Macchine Ibride

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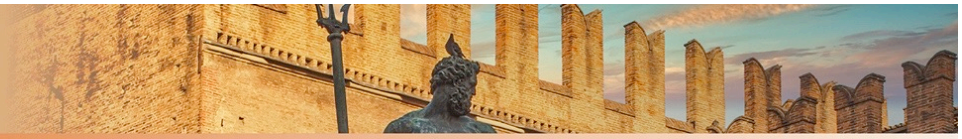


DICHIARAZIONE

Relatore: Maria Antonietta Gambacorta

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.

- Posizione di dipendente in aziende con interessi commerciali in campo sanitario: Niente da dichiarare
- Consulenza ad aziende con interessi commerciali in campo sanitario: Niente da dichiarare
- Fondi per la ricerca da aziende con interessi commerciali in campo sanitario: MSD
- Partecipazione ad Advisory Board: Astra Zeneca
- Titolarità di brevetti in compartecipazione ad aziende con interessi commerciali in campo sanitario: Niente da dichiarare
- Partecipazioni azionarie in aziende con interessi commerciali in campo sanitario: Niente da dichiarare Altro

Criteri per innovatività terapeutica (AIFA)

1. Bisogno terapeutico
2. Valore terapeutico aggiunto
3. Qualità delle prove
4. Impatto economico

Barbieri M. *Opening Ceremony; AIRO 2022*

Criteri per innovatività terapeutica

1. **Bisogno terapeutico**
2. Valore terapeutico aggiunto
3. Qualità delle prove
4. Impatto economico

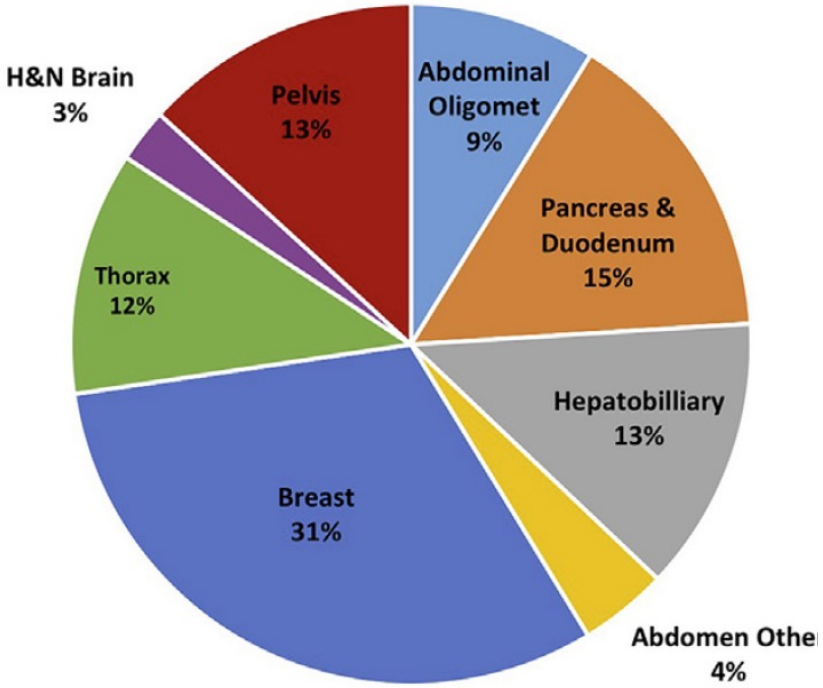
Hybrid Machines: MRgRT

- Improvement of soft tissue **contrast**
- No IGRT **extra dose**
- Inter-intrafraction **motion** management

To see
To treat
To adapt

The 'ideal' target for MRgRT

SITE	similar HU densities/sensitive OAR
MOBILITY	high intra-fraction motion
MODIFICATION	tumor shrinkage
TREATMENT	high dose



Henke et al *Clin Oncol (R Coll Radiol). 2018*

Criteri per innovatività terapeutica

1. Bisogno terapeutico
2. Valore terapeutico aggiunto
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The 'ideal' target for MRgRT

SITE	similar HU densities/sensitive OAR
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MODIFICATION	tumor shrinkage
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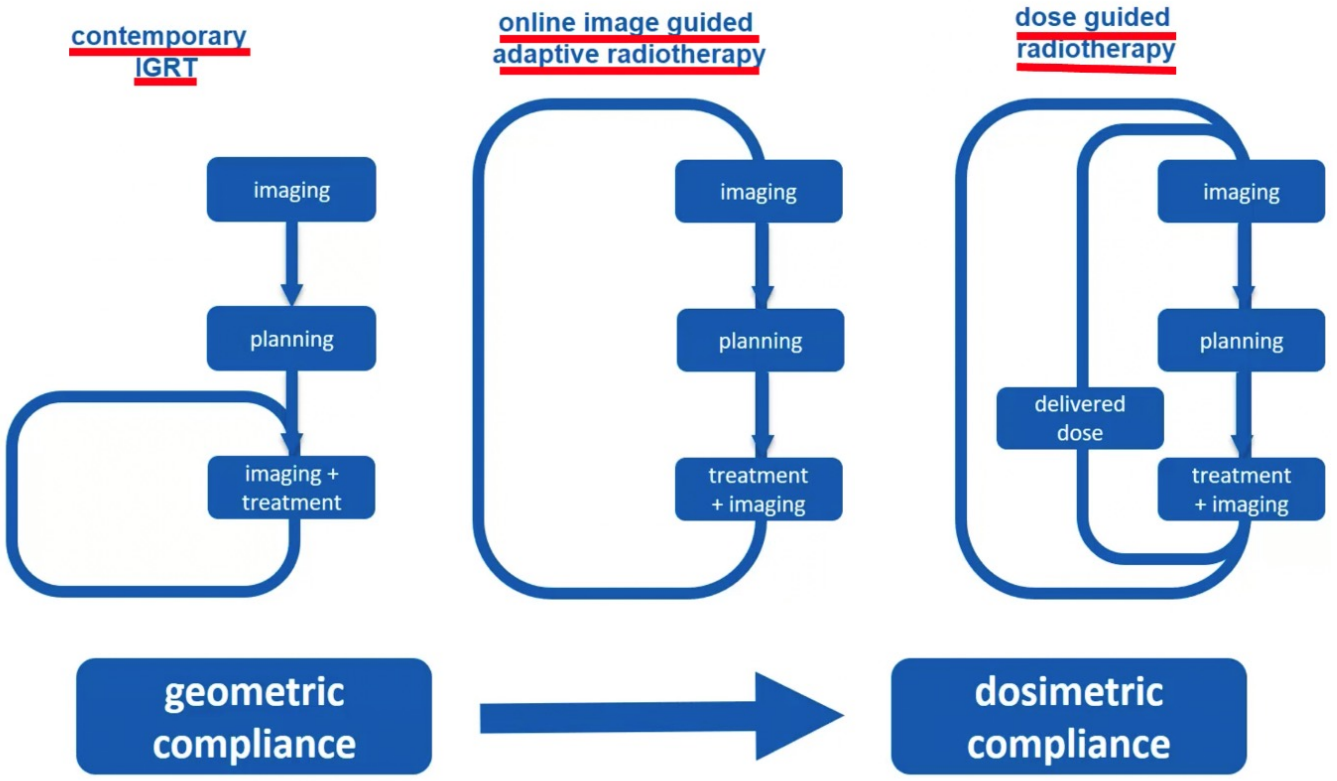
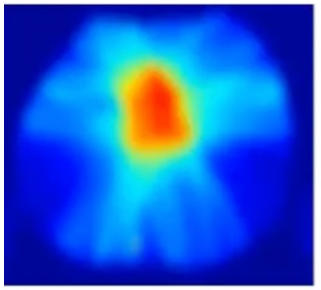
Which compliance to be measured in technical innovations?



Accumulated dose



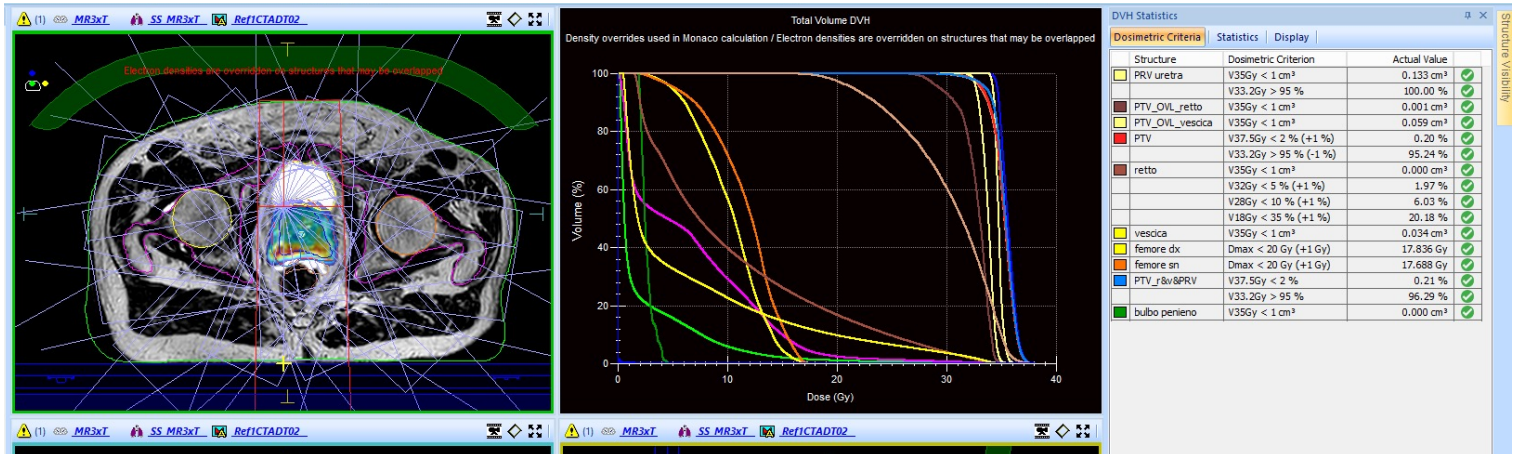
By courtesy of G.Meyer

On-line adaptive RT

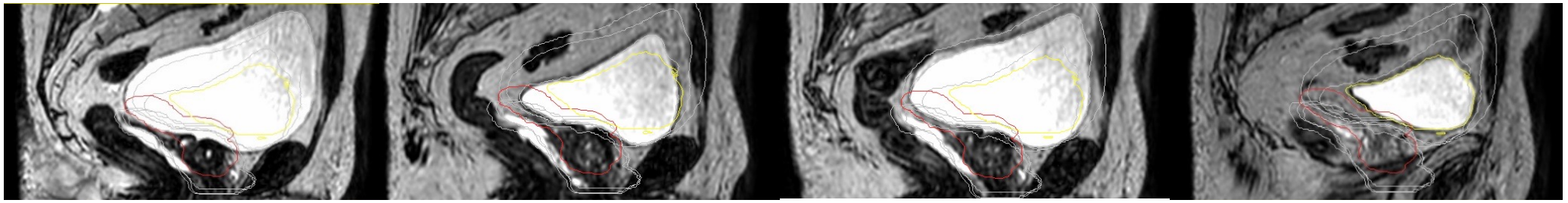
Prostate SBRT

35 Gy in 5 fr

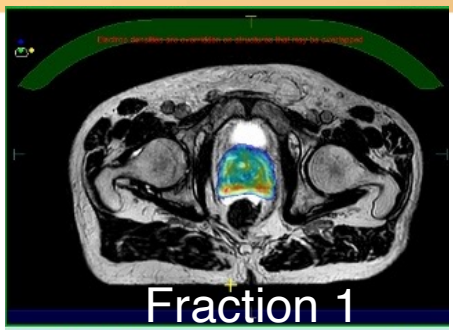
16 field IMRT(VMAT like)

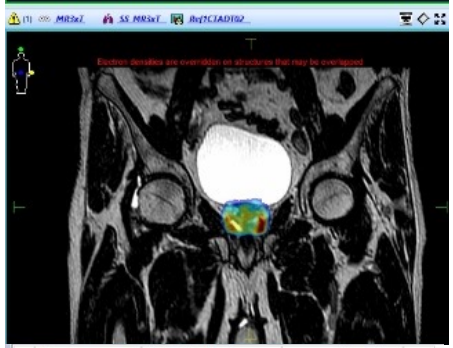


Fraction 1 **Fraction 2** **Fraction 3** **Fraction 4**



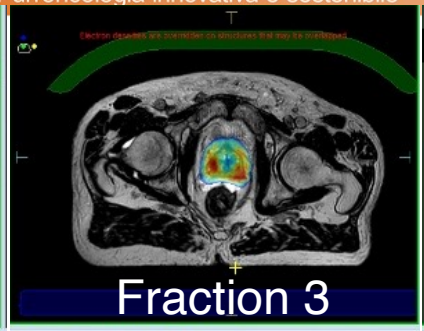
Courtesy of *F. Alongi*



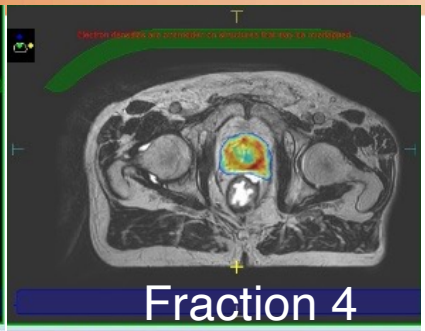


Structure	Dosimetric Criterion	Actual Value	
PRV uretra	V35Gy < 1 cm³	0.133 cm³	✓
	V33.2Gy > 95 %	100.00 %	✓
PTV_OVL_retto	V35Gy < 1 cm³	0.001 cm³	✓
PTV_OVL_vescica	V35Gy < 1 cm³	0.059 cm³	✓
PTV	V37.5Gy < 2 % (+1 %)	0.20 %	✓
	V33.2Gy > 95 % (-1 %)	95.24 %	✓
retto	V35Gy < 1 cm³	0.000 cm³	✓
	V32Gy < 5 % (+1 %)	1.97 %	✓
	V28Gy < 10 % (+1 %)	6.03 %	✓
	V18Gy < 35 % (+1 %)	20.18 %	✓
vescica	V35Gy < 1 cm³	0.034 cm³	✓
femore dx	Dmax < 20 Gy (+1 Gy)	17.836 Gy	✓
femore sn	Dmax < 20 Gy (+1 Gy)	17.688 Gy	✓
PTV_r&v&PRV	V37.5Gy < 2 %	0.21 %	✓
	V33.2Gy > 95 %	96.29 %	✓
bulbo penieno	V35Gy < 1 cm³	0.000 cm³	✓

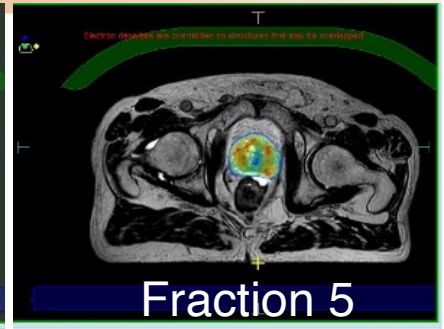
Structure	Dosimetric Criterion	Actual Value	
PRV uretra	V35Gy < 1 cm³	0.170 cm³	✓
	V33.2Gy > 95 %	100.00 %	✓
PTV_OVL_retto	V35Gy < 1 cm³	0.009 cm³	✓
PTV_OVL_vescica	V35Gy < 1 cm³	0.048 cm³	✓
PTV	V37.5Gy < 2 % (+1 %)	1.08 %	✓
	V33.2Gy > 95 % (-1 %)	98.21 %	✓
retto	V35Gy < 1 cm³	0.004 cm³	✓
	V32Gy < 5 % (+1 %)	2.01 %	✓
	V28Gy < 10 % (+1 %)	5.43 %	✓
	V18Gy < 35 % (+1 %)	17.98 %	✓
vescica	V35Gy < 1 cm³	0.030 cm³	✓
femore dx	Dmax < 20 Gy (+1 Gy)	17.277 Gy	✓
femore sn	Dmax < 20 Gy (+1 Gy)	17.032 Gy	✓
PTV_r&v&PRV	V37.5Gy < 2 %	1.12 %	✓
	V33.2Gy > 95 %	98.17 %	✓
bulbo penieno	V35Gy < 1 cm³	0.000 cm³	✓



Structure	Dosimetric Criterion	Actual Value	
PRV uretra	V35Gy < 1 cm³	0.109 cm³	✓
	V33.2Gy > 95 %	100.00 %	✓
PTV_OVL_retto	V35Gy < 1 cm³	0.000 cm³	✓
PTV_OVL_vescica	V35Gy < 1 cm³	0.030 cm³	✓
PTV	V37.5Gy < 2 % (+1		
	V33.2Gy > 95 % (-1		
retto	V35Gy < 1 cm³		
	V32Gy < 5 % (+1 %		
	V28Gy < 10 % (+1 %		
	V18Gy < 35 % (+1 %		
vescica	V35Gy < 1 cm³		
femore dx	Dmax < 20 Gy (+1 G		
femore sn	Dmax < 20 Gy (+1 G		
PTV_r&v&PRV	V37.5Gy < 2 %		
	V33.2Gy > 95 %	97.97 %	✓
bulbo penieno	V35Gy < 1 cm³	0.000 cm³	✓



Structure	Dosimetric Criterion	Actual Value	
PRV uretra	V35Gy < 1 cm³	0.454 cm³	✓
	V33.2Gy > 95 %	100.00 %	✓
PTV_OVL_retto	V35Gy < 1 cm³	0.000 cm³	✓
	V33.2Gy > 95 %	98.96 %	✓
bulbo penieno	V35Gy < 1 cm³	0.000 cm³	✓



Structure	Dosimetric Criterion	Actual Value	
PRV uretra	V35Gy < 1 cm³	0.193 cm³	✓
	V33.2Gy > 95 %	100.00 %	✓
PTV_OVL_retto	V35Gy < 1 cm³	0.001 cm³	✓
	V33.2Gy > 95 %	99.48 %	✓
bulbo penieno	V35Gy < 1 cm³	0.000 cm³	✓

- Sexual structures preservation
- Boost to the dominant intraprostatic lesion (DIL)
- Margins reduction/single shot treatments

Courtesy of *F. Alongi*

25 Prostate cacancer

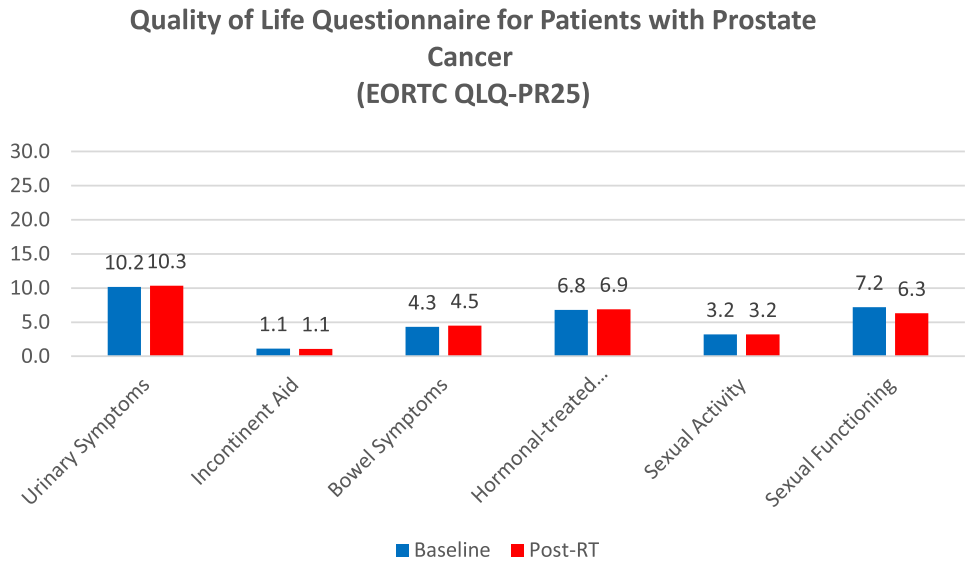
SBRT 35 Gy in 5 fr in 2 wks

Table 4 Quality of Life Questionnaire for Patients with Prostate Cancer (EORTC QLQ-PR25)

EORTC QLQ-PR25	Baseline (Mean ± SD)	Post-Rt (Mean ± SD)	p
Urinary Symptoms	10.2 ± 3.1	10.3 ± 3	0.21
Incontinent Aid	1.1 ± 0.5	1.1 ± 0.5	1
Bowel Symptoms	4.3 ± 0.6	4.5 ± 1.8	0.33
Hormonal-treated Related Symptoms	6.9 ± 1	6.8 ± 1.2	0.19
Sexual Activity	3.2 ± 1.7	3.2 ± 1.5	0.71
Sexual Functioning	7.2 ± 4	6.3 ± 3.4	0.76

Table 2 Acute Toxicity Rates (CTCAE v.5)

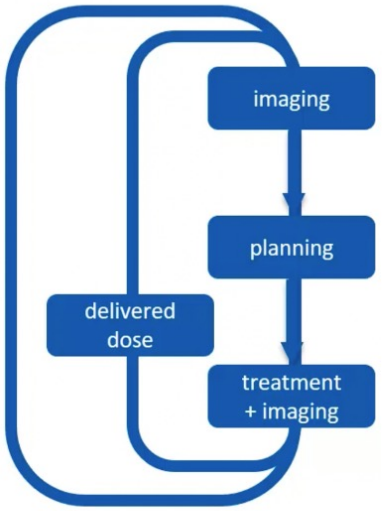
Genitourinary (frequency, urgency, pain)
G2: 3 (12%)
G1: 6 (24%)
Gastrointestinal (rectal pain)
G2: 1 (4%)
G1: 2 (8%)



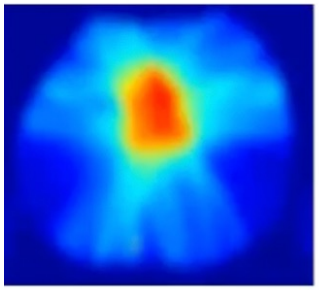
Alongi F et al. *Radiat Oncol 2020*

Which compliance to be measured in technical innovations?

dose guided radiotherapy



Accumulated dose



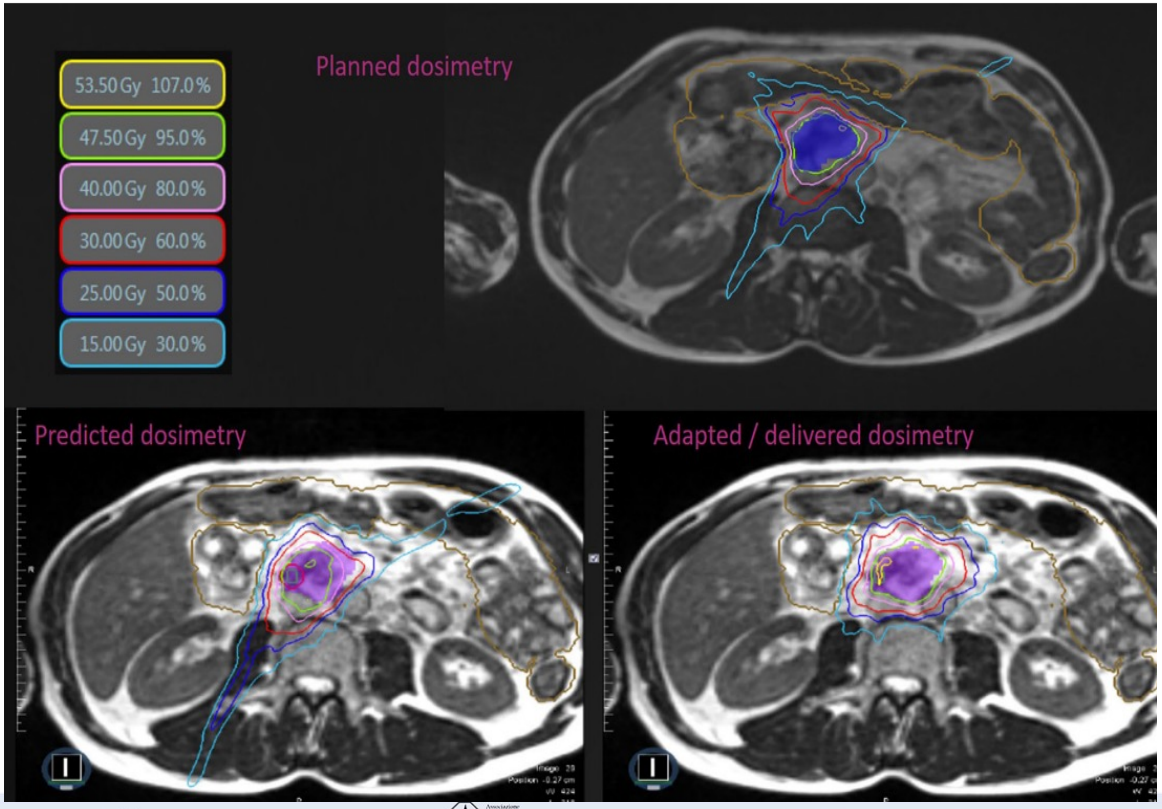
geometric compliance → **dosimetric compliance**

By courtesy of G.Meyer

Dose guided RT

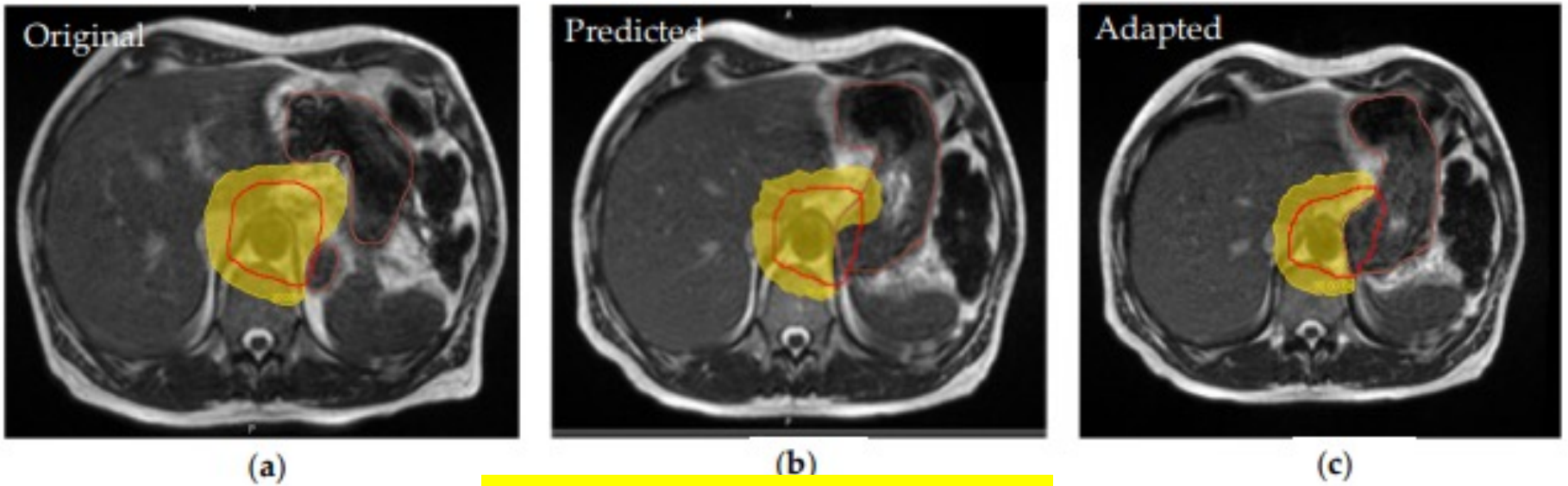
Target adaptation

- 30 pancreatic cancer patients
- SMART (Stereotactic MR-guided adaptive radiotherapy)
- median dose prescription 50 Gy.



Michalet M et al. *Front. Oncol 2022*

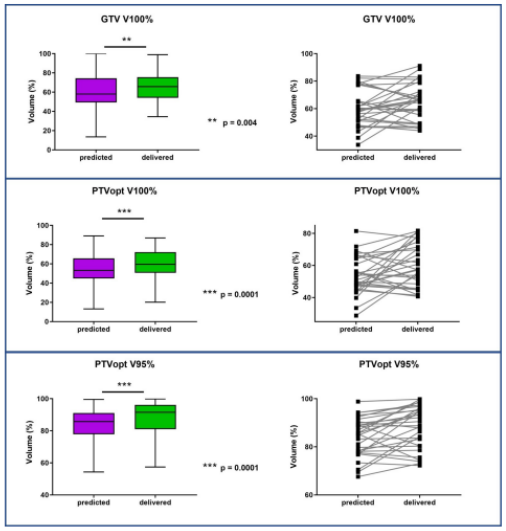
Dose guided RT OAR adaptation



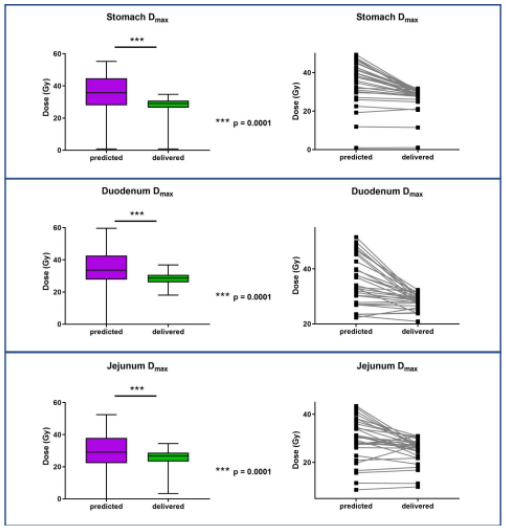
30 Gy isodose

Randall JW et al. *J clin Med 2022*

Dosimetric advantage



PTV



OAR

Clinical advantage

TABLE 5 | SMART-related acute and late toxicities.

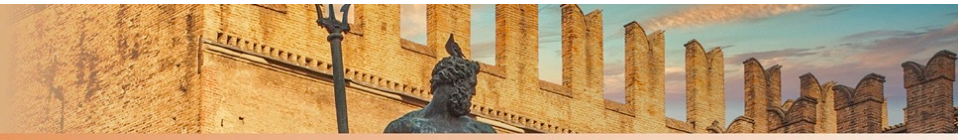
CTCAE v5.0	Acute toxicity (0–90 days)	Late toxicity (90 days–1 year)
Abdominal pain		
g0	18 (60%)	13 (43.3%)
g1	12 (40%)	8 (26.7%)
g2	0	1 (3.3%)
g3	0	0
Ongoing	0	7 (23.3%)
Nausea/Vomiting		
g0	17 (56.7%)	19 (63.3%)
g1	7 (23.3%)	2 (6.7%)
g2	6 (20%)	2 (6.7%)
g3	0	0
Ongoing	0	7 (23.3%)
Gastritis/enteritis		
g0	29 (96.7%)	23 (66.7%)
g1	1 (3.3%)	0
g2	0	0
g3	0	0
Ongoing	0	7 (23.3%)
Gastroduodenal ulcer		
g0	30 (100%)	23 (66.7%)
g1	0	0
g2	0	0
g3	0	0
Ongoing	0	7 (23.3%)
Digestive fistula		
g0	30 (100%)	23 (66.7%)
g1	0	0
g2	0	0
g3	0	0
Ongoing	0	7 (23.3%)
Diarrhea		
g0	22 (63.3%)	16 (53.3%)
g1	7 (23.3%)	4 (13.3%)
g2	1 (3.3%)	3 (10%)
g3	0	0
Ongoing	0	7 (23.3%)

SMART, stereotactic MR-guided adaptive radiotherapy; CTCAE, Common Terminology Criteria for Adverse Events.

NO grade > 2 acute TOX

- asthenia (40%)
- abdominal pain 40%
- nausea 43%

Michalet M et al. *Front. Oncol 2022*



The 'ideal' target for MRgRT

SITE	similar HU densities/sensitive OAR
MOBILITY	high intra-fraction motion
MODIFICATION	tumor shrinkage
TREATMENT	high dose

Contents lists available at ScienceDirect
Radiotherapy and Oncology
journal homepage: www.thegreenjournal.com

Predicting tumor motion

Predicting tumour motion during the whole radiotherapy treatment: a systematic approach for thoracic and abdominal lesions based on real time MR

Davide Cusumano [a,b,1], Jennifer Dhont [c,d,e,1], Luca Boldrini [b,*], Giuditta Chiloiro [b,f], Stefania Teodoli [a], Mariangela Massaccesi [f], Bruno Fionda [f], Francesco Cellini [f], Luigi Azario [a,g], Jef Vandemeulebroucke [d,e], Marco De Spirito [a,g], Vincenzo Valentini [b,f], Dirk Verellen [c,h]

20 Patients treated on **MR-Linac**

lung & abdominal lesions

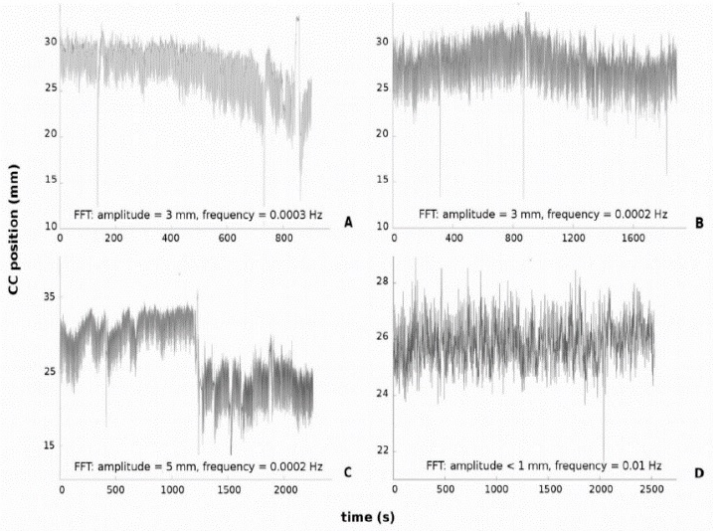
4DCT vs 2D-cine MR motion data @ **simulation**

2D-cine MR over **entire** treatment

- Cine MR better predict motion during treatment
- Large motion at simulation **more variable amplitudes** throughout the treatment course
- **Max** *intrafraction* **1.6 cm CC and 1.2 cm AP,** which highlights the importance of continuous IGRT.

One direction drift

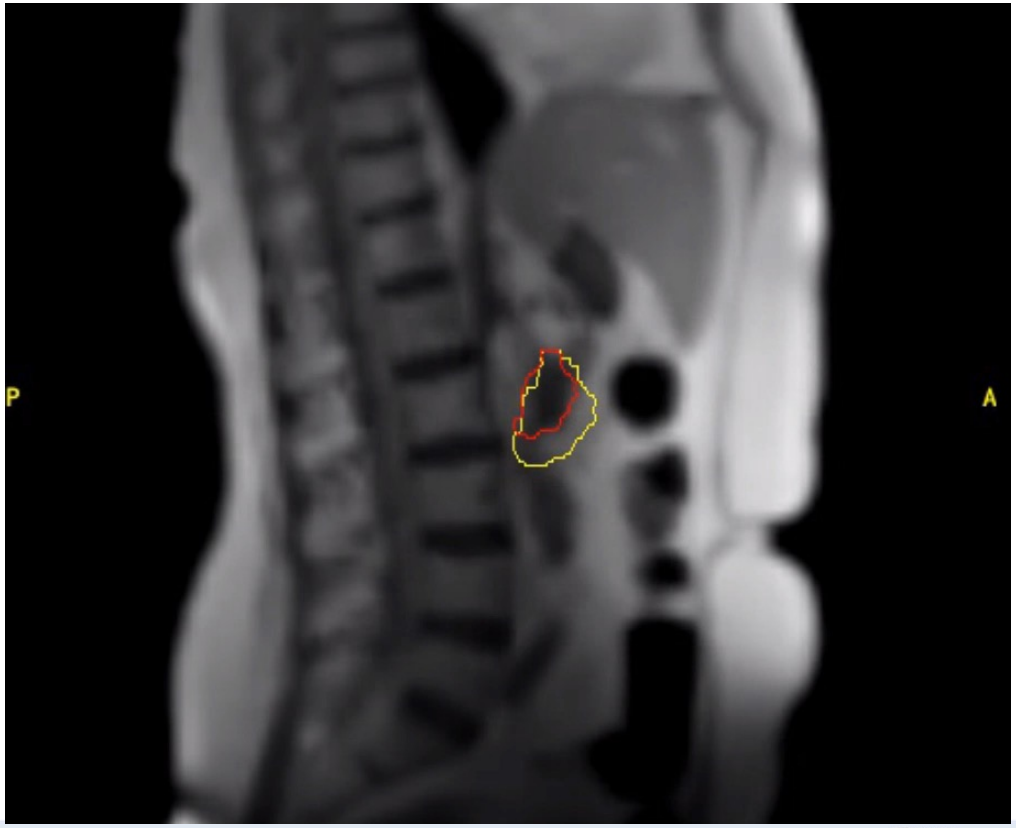
Sine-like drift

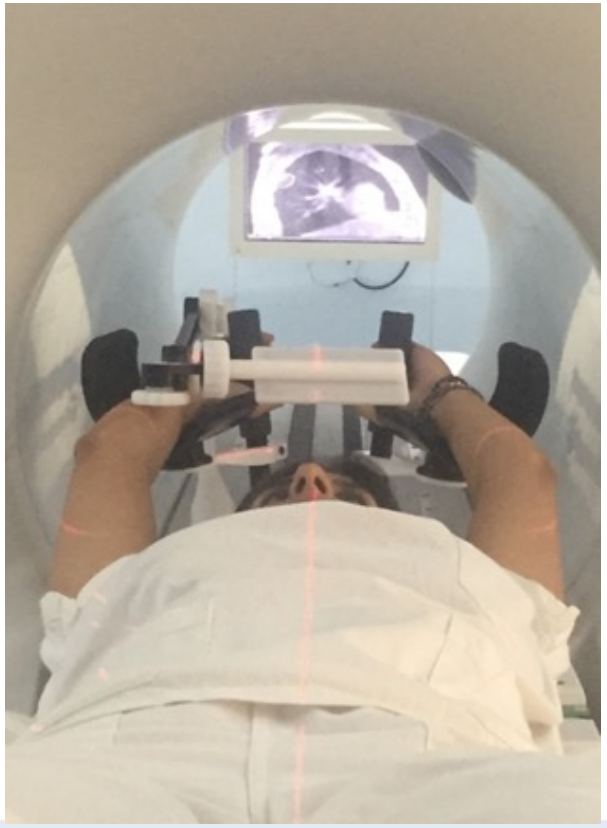


Fast baseline shift

Chaotic breath

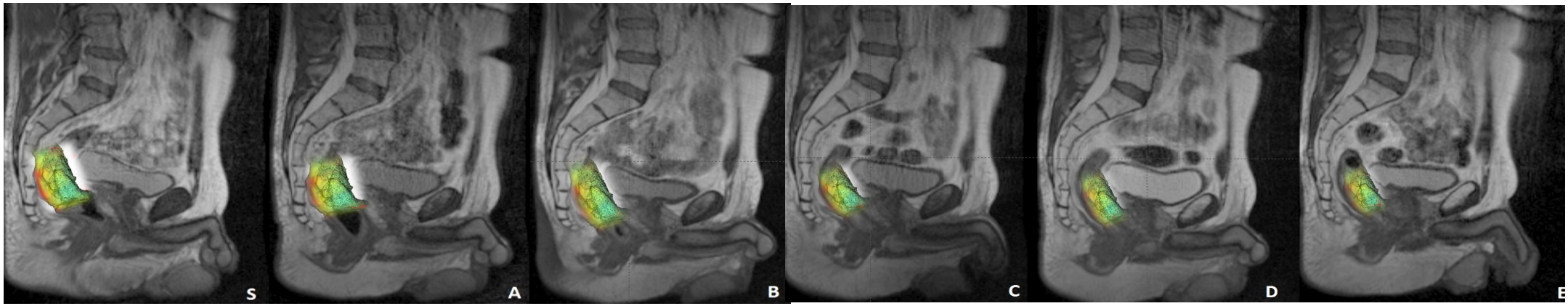
Motion management: patient engagement





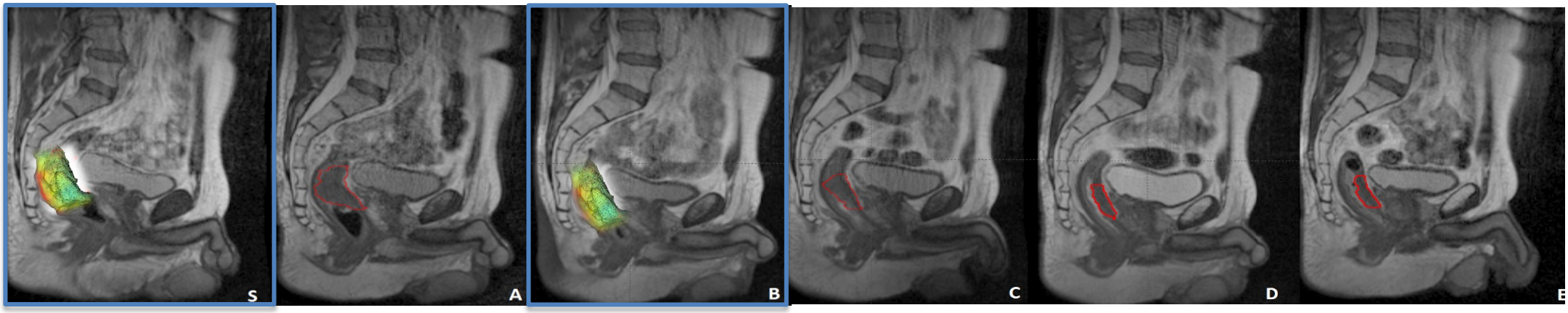
The 'ideal' target for MRgRT

SITE	similar HU densities/sensitive OAR
MOBILITY	high intra-fraction motion
MODIFICATION	tumor shrinkage, model based adapt
TREATMENT	high dose



Boldrini et al. *Rad Med*, 2019

DELTA ERI + radiomic



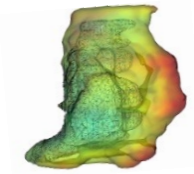
22 Gy

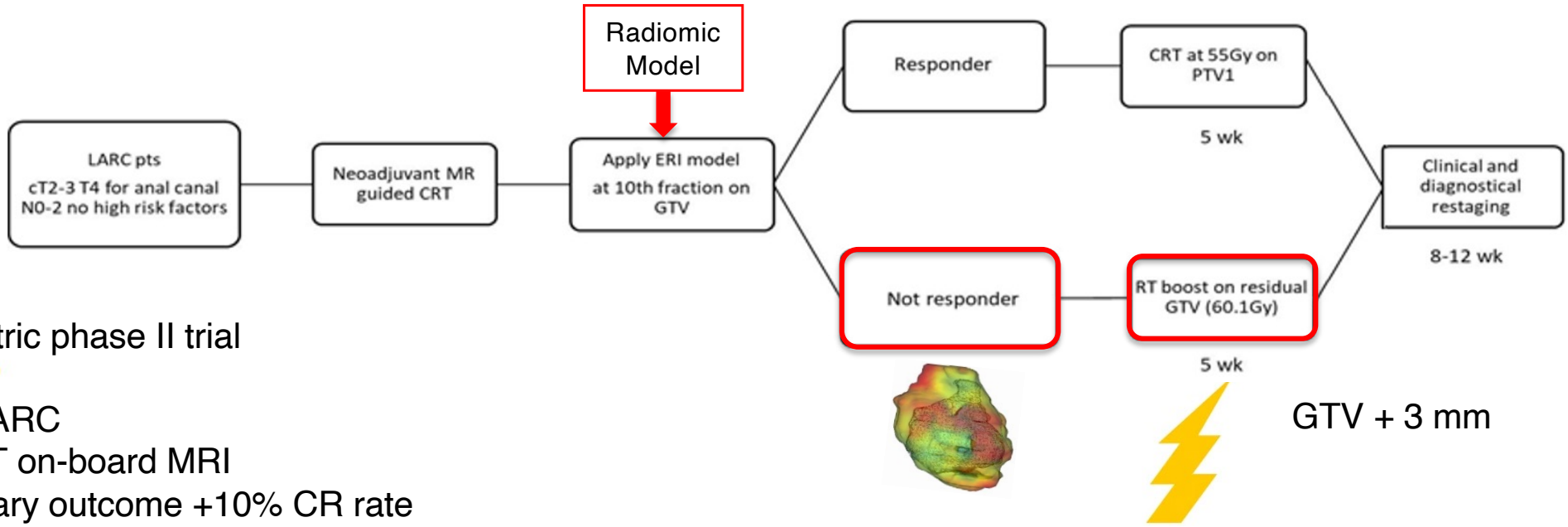
Cusumano D et al. *IJROBP 2020*

Boldrini et al. *Rad Med* 2019

THUNDER-2 trial **TH**eragnostic **U**tilities for **N**eoplastic **D**iseases of the r**E**ctum by MRI guided **R**adiotherapy

Actionable Radiomics





GTV + 3 mm

Monicentric phase II trial

- 63 LARC
- 0.35T on-board MRI
- Primary outcome +10% CR rate
- Volume/Radiomics predictive model validation

Chiloiro G. et al. BMC Cancer 2022 *active trial* : NCT04815694

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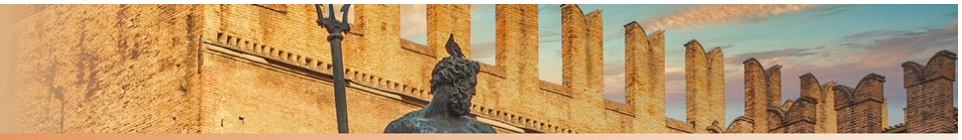
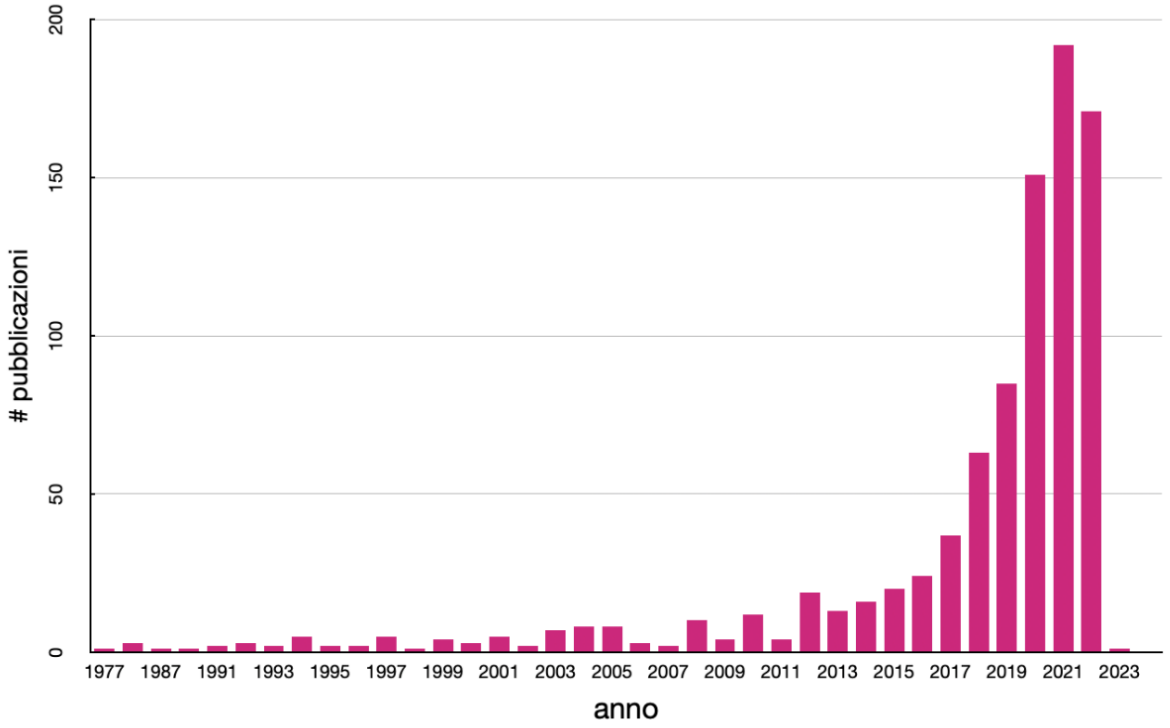


Author	Tumor site	N° of patients	Reported outcome
Alongi *Radiat Oncol 2020*	Prostate	25	Acute tox Early QoL
Michalet *Front Oncol 2022*	Pancreas	30	Dosimetric benefits
Randall *Clin Med 2022*	Pancreas	/	Review
Cusumano *Radiother Oncol 2018*	Lung Abdomen lesions	20	Dosimetric benefits
Chiloiro G *BMJ 2022*	Rectum	63	No results

Increasing evidences



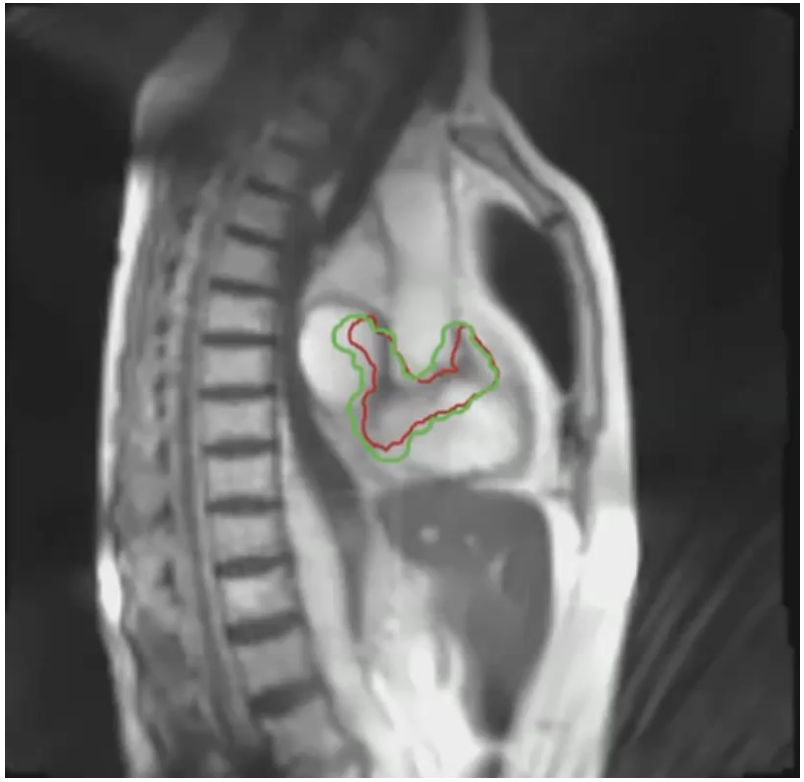
The 'ideal' target for MRgRT

SITE	similar HU densities/sensitive OAR
MOBILITY	high intra-fraction motion
MODIFICATION	tumor shrinkage
TREATMENT	high dose-CTV/PTV > 0.95

Complex case solution

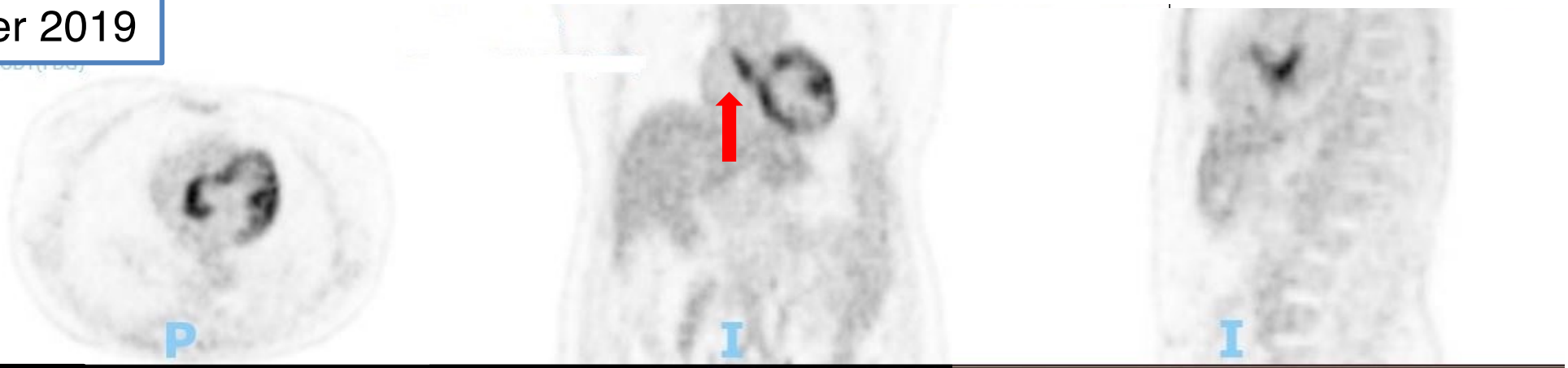
Heart lymphoma radical treatment

- 60 y.o., female
- Lymphoblastic B heart lymphoma
- 30.6 Gy in 17 fractions
- BHI conditions 8fps



Corradini S et al *Radiat Oncol* 2021

November 2019



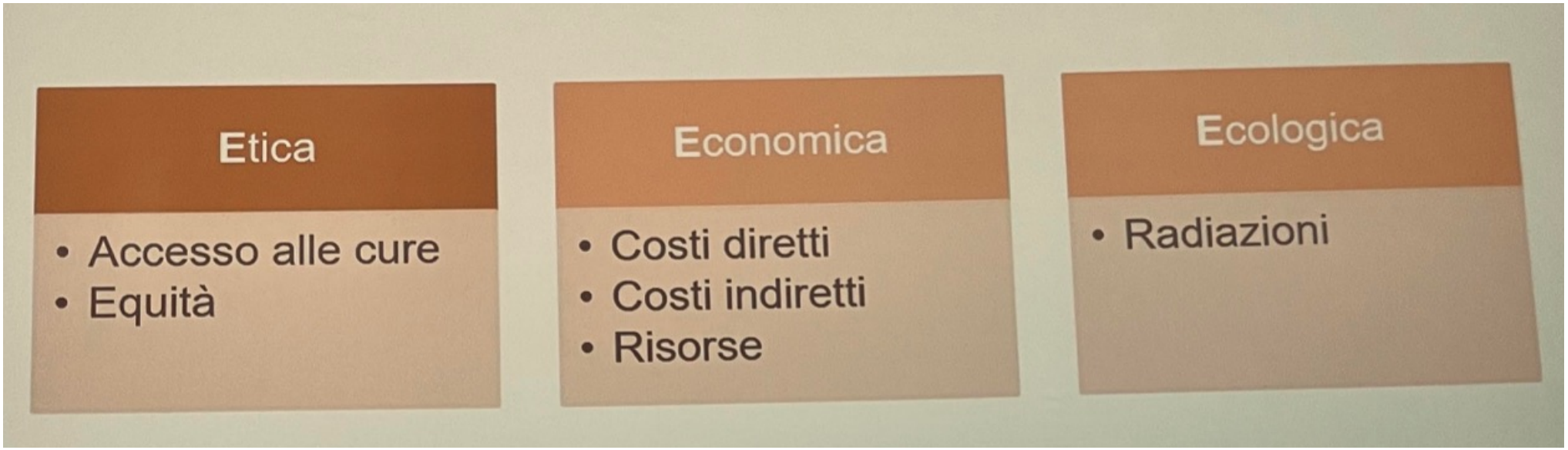
March 2020

4 months FUP PET-CT

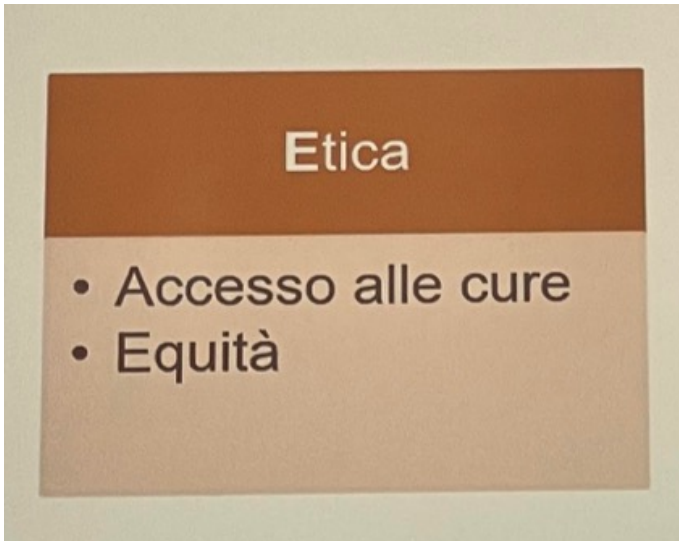
almost complete response, no toxicity

Criteri per innovatività terapeutica

1. Bisogno terapeutico
2. Valore terapeutico aggiunto
3. Qualità delle prove
4. Impatto economico



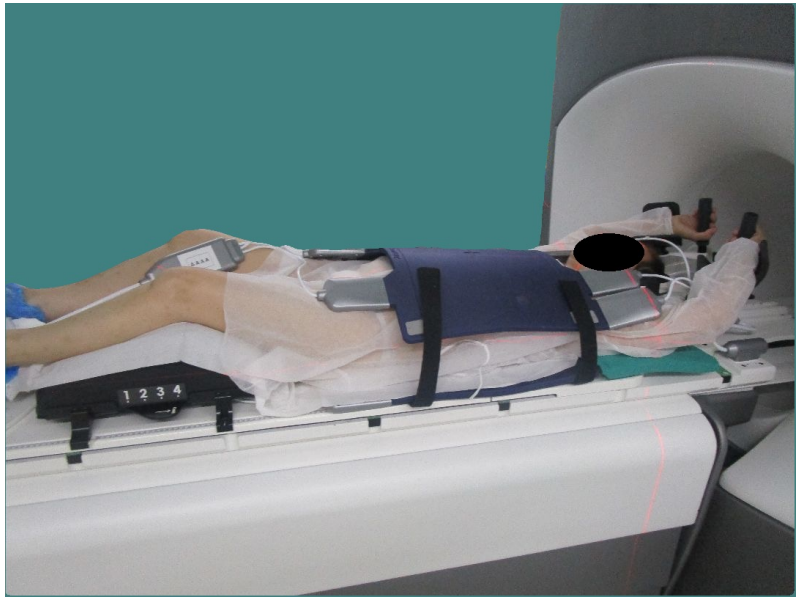
Captured from L. Evangelista, *AIRO 2022*



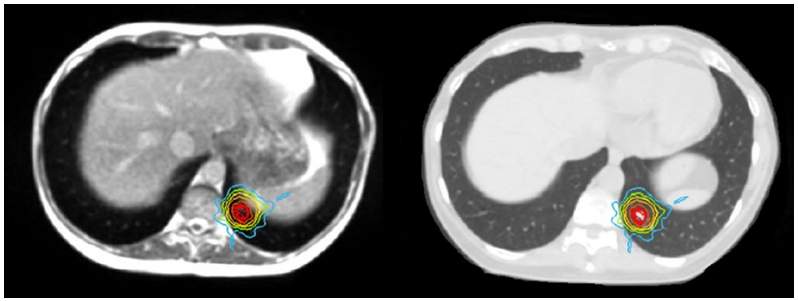
Captured from L.Evangelista, *AIRO 2022*

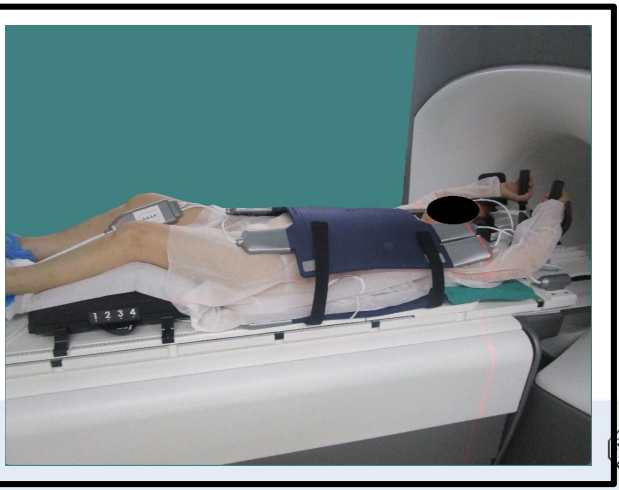
The **'ideal' patient** for MRgRT

physically not compatible	(i.e. pace maker carriers)
clinically not compatible	(i.e. major psychiatric disorder, severe claustrophobia)
border line compatible	(i.e. mild claustrophobia)
fully compatible	



MRgRT WORK-FLOW





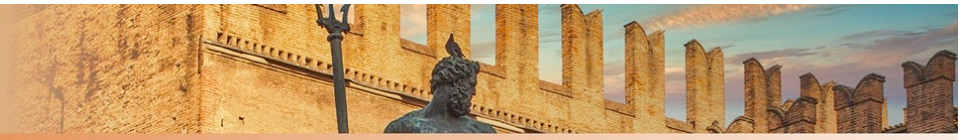
Simulation:

Patient positioning → Pilot scan → HR (**breath-hold)** scan → Contouring (tumor/ normal organs) → Plan generation / QA

For each fraction:

Patient positioning → Pilot scan → HR (**breath-hold)** scan → Matching with baseline MR (on tumor) → Deformation and adaptation of normal organs → Plan prediction → Re-optimalisation of the plan → QA → Positioning verification → **Treatment delivery (in breath-hold periods)**

Tetar et al. *Cureus 2018*

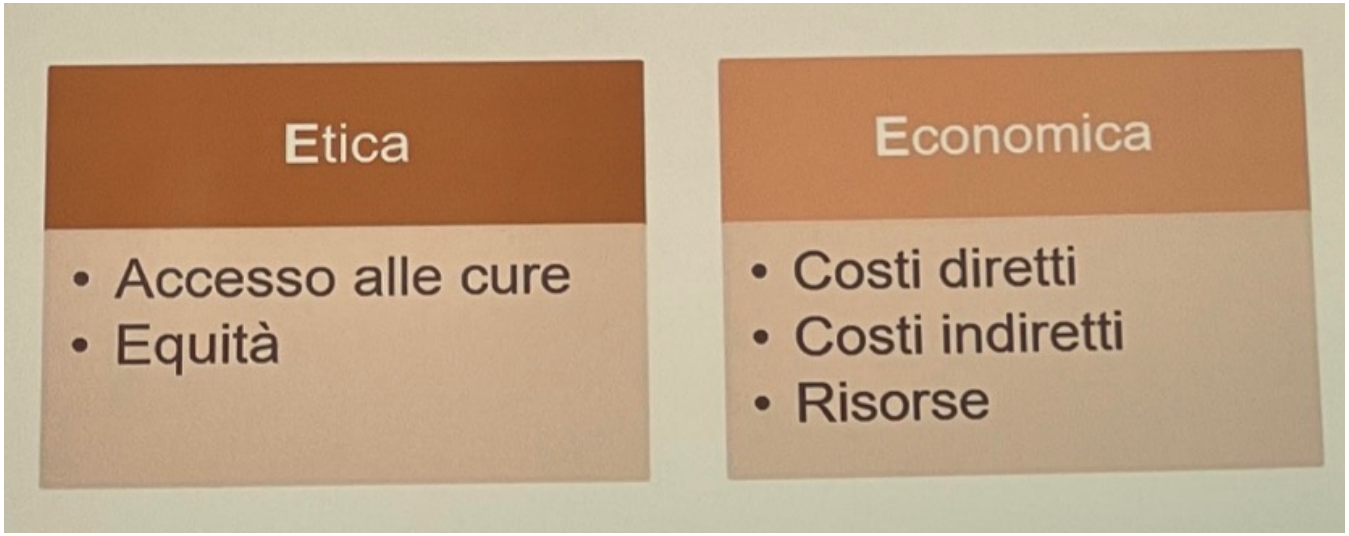


MRgRT WORK-FLOW

	MEAN	RANGE
BEAM-ON TIME	16.7 min	6-62 min
TOTAL TREAT TIME	47 min	21-125 min

15-18 patients per day
Short Treatments → 320 patients per year

Bilgehan S et al. *Cureus 2019*



Captured from L.Evangelista, *AIRO 2022*

AUTHOR	COUNTRY	Methodology	DISEASE	INNOVATIVE TREATMENT	STANDARD TREATMENT	RESULTS
Parikh 2020	USA	ABC	HCC	0.35 T 5f-MRIgRT SBRT	5f-CTIgRT SBRT	**Cost 18% higher**
Parikh 2021	USA	ABC	Prostate Ca	0.35 T 5f-MRIgRT SBRT	5f-CTIgRT SBRT	**+ 1497 USD**
Beerber 2020	AUSTALIA	CMA	Prostate Ca	0.35 T 5f-MRIgRT SBRT	5f-CTIgRT SBRT	**In favour of MRIgRT considering medical benefits**
Schumacher 2020	USA	CUA	Prostate Ca	0.35 T 5f-MRIgRT SBRT; 0.35 T 39f-MRIgRT	5f-CTIgRT SBRT; 39f-CTIgRT	**Sfavous MRIgRT if 50,000 USD/QALY** **Favours MRIgRT if 100,000 USD/QALY**
Hehakay 2021	The Netherldnds	CUA	Hypotetical Prostate Ca	1.5 T 5f-MRIgRT SBRT	5f-, 20f- or 39f-EBRT	**Favours MRIgRT compared to 20-39 f**

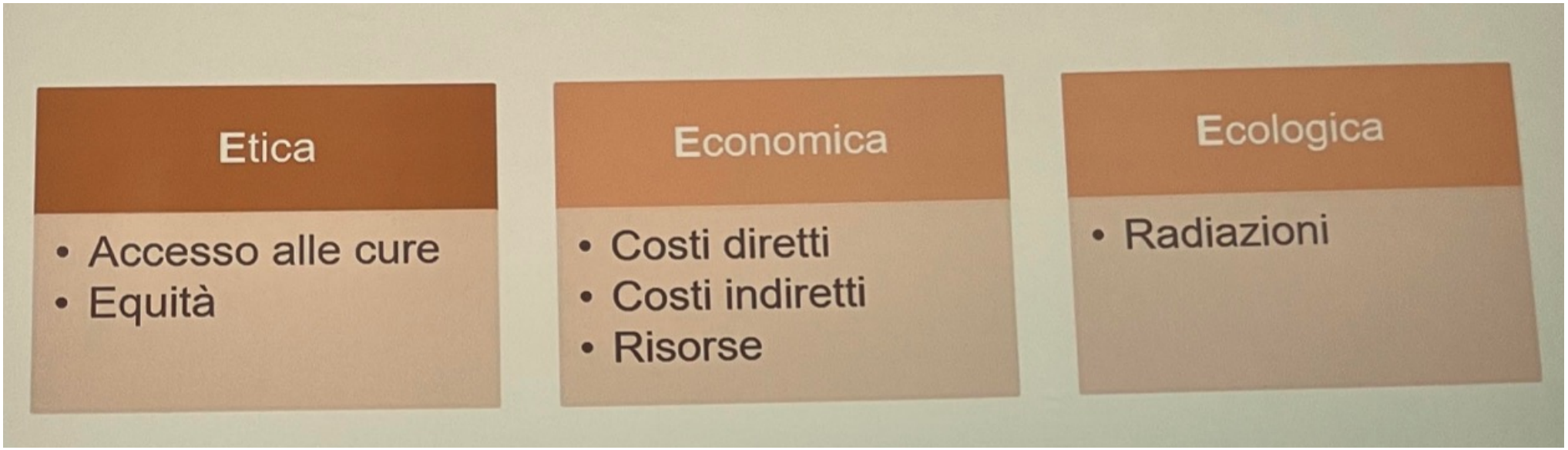
ABC: Activity Based Cost; CMA: Cost Minimization Analysis; CUA: Cost Utility Analysis

Castelluccia A et al, *Int J Env Res 2022*

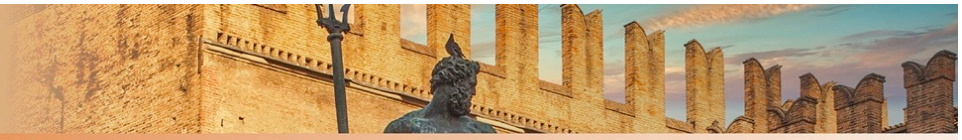
The high-speed technology

The visual story of iPhone

Dec 2014	• ^{60}Co system Contract Signature
Aug 2015	• Site installation
Jul 2016	• Authorization site Category A
Oct 2016	• Magnets installation
Nov 2016	• RT source installation
Dec 2016	• FTP & ATP
Jan 2017	• Commissioning
Feb 2017	• First ^{60}Co Treatment
Dec 2018	• ^{60}Co system dismission
May 2019	• First Linac Irradiation
March 2020	• Smart Vision & HSMLC
Feb 2023	• A3i first patient



Captured from L.Evangelista, *AIRO 2022*



› Acad Radiol. 2020 Nov;27(11):1594-1600. doi: 10.1016/j.acra.2019.11.011. Epub 2019 Dec 13.

"Green Fingerprint" Project: Evaluation of the Power Consumption of Reporting Stations in a Radiology Department

Nicolin Hainc [1], Philipp Brantner [2], Caroline Zaehringer [2], Joachim Hohmann [3]

› Acad Radiol. 2014 Dec;21(12):1563-6. doi: 10.1016/j.acra.2014.07.010. Epub 2014 Aug 27.

"EcoRadiology"--pulling the plug on wasted energy in the radiology department

Colin J McCarthy [1], Jan F Gerstenmaier [2], Ailbhe C O' Neill [2], Sinead H McEvoy [2], Chris Hegarty [2], Eric J Heffernan [2]

Canadian Association of Radiologists Journal
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Article

Quantitative Assessment of Computed Tomography Energy Use and Cost Savings Through Overnight and Weekend Power Down in a Radiology Department

Maura Brown, MD, FRCPC [1], Eric Snelling, PEng, CEM, CMVP [2], Moises De Alba, PEng, CEM, MEng, LEED AP BD+C [3], Ghazal Ebrahimi, PhD, MSc, B.Arch [4], and Bruce B. Forster, MSc, MD, FRCPC, FCAR [5]

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Switching off for future—Cost estimate and a simple approach to improving the ecological footprint of radiological departments

L. Büttner [a,*,1], H. Posch [a,1], T.A. Auer [a], M. Jonczyk [a,c], U. Fehrenbach [a], B. Hamm [a], H. C. Bauknecht [b], G. Böning [a]

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Criteri per innovatività terapeutica

1. Bisogno terapeutico ✓
2. Valore terapeutico aggiunto ✓
3. Qualità delle prove ✗
4. Impatto economico ✓ ✗

Barbieri M. *Opening Ceremony; AIRO 2022*


AIRO2022
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XII CONGRESSO NAZIONALE AIRO GIOVANI
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