



# Multidisciplinary approach in the **Omics** and **AI** era

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# Multidisciplinary approach



**First Contact**



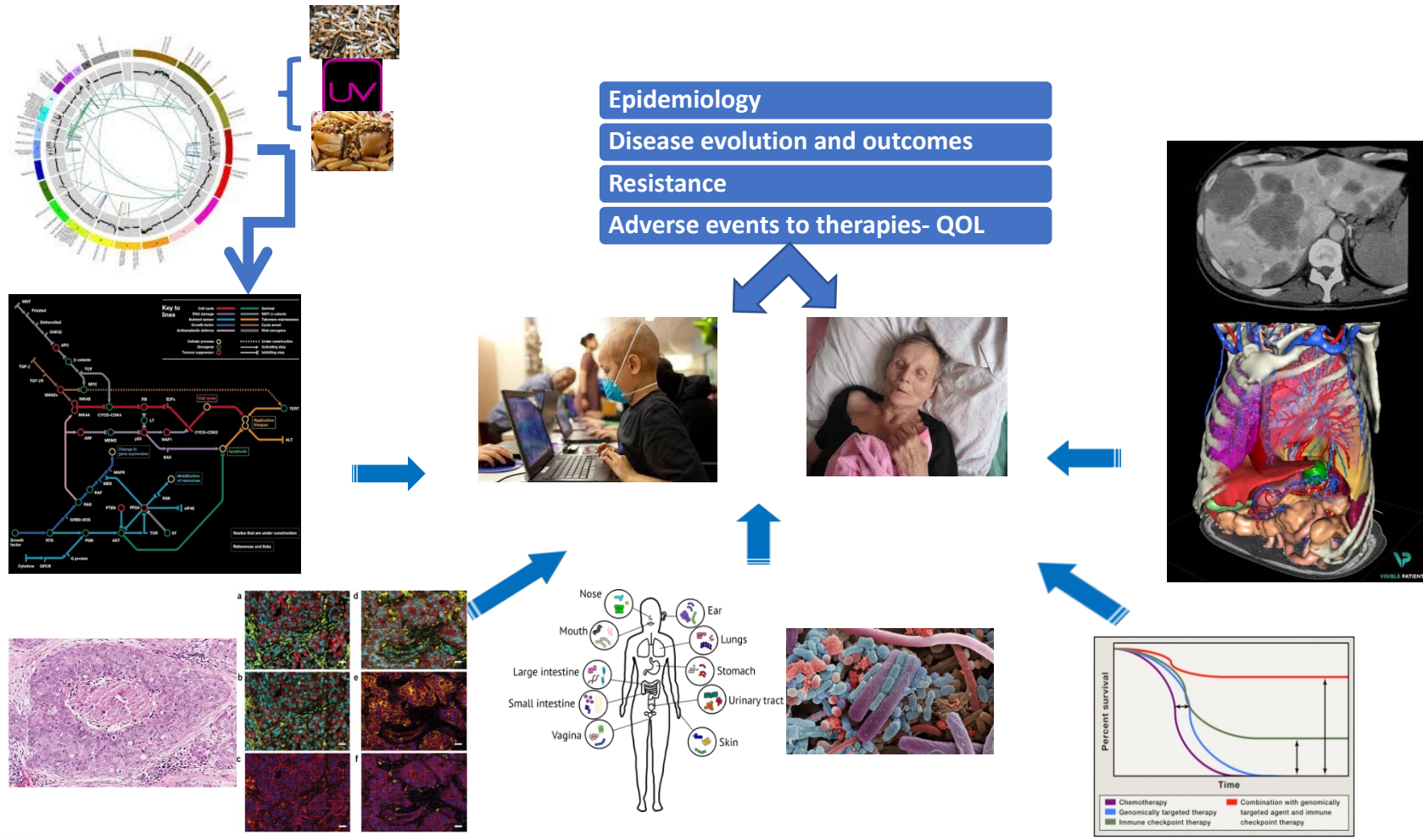
**Restaging**



**After surgery**

- **interdisciplinary approach** for decision-making in cancer care
- originally intended to **educate health care professionals**
- positively affectes the **quality** of medical service and **clinical outcomes**

# Cancer complexity in the 21st Century



# How OMICS integrates the Multidisciplinary Approach?

- Omics Guided Oncology
- Omics Guided Radiotherapy
- Image Omics Guided Radiotherapy



# OMICS for Precision Oncology

Use in Precision Oncology		Examples
well established in clinical practice	<b>Genomics</b> Mutation Analysis	Alexandrow et al. (2013) [20] Burrell et al. (2013) [21] Tomczak et al. (2015) [22] Bailey et al. (2018) [30]
well established in clinical practice	<b>Genomics</b> Copy Number Variation	Hu et al. (2018) [29] Davoli et al. (2017) [33] Zak et al. (2013) [34] Lee et al. (2012) [35]
extensive research data	<b>Transcriptomics</b>	Cancer Genome Atlas (2013) [41] Pratt et al. (2011) [43] Duarte et al. (2012) [44] Li et al. (2012) [45] Botling et al. (2013) [46]
significant research data	<b>Epigenetics</b> DNA Methylation	Kulis and Esteller (2010) [55] Hegi et al. (2005) [60] Neureiter et al. (2014) [63]
significant research data	<b>Epigenetics</b> microRNA	Kohlhapp et al. (2015) [57] Teplyuk et al. (2016) [64]
increasing research data	<b>Proteomics</b>	Swiatly et al. (2018) [66] Yanovich et al. (2018) [67]
emerging research data	<b>Metabolomics</b>	Chaturvedi et al. (2013) [70] Zhang et al. (2016) [71] Giskeodegard et al. (2013) [72]
exploratory data	<b>Other Omics</b>	

Early diagnosis/familiarity  
(Lynch syndrome, BRCA breast and ovarian)

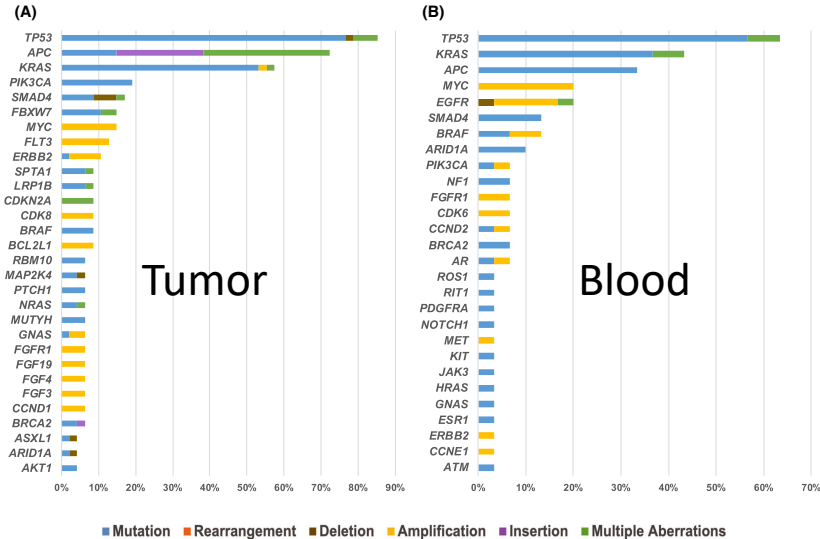
PROGNOSIS

PERSONALIZED treatments  
Molecular Targeted Drugs

**Figure 1.** Summary of the applications of individual omics technologies to study cancer and other human disorders.

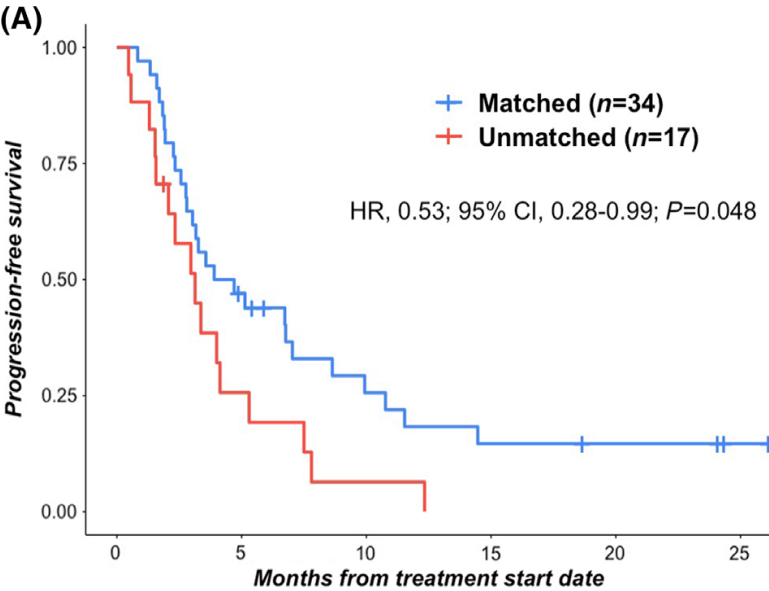
# Molecular Tumor Board

51 metastatic colorectal cancer patients:  
 67% received  $\geq 1$  based on individual tumor characteristics,  
 33% patients received unmatched therapies

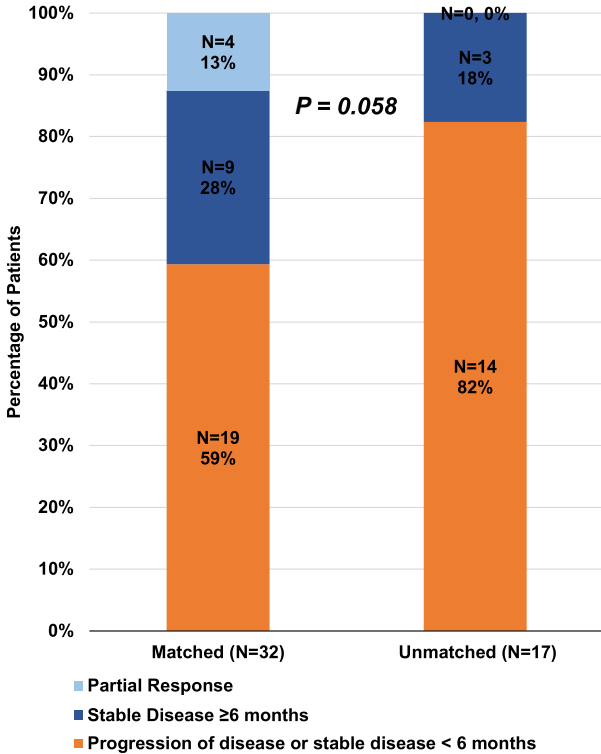


**Fig. 2.** Frequency of characterized genomic alterations from tissue NGS and cfDNA of colorectal cancer. (A) Alterations identified by tissue NGS ( $N = 47$ ). Alterations present in  $\geq 4\%$  of patients were included. (B) Alterations identified by cell-free DNA ( $N = 30$ ). Alterations present in  $\geq 3\%$  of patients were included. Colored bars show the percent of patients with the specific type of genomic alteration for each gene. Multiple aberrations indicates that some patients harbored multiple types of alterations (e.g., mutation, deletion, insertion) within the same gene.

molecular profiling information



Progression-Free Survival



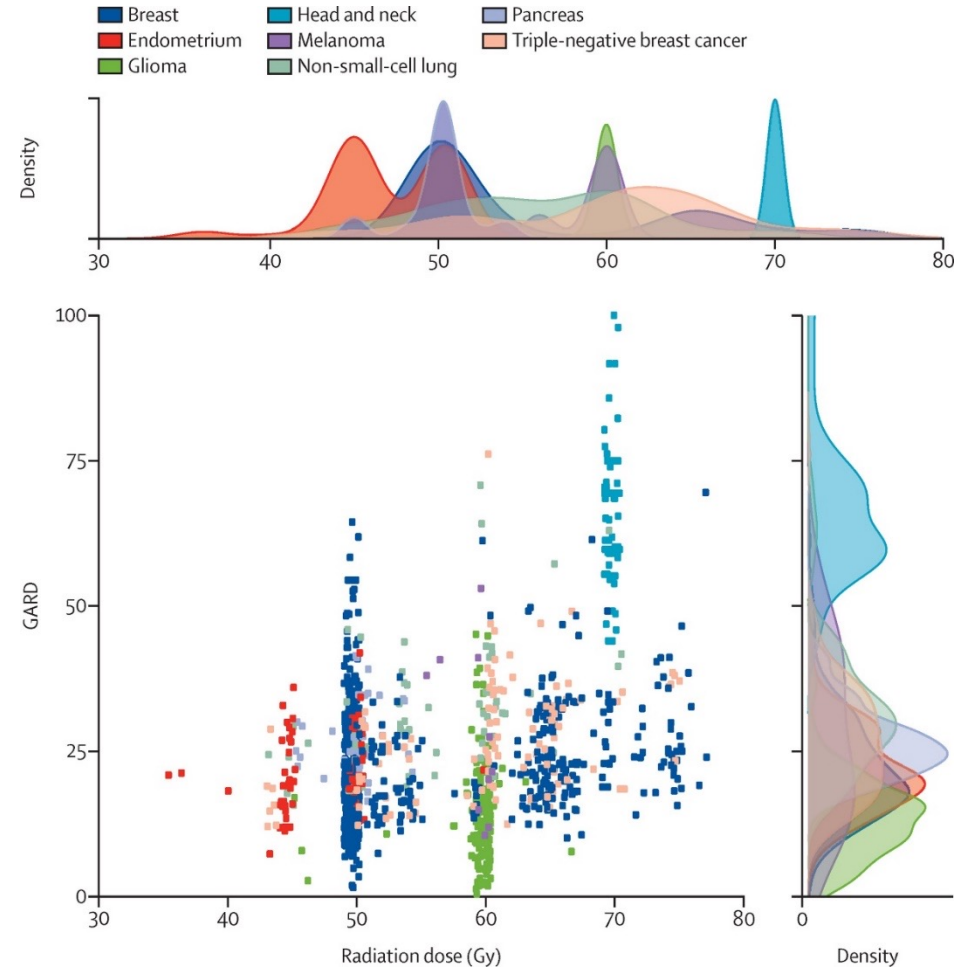
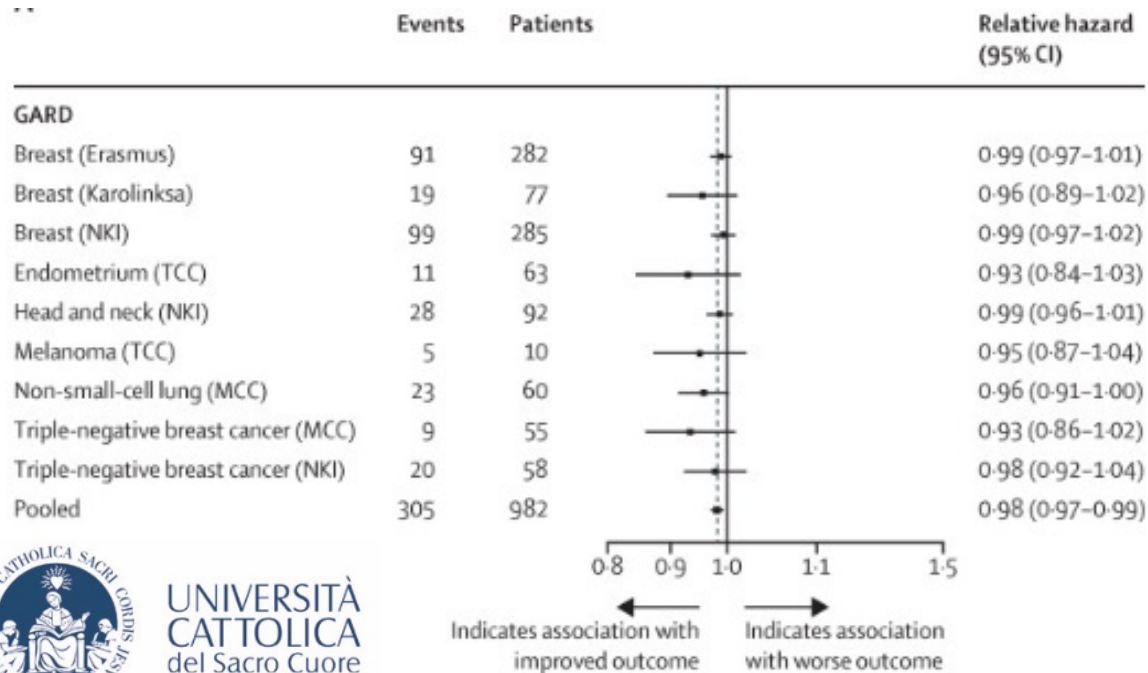
# How OMICS integrates the Multidisciplinary Approach?

- Omics Guided Oncology
- Omics Guided Radiotherapy
- Image Omics Guided Radiotherapy

# Omic guided radioterapy

## New radiotherapy dose definition protocols Genomic-Adjusted Radiation Dose (**GARD**)

Correlation with time to first recurrence and overall survival





# The «omics burden»

Of 100 cancer patients analysed with genomics

100

A driver alteration can be found in 60%

60

50% can be treated by an appropriate drug

30

50% of the patients will respond to treatment

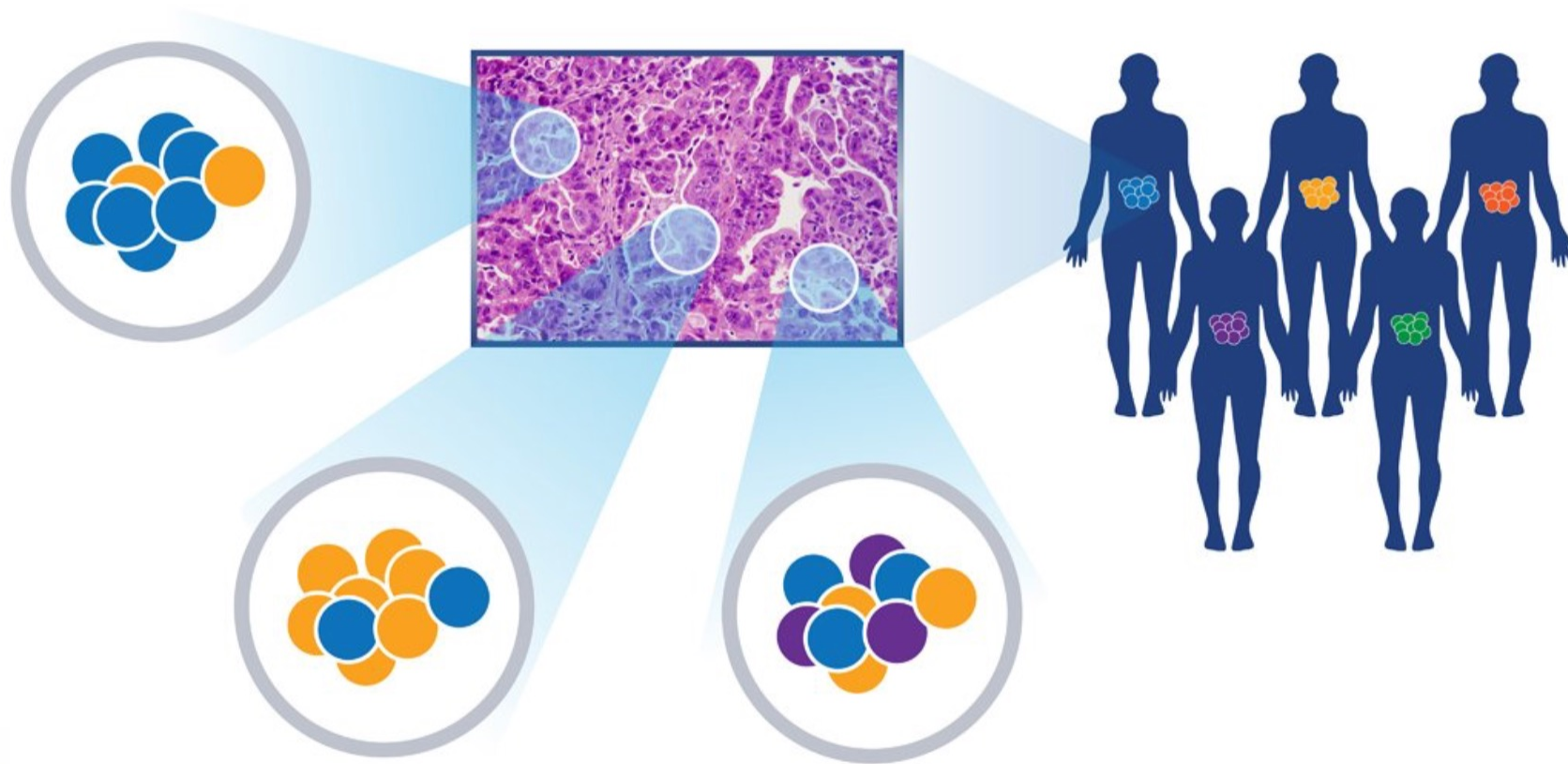
15

50% of these responses will be of quality

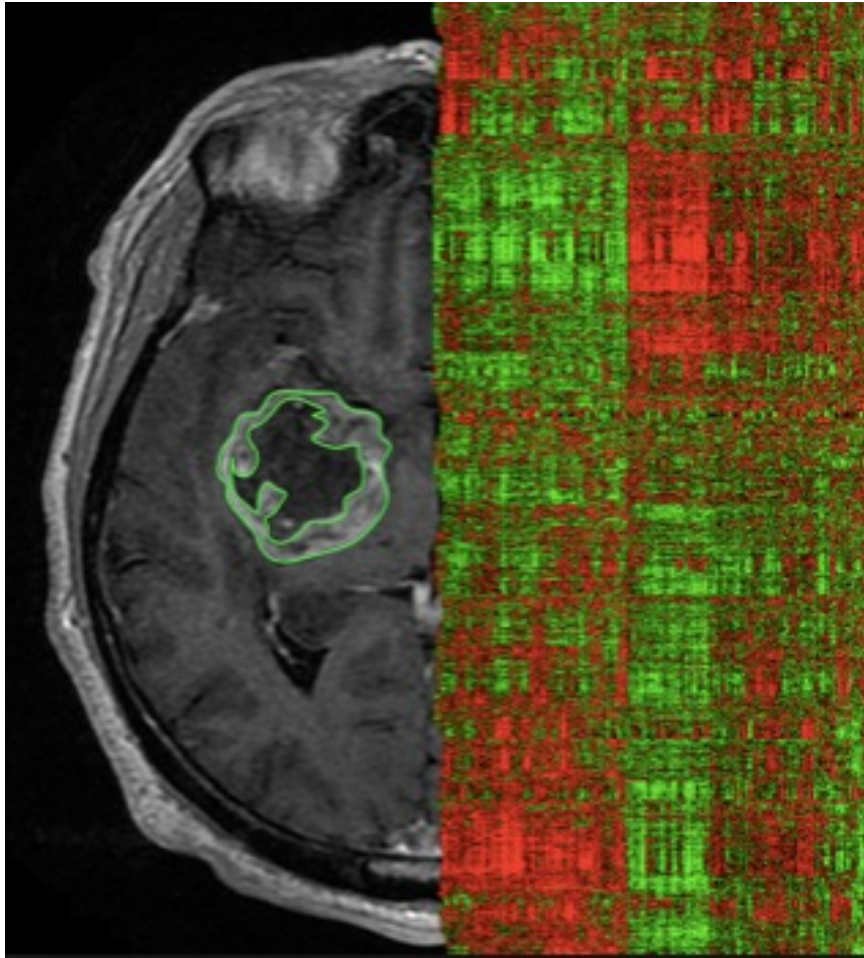
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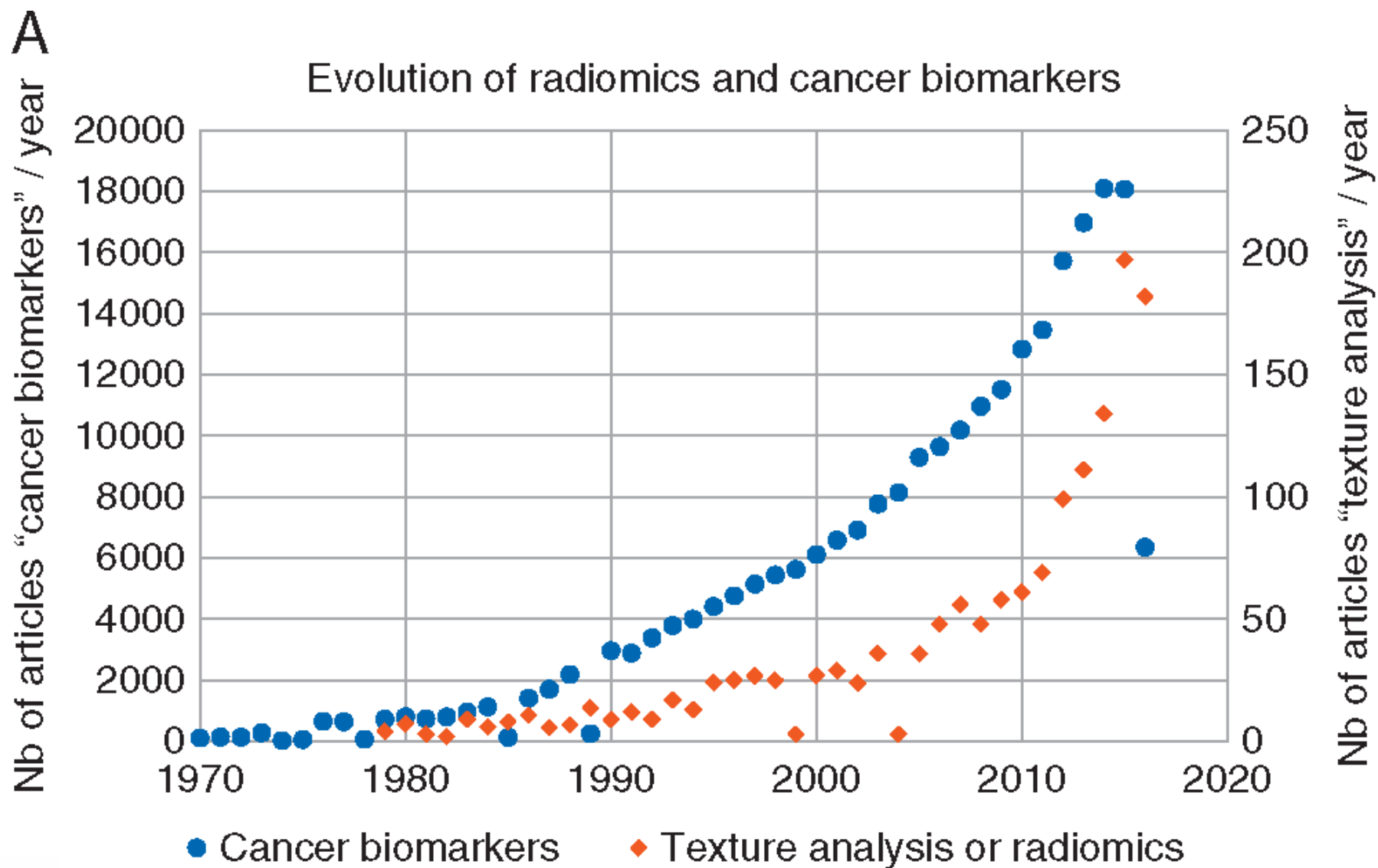
# Tumor Complexity and Heterogeneity



# Radiomics



- Not invasive
- Repeatable
- **Analyzes entire tumor volume**
- Uses already available diagnostic exams
- Cheap





Can we really know the real meanings of radiomics features?

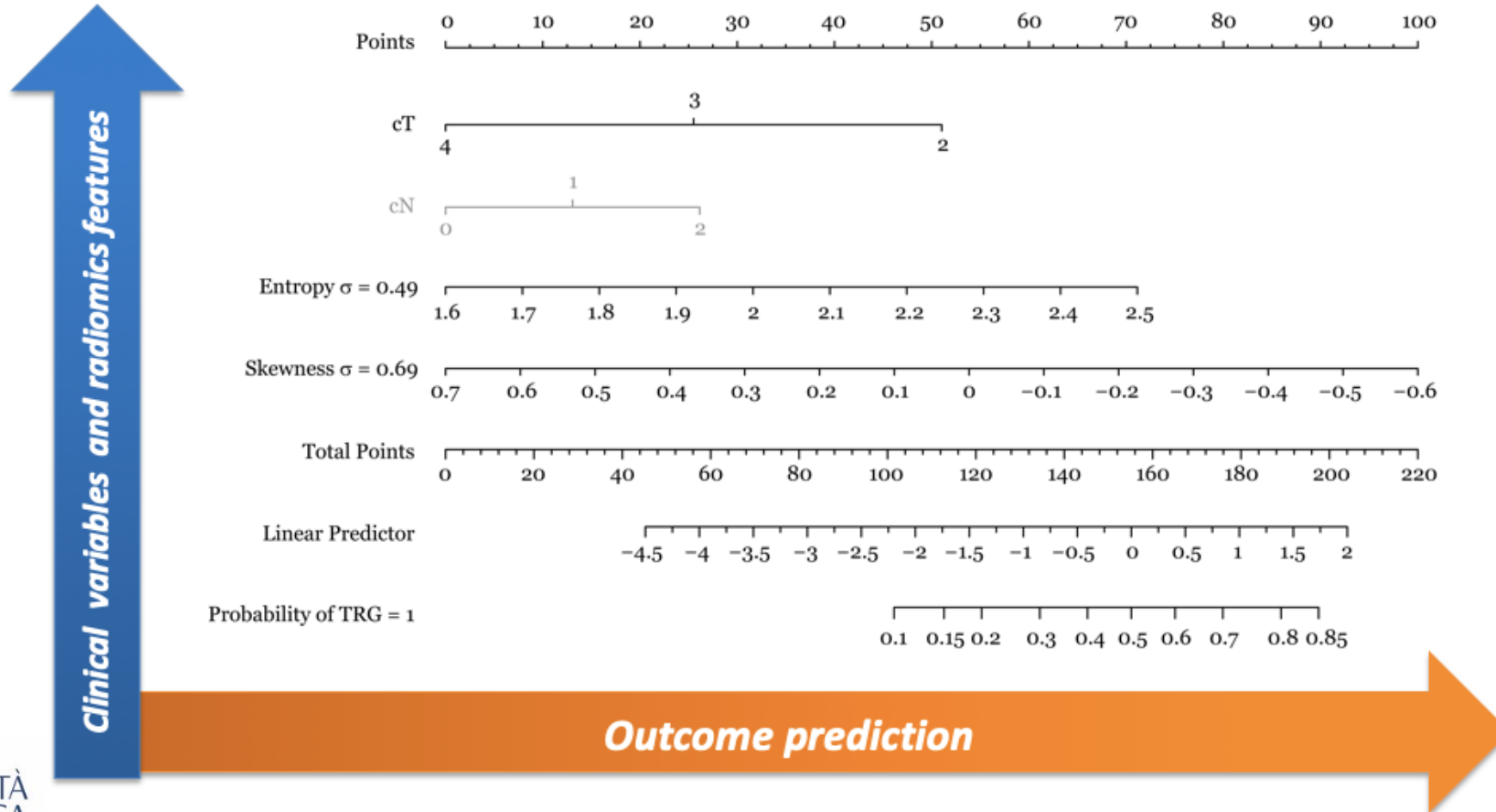


No, but we can start integrating them in multivariable predictive models



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# Radiomics



# Hybrid Machine



**DELTA RADIOMICS**

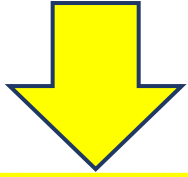


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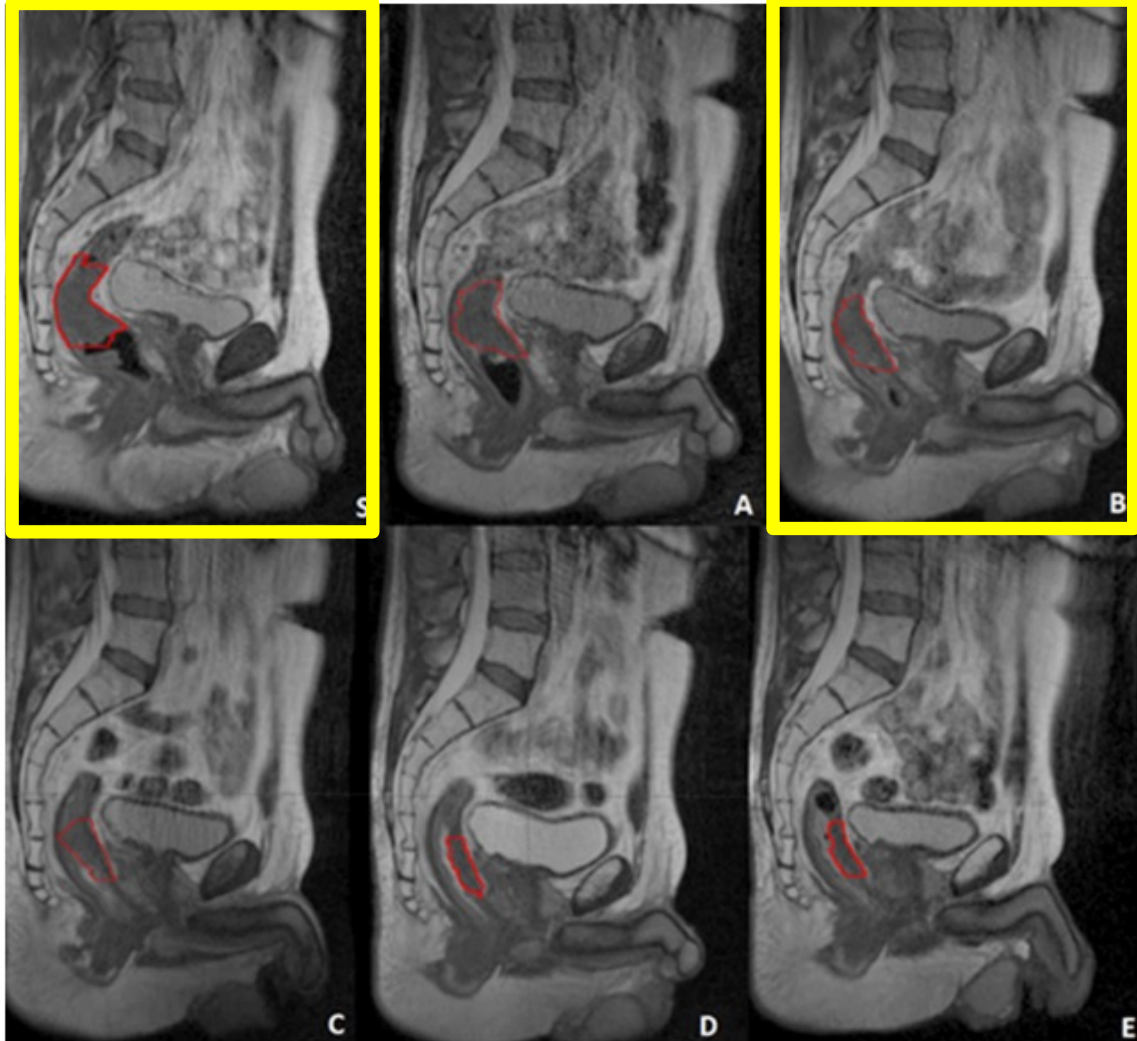
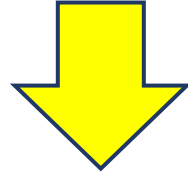
# Hybrid machine

Simulation

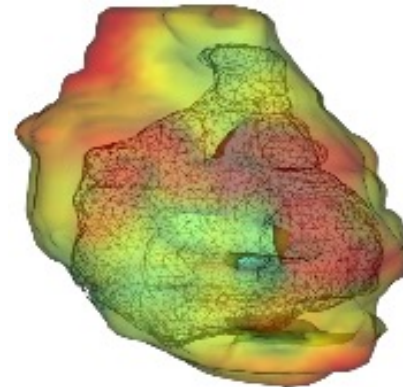
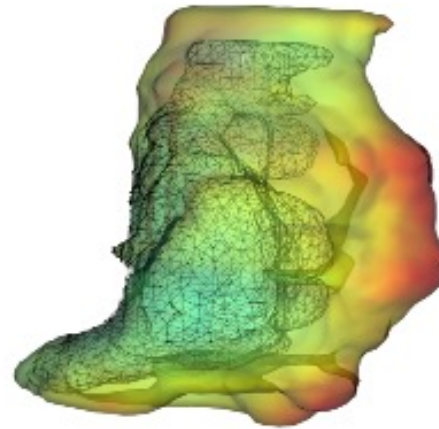


MR-LINAC

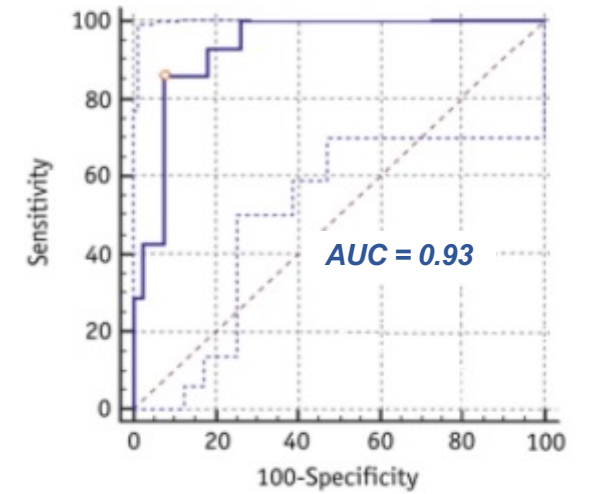
2° week



## pCR prediction during treatment



2020



**Early regression index**

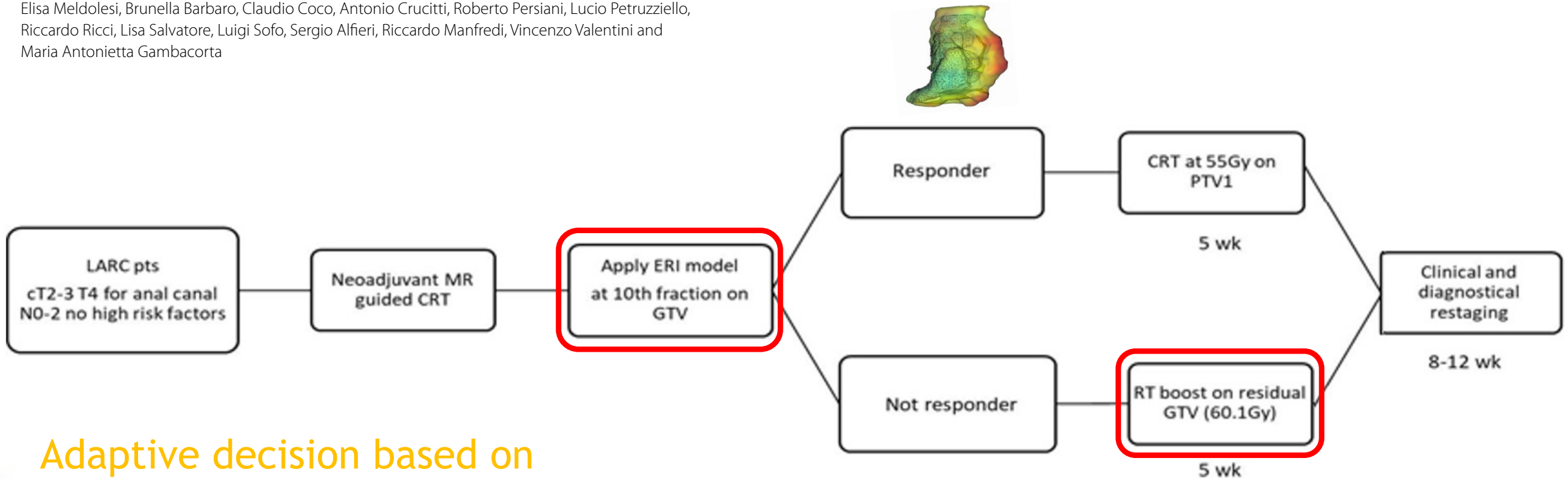




# THUNDER 2: THERAGNOSTIC UTILITIES FOR NEOPLASTIC DISEASES OF THE RECTUM BY MRI GUIDED RADIOTHERAPY

Giuditta Chiloire, Davide Cusumano, Luca Boldrini, Angela Romano <sup>\*</sup>, Lorenzo Placidi, Matteo Nardini, Elisa Meldolesi, Brunella Barbaro, Claudio Coco, Antonio Crucitti, Roberto Persiani, Lucio Petruzzello, Riccardo Ricci, Lisa Salvatore, Luigi Sofo, Sergio Alfieri, Riccardo Manfredi, Vincenzo Valentini and Maria Antonietta Gambacorta

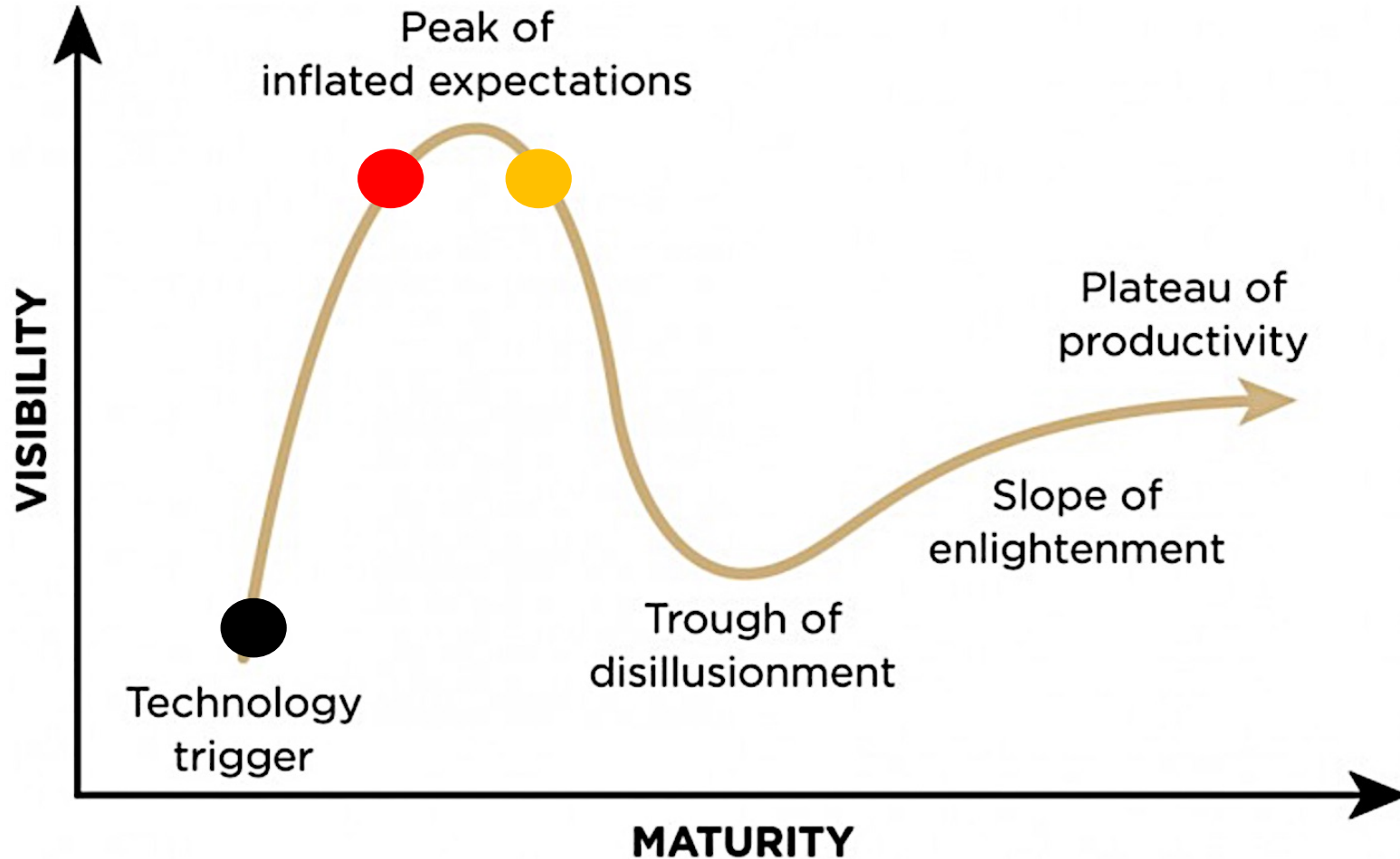
## ACTIONABLE prediction (iOGRT)






### Adaptive decision based on

- On-board 0.35 T imaging
- Response prediction model
- Radiomics

# Innovation Hype: Omic



-  *Omic driven oncology*
-  *Omic Driven RT*
-  *Radiomic*

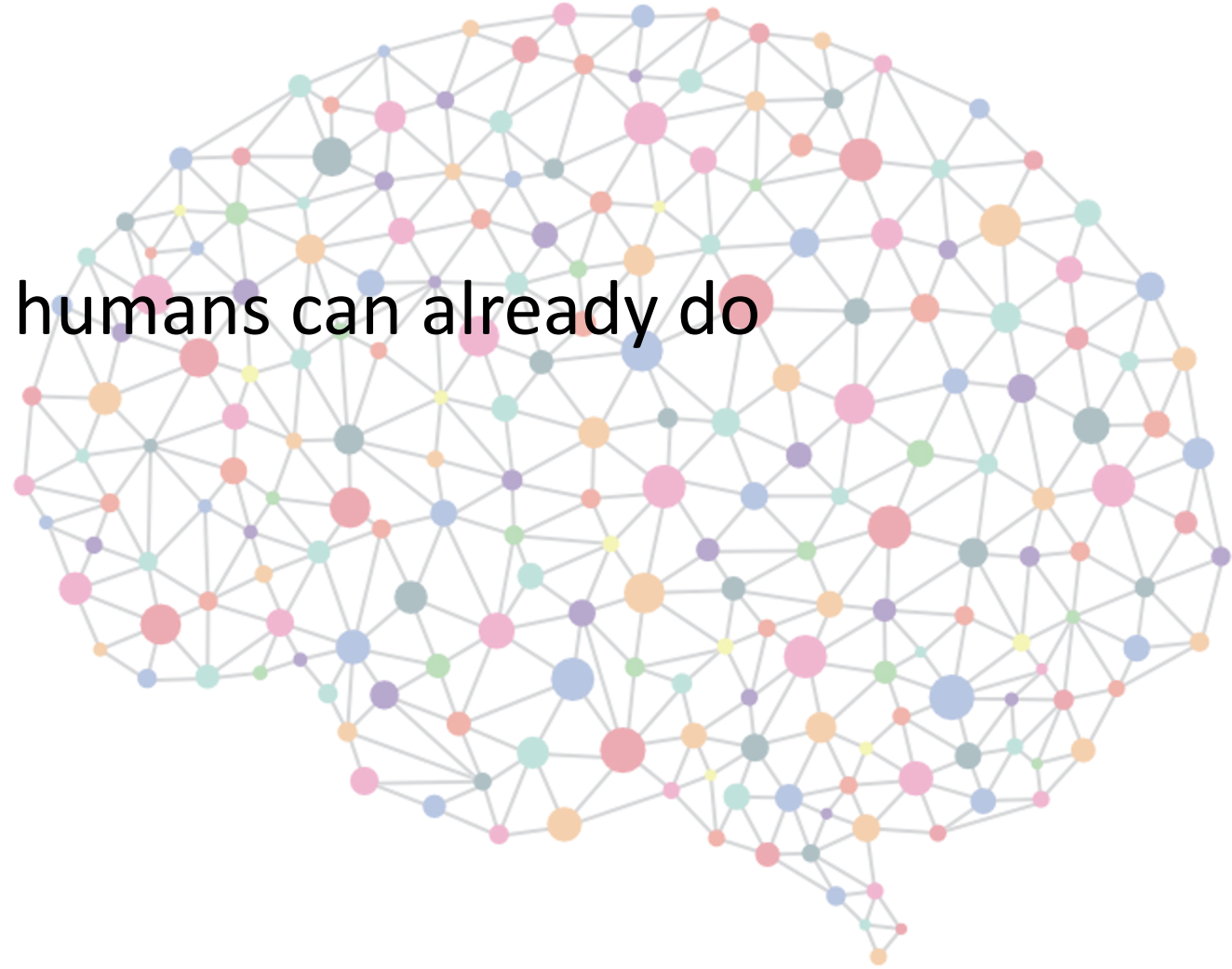
# Rationale for using AI in healthcare

- **TASK REPLACEMENT**

To do quicker (and better) what humans can already do

- **DECISION SUPPORT**

To do what humans can not do



# How AI may support MTD?



**First Contact**



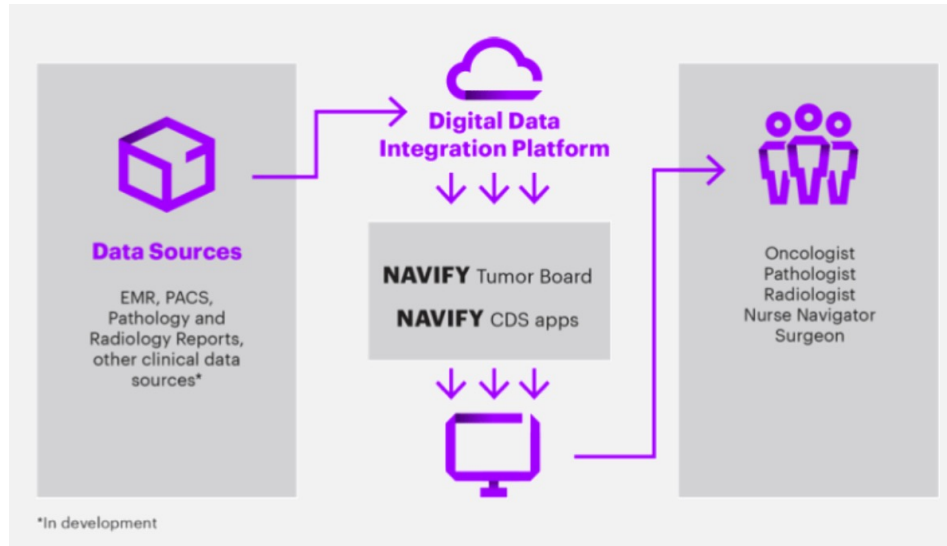
**Restaging**



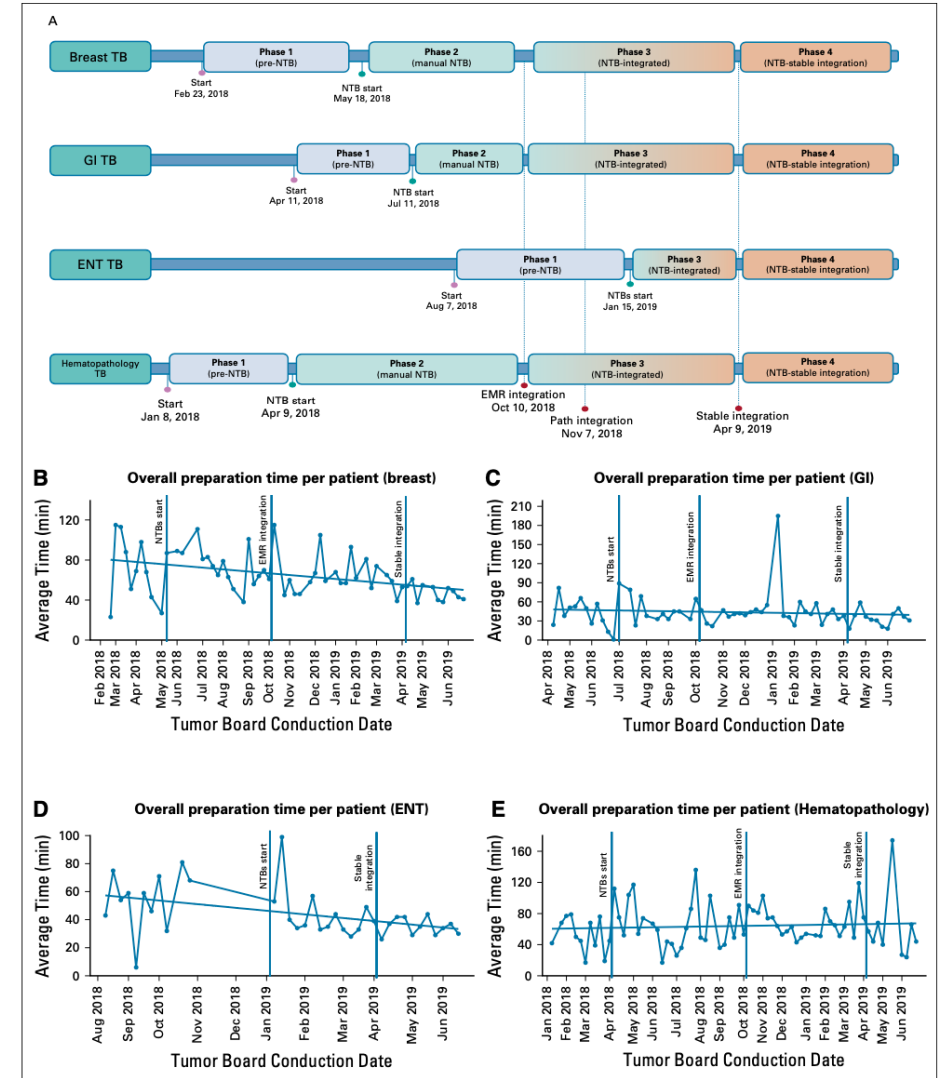
**After surgery**



# PREPARATION TIME: task replacement



Roche Molecular Systems, Santa Clara, CA



Mean **PREPARATION TIME REDUCTION** per PTS

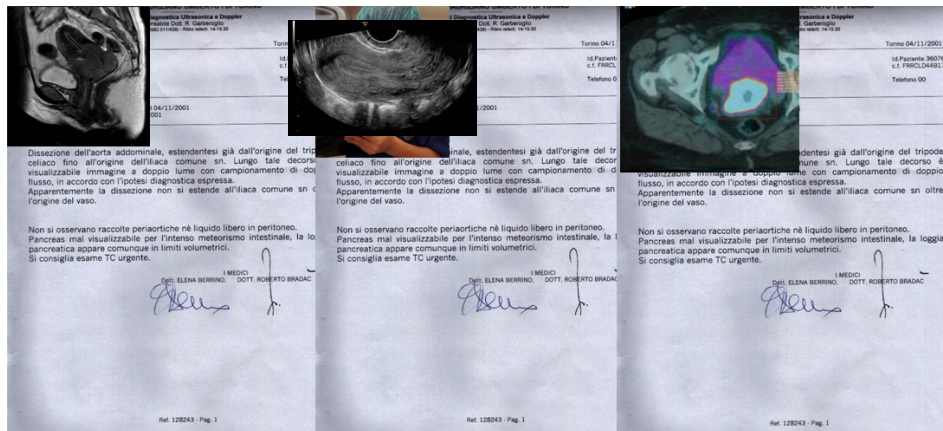
Breast: **28%**

GI: **23%**

ENT: **33%**

# PATIENTS PRIORITIZATION: task replacement

## SMART CLINICAL ASSISTANT



### Variables

- Parametrium involvment
- Lower Third involvment
- Middle Third involvment
- Upper Third involvment
- Bladder involvment
- Rectum involvment
- Vesico-vaginal septum inv.
- Recto-vaginal septum inv.
- Hydronephrosis
- Lymph nodes involvment
- Lymph nodes activity
- Cervical lesion
- Cervical activity
- Fornix involvment
- Stromal involvment
- Metabolic activity
- “Other” Activity

### MR

### EUA

### PET-CT

Parametrium involvment	Present	Absent	Absent
Lower Third involvment	Absent	Absent	Absent
Middle Third involvment	Absent	Absent	Absent
Upper Third involvment	Absent	Absent	Absent
Bladder involvment	Absent	Absent	Absent
Rectum involvment	Absent	Absent	Absent
Vesico-vaginal septum inv.	Absent	Absent	Absent
Recto-vaginal septum inv.	Absent	Absent	Absent
Hydronephrosis	Present	Absent	Absent
Lymph nodes involvment	Absent	Absent	Absent
Lymph nodes activity	Present	Absent	Absent
Cervical lesion	Absent	Absent	Present
Cervical activity	Present	Absent	Absent
Fornix involvment	Absent	Absent	Present
Stromal involvment	Absent	Absent	Absent
Metabolic activity	Present	Present	Absent
“Other” Activity	Absent	Absent	Absent
“Other” Activity	Absent	Absent	Absent

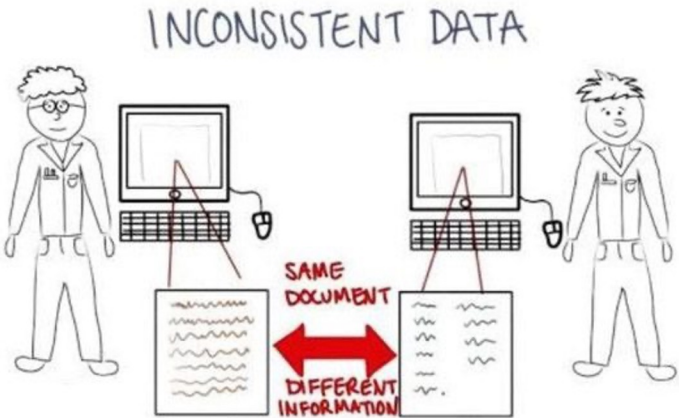
### Legend

Features absent

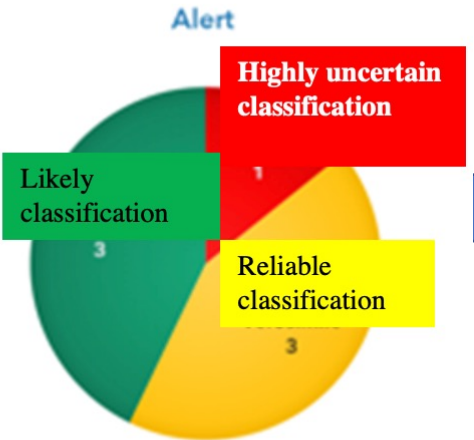
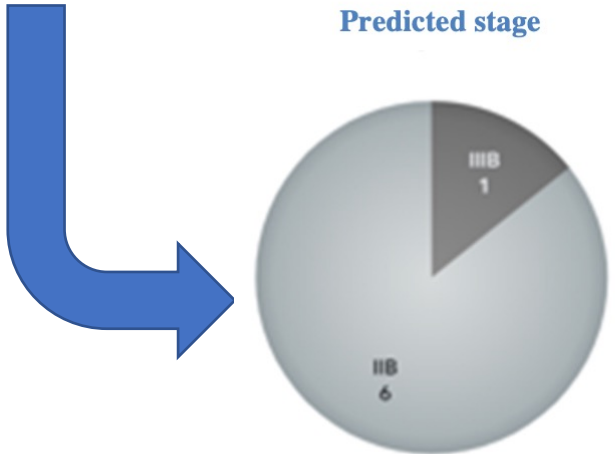
Features present

# PATIENTS PRIORITIZATION

## SMART VIRTUAL ASSISTANT



Patients		Predicted stage	Alert
Patient name; hospital code, age: 59; BMI: 23.4	IIIB	Green	
Patient name; hospital code, age: 55; BMI: 21.4	IIIB	Green	
Patient name; hospital code, age: 56; BMI: 30.1	IIIB	Green	
Patient name; hospital code, age: 29; BMI: 26.4	IIIB	Yellow	
Patient name; hospital code, age: 76; BMI: 29.1	IIIB	Yellow	
Patient name; hospital code, age: 44; BMI: 28.5	IIIB	Red	



# ACCESS TO CURE: task replacement

Table 1. Fields chosen by the professionals of the Breast Cancer Working Group, in order to classify the patients inserted in the platform.











Field	Value Type	Values	Notes
TNM	Text	T (1,2,3,4, IS) N (0,1,2,3) M (0,1)	
TNM stage	Numerical	From 0 to 4	If 1,2,3 specify the TNM
Age	Numerical	Range	
Immunophenotype	Text	Luminal A Luminal B Triple Negative HER 2 +	
Histological examination	Bit	Internal External	
BMI	Numerical	Mathematic formula Neoadjuvant Adjuvant	Specify if $\geq 25$
Therapy stage	Text	First line metastatic After the first line	
Genetic test	Ternary	Positive Negative Not applicable	Possibility to specify the test
Mutated PI3K	Ternary	Yes No Not applicable	

## DIGITAL RESEARCH ASSISTANT

to report real-time every available **clinical trial** and support clinician in matchmaking single patients with existing trials

Moduli Abilitati: **Neoplasia Mammaria** Neoplasia Polmonare

+ Codice Anonimo Esame Istologico BMI Stadio Immunofenotipo Tipo Terapia

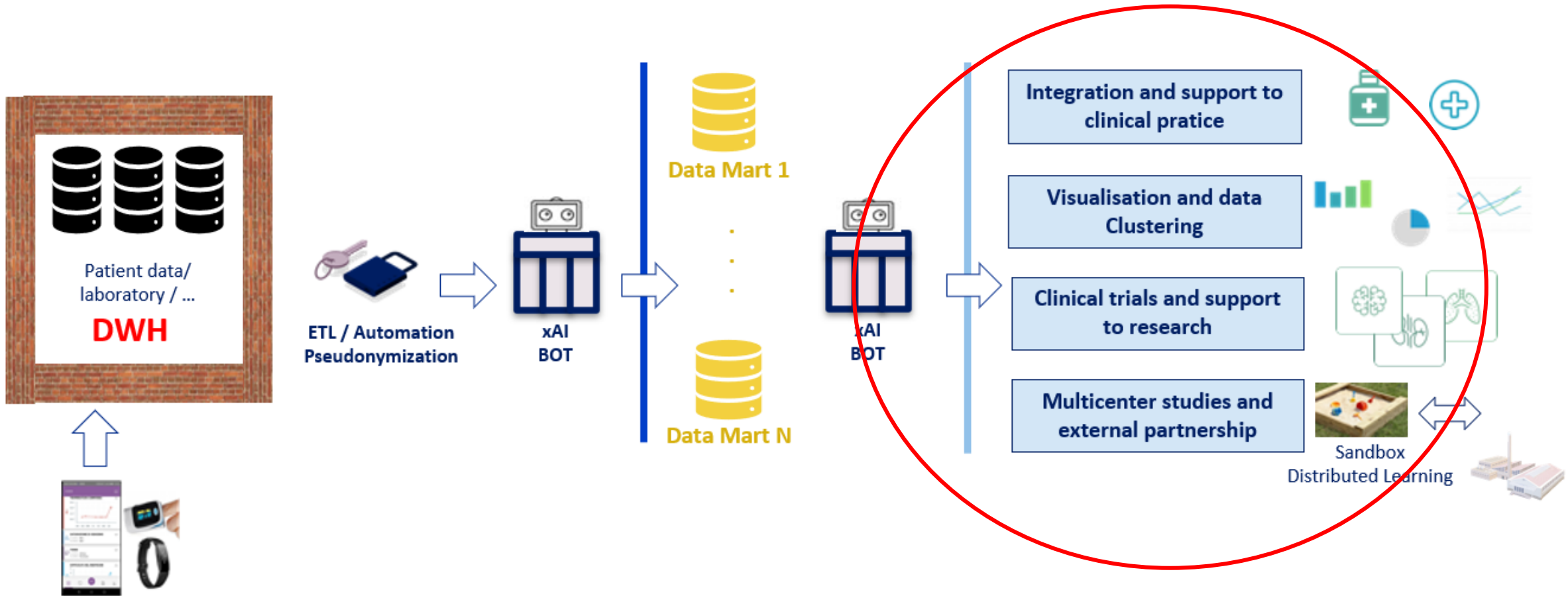
	Codice Anonimo	Età	Esame Istologico	BMI	T	N	M	Stadio	Immunofenotipo	Tipo Terapia	Test Genetico	Specifica Test Genetico	PI3K Mutato	Cognome Nome	Azioni Possibili
●	giorgino	74	Interno	24.44	T2	N1	M0	Stadio IIB	Triplo Negativo	Adiuvante	sadasd	adad	adsafsd	null null	 
●	prova 1000	44	Interno	27.51	T2	N2	M0	Stadio IIIA	Triplo Negativo	Prima Linea Metastatica	asasda	dadas	asdasd	null null	
●	sfsddf	2	Esterno	2.00	T3	N2	M0	Stadio IIIA	Luminale B	Adiuvante	asdasd	sdasdasdas	dasda	null null	 
●	prova put	33	Interno	26.12	T3	N0	M0	Stadio IIB	Luminale A	Neoadiuvante	a3	b2	K4	null null	
●	dfsdfsdf	22	Esterno	45.00	T2	N1	M0	Stadio IIB	Luminale A	Neoadiuvante	asdasd	asdasd	adasdasd	null null	
●	dfsdfsdf	22	Esterno	45.00	T1s	N0	M0	Stadio 0	Luminale A	Neoadiuvante	asdasd	asdasd	adasdasd	null null	 
●	dfsdfsdf	22	Esterno	45.00	T2	N1	M0	Stadio IIB	Luminale A	Neoadiuvante	asdasd	asdasd	adasdasd	null null	



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# CLINICAL DECISION based on AI and BIG DATA



DWH and ODW FPG  
Integration Real World Data


Compliance with policies and procedures:  
- Ethics Committee FPG  
- Data Privacy Officer

- Ontologies and standard data on clinical activity
- Data Clustering for Pathology
- Processing of pseudonymised data


Predictive models  
Clinical workflow integration  
Data visualisation  
Research and Industry  
Privacy-preserving Methods



# DIGITAL AVATAR - SURGICAL COMPLICATIONS



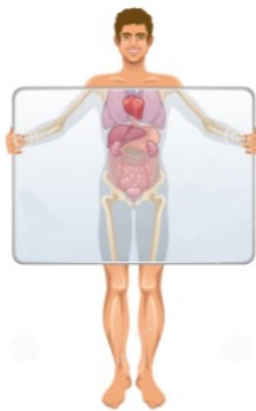
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COLON
RETTO

	Variabile	Valore
^		
Anamnesi		
Chimica		
Chirurgia		
Ematologia		
Emogas		
Microbiologia		
Dati Oncologici		
Parametri-Valori		
∨		

	Variabile	Valore
	con_post30_Ematocrito	33.6
	con_post30_Emoglobina	11.4
	con_post30_Globuli_Bianchi	9.77
	con_post30_Globuli_Rossi	4.11
	con_post30_Linfociti	1.19
	con_post30_Linfociti_perc	12.2
	con_post30_MCH	27.7
	con_post30_MCHC	33.9
	con_post30_MCV	81.7
	con_post30_MPV	11.6
	con_pre90_Ematocrito	41.5
	con_pre90_Emoglobina	13.4
	con_pre90_Globuli_Bianchi	3.83



**Variabili Categoriche**

categ_ASA5	▼	categ_COM_CARDIACHE	▼
0	▼	0	▼
Variabile	▼	Variabile	▼
	▼		▼

**Variabili Numeriche**

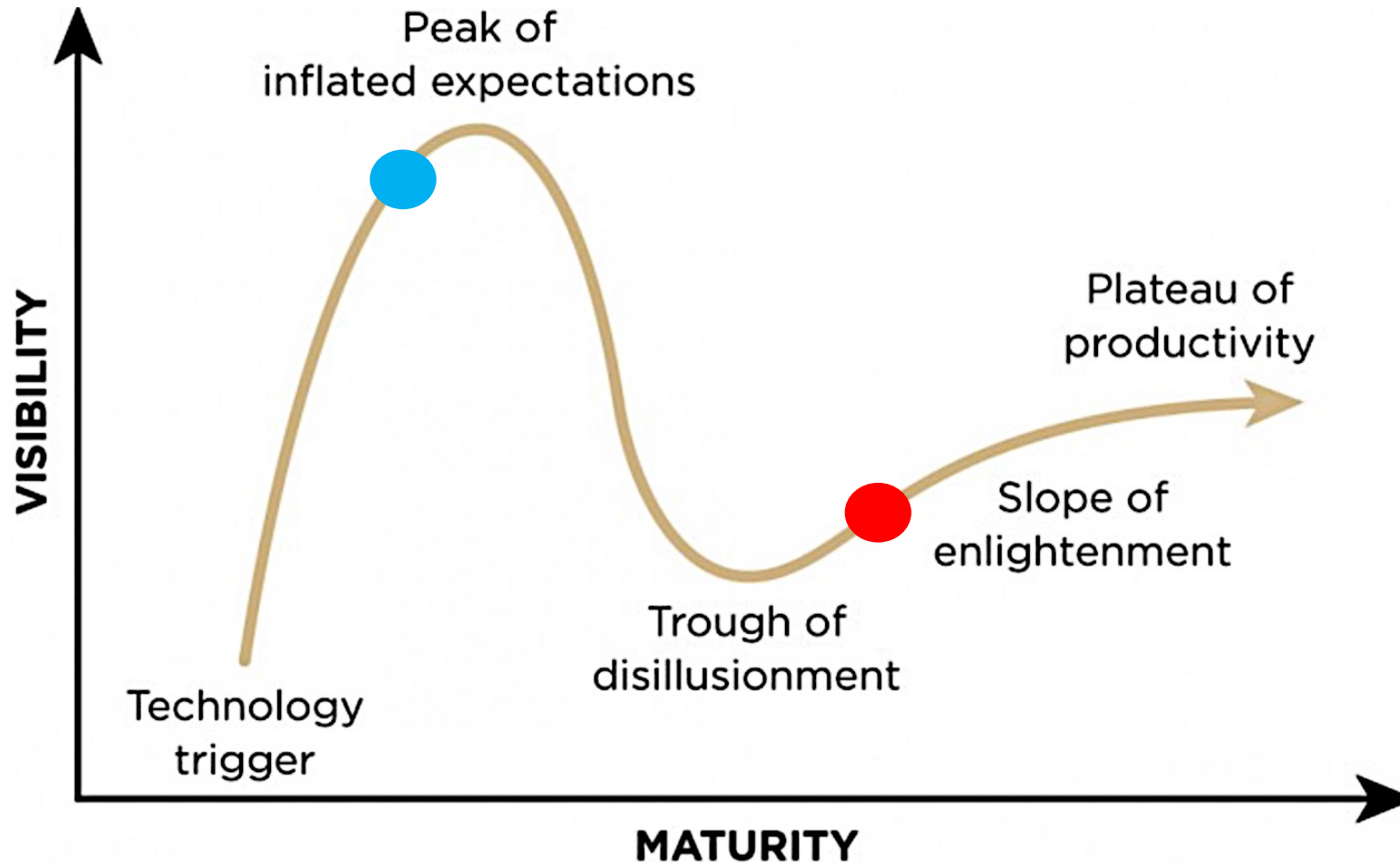
con_ETA	▼	con_BMI	▼
71	▼	22.83	▼
Variabile	▼	Variabile	▼
.	▼		▼

Frequenze	Occlusione	Polmonite	SSI	Emorragia	Deiscenza
124.85	7.21%	3.20%	1.60%	3.20%	3.20%

Frequenze	Occlusione	Polmonite	SSI	Emorragia	Deiscenza
1,571.69	6.36%	2.29%	2.80%	2.48%	2.10%

# Innovation Hype: AI



- *Task Replacement*
- *Decision Supportive Systems*

*'If you are not failing every now and again, it's a sign  
you're not doing anything very innovative'*

*Woody Allen*



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