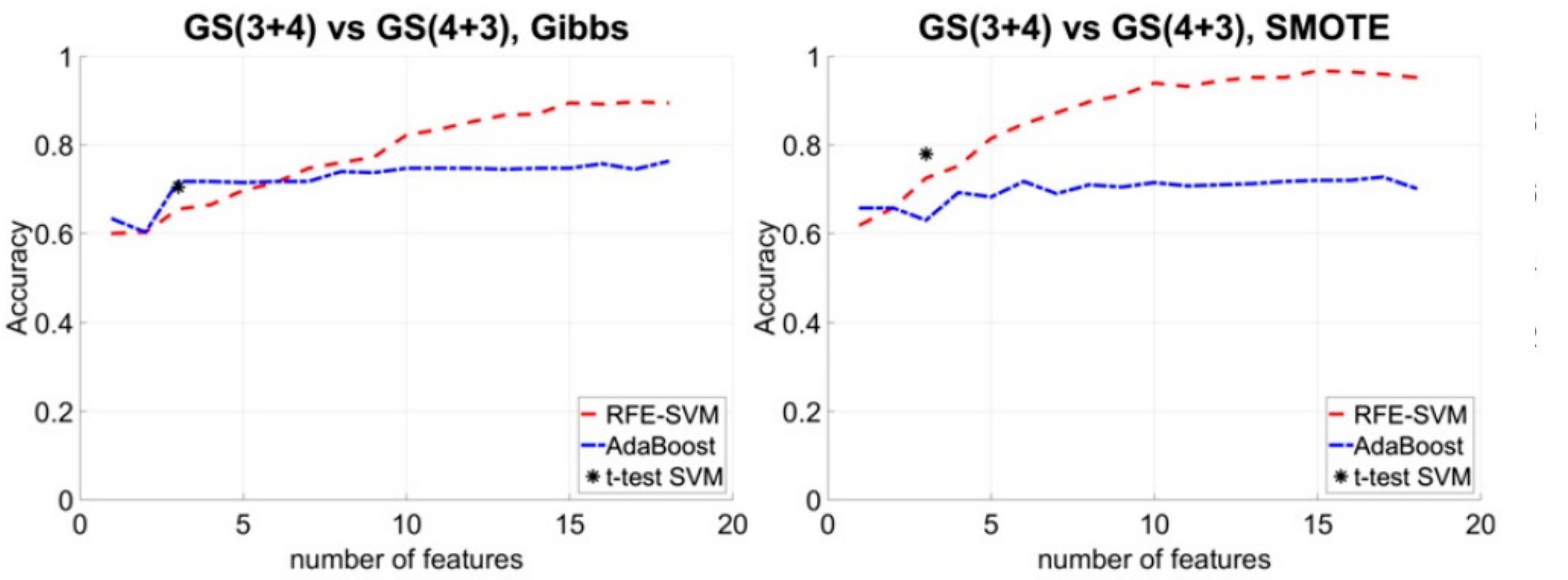
- Personalised radiotherapy ………….
  - dose,
  - volume,
  - fractionation,
  - sensitiser,
  - chemorads ……………

- Identify those better treated with other modalities

Automatic classification of prostate cancer Gleason scores from multiparametric magnetic resonance images

Duc Fehr[a,1], Harini Veeraraghavan[a,1,2], Andreas Wibmer[b], Tatsuo Gondo[c], Kazuhiro Matsumoto[c], Herbert Alberto Vargas[b], Evis Sala[b], Hedvig Hricak[b], and Joseph O. Deasy[a]

www.pnas.org/cgi/doi/10.1073/pnas.1505935112

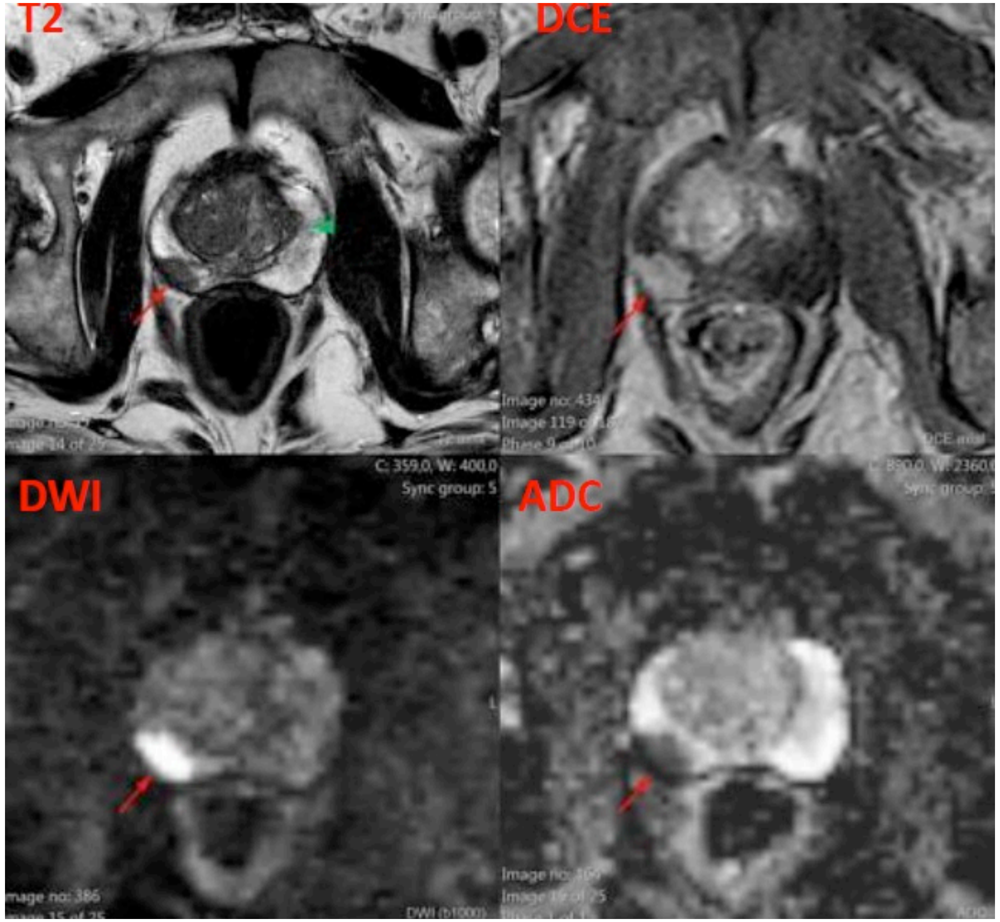


Gibbs

SMOTE

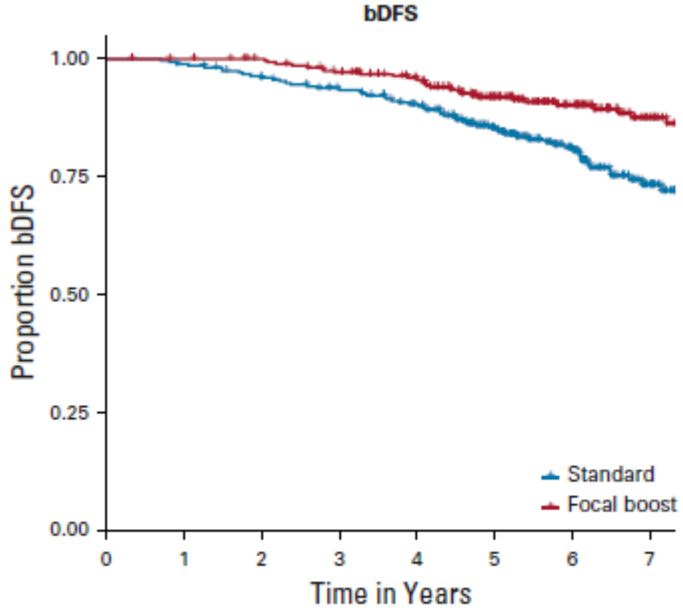
MRO. ART
MODERN RADIATION ONCOLOGY

Anatomical and functional imaging
Can identify the DIL



Focal Boost to the Intraprostatic Tumor in External Beam Radiotherapy for Patients With Localized Prostate Cancer: Results From the FLAME Randomized Phase III Trial

J Clin Oncol 39:787-796. © 2021



N at risk (cumulative events)

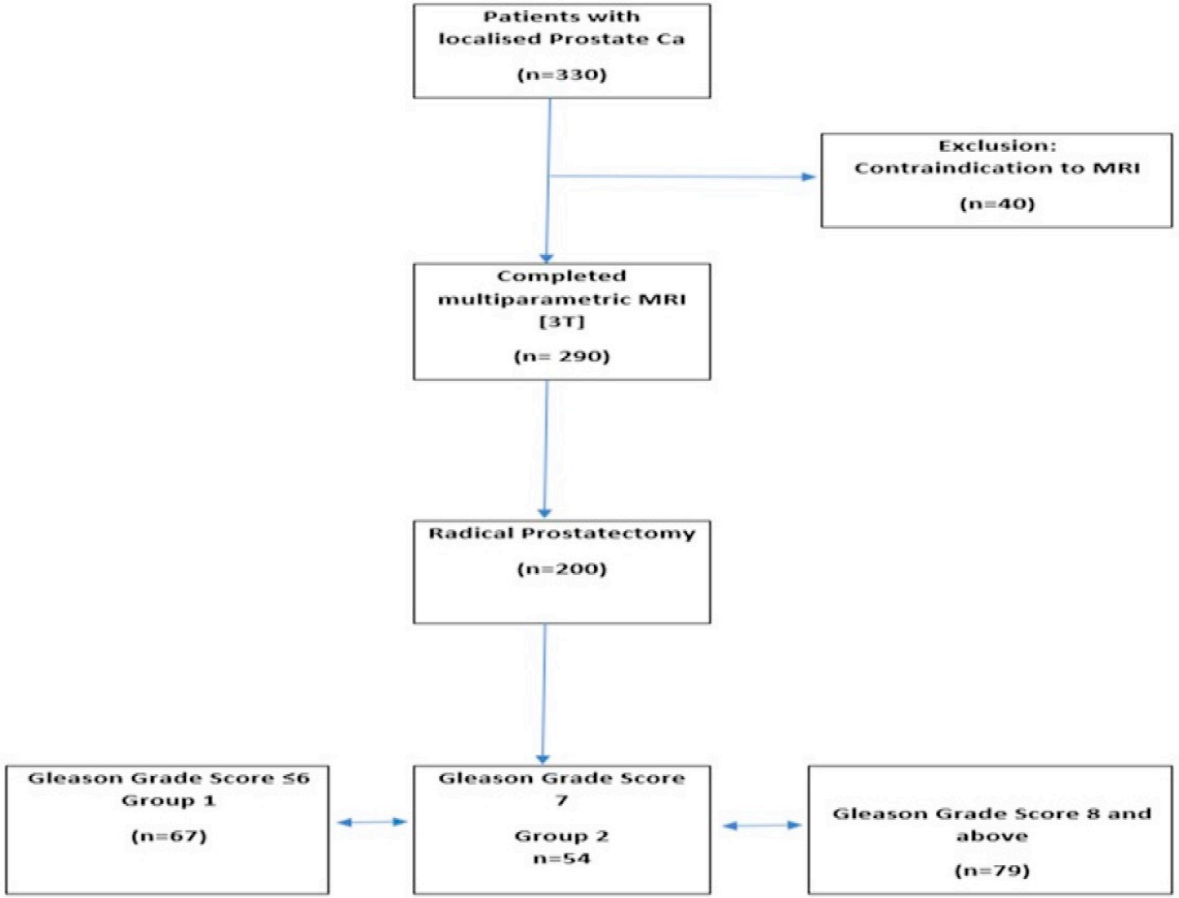
	0	1	2	3	4	5	6	7
Standard	276 (0)	272 (3)	260 (11)	247 (17)	229 (26)	182 (38)	127 (46)	67 (56)
Focal boost	281 (0)	279 (0)	274 (0)	261 (8)	244 (11)	188 (21)	135 (24)	80 (27)

Cumulative censoring

	0	1	2	3	4	5	6	7
Standard	0	1	5	12	21	56	103	153
Focal boost	0	2	7	12	26	72	122	174

Prediction of Clinically Significant Cancer Using Radiomics Features of Pre-Biopsy of Multiparametric MRI in Men Suspected of Prostate Cancer

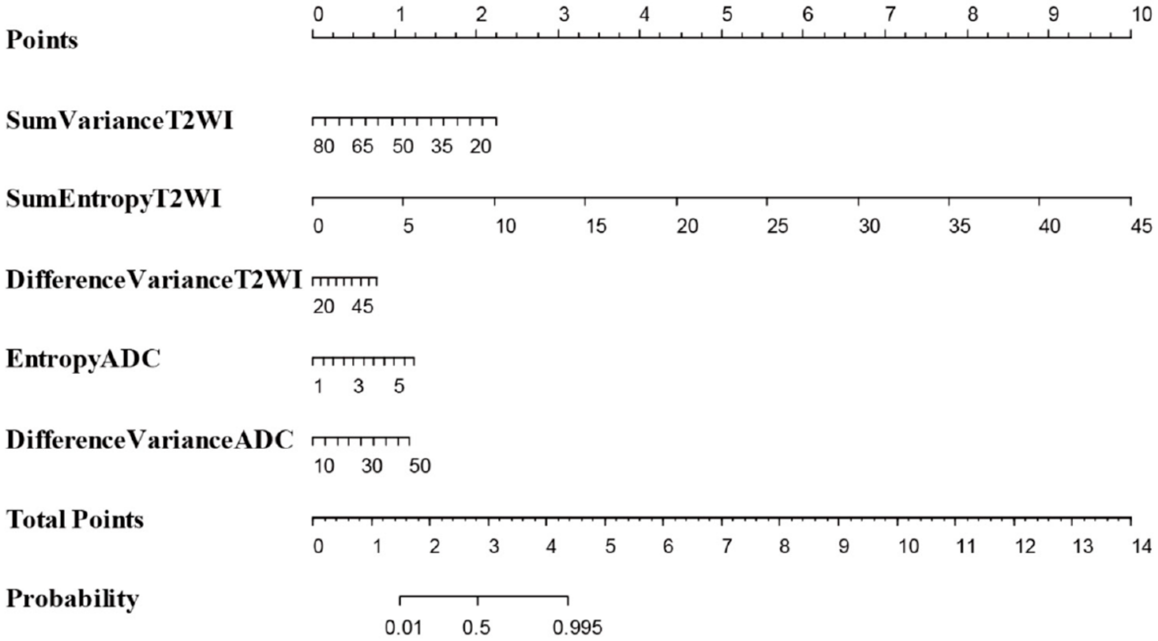
Cancers 2021, 13, 6199

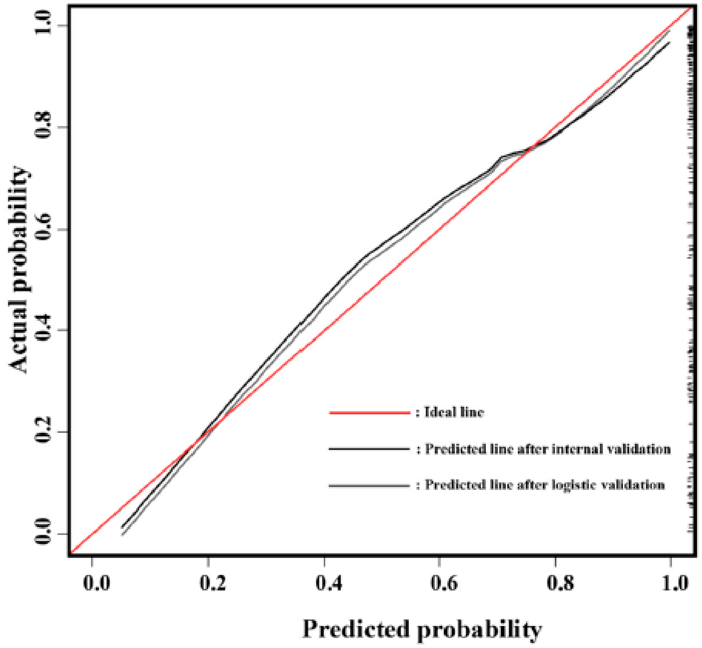


Prediction of Clinically Significant Cancer Using Radiomics Features of Pre-Biopsy of Multiparametric MRI in Men Suspected of Prostate Cancer

Cancers 2021, 13, 6199

	Actual Significant PCa	Actual Non Significant PCa	AUC	Standard Error	Difference AUC	Standard Error of Difference	z Value	*p* Value
Radiomic Features	72	128	0.901	0.021	0.350	0.048	7.274	<0.001
PIRADS	67	123	0.551	0.044				
Radiomic Features	72	128	0.901	0.021	0.344	0.045	7.577	<0.001
PSAD	67	123	0.557	0.045				





A pilot study on dosimetric and radiomics analysis of urethral strictures following HDR brachytherapy as monotherapy for localized prostate cancer

Br J Radiol 2020; **93**: 20190760.

[1]YAT MAN TSANG, PhD, [2]DINESH VIGNARAJAH, [3]ALAN MCWILLIAM, [1]HANNAH THARMALINGAM, [1]GERRY LOWE,
[3]ANANYA CHOUDHURY and [1,3]PETER HOSKIN

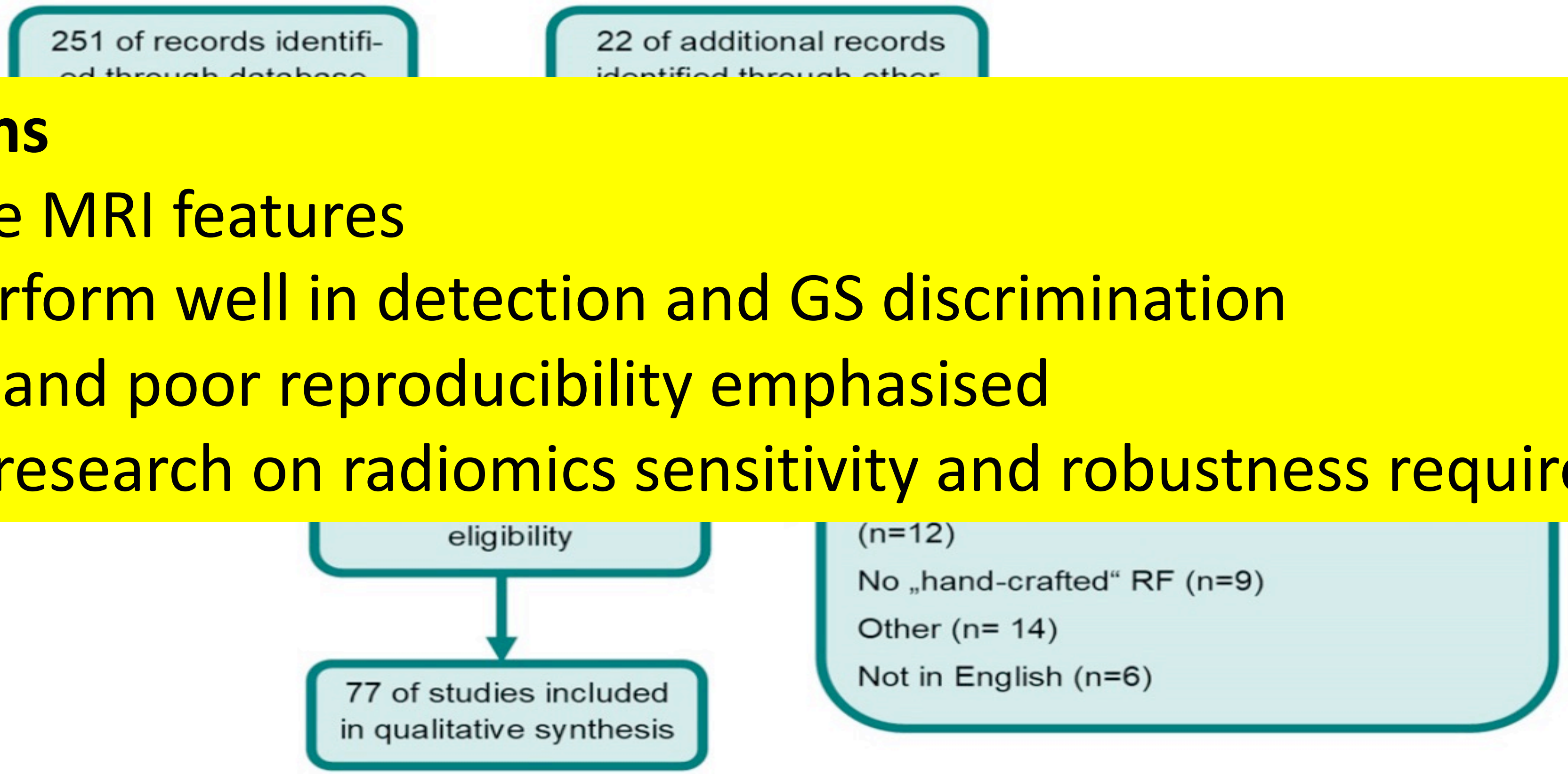
N=178 HDR BT monotherapy – 19Gy
5 (3%) strictures identified
Case control comparison of MR radiomics features

		Patients with ≥Grade II stricture ($n = 5$)	Patient without ≥Grade II stricture ($n = 5$)	
		Median value (range)	Median value (range)	*p*-value
MRI radiomics features	Energy	0.0036 (0.0020–0.0060)	0.0018 (0.0017–0.0053)	0.28
	Contrast	30.1 (25.9–42.1)	50.3 (30.1–68.4)	0.04
	Homogeneity	13.7 (11.8–17.7)	22.1 (14.4–30.7)	0.04

Radiomics in prostate cancer imaging for a personalized treatment approach – current aspects of methodology and a systematic review on validated studies

Theranostics 2021

Simon K.B. Spohn[1,2,11]*, Alisa S. Bettermann[1*], Fabian Bamberg[3], Matthias Benndorf[3], Michael Mix[4], Nils H. Nicolay[1,2], Tobias Fechter[5], Tobias Hölscher[6,7], Radu Grosu[8], Arturo Chiti[9,10], Anca L. Grosu[1,2], Constantinos Zamboglou[1,2,11,12]



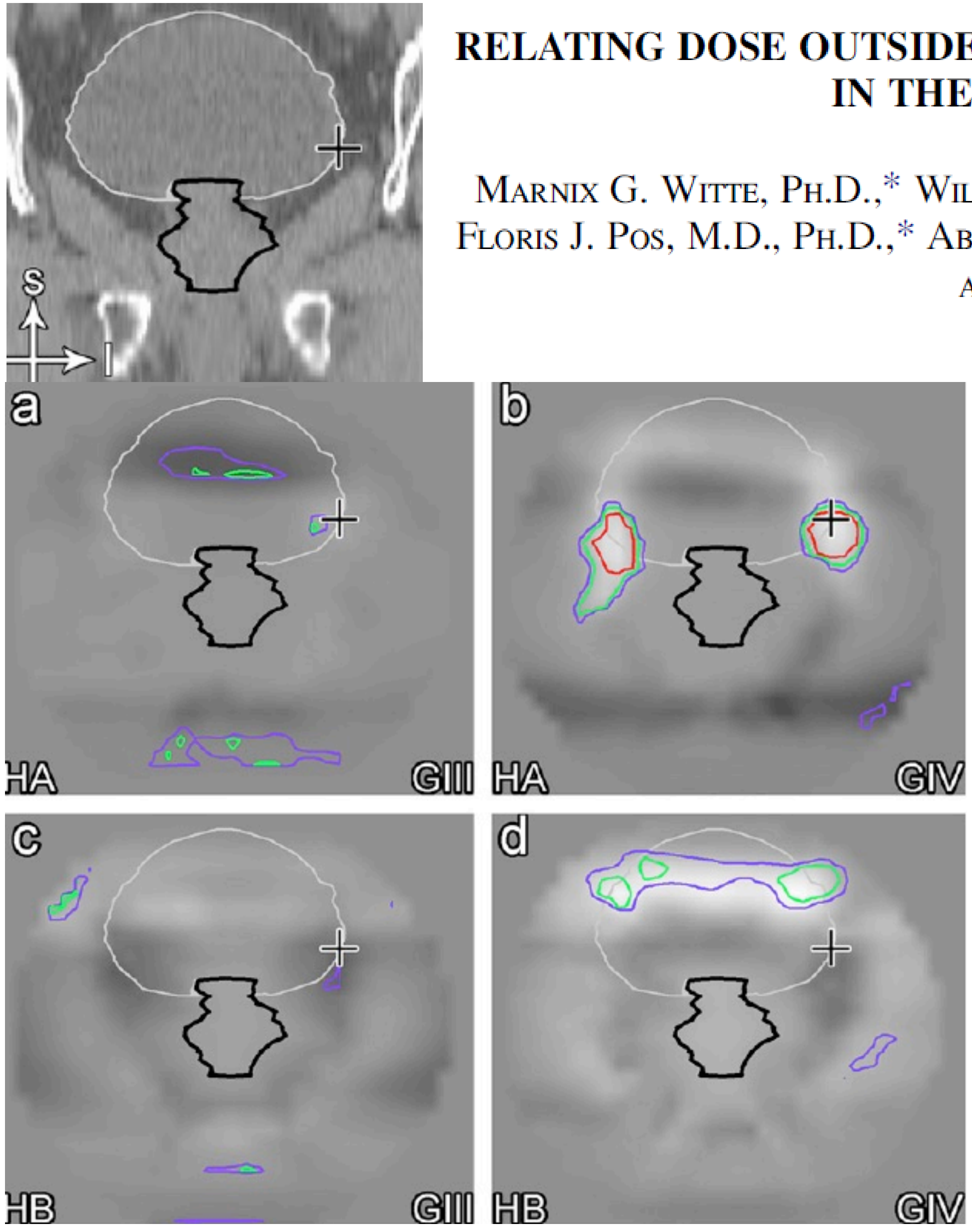
Conclusions

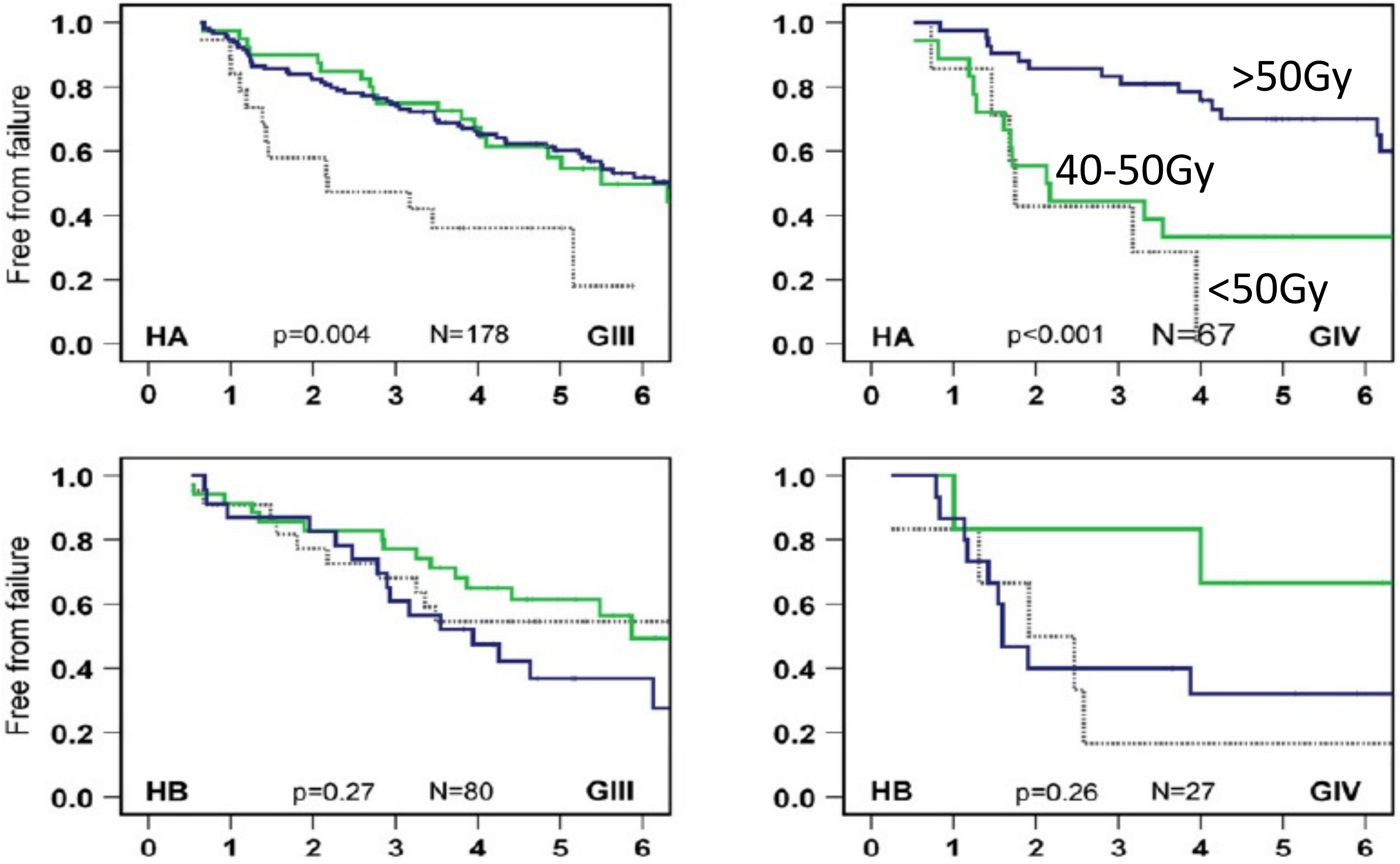
- Most use MRI features
- Most perform well in detection and GS discrimination
- Fragility and poor reproducibility emphasised
- Further research on radiomics sensitivity and robustness required

RELATING DOSE OUTSIDE THE PROSTATE WITH FREEDOM FROM FAILURE IN THE DUTCH TRIAL 68 GY VS. 78 GY

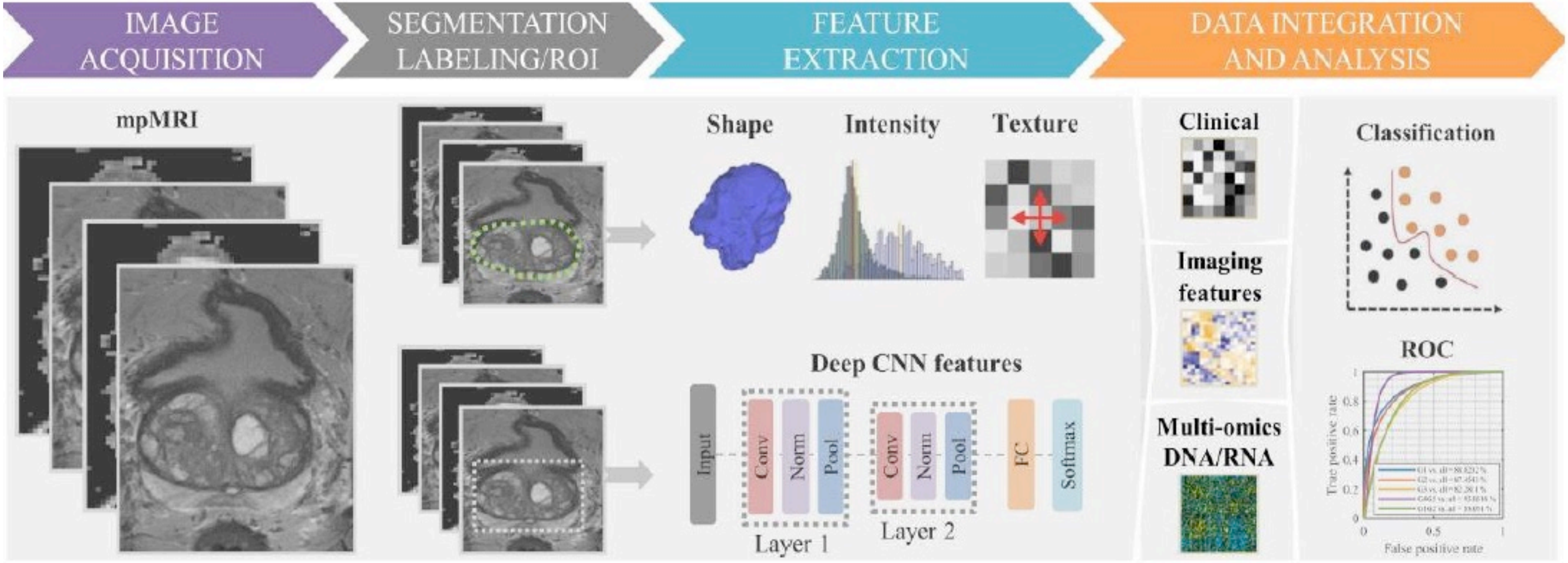
Marnix G. Witte, Ph.D.,* Wilma D. Heemsbergen, Ph.D.,* Román Bohoslavsky, M.Sc.,* Floris J. Pos, M.D., Ph.D.,* Abrahim Al-Mamgani, M.D.,† Joos V. Lebesque, M.D., Ph.D.,* and Marcel van Herk, Ph.D.*

Int. J. Radiation Oncology Biol. Phys., Vol. 77, No. 1, pp. 131–138, 2010





Biomarkers/ Radiomics/ Radiogenomics



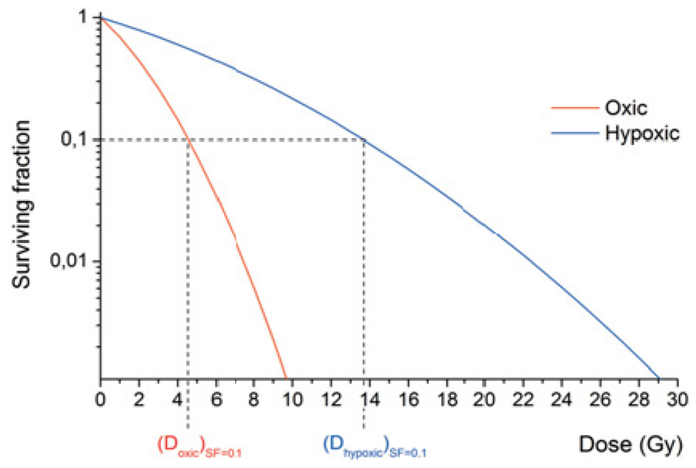
Chaddad et al. 2016

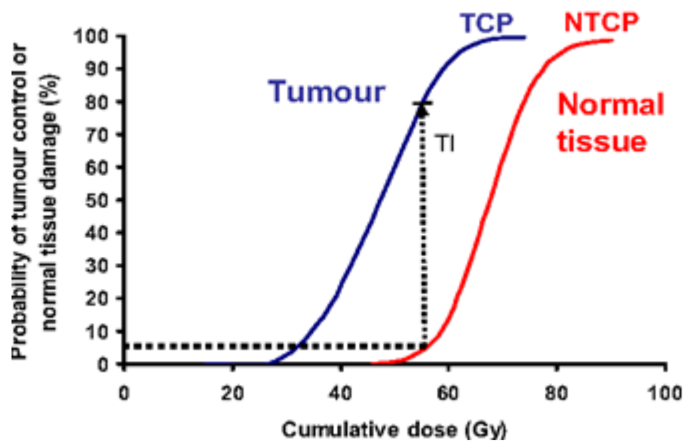
Transcriptomics

……..the study of cellular RNA

Hypoxia signature

Radiation sensitivity index (RSI)

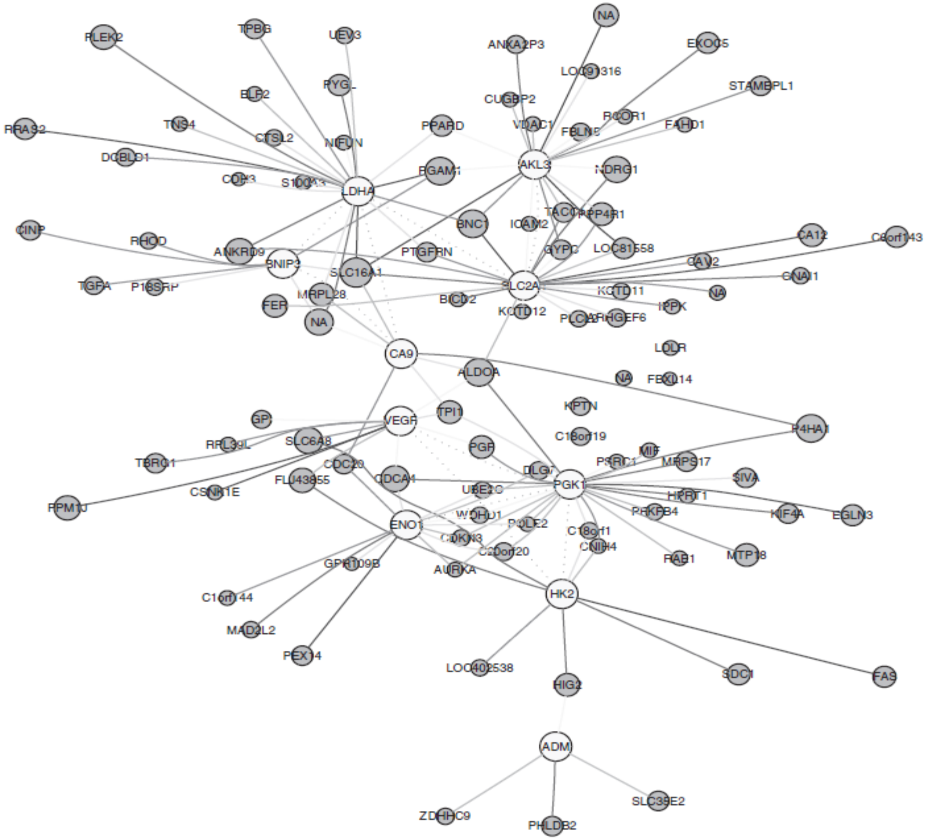


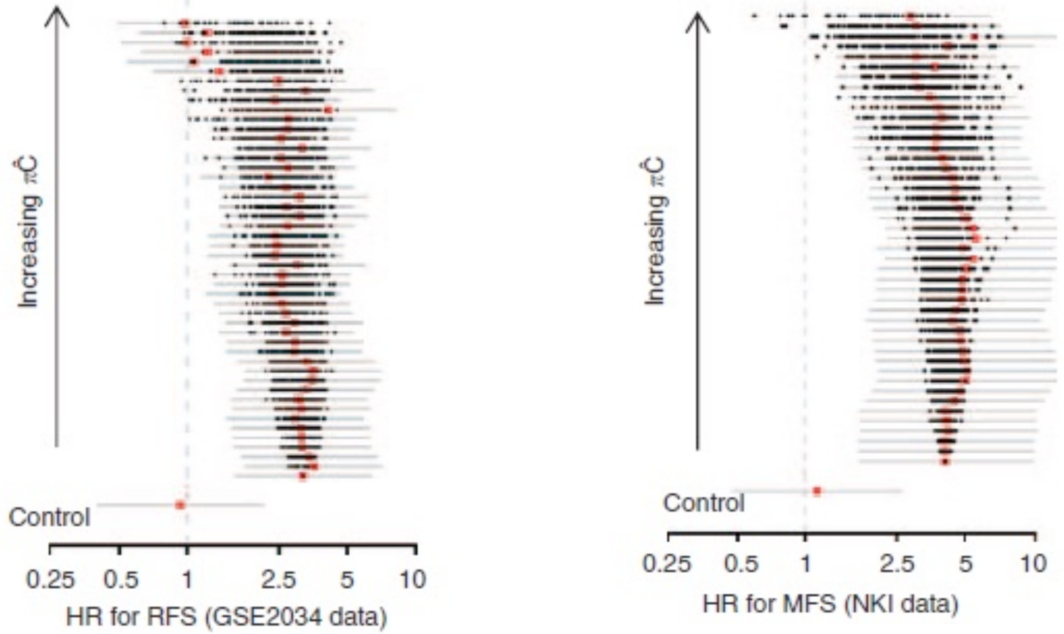


Large meta-analysis of multiple cancers reveals a common, compact and highly prognostic hypoxia metagene

FM Buffa*[,1], AL Harris[1], CM West[2] and CJ Miller[3]

British Journal of Cancer (2010) 102, 428–435

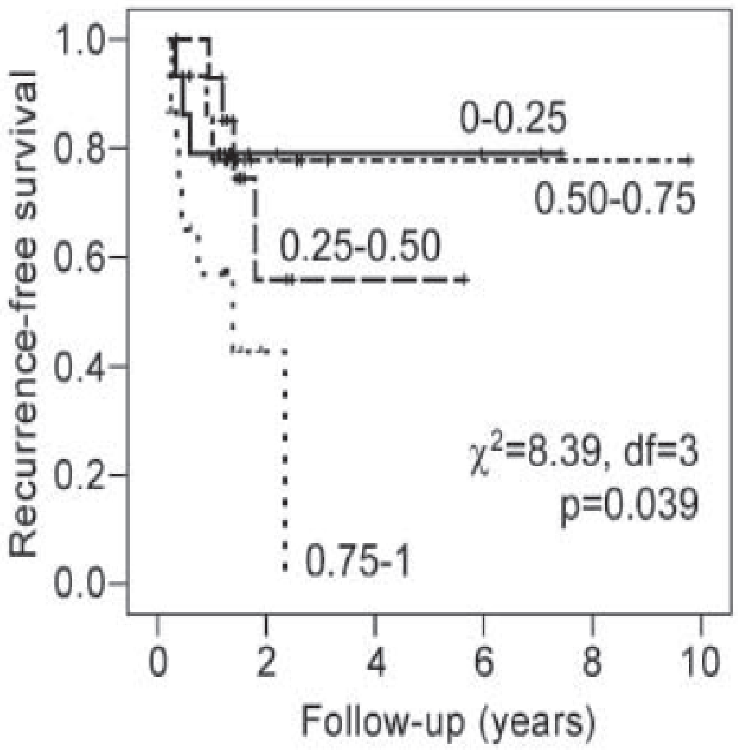


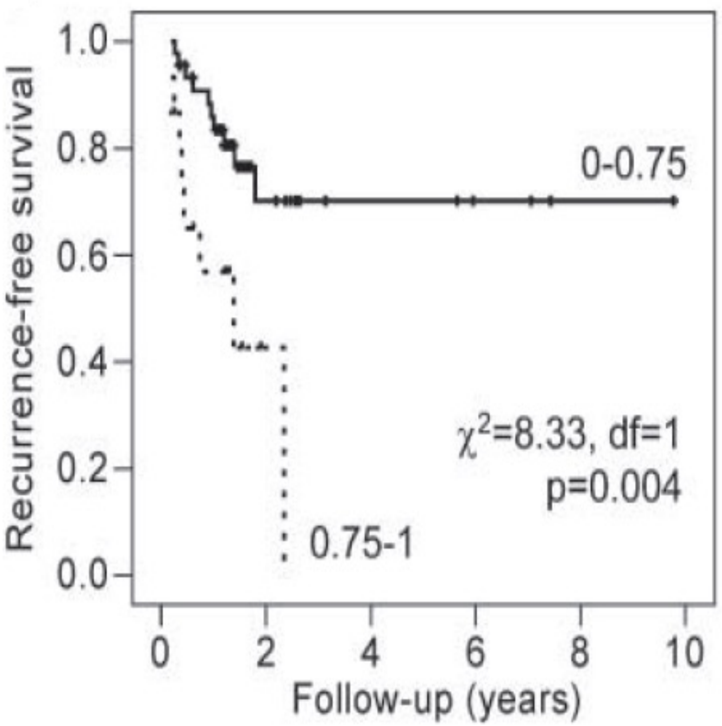


Relation of a Hypoxia Metagene Derived from Head and Neck Cancer to Prognosis of Multiple Cancers

Cancer Res 2007;67(7):3441–9

MTX1	*P4HA1*	*GAPD*	*PSMA7*
ADORA2B	*PFKFB4*	*GMFB*	*PSMB7*
AK3	*PGAM1*	*GSS*	*PSMD2*
ALDOA	*PVR*	*HES2*	*PTGFRN*
ANGPTL4	*SLC16A1*	*HIG2*	*PYGL*
C20orf20	*SLC2A1*	*IL8*	*RAN*
MRPS17	*TEAD4*	*KCTD11*	*RNF24*
PGF	*TPBG*	*KRT17*	*RNPS1*
PGK1	*TPI1*	*Kua*	*RUVBL2*
AFARP1	*TUBB2*	*LOC149464*	*S100A10*
ANLN	*VEGF*	*LOC56901*	*S100A3*
B4GALT2	*VEZT*	*LRP2BP*	*SIP1*
BCAR1	*AD-003*	*MGC14560*	*SLC6A10*
BMS1L	*ANKRD9*	*MGC17624*	*SLC6A8*
BNIP3	*C14orf156*	*MGC2408*	*SLCO1B3*
HOMER1	*C15orf25*	*MIF*	*SMILE*
HSPC163	*CA12*	*MRPL14*	*SNX24*
IMP-2	*CA9*	*NUDT15*	*SPTB*
KIAA1393	*CDCA4*	*PAWR*	*TFAP2C*
LDHA	*COL4A5*	*PDZK11*	*TIMM23*
LDLR	*CORO1C*	*PLAU*	*TMEM30B*
MGC2654	*CTEN*	*PLEKHG3*	*TPD52L2*
MNAT1	*DKFZP564D166*	*PPARD*	*VAPB*
NDRG1	*DPM2*	*PPP2CZ*	*XPO5*
NME1	*EIF2S1*	*PPP4R1*	



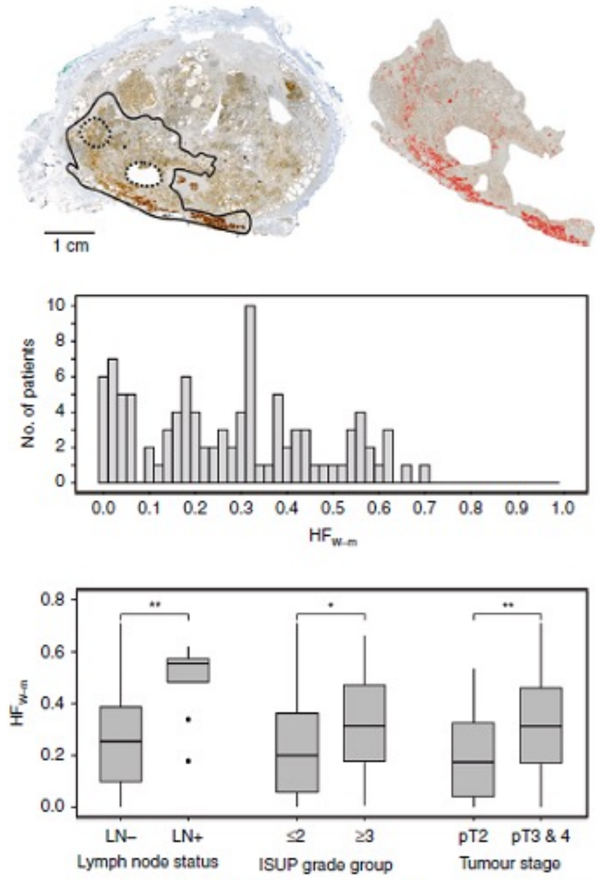


Prognostic but NOT predictive

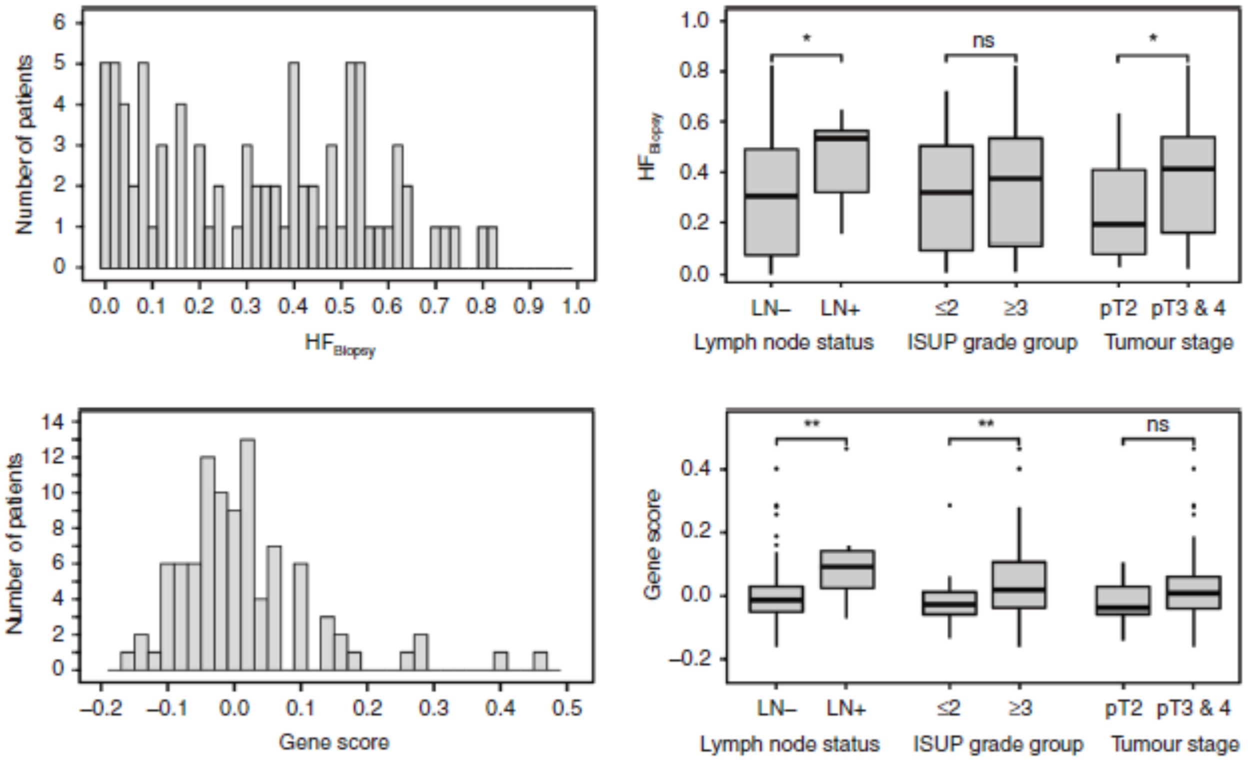
A prognostic hypoxia gene signature with low heterogeneity within the dominant tumour lesion in prostate cancer patients

Unn Beate Salberg[1,2], Vilde Eide Skingen[1,3], Christina Sæten Fjeldbo[1], Tord Hompland[1], Harald Bull Ragnum[1,4], Ljiljana Vlatkovic[5], Knut Håkon Hole[2,6], Therese Seierstad[6] and Heidi Lyng[1,3]

British Journal of Cancer (2022) 127:321–328;



Pimonidazole-defined hypoxia in the index lesion in relation to tumour aggressiveness.



MODERN RADIATION ONCOLOGY
MRO. ART

A prognostic hypoxia gene signature with low heterogeneity within the dominant tumour lesion in prostate cancer patients

Unn Beate Salberg[1,2], Vilde Eide Skingen[1,3], Christina Sæten Fjeldbo[1], Tord Hompland[1], Harald Bull Ragnum[1,4], Ljiljana Vlatkovic[5], Knut Håkon Hole[2,6], Therese Seierstad[6] and Heidi Lyng[1,3]

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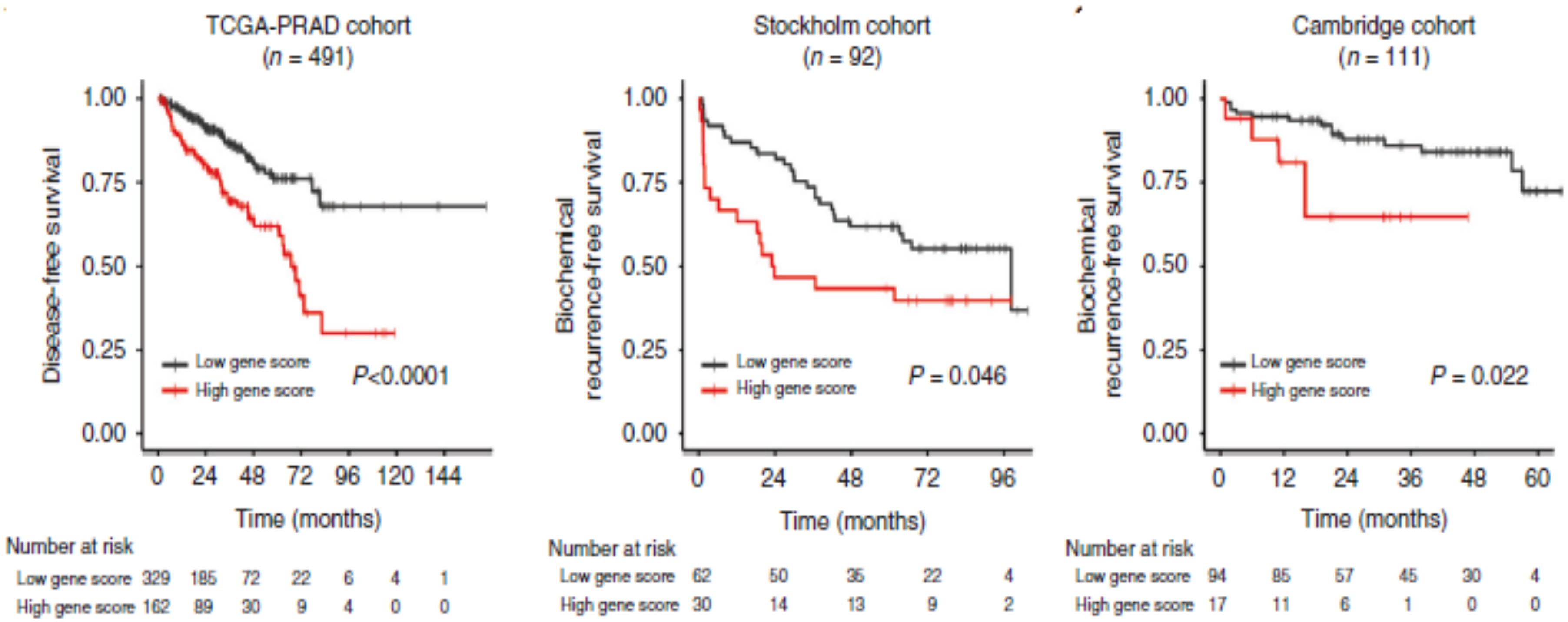


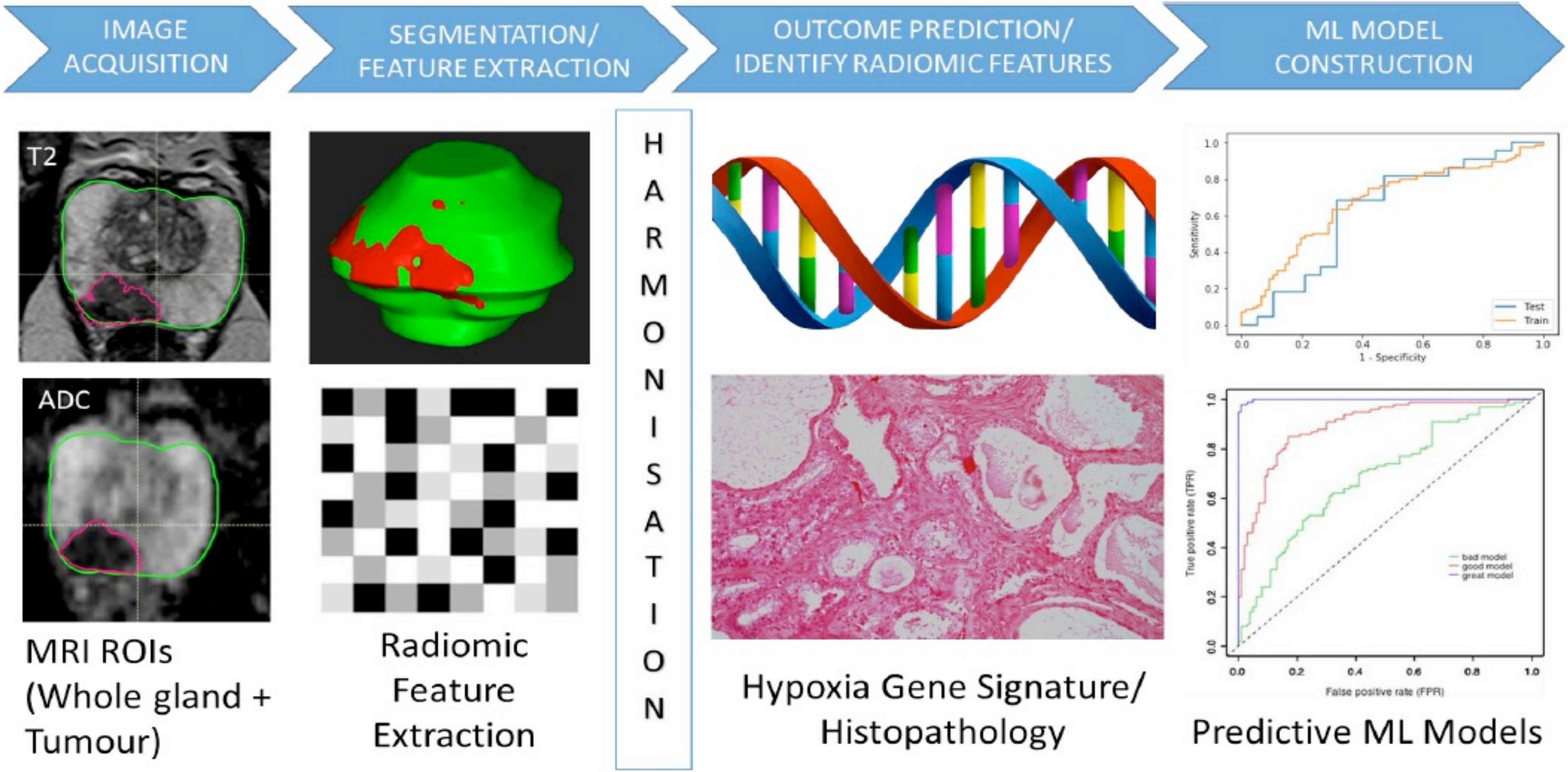


IMAGE ACQUISITION
SEGMENTATION/ FEATURE EXTRACTION
OUTCOME PREDICTION/ IDENTIFY RADIOMIC FEATURES
ML MODEL CONSTRUCTION
T2
ADC
MRI ROIs (Whole gland + Tumour)
Radiomic Feature Extraction
HARMONISATION
Sensitivity
1 - Specificity
Test
Train
True positive rate (TPR)
False positive rate (FPR)
bad model
good model
great model
Hypoxia Gene Signature/ Histopathology
Predictive ML Models

What is the goal ……………..

- Identify subpopulations within any tumour group with different radiation response characteristics

- Personalised radiotherapy ………….
  - dose,
  - volume,
  - fractionation,
  - sensitiser,
  - chemorads ……………

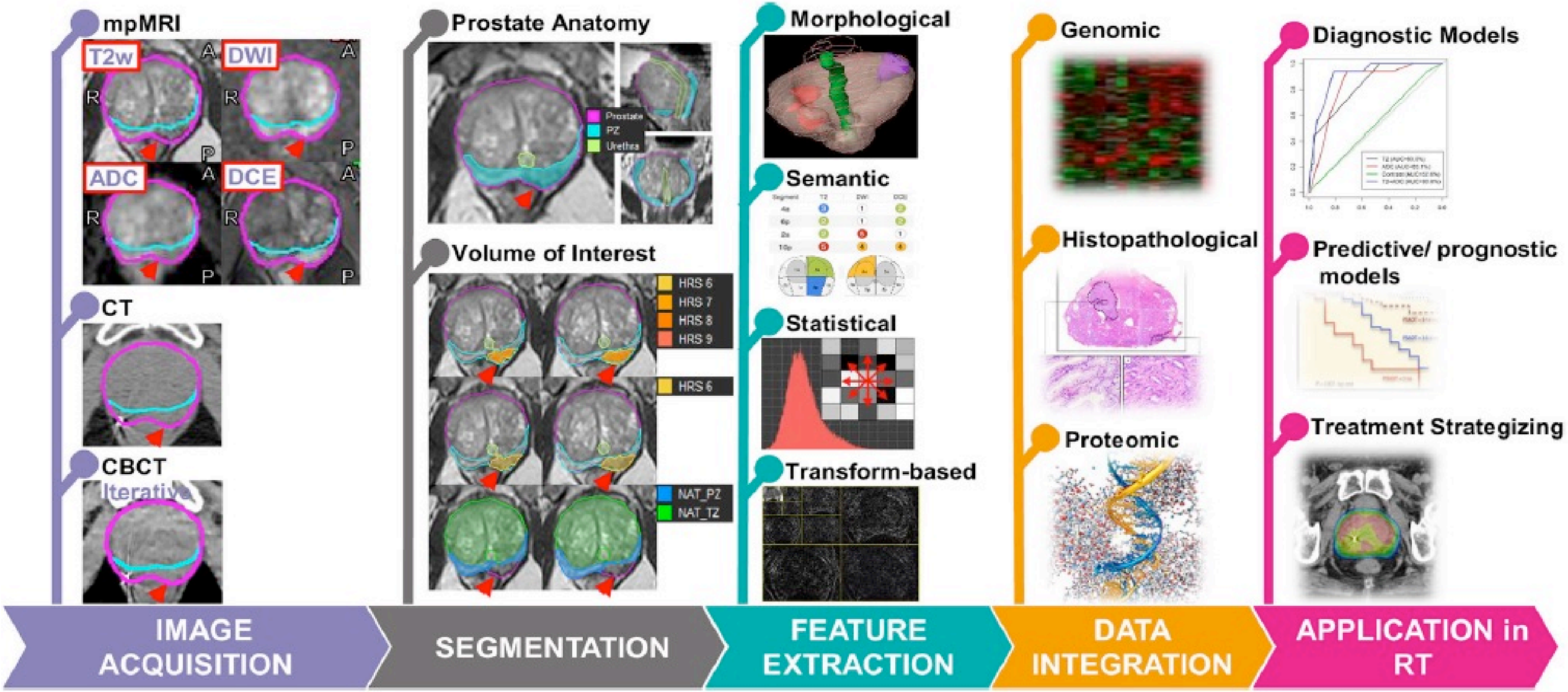
……….PREDICTIVE

- Identify those better treated with other modalities ………PREDICTIVE

The Role of Radiomics in Prostate Cancer Radiotherapy

Rodrigo Delgadillo, John C. Ford, Matthew C. Abramowitz, Alan Dal Pra, Alan Pollack, Radka Stoyanova*

Strahlenther Onkol. 2020 October ; 196(10): 900–912.



Omics driven radiotherapy approaches

Great potential but ……………….

- ***Predictive*** omic biomarkers needed to define changes in treatment
- Rigorous validation and qualification in prospective trials needed
- Problems:
  - No universal predictive signatures identified
  - Current signatures appear tumour and even cohort specific
  - Statistical trawling vs Hypothesis driven signatures

Future application of 'omics' to radiotherapy