

Dott.ssa Ester Orlandi

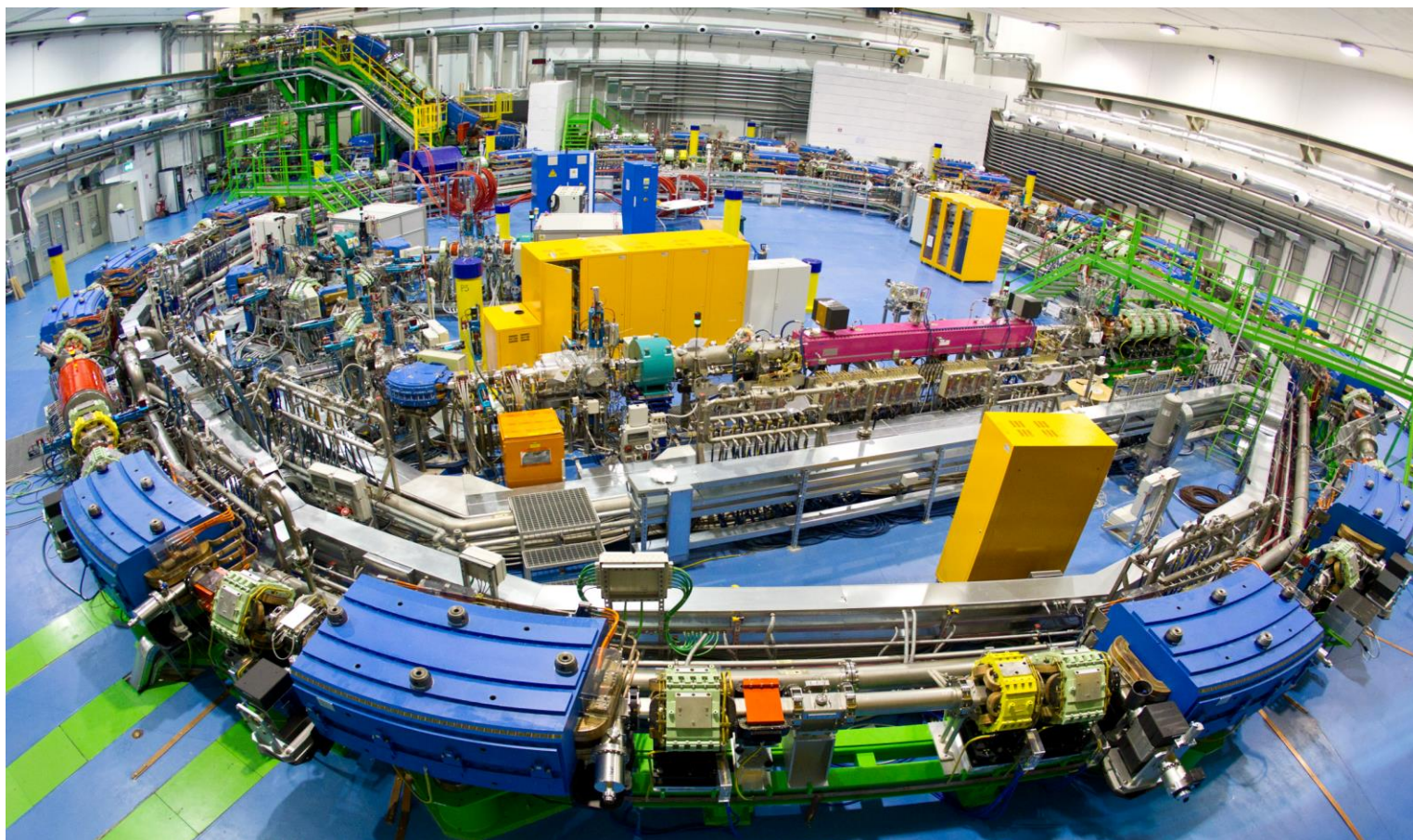
Chief of Clinical Department
Fondazione CNAO,
National Center for Oncological
Hadrontherapy

21/05/2021



CNAO in Pavia

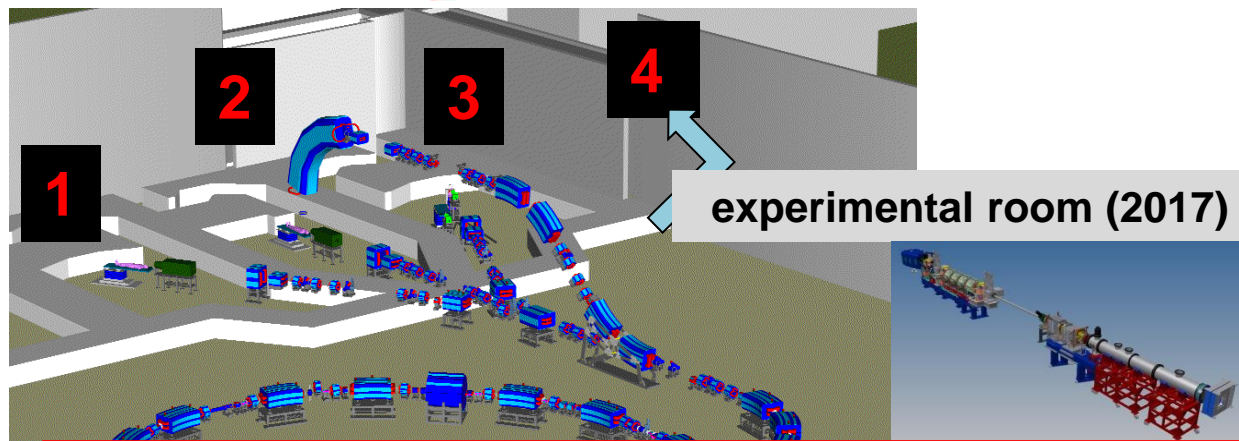
dual center
Protons/Carbon Ions



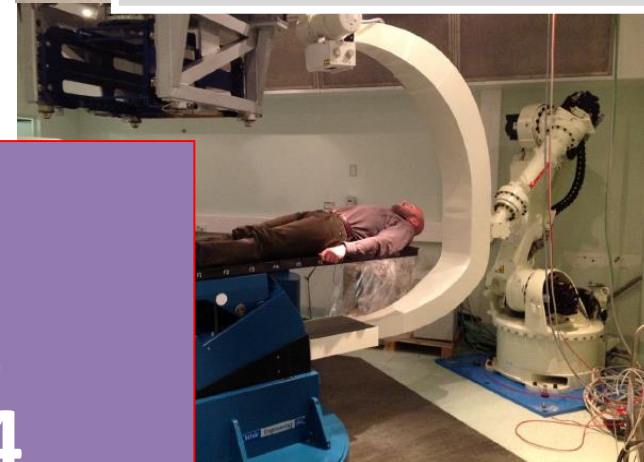
Experimental Phase
179 patients
September 2011-
December 2013

CNAO in Pavia
dual center
active scanning
Protons /Carbon Ions

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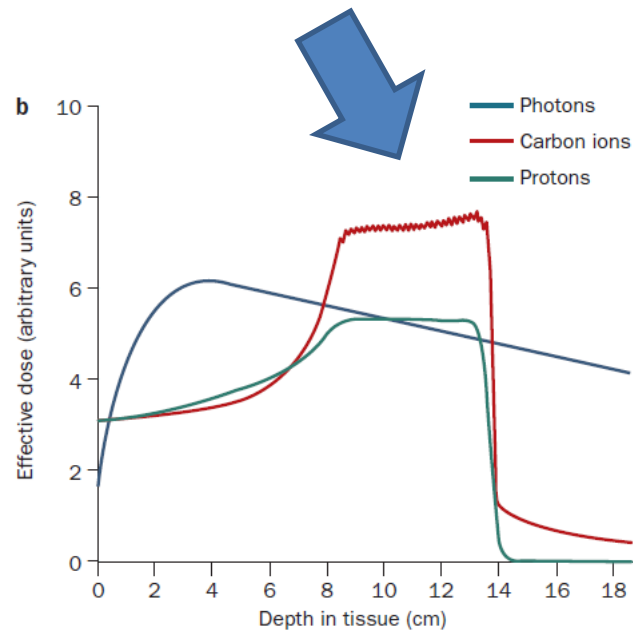
in room 3D imaging



Clinical Phase
(National Health System)
Started since January 2014

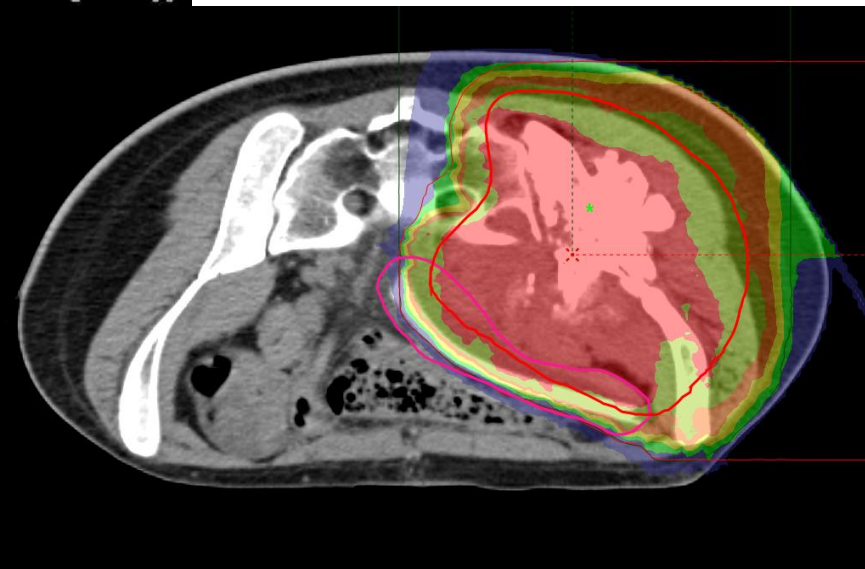
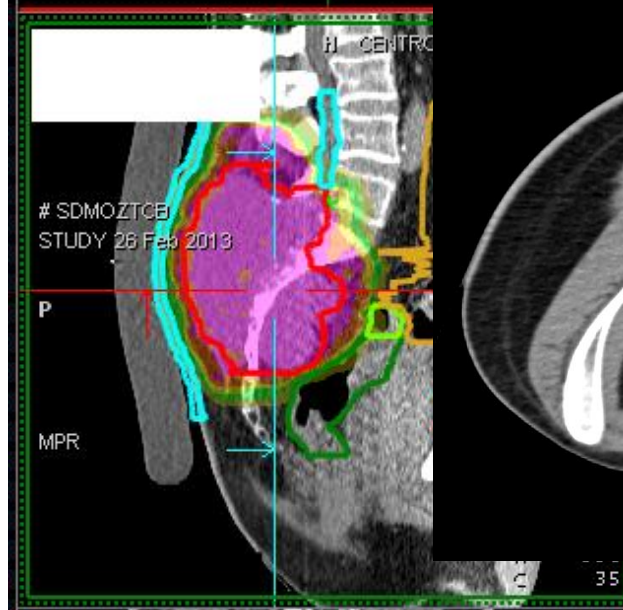
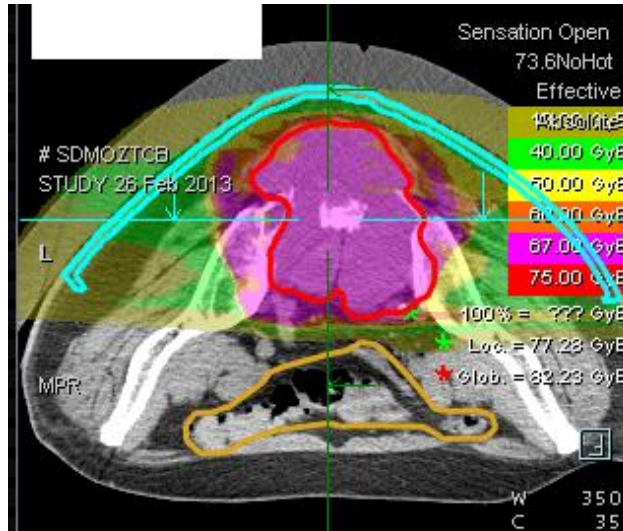
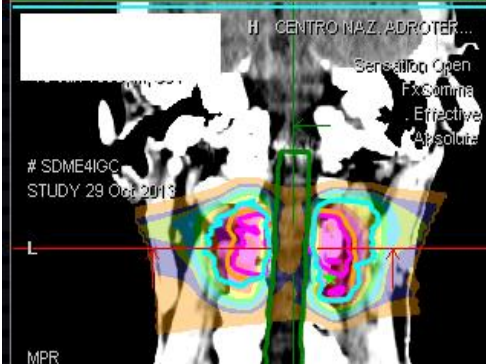
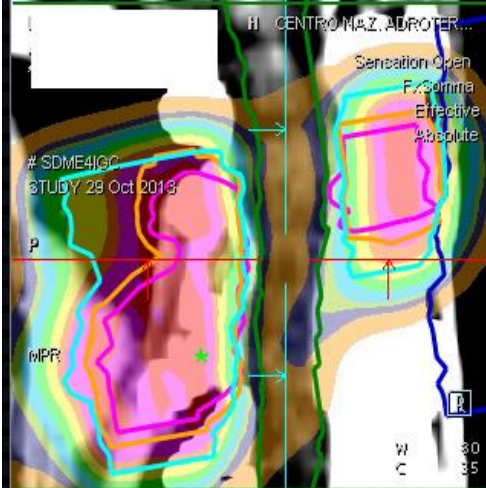
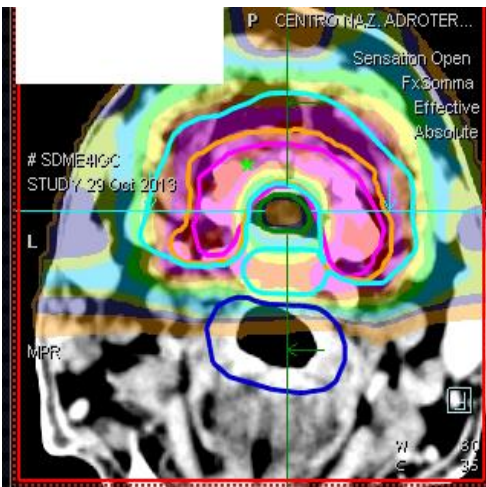
Hadrontherapy

SOBP, spread-out Bragg peak.



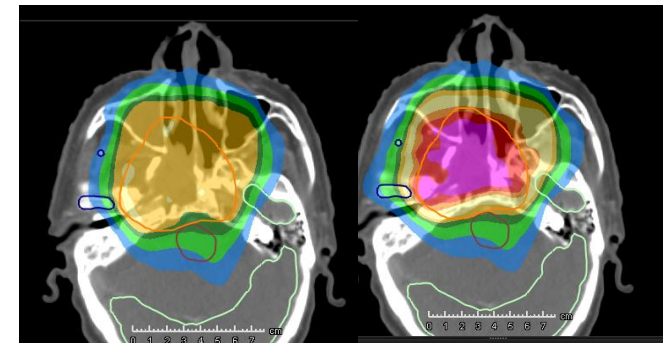
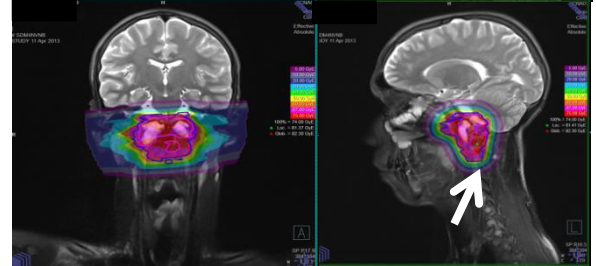
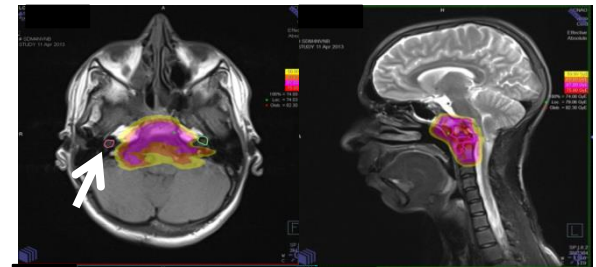
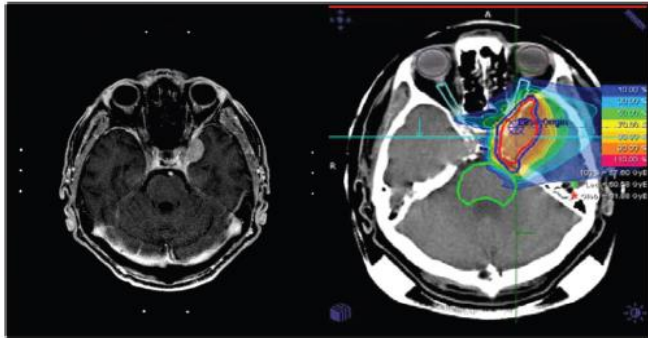
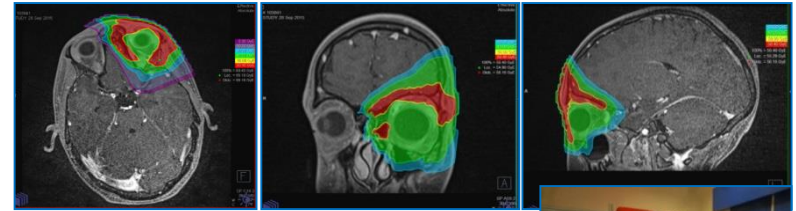
Dosimetric proprieties

Main Goal: OARs Sparing



Selection Criterias

Proton : Complex shaped tumor and radisensitive structures sensible to mean dose



Dose prescription could be increased without increasing the dose to organ at risk.

*Neurocognitive function preservation
Endocrinal and Coclear function sparing*

Radiobiological properties

Main Goal: prevent DNA repair mechanisms



Low LET (photons, protons)

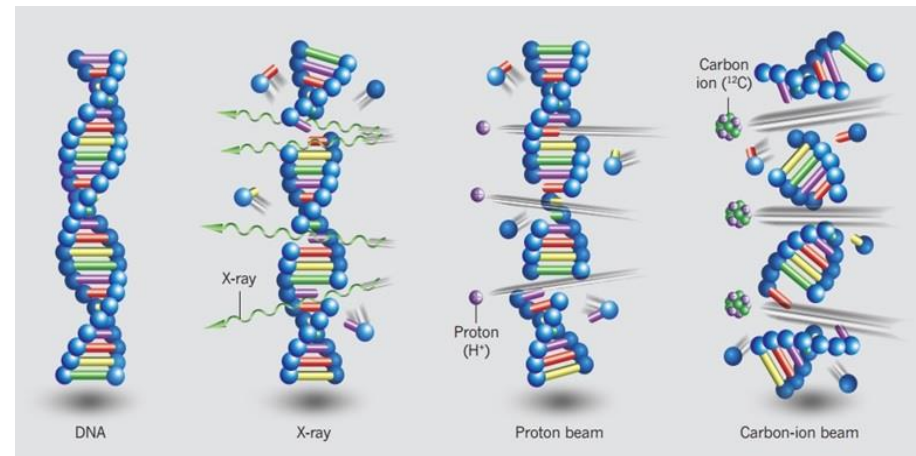
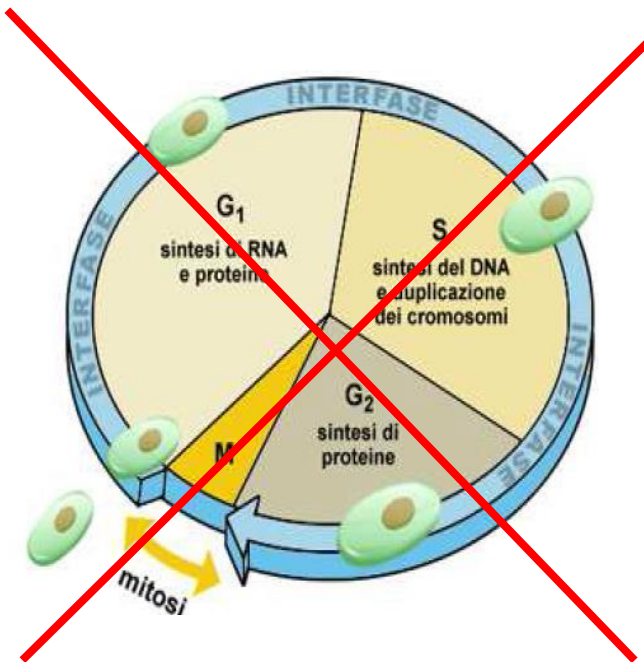
1-----1-----1-----1-----

(<20 Ke V/micron)

High LET (carbon ions)

1---1---1---1---1---1---1---1--- 1--- 1---

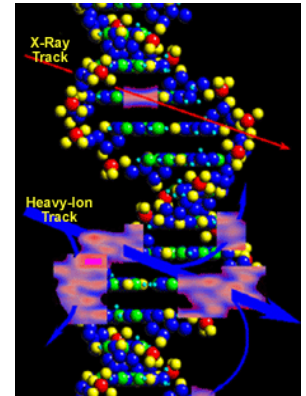
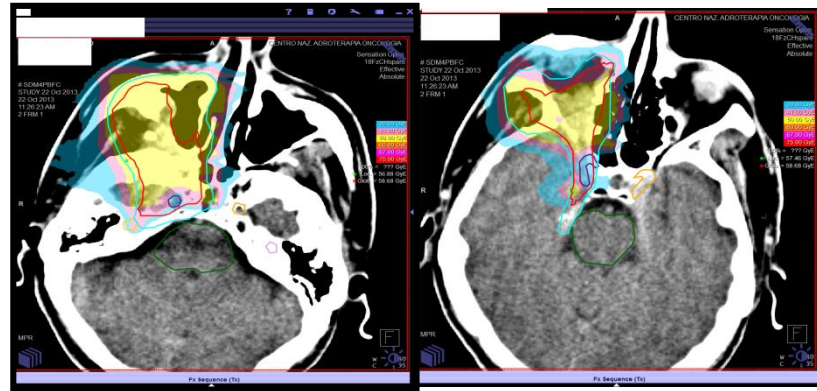
(> 20 – 100 KeV/micron)



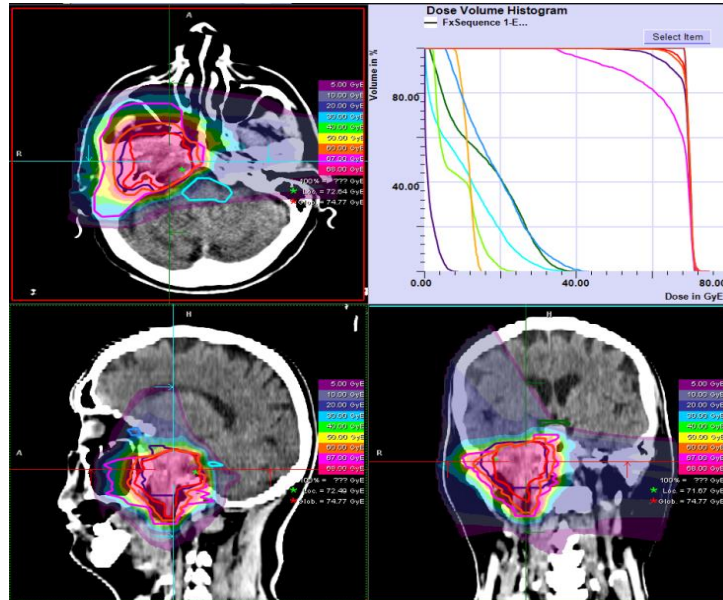
Selection Criterias

Carbon Ions More efficacy in radioresistant clones

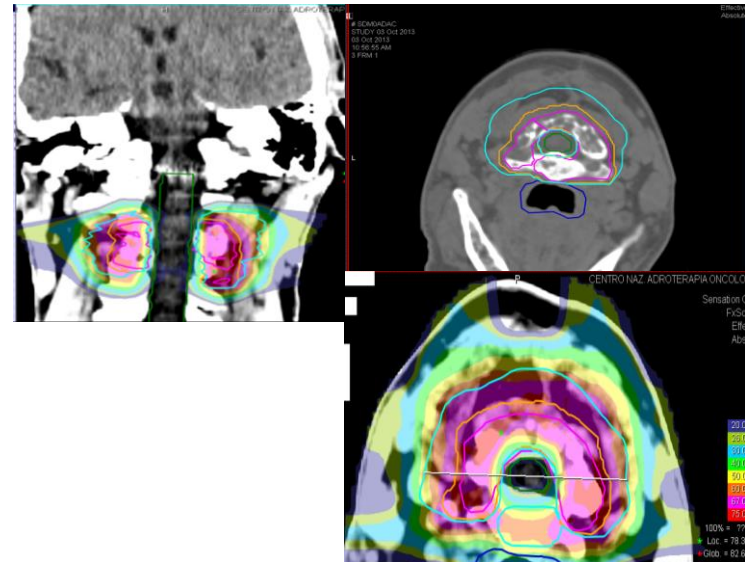
Complex shaped tumor:



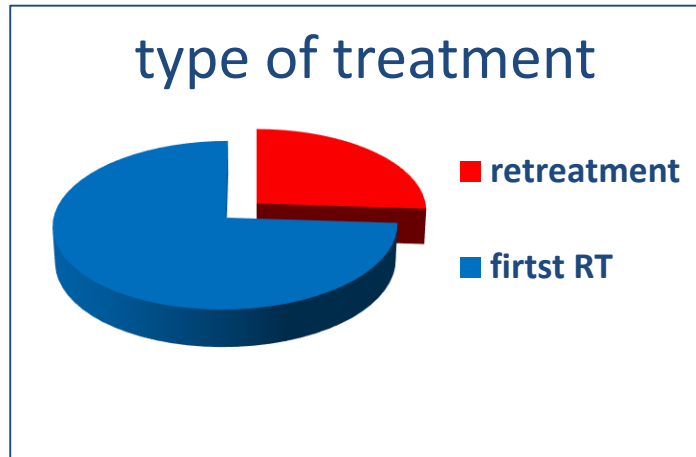
Selective OAR Sparing



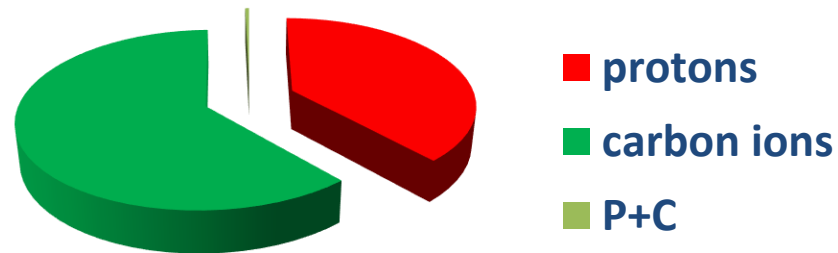
Steep dose gradient

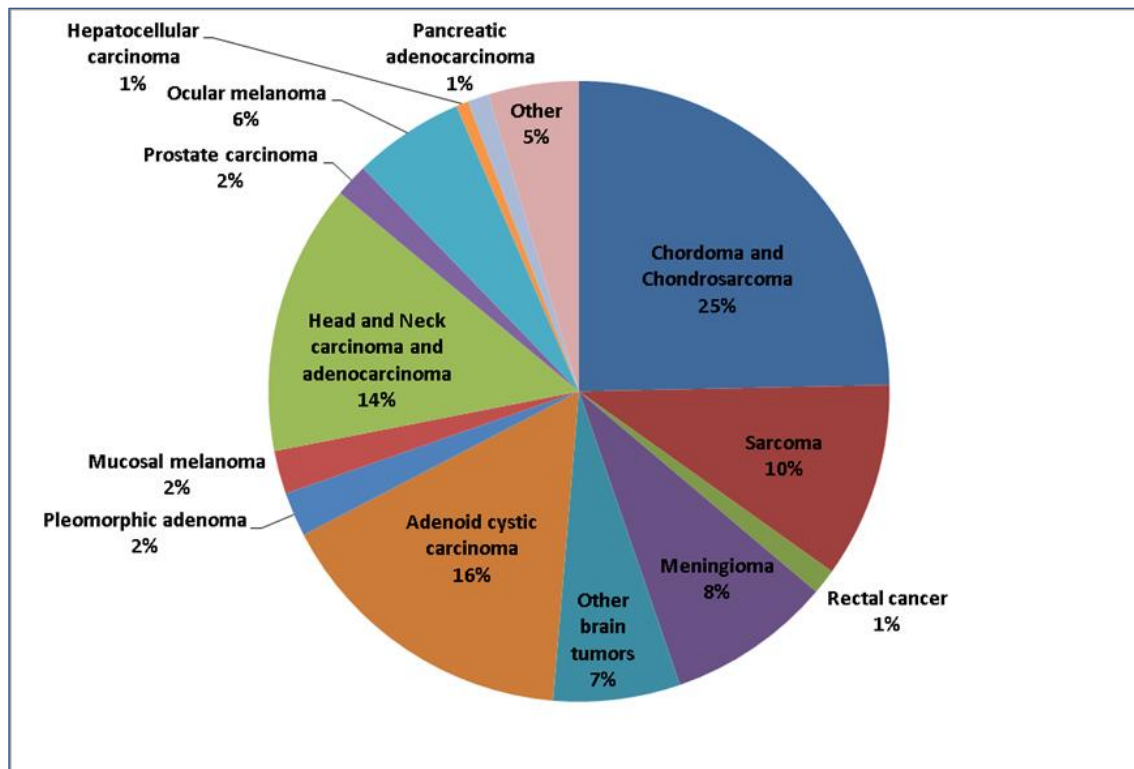


Patients 3208

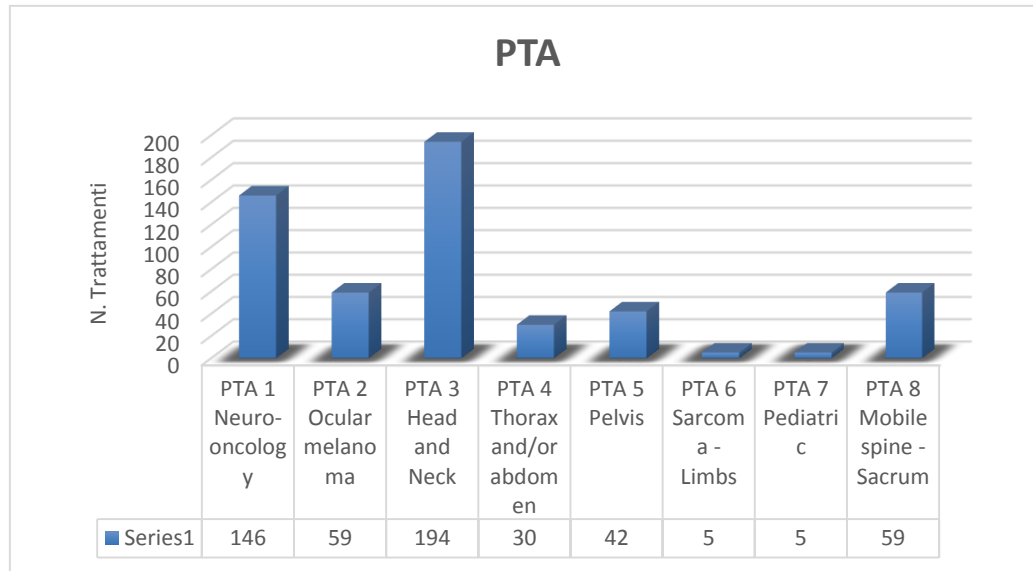


- ✓ Radio resistant tumors
- ✓ Complex shape tumors
- ✓ Located close to critical structures





2020



PTA 1: NEURONCOLOGIA, TOT 146

PTA 2: TRATTAMENTO CON PROTONI DEI MELANOMI OCULARI, TOT 59

PTA 3: TUMORI DISTRETTO CERVICO CEFALICO, TOT 194

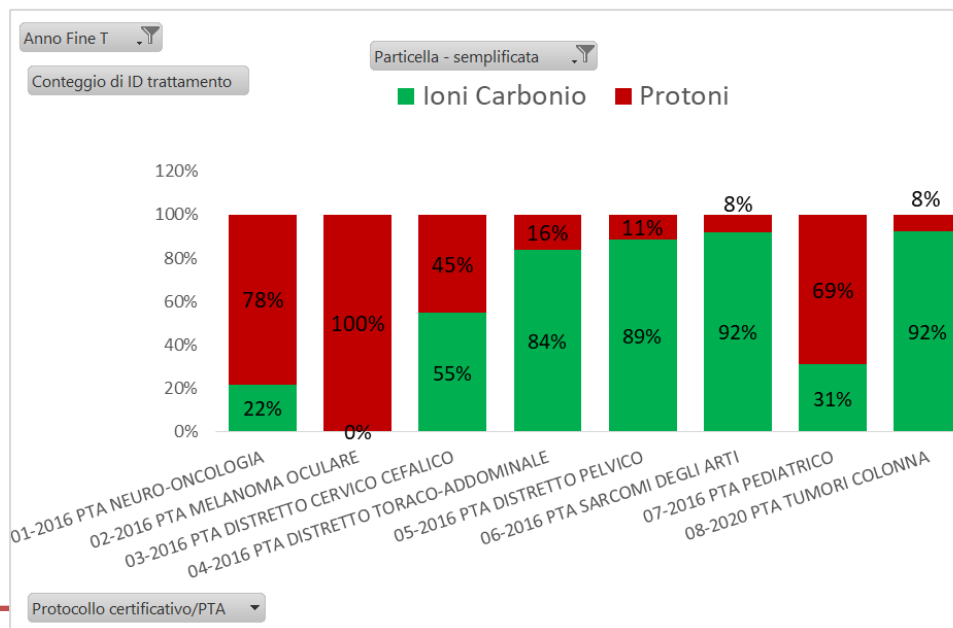
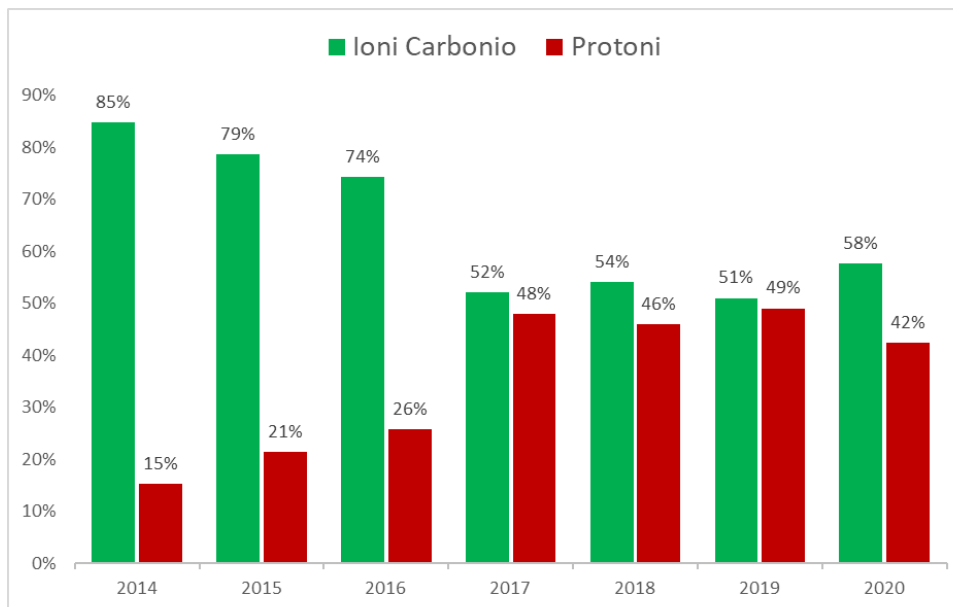
PTA 4: DISTRETTO TORACO-ADDOMINALE, TOT 30

PTA 5: ADROTERAPIA NEI TUMORI DEL DISTRETTO PELVICO, TOT 42

PTA 6: ADROTERAPIA NEI TUMORI (SARCOMI) DEGLI ARTI, TOT. 5

PTA 7: PAZIENTI PEDIATRICI (MINORI DI 17 ANNI), TOT 5

PTA 8: PATOLOGIE DELLO SCHELETRO TOT 53



CNAO clinical experience : Skull Base Chordomas

135 pts

FU = 44 months (6 – 87 range)

RT Timing: At primary diagnosis 79 % (107/135)
At recurrence: 21% (28/135)

Intent of RT treatment

Exclusive RT: 4 % (5/135)
Post-operative RT: 96% (130/135)

Surgery 130 pts

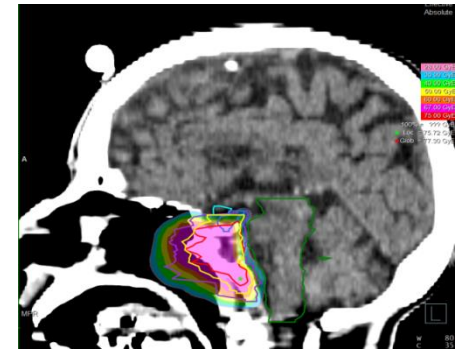
Macroscopic complete resection : 15% (19/130)
Macroscopic incomplete resection : 85% (111/130)

Protons : 3 yrs LC 89 % 5 yrs LC 84 %
5 yrs LC 100 % in R0 pts

Carbon ions : 3 yrs LC 77 % 5 yrs LC 71 %

Protons : 3 yrs OS 93 % 5 yrs OS 83 %

Carbon ions : 3 yrs OS 90 % 5 yrs OS 82 %



Proton 74 Gy
(RBE) /37 fx/ 65 pts

Carbon ions 70.4 Gy
(RBE) 16 fx/ 70 pts

Acute Tox G \geq 3 = 0
Late Tox G \geq 3 = 11%

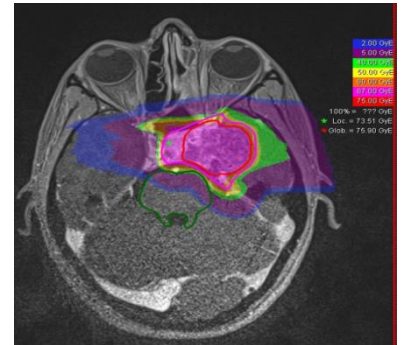
CNAO clinical experience : Skull Base Chondrosarcoma

50 pts

Intent of RT treatment

Exclusive RT:	51%
Post-operative RT:	49%

Proton	74 Gy (RBE) /37 fx/	50%
Carbon ions	70.4 Gy(RBE) /16 fx/	50%



Median gross tumor volume (GTV) was 16,4 cm³ (range, 1,64 – 28,28).

The median follow-up was 34 months (range, 5-70 months)

Local Control : 97%. (1-year, 3-year and 5-year LC rates were 100%, 96% and 96%)

Overall Survival : 97%, 93% and 93% respectively

No pts developed late G4 treatment-related toxicity.

G3 late toxicity :2 (5.7%) of pts: 1 pz hearing impairment (expected)

1 pz optic neuropathy (sight reduction) (expected)

CNAO clinical experience : Adenoid Cystic Carcinoma

255 pts

RT Timing: At primary diagnosis 86%
At recurrence: 14%

Intent of RT treatment

Exclusive RT: 38%
Post-operative RT: 62%

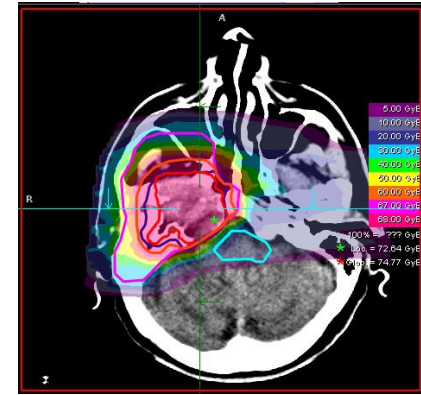
Surgery

Biopsy : 30%
Macroscopic complete resection : 20%
Macroscopic incomplete resection : 50%

PFS a 12 and 24 months was 81% and 67%

Distant Metastasis Free Survival 12 and 24 months was 86% and 81%

OS at 12 and 24 months: 95% and 85%



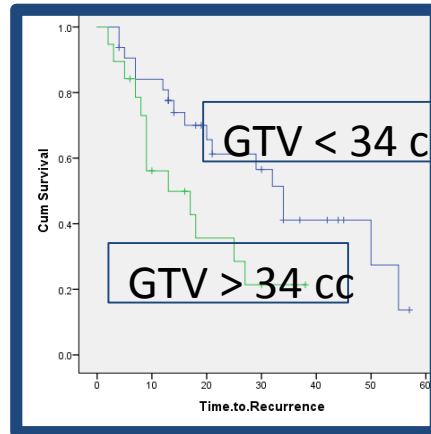
No G4

Carbon ions 68,8 Gy(RBE) /
16 fx/4 fx/wk

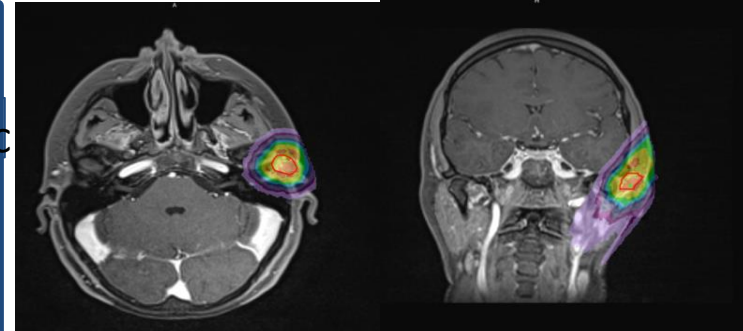
CNAO clinical experience : Salivary Gland tumors - Retreatment

pts 51

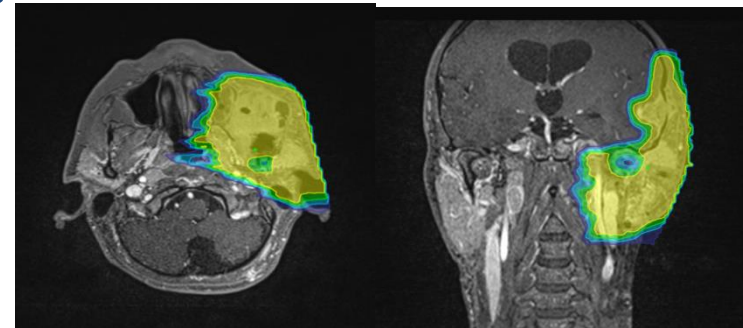
T-Stage	n	%
rcT2	1	2%
rcT3	5	10%
rcT4a	26	51%
rcT4b	19	37%



CIRT 60 GyE



CIRT 48 GyE



Prior RT dose : median 60 Gy (24 – 78 Gy)
Infield recurrences : 82 %

Median GTV 29 cc (1.75-205.54 cc)
Re-RT Carbon Ions: median 60 Gy RBE (46,8 – 74GyE)

Acute toxicity G3 :3.5%

Late toxicity G3 : 17%

3-yr PFS: 43.5%

3-yr OS: 54.5%

CNAO clinical experience : **LA Pancreatic Cancer**

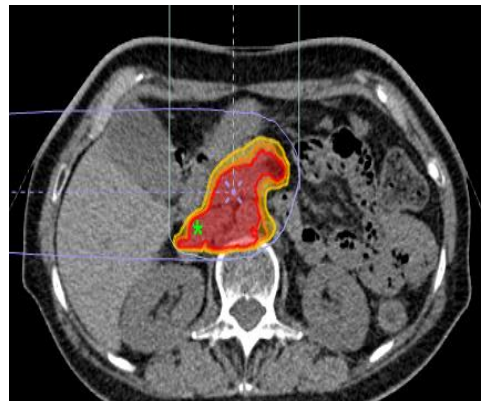
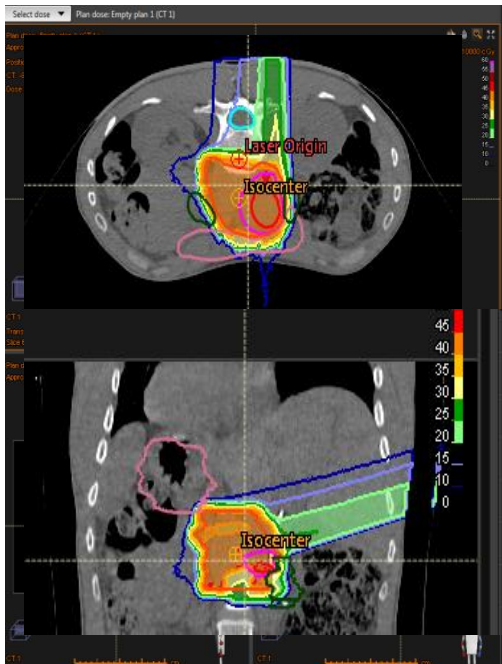
20 Patients

After chemotherapy (Gem/Gemox/Folfirinox)

CT

CIRT: 57.6 GyE (12 fx)

Toxicity: G2 – G3 0%



Age (median, range)	71 (43-78)
cT3	1
cT4	11
pT3	4
N1	9
N0	7
M1	2

1-y-LC: 71%

MDFS mediana:

11 months (4-55 m)

OS mediana:

12 months (5-55 m)

CNAO clinical experience : Spine Chordomas

48 pts

RT Timing: At primary diagnosis 40
At recurrence: 8

Intent of RT treatment

Exclusive RT: 12
Post-operative RT: 36

Surgery

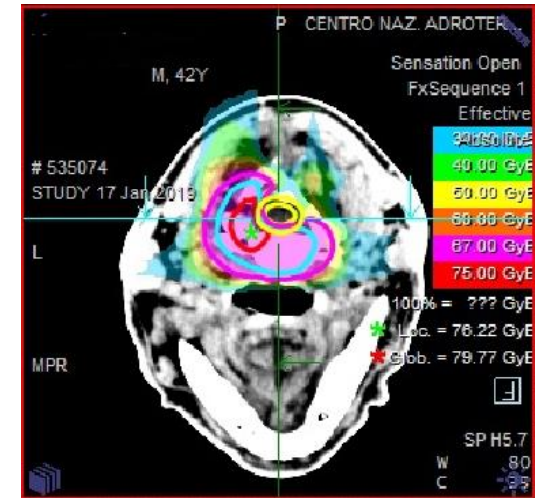
Macroscopic complete resection : 0
Macroscopic incomplete resection : 72%
Unresectable : 28%

Proton 74 Gy (RBE) /37 fx
Carbon ions 70.4 Gy(RBE) /16 fx

The median follow-up was 16 months (range, 4-74 months)

Local Control : 1-year, 2 years 97% and 70%

Overall Survival : 1-year, 2 years 95 %



No G3

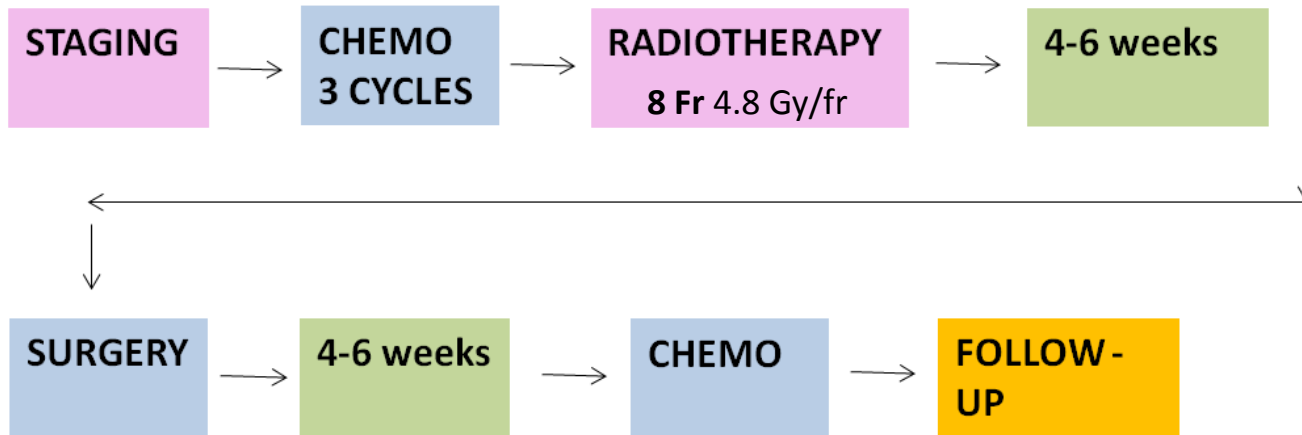


Ongoing trials

PIOPPO STUDY

(Preoperative IOn carbon Per Pancreas Operable)

Phase II trial, PROSPECTIVE, SINGLE ARM



PRIMARY END POINT:

Progression free survival

SECONDARY ENDPOINTS:

Overall survival

Resectability R0 (operable vs Borderline operable)

Acute and late toxicity

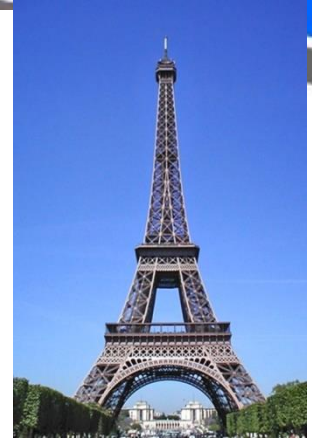
Intra e perioperative Toxicity



8 patients enrolled

PROTOCOL

Randomized study comparing the carbon ion radiotherapy with conventional radiation treatments including proton therapy - for the treatment of radioresistant tumors. PHRC ETOILE-ULICE



15 pts enrolled

SACral Chordoma: a Randomized & Observational study on surgery versus definitive radiation therapy in primary localized disease (SACRO)



**40 pts enrolled from February 2017;
22 pts ARM B Carbon ions radiotherapy @ CNAO**

Phase II trial



Carbon Ion re-irradiation in intra-axial gliomas recurrences
Carbon Ion re-irradiation in intra-axial non gliomas brain tumor recurrences
Carbon Ion re-irradiation in meningiomas recurrences

Study Protocol SINTART1

26 February 2013

**Multidisciplinary approach for poor prognosis sinonasal tumors:
Phase II study of chemotherapy, surgery, photon and heavy ion
radiotherapy integration for more effective and less toxic
treatment in operable patients.**

concluded

Study Protocol SINTART2

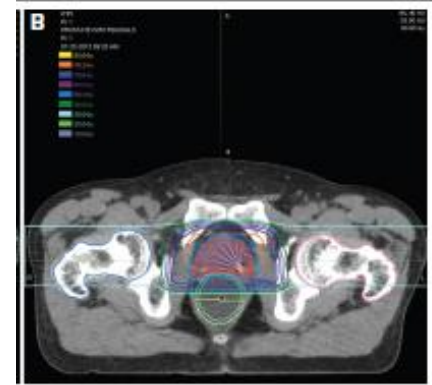
26 February 2013

**Multidisciplinary approach for poor prognosis sinonasal tumors:
Phase II study of chemotherapy, photon and heavy ion
radiotherapy integration for more effective and less toxic
treatment in inoperable patients.**

concluded

Phase II trial GU and GYN

Carbon Ion Boost and pelvic IG-IMRT in high risk Prostate cancer patients



Carbon ions re-irradiation of lymph node/pelvic recurrences of gynecological tumors

Carbon ions treatment of gynecological melanomas +/- immunotherapy

Boost with **carbon ions** in locally advanced cervical tumors for radio-resistant histologies and/or tumors unfit for brachytherapy boost.





Thanks

“True progress is when the advantages of new technology are available for all”

H. Ford