


XXXII CONGRESSO NAZIONALE AIRO
XXXIII CONGRESSO NAZIONALE AIRB
XII CONGRESSO NAZIONALE AIRO GIOVANI

AIRO2022

Radioterapia di precisione per un'oncologia innovativa e sostenibile

BOLOGNA, 25-27 NOVEMBRE
PALAZZO DEI CONGRESSI

 Associazione Italiana
Radioterapia e Oncologia clinica

 Società Italiana di Radiobiologia

 Associazione
Italiana
Radioterapia
e Oncologia
clinica




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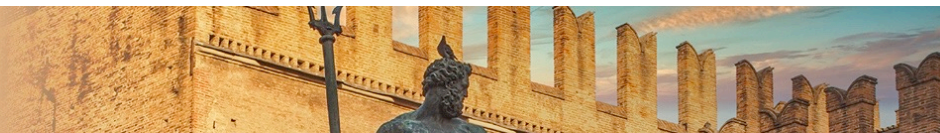
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Innovazione e sostenibilità nelle scienze radiologiche: *il punto di vista in radioterapia*

Vincenzo Valentini



DICHIARAZIONE

Relatore: Vincenzo VALENTINI

Come da nuova regolamentazione della Commissione Nazionale per la Formazione Continua del Ministero della Salute, è richiesta la trasparenza delle fonti di finanziamento e dei rapporti con soggetti portatori di interessi commerciali in campo sanitario.

Research collaborations incl. funding, consultancy and speaker honoraria

- Pharma: AstraZeneca, Bayer, MSD, Pfizer, Sofar
- MedTech: Accuray, Bebig, Elekta, GE, Siemens, Varian Medical Systems, ViewRay

Spin-offs and commercial ventures

- KBO.com
- Gemelli Digital Medicine & Health

Various patents on RTO

Public research funding:

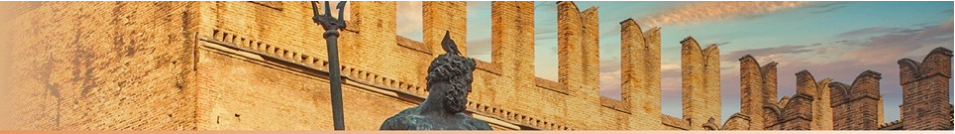
- H2020 Termet
- H2020 iHelp
- H2020 Re-Sample
- H2020 Care4Covid



What is innovation (technologies)?

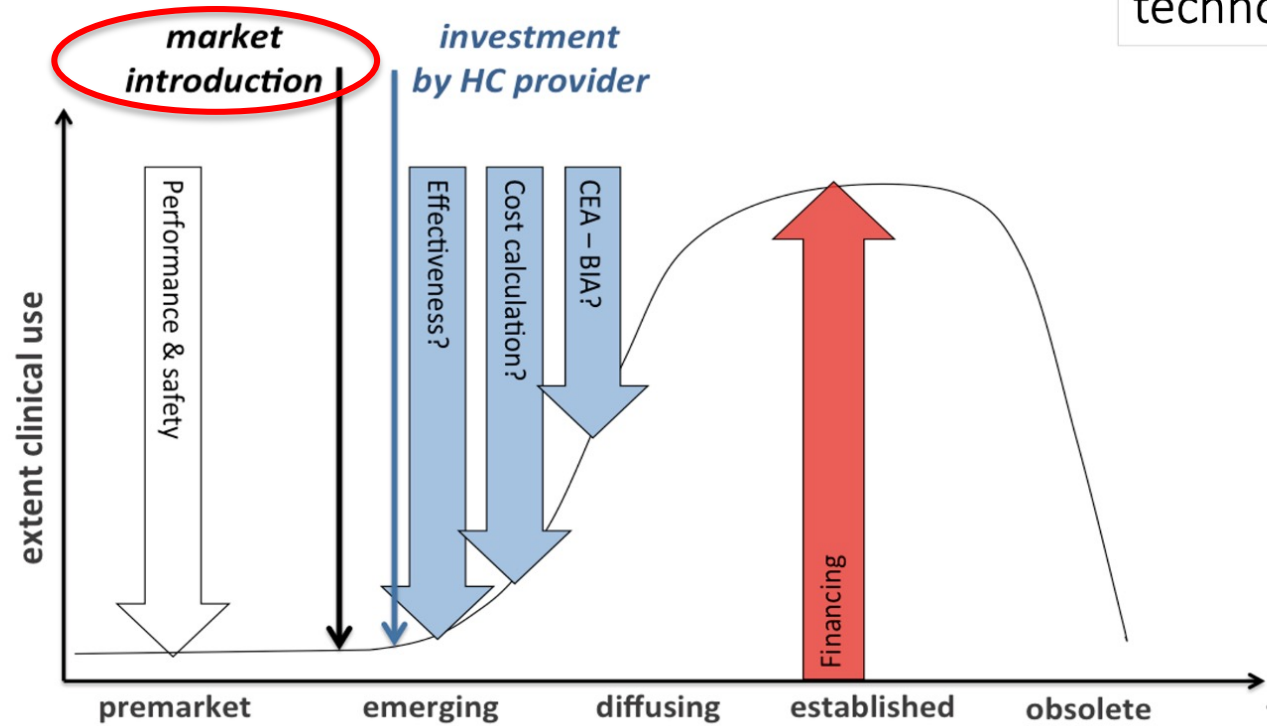
“A new method or new product
that **becomes a new practice** somewhere in the world”

Edmund Phelps

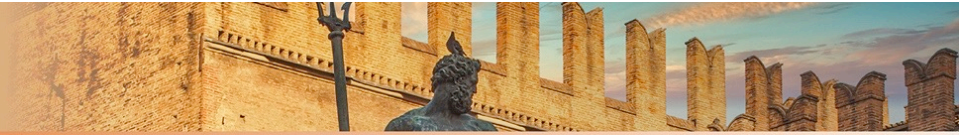


Market introduction and reimbursement

technologies



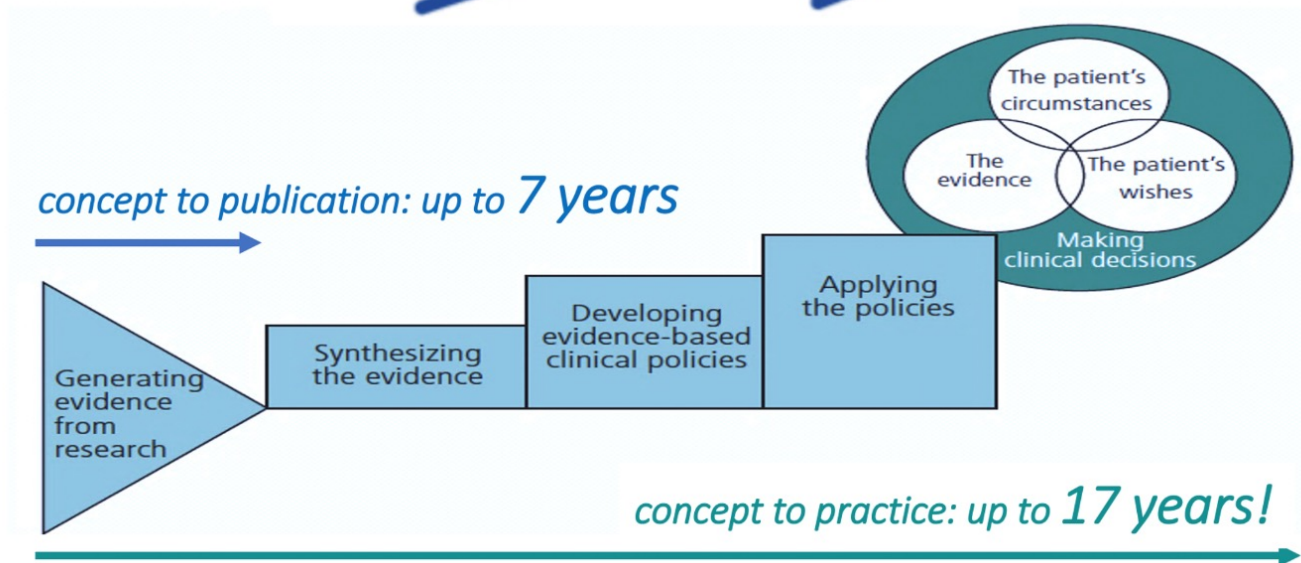
Lievens et al. Acta Oncol 2015

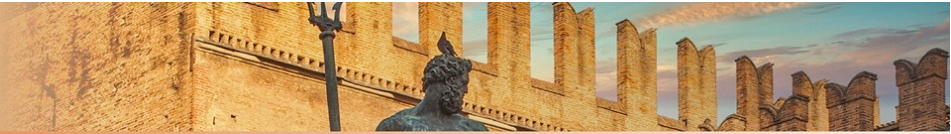


innovation



clinical practice





What is innovation (drugs)?

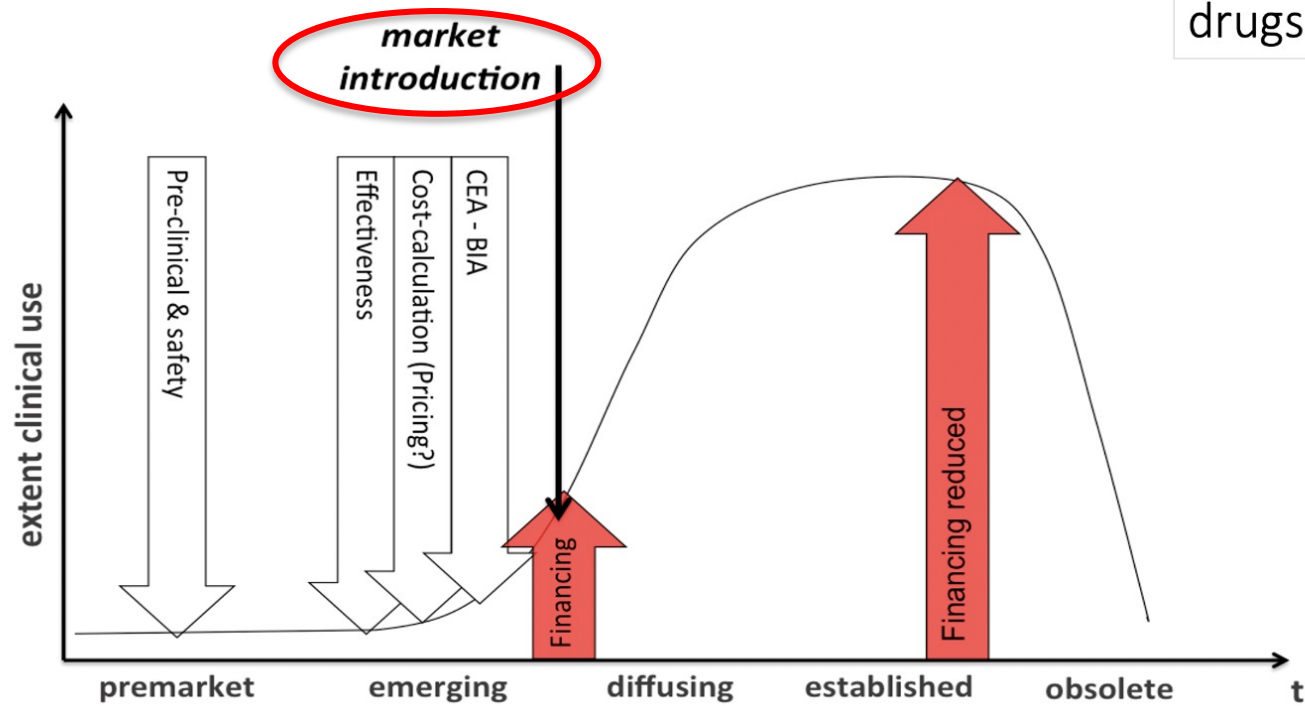
Criteri per innovatività terapeutica (AIFA)

- **1. BISOGNO TERAPEUTICO:** basato sulla disponibilità di terapie per la patologia in oggetto ed indica quanto l'introduzione di una nuova terapia sia necessaria per dare risposta alle esigenze terapeutiche di una popolazione di pazienti (massimo/importante/moderato/scarso/assente)
- **2. VALORE TERAPEUTICO AGGIUNTO:** Il valore terapeutico aggiunto è determinato dall'entità del beneficio clinico apportato dal nuovo farmaco rispetto alle alternative disponibili, se esistenti, su esiti riconosciuti come clinicamente rilevanti e validati per la patologia in oggetto. *Per i farmaci oncologici il gold standard è OS. La mancanza di dati di OS dovrà essere adeguatamente giustificata e, in relazione al tipo di neoplasia ed al setting terapeutico, potranno essere considerati la PFS, DFS), la durata della risposta completa o altri esiti surrogati* (massimo/importante/moderato/scarso/assente)
- **3. QUALITA' DELLE PROVE:** La corretta valutazione del potenziale innovativo di un farmaco dipende dalla qualità delle prove scientifiche portate a supporto della richiesta. Per la valutazione di questo parametro l'AIFA decide di adottare il metodo GRADE (alta/moderata/bassa/molto bassa)
- **Impatto economico: quarto ostacolo?**

By courtesy Prof M.Barbieri – AIRO - 2022



Market introduction and reimbursement

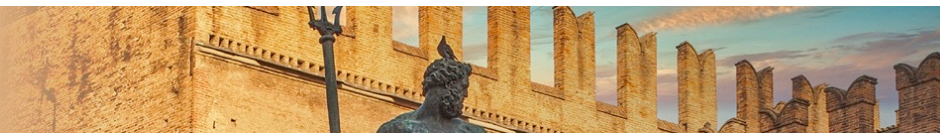


Lievens et al. Acta Oncol 2015

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PHARMASTAR[★]
il Giornale online sui Farmaci

ONCOLOGIA MEDICA
Congresso ESMO 2022

121 PAGINE
18 INTERVISTE
26 ARTICOLI

Tumori, 4 mld la spesa per i farmaci nel 2021, +73% in 8 anni, ma nei programmi elettorali manca l'oncologia

Venerdì 9 Settembre 2022  Redazione

 Associazione Italiana
Radioterapia e Oncologia clinica

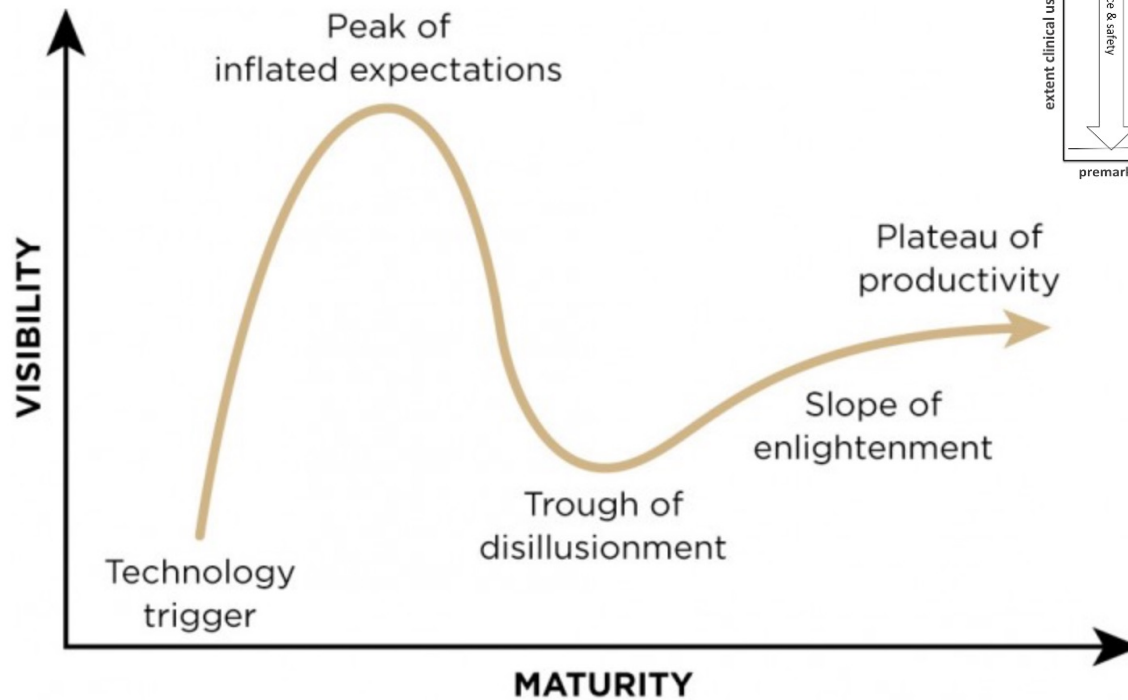
 Società Italiana di Radiobiologia

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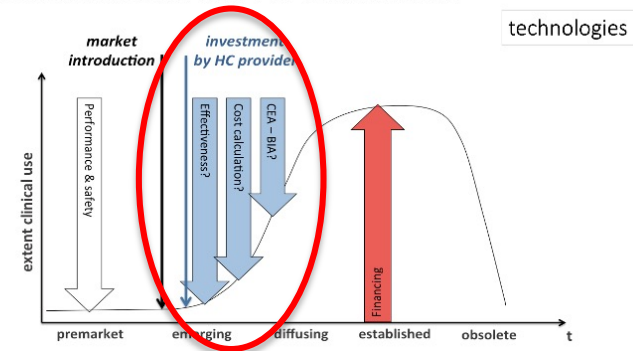
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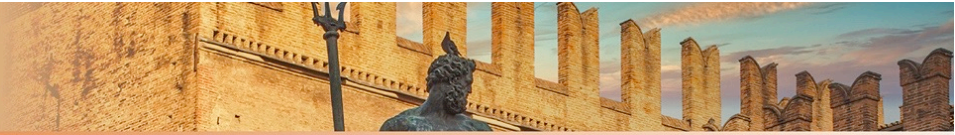


What is innovation?



Market introduction and reimbursement





FLASH



First treatment of a patient with FLASH (Lausanne, Oct 2018)

Multiresistant
T cell lymphoma

150 Gy/s
Overall time
90 ms



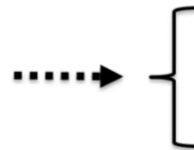
Day 0



5 months



J.Bourhis



Feasible

Safe, including with long term follow-up (> 2.5 years)

(Bourhis et al 2019)



Associazione Italiana
Radioterapia e Oncologia clinica



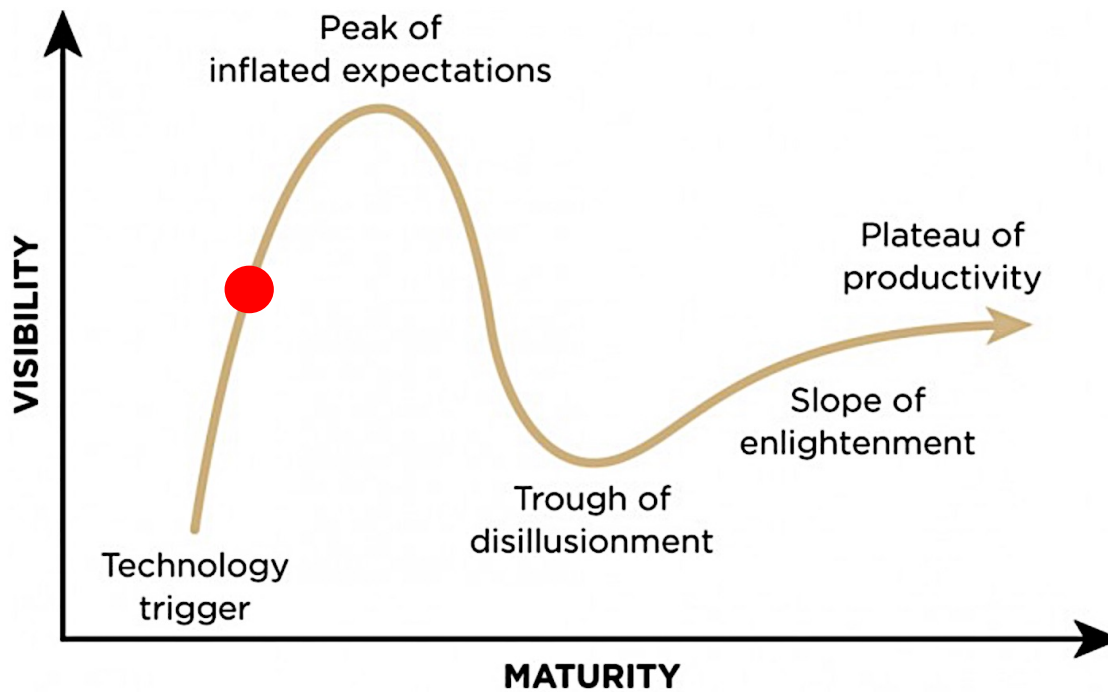
Società Italiana di Radiobiologia



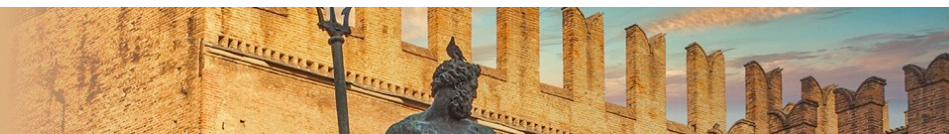
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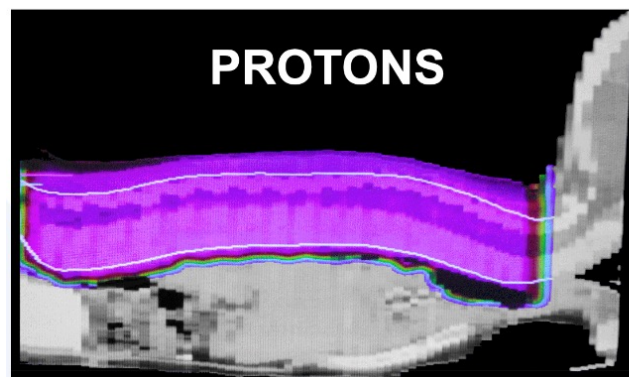
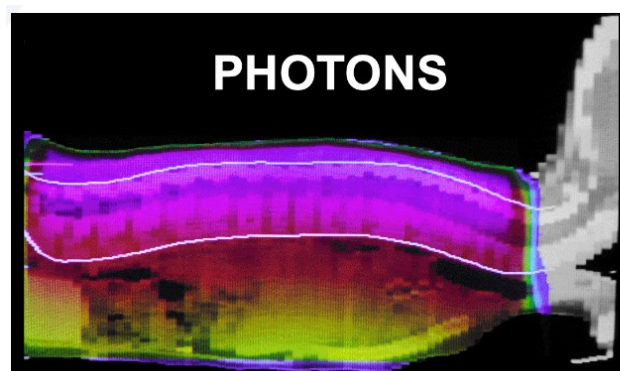
Innovation Hype: Flash



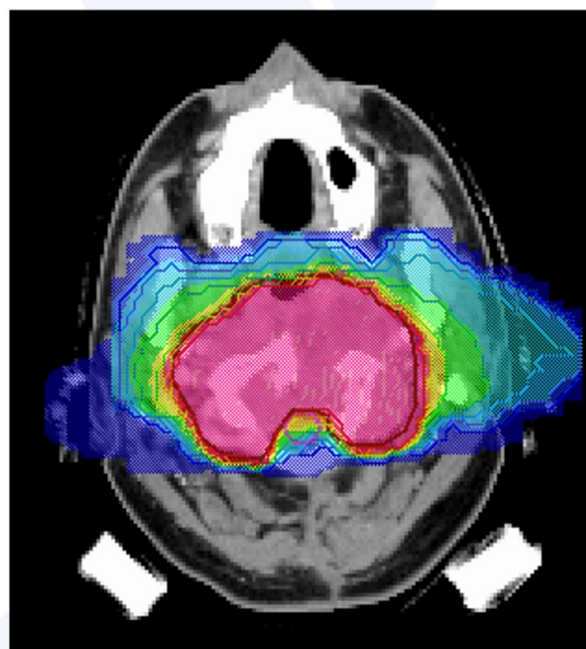
● *Flash*

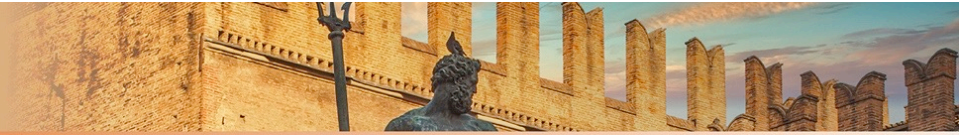


Adrons

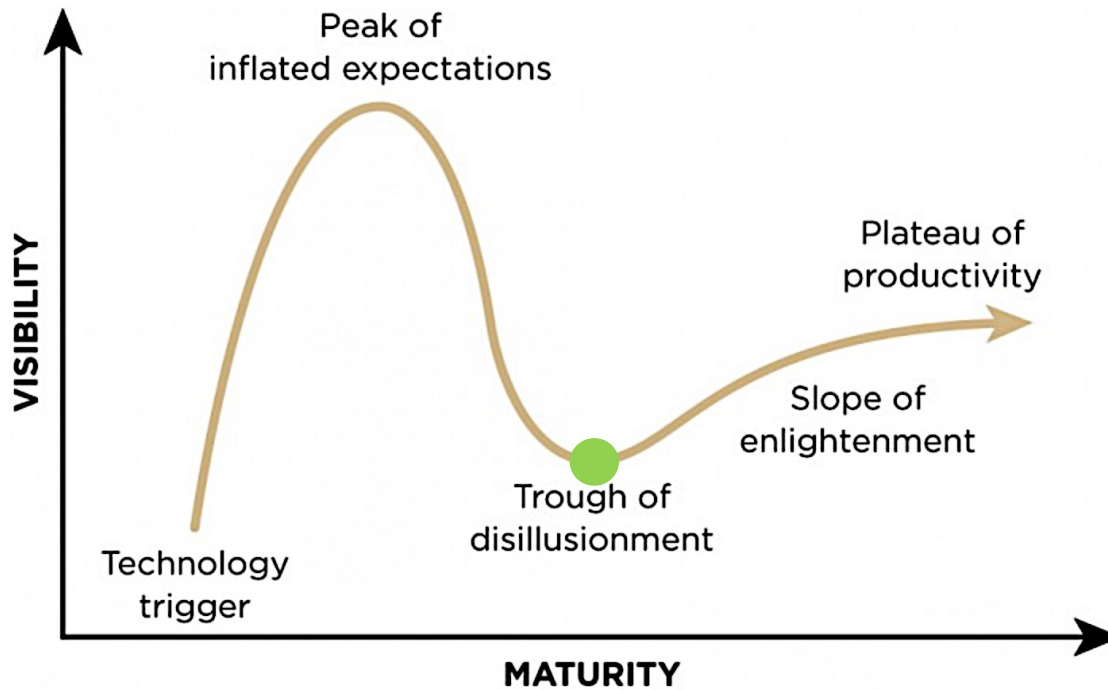


^{12}C -ions, 2 fields





Innovation Hype: Adrons



● *Flash*



Radiation oncologists: where are we going?

- **Image Guided Radiotherapy**
- **AI Guided Radiotherapy**
- **Omic Guided Radiotherapy**
- **Humanist Guided Radiotherapy**



I-GRT

- IGRT has drastically diminished the need for immobilization, potentially increasing eligibility (and compliance)
- IGRT has decreased dose to the surrounding tissues enhancing treatment compliance
- MRgRT well tolerated for hypofractionated regimens
- However, the true merit of IGRT/MRgRT is the increased possibility of non-invasively eradicating macroscopic disease thereby further bridging the gap between radiotherapy and surgery

G-Meyer



By courtesy of G.Meyer



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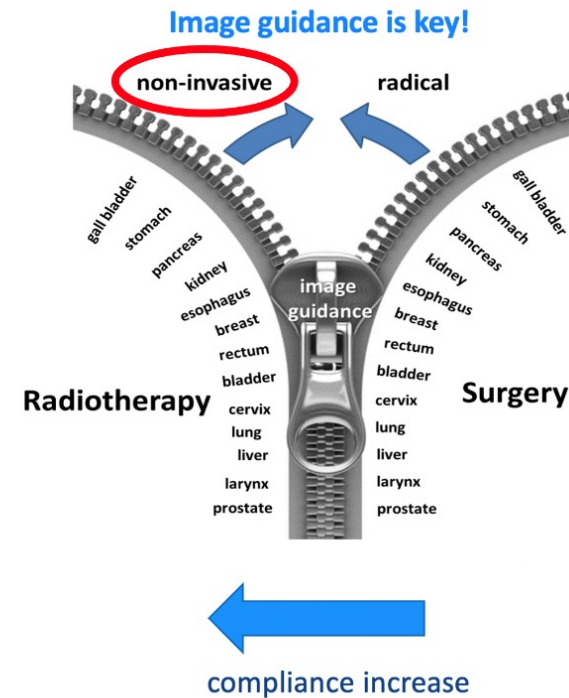


By courtesy of G.Meyer



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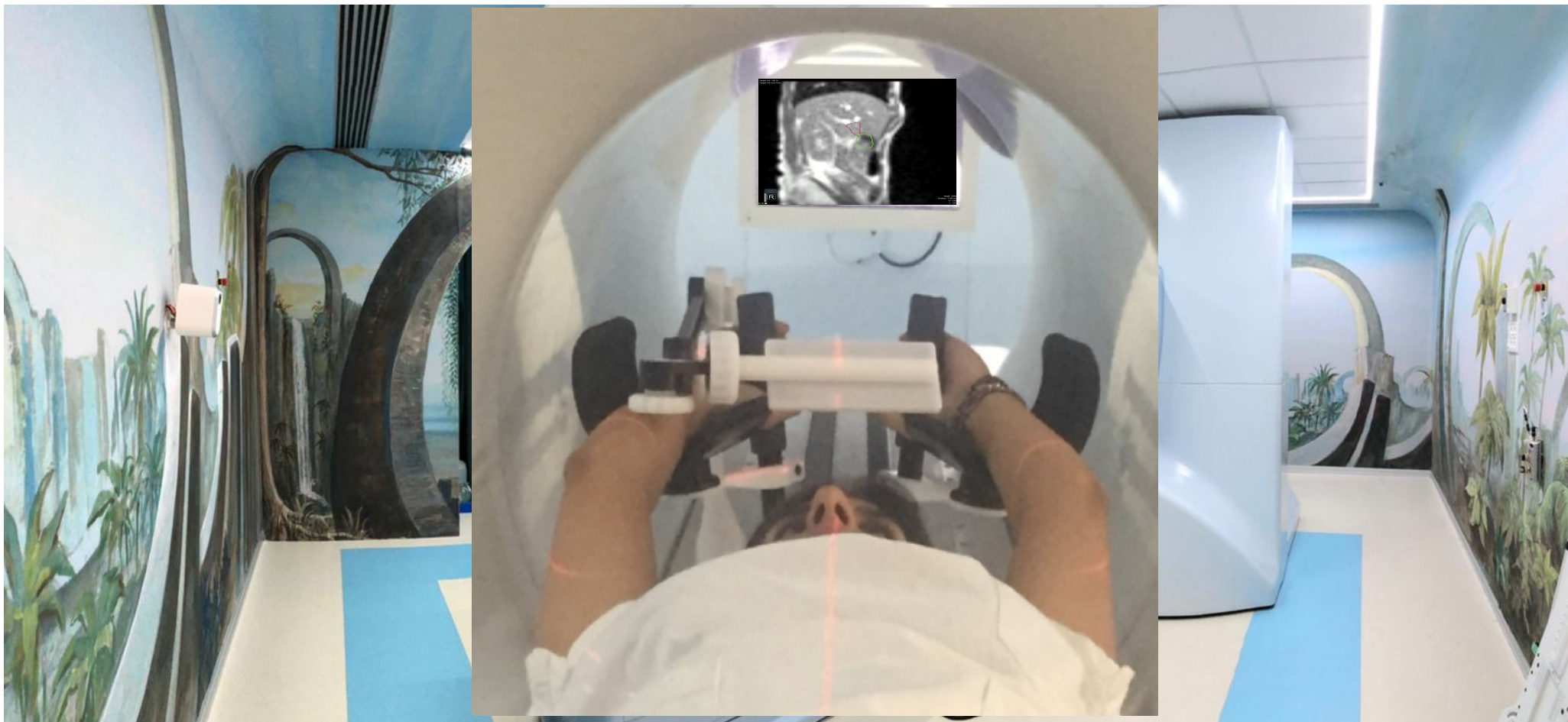
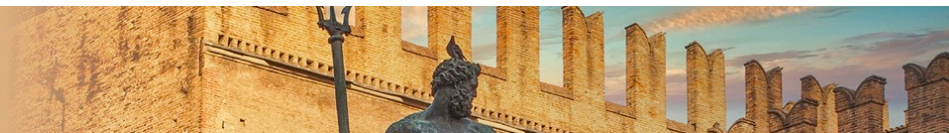


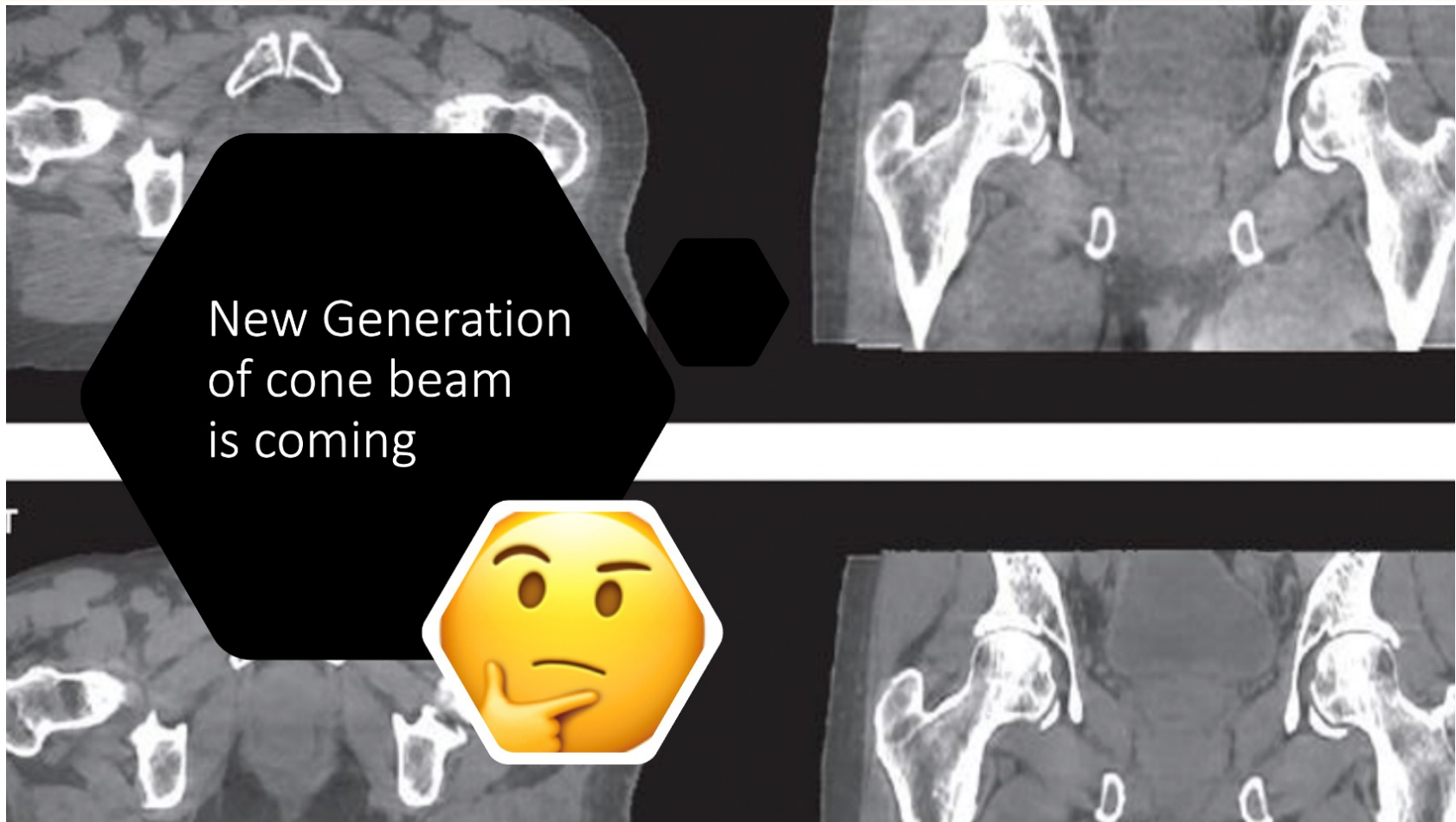
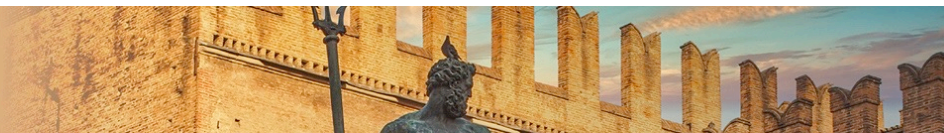
By courtesy of G.Meyer

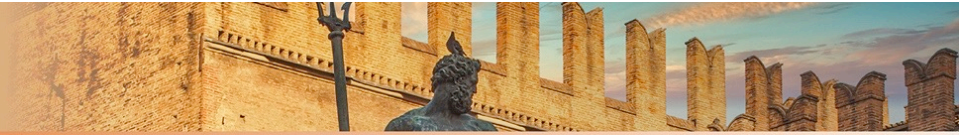
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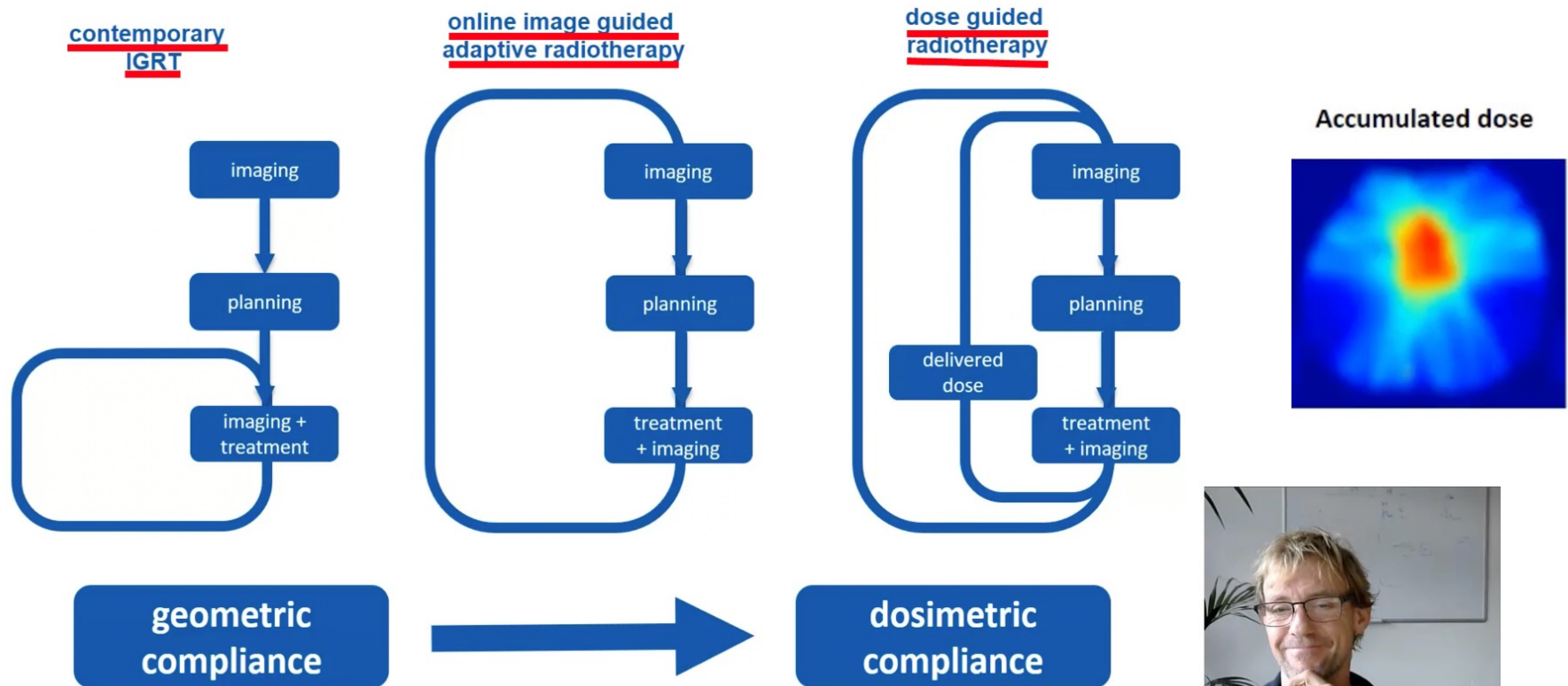
Radioterapia di precisione per un'oncologia innovativa e sostenibile

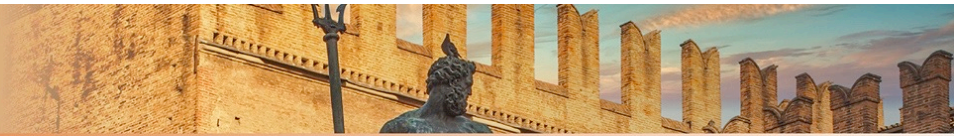




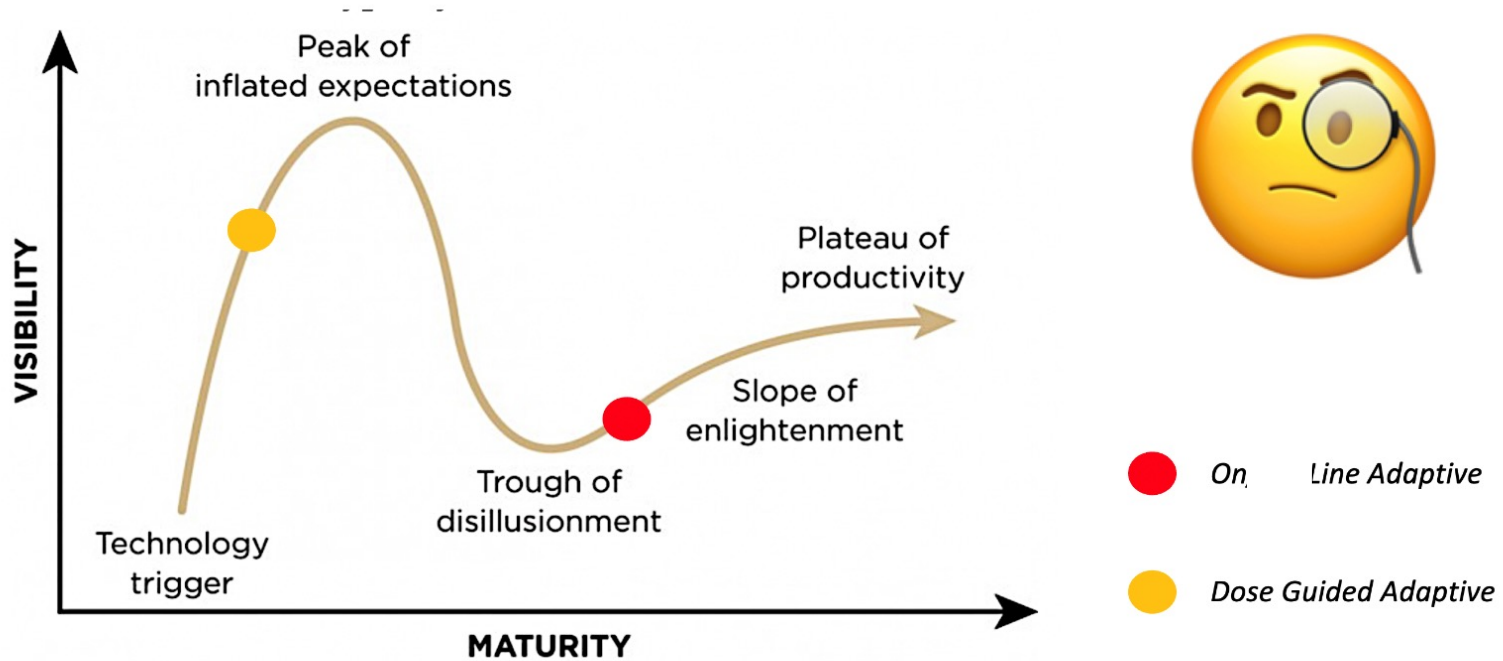


Which compliance to be measured in technical innovations?





Innovation Hype: Adaptive





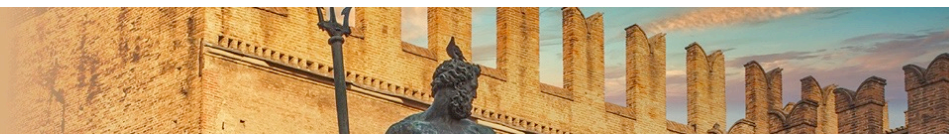
Radiation oncologists: where are we going?

- *Image Guided Radiotherapy*
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Radioterapia di precisione per un'oncologia innovativa e sostenibile



Artificial Intelligence: *Impact on RT*





Artificial Intelligence: *Impact on RT*



Providing clinical decision support



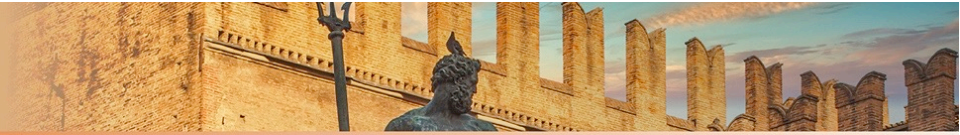
Mining *-omics*, analysing data



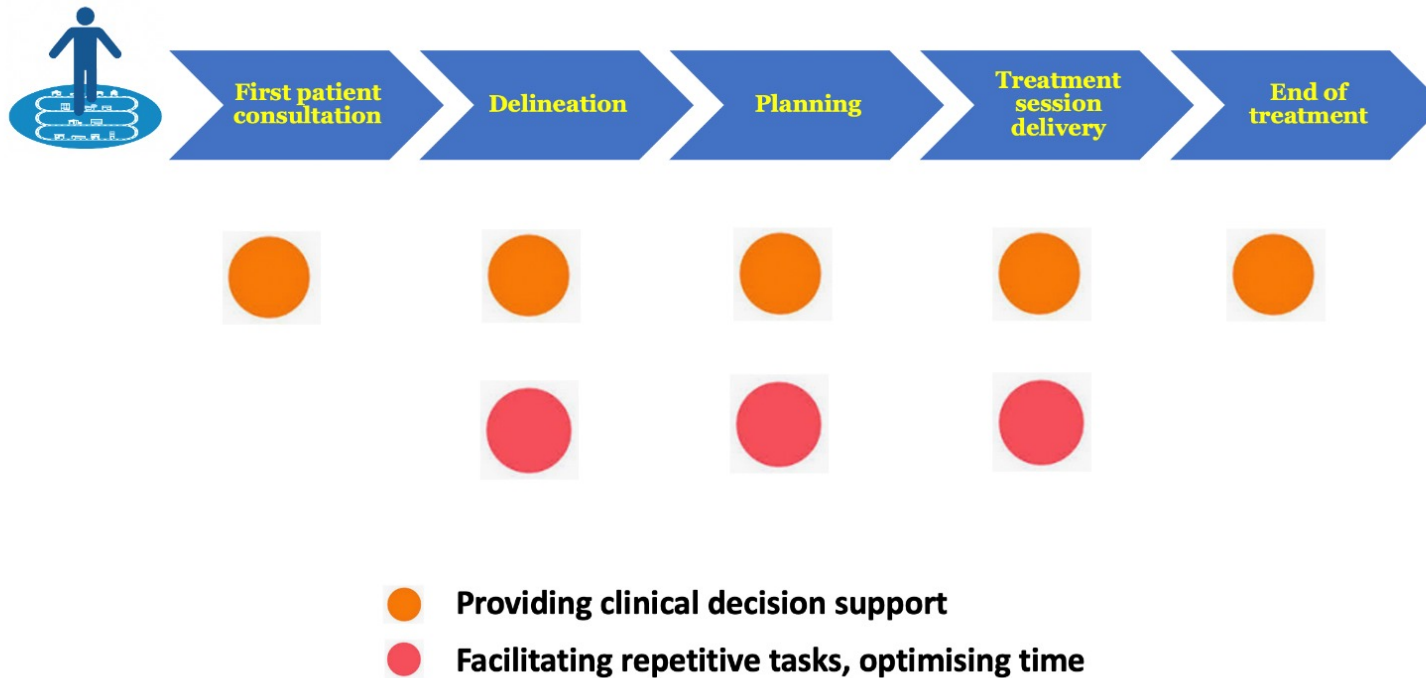
Facilitating repetitive tasks, optimising time



Modeling behaviors, in heterogeneous contexts

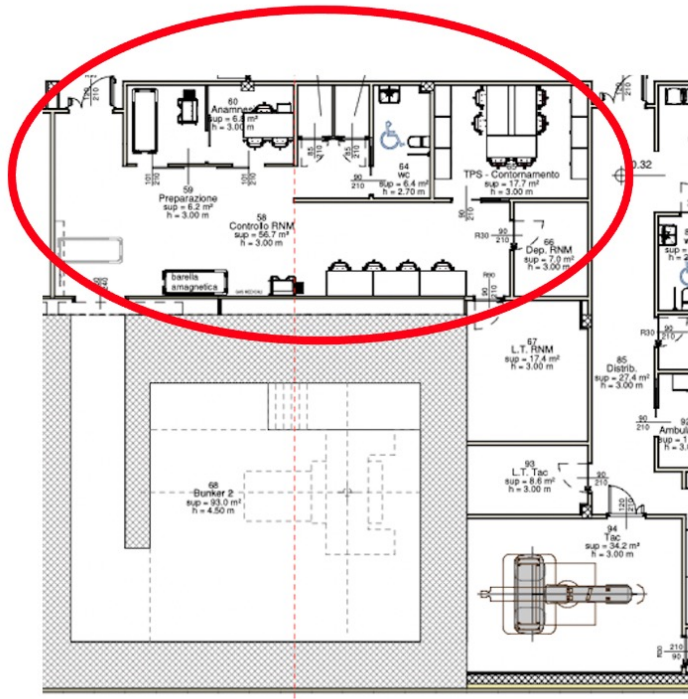


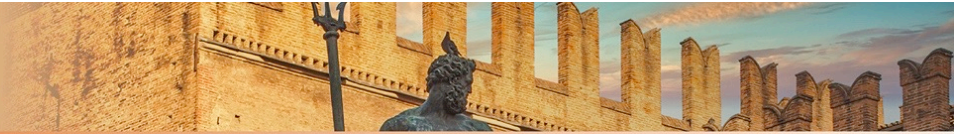
AI and the patient pathway



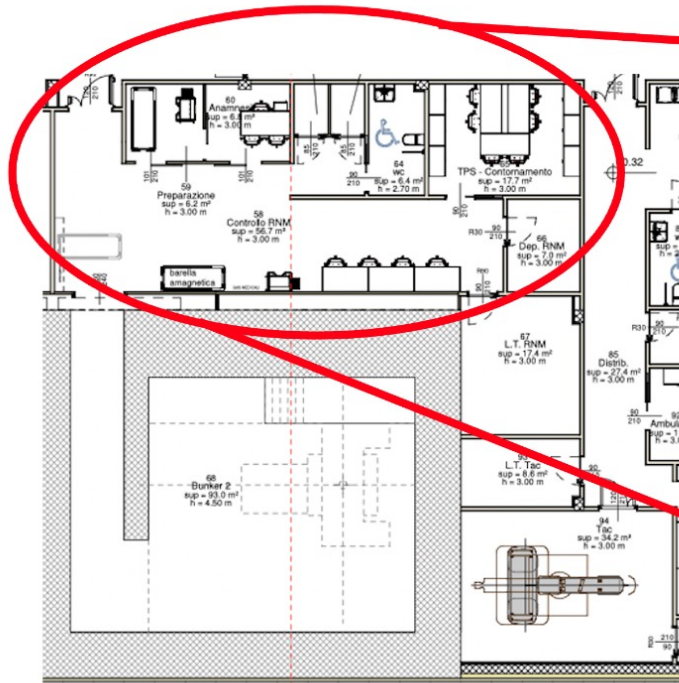


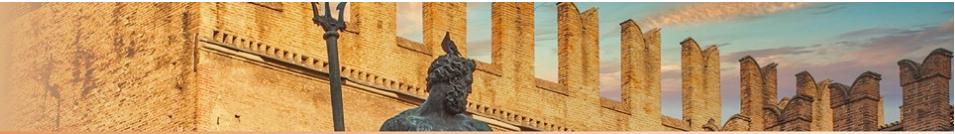
Non Invasive Interventional Radiotherapy



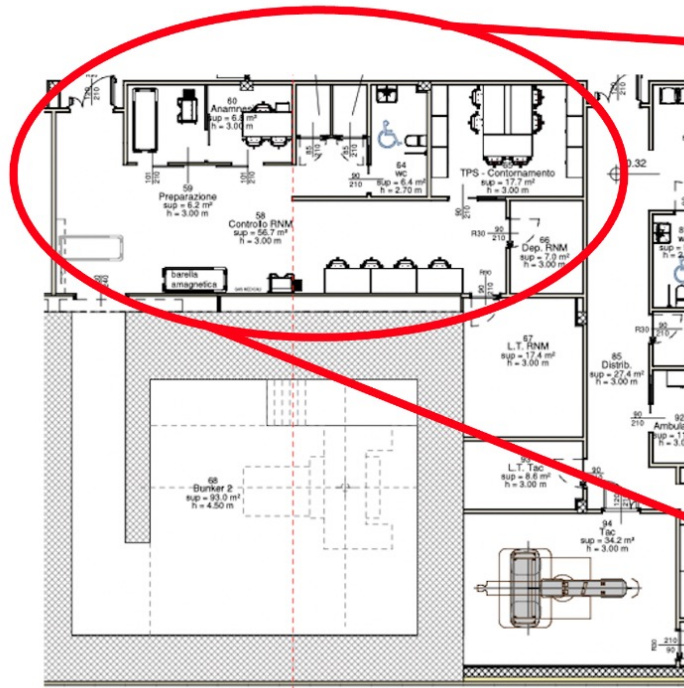


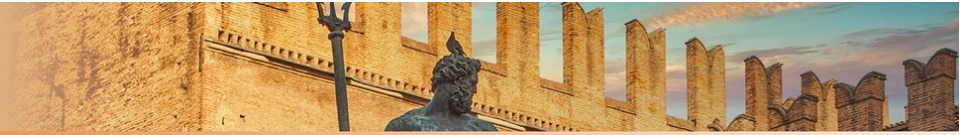
Non Invasive Interventional Radiotherapy





Non Invasive Interventional Radiotherapy





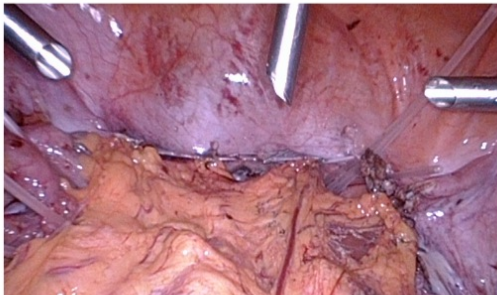
Invasive INTERVENTIONAL RADIO THERAPY

1D

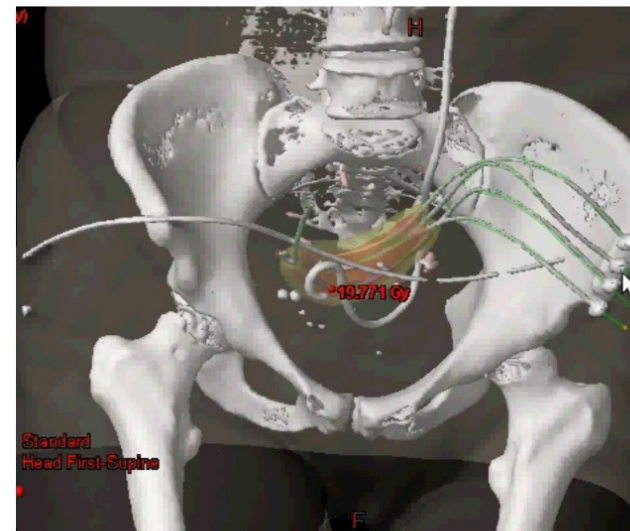
2D

3D

4D

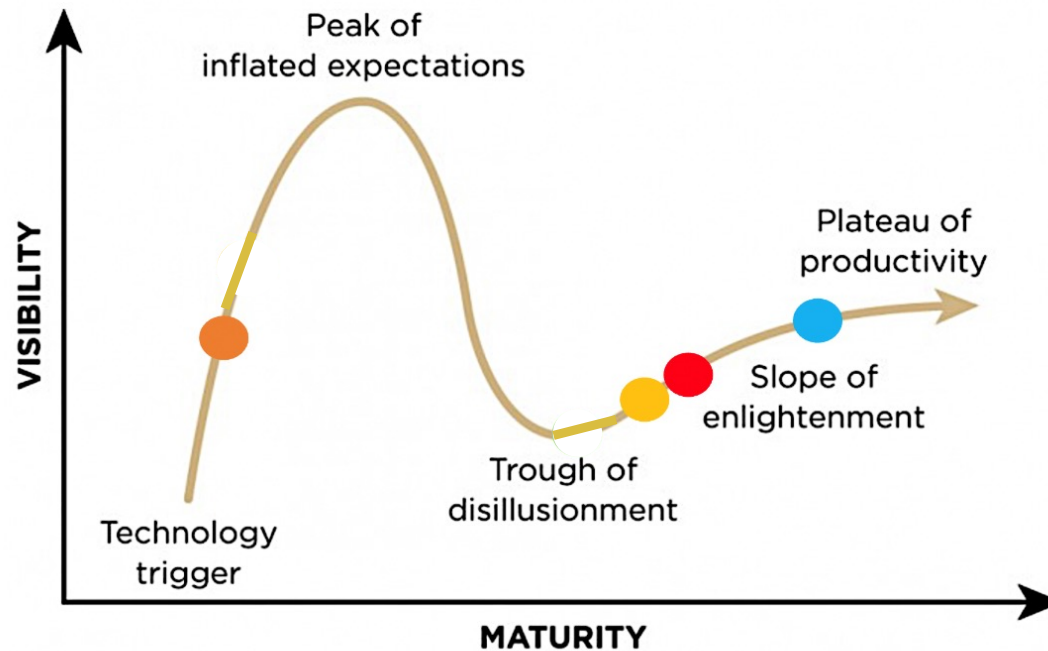


Laparoscopy Guided Procedure





Innovation Hype: Planning, I-RTO



- *Inv interventional RTO*
- *Auto-counturing*
- *Auto-planning*
- *Not Inv interventional RTO*



Radiation oncologists: where are we going?

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Omic gRT – From Sample to Data

Repository



PACS



Biobank

Sample



Imaging



Blood



Feces



Urine



Tumour Biopsy



Tissue Biopsy

Data



Radiomics



Genomics



Proteomics



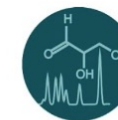
Trascritomics



MetaProteomics



Microbiomics



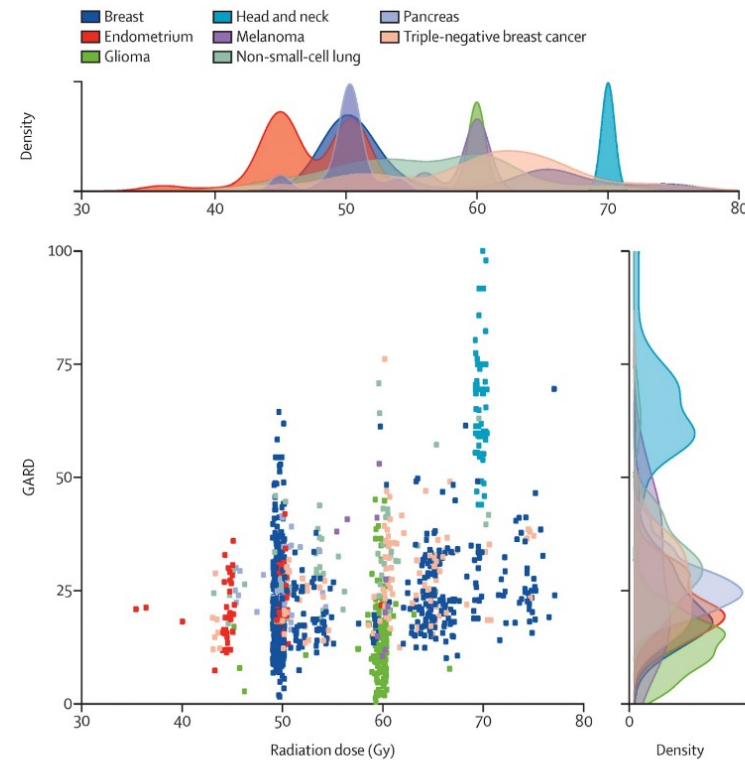
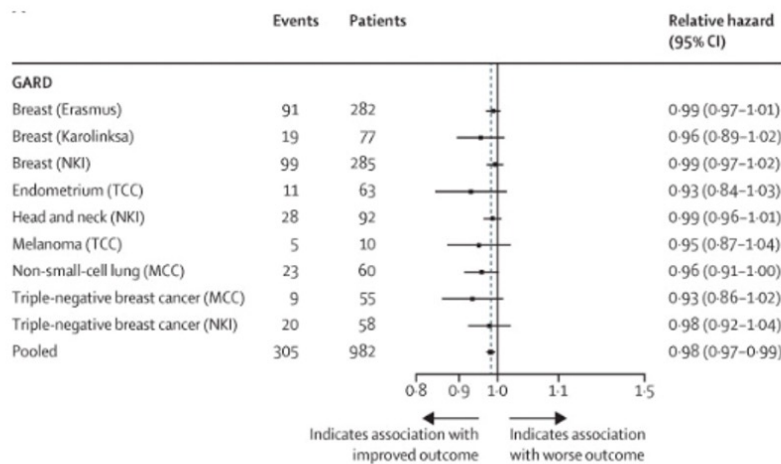
Metabolomics

Cognitive Platform



Treatment optimization

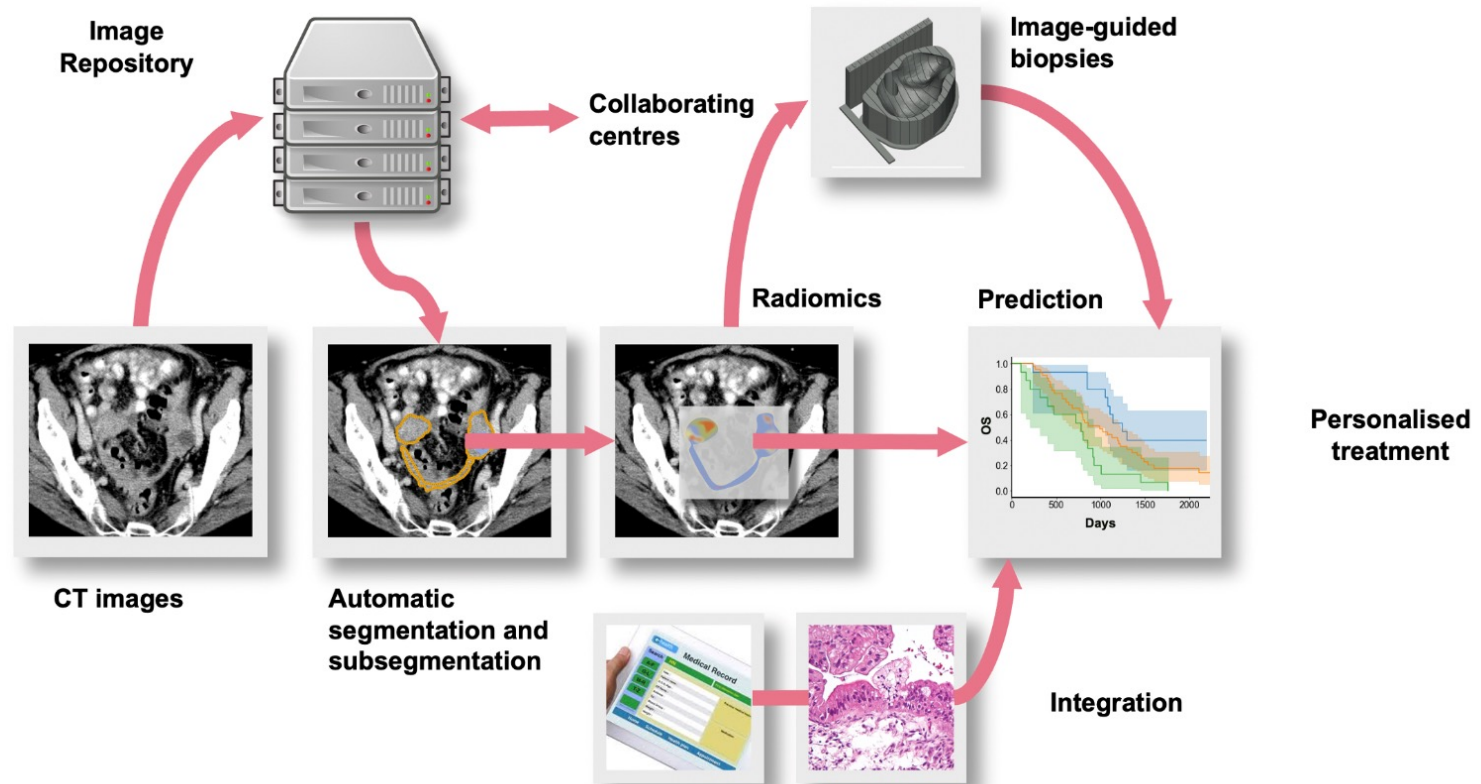
Radiotherapy : New dose definition protocols
Genomic-adjusted radiation dose (GARD)
 Correlation with time to first recurrence and overall survival



Scott JG et al. *Lancet Oncol.* 2021 Sep;22(9):1221-1229



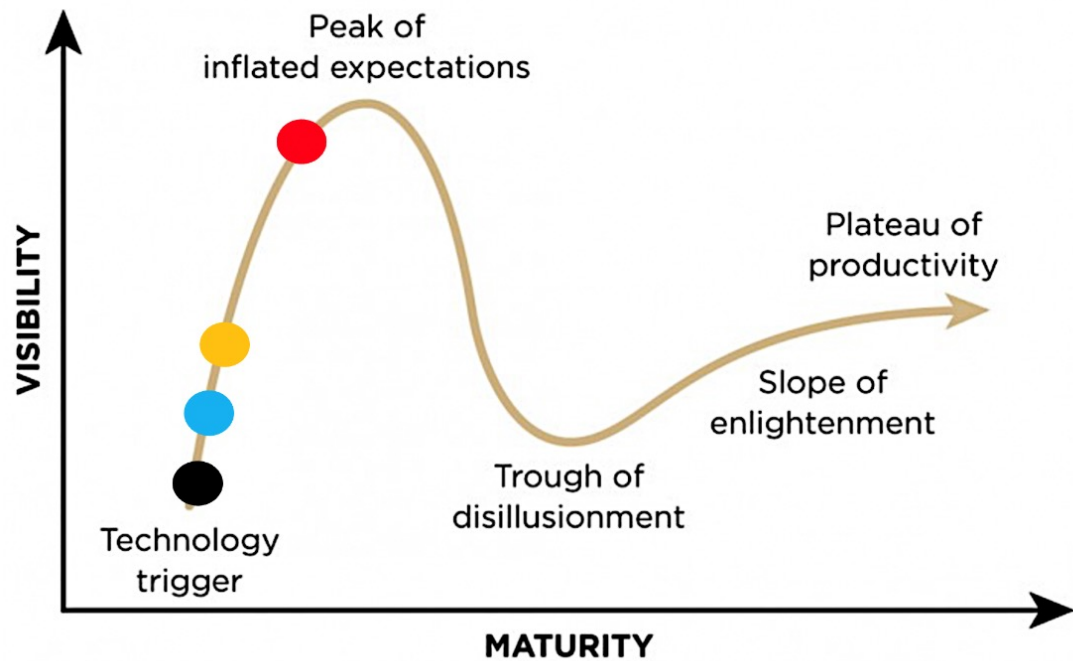
Radiogenomics/Multiomics framework



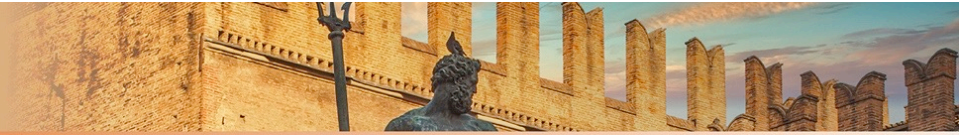
By courtesy Prof E.Sala



Innovation Hype: Omic

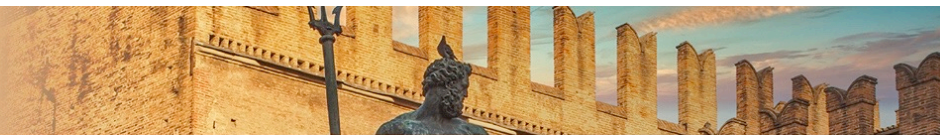


- *Radiomic*
- *Radiogenomic*
- *Omic integration*
- *Omic Driven Drug + RT*



Radiation oncologists: where are we going?

- *Image Guided Radiotherapy*
- *AI Guided Radiotherapy*
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- ***Humanist Guided Radiotherapy***



Personalized against Precision Medicine

Two dimension of the human should be identified:

Actionable Values (emotion, culture, spirituality..)

ART suggests **words** to narrate the **sense of the life**

Given World (science, deterministic rules, adaptation ..)

SCIENCE enables you to **live and interact** with the **world**



Personalized against Precision Medicine

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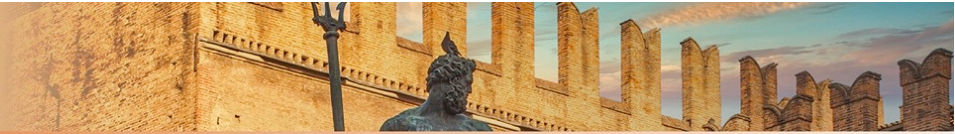
ART suggests words to narrate the sense of the life

Personalized Medicine

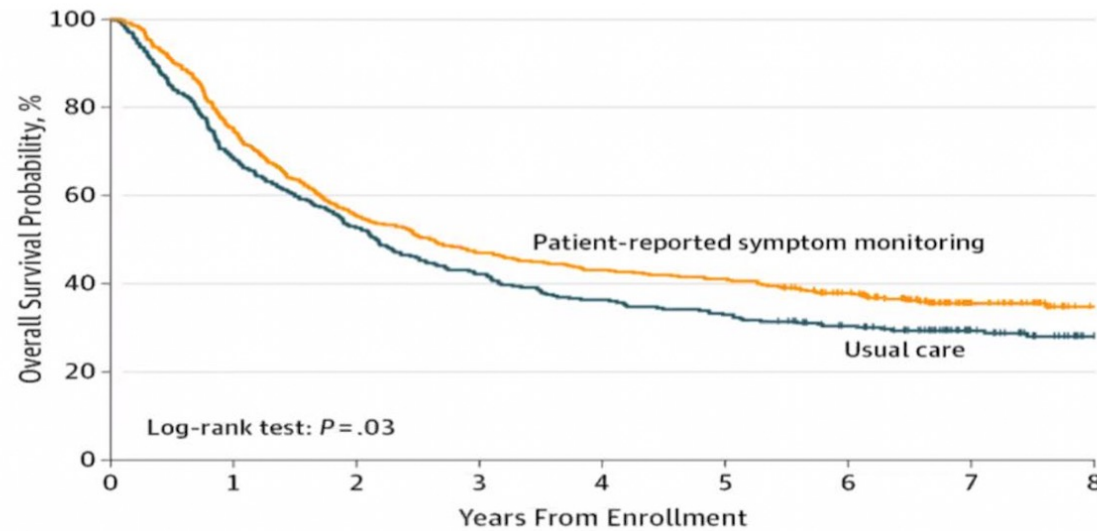
Given World (science, deterministic rules, adaptation ..)

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Precision Medicine



Caring makes us live longer



No. at risk	0	1	2	3	4	5	6	7	8
Patient-reported symptom monitoring	441	331	244	207	190	181	148	65	33
Usual care	325	223	171	137	118	107	89	50	27

E.Basch et al, YAMA, 2017

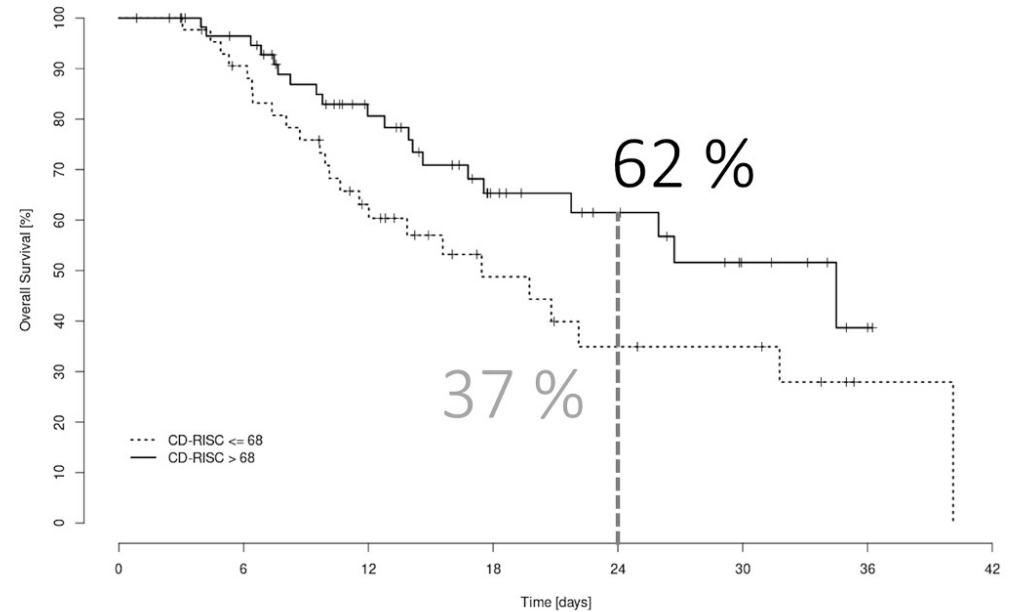


SPIRITUALITY AND RESILIENCE IN GLIOBLASTOMA

SPIRITUALITY is “a framework that provides people with a *sense of ultimate purpose and meaning in life*”

RESILIENCE is the “ability to withstand adversity and *bounce back and grow despite life’s downturns*”

- Multicentric observational protocol
- Tests: **Spirituality (FACIT-SP12); Resilience (CD-RISC).**
- 104 patients: 68 male, 36 female, median age 59.
- Median FUP was 338 days.



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Radioterapia di precisione per un'oncologia innovativa e sostenibile



... a good practice

- Too many **changes**
- Too much **time!**
- Being **alone?!**
- It's **complicated!**



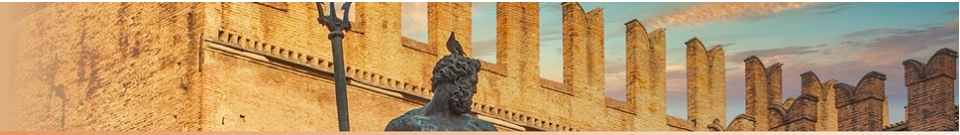
... a good practice

	PLA	FAZ1	FAZ2	FAZ3	FAZ4	FAZ5	FAZ6	FAZ7	FAZ8	FAZ9	FAZ10
12/01/2022											
13/01/2022											
14/01/2022											
15/01/2022											
16/01/2022											
17/01/2022											
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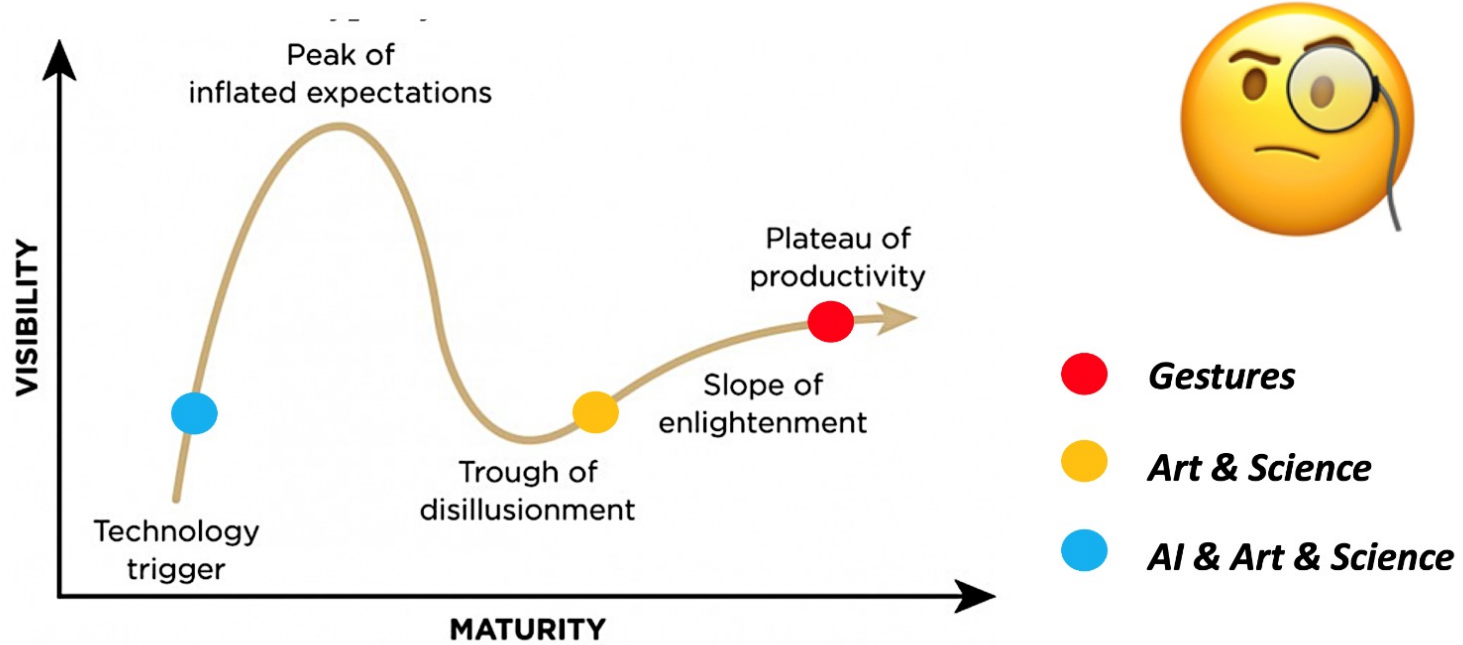


... a good practice





Innovation Hype: Humanism

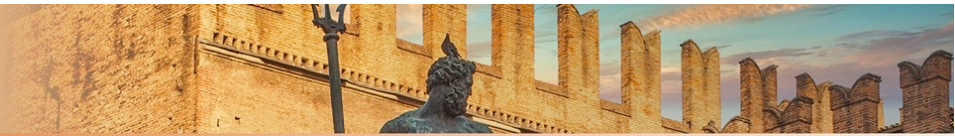




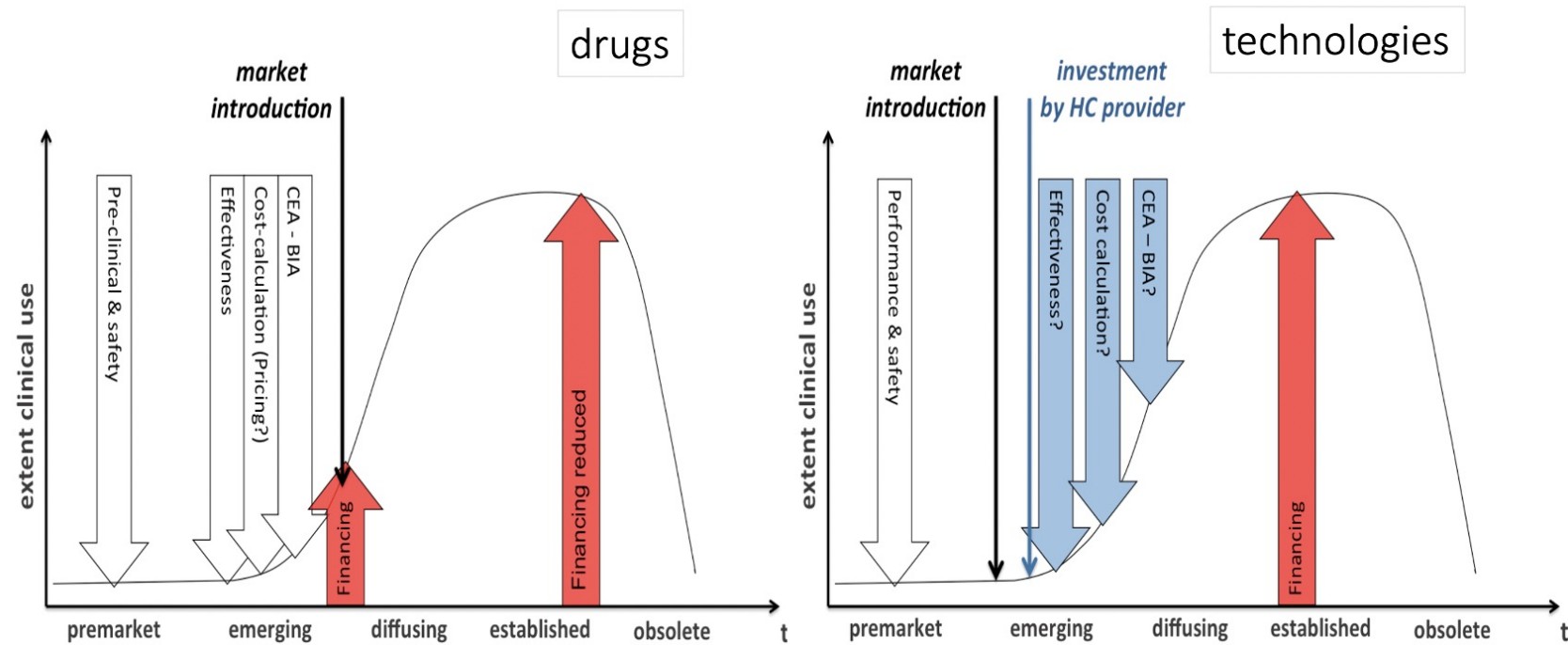
R-IDEAL: evaluation of innovation in radiotherapy

	Radiotherapy— predicate studies	Idea	Development	Exploration	Assessment	Long-term evaluation
	Stage 0	Stage 1	Stage 2a	Stage 2b	Stage 3	Stage 4
Purpose	Answer the following questions before actual use of the innovation for treatment of patients 1. How to use the innovation (software, coils needed)? 2. Why and in whom to use the innovation?	First time use of the innovation for treatment delivery in men	Technical optimization of the innovation for treatment delivery	Provide proof of early clinical effectiveness and safety of the innovation	Formal comparison of innovation against standard treatment	Long-term outcomes of the innovation, post-marketing, and surveillance
Outcomes	<ul style="list-style-type: none"> MR sequences, dedicated coils, etc. Inter-rater reproducibility Treatment strategies, patient selection 	Proof of concept	Technical improvements, feasibility, and safety	<ul style="list-style-type: none"> Early effectiveness toxicity tumor response local recurrence (with spacious information) 	<ul style="list-style-type: none"> Effectiveness compared to standard treatment (disease-free) survival recurrence toxicity PROMs, CTC-PRO, Cost effectiveness 	<ul style="list-style-type: none"> Long-term toxicity, long-term (disease-free) survival, rare side effects, Patient-Reported Outcomes
Study design	Phantom studies, delineation studies, planning studies, model-based studies	Structured case report	Prospective small uninterrupted case series	Prospective study with preferably randomized component: RCT; cmRCT; random allocation of limited available treatment slots to eligible patients; Comparison with matched (historical) controls	RCT, cmRCT, registry-based trial	Prospective registries, including all patients treated with the innovation

Verkooijen HM et al. - Front Oncol - 2017



Market introduction and reimbursement



Dynamics of evidence generation, market introduction and financing are different between drugs and technologies

Lievens et al. Acta Oncol 2015



Radiation oncologists: where are we going?

- **Image Guided Radiotherapy**
- **AI Guided Radiotherapy**
- **Omic Guided Radiotherapy**
- **Humanist Guided Radiotherapy**