LE SFIDE FUTURE DELLA RADIOTERAPIA

TRA CLINICA E SOSTENIBILITÀ: adroterapia

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Fondazione Umberto Veronesi – per il progresso delle scienze

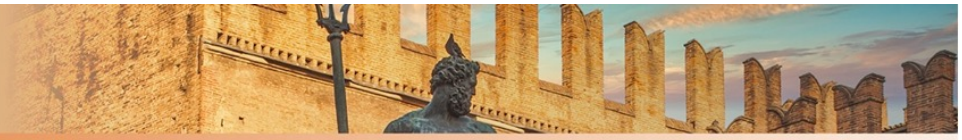
CORE FACULTY

Fondazione IEO · MONZINO
ISTITUTO EUROPEO DI ONCOLOGIA
CENTRO CARDIOLOGICO MONZINO

AIRC

Associazione Italiana Radioterapia e Oncologia clinica

Società Italiana di Radiobiologia



DICHIARAZIONE

Relatore: Barbara Jereczek

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: no
- Consulenza ad aziende con interessi commerciali in campo sanitario: no
- Fondi per la ricerca da aziende con interessi commerciali in campo sanitario: istituzionali – **IBA, Accuray, charity – AIRC, FIEO-CCM. Fondazione Veronesi**
- Partecipazione ad Advisory Board: **IBA, Bayer**
- Titolarità di brevetti in compartecipazione ad aziende con interessi commerciali in campo sanitario: no
- Partecipazioni azionarie in aziende con interessi commerciali in campo sanitario: no
- Partecipazione ai congressi (fee, spese viaggi): **Janssen, Ferring, Bayer, Roche, Astellas, Elekta, Carl Zeiss, Ipsen, Accuray, IBA**

AGENDA

- Green radiotherapy
- Radiotherapy development
- Hadrontherapy (particle beam RT) and how to do it best
- Green particle beam radiotherapy

SUSTAINABILITY

SOSTENIBILITA’

WIKIPEDIA
L’enciclopedia libera

Pagina principale
Ultime modifiche
Una voce a caso
Nelle vicinanze
Vetrina
Aiuto
Sportello informazioni

Comunità

Portale Comunità
Bar
Il Wikipediano
Fai una donazione
Contatti

Strumenti

Voce | Discussione | Leggi | Modifica | Modifica wikitesto | Cronologia | Cerca in Wikipedia

Sostenibilità

Da Wikipedia, l'enciclopedia libera.

La **sostenibilità** è la caratteristica di un processo o di uno stato che può essere mantenuto a un certo livello indefinitamente. In ambito ambientale, economico e sociale, essa è il processo di cambiamento nel quale lo sfruttamento delle risorse, il piano degli investimenti, l'orientamento dello sviluppo tecnologico e le modifiche istituzionali sono tutti in sintonia e valorizzano il potenziale attuale e futuro al fine di far fronte ai bisogni e alle aspirazioni dell'uomo.[1]

Il principio guida della sostenibilità è lo sviluppo sostenibile, che riguarda, in modo interconnesso, l'ambito ambientale, quello economico e quello sociale. I settori culturali, tecnologici e politici sono, invece, considerati come sotto-settori dello sviluppo sostenibile.[2][3] Per sviluppo sostenibile si intende lo sviluppo volto a soddisfare i bisogni della generazione presente senza compromettere la capacità delle generazioni future di far fronte ai propri bisogni.[1] Tuttavia, il primo riferimento storico al concetto di sostenibilità "intergenerazionale" è contenuto nella costituzione pastorale Gaudium et spes pubblicata a conclusione del Concilio Vaticano II nel 1965 [4]. Il termine "sviluppo sostenibile" è stato introdotto per la prima volta dal Rapporto Brundtland

Raggiungere gli obiettivi di sostenibilità permetterà all'uomo di continuare a vivere sulla Terra

https://www.wekiwi.it/main/sostenibilita-energia-del-futuro/
https://it.wikipedia.org/wiki/Sostenibilit%C3%A0

GREEN RADIOTHERAPY

1. Innovation through energy saving new technologies

2. Telemedicine (telehealth)

3. Paper usage reduction (treatment charts, RT plans, Q&A documentations, instructions etc.)

4. Hypofractionation

GREEN RADIOTHERAPY

5. Strategies that improve therapeutic index like particle beam treatments, FLASH, BNCT etc.

6. Personalised radiation oncology (new combinations, biomarkers including AI, radiomics etc.)

7. Evidence based use of radiotherapy as an alternative to more expensive treatments (for example, ablative radiotherapy instead of surgery, radiotherapy for oligoprogressive disease, palliative radiotherapy).

8. **Choosing wisely campaign** – aiming in the resources optimisation (limitation of waste resources)

Associazione Italiana Radioterapia e Oncologia clinica

Slow Medicine

CHOOSING WISELY ITALY

Doing more does not mean doing better

Work in progress

1. Define a therapeutic program forseeing the use of radiation therapy only having previously involved (usually, at time of the tumor first diagnosis**) the radiation oncologist in defining the whole treatment program.**

2. Do not recommend the use of “special” techniques or radiation therapy machines without having previously obtained the **recommendation by a radiation oncologist.**

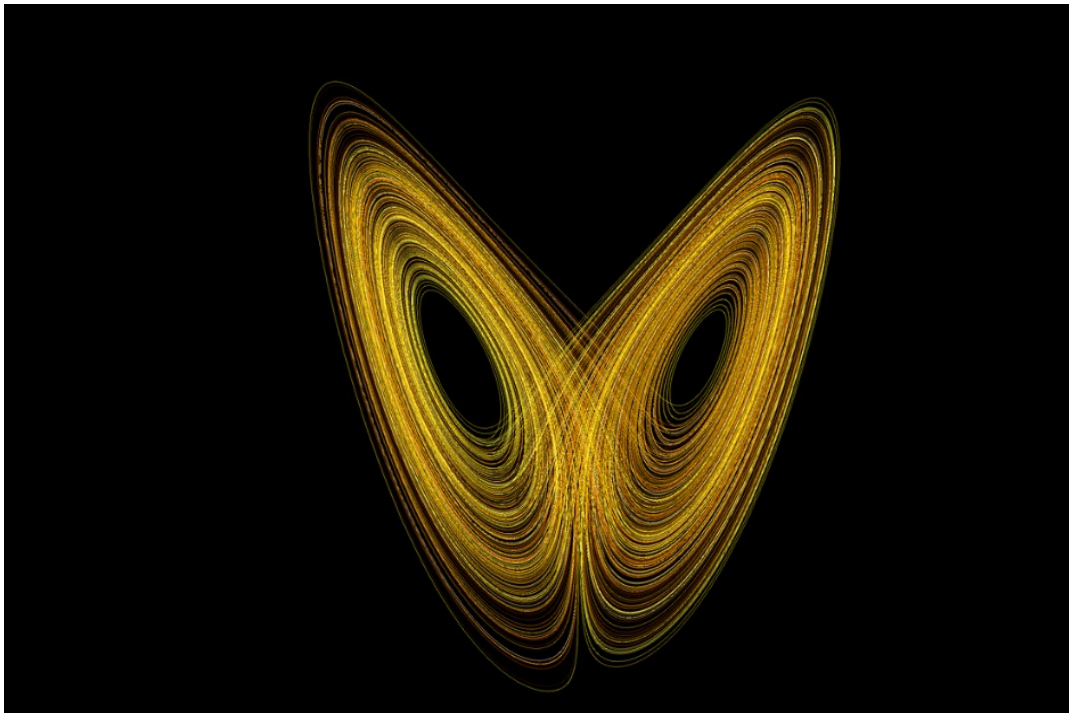
3. Offer radiotherapy delivered with **hypofractionated** schedules when the scientific evidence is already available

4. Use **short radiotherapy schedules for palliative treatments** in frail patients with a short life expectancy

5. **Limit the use of diagnostic procedures** in case of low-risk prostate and breast cancer. Avoid the use of serum biomarkers in early stage breast cancer**.**

BUTTERFLY EFFECT

“il battito di ali di una farfalla può provocare un uragano dall'altra parte del mondo”



https://en.wikipedia.org/wiki/File:Lorenz_attractor_yb.svg

LANDSCAPE OF RT DEVELOPMENT

S. Espenel et al. / European Journal of Cancer 171 (2022) 242e258

AGENDA

- Green radiotherapy
- Radiotherapy development
- **Particle beam RT and how to do it best**
- Green particle beam radiotherapy

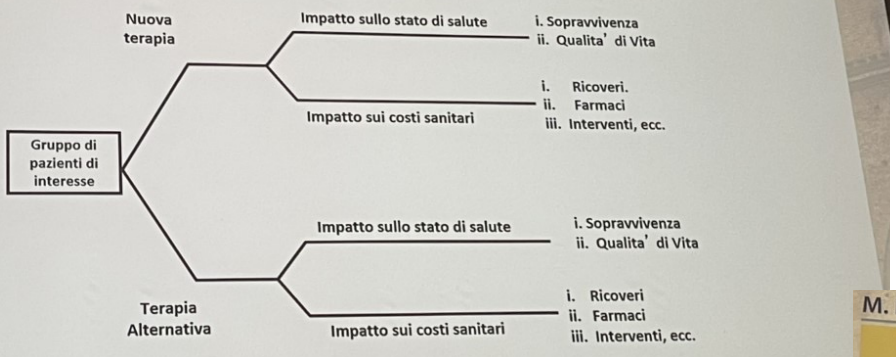
M. Barbieri

AIRO2022

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

Radioterapia di precisione per un'oncologia innovativa e sostenibile

Percorso della valutazione economica in sanità



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Società Italiana di Radiobiologia

BOLOGNA, 25-27 NOVEMB
PALAZZO DEI CONG

M. Barbieri

AIRO2022

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

Radioterapia di precisione per un'oncologia innovativa e sostenibile

Rapporto costi-efficacia incrementale (ICER)

A = Intervento innovativo B = Intervento *standard*

$$ICER = \frac{\text{Costi tot. di A - Costi tot. di B}}{\text{Efficacia di A - Efficacia di B}} = \frac{\Delta \text{ costi}}{\Delta \text{ efficacia}}$$

$$ICER = \frac{\text{Costi incrementali}}{\text{Efficacia incrementale}}$$

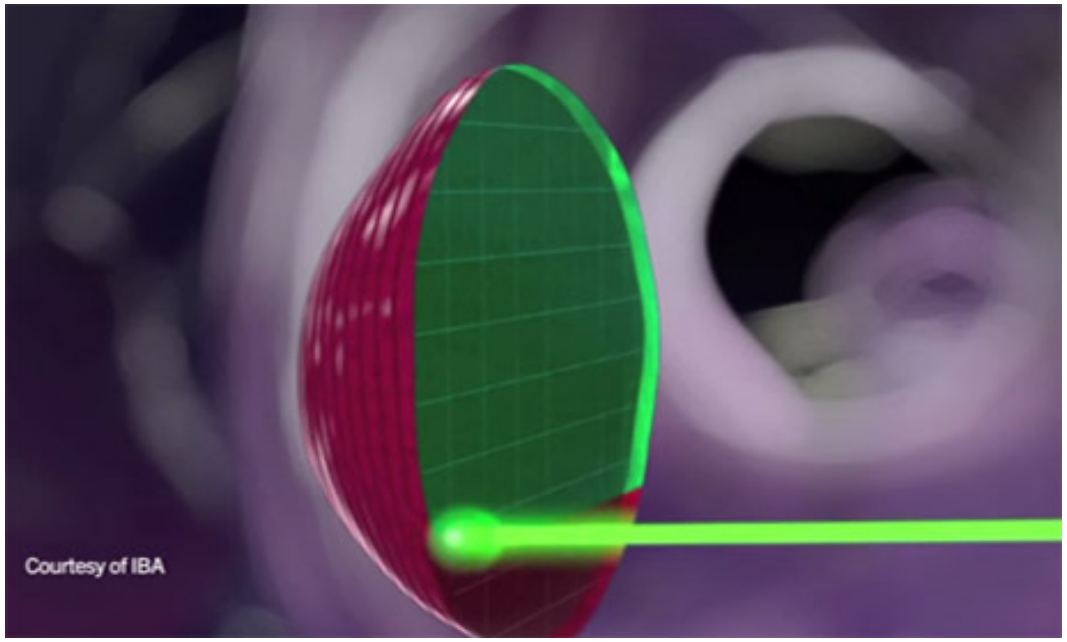
Associazione Italiana Radioterapia e Oncologia clinica
Società Italiana di Radiobiologia

BOLOGNA, 25-27 NOVEMBRE
PALAZZO DEI CONGRESSI

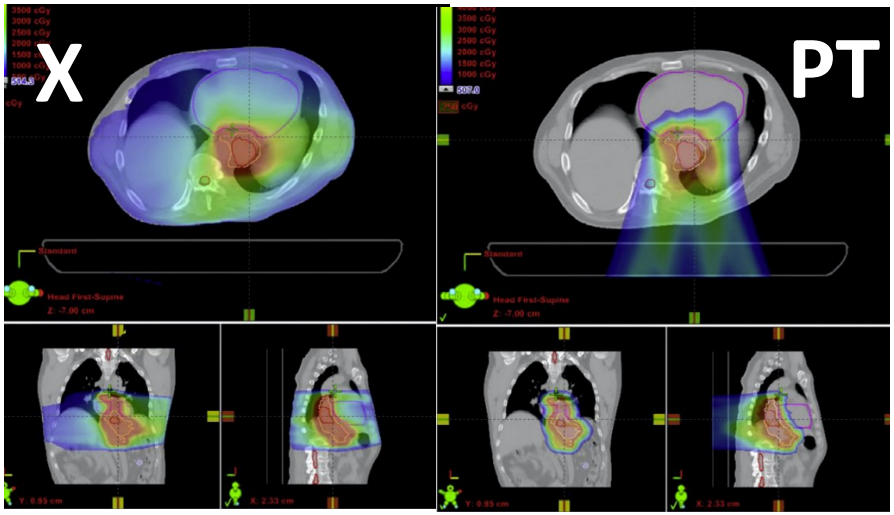
HOW TO MAKE GREEN PT RT

- Planning of new centers
- Networking
- Patient selection
- Multicentric studies
- Hypofractionation

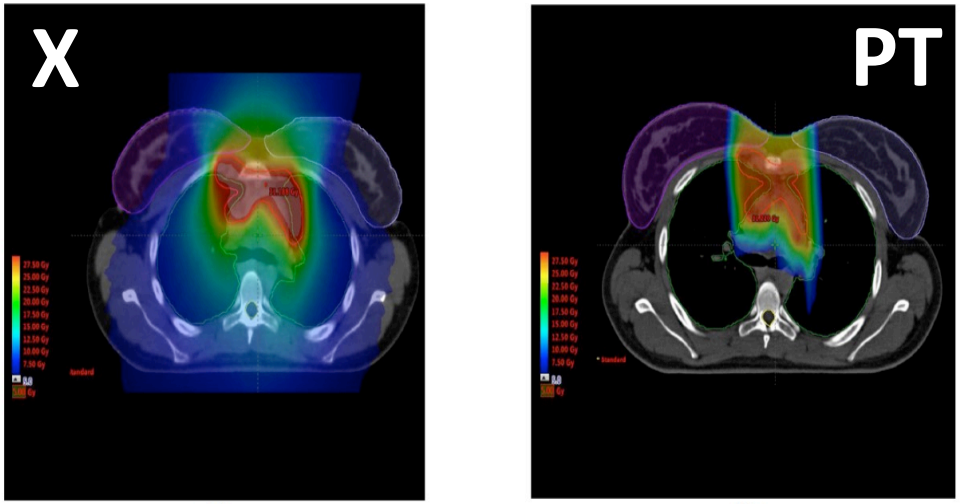
Proton Therapy with pencil beam scanning: increased conformality



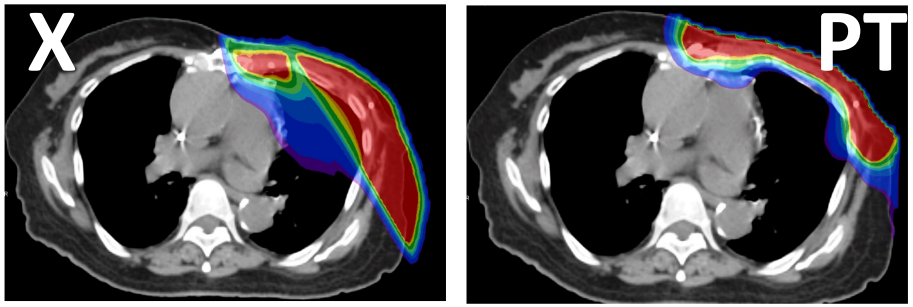
Hard-to-treat-tumors



Oesophageal cancer

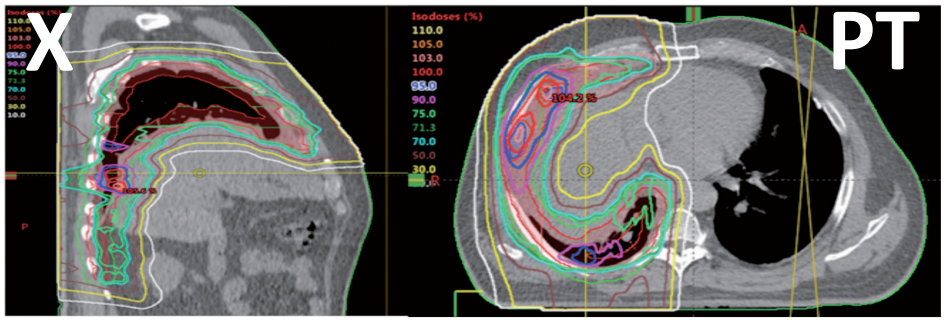


Hodgkin lymphoma



Photons Protons

Breast cancer

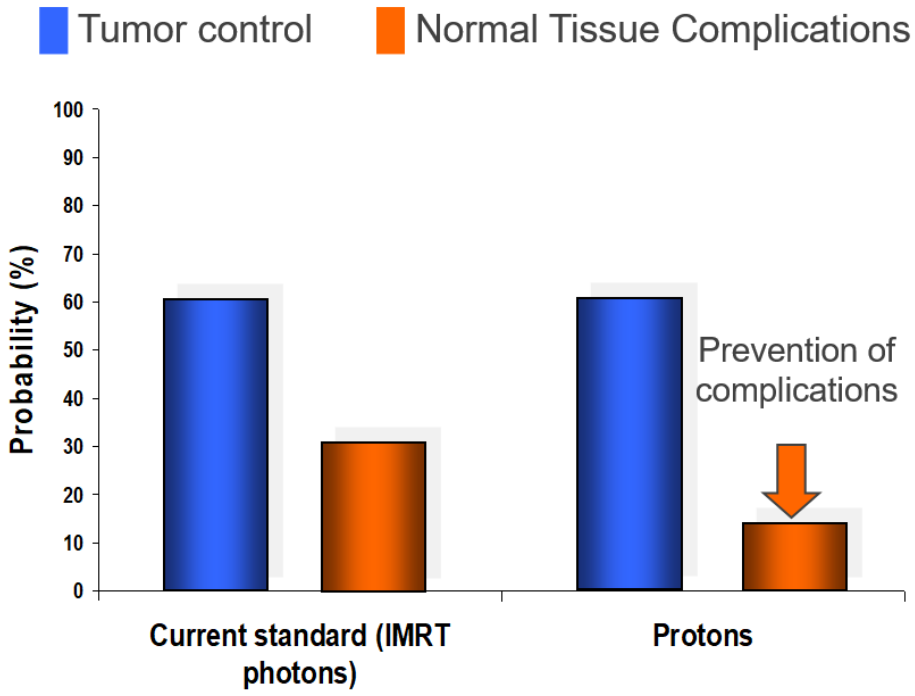


Mesothelioma

Badiyan SN et al Transl Lung Cancer Res 2018;7(2):189-198
Loap et al. Cancers 2021, 13, 3746.

Potential benefits of proton therapy

- **Dose escalation**
  = improvement of local control
- **Better Organ at risk sparing** = reduction of side effects
- **Treatment of choice for re-RT**
- **Lower risk of carcinogenesis**



Graph courtesy of Johannes A. Langendijk, MD, PhD

Which patients could benefit from Proton Therapy?

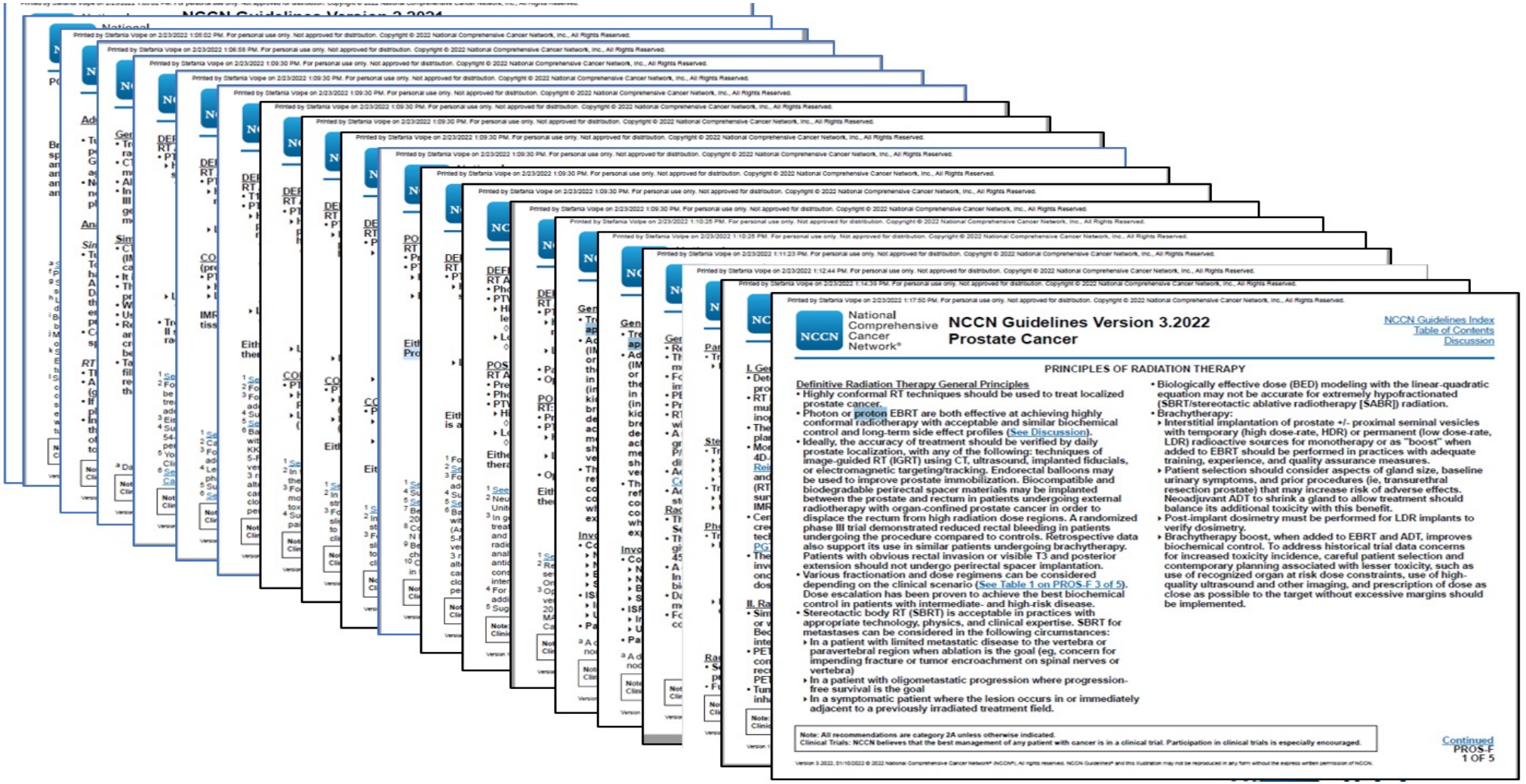
- **Treat standard indications** (0.6%)
  - Uveal Melanoma
  - **Pediatrics**
  - Base of Skull
  - Brain
- **Improvement of local control** (3.0%)
  - **Head & Neck**
  - Prostate
  - Bladder
  - NSCLC
  - Sarcoma
- **Reduce side effects** (12.1%)
  - Intracranial
  - **Head & Neck**
  - GU
  - GI
  - **Breast**
  - **Lung**
  - Re-irradiation
- **Lower risk of induced disorders** (2.0%)
  - Breast
  - **Lymphoma**
  - Testis

Potential of ~ 20% of RT patients

(based on Proton Radiotherapy Horizon scanning report in the Netherlands)

https://www.gezondheidsraad.nl/sites/default/files/proton_radiotherapy200917E_0.pdf

Evidence and guidelines

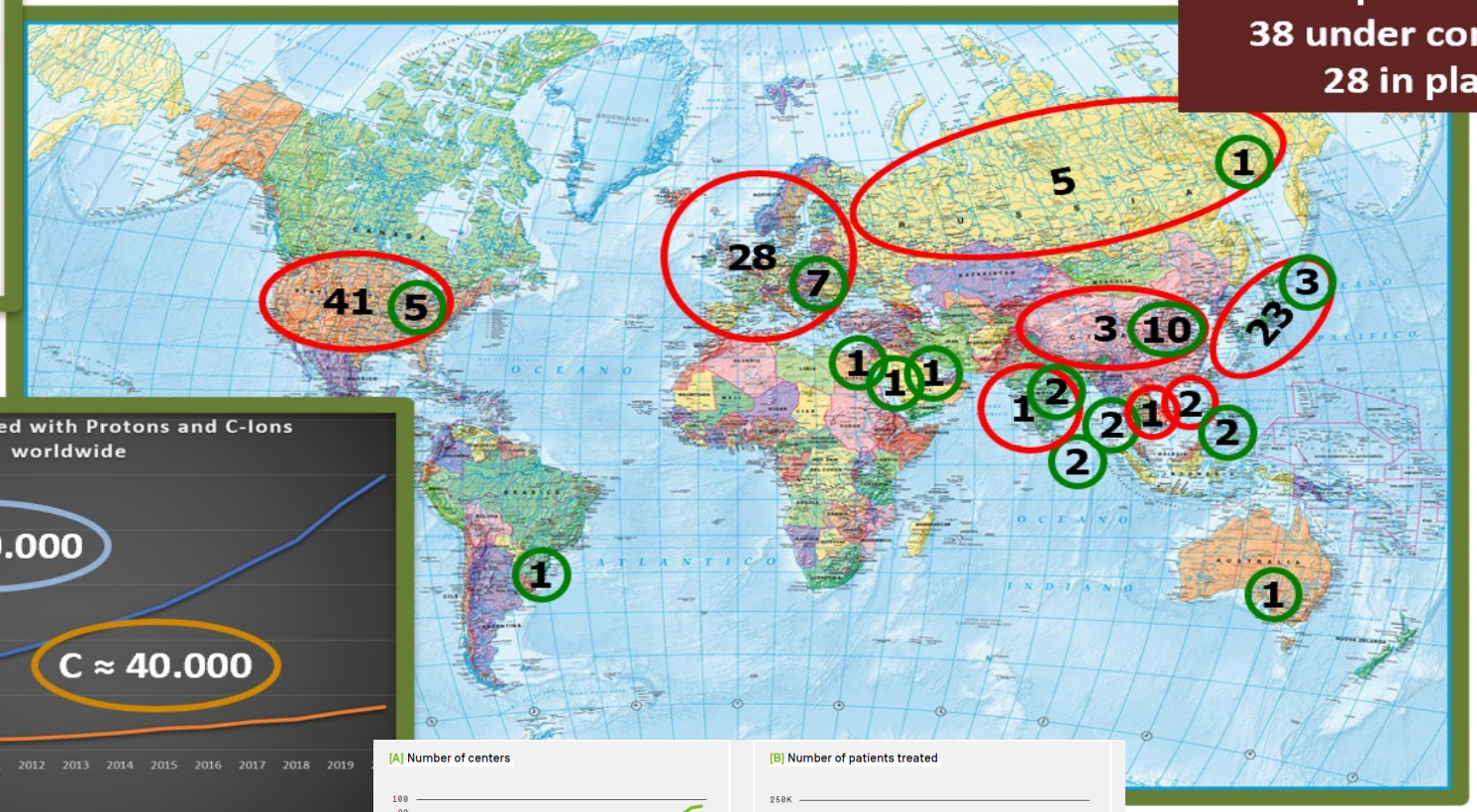


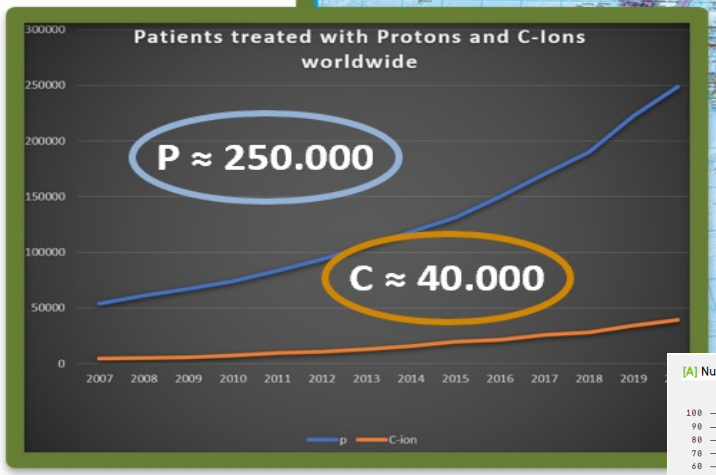
Particle therapy centers worldwide

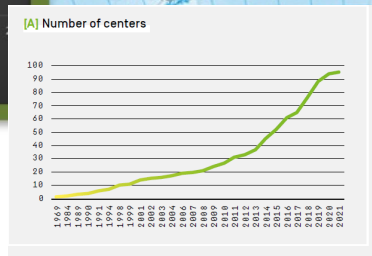
In operation

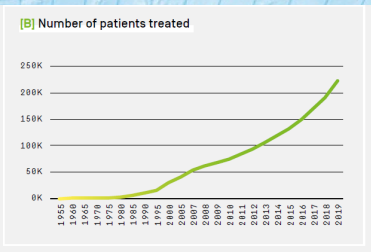
Under construction

104 operating centers
38 under construction
28 in planning



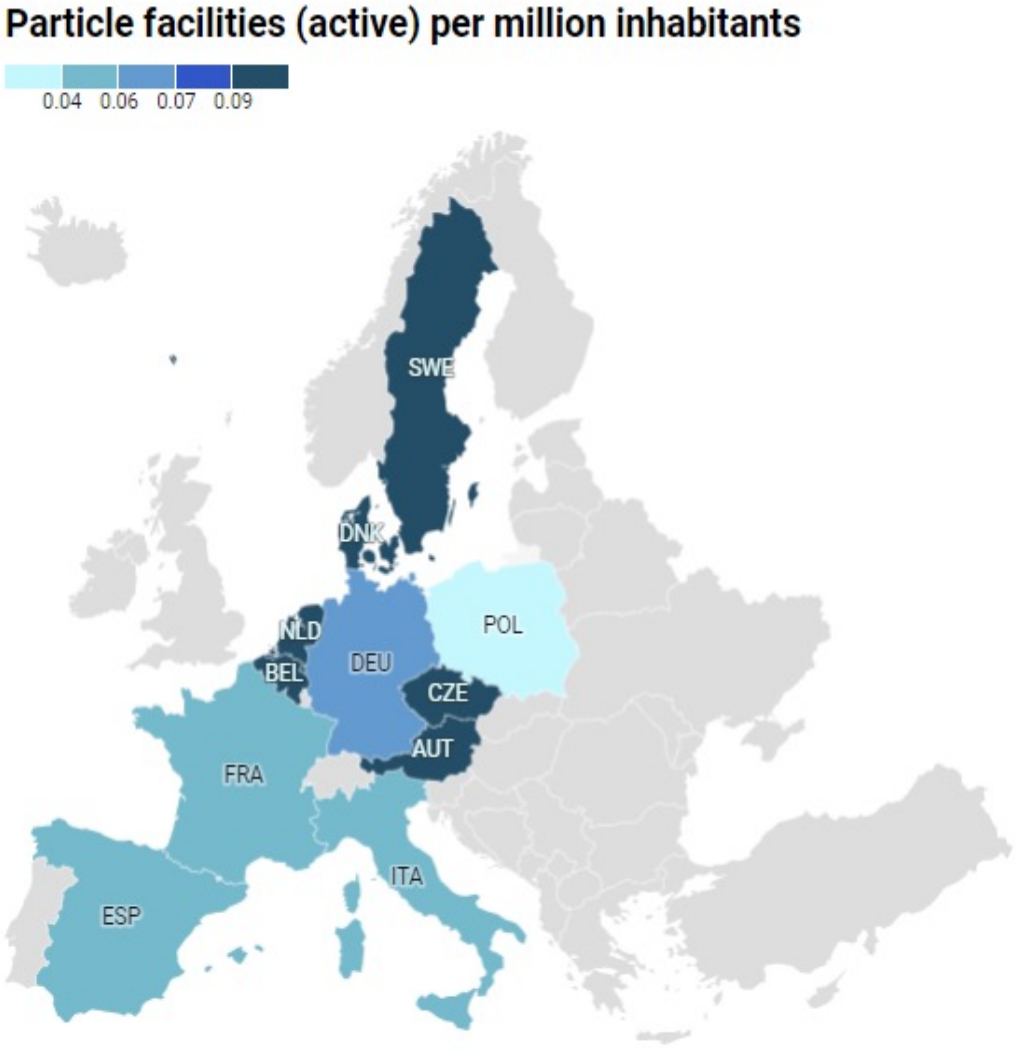




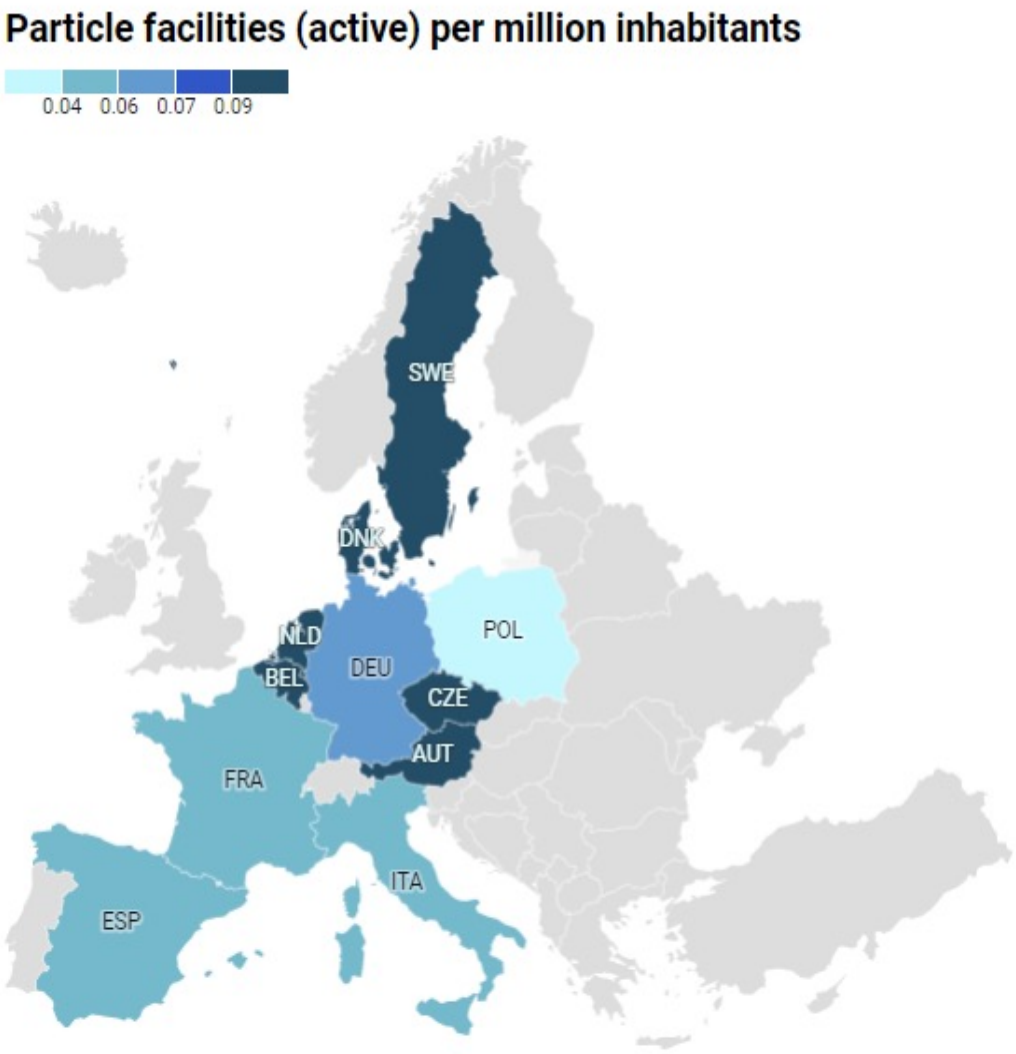


PTCOG Website, April 2022

ratio $P+/C_{-12}$ 6.4 : 1



Mazzola G, Bergamaschi L et al submitted



Mazzola G, Bergamaschi L et al submitted

Iulia-Elena Cazan
August 10, 2020

Who has an access to proton therapy?

Access

in adults patients

1. Clinical decision-making tools (list)

2. Dose comparison methods:

- Normal Tissue Complication Probability model
- Cost-effectiveness modelling
- Dosimetry comparison

Zientara N et Al. J Med Radiat Sci 2021

Who has an access to proton therapy?

Access

in adults patients

1. Clinical decision-making tools (list)

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- Cost-effectiveness modelling
- Dosimetry comparison

Clinical Indication	Country/region				
	UK[18]	United States [22]	Canada[21]	Netherlands[20]	Australia & New Zealand[19]
Chondrosarcoma base of skull/spine					
Chordoma base of skull/spine					
Intraocular melanoma				NR	
Craniopharyngioma		NR			NR
Optic pathway and other selected low-grade glioma		NR			NR
Spinal/paraspinal bone and soft tissue sarcoma (non-Ewing)		NR		NR	
Ependymoma	NR	NR			NR
Hepatocellular cancer	NR		NR	NR	
Intracranial arteriovenous malformation		NR		NR	NR
Lymphoma	NR			<30years	NR
Medulloblastoma		NR	NR		NR
Pelvic sarcoma		NR	NR		NR
Rhabdomyosarcoma	NR	NR			NR
Advanced and/or unresectable head and neck cancers	NR		NR	NR	NR
Esthesioneuroblastoma		NR	NR	NR	NR
Nasopharyngeal carcinoma		NR	NR	NR	NR
Nephroblastoma	NR	NR	NR		NR
Paranasal sinus or nasal cavity	NR	NR		NR	NR
Pineal parenchymal tumours (*excluding pineoblastoma*)	NR	NR		NR	NR
Primitive neuroectodermal tumours	NR	NR		NR	NR
Re-irradiation	NR		NR	NR	
Retinoblastoma	NR	NR	NR		NR
Oesophageal cancer	NR		NR	NR	
Pancreatic cancer	NR		NR	NR	
Prostate cancer	NR	No M	NR	NR	
Lung cancer	NR		NR	NR	
Breast cancer	NR		NR	NR	

Zientara N et Al. J Med Radiat Sci 2021

ITALY: LEA LIST (2022)

- Cordoma & condrosarcoma 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

https://en.wikivoyage.org/wiki/Italy

Radiotherapy and Oncology 167 (2022) 7–13

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Original Article

Current practice in proton therapy delivery in adult cancer patients across Europe

Makbule Tambas [a,*], Hans Paul van der Laan [a], Roel J.H.M. Steenbakkers [a], Jerome Doyen [b], Beate Timmermann [c,d], Ester Orlandi [e], Morten Hoyer [f], Karin Haustermans [g], Petra Georg [h], Neil G Burnet [i], Vincent Gregoire [j], Valentin Calugaru [k], Esther G.C. Troost [l,m,n,o,p,q,r], Frank Hoebers [s], Felipe A. Calvo [t], Joachim Widder [u], Fabian Eberle [v], Marco van Vulpen [w], Philippe Maingon [x], Tomasz Skóra [y], Damien C. Weber [z], Kjell Bergfeldt [aa], Jiri Kubes [ab], Johannes A. Langendijk [a]

https://en.wikipedia.org/wiki/Europe

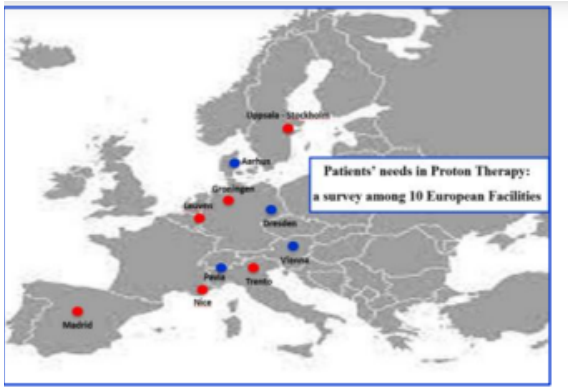
Tumour-site specific factors considered while selecting patients for PT.

Tumour site	Factors
CNS tumours	Good neurocognitive function Molecular type and histology Good prognosis Tumour close to critical structures such as the brain stem
HNC	Good immobilization capacity of the patient during long treatment time Locally advanced HNC with primary tumour close to skull base Tumours of nasopharynx, salivary gland, and paranasal sinus tumours Unilateral tumours Dose reduction to the brain
Lymphoma	Supradiaphragmatic localisation (mediastinal, HNC, axillary, precardiac) Gender (female) Cardiovascular risk factors
Lung cancer	Non-small cell lung cancer Maximal tumour motion <2 cm
Breast cancer	Cardiovascular risk factors Left-sided tumours Internal mammary chain RT Accelerated partial breast RT
Prostate cancer	Difficult anatomic situations (such as bowel loops) Comorbidities (such as colitis ulcerosa) Patient preference
GI cancers	Technical feasibility Reproducibility of tissues
Gynaecological cancers	Pelvic side wall recurrences of cervical cancer Para-aortic RT Oligorecurrences

Reasons for non treating adult pts with PT (by site)

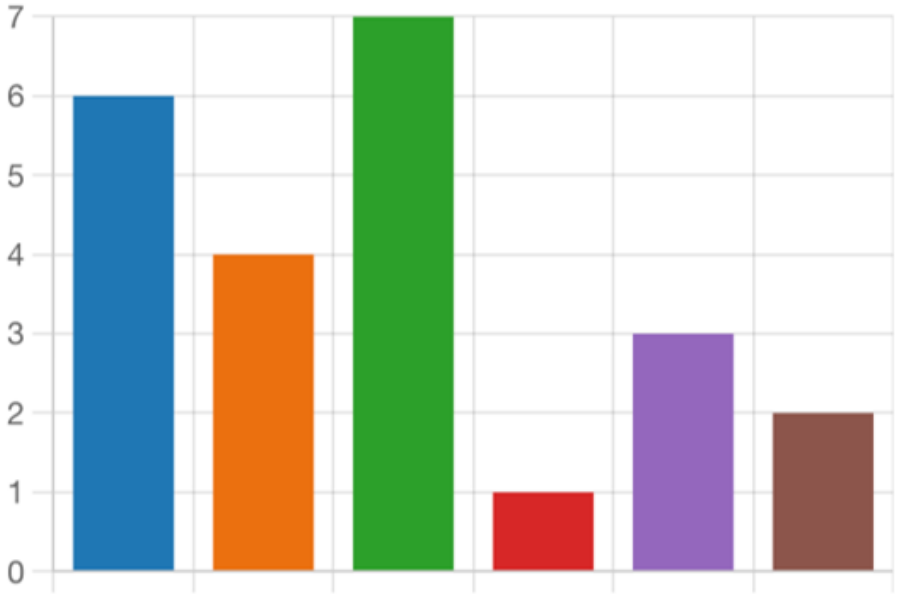
	CNS	HNC	Lymphoma	GI	Breast	Prostate	Lung	Gynaecology	Total
Lack of evidence	0	1	2	4	6	8	6	5	30%
No Reimbursement	0	1	3	4	5	5	5	8	29%
Technical limitations	0	1	5	1	4	1	6	3	20%
No patient referral	0	0	1	2	3	3	3	2	13%
Treatment capacity	0	0	2	0	1	0	0	0	3%
Other	0	0	1	1	0	1	1	1	5%

Thambas M et al. Radiother Oncol 2021, DOI:https://doi.org/10.1016/j.radonc.2021.12.004

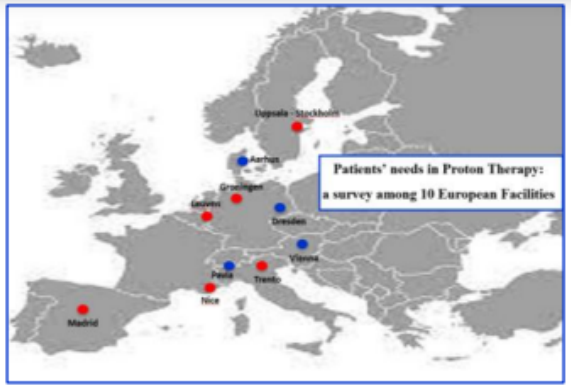


Indications at your center are discussed…

National meetings	6
Regional meetings	4
Institutional multidisciplinary m...	7
In division meetings	1
On individual basis	3
Other	2



Mazzola G, Bergamaschi L et al submitted



Logistic support for PT patients

		Center ID									
		1	2	3	4	5	6	7	8	9	10
Health National System	Economic support for patients' accommodation	✗	✗	✗	✓	✓	✓	✓	✓	✓	✓
	Logistic support for patients' accommodation	✓	✗	✗	✗	✗	✓	✗	✗	✗	✗
	Logistic support for parents of pediatric patients	✗	✓	✗	✓	✗	✓	✗	✗	✗	✗
	Support for meal	✓	✓*	✗	✗	✗	✓	✗	✗	✓*	✗
PT Facilities	Economic/logistic support for patients' accommodation	✓	✓	✓	✓	✓	✓	✓	✓	✗	✓
	Support for meal	✗	✗	✗	✗	✗	✗	✗	✗	✗	✗

Legend: 1. Belgium; 2. Italy-1; 3. Italy-2; 4. France; 5. Netherlands; 6., Denmark; 7. Germany; 8. Austria; 9. Sweden; 10. Spain.; *Regional or Provincial support

Mazzola G, Bergamaschi L et al submitted

Hypofractionation

- Reduces overall treatment time
- Improves patient quality of life
- Increases system capacity
- Reduces direct and indirect costs
- Ecological benefit: **go green**

https://www.appa.org/editorial-guidelines/

Hypofractionated radiotherapy

Tumor site	Examples of randomized studies
Breast Cancer	START-A, START-B, FAST, FAST-FORWARD
Prostate Cancer	HYPRO, HYPO-RT-PC, PACE-B, PACE-C
NSCLC	SPACE, TROG 09.02 CHISEL
Rectum	Swedish trial, Polish II trial
Oligometastic cancer	SABR-COMET, SAFRON

Hypofractionated radiotherapy

Tumor site	Examples of randomized studies
Breast Cancer	START-A, START-B, FAST, FAST-FORWARD
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NSCLC	SPACE, TROG 09.02 CHISEL
Rectum	Swedish trial, Polish II trial
Oligometastic cancer	SABR-COMET, SAFRON
Proton therapy	

Tab. 3.5: Le categorie di costo nella valutazione economica

Costi diretti sanitari: risorse associate al trattamento e all'assistenza sanitari.

- Farmaci
- Visite mediche (medico di famiglia, specialista, Pronto Soccorso)
- Terapie di supporto (riabilitazione, lungodegenza, psicoterapie, ecc.)
- Esami di laboratorio
- Diagnostica strumentale
- Assistenza infermieristica domiciliare
- Ospedalizzazioni (ricoveri e day hospital)

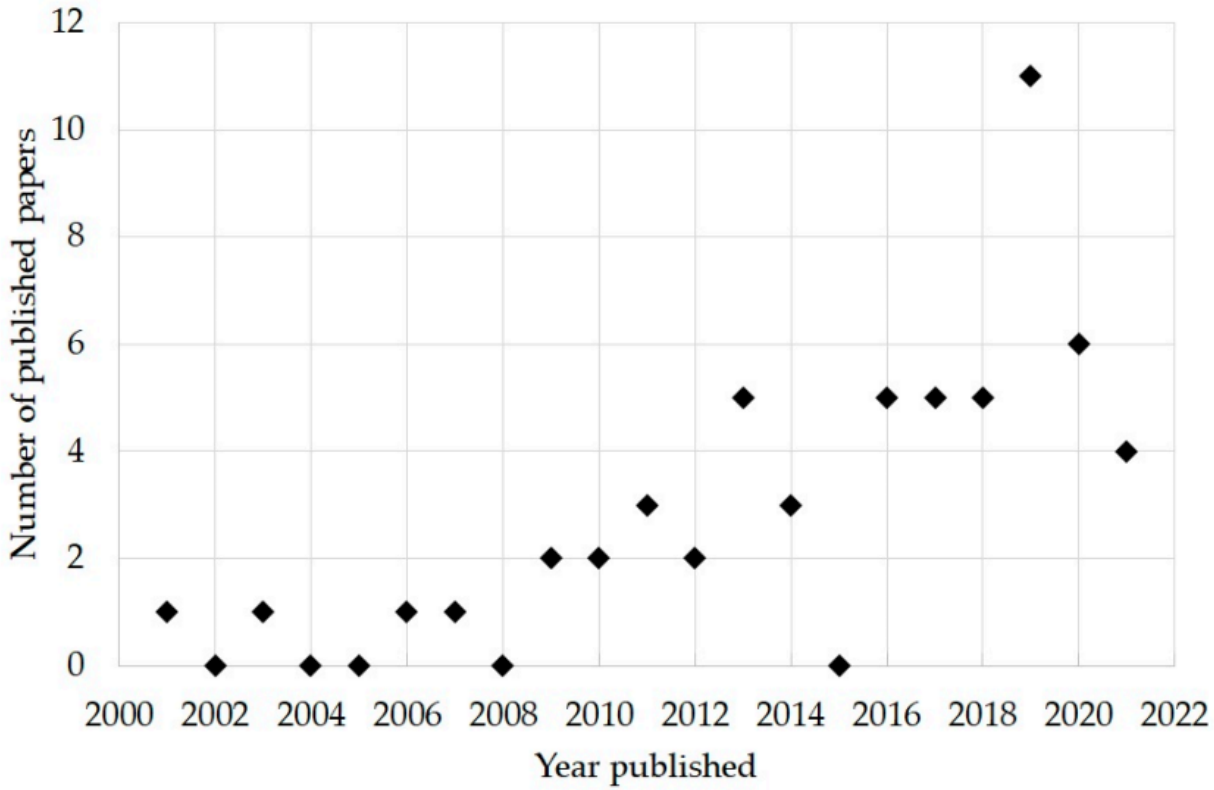
Costi diretti non sanitari: risorse non sanitarie impiegate da enti assistenziali non sanitari, dai pazienti e dai familiari.

- Servizi sociali (assistente sociale)
- Assistenza domestica (servizi pasti, pulizie)
- Trasporto (ad esempio per recarsi presso il medico per la visita)
- Assistenza fornita dai familiari al di fuori dell'orario di lavoro

Costi indiretti: risorse non prodotte a causa della malattia, sia da parte dei pazienti che dei familiari.

- Giornate di lavoro perdute per trattamento eassistenza sanitaria
- Giornate di lavoro perdute dai pazienti per la disabilità momentanea
- Giornate di lavoro perdute dai familiari per l'assistenza ai pazienti

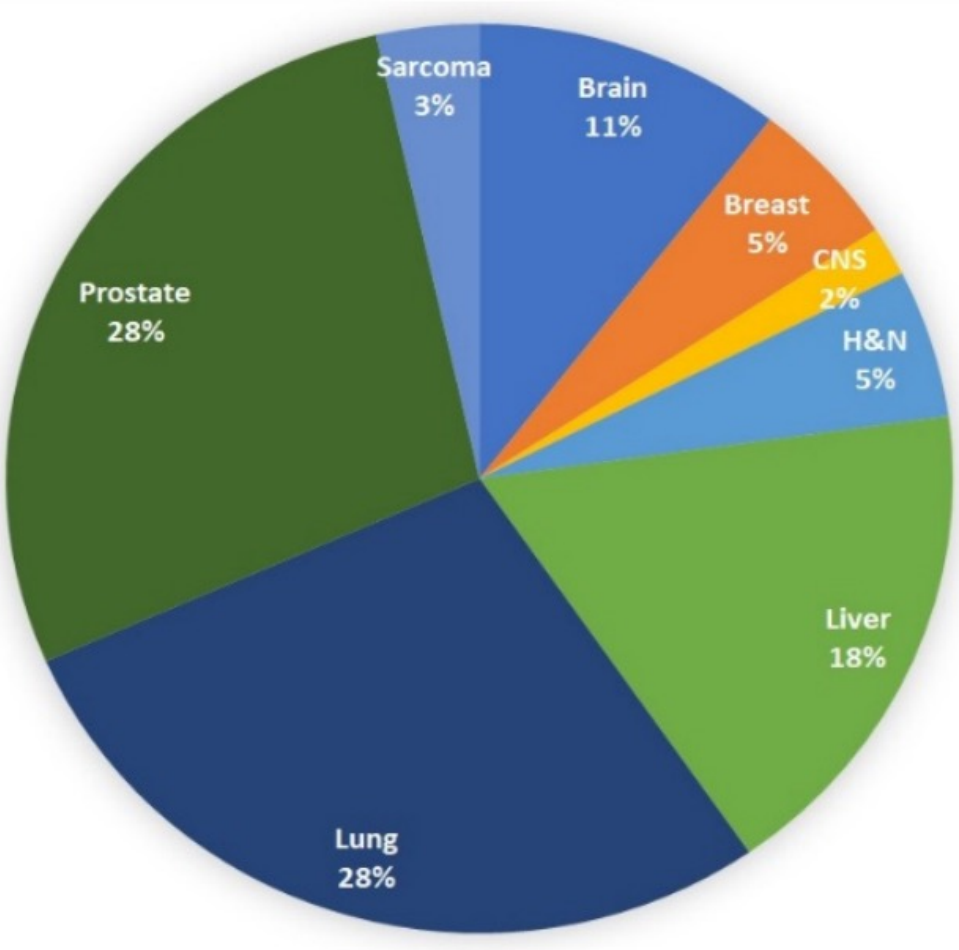
Hypofractionated proton radiotherapy



Percentage of publications reporting on clinical outcomes with hypofractionated proton therapy between 2001 and 2021.

Santos, A et al. The Role of Hypofractionation in Proton Therapy. Cancers 2022, 14, 2271. https:// doi.org/10.3390/cancers14092271

Hypofractionated proton radiotherapy



Santos, A et al. The Role of Hypofractionation in Proton Therapy. Cancers 2022, 14, 2271. https:// doi.org/10.3390/cancers14092271

Breast Cancer Research and Treatment (2022) 192:249–263
https://doi.org/10.1007/s10549-022-06516-4

REVIEW

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

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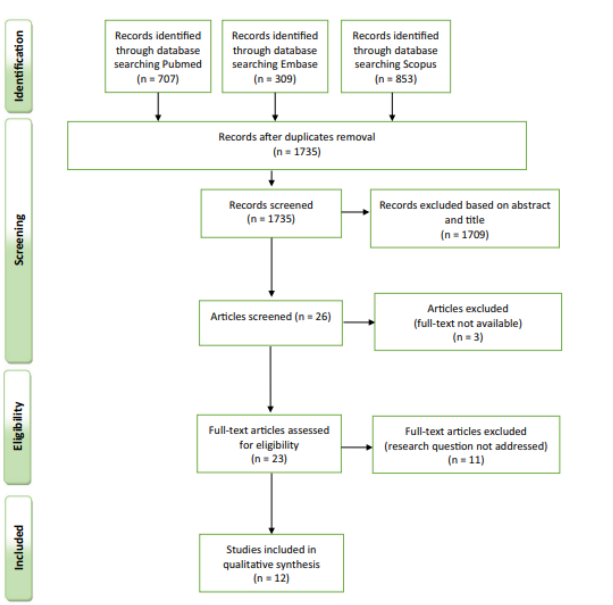
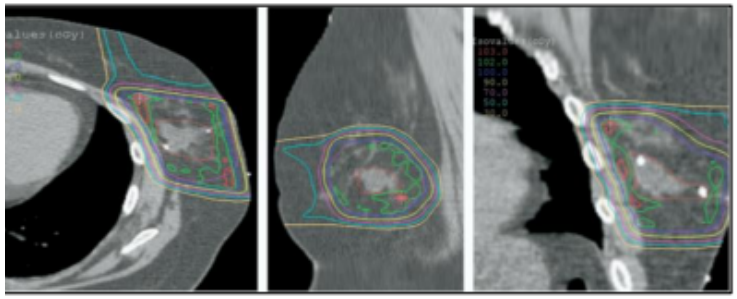


Breast Cancer



All studies but one focused on **accelerated partial breast irradiation (APBI).**

The **dosimetric profile of PT compared favorably** with both photon-based 3D conformal and intensity-modulated techniques

More extended follow-up is warranted to fully assess both the long-term toxicities and the non-inferiority of oncological outcomes.

Courtesy of Daniela Alterio

Courtesy of Daniela Alterio

Lung cancers

Cancer Treatment Reviews 110 (2022) 102464

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

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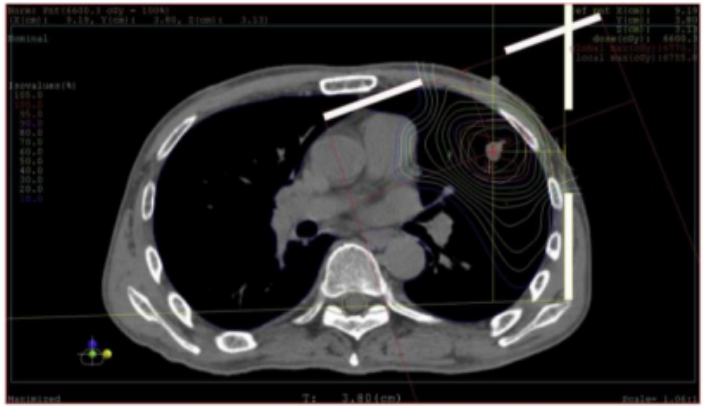
Systematic review- meta-analysis

Curative-intent hypofractionated PBT

ES-NSCLC (≥3 Gy(RBE)/fraction)



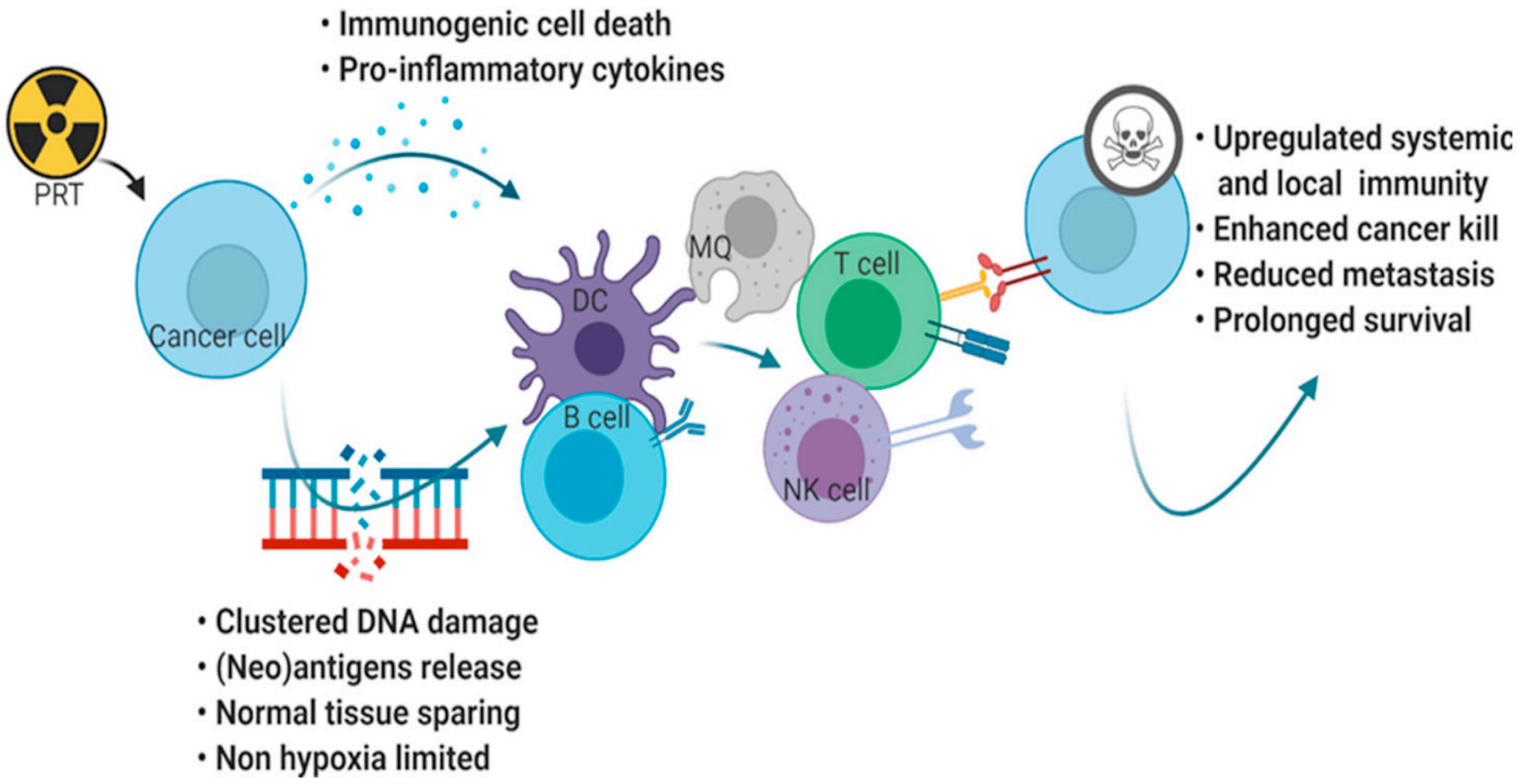
Methods

The **BED** was calculated for each included study (α/β = 10 Gy)
the **median BED** was used as a **threshold** for stratifying into **"high" and "low"-dose subgroups**.

Eight studies and **401 patients**
Median follow-up was **32.8 months**.

Hypofractionated PBT is a safe and effective treatment option for ES-NSCLC; the delivery of BED ≥ 105.6 Gy(RBE) with advanced techniques for uncertainty management has been associated with improved oncological outcomes across all considered time point

Proton therapy and immunotherapy: improved therapeutic index?



Marcus D et al Cancers **2021**, 13, 1468. https://doi.org/10.3390/cancers13061468

TAKE HOME MESSAGES

- Particle beam RT is an innovative treatment option for selected cases
- Indicated for difficult cases (tumor position, radioresistance)
- New combinations (immunotherapy, target therapy, surgery)
- New areas of research (biology, radiomics, hypofractionation)
- Key words for sustainability:

  integration, networking, hypofractionation

https://velvetpets.it/2017/07/11/farfalle-quanto-vivono/