

#### L' adroterapia : indicazioni, vantaggi e risultati preliminari di tossicità e risposta

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#### 42 centri di protoni

(USA 14, Europa 12, Giappone 8, ....)

6 centri di loni carbonio(Giappone 3,

Europa 2, Cina 1)

107.792 pazienti trattati

93.452 con Protoni,

10.753 con Carbonio

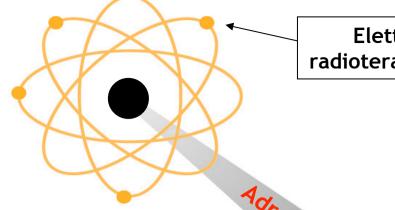
3 centri (protoni+ ioni carbonio)

+ 46.000 negli ultimi 5 anni

≈ 10.000 pazienti per anno

24 centri di protoni nei prox 3 anni





Elettroni (raggi X): radioterapia convenzionale

#### Adroterapia?

Lo ione carbonio è 12×2000 volte più pesante dell'elettrone

but bu

Nucleo del Carbonio fatto di 6 protoni (p) e 6 neutroni (n)

p

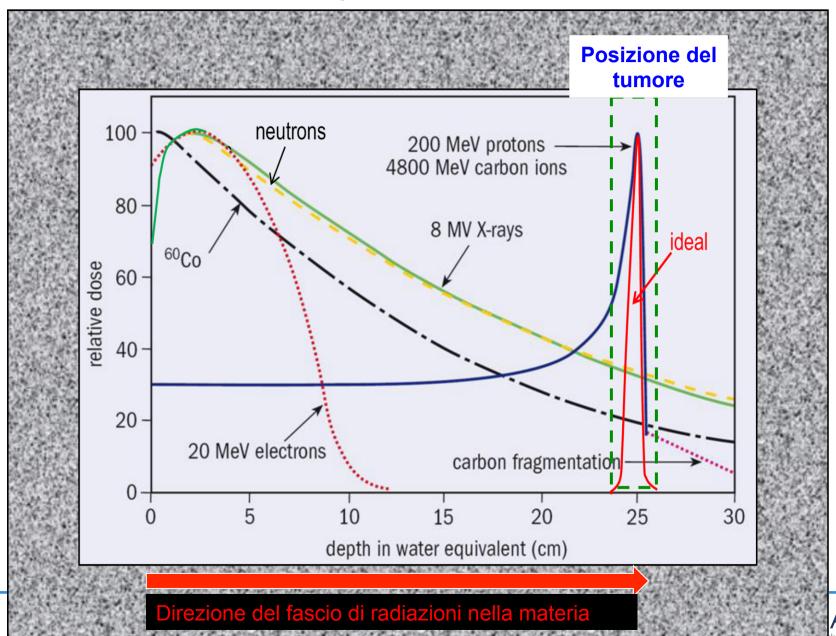
Nucleo più semplice: il protone (p)

Il protone è 2000 volte più pesante dell'elettrone

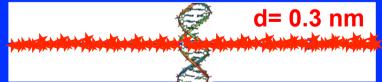




#### Precisione dell'adroterapia





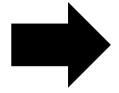






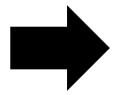
#### Adroterapia consente di trattare casi "difficili"





Tumori vicini ad organi critici

**EFFICACIA** 

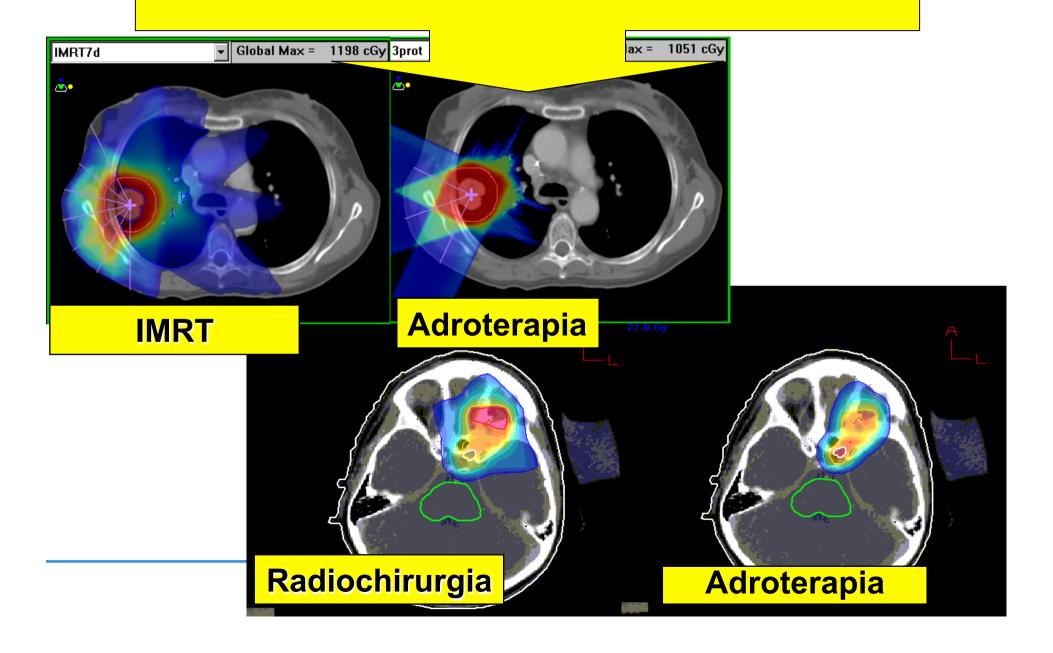


Tumori radioresistenti, che non rispondono alla radioterapia convenzionale

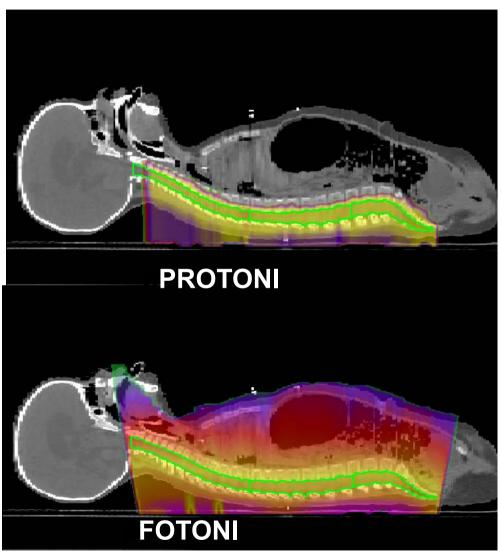




#### Selettività fisica



#### Protoni in tumori pediatrici



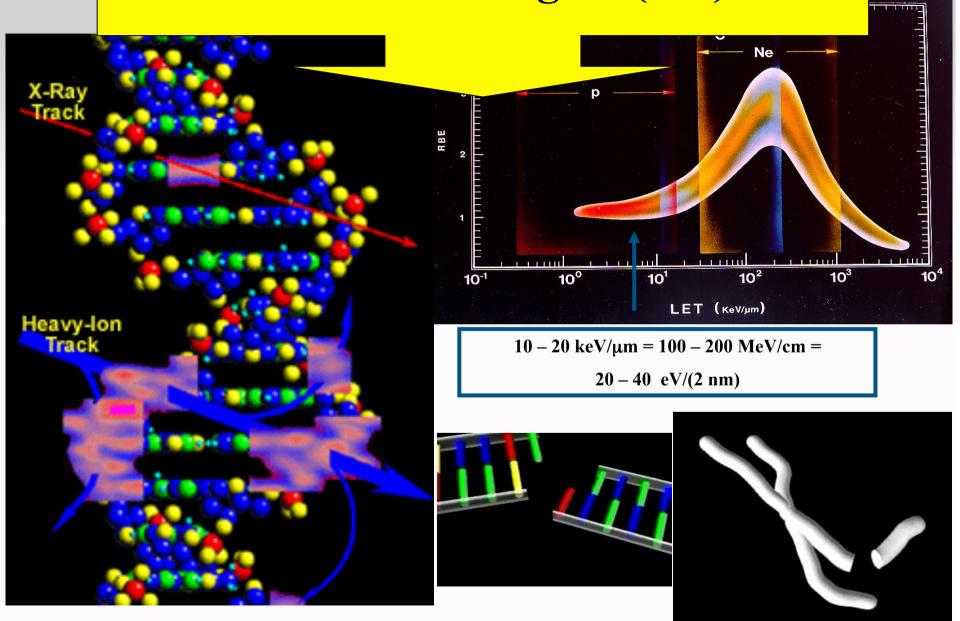
	X-ray	<u>IMRT</u>	<u>Protoni</u>
CTV	90%	90%	90%
Heart	18.2	17.4	0.1
Right lung	3.5	21.9	0.1
Esophagous	11.9	32.1	10.2
Stomach	3.7	20.6	0.1
Right kidney	3.3	29.8	0.1
Transvers colon	2.6	18.0	0.1

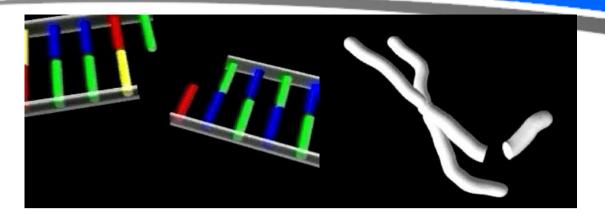


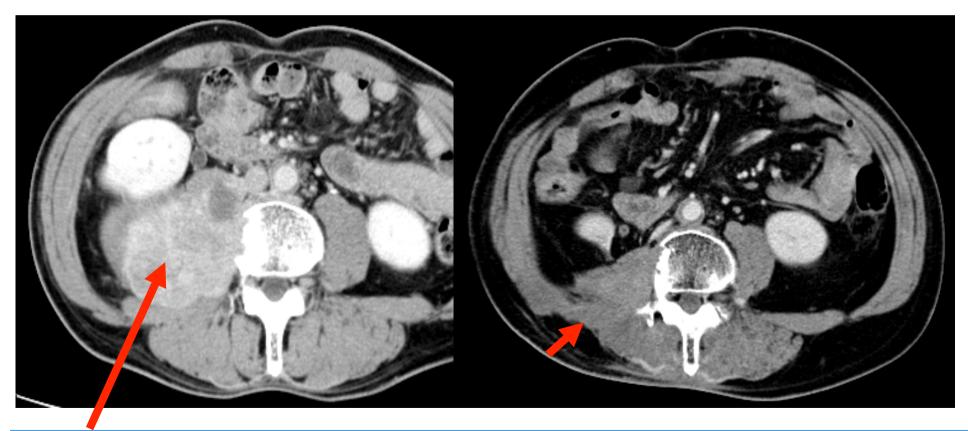




#### Efficacia Biologica (C12)









Which tumors might benefit of high LET particles?

Up-regulated oncogenes

Mutated tumor suppresor genes

Radioresistant for genetic alteration

Dis-regulated apoptosis

Radioresistant for intratumoral micromilieau

Deprivation of oxigen

Up-regulated defense system

High angiogenetic potential

Radioresistant for proliferation status

High content of quiescent cell clones

Slow proliferation activity







Fonte: Airo



# Working Group 1998,2003, 2008, 2009

Si stima che in Italia ci siano 15.000 casi l'anno di pazienti che richiedono un trattamento con protonterapia

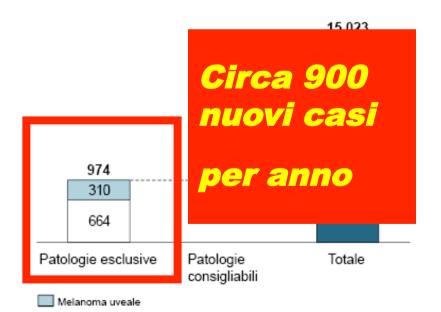
Co

Le principali pa

oncologic

Domanda di trattamenti con protonterapia in Italia

Numero di pazienti all'anno in Italia con patologie trattabili con proton terapia [2008]



**Cordoma** 

Condrosarcoma

- 250 nuovi casi/anno melan. delle patois cranica e de" **Melanoma oculari** condro tronce tumor 300 nuovi casi/anno cranici, g. pediatrici
- risulta parti tumori a al fega Tumori solidi pediatrici In futu del car 180 nuovi casi/anno protoni





#### Working Group 1998,2003, 2008, 2009

Le terapie con ioni di carbonio potrebbero essere adottate in quasi il 20% dei casi di alcune categorie di tumori radioresistenti

Domanda di trattamenti con ioni Carbonio in Italia

Numero di pazienti all'anno in Italia con tumori radioresistenti [2008]

7.672

Circa 1500 nuovi casi per anno

Casi tumori radioresistenti

Casi non trattabili con ioni 19%

1.436

Casi trattabili con ioni

**Head&Neck** 

**No SC carcinoma** 

350 nuovi casi/anno

Sarcomi ossei e delle parti molli

520 nuovi casi/anno

**Prostata** 

**Fegato e Pancreas** 

"Selected cases"

estenti

Table I: "Consolidated" indications resulting from ETOILE's work

Tumour location	Detailed definition of indications	Recommended form of hadron therapy	Estimated incidence <sup>§</sup> (cases/year in France)
Salivary gland (parotid gland) tumours	Inoperable tumours <u>or</u> refusal of surgery <u>or</u> R2 resections <u>or</u> local recurrences <sup>®</sup> All types of histology: adenoid cystic carcinomas, mucoepidermoid adenocarcinomas, acinar cell carcinomas, etc.	Carbon alone or in combination with a dose of locoregional photon therapy	≈ 100
Paranasal sinus tumours	Inoperable tumours <u>or</u> refusal of surgery <u>or</u> R2 resections <u>or</u> local recurrences Adenocarcinomas and adenoid cystic carcinomas	Carbon alone in primary location	≈ 250
Adenoid cystic carcinomas with skull base involvement	Inoperable tumours <u>or</u> refusal of surgery <u>or</u> R2 resections <u>or</u> local recurrences	Carbon alone in primary location	≈ 10
Malignant mucosal melanomas (primarily ENT)	Any location without immediately threatening metastasis Tumour without surgery if possible <u>or</u> emergency after R2 resections or non-irradiated local recurrence	Carbon alone in primary location; urgent treatment	≈ 40
Chordomas at the base of the skull, spine and sacrum	Any clinical presentation	Carbon or proton therapy alone in primary location	≈ 30–50
Chondrosarcomas of the	Base of skull	Proton therapy alone in primary location	≈ 20
axial skeletal	Spine and sacrum	Proton therapy or carbon alone in primary location	<10
Soft-tissue (non- retroperitoneal) sarcomas	Weak-grade M0, any histology, any location Unresectable or surgery refused or "definitive R2": R2 with no possible repeat surgery or R2 following repeat surgery or local recurrence in R2 resection  Non-threatening M+ with incapacitating T or rT		≈ 100 ≈ 80
Retroperitoneal sarcomas	Following local recurrence <u>and</u> surgical resection: R0 or R1 and M0 (for unresectable T and R2, see above) Initial status R1 M0	Carbon alone in primary location	≈ 40
Soft-tissue sarcomas of the head, neck and limbs	"Definitive R1": R1 resection with no acceptable possibility for		≅ 200
Osteo- and chondrosarcomas (any location except axial skeleton)	repeat surgery  Tumours without surgery <u>or</u> resections: R2, M0  M+ accepted for osteosarcomas only  Discussion according to grade		≈ 10
Pelvic recurrence of rectal adenocarcinomas	Unresectable unifocal locoregional pelvic recurrences in irradiated or non-irradiated location, and M0 (CT, liver MRI, PET)	Carbon alone	≈ 200
Hepatocellular carcinomas	or non-irradiated location, and MO (C1, liver MRI, PE1)  Single hepatocellular carcinoma, Ø > 4–5 cm, unresectable, MO, not suitable for conventional treatment methods or photon therapy, no threatening comorbidity	Carbon alone in primary location	≈ 50

1150 pz

#### Notes:

<sup>9</sup>The annual estimated incidence is the estimated total annual number of tumours that match the detailed descriptions. This is the maximum recruitment potential. It does not take into account feasibility of treatment or the care services actually available.

Local recurrence is taken to mean the reappearance of the tumour in its primary location, with no other regional or metastatic manifestation.





Table II: "Prospective" indications resulting from ETOILE's work

Tumour location	Detailed definition of indications	Recommended form of hadron therapy	Estimated incidence <sup>§</sup> (cases/year in France)
Non-small cell lung cancer	Inoperable initial status, stage (UICC/AIC 1997) IA and IB: T1T2N0 (CT, PET) M0 (brain MRI); purely endobronchial tumours excluded Second cancer in patients who underwent radiotherapy and/or pneumonectomy >2 years ago; inoperable stage I Inoperable initial status, stage (UICC/AIC 1997) IIB-IIIB limited to T3T4N0 (CT, PET) M0 (brain MRI); purely endobronchial tumours excluded Second cancer in patients who underwent radiotherapy and/or	Carbon alone in primary location with respiratory gating	≈ 750–1000
	pneumonectomy >2 years ago; inoperable stage II Any histology		× 10
Nasopharynx	Strictly local recurrences after initial radiation	Protons or carbon	
High-grade gliomas	Recurrence after initial radiotherapy +/- chemotherapy and progressing during chemotherapy	Carbon alone in primary	≈ 50
(grade 3 or glioblastomas)	Initial treatment, possibly following surgery	location	≅ 300
Epidermoid ENT carcinomas	Unresectable recurrences or second location, in irradiated area and M0 (CT, liver MRI, PET) (proposal to be assessed) Initial status T3—T4, N ≤2, M0 of the oropharynx or oral cavity (proposal to be assessed)	Carbon alone	№ 500
Prostate adenocarcinomas	Intermediate risk groups: T2b, T3a/b <u>and</u> (PSA 10–20 <u>and/or</u> Gleason≥7) <u>and</u> pN0	Comparison IMRT ± hormone therapy versus carbon versus protons	≈ 1000
Highly radioresistant tumours of the digestive tract	Unresectable single nodular bile duct cancer <u>or</u> pancreatic adenocarcinoma, M0, not previously irradiated <u>and</u> not progressing during chemotherapy after 4–6 months	Carbon alone or in combination with dose of locoregional photon therapy	≈ 900
	M0 endocrine tumour of the pancreas, progressing after multiple treatments: isotopic and/or chemotherapy <u>and</u> somatostatin	Carbon alone in primary location	≈ 20

Table III: "Exceptional" indications proposed by ETOILE

Tumour location	Detailed definition of indications	Recommended form of hadron therapy	Estimated incidence <sup>§</sup> (cases/year in France)
Paediatric tumours	Large (more than 100 or 200 ml, depending on age), inoperable Ewing's sarcomas of the pelvis Aggressive chordomas in small children (<3–4 years) Unresectable pelvic osteosarcomas	Carbon alone in primary location	<100
Various locations, highly functional	Benign tumours or locally-invasive malignant tumours that are incapacitating <u>and</u> have a high risk of local recurrence (desmoid tumours, neurinomas, schwannomas, meningiomas, etc.)	Carbon alone	Very rare

3600 pz

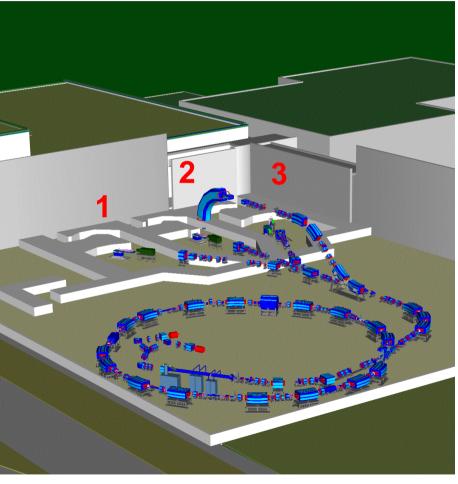
100 pz





#### **CNAO** a Pavia

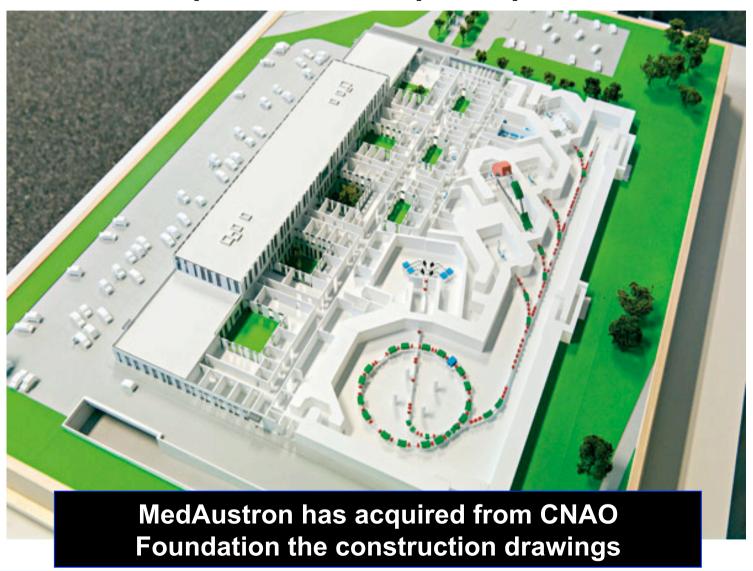






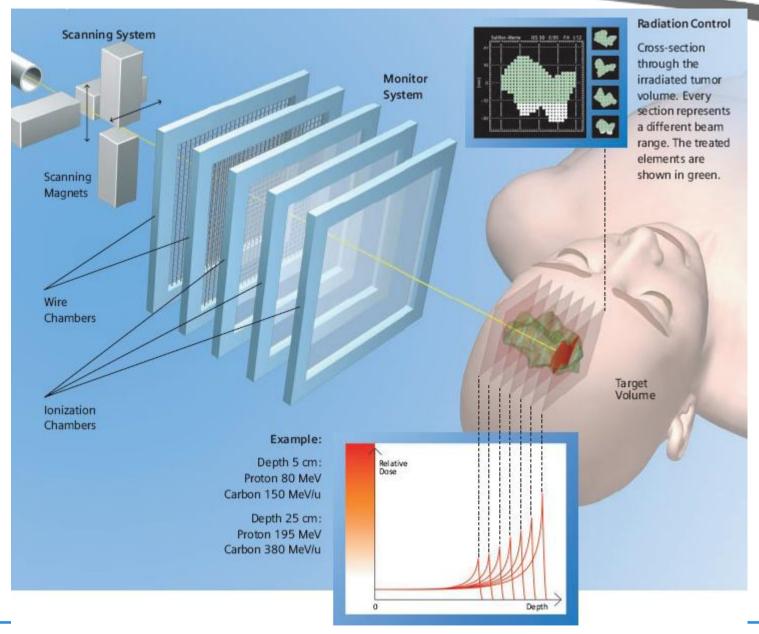


#### MedAustron promoted and participated in PIMMS



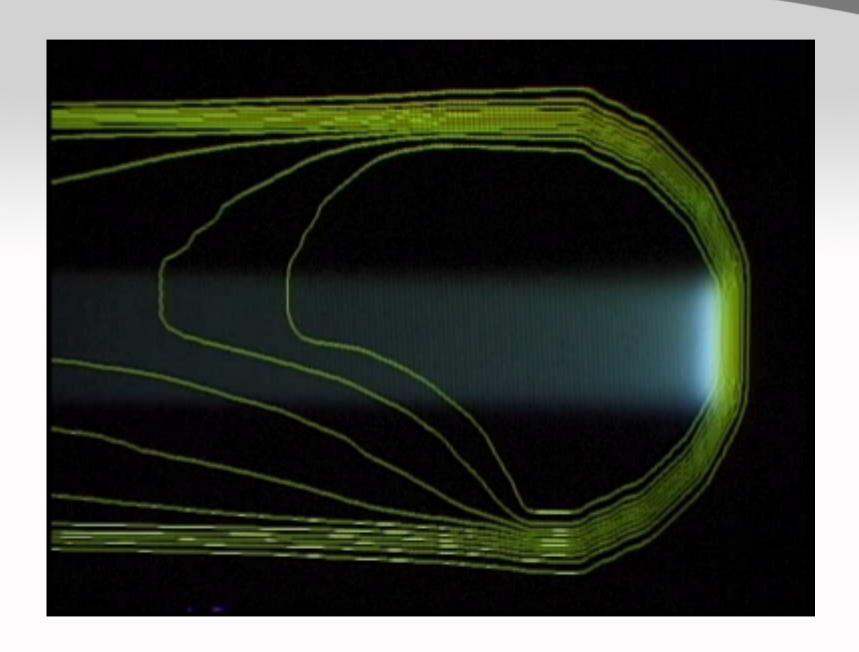


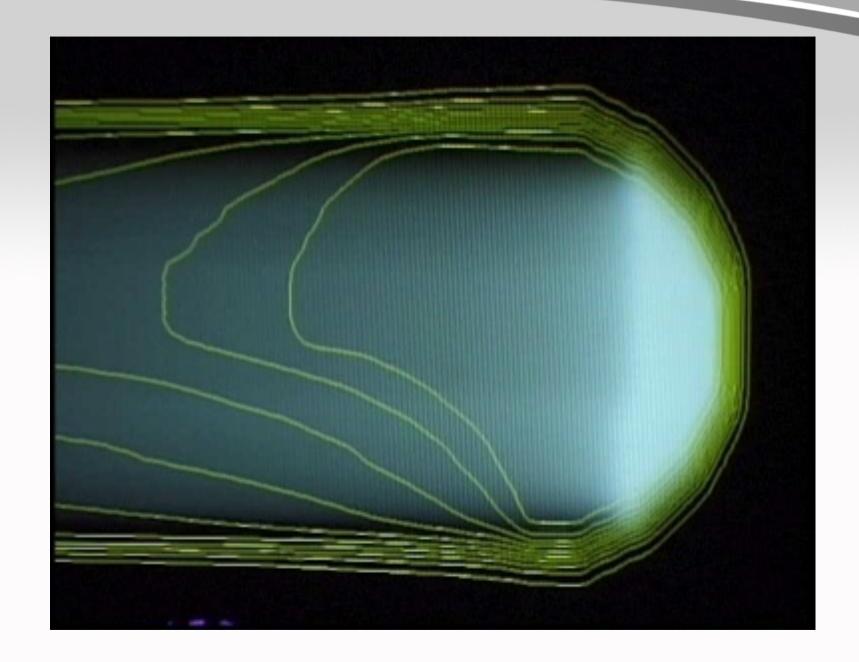


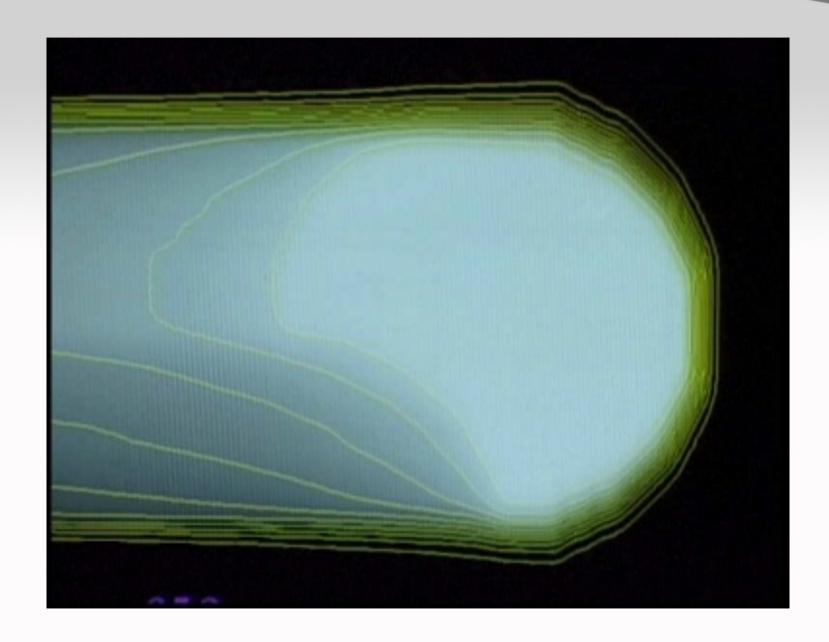














# File Acquesion Graphics View Help 1.2:30:34 Guido Baroni logged in Administrator Treatment Data

Patient Sex: Date of Birth:

Indexing position:

Table Lateral[mm]:

Table Vertical[mm]: Table Pitch[deg]: Table Roll[deg]:

Table Longitudinal[mm]: -1123.6

Table Rotate (Yaw)[deg]: 71.7
Acquisition Data
Acquired Frames:
Displayed Frames:
Saved Frames:
Sample Rate [H2]:

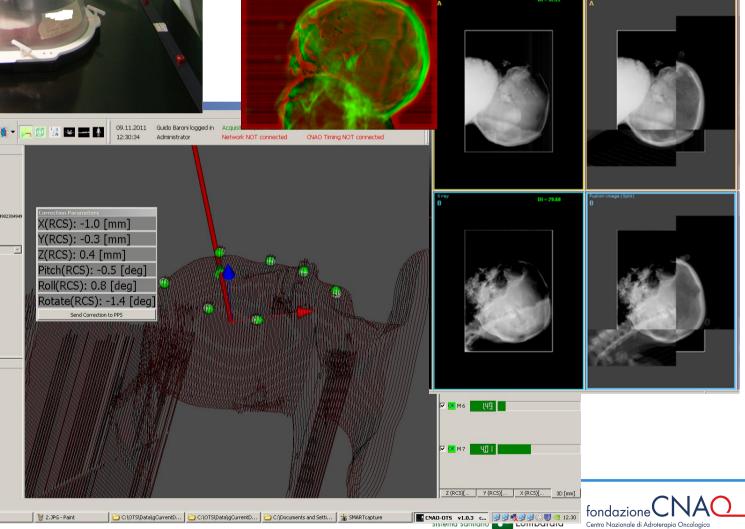
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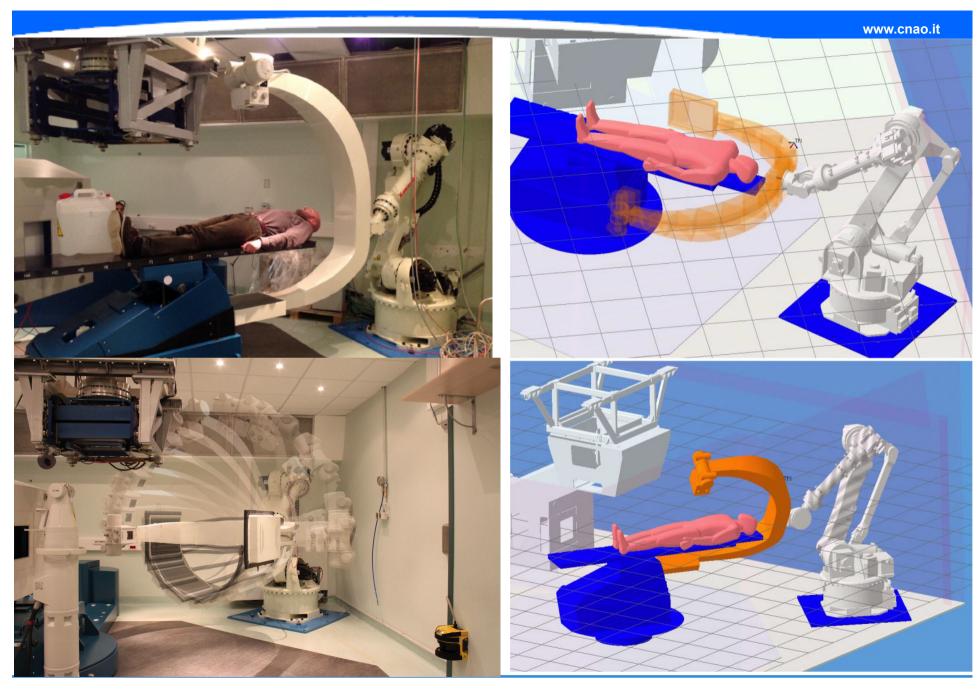
Y-0.0 Y-273.0 7-0.0

Lock PPS/Treat Enable

-0.8

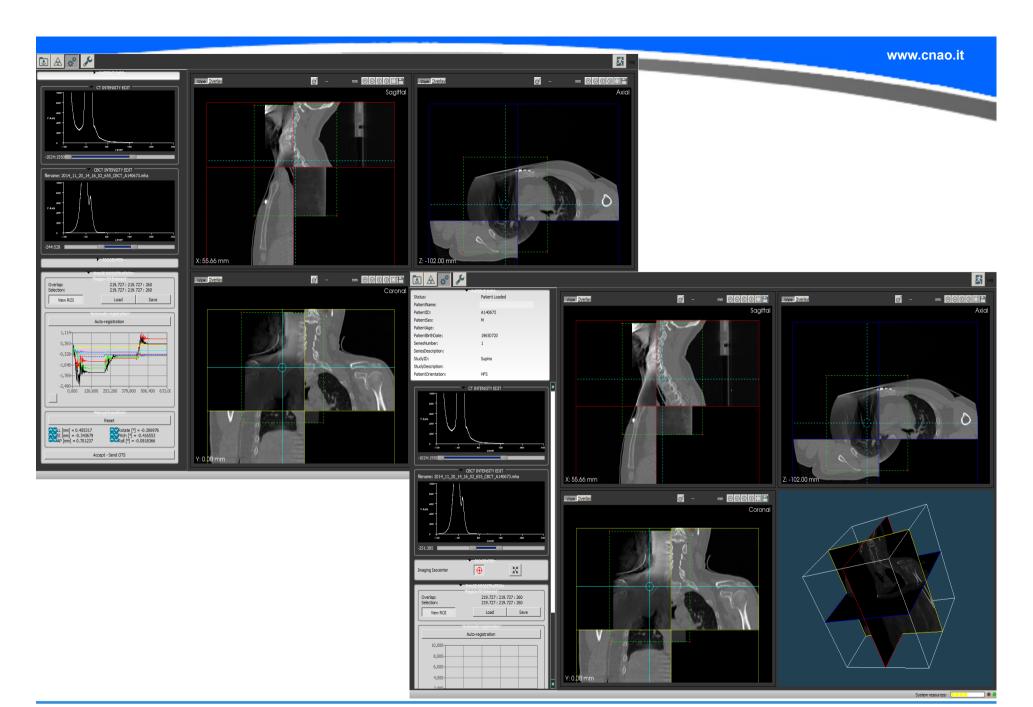
## Optical & X-ray tracking per la verifica del set up





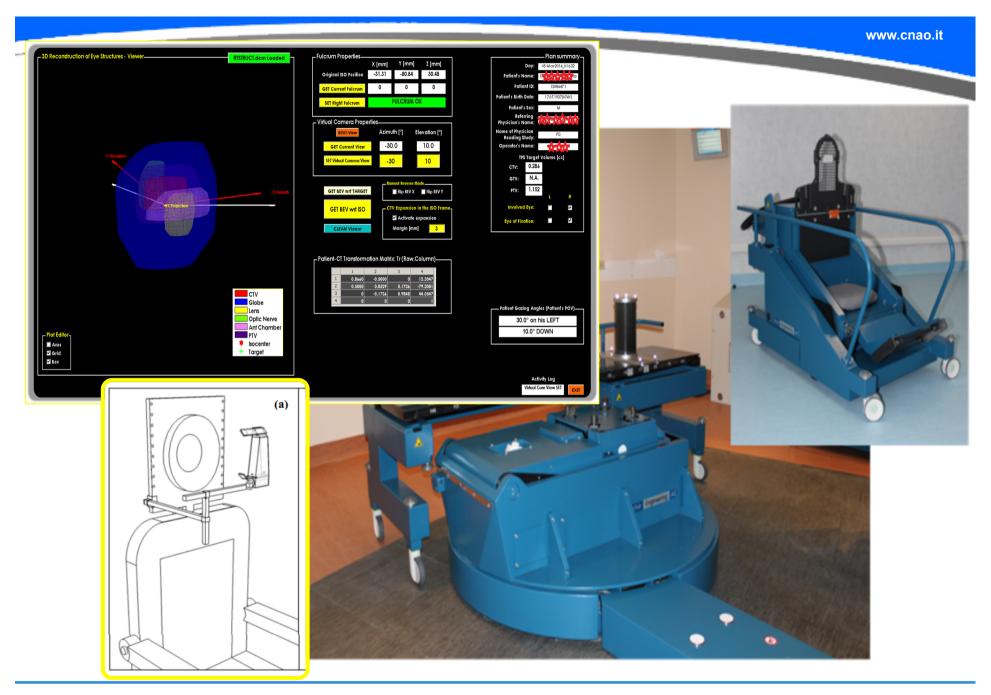








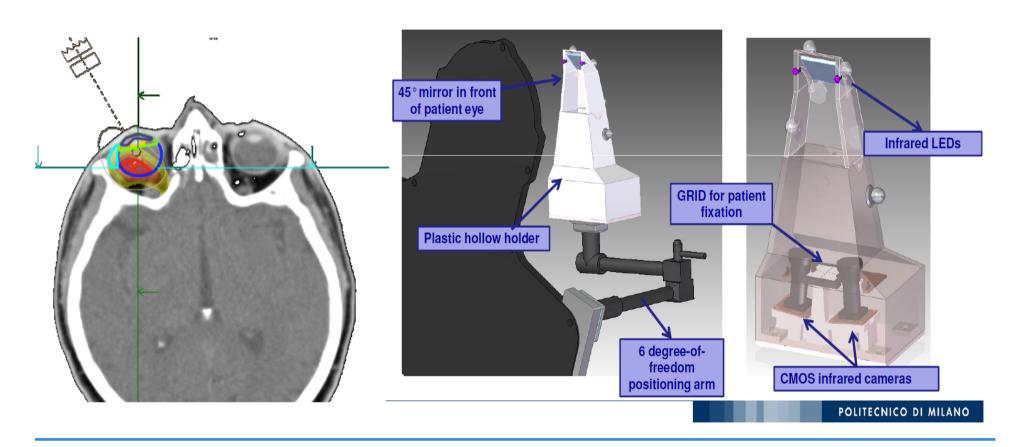








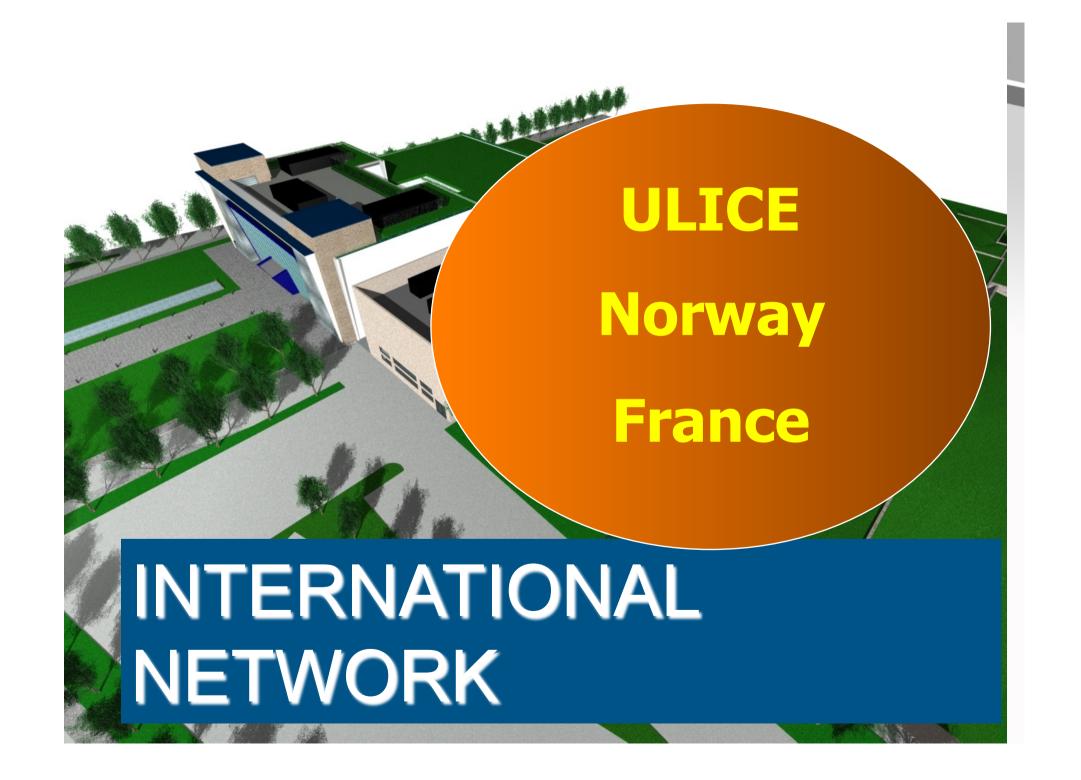
### Non invasive eye tracking system for intraocular tumor localization in proton therapy treatment













direzionemedica@cnao.it

serviziomedico@cnao.it



Tel 0382 078963



Protocolli CNAO



**Prima Visita Virtuale** 



Prima Visita

http://folder.cnao.it

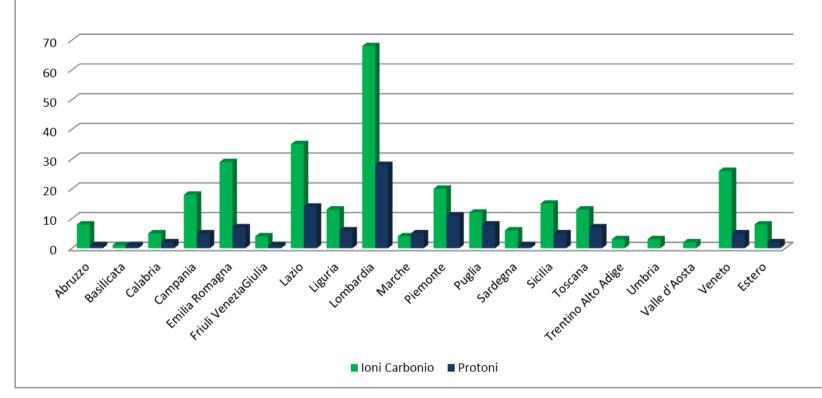




#### Distribuzione geografica dei pazienti del CNAO

22 Settembre 2011 – 21 Novembre 2014

Totale 402 pazienti (133 in sperimentazione + 252 post sperimentazione + 17 compassionevoli)



•Protoni: 109 pazienti

•Carbonio: 293 pazienti









Waiting list

Avvio procedure per trattamento radiante



**REGIONI** 





#### Numero Contatti Servizio medico 1233

MACRO CATEGORIA	CATEGORIA	2014
VISITE	PRIME VISITE	481
	ESAME DOCUMENTAZIONE CLINICA	263
Totale VISITE PRELIMINARI		744
IMAGING	PET	54
	RM	599
	TAC	399
Totale IMAGING per ADROTERAPIA		1.052
SEDUTE ADROTERAPIA	PROTONI	1.103
	IONI CARBONIO	3.380
Totale SEDUTE		4.483
ADROTERAPIA ALTRO	DEFINIZIONE DEL VOLUME BERSAGLIO E DEGLI ORGANI A RISCHIO	250
	FUSIONE DI IMMAGINI PER PREPARAZOINE PIANO DI TRATTAMENTO	250
	SISTEMA DI IMMOBILIZZAZIONE PERSONALIZZATO	265
	STUDIO FISICO-DOSIMETRICO	250
	VISITE CONTROLLO	1.309
	INIEZIONI FARMACI SPECIFICI	8
	MEDICAZIONI	13
Totale ALTRE PRESTAZIONI per ADROTERAPIA		2.345
Totale ADROTERAPIA		7.879
IMAGING	RM	962
	TAC	48
Totale IMAGING		1.010
VISITE	VISITE CONTROLLO	1.010
Totale PRESTAZIONI DI FOLLOW UP		2.019
TOTALE PRESTAZIONI		10.642



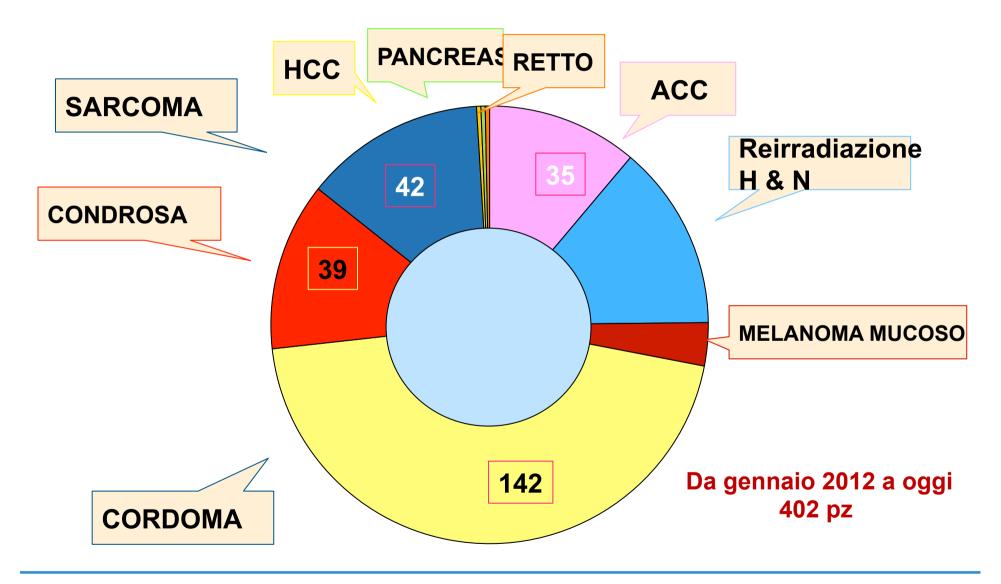
#### **Attività Clinica:**

- Cordoma e condrosarcoma
- Tumori delle ghiandole Salivari
- Sarcoma delle parti molli
- Melanoma mucoso
- Recidive di Adenoma pleomorfo
- Meningioma
- Tumori dell'orbita (melanomi dell'occhio)
- Tumori avanzati della testa e del collo
- Tumori della prostata ad alto rischio
- Tumori del pancreas inoperabili
- Epatocarcinoma
- Re-irradiazione delle recidive di tumori del retto
- Re-irradiazione di tumori della testa e del collo





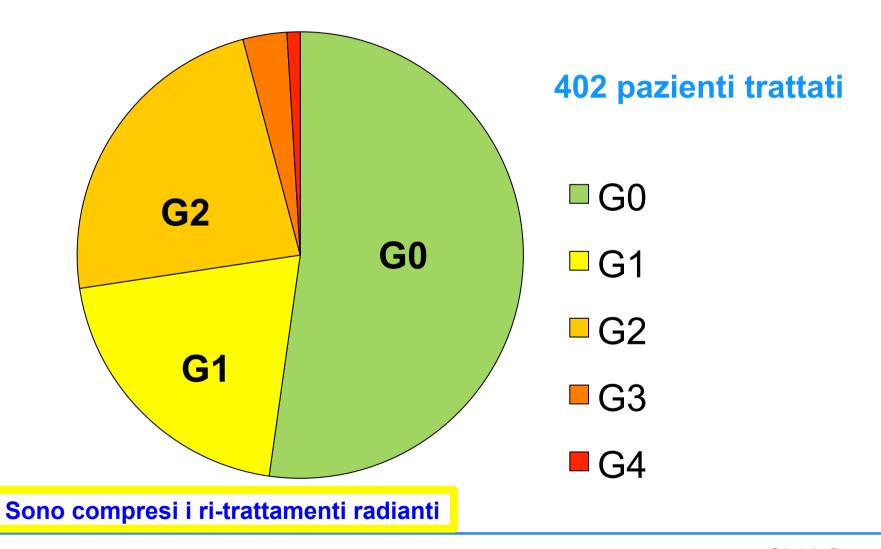
#### Patologie trattate con Adroni al CNAO di Pavia







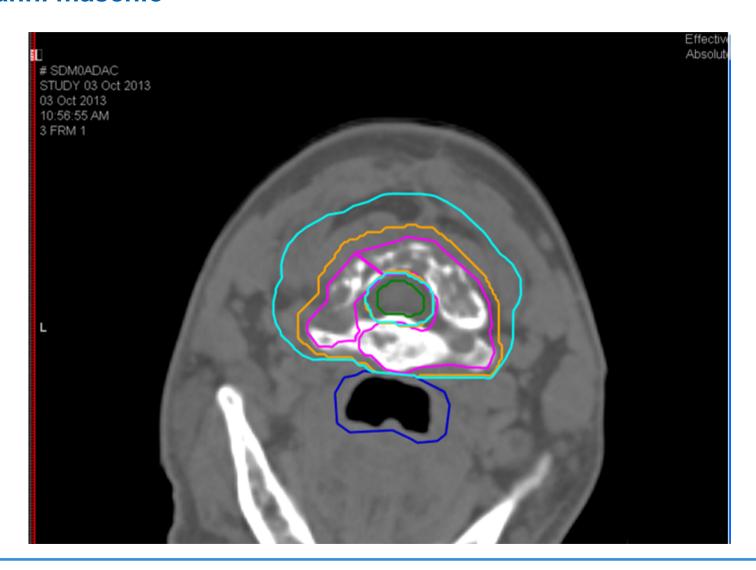
#### Tossicità acuta secondo criteri CTCAE





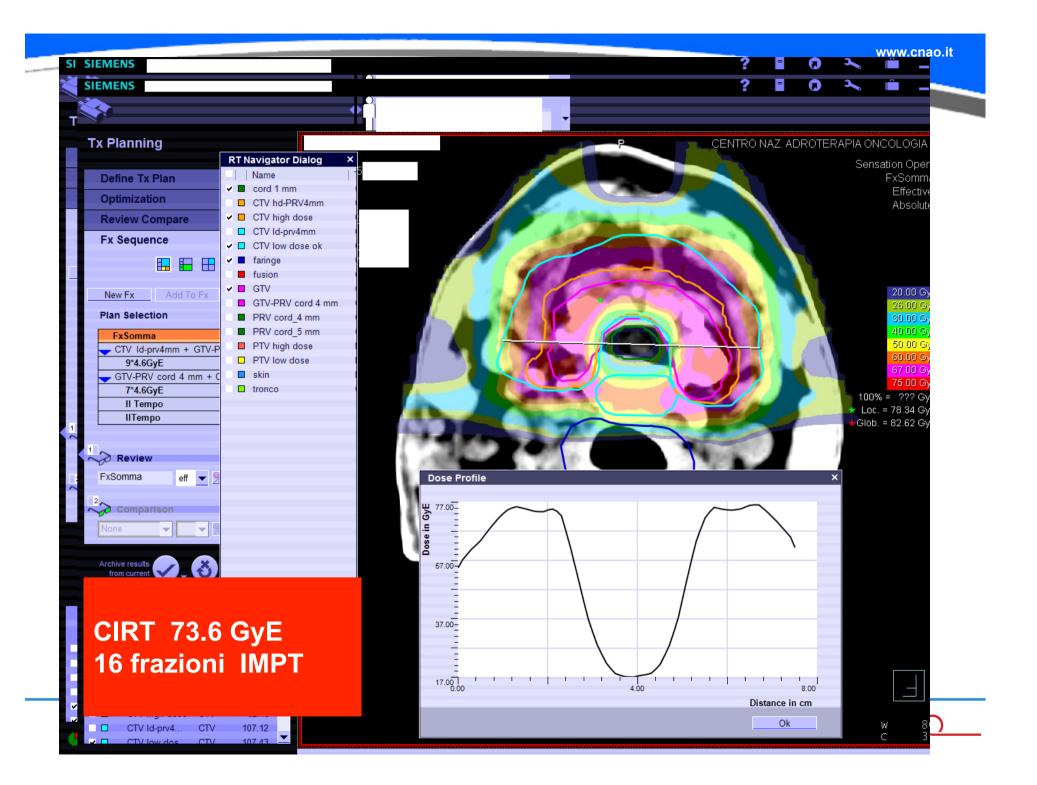


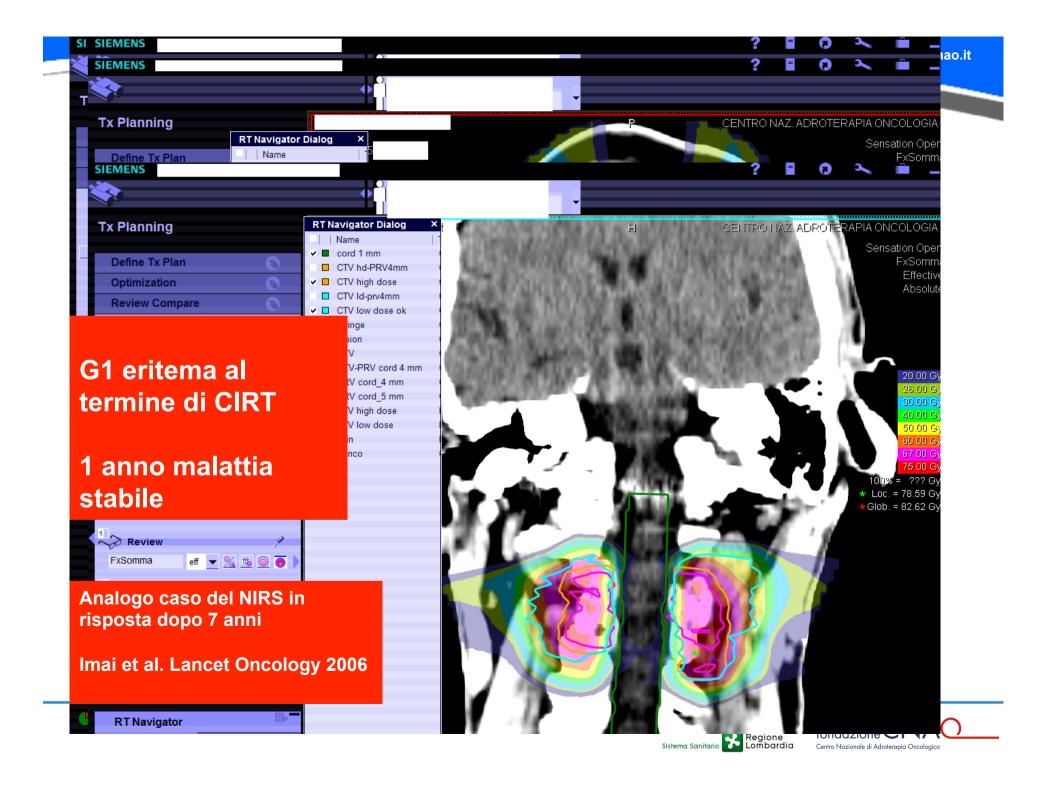
### osteosarcoma di basso grado delle vertebre cervicali, C1-C2 56 anni maschio







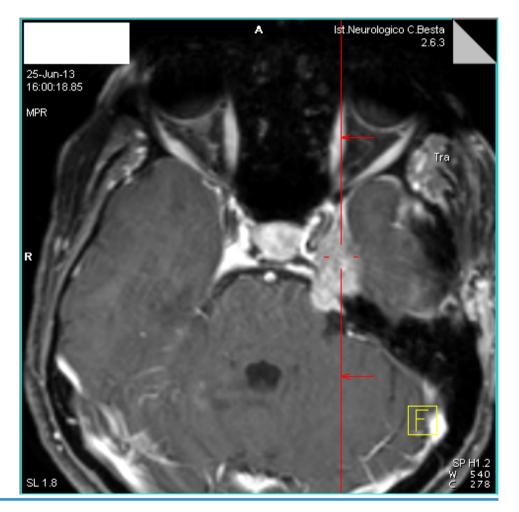




#### **Pre-CIRT**

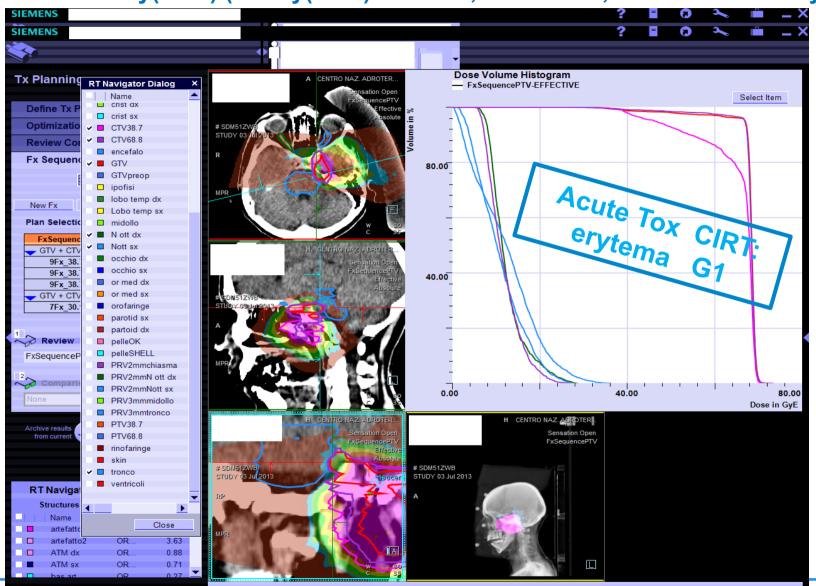
Donna di 62 anni Carcinoma adenoido-cistico del cavo di Meckel

21/05/2013 craniotomia temporale e biopsia



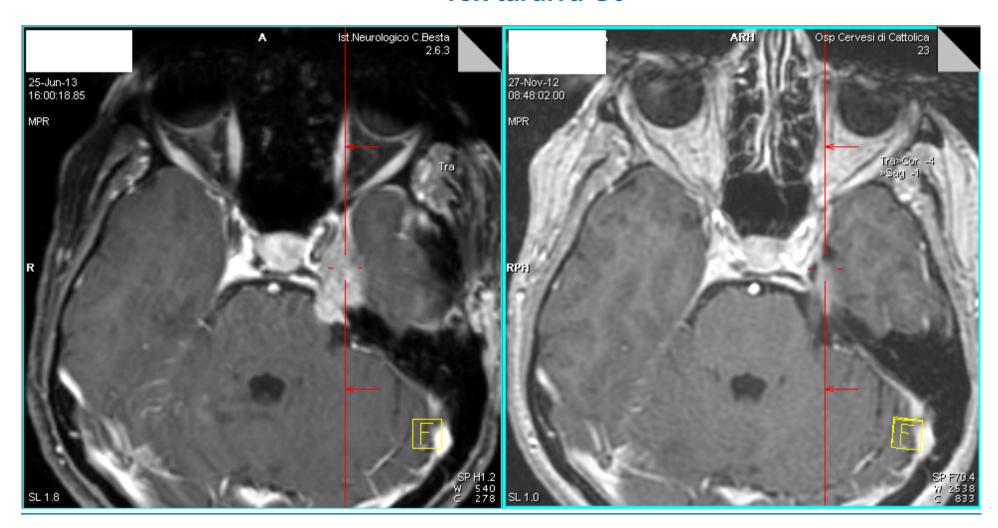


### CIRT: 68.8 Gy(RBE) (4.3 Gy(RBE)/frazione, 16 frazioni, 4 fractions/weekly



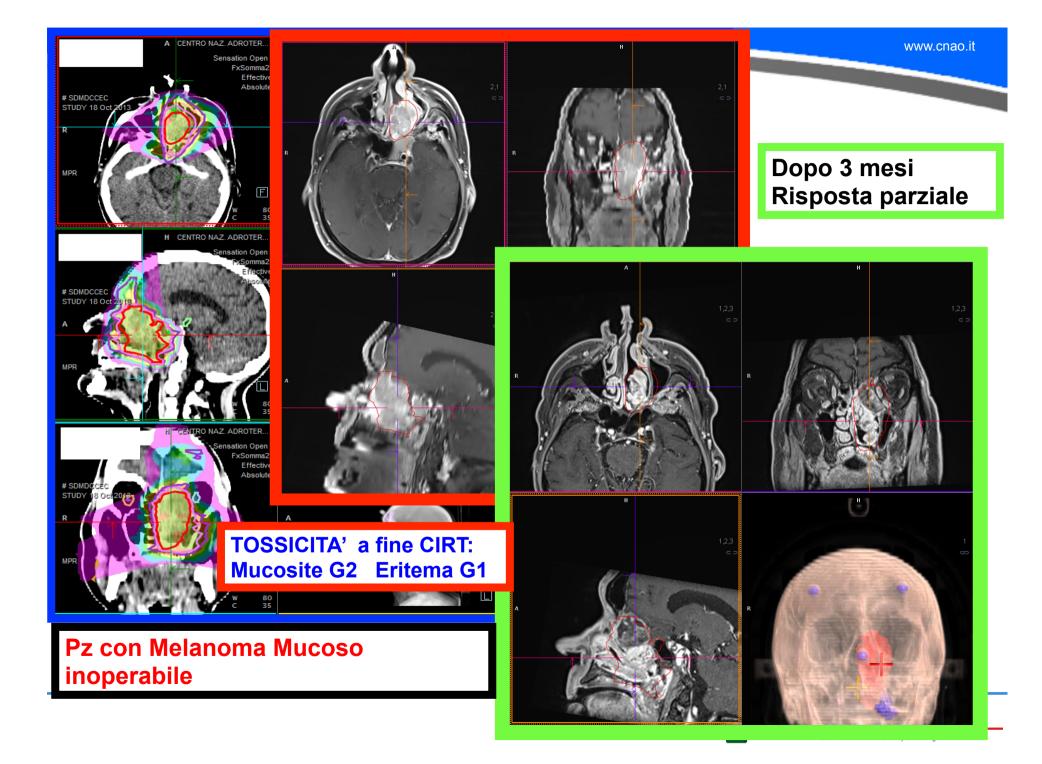


# Maggio 2014 ( 9 mesi) controllo radiologico di malattia confermato dalla MRI. Tox tardiva G0









### **Durante CIRT**

**Fine CIRT** 





**Mucosite G2** 

**Eritema G1** 





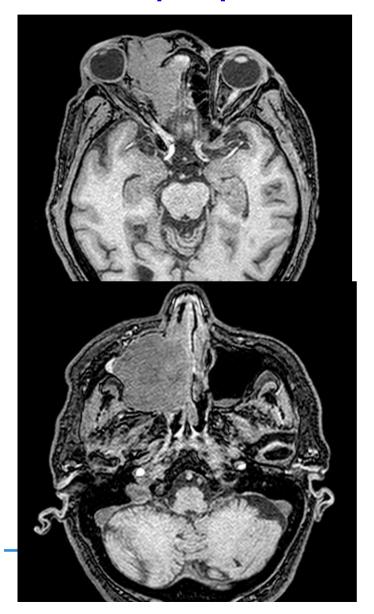


9 mesi





### paziente analogo sottoposto a chirurgia demolitiva: RNM preoperatoria esiti dell'intervento

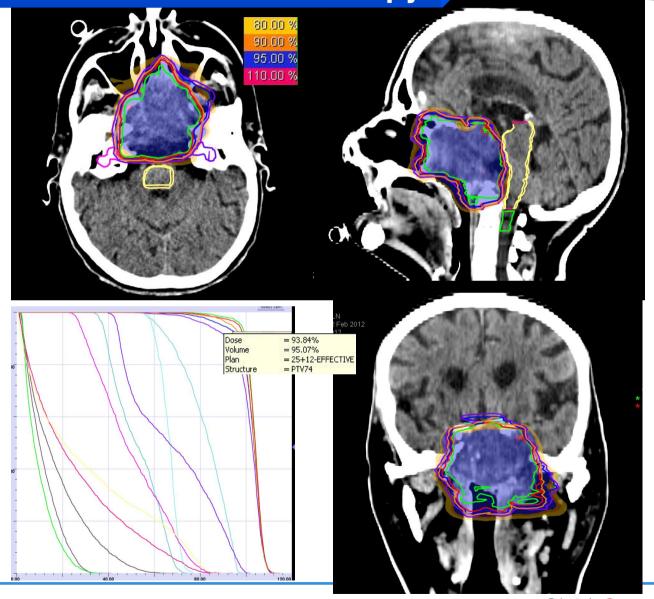








### **SKULL BASE CHORDOMA: Proton therapy**







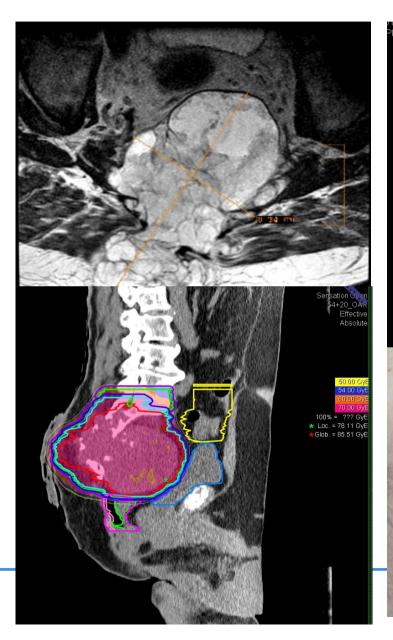
### **SKULL BASE CHORDOMA: Proton therapy**

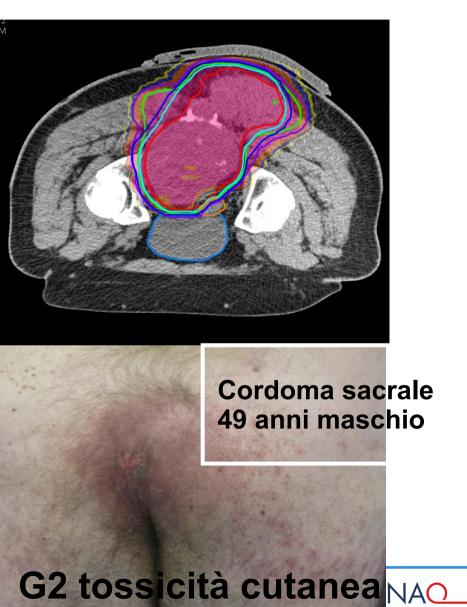


### 10 months F-up



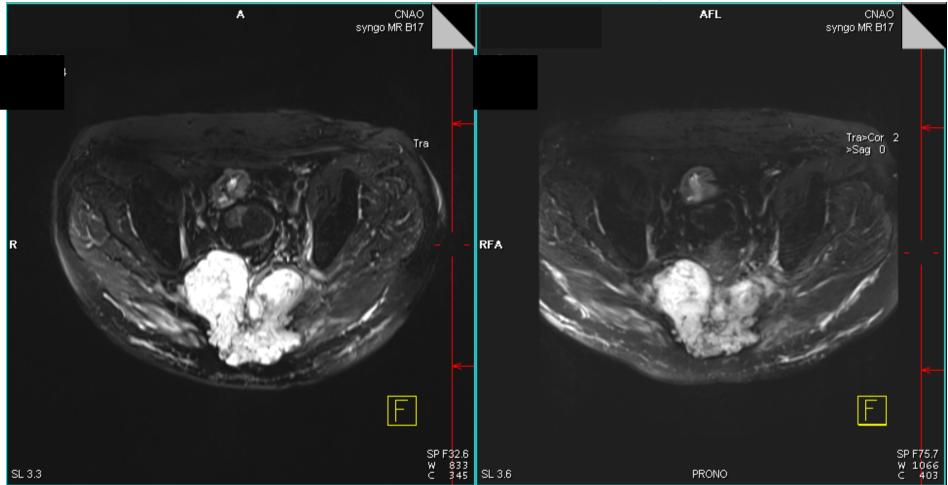
### **CORDOMA SACRALE: Terapia con Ioni Carbonio**





#### **Prima del**

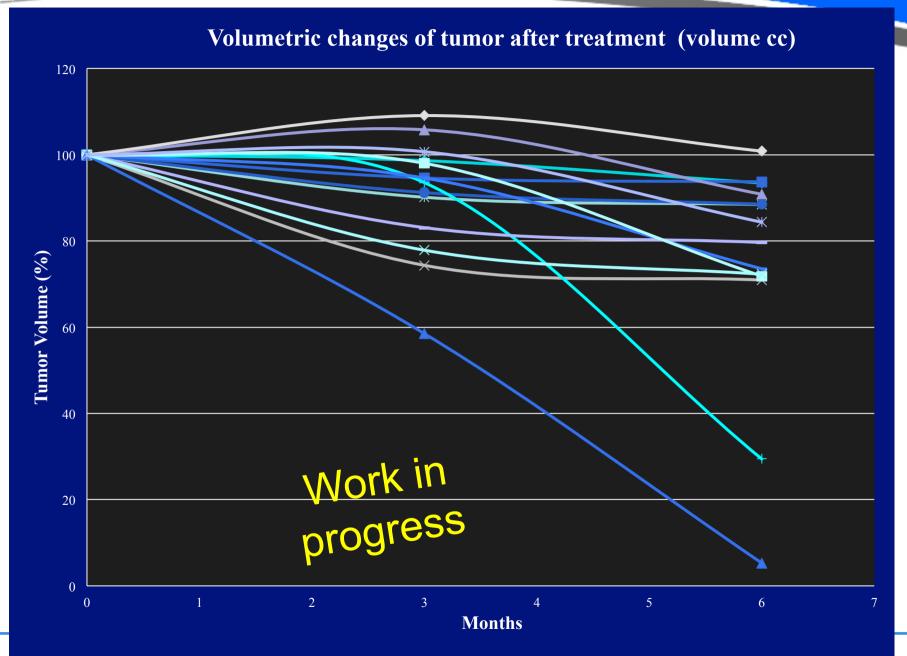
### 1 anno dopo il trattamento



Dopo 1 anno dal trattamento residua ipoestesia alla gamba sx : G1 tossicità, miglioramento della funzione urinaria e della continenza rettale, scomparsa del dolore, il paziente sta seduto senza problemi e cammina per 15-20 minuti



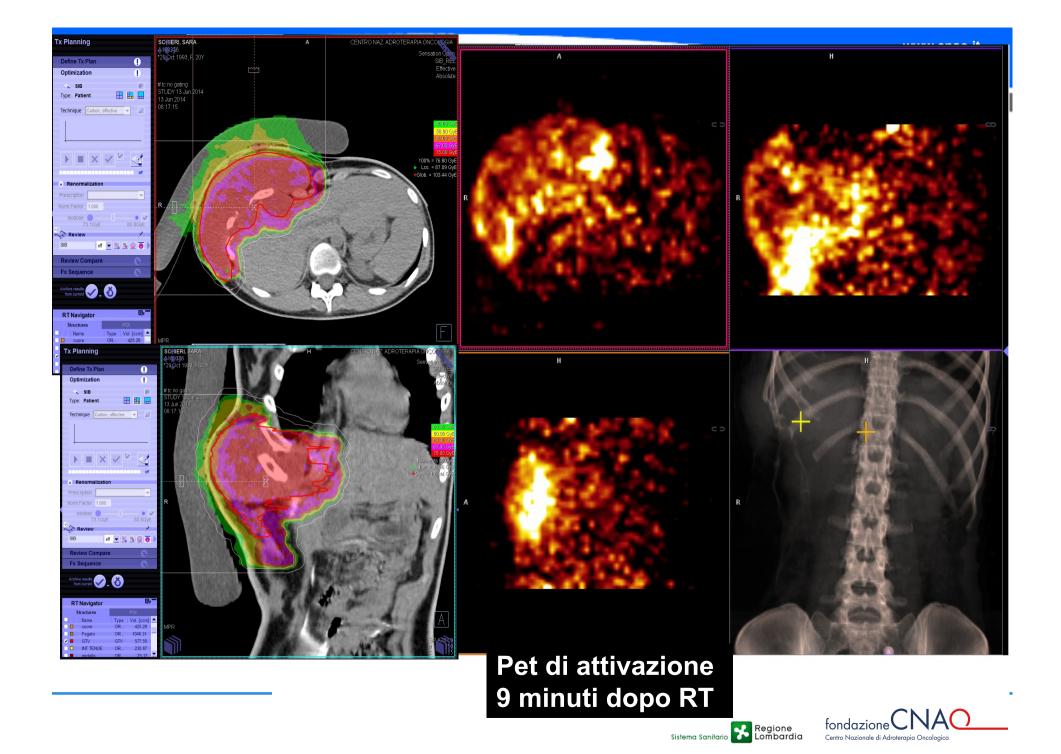






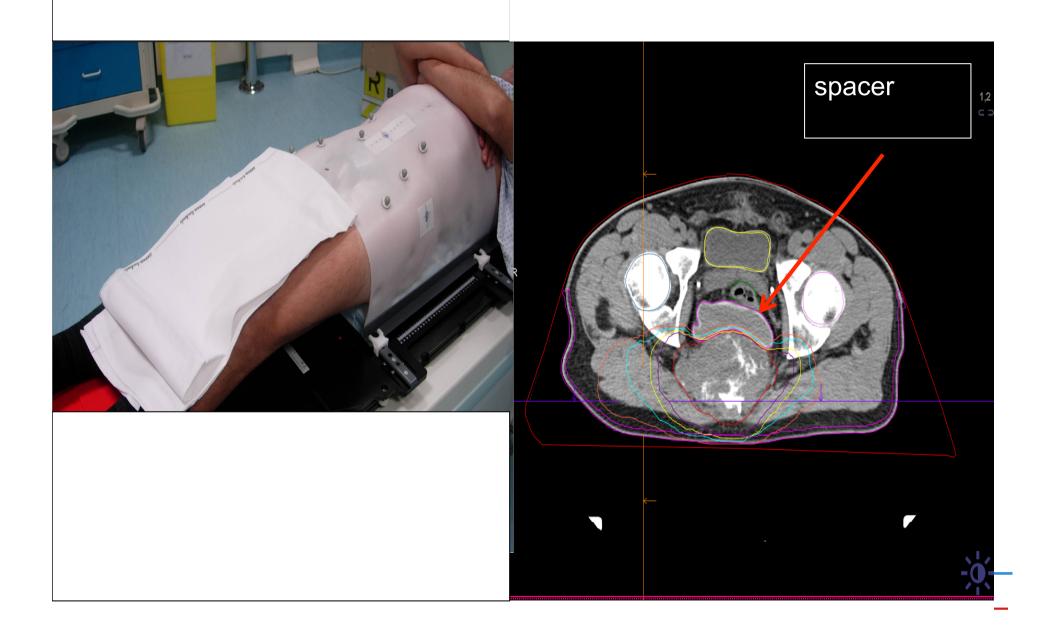


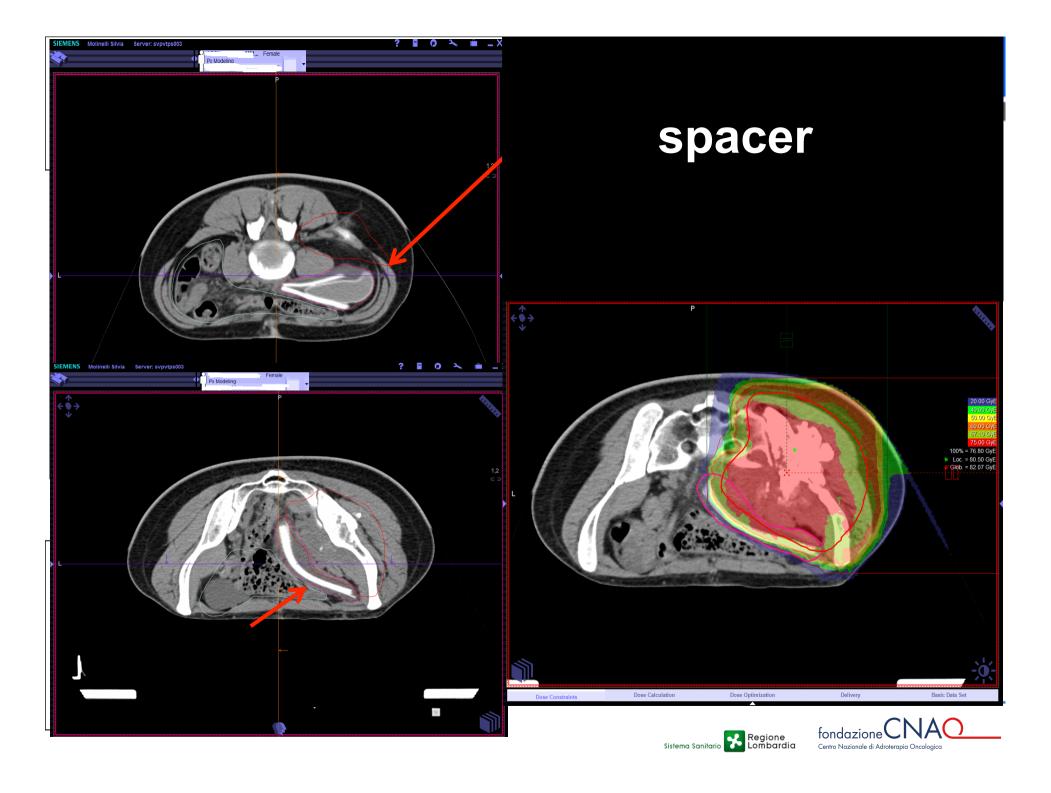






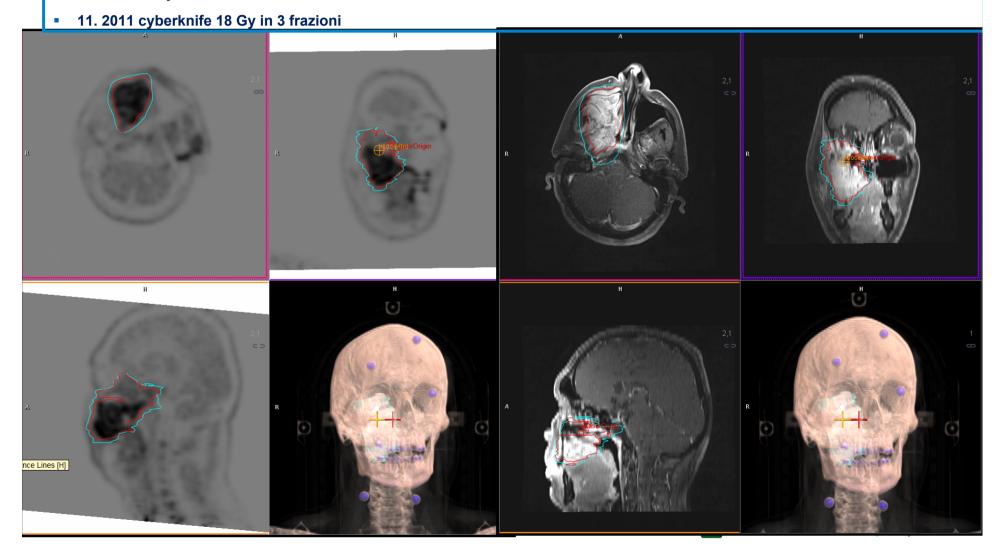






### Reirradiazione

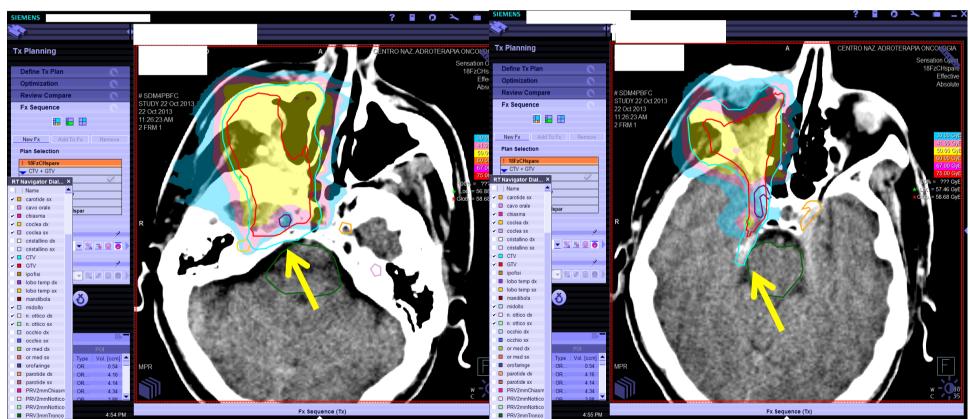
- 50 anni maschio carcinoma adenoido- cistico orbita destra, seno mascellare e fossa pterigoidea
- 2010 cyberknife 24 Gy in 4 frazioni
- 10. 2011 50 Gy IMRT in 25 frazioni



### Reirradiazione

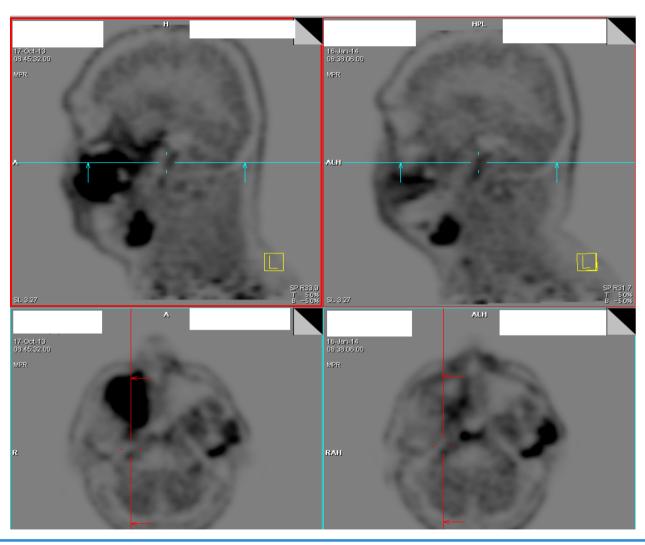
# Risparmio Selettivo della Carotide

# Risparmio Selettivo del tronco cerebrale





### PET (C11-Metionina) 1 mese dopo



Ridotto uptake del radionuclidde





### Reirradiazione

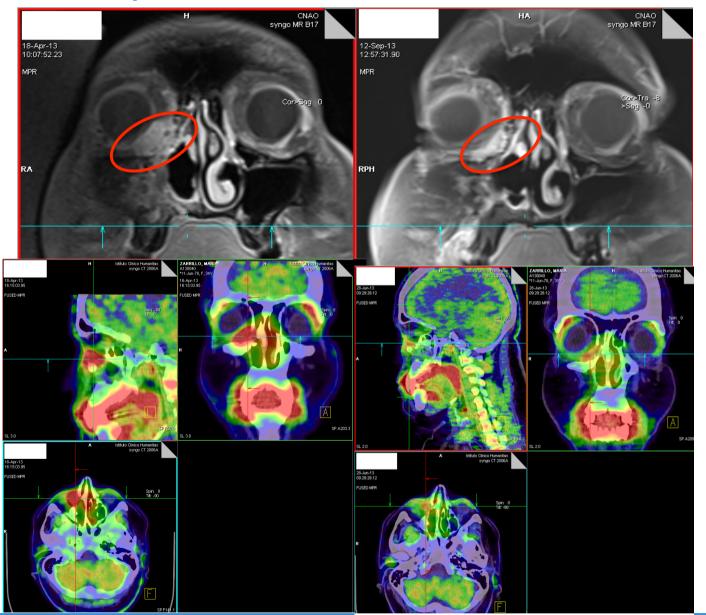
- 2006: diagnosi di ACC cavità nasale-rinofaringe
- 2006 RT 50 Gy in 25 fr.
- 2009: diagnosi 3 mts polmonari
- 2009 lobectomy
- 2012: MRI lesione solida di 17 mm in regione orbitaria ds in contatto con il globo oculare → ripresa di malattia
- 01/2014 chirurgia
- PET C11 Met → positiva





### Aprile 2013

### Settembre 2013





### Reirradiazione



Fine del trattamento G1 eritema e congiuntivite



3 mesi dopo G0

Il trattamento con loni carbonio è stato impiegato:

-per la sua elevata efficacia in ACC

-per l'ottima conformazione della dose al bersaglio che ha permesso la preservazione dell'occhio



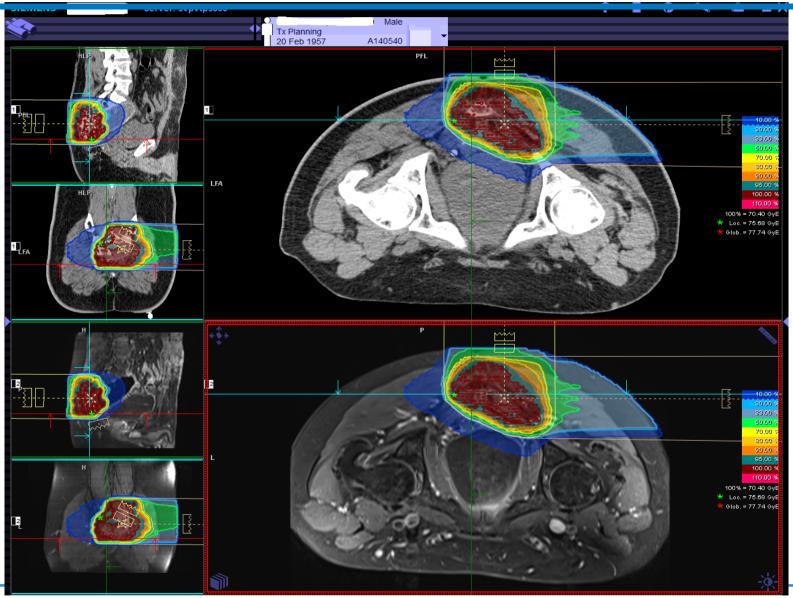
# Risultati dell' Adroterapia nelle recidive locali da carcinoma del retto

			Transmant	Survival Rate		Local	
		n	Treatment	2 y	5 y	Control	
Lybeert M	1992	76	RT	61%(1y)	3%	28%(3y)	
Knol HP	1995	50	RT	27%	8%	-	
Kim MS	2008	23	RT	82%	23%	74%(5y)	
Lee JH	2011	22	RT	66%	40%	56%(5y)	
Wanebo	1999	53	Surgery	62%	31%		
Morja	2004	48	Surgery	76	36		
Melton	2007	29	Surgery	65	20		
NIRS	2011	107	73.6	87%	45%	95%(5y)	



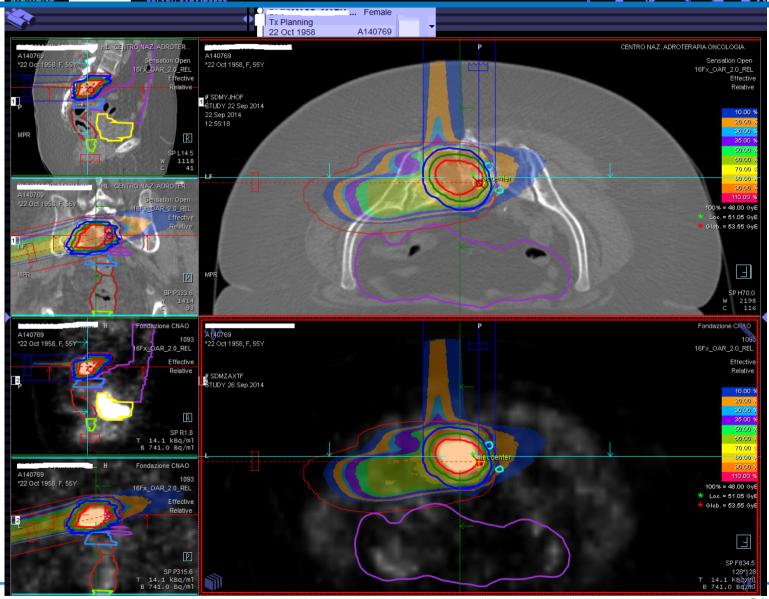


### REIRRADIAZIONE recidiva da carcinoma del retto





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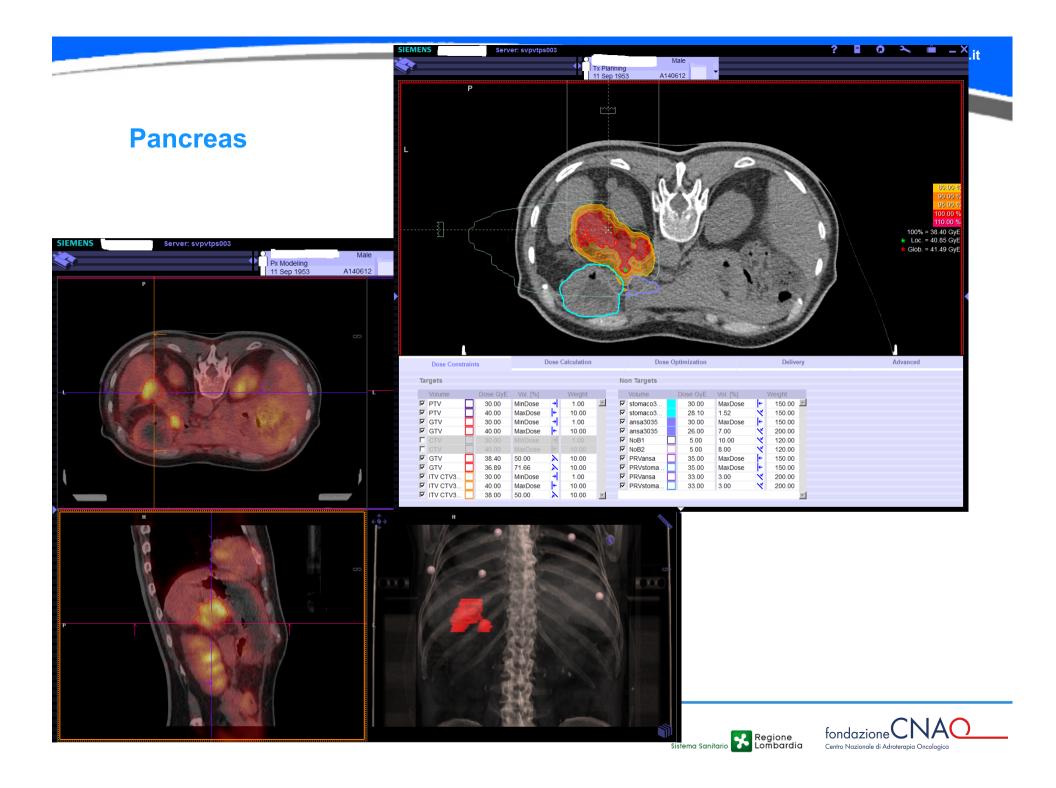




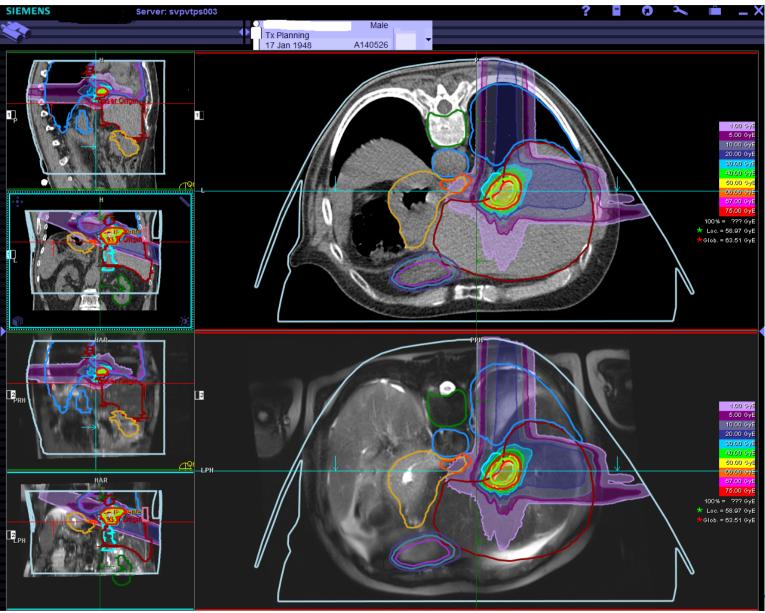
### **GEM+CIRT** carcinoma del pancreas localmente avanzato

	Year	n	Treatment	Dose	Survival	
i Gai		n	Heatment	Dose	1yr	2yr
ECOG	2008	34	GEM+RT	50.4Gy	50%	12%
		37	GEM	-	32%	4%
Ishii	2010	50	GEM	-	64%	14%
Sudo	2011	34	S-1+RT	50.4Gy	71%	25%
Small	2011	28	GEM+BZ* +RT	36Gy/15fr.	45%	17%
Schellenberg	2011	20	GEM+ SBRT 25Gy/1		50%	20%
NIRS		34	GEM+CIRT	45.6-52.8 GyE	<b>72</b> %	68%



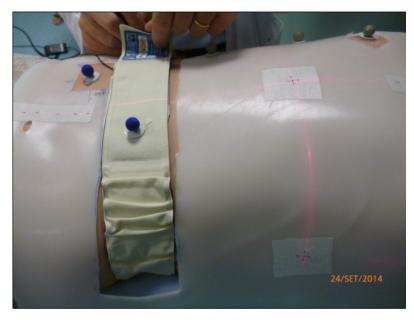


### **HCC**





### Moving organs: 4-D treatment strategies at CNAO

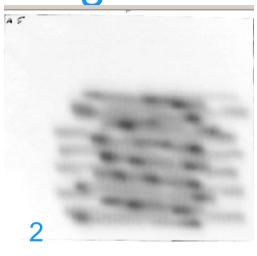


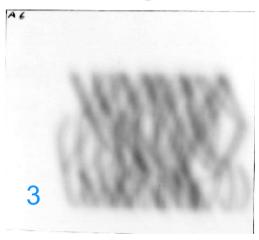
- Riduzione movimento respiratorio (meno di 5 mm) usando maschera termo-plastica o fascia di compressione
- Multiple porte di entrata (2-3) e trattamento frazionato
- Gating (ref. phase: max espirio; ANZAI system and OTS) + rescanning (N=5)

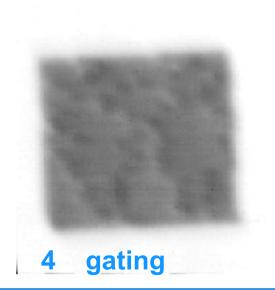


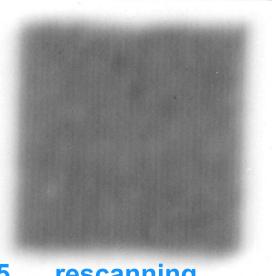


### Organ motion management









rescanning 5



#### Future direzioni

- Ipofrazionamento con Protoni
- Studio di fase III: protoni / ioni Carbonio vs RT convenzionale (ACC e Sarcomi)
- Melanoma del retto e della vagina
- Linfomi
- Ritrattamento di neoplasie cerebrali
- Neoplasie polmonari avanzate
- Pazienti Pediatrici
- Studio di fase III : ioni Carbonio vs RT/CT in pancreas localmente avanzato
- Attivazione di linea sperimentale
   Studi di efficacia di nuove particelle







"C'è vero progresso solo quando i vantaggi di una nuova tecnologia diventano per tutti

H. Ford

**Grazie per l'attenzione** 

