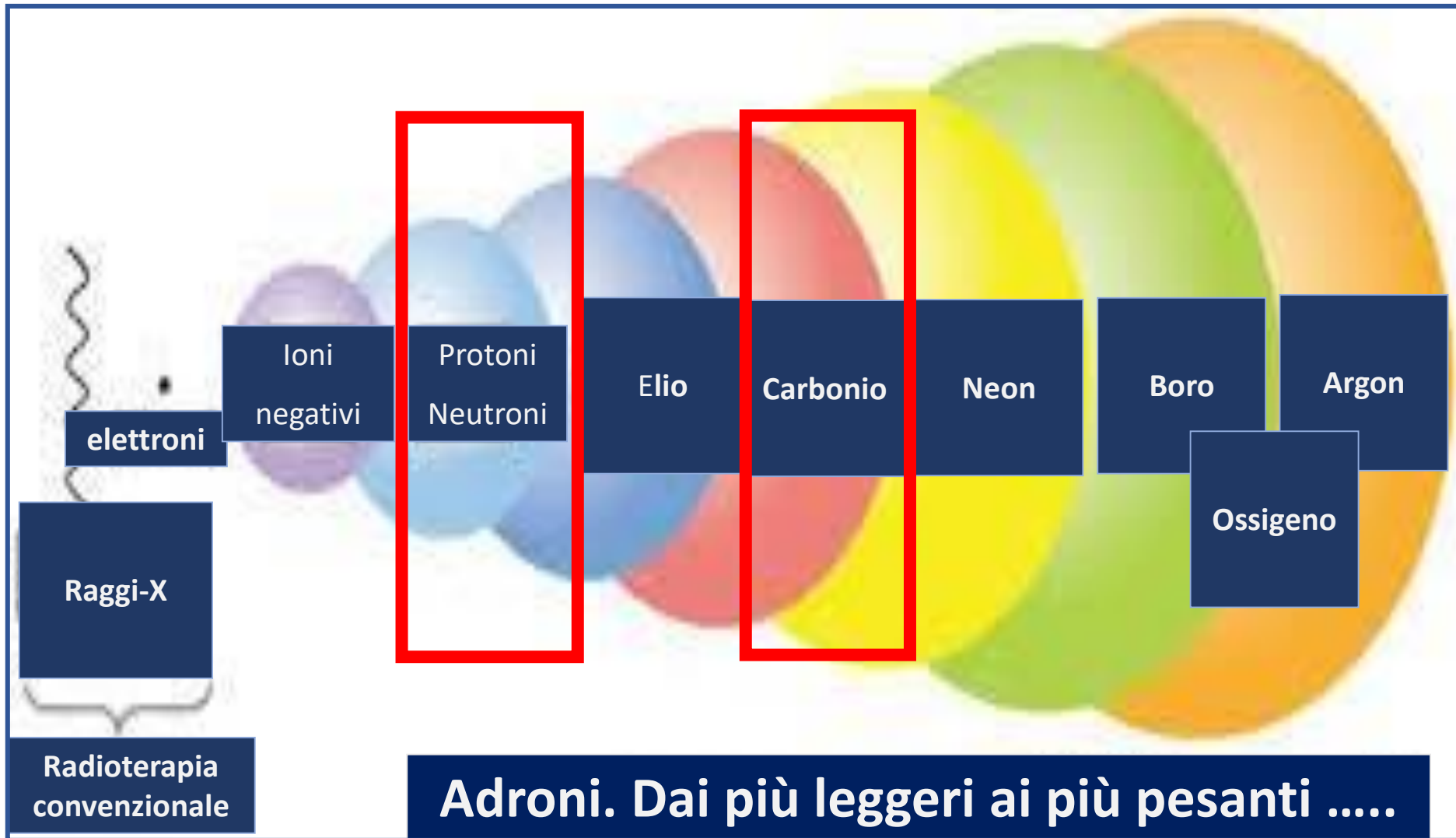
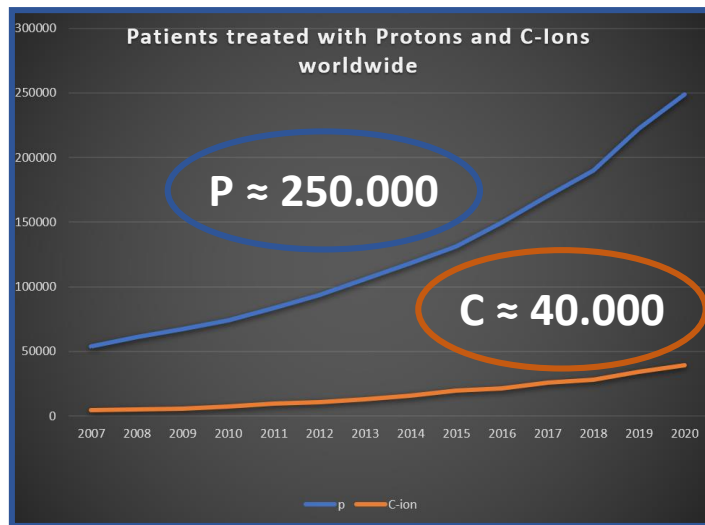


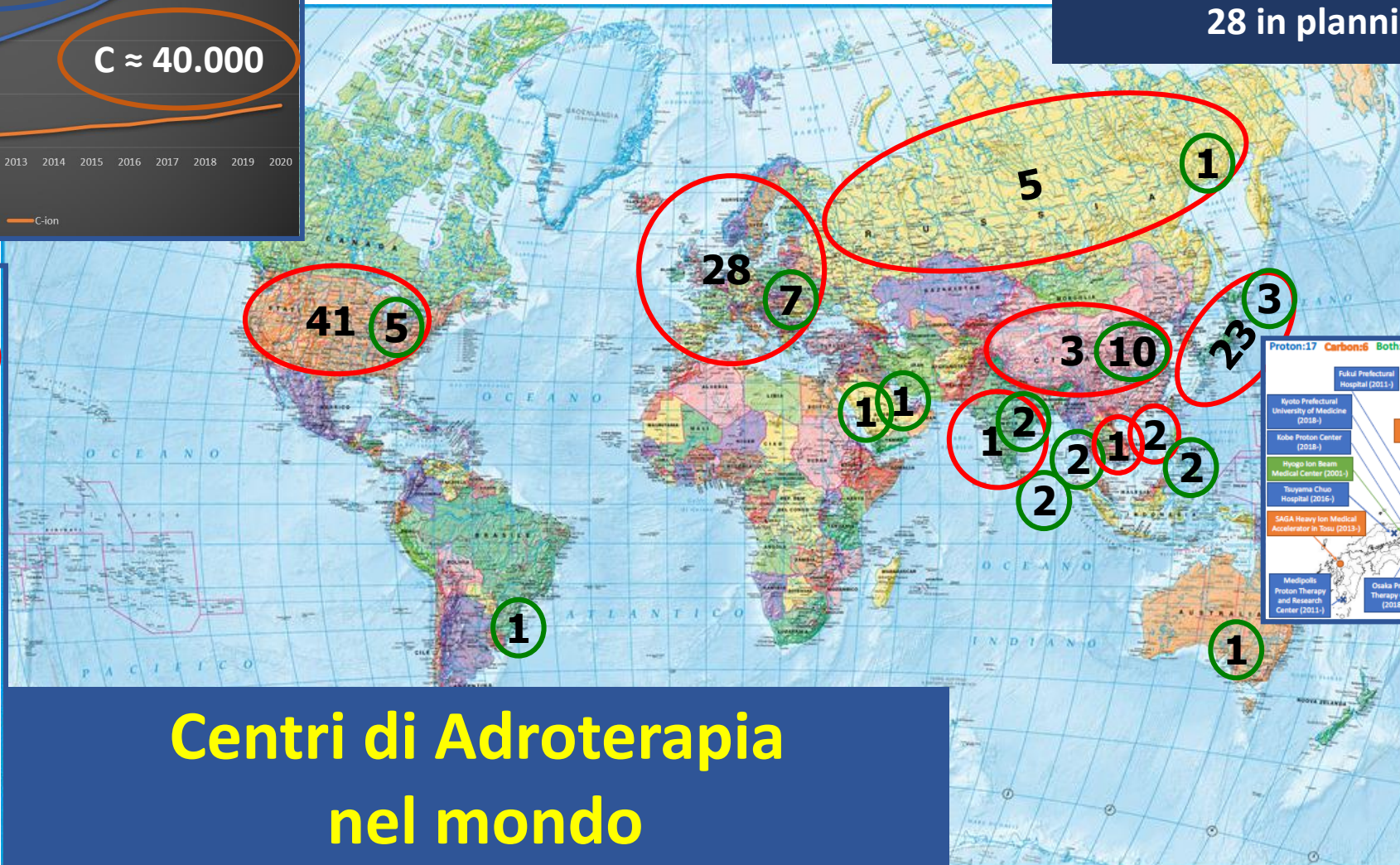
Stato dell'arte dell'adroterapia: Aspetti clinici

Roberto Orecchia





104* Centri in attività
38** in costruzione
28 in planning



In attività

In costruzione

***12 con
Ioni Carbonio
**5
in costruzione**

Centri di Adroterapia nel mondo



Vent'anni di Cnao.



Centri con Ioni Carbonio



Mayo, Jacksonville

PARALLEL OPPOSED EDITORIAL

We are ready for clinical implementation of Carbon Ion Radiotherapy in the United States

J Appl Clin Med Phys 2020; 21:12-6-9



PTCOG website, Ottobre 2021



Vent'anni di Cnao.

California, PBT (2003-2016) [11]		Japan, PBT (1979-2013) [77]		Japan, CIRT (1994-2017) [78]		UK (Christie), PBT (2018-2019) [8]		
Site	Percentage	Site	Percentage	Site	Percentage	Population	Site	Percentage
Prostate	41.3	Prostate	30.0	Prostate	24.7	Pediatric and young adult (~24 yr)	CNS	38.9
Breast	14.0	Liver	19.0	Bone and soft tissue	11.5		H&N	15.7
Eye/orbit	11.8	H&N	13.0	H&N	9.6		Body	10.2
Lung	6.1	Lung	12.0	Lung	9.2		Spine	6.5
CNS	6.0	GI	6.0	Pancreas	5.4		CSI	1.9
Lymphoma/leukemia	2.9	Pancreas	4.0	Liver	5.3	Adult	CNS	8.3
Liver	2.4	Sarcoma	3.0	Rectum (recur)	4.9		H&N	3.7
H&N	2.3	CNS	3.0	Uterus	2.5		Body	0.9
Female genital	2.1	Others	10.0	Uveal melanoma	1.8		Spine	13.9
Colon and rectum	3.0			Abdominal LN	1.2			
Others	9.1			CNS	0.9			
				GI tract	0.8			
				Re-irradiation	9.2			
				Others	13.0			
Total	100 (n=8,609)	Total	100 (n=15,000)	Total	100 (n=11,580)	Total		100 (n=108)

Pazienti trattati nelle varie sedi

Stati Uniti

Astro Model Policy, group 1: disease sites that frequently the use of proton ocular tumors, including intraocular melanomas

Tumors that approach or are located at the base of skull, including but not limited to chordoma or chondrosarcomas

Primary or metastatic tumors of the spine where the spinal cord tolerance may be exceeded with conventional treatment or where the spinal cord has previously been irradiated

Hepatocellular cancer

Primary or benign solid tumors in children treated with curative intent and occasional palliative treatment of childhood tumors when at least one of the four criteria noted above apply

Patients with genetic syndromes making total volume of radiation minimization crucial such as but not limited to NF-1 patients and retinoblastoma patients

Malignant and benign primary CNS tumors

Advanced (e.g., T4) and/or unresectable head and neck cancers

Cancers of the paranasal sinuses and other accessory sinuses

Non-metastatic retroperitoneal sarcomas

Re-irradiation cases (where cumulative critical structure dose would exceed tolerance dose)

Base cranica, spinali, occhio, pediatrici, fegato, re-irradiazioni, H&N, SNC, sarcomi, sindromi genetiche

Base cranica, spinali, pediatrici, seni paranasali

Gran Bretagna

Pediatric tumor
Most pediatric tumors, malignant and benign

Adult
Base of skull tumors (radioresistant)
Spinal and paraspinal tumors (radioresistant)
Paranasal sinus tumors with base of skull involvement

Giappone

PBT
Pediatric cancer
Bone and soft tissue sarcoma
Head and neck
Prostate

CIRT
Bone and soft tissue sarcoma
Head and neck
Prostate

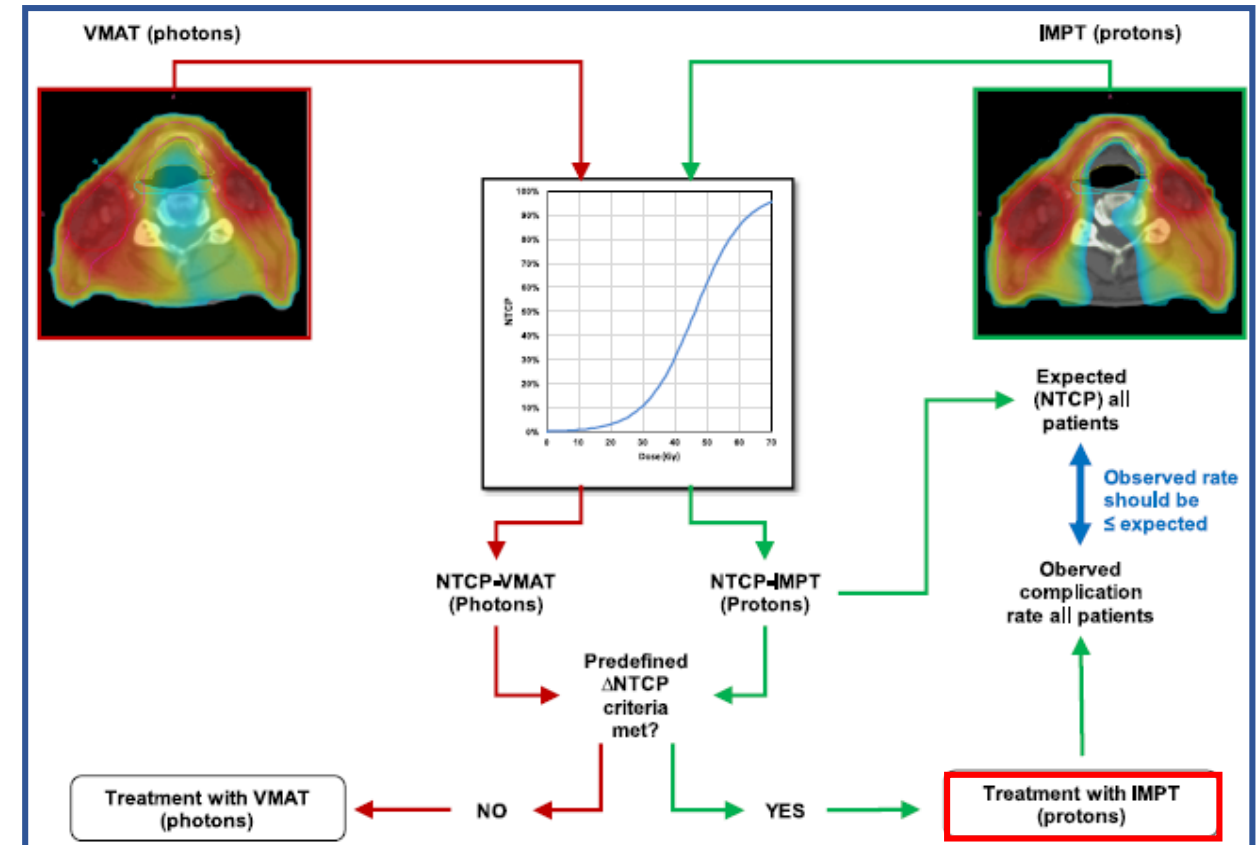
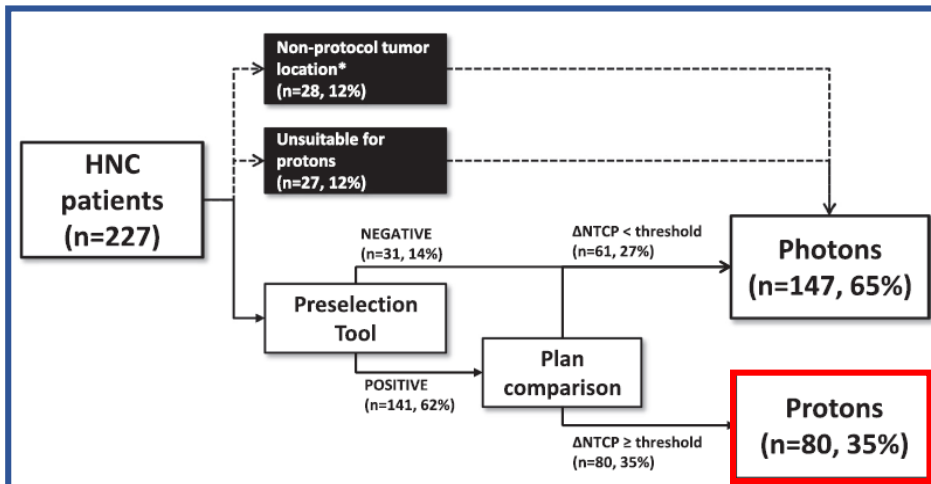
Sarcomi, H&N, prostata, pediatrici

Raccomandazioni sulle indicazioni in vari Paesi

Standard indication
Skull base or spinal chordoma and chondrosarcoma
Other intracranial, spinal, and paraspinal tumors, including meningioma
Pediatric tumors, including bone tumors, soft-tissue sarcoma, low-grade glioma, meningioma, medulloblastoma, ependymoma, and neuroblastoma
Potential indications (cases for which protons may be specifically utilized to improve local control)
Re-irradiation (malignant brain tumors, head and neck cancer)
Paranasal sinus tumors, nasopharyngeal carcinoma, prostate, NSCLC, retroperitoneal sarcoma
Model based indication (cases where proton will be utilized to reduce side effect)
Re-irradiation (meningioma, head and neck cancer)
Head and neck cancers, prostate
Reduction of secondary cancer
Breast cancer
Lymphoma
Testis

Base cranica, spinali, pediatrici,
re-irradiazioni, H&N, prostata, polmone,
mammella, linfomi, testicolo

National Protocol for **Model-Based** Selection for Proton Therapy in Head and Neck Cancer



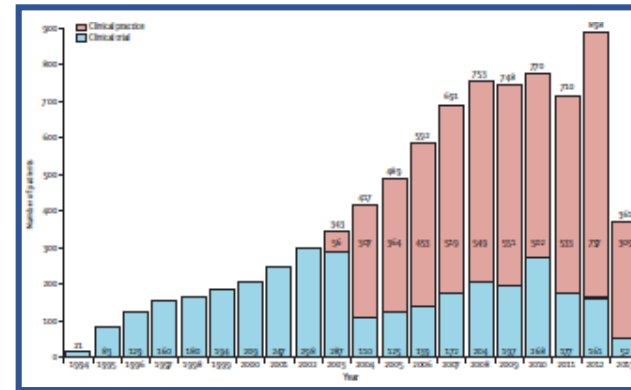
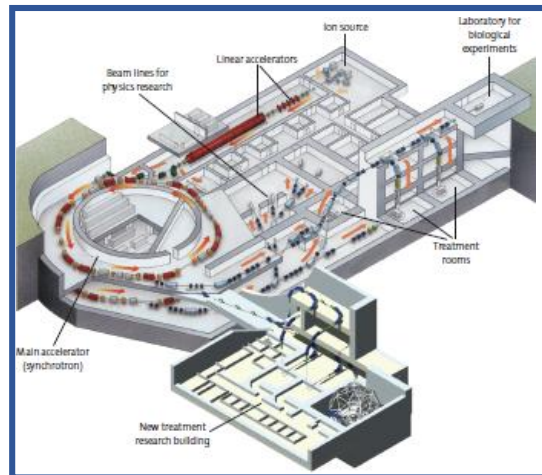
Il modello olandese

Carbon ion radiotherapy in Japan: an assessment of 20 years of clinical experience

Tadashi Kamada, Hirohiko Tsujii, Eleanor A Blakely, Jürgen Debus, Wilfried De Neve, Marco Durante, Oliver Jäkel, Ramona Mayer, Roberto Orecchia, Richard Pötter, Stanislav Vatnitsky, William T Chu



Vent'anni di Cnao.



CIRT provided favourable outcomes for patients with radioresistant H&N tumours such as **malignant mucosal melanoma and ACC**

In **lung cancer**, a single-fraction dose is escalated to 50GyE with high LC and acceptable adverse effects

In **sacral chordoma**, a 5-year LC and OS rates of 88% and 86% was reported. Good LC was reported also in **skull-base tumours**

About 1000 patients with **prostate cancer** have been treated with hypo-fractionation with very good biochemical control and minor toxic effects

In **hepatocellular carcinoma** a 5-year LC of 81% with a negligible hepatic impairment. Two fractions in days have been used, with minor toxic effects

In locally **recurrent rectal cancer**, high LC and OS was reported (93% and 45%), even in patients previously irradiated (DFS 51%)

I 20 anni di Chiba

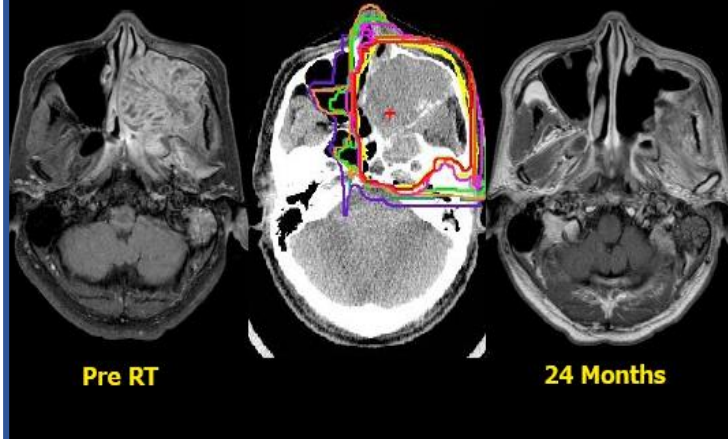
	Total number of patients (%)	Clinical practice
Prostate	1731 (22%)	1399
Bone and soft tissue	1033 (13%)	780
Head and neck	854 (11%)	529
Lung	795 (10%)	207
Liver	485 (6%)	250
Post-operative rectum	408 (5%)	338
Pancreas	353 (4%)	113
Gynaecological	207 (3%)	10
Eye	128 (2%)	86
CNS	106 (1%)	0
Para aortic lymph node	94 (1%)	87
Skull base	85 (1%)	56
Oesophagus	71 (1%)	0
Lacrimal gland	24 (<1%)	1
Scanning	11 (<1%)	0
Miscellaneous	1547 (20%)	715

In **pancreatic cancer**, the combination of CIRT and gemcitabine resulted in a 2-year LC and OS of 58% and 54%. Median survival was 2 times longer than for the best standard option



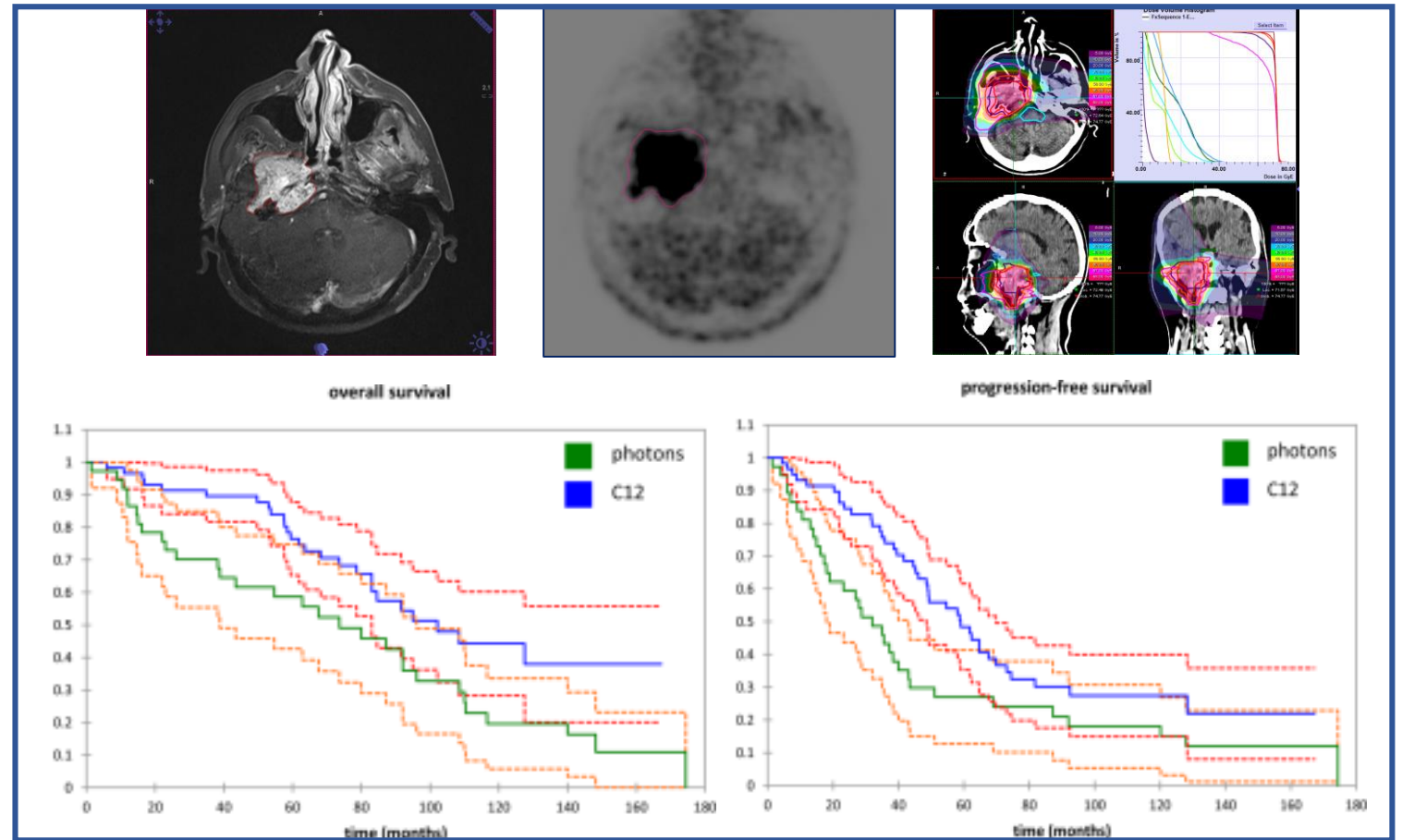
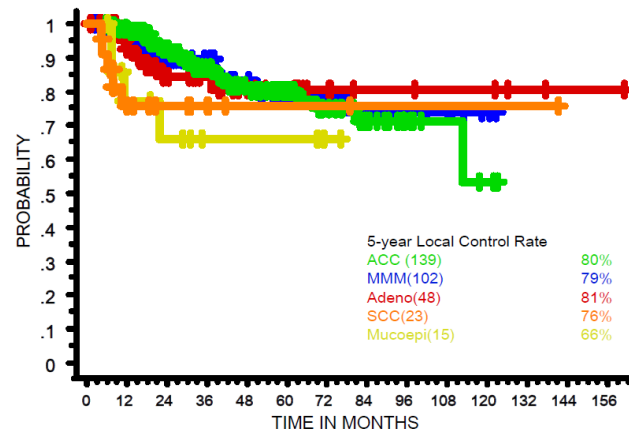
Vent'anni di Cnao.

ACC 57.6GyE/16fr/4
wks



Phase II (9602) for Malignant Head-and-Neck Tumors

Local Control according to Histological Type (Apr 97~Aug 10)

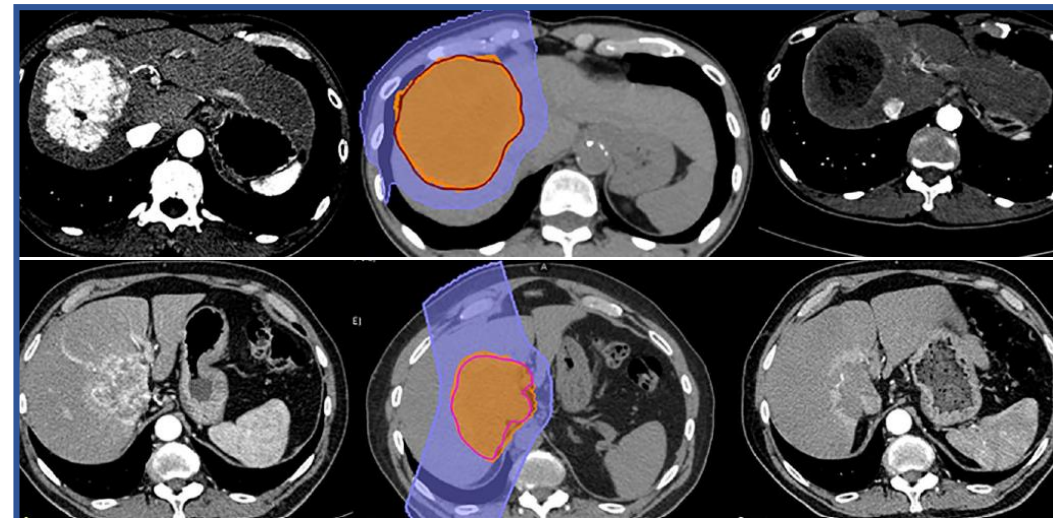
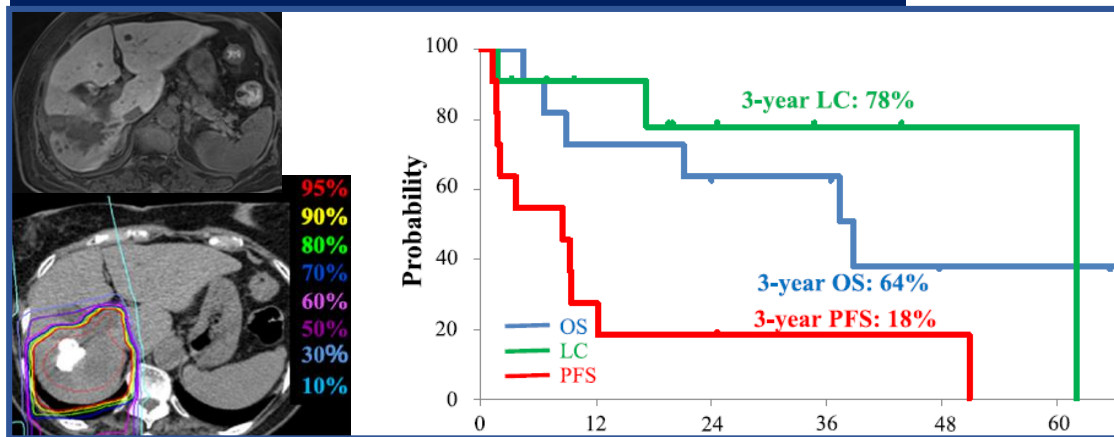


Carcinomi adenoideo-cistici
Le esperienze a Chiba ed in Germania

Esperienza di Gumna

11 Pazienti, dose media 60 Gy/4 fr o 60 Gy/12 fr
Tossicità minima

20
Vent'anni di Cnao.



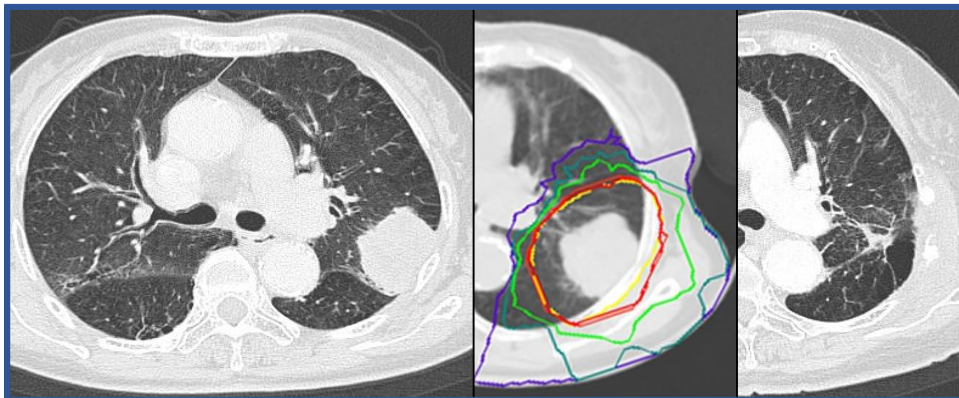
Esperienza di Trento

La prima esperienza clinica in Europa
18 Pazienti, dose media 58.05 Gy
Sopravvivenza globale (OS) ad un anno 63%
Forte correlazione tra OS e performance status,
invasione vascolare, e stadio di T
Controllo locale ad un anno 90%
Bassa tossicità
Nessun caso di RILD

Reference	Year	n	Treatment Method	OS
Kudo M, et al. [3]	2018	250	Lenvatinib	Median OS: 11.5 months
Bruix J, et al. [4]	2012	108	Sorafenib	Median OS: 8.1 months
Yoon SM, et al. [5]	2018	45	Sorafenib	Median OS: 9.9 months
Kodama K, et al. [21]	2018	36	Sorafenib	Median OS: 5.3 months
Kodama K, et al. [21]	2018	36	HAIC with RT	Median OS: 9.9 months
Yoon SM, et al. [5]	2018	45	TACE with RT	Median OS: 12.7 months
Zhang X, et al. ^a [22]	2017	21–604	Sorafenib	Median OS: 7.0–13.0 months
Kudo M, et al. [15]	2019	1101	Surgery	3y-OS: 40%
Liu PH, et al. [23]	2014	247	Surgery	3y-OS: 68%
Shi J, et al. [24]	2010	406	Surgery	3y-OS: 13%
Komatsu S, et al. [25]	2017	19	Particle RT (proton beam therapy and C-ion RT)	Median OS: 24.6 months
Present study		11	C-ion RT	Median OS: 36.4 months, 3y-OS: 64%

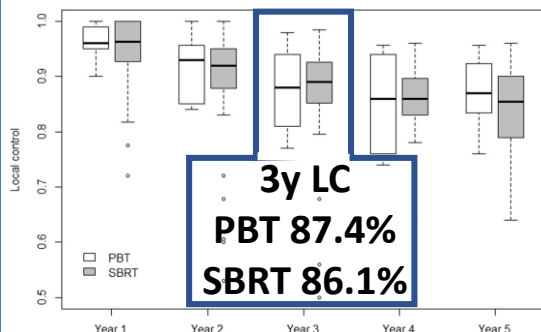
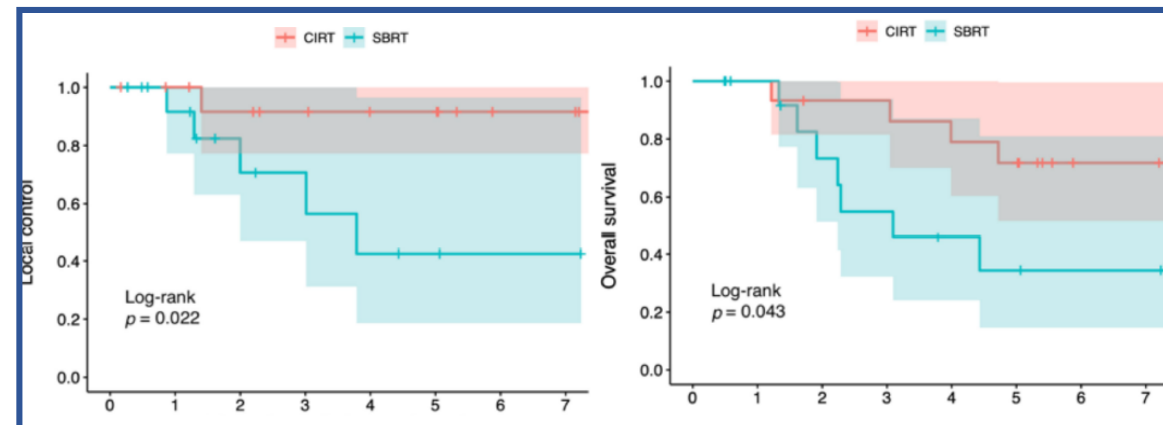
Tumori epatici

Shiba S et Al. Radiat Oncol 2020; Dionisi F et Al. Tumori J 2021



Vent'anni di Cnao.

Carcinoma polmonare



3y OS: PBT 69.5%, SBRT 58.8%
5y OS: CIRT 60.0%, SBRT 41.3%
p<0.05

3y PFS: PBT 63.5%, SBRT 50.7%
5y PFS: PBT 57.2%, SBRT 37.7%
P<0.05

Meta-analisi
PBT: 9 studi
SBRT: 72 studi

Toxicity type	PBT (N = 614) Events percentage (95% CI)	SBRT (N = 4805) Events percentage (95% CI)	p value
Grade 3–5 toxicity	4.8% (3.4%, 6.7%)	6.9% (6.1%, 7.9%)	0.05
Grade 5	0% (0%, 0.6%)	0.2% (0.1%, 0.4%)	0.41
Grade 4	1.8% (1.0%, 3.1%)	1.3% (1.0%, 1.6%)	0.34
Radiation Pneumonitis (≥grade 3)	0.9% (0.4%, 1.9%)	3.4 % (2.9%, 4.0%)	<0.001
Chest wall toxicity (≥grade 3)	1.9% (1.1%, 3.3%)	0.9% (0.6%, 1.3%)	0.03
Rib fractures	13% (11%, 16%)	3.2% (2.7%, 3.8%)	<0.001

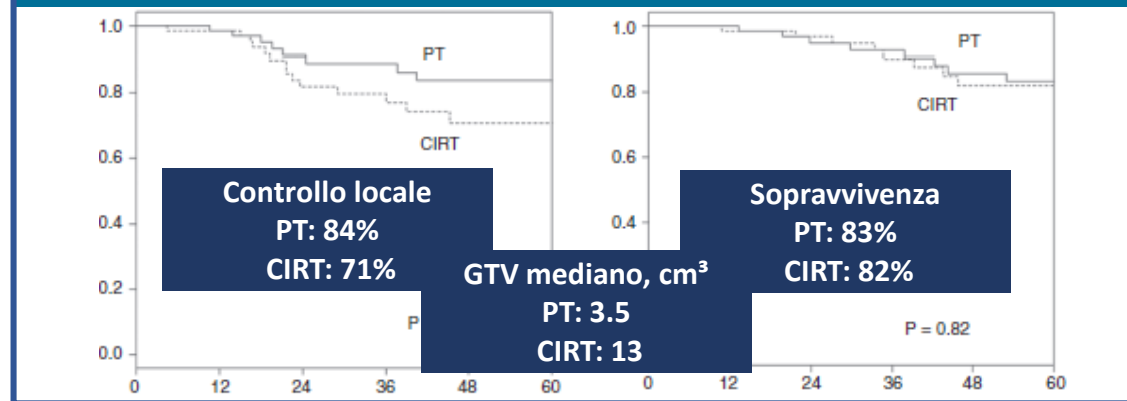
Comparison of Oncologic Outcomes between Carbon Ion Radiotherapy and Stereotactic Body Radiotherapy for Early-Stage Non-Small Cell Lung Cancer

Propensity score matching/adjusted analysis
CIRT: 52.8-60 Gy / 4 frazioni
SBRT: 48 Gy / 4 frazioni

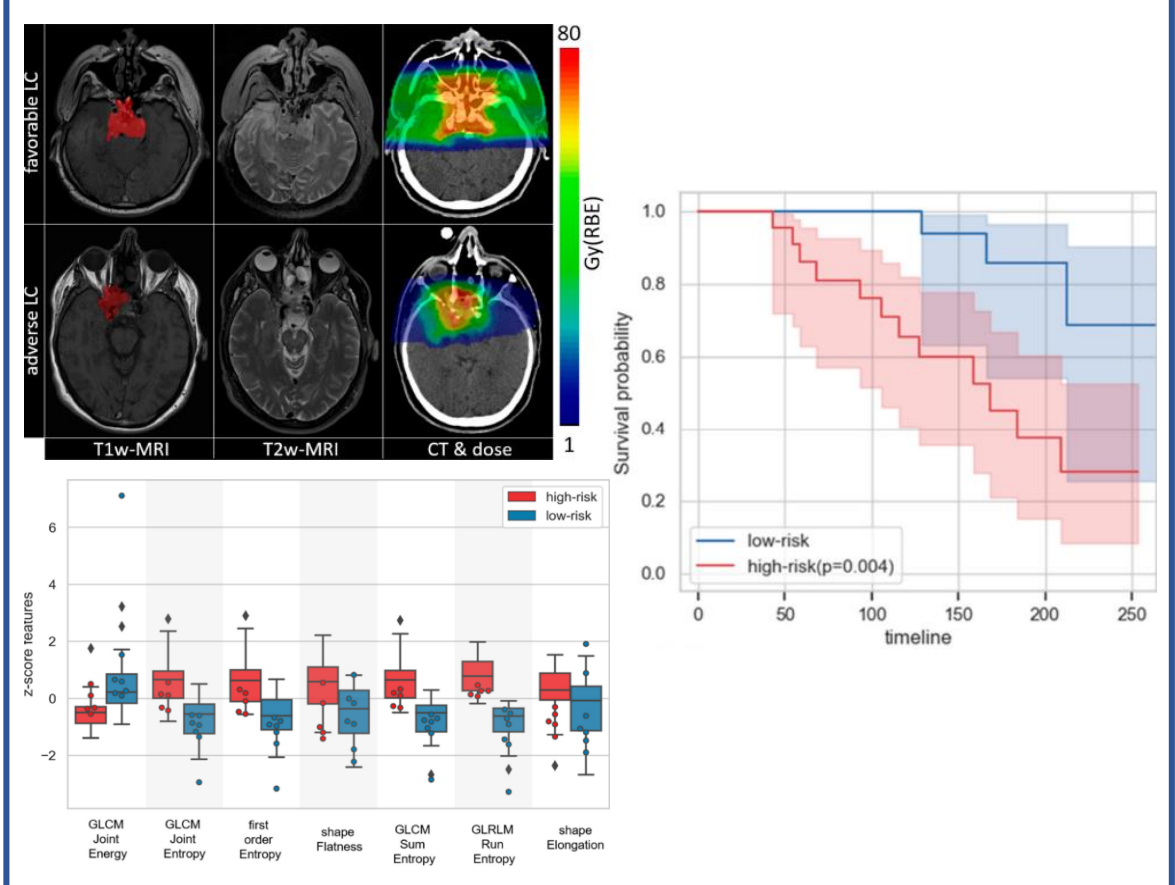
3y OS: CIRT 93.3%, SBRT 55.0%
5y OS: CIRT 71.8%, SBRT 34.4%

3y LC: CIRT 92.3%, SBRT 70.7%
3y LC: CIRT 92.3%, SBRT 42.4%

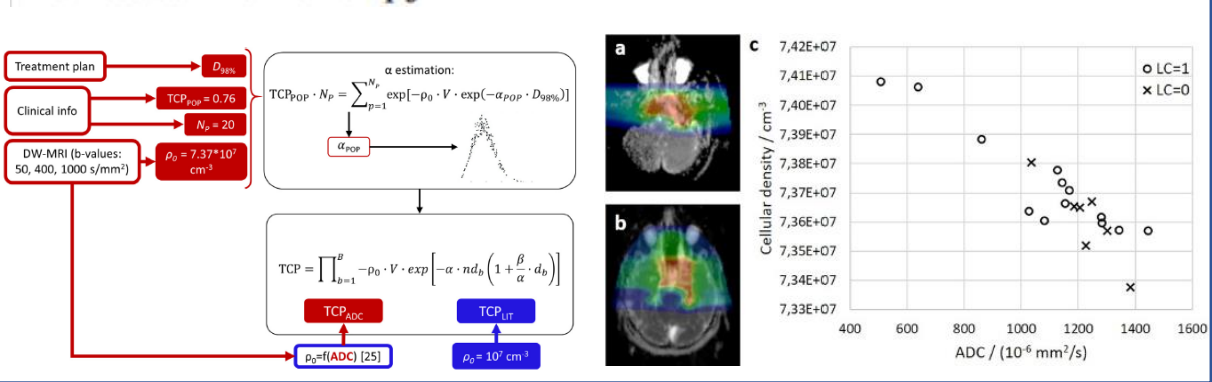
Proton and carbon ion radiotherapy in skull base chordomas: a prospective study based on a dual particle and a patient-customized treatment strategy



Radiomics and Dosiomics for Predicting Local Control after Carbon-Ion Radiotherapy in Skull-Base Chordoma



MRI-based tumour control probability in skull-base chordomas treated with carbon-ion therapy



Real World Evidence

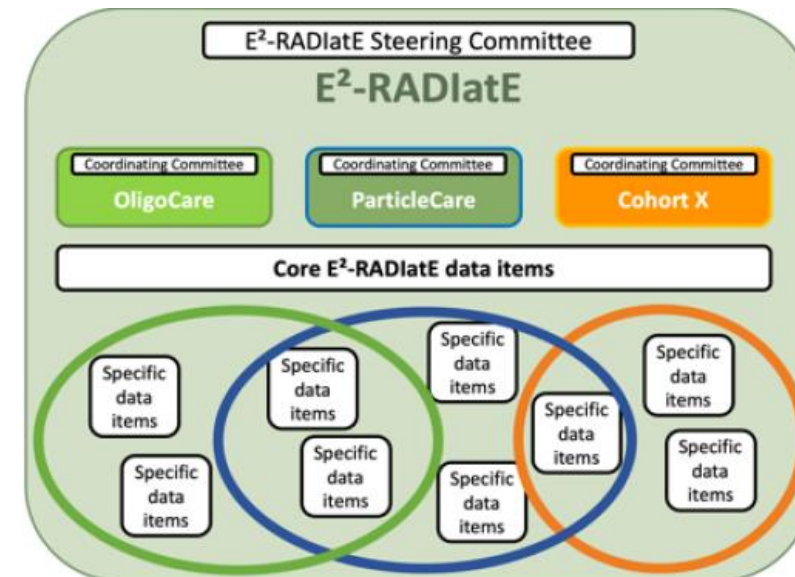
EPTN - European Particle Therapy Network

Prospective data registration and clinical trials for particle therapy in Europe

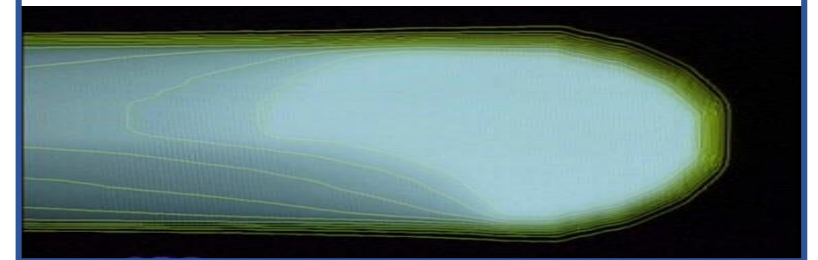
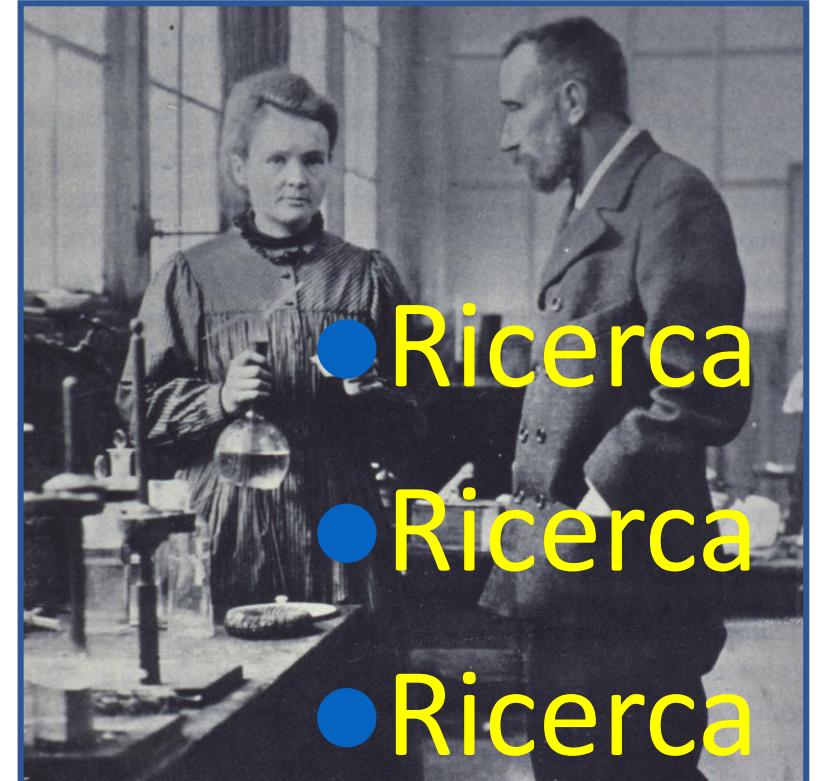
Johannes A. Langendijk^{a,*}, Roberto Orecchia^b, Karin Haustermans^c, Daniel Zips^d, Jacques Balosso^{e,f,g}, Denis Lacombe^h, Yolande Lievensⁱ, Damien C. Weber^{j,k}, Cai Grau^l, Esther G.C. Troost^{m,n,o}



**The European Particle Therapy Network
ESTRO & EORTC Vision**



- Studi randomizzati difficilmente fattibili (livello I)
- Ci sono comunque circa 300 studi clinici attivi, in varie parti del mondo, che daranno ulteriori dati di valutazione
- Ad oggi, sulla base delle analisi comparative i risultati clinici dell'adroterapia non sono mai inferiori a quelli ottenibili con la radioterapia convenzionale
- Al contrario, spesso si osserva un incremento del controllo locale in molte situazioni cliniche (sedi complesse, istologie diverse, tumori ipossici, ecc.) con possibili riflessi positivi sulla sopravvivenza
- In alcune sedi (H&N in particolare) si assiste ad una riduzione degli effetti collaterali, con positivo impatto sulla qualità di vita dei pazienti
- La combinazione con altre terapie rappresenta una prospettiva di grande interesse, sinora non sufficientemente esplorata

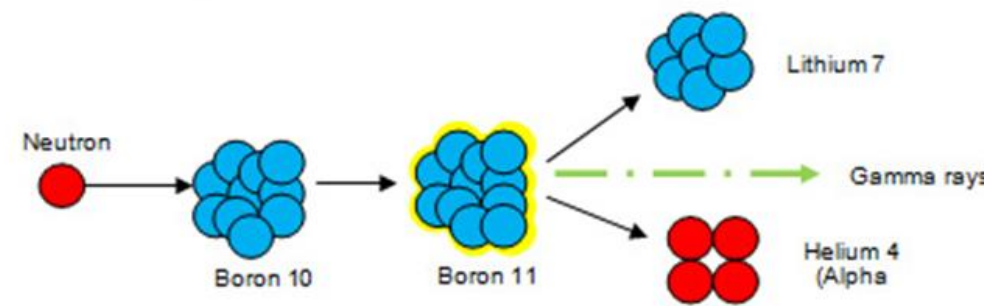
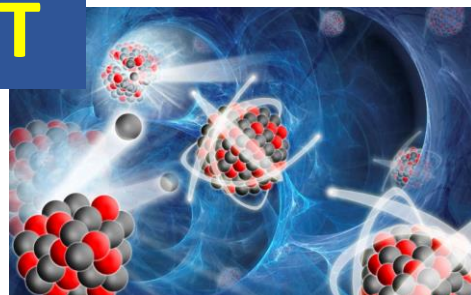




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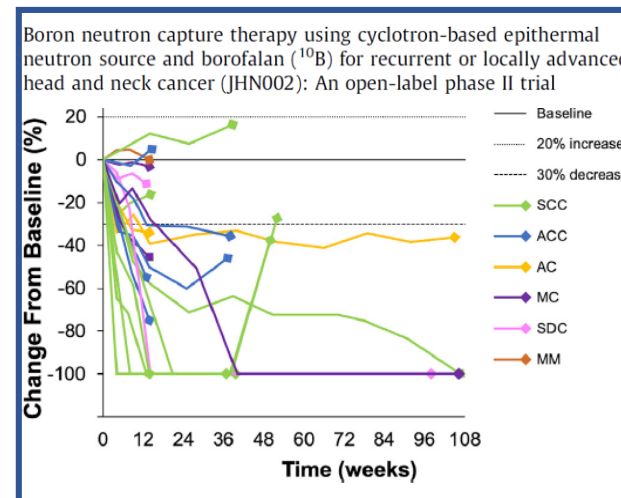
Vent'anni di Cnao.

BNCT



Finlandia, USA, Taiwan, Olanda,
Germania, Argentina, Cechia, Italia

- Gliomi ad alto grado
- Melanomi cutanei
- Tumori H&N (recidive)



Long-term outcome of cutaneous melanoma patients treated with boron neutron capture therapy (BNCT)

