

MIDSUMMER SCHOOL 2025

IL FUTURO DELLE CURE ONCOLOGICHE SI INCONTRA A MILANO

9 LUGLIO 2025 | MILANO

Palazzo Lombardia, Sala Marco Biagi
Piazza Città di Lombardia, 2

10-11 LUGLIO 2025 | MILANO

Aula Magna la Pietra - Istituto Europeo di Oncologia
Via G. Ripamonti, 435

In collaborazione con



Con il patrocinio di



f x @ v in

www.motoresanita.it



Promuovere la radioterapia: innovazione tecnologica e approcci traslazionali

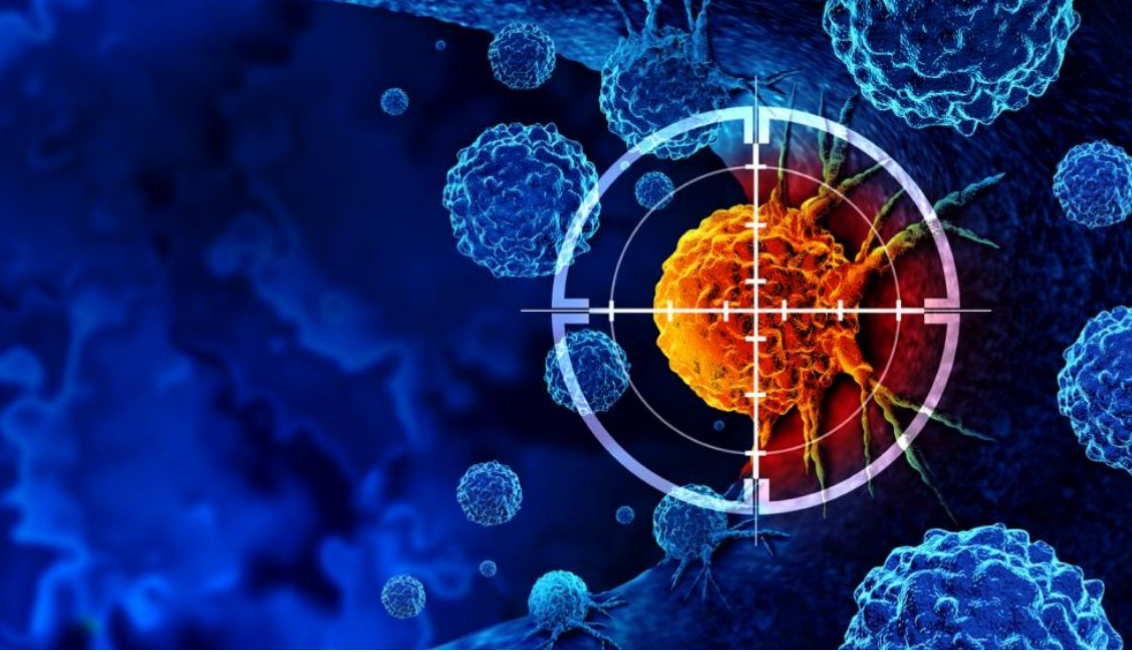
Barbara Alicja Jereczek-Fossa MD PhD

European Institute of Oncology and University of Milan, Italy

barbara.jereczek@ieo.it @BarbaraJereczek

UNIVERSITÀ
DEGLI STUDI
DI MILANO





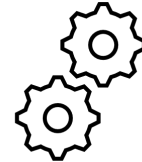
ONCOLOGY TODAY



- Incidence is growing



- Cure rates are improving



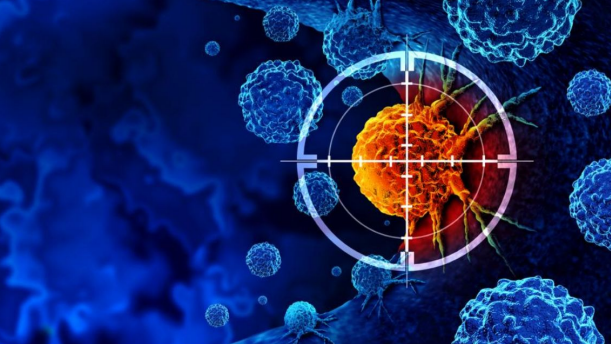
- Treatments are more complex



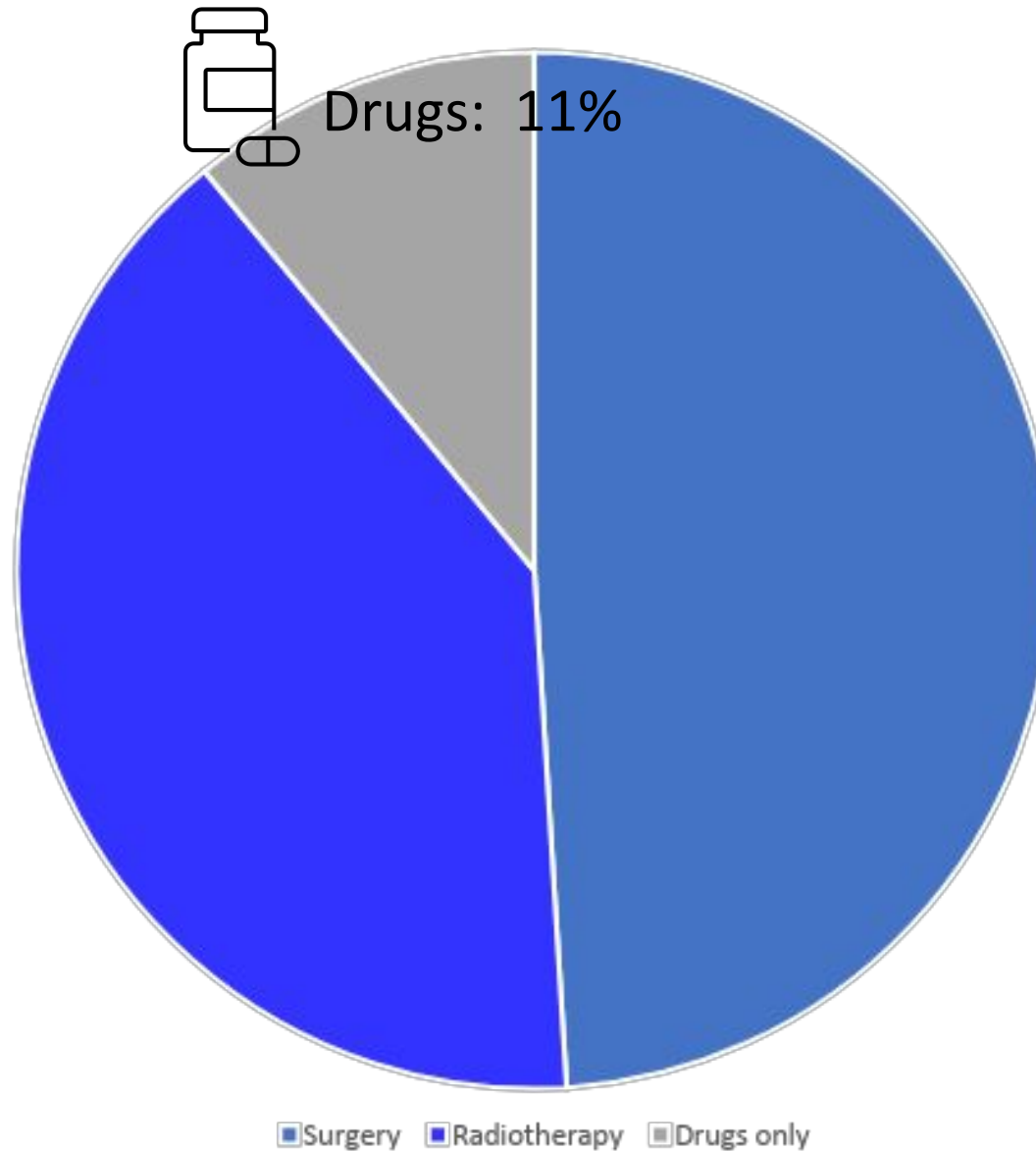
- Multidisciplinary care is standard



- Patient expectations are higher



WHO CURES CANCER?



Radiotherapy: 40%



Surgery: 49%

RADIOTHERAPY

60% of all patients need RT

- Curative therapy
- Adjuvant
- Palliative
- Ablative
- T, N, M



RADIOTHERAPY

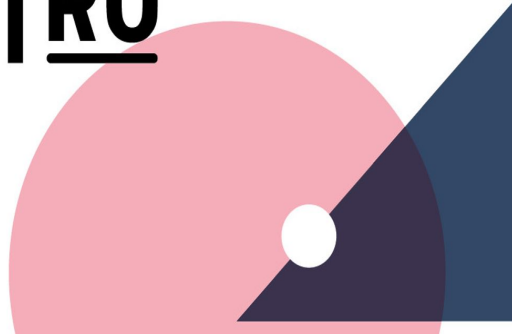
- **The request for RT will grow by 15-20%**
- **Cost-effective:** <5% of cancer care costs
- **Optimizes spending:** Hypofractionation, oligoproggression, virtual surgery etc.
- **Underfunded:**
Only 2.8% of public/philanthropic cancer research funds



1980
The European Society for Radiotherapy and Oncology
Almost 10.000 members
Almost 100 national societies



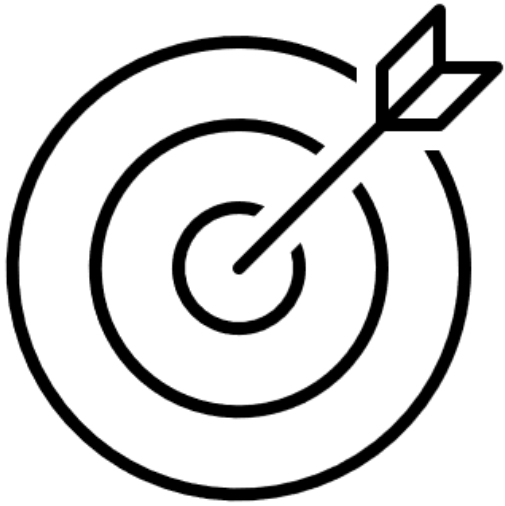
ESTRO



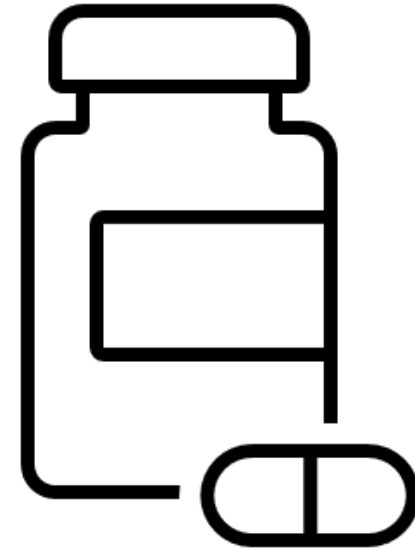
**1 in 4 cancer patients in EU
does not receive
the radiation oncology treatment needed**

$$KPI = \frac{\text{patients receiving RT}}{\text{patients who should receive RT}}$$

Two important directions in radiation oncology



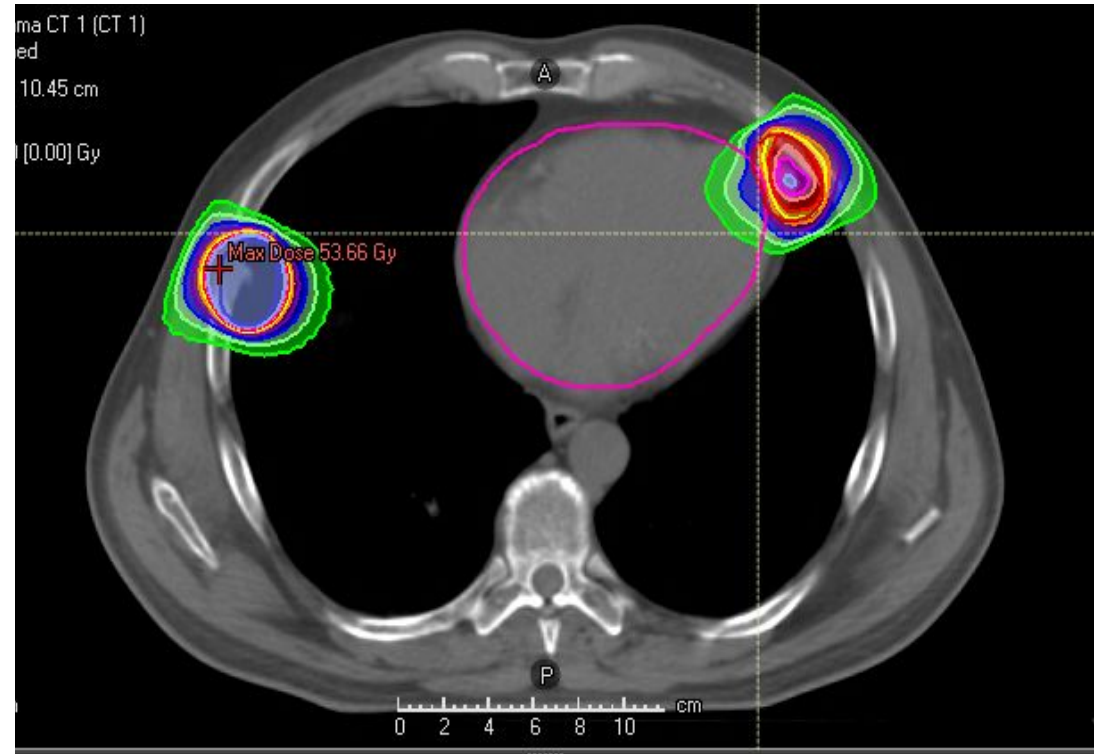
Technological and biological precision



RT + new drugs

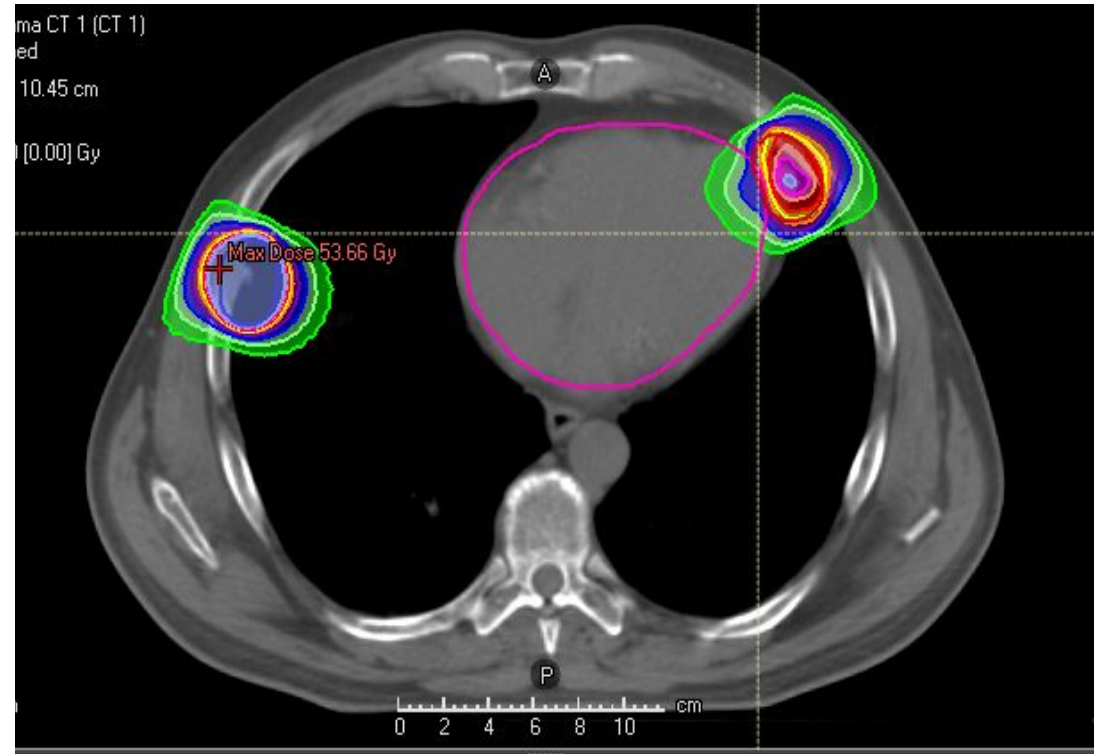
FUTURE of Radiation Oncology

- AI and innovation
- New Combinations
- New indications
- Green RT



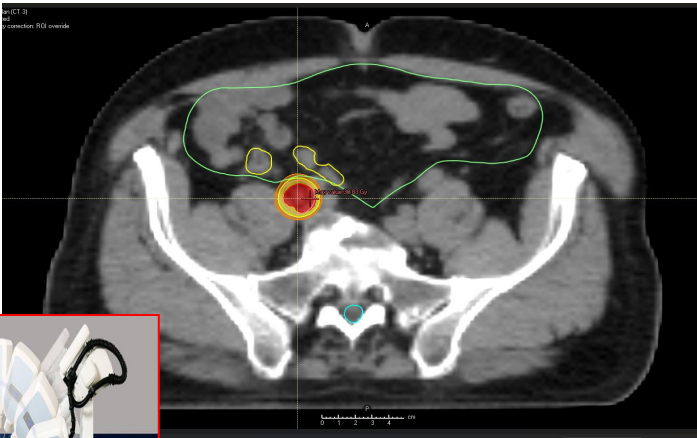
FUTURE of Radiation Oncology

- **AI and innovation**
- **New Combinations**
- **New indications**
- **Green RT**

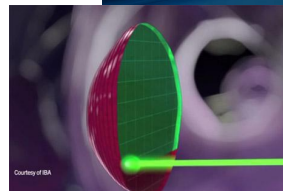
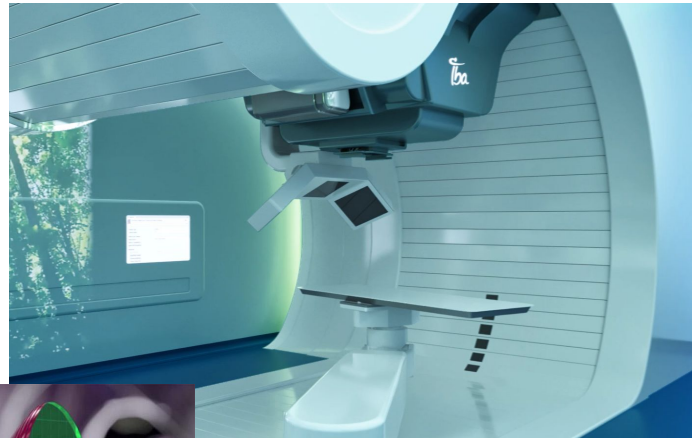


Understanding the Disruptive Potential of MDT in Metastatic Prostate Cancer Treatment, Exploring Hypotheses for Future Studies

January 29, 2025



SBRT



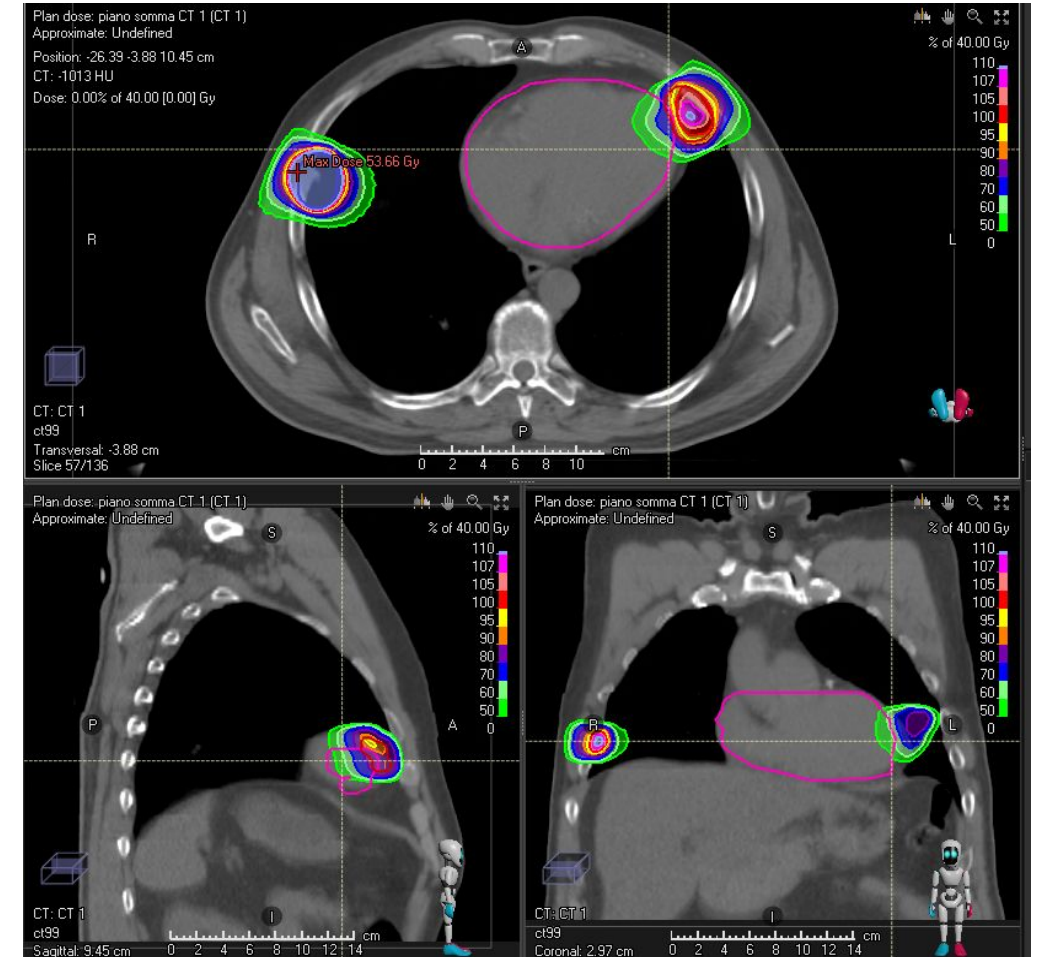
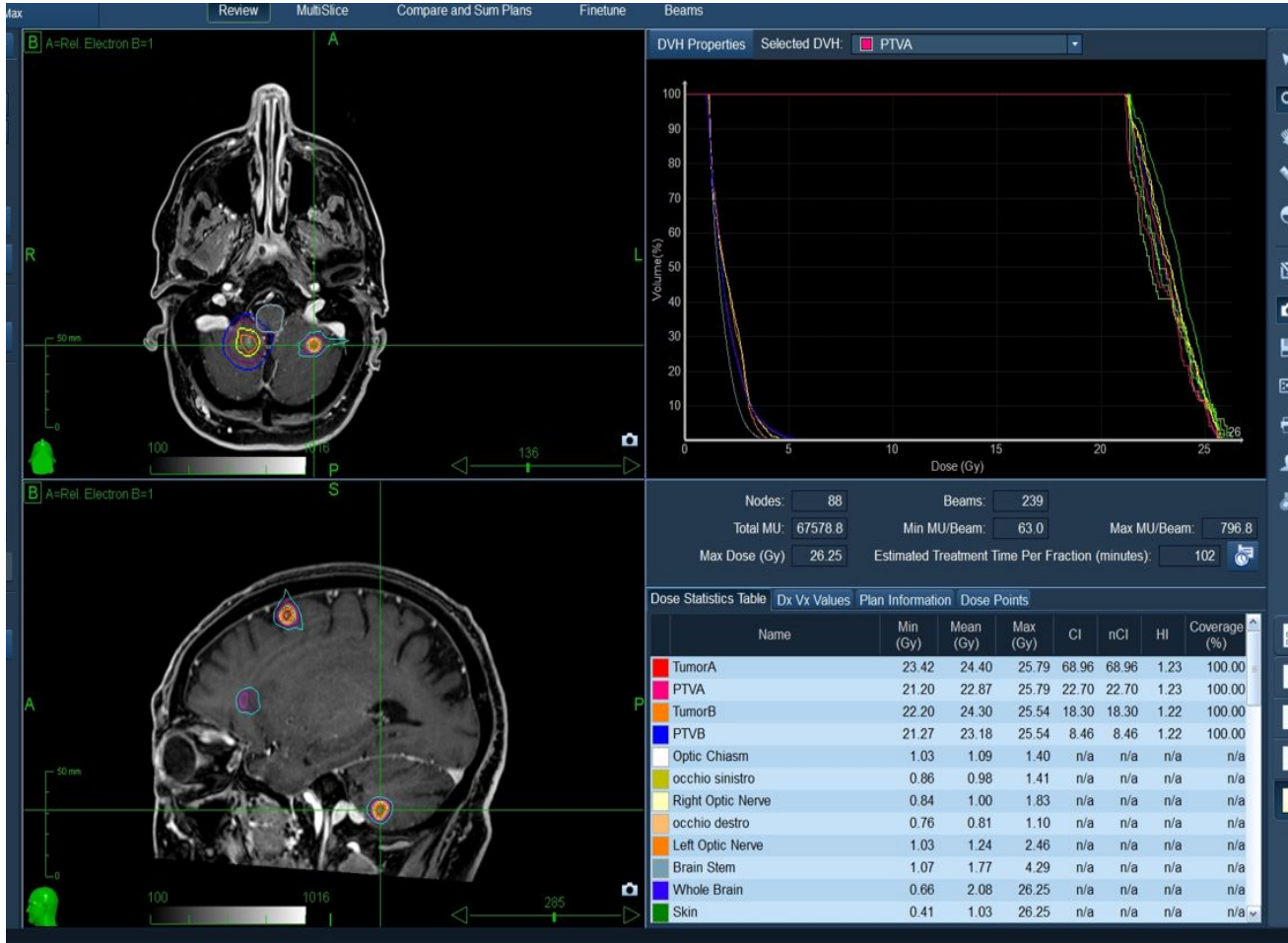
Proton ther.



MRI-linac

Ablative stereotactic RT (SBRT, SABR): any site can be treated

Primary, recurrent, oligometastatic and oligoprogressive disease





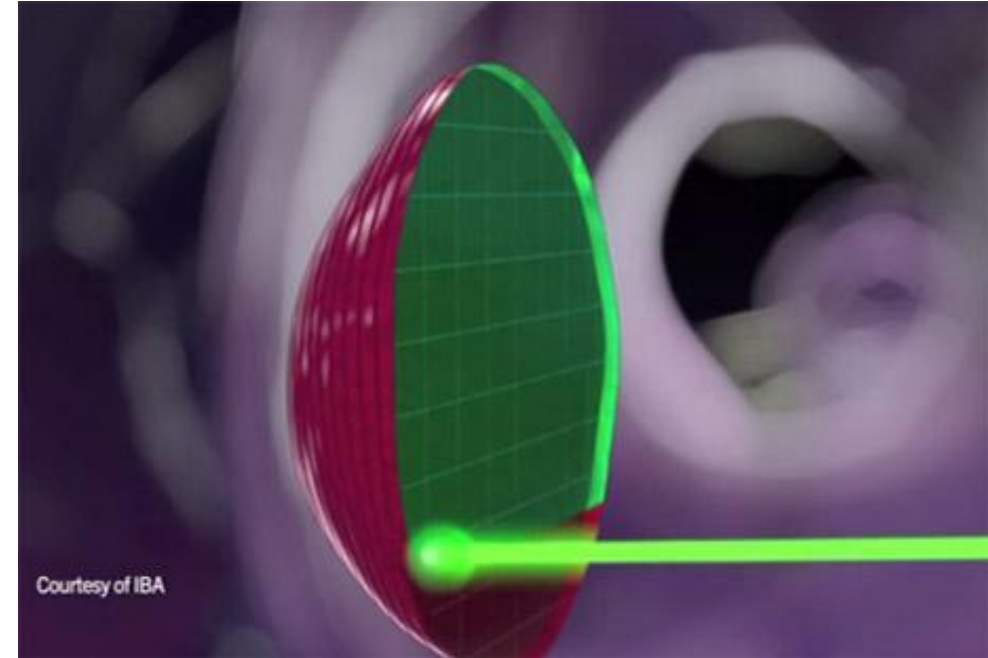
PROTONTHERAPY

European Institute of Oncology
IEO Advanced Radiotherapy Center ARC
& Proton Center

PROTON THERAPY: compact system Proteus One



1 room (1 gantry), 3 floor building
Possible upgrade: FLASH, Arc therapy



30+ in Europe
100+ in the world

Pencil beam scanning (PBS)



Radiotherapy in Italy (59 million inhab.)

Italy: 183 RT centers, 2 PT (eye-center is now inactive)

Candidates to PT: 15% of all pts undergoing RT (7.000-20.000p/y)

2 existing PT centers treat: < 1.000 pts/year...

unmet need

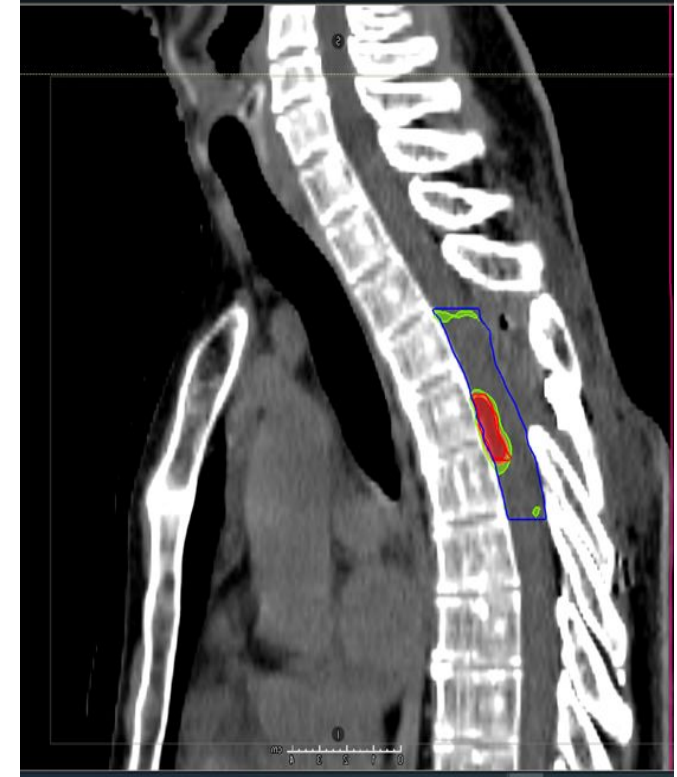


Italy: Health Ministry list of indications for PT

- Chordoma & chondrosarcoma of skull base & spine
- Brain stem and spinal cord
- Sarcoma of head&neck, paraspinal, retroperitoneal, pelvic
- Osteo & condrosarcoma of the limbs
- Orbit al & paraorbital tumors (included melanoma)
- Adenoid cystic tumor of salivary gland
- Patients with genetic syndroms (radiosensitivity) & connective tissue disorders
- Pediatric solid tumors
- Re-irradiation

Hard-to-treat-tumors

Example: meningeal melanoma



Dose Prescription

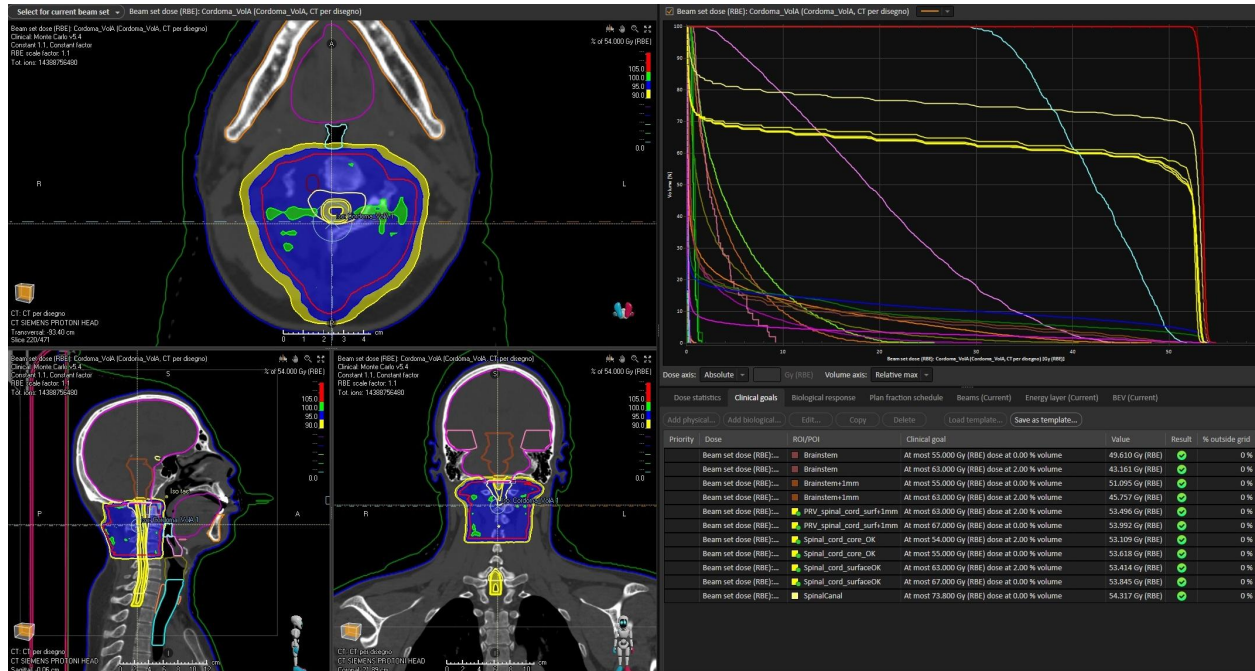
Low risk area 25 fr x 1.8 Gy/fr \square 45 Gy (RBE)

Surgical bed 25 fr x 2 Gy \square 50 Gy (RBE)

Example: schwannoma of the hypoglossus nerve



Example: chordoma (postop PT)



Diagnosis: chordoma of the cervical spine (persistence after surgery)

Age: 33 Gender M

Proton therapy doses: 73.8 Gy (RBE) and 54 Gy RBE (sequential boost)



Future indications?

- Young adults
- Glioma (Dutch guidelines: 5% dose reduct to supratentorial brain or hippocampus)
- Oropharynx HPV positive
- Nasopharynx
- All parotid tumors
- H&N with monolat neck RT
- HCC
- Oligometastatic disease
- Cases with dosimetric advantage



PI: Prof. Roberto Orecchia

Alterio et al. BMC Cancer (2024) 24:333
https://doi.org/10.1186/s12885-024-12059-2

BMC Cancer

STUDY PROTOCOL

Open Access

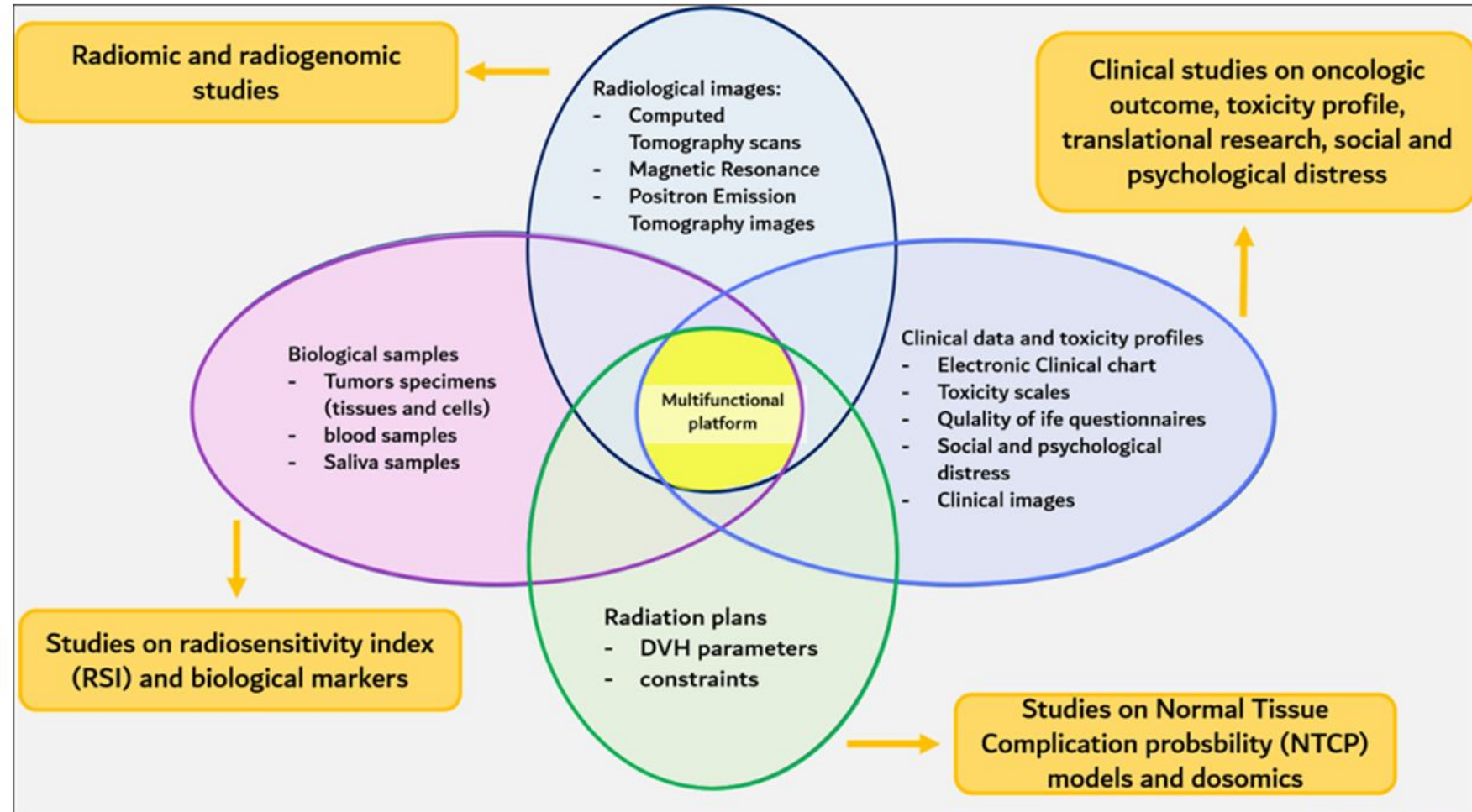
A multicenter high-quality data registry for advanced proton therapy approaches: the POWER registry

Daniela Alterio¹, Maria Giulia Vincini^{1*}, Stefania Volpe^{1,2}, Luca Bergamaschi¹, Mattia Zaffaroni¹, Sara Gandini³, Giulia Peruzzotti⁴, Federica Cattani⁵, Cristina Garibaldi⁶, Barbara Alicja Jereczek-Fossa^{1,2†} and Roberto Orecchia^{7†}

Supported by IBA

1. POWER REGISTRY

Multicentric High Quality Data Registry



Prostate cancer

Online ahead of print.

Photon vs proton hypofractionation in prostate cancer: A systematic review and meta-analysis

Giulia Corrao¹, Giulia Marvaso¹, Federico Mastroleo¹, Annalisa Biffi², Giacomo Pellegrini², Samuele Minari³, Maria Giulia Vincini⁴, Mattia Zaffaroni⁵, Dario Zerini⁶, Stefania Volpe¹, Simona Gaito⁷, Giovanni Carlo Mazzola⁶, Luca Bergamaschi⁶, Federica Cattani⁸, Giuseppe Petralia⁹, Gennaro Musi¹⁰, Francesco Ceci¹¹, Ottavio De Cobelli¹², Roberto Orecchia¹³, Daniela Alterio⁶, Barbara Alicja Jereczek-Fossa¹

Hypofractionated proton therapy for ocular melanoma

In preparation

Eye melanoma

Submitted to CTR

Reirradiation with Proton Therapy Using Hypofractionated Schedules:

a Systematic Review of the Literature

Daniela Alterio^{1,*}, Vanessa Eleonora Pierini^{1,2,*}, Stefania Volpe^{1,2,§}, Maria Giulia Vincini^{1,§}, Mattia Zaffaroni¹, Annamaria Ferrari¹, Marvaso Giulia¹, Federico Mastroleo¹, Nicolaus Andruschke³, Matthias Guckenberger³, Jiri Kubeš^{4,5}, Icro Meattini^{6,7}, Carsten Nieder^{8,9}, Yvette Orecchia¹³ and Barbara Alicja Jereczek-Fossa^{1,2}

Re-irradiation, all sites

Epub 2022 Jan 13.

Breast cancer

Hypofractionated proton therapy in breast cancer: where are we? A critical review of the literature

Daniela Alterio^{# 1}, Eliana La Rocca^{# 1 2}, Stefania Volpe^{3 4}, Anna Maria Camarda^{1 2}, Alessia Casbarra^{1 2}, William Russell-Edu⁵, Maria Alessia Zerella¹, Roberto Orecchia⁶, Viviana Galimberti⁷, Paolo Veronesi⁷, Maria Cristina Leonardi^{# 1}, Barbara Alicja Jereczek-Fossa^{# 1 2}

Epub 2023 Sep 6.

CNS

Hypofractionated proton therapy for benign tumors of the central nervous system: A systematic review of the literature

Gaia Piperno¹, Annamaria Ferrari¹, Stefania Volpe², Federica Cattani³, Mattia Zaffaroni¹, Stefania Comi³, Floriana Pansini³, Luca Bergamaschi¹, Giovanni Carlo Mazzola¹, Francesco Ceci⁴, Marzia Colandrea⁵, Giuseppe Petralia⁶, Roberto Orecchia⁷, Barbara Alicja Jereczek-Fossa⁸, Daniela Alterio¹

Epub 2022 Sep 20.

Lung cancer

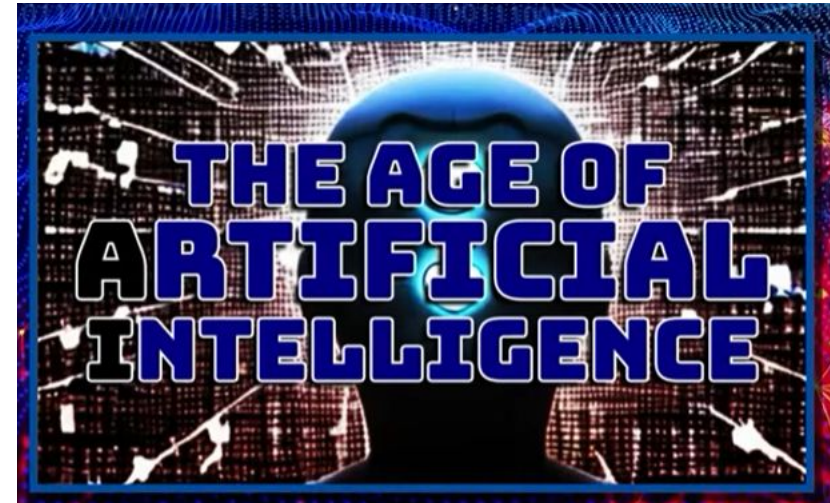
Hypofractionated proton therapy for non-small cell lung cancer: Ready for prime time? A systematic review and meta-analysis

Stefania Volpe¹, Gaia Piperno², Francesca Colombo³, Annalisa Biffi⁴, Stefania Comi⁵, Federico Mastroleo⁶, Anna Maria Camarda⁷, Alessia Casbarra⁷, Federica Cattani⁵, Giulia Corrao², Filippo de Marinis⁸, Lorenzo Spaggiari⁹, Matthias Guckenberger¹⁰, Roberto Orecchia¹¹, Daniela Alterio², Barbara Alicja Jereczek-Fossa⁷



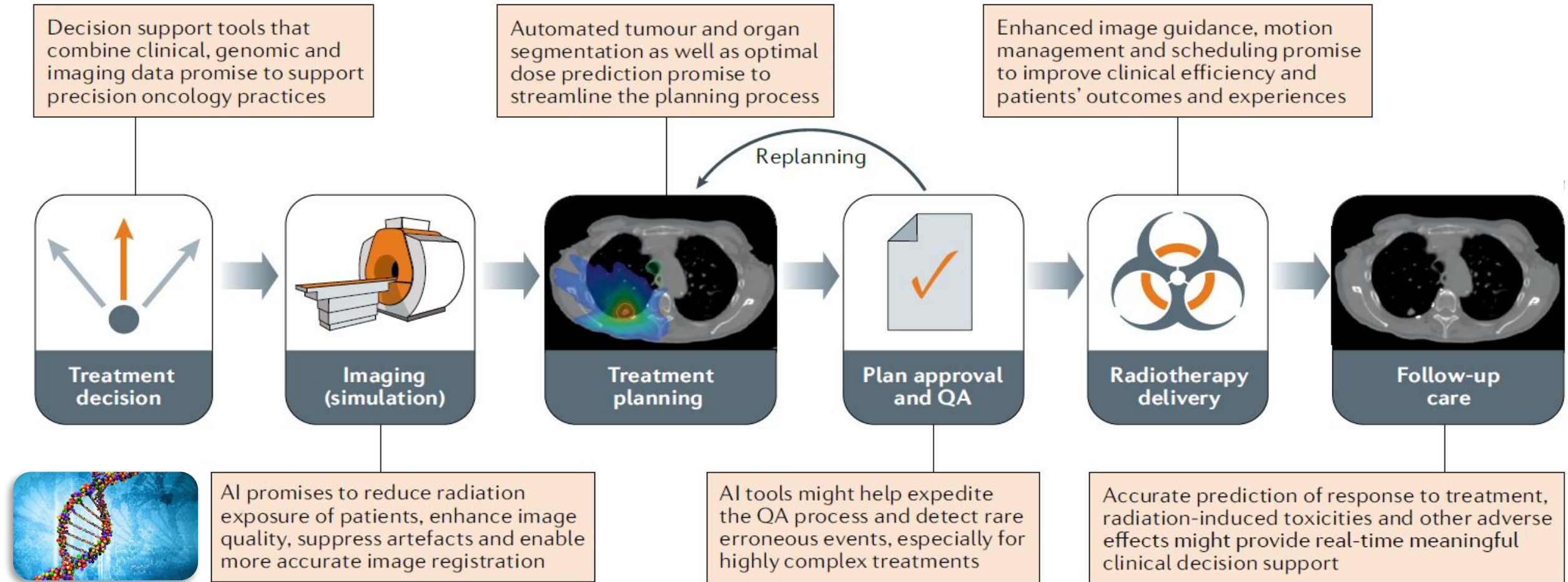
AI is everywhere and will change EVERYTHING

- Every human activity
- Every job
- Unlocking enormous potential
- But needs regulations



https://www.youtube.com/watch?v=ypEDNu0_kRk

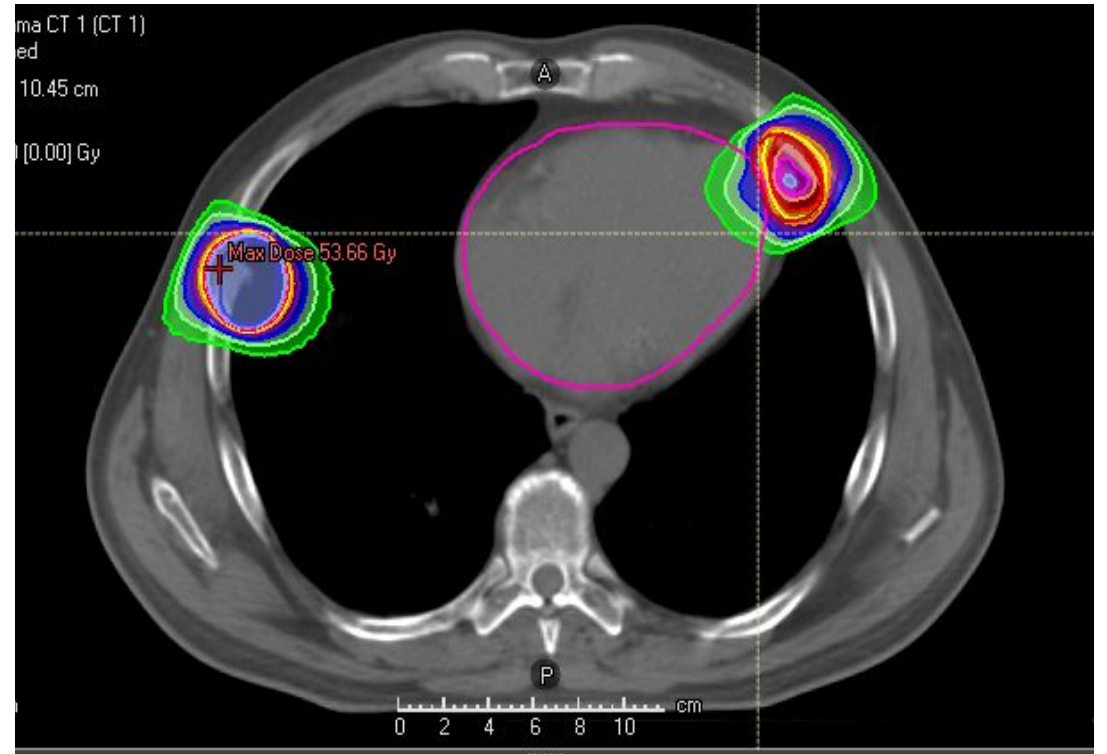
RT has technology and data-driven WORKFLOW



Huynh E. et al. doi:
10.1038/s41571-020-0417-8.

FUTURE of Radiation Oncology

- AI and innovation
- **New Combinations**
- New indications
- Green RT





New combinations: RT plus

- surgery
- drugs
- other modalities
- translational research**



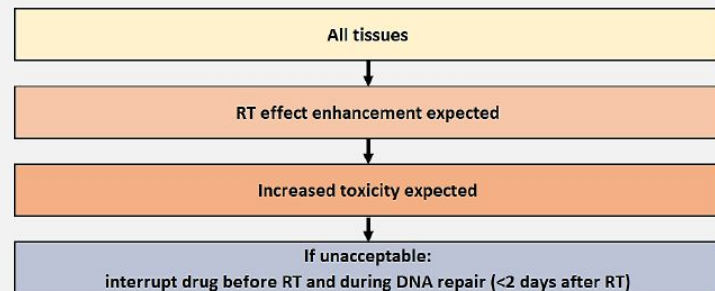


Original Article

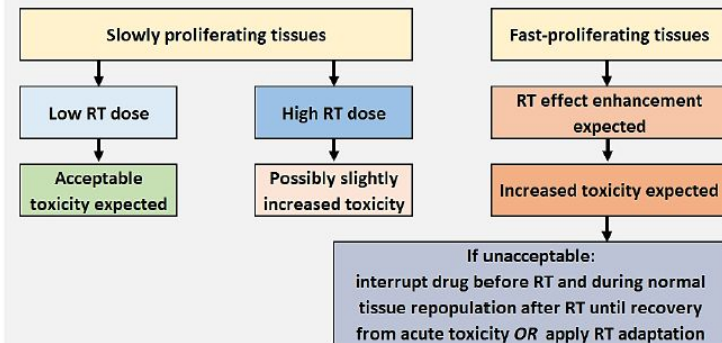
ESMO-ESTRO framework for assessing the interactions and safety of combining radiotherapy with targeted cancer therapies or immunotherapy

Evert S.M. van Aken^{a,b,*}, Bharti Devnani^{c,1}, Luis Castelo-Branco^{d,1}, Dirk De Ruyscher^{e,f}, Diogo Martins-Branco^g, Corrie A.M. Marijnen^{a,b}, Barbara Muoio^h, Claus Belkaⁱ, Florian Lordick^j, Stephanie Kroeze^k, George Pentheroudakis^g, Dario Trapani^{l,m}, Umberto Ricardiⁿ, Ajeet Kumar Gandhi^{o,2}, Arsela Prelai^{p,2}, Sean M. O'Cathail^{q,r,3}, Monique C. de Jong^{a,3}

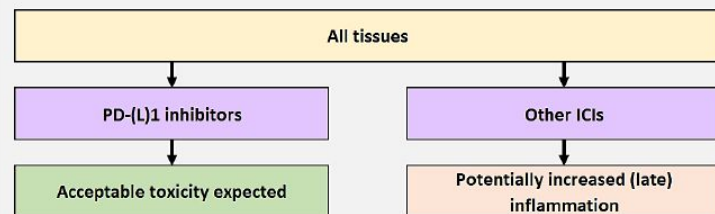
RT + agents interfering with DNA repair



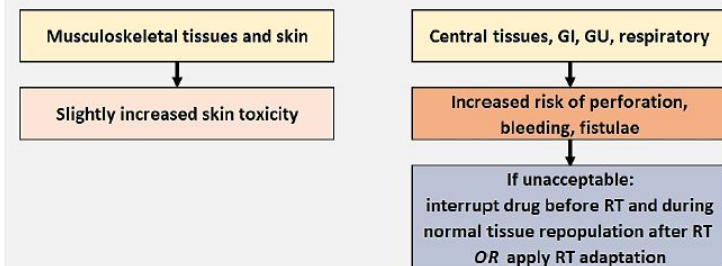
RT + proliferation inhibitors



RT + immune checkpoint inhibitors



RT + angiogenesis inhibitors





CRYSTAL study PI: Maria C Leonardi MD



AIRC19-IG- IEO 1308

NCT04679454

Single fraction ablative preoperative RT with Cyberknife for early-stage BC

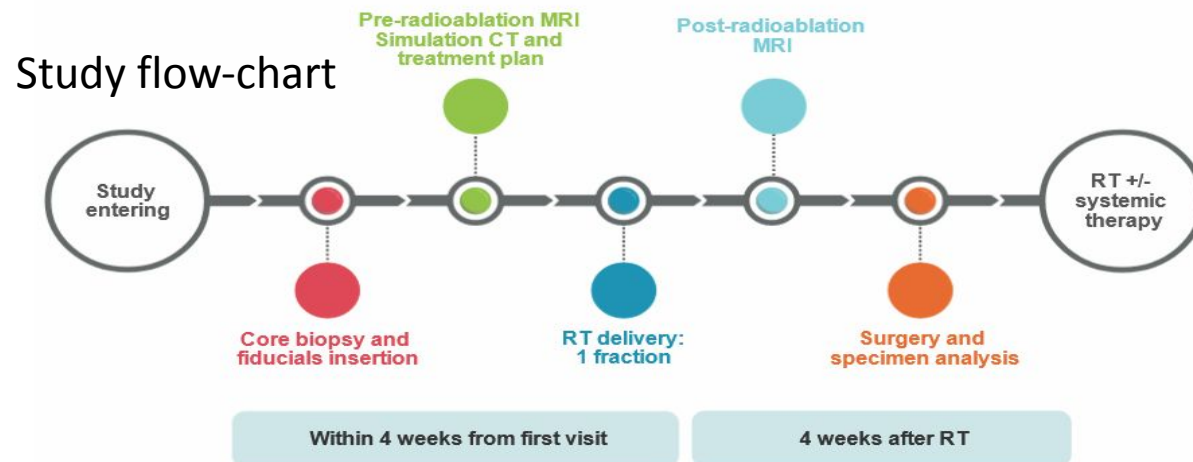
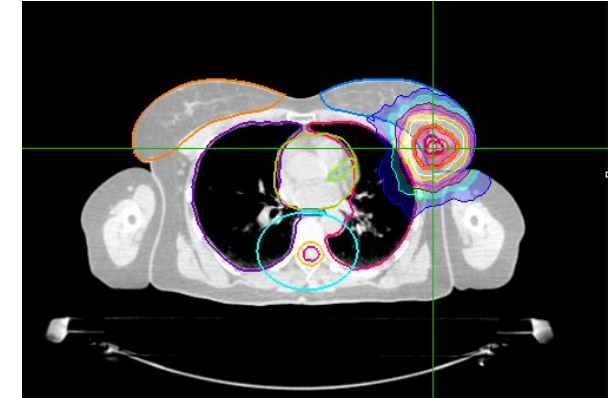
Phase I, dose escalation: 3+3 design (18, 21, 24 Gy)

endpoint: acute toxicity

Completed: 9 pts, no toxicity **MTD:** 24 Gy

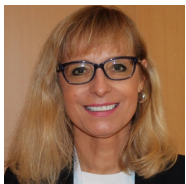
Phase II, endpoint: pCR. Ongoing, 5/60 pts enrolled

So far: no toxicity, no pCR observed in 14 pts, 50% reduction in Ki-67



Eligibility: T size up to 2.5 cm, cN0

- **Clinical Task:** *tolerance and efficacy*
- **Pathology Task:** *pathways of apoptosis, hypoxia response and specific lymphocytic response*
- **Molecular pathology Task:** *targeted next generation sequencing (NGS) gene expression assay (Oncomine Immune Response Research) to measure the expression of genes involved in tumor-immune system interactions*
- **Radiomics Task:** *MRI changes and MRI-histology correlation study («Historadiomics»)*



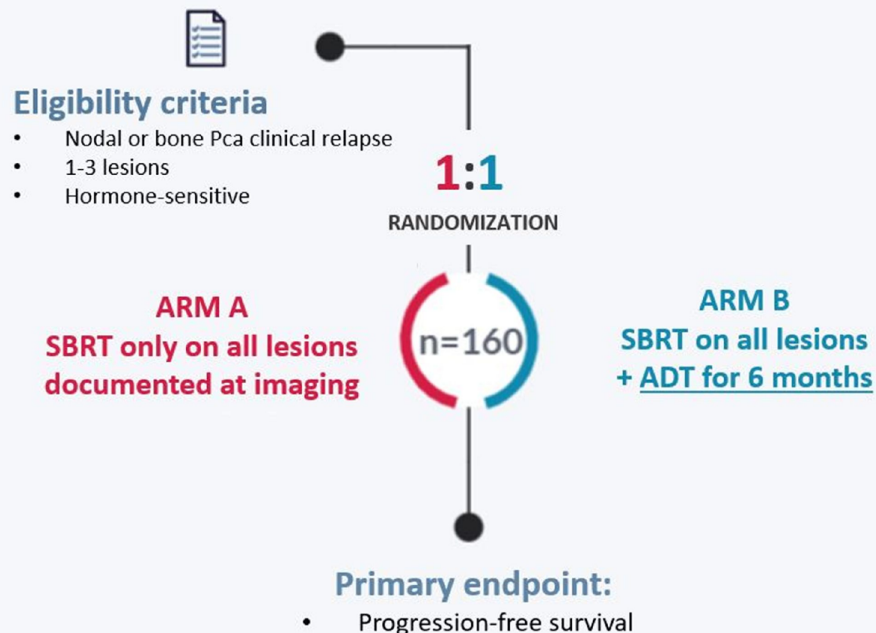
RADIOSA trial PI: Barbara Jereczek-Fossa MD PhD



AIRC IG- 22159
NCT03940235

Phase II randomised trial: SBRT +/- ADT

STUDY DESIGN



AIM: Compare two different approaches to treating oligorecurrent prostate disease

- SBRT alone versus
- SBRT combined with hormonal therapy

RESULTS

- Between September 2019 and April 2023, **100 patients** were enrolled in the trial.
- **50** were assigned to arm A and **50** assigned to arm B.

Clinical progression free survival

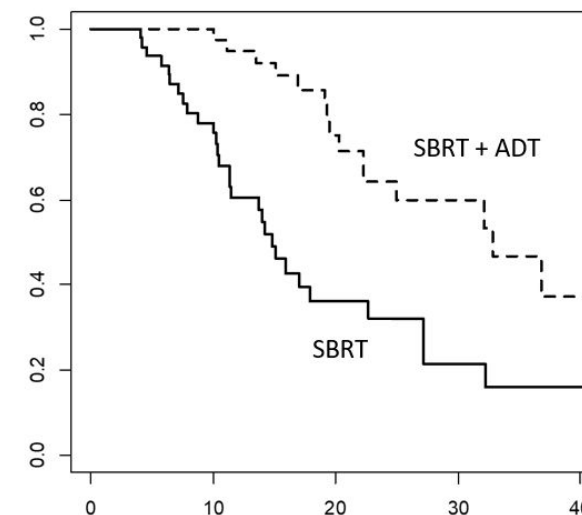
Log rank P-value= 0.0001

HR=0.30 (95%CI: 0.16-0.56) adjusted for PSA at baseline

MEDIAN TIME TO CLINICAL PROGRESSION

SBRT: 15 months

SBRT+ADT: 33 months

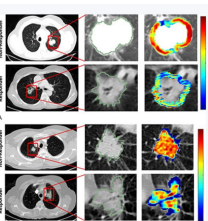
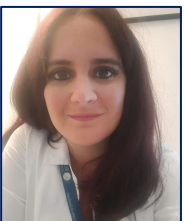


ADT with SBRT versus SBRT alone for hormone-sensitive oligorecurrent prostate cancer (RADIOSA): a randomised, open-label, phase 2 clinical trial

Giulia Marvaso*, Giulia Corrao*, Mattia Zaffaroni, Maria Giulia Vincini, Chiara Lorubbio, Sara Gandini, Cristiana Fodor, Sofia Netti, Dario Zerini, Stefano Luzzago, Francesco Alessandra Mistretta, Konstantinos Venetis, Giulia Cursano, Tiziana Burla, Ketti Mazzocco, Federica Cattani, Giuseppe Petralia, Nicola Fusco, Gabriella Pravettoni, Gennaro Musi, Ottavio De Cobelli, Chad Tang, Piet Ost, David A Palma, Roberto Orecchia, Barbara Alicja Jereczek-Fossa

Summary

Background Metastasis-directed therapy by stereotactic body radiotherapy (SBRT) has been shown to improve clinical outcomes in the oligometastatic prostate cancer setting. We aimed to investigate whether short-course androgen deprivation therapy (ADT) and SBRT at all oligometastatic sites versus SBRT alone improves clinical progression-free survival in men with metachronous oligorecurrent hormone-sensitive prostate cancer.



MONDRIAN PI: Stefania Volpe MD PhD



AIRC 28282

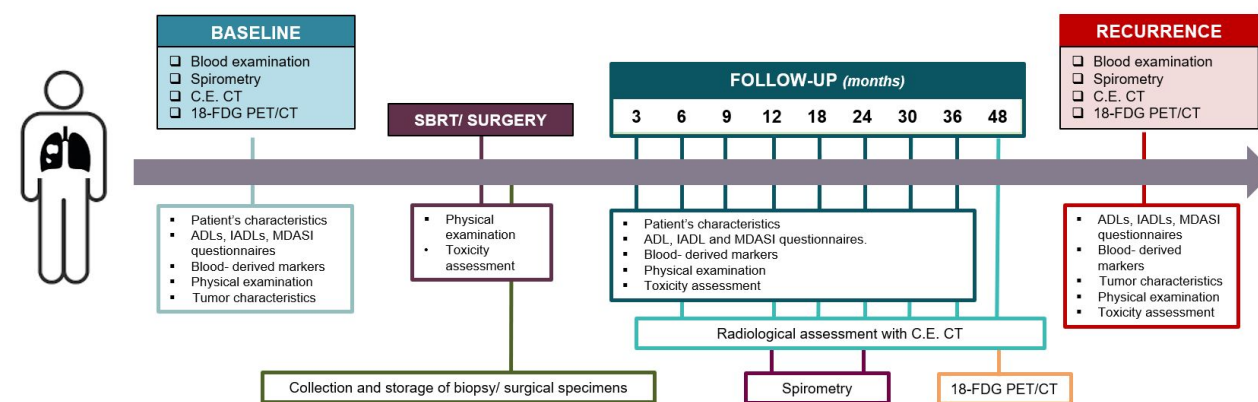
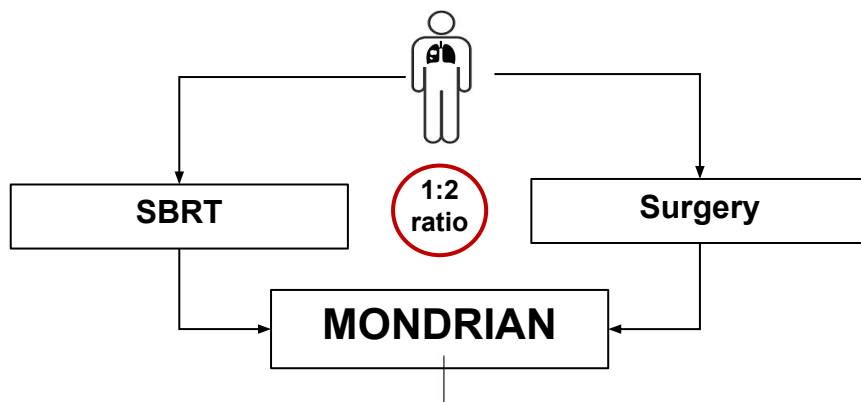
Next Gen
Clinician Scientist
2022

NCT05974475

Multi-omics integrative modelling for Stereotactic Body Radiotherapy in Early-Stage NSCLC

AIM: To identify multiomic biomarkers of SBRT response through advanced computational integration of clinical, radiomic, genomic and proteomic information layers.

STUDY DESIGN: Prospective observational explorative cohort clinical study



CLINICAL TASK

T1

- Validation of the MDASI Lung Cancer Module for the Italian Language
- Blood immunological biomarkers studies

IMAGING TASK

T2

- Methodological radiomic studies
- Analytic morphomics
- Dosomics

TRANSLATIONAL TASKS

T3

- Longitudinal validation of a non-invasive mutational signature in liquid biopsy

T4

- Longitudinal validation of a non-invasive proteomic signature in liquid biopsy

MODELING TASK

T5

- Single- and dual-omics outcome modeling

Patient-specific Microstructural and radiobiological model for personalised external beam radiation therapy in localised tumours

Host institution: Politecnico di Milano

PI IEO: Giulia Marvaso MD



POLITECNICO
MILANO 1863

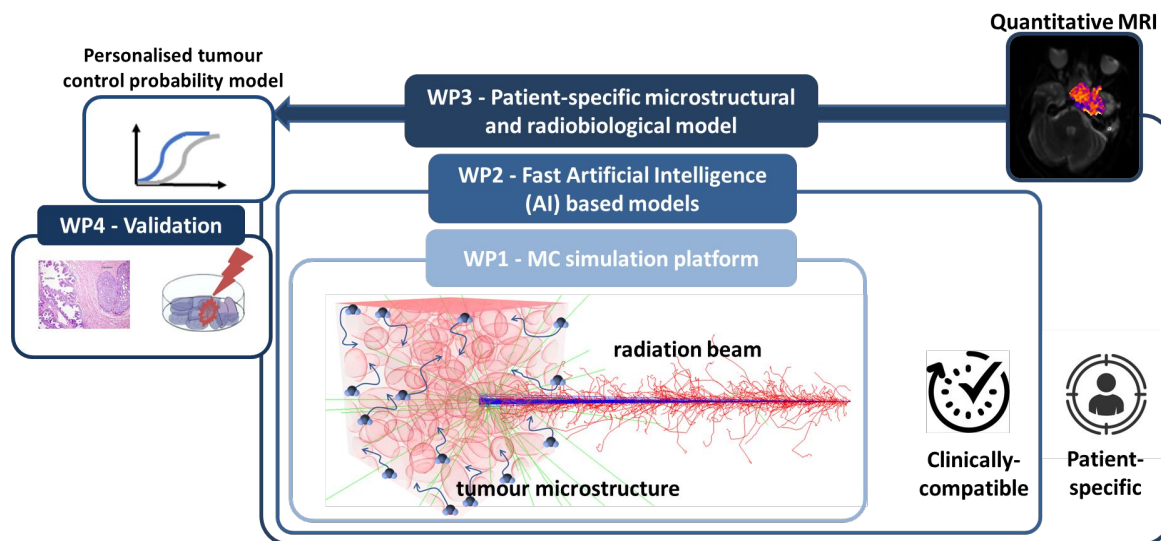
AIM:

To implement a model able to provide a description of the tumor structure down to the micro-scale and its interaction with the radiation beam, supported by simulations of the MR diffusion signal with radiation damage.

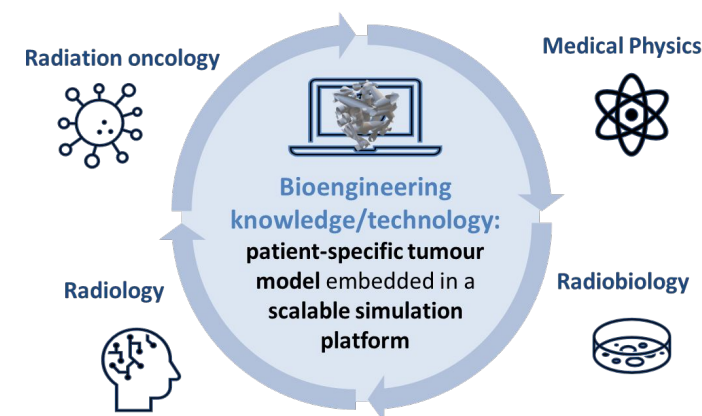
VISION

Novel modellistic framework towards the implementation of **biologically-guided radiotherapy treatments**

METHODOLOGY

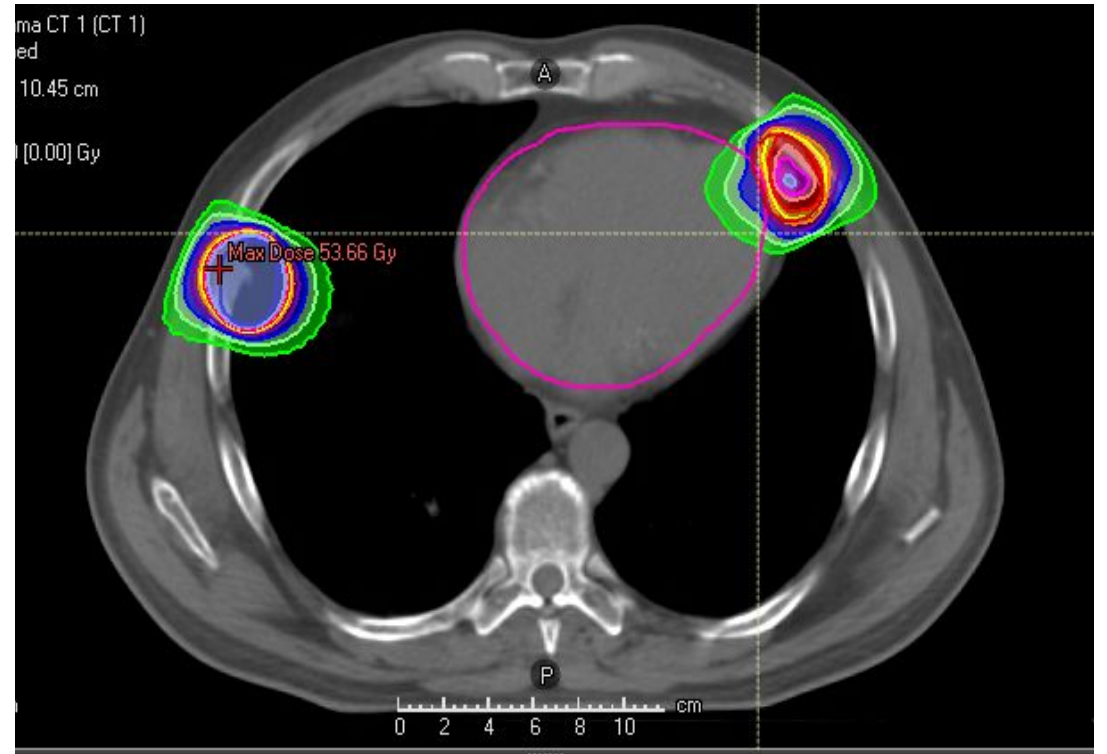


RESULTS AND IMPACT



FUTURE of Radiation Oncology

- AI and innovation
- New Combinations
- New indications
- Green RT



CLINICAL INVESTIGATION

A Phase 1 Trial of Salvage Stereotactic Body Radiation Therapy for Radiorecurrent Prostate Cancer After Brachytherapy

Krishnan R. Patel, MD,* Nicholas R. Rydzewski, MD, MPH,* Erica Schott, CRNP,* Theresa Cooley-Zgela, RN,* Holly Ning, PhD,* Jason Cheng, PhD,* Kilian Salerno, MD,* Erich P. Huang, PhD,† Liza Lindenberg, MD,‡ Esther Mena, MD,‡ Peter Choyke, MD,‡ Baris Turkbey, MD,‡ and Deborah E. Citrin, MD*

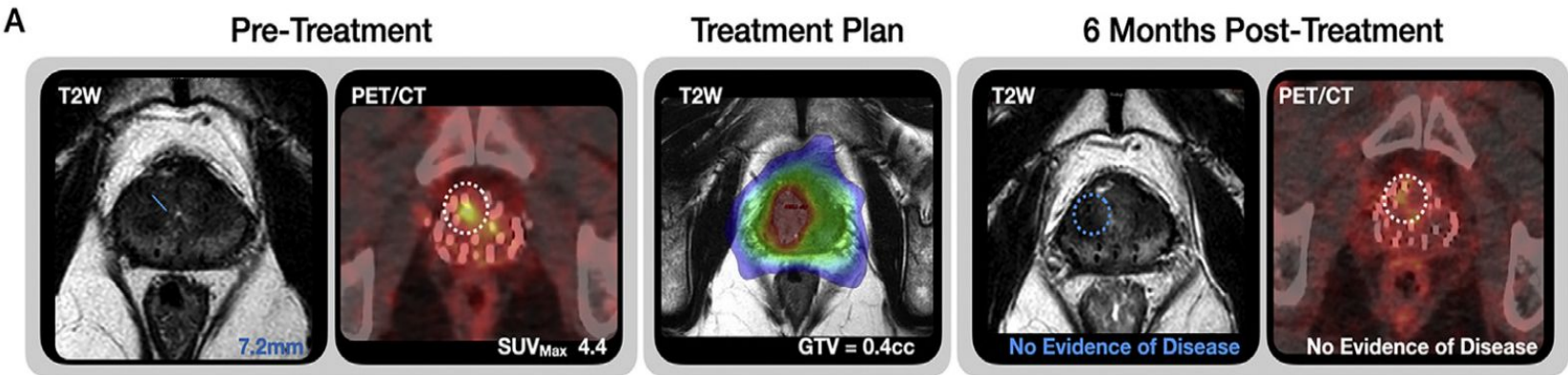
NCT03253744
doi:10.1016/j.ijrobp.2024.02.014



- 9 patients
- mpMRI and PSMA7PET
- Doses: 40Gy, 42.5Gy, 45Gy in 5 fr (DIL) and whole gland 30 Gy

RESULTS: maximum tolerated dose MTD was **42.5 Gy in 5 fr**

- 86% 2-year biochemical progression-free survival rate
- with 1 poststudy failure at 20 months



Case 1: Complete Response (CR) on both MRI and PET/CT at 6 months post salvage SBRT

Case series on multiple prostate re-irradiation for locally recurrent prostate cancer: something ventured, something gained.
Volpe S, Jerezek-Fossa BA, Zerini D, Rojas DP, Fodor C, Vavassori A, Romanelli P, Vigorito S, Rondi E, Comi S, Cambria R, Cattani F, Dicunzio S, De Marco P, Beltramo G, Musi G, De Cobelli O, Marvaso G, Orecchia R.
Neoplasma. 2019 Mar 5;66(2):308-314. doi: 10.4149/neo_2018_180723N520. Epub 2018 Nov 25. PMID: 30509110

ESTRO 2025
Putzu C et al:
Outcomes and Toxicity of a Third Radiotherapy Course for Prostate Cancer Local Recurrence: A Retrospective Analysis





STRA-MI-VT (STereotactic RadioAblation by Multimodal Imaging for Ventricular Tachycardia): rationale and design of an Italian experimental prospective study

C. Carubicchio¹ · B. A. Jereczek-Fossa^{2,3} · D. Andreini^{4,5} · V. Catto¹ · G. Piperno³ · E. Conte⁴ · F. Cattani⁶ · E. Rondi⁶ · S. Vigorito⁶ · C. Piccolo^{6,7} · A. Bonomi⁸ · A. Gorini^{2,9} · M. Pepa³ · S. Mushtaq⁴ · G. Fassini¹ · M. Moltrasio¹ · F. Tundo¹ · G. Marvaso^{2,3} · F. Veglia⁸ · R. Orecchia¹⁰ · E. Tremoli¹¹ · C. Tondo^{1,2}

Received: 16 June 2020 / Accepted: 17 August 2020 / Published online: 27 August 2020
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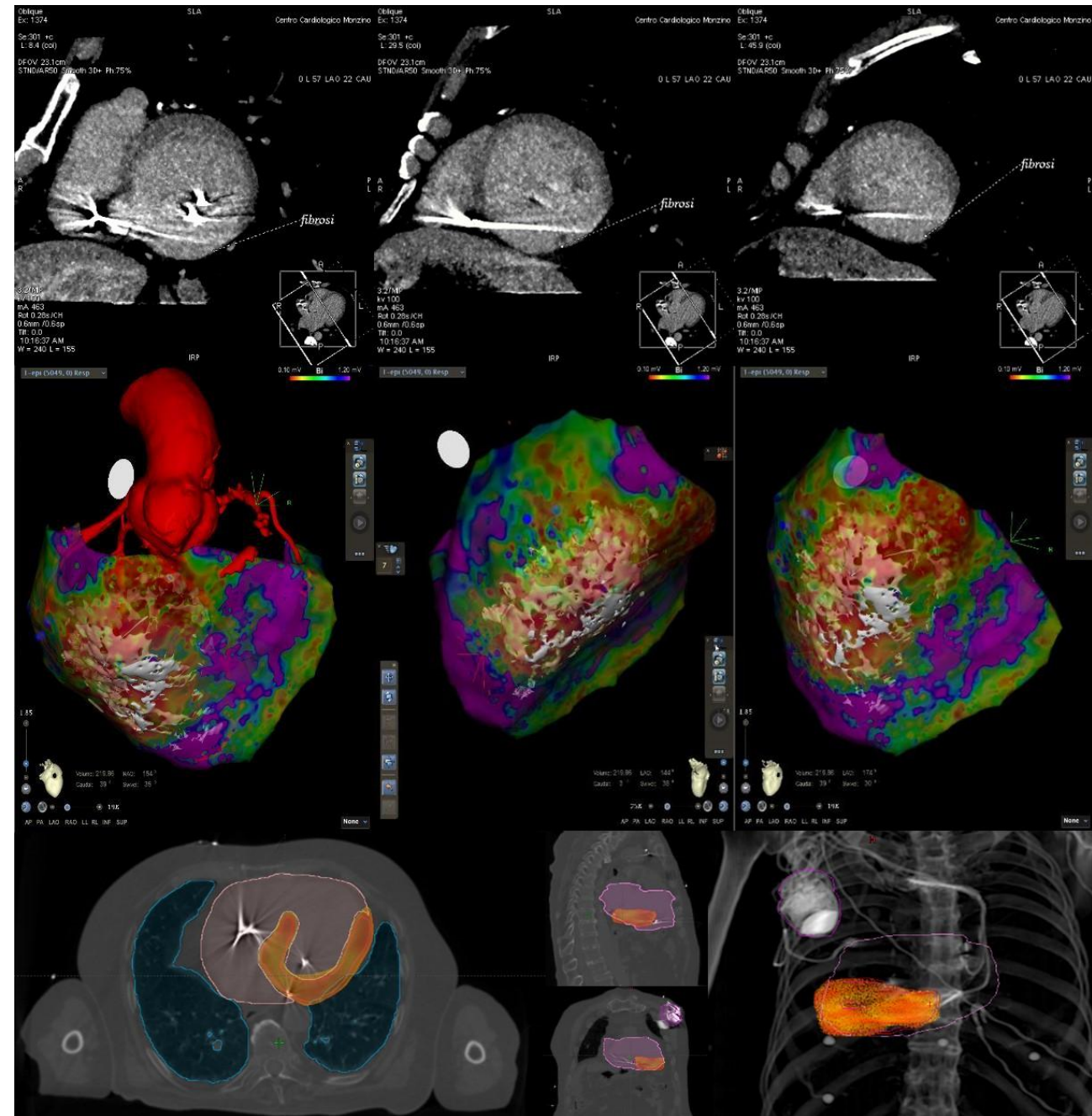
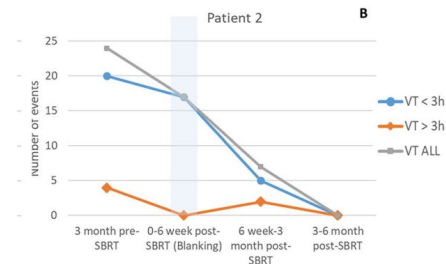
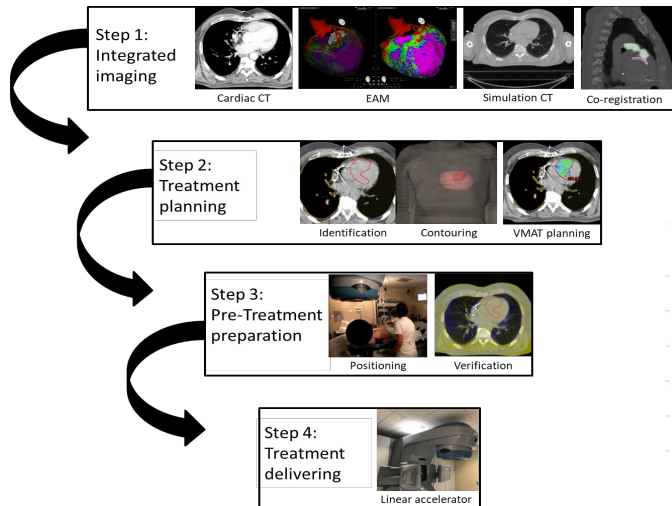
STRA-MI-VT

Journal of Interventional Cardiac Electrophysiology (2021) 62:427–439
https://doi.org/10.1007/s10840-021-01060-5



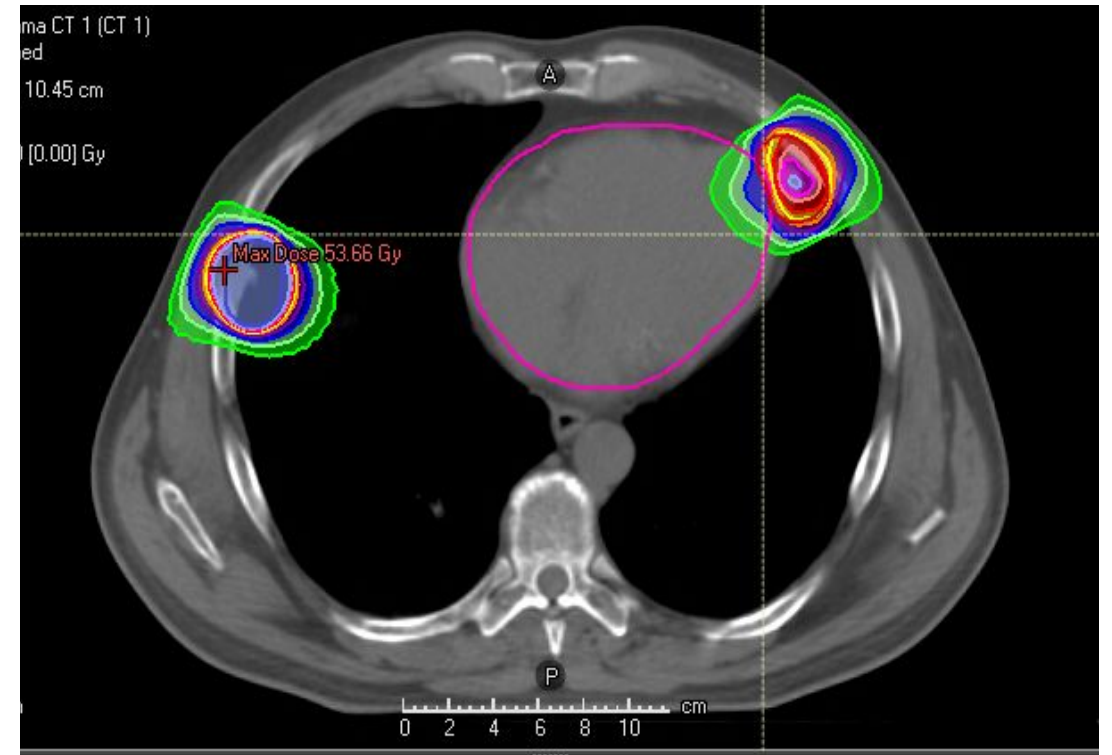
Stereotactic radioablation for the treatment of ventricular tachycardia: preliminary data and insights from the STRA-MI-VT phase Ib/II study

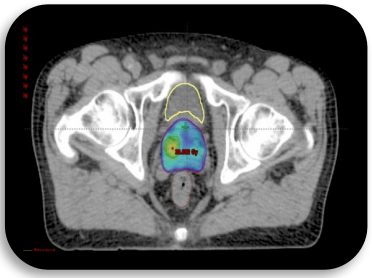
Corrado Carubicchio¹ · Daniele Andreini^{2,3} · Gaia Piperno⁴ · Valentina Catto¹ · Edoardo Conte² · Federica Cattani² · Alice Bonomi² · Elena Rondi² · Consiglia Piccolo² · Sabrina Vigorito² · Annamaria Ferrari⁴ · Matteo Pepa⁴ · Mattia Giuliani⁷ · Saima Mushtaq² · Antonio Scara⁸ · Leonardo Calò⁸ · Alessandra Gorini^{7,9} · Fabrizio Veglia⁸ · Gianluca Pontone² · Mauro Pepi¹⁰ · Elena Tremoli¹¹ · Roberto Orecchia¹² · Giulio Pompilio^{13,14} · Claudio Tondo^{1,14} · Barbara Alicia Jereczek-Fossa^{4,9}



NEW FRONTIERS in Radiation Oncology

- AI and innovation
- New Combinations
- New indications
- Green RT



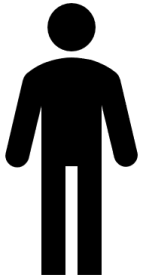


HYPOFRACTIONATION Green Radiotherapy

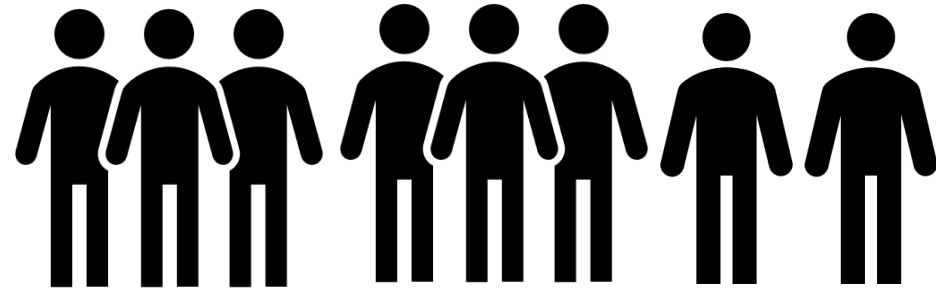
carbon emissions

28 fractions: **17.34 kg CO₂**

5 fractions: **2.18 kg CO₂**



Prostate cancer 40 fractions



8 patients with prostate cancer receiving 5 fractions



GREEN RADIOTHERAPY PI: B Jereczek-Fossa MD PhD

MUSA Multilayered Urban Sustainability Action: smart solutions for renewable energy, new green mobility models, optimize the use of big data for the health and well-being of citizens



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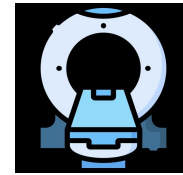
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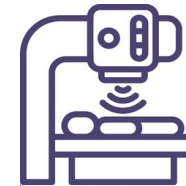
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1. patient travel – average distance to hospital from rural, suburban and urban community

2. pre-treatment imaging – diagnostic imaging and simulation CT



3. LINAC beam-on power per manufacturing data



Carbon-footprint score

6. paper consumption for documentations

5. number of fractions per patient

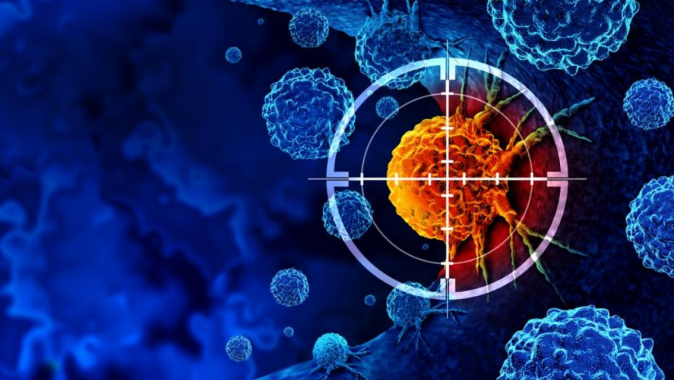
4. LINAC beam-on time, estimated by average time of treatment

Milestone 1-2 (months 6-18):

Development of a **carbon footprint score** that estimate CO2 emissions generated per patient at the end of RT:

- Patients' screening finalized (35000+ patients included from 2012 to 2022)
- Ongoing ML-based analysis to develop a predictive model for carbon footprint
- Assessing the role of hypofractionation

Milestone 3 (months 18-32): Extend the developed score to radiation oncology departments in Lombardy and Italy.



TAKE HOME MESSAGES



- **Radiotherapy is evolving rapidly**, offering personalized precise treatments that improve outcomes and quality of life
- **Hypofractionated and ablative RT** provide excellent efficacy while reducing costs and environmental impact, making treatment more sustainable
- **A strong multidisciplinary team** that integrates RT ensures the best care for patients

