

Case Study

Salivary Gland and Paranasal Sinus

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Case 1

- L.G. Italian Male, 64 y
- Smoke: <10 py
- Job: Carpenter
- Comorbidities: no

In **February 2018** appearance of right nasal obstruction

Fiber-optic nasal endoscopy: **subtotal obstruction of right nasal cavity.**

✓ **CT-scan**
✓ **Biopsy**



Carcinoma of Ethmoid and right Maxillary sinus



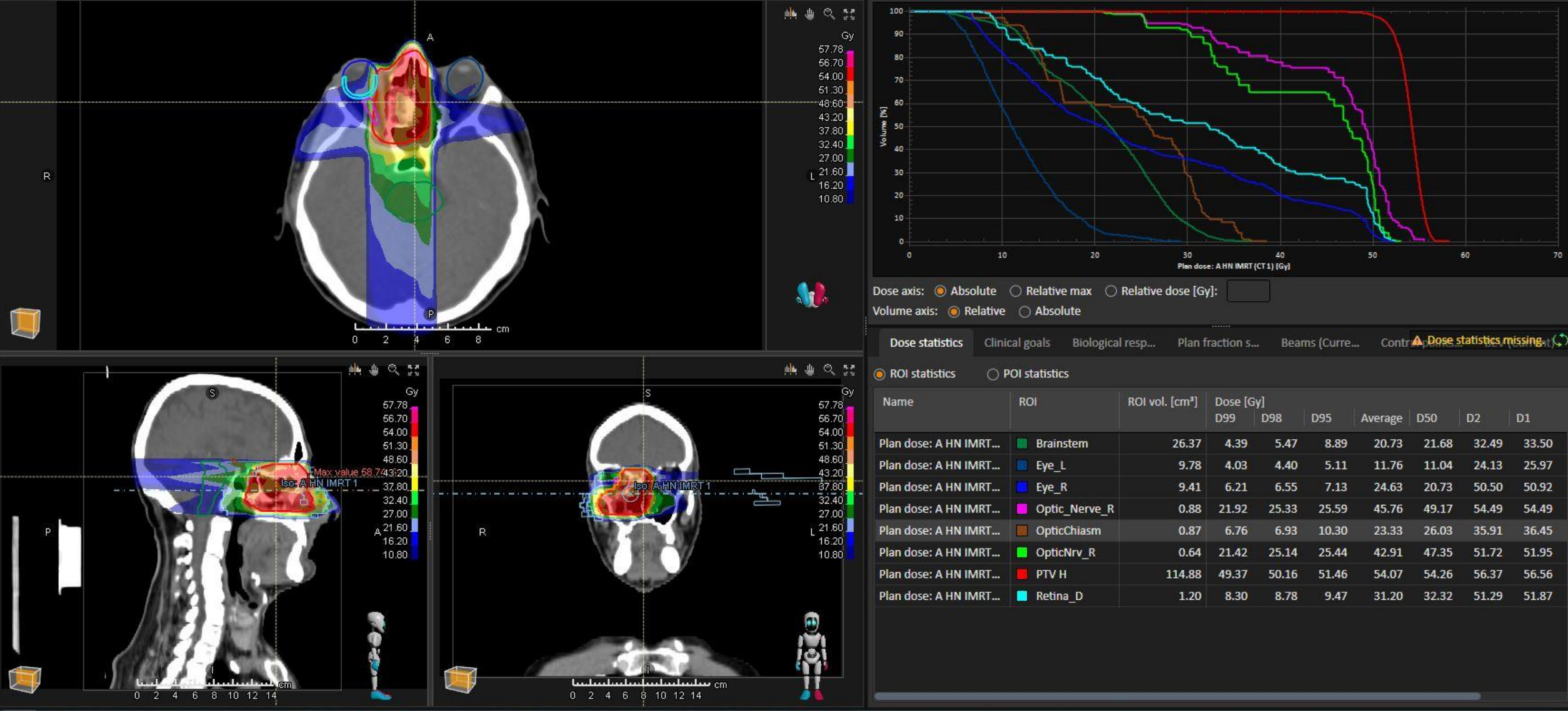
✓ **Surgery:** Ethmoidectomy with a right paralateral-nasal approach

Histological report: *Intestinal-type adenocarcinoma with extensive areas of necrosis, infiltrates the mucosa occasionally lined with squamous metaplasia epithelium.*

pT2cN0, stage II AJCC 8th edition

✓ Radiotherapy: IMRT 54 Gy in 27 fractions (2 Gy/fr)

ended at June 2018



July 2019

Surgical revision for local relapse

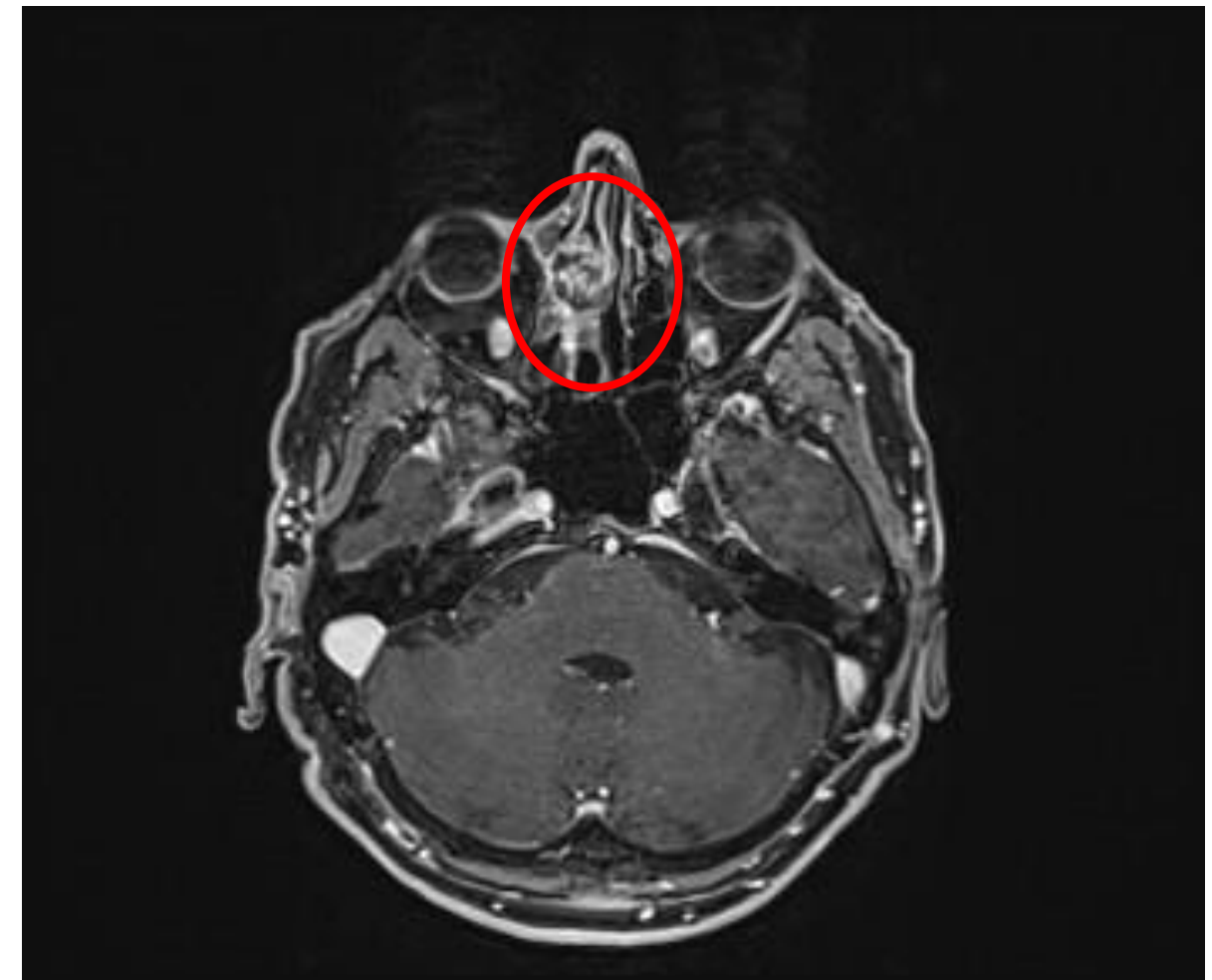


Clinical and instrumental follow-up NED



September 2020

H/N CE-MRI: pseudonodular and polypoid lesion, approximately 15 mm, in the middle-posterior right nasal fossa with strong post-contrast enhancement. This finding is compatible with locoregional recurrence of the previously diagnosed pathology and warrants biopsy confirmation.



Biopsy: confirm ITAC with necrotic component

December 2020

CNAO First evaluation

KPS 100

No relevant symptoms

Absence of late effect from previous RT

Required:

- TB CT-scan
- Histological revision (high expertise center)
- Previous RT-plan



- No distant metastasis
- **Histological revision** "*Confirmed intestinal-type sinonasal adenocarcinoma, with elevated MIB1. Mutational analysis of the TP53 gene revealed the presence of a CGA-TGA mutation, resulting in the amino acid substitution p.R213Ter in exon 6 of the TP53 gene.*"

Base line exams

- Eye examination
- Color-Doppler Ultrasound of the neck
- Odontoiatric evaluation
- Audiometric test

WHAT'S NEXT?

Tumor board



ITAC of the right nasal cavity TP53 mut rcT1 rcN0 M0

Surgery



Not indicated
-previous treatment (2 surgery, 1 radiotherapy)

Chemotherapy



Not indicated
-controversial role; TP53 mut



Feasibility Re-RT study

Planning

Patients characteristics

Performance status → **KPS 100**

Comorbidities → **no**

Age → **64 y**

Previous RT characteristics

Time to first radiotherapy → **< 2y (19 m)**

Late effects from previous RT → **none**

Previous dose exposure → **54 Gy**



Tumor characteristics

Site of relapse (in field, marginal, out of field) → **in field**

Local recurrence versus new primary → **local recurrence**

Radiotherapy files to generate a sum plan, is recommended if available in order to evaluate total cumulative doses and better optimize the reirradiation plan

Planning

OARs

Name	ROI	ROI vol. [cm ³]	Dose [Gy]						
			D99	D98	D95	Average	D50	D2	D1
Deformed Dose: A HN...	CTV	15.62	34.31	37.06	52.00	53.61	54.01	56.35	56.63
Deformed Dose: A HN...	Eye_L	5.63	6.25	6.61	6.99	12.48	12.19	19.13	19.83
Deformed Dose: A HN...	Eye_R	5.93	7.43	7.89	8.73	27.54	25.97	49.93	50.42
Deformed Dose: A HN...	optic chiasm	1.00	6.34	6.41	8.74	24.08	26.99	35.01	35.09
Deformed Dose: A HN...	Optic nerve L	0.99	13.34	13.57	14.63	19.20	19.43	22.85	23.37
Deformed Dose: A HN...	Optic Nerve R	0.93	25.74	26.29	32.22	45.27	47.33	52.49	52.71
Deformed Dose: A HN...	Retina_L	0.50	8.81	8.81	9.53	13.60	13.53	19.08	20.08
Deformed Dose: A HN...	Retina_R	0.44	12.93	12.93	15.49	32.67	33.16	51.04	51.62



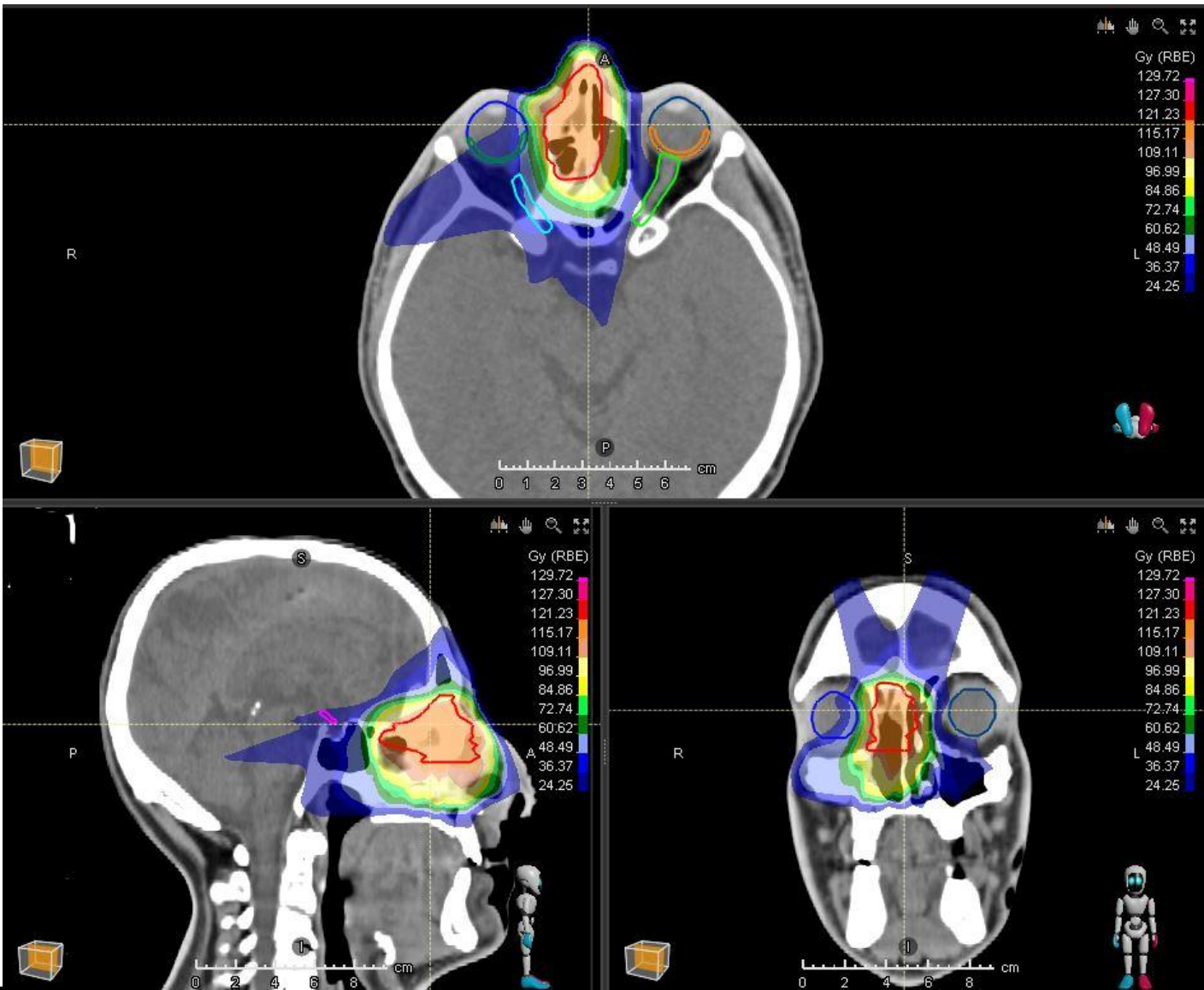
Optical structures

From 09/02/2021 to 04/03/2021 Radiotherapy with Carbon Ions with a Total dose of 64 Gy (RBE) in 16 fx (4 Gy/fx)



Planning

Sum Plan



Name	ROI	ROI vol. [cm³]	Dose [Gy (RBE)]						
			D99	D98	D95	Average	D50	D2	D1
Summed Dose (RBE): S...	CTV	15.68	99.12	102.31	111.26	117.09	117.85	120.07	120.39
Summed Dose (RBE): S...	Eye_L	5.64	7.06	7.37	8.11	13.07	12.98	18.80	19.25
Summed Dose (RBE): S...	Eye_R	5.94	8.59	9.12	10.55	29.84	28.99	57.79	60.05
Summed Dose (RBE): S...	optic chiasm	1.02	6.15	8.09	10.03	24.02	26.92	34.46	37.53
Summed Dose (RBE): S...	Optic nerve L	1.01	14.52	14.99	15.67	19.59	19.71	23.16	23.46
Summed Dose (RBE): S...	Optic Nerve R	0.96	29.01	31.45	32.64	46.19	48.10	54.04	54.52
Summed Dose (RBE): S...	Retina_L	0.50	9.99	10.40	10.54	14.55	14.32	19.19	19.44
Summed Dose (RBE): S...	Retina_R	0.45	13.99	13.99	16.54	34.68	31.68	57.30	58.63

Cumulative Dose at OARs

Constraints

Optic Nerve_R → D1% 58,63

D1% < 60

Retina_R → D1% < 58,63
Dmed < 34,68

D1% < 50-55
Dmed < 30

Eye_R → Dmean < 29,84

Dmed < 30

Follow-up

Baseline

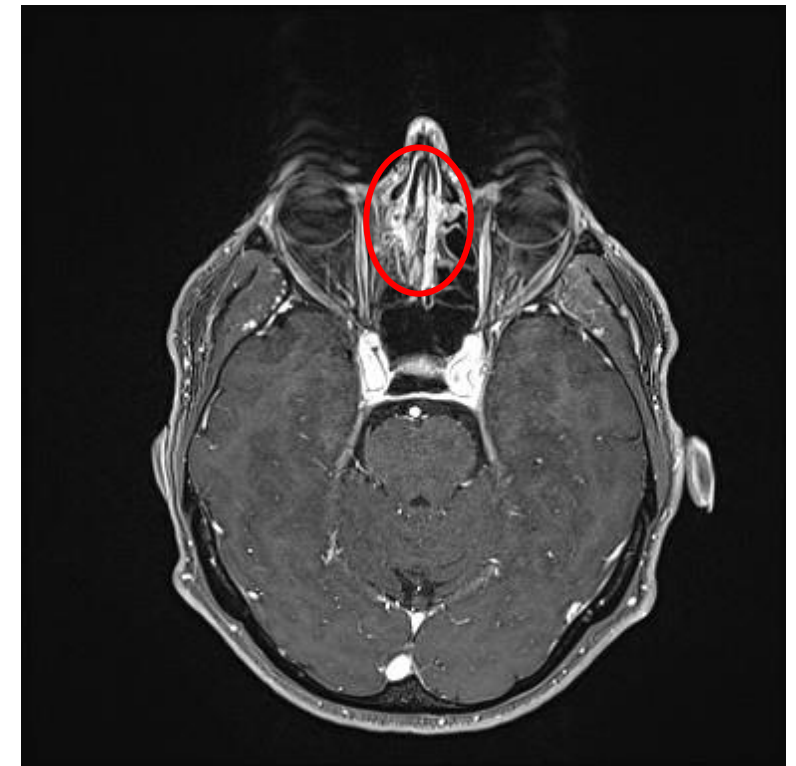
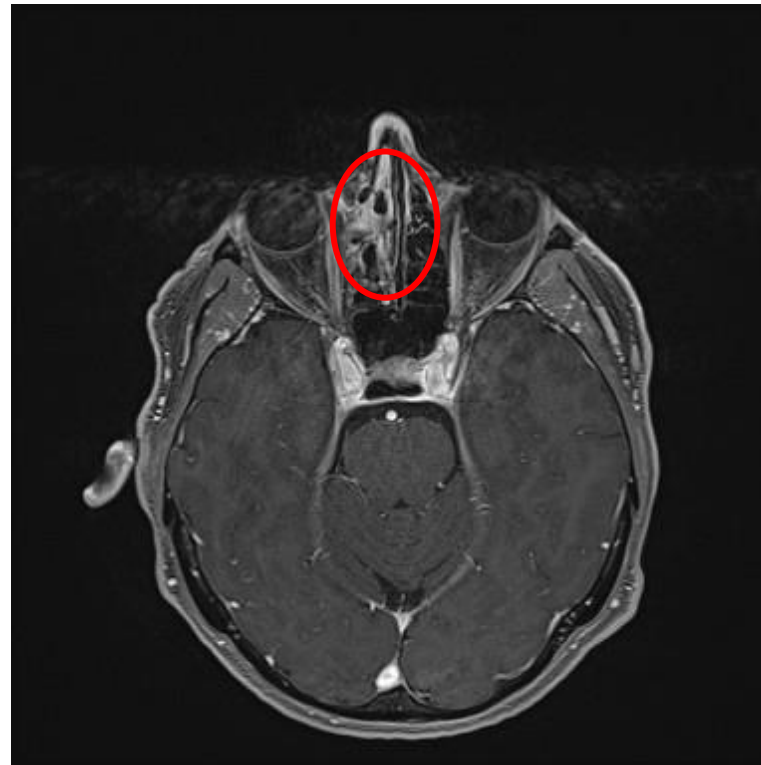
3 months

15 months

MRI: CR. presence of signal alteration characterized by low contrast enhancement, as for radiation treatment effect.

Toxicity:G0

Toxicity: watering eyes G1



26 months

- At the last follow-up patients was in good clinical condition without new symptoms except **watering eyes G1**
- The instrumental evaluation confirmed no signs of local or systemic relapse
- The last Eye examination didn't showed visual loss or other optical issue

Article

Particle Reirradiation of Malignant Epithelial and Neuroectodermal Sinonasal Tumors: A Case Series from CNAO

Barbara Vischioni ^{1,*}, Rossana Ingargiola ^{1,†}, Maria Bonora ¹, Sara Ronchi ¹, Anna Maria Camarda ¹, Stefania Russo ², Eleonora Rossi ², Giuseppe Magro ², Alfredo Mirandola ² and Ester Orlandi ¹

15 pz

Median time from first RT 37 months

Median Re-RT dose 54 Gy RBE (range 45-64)

LC was 44% 1-y and 35.2% at the 3-y

OS at 1 and 3 years were 92.9% and 38.2%, respectively.

10 patients developed at maximum G1–2 events

1 G3 late toxicity event was reported (dysphagia requiring a percutaneous endoscopic gastrostomy).

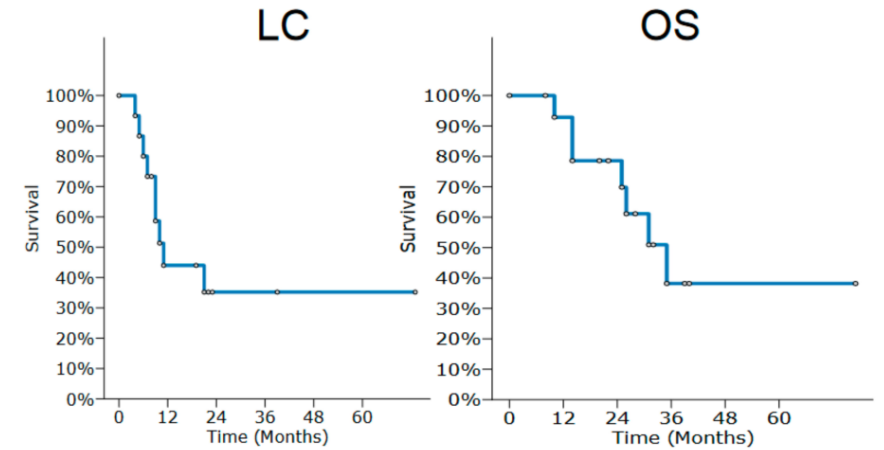


Table 3. Acute and late toxicity details after particle re-RT.

Grade of Toxic Effects	Number of Toxic Effects			
	Grade 1	Grade 2	Grade 3	Grade 4
ACUTE				
Mucositis	2	4	0	0
Dermatitis	6	3	0	0
Edema	0	1	0	0
Conjunctivitis	2	2	0	0
Neuropathy	0	2	0	0
Dry mouth	0	1	0	0
LATE				
Dry mouth	1	1	0	0
Dysphagia	1	1	1	0
Neuropathy	0	3	0	0
Brain necrosis	1	2	0	0
Periorbital edema	0	1	0	0
Dry Eye	1	0	0	0
Soft tissue necrosis	0	1	0	0
Hypopituitarism	0	1	0	0
Alopecia	1	0	0	0
Fibrosis	1	0	0	0
Trismus	1	0	0	0

Case 2

- Z.M. Italian Male, 70 y
- Smoke: former smoker
- Job: Dentist
- Comorbidities: prostatic cancer treated with surgery

November 2019 paralysis of the right VII cranial nerve

H/N CE-MRI: Right parotid lesion in contiguity with VII cranial nerve

✓ **Surgery** (December 2019): Right parotidectomy with reconstruction of the right facial nerve using sural nerve graft and right nodal dissection (level I-IV)

Histopathological report: **Salivary duct carcinoma** with massive perineural invasion and focal aspects of vascular invasion.

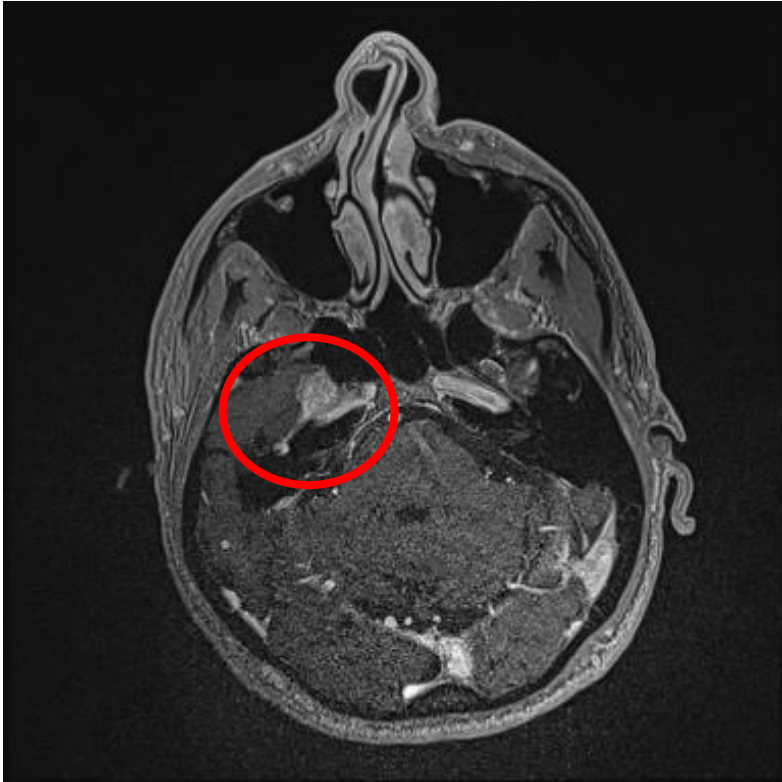
Immunophenotype shows absence of CK7, DOG1, vimentin, GCP15, CD117, ER, and PgR; weak incomplete membrane immunoreactivity for HER2/neu in more than 10% of neoplastic cells (1+); S100 and androgen receptors are present in over 95%.

pT4aN0, PNI+ R1

✓ **Radiotherapy: 3D-CRT 56 Gy in 28 fractions (2Gy/fr)**
ended at March 2020



April 2021



H/N CE-MRI: Presence of a **solid mass** at the right **foramen ovale**, extending cranially to the **Meckel's cave**, and also presenting a protrusion into the right middle cranial fossa, achieve the dura and the temporal lobe without signs of infiltration. The described finding **represent a perineural disease recurrence along the V3 branch**. A protrusion extends caudally along the course of the **inferior alveolar nerve** in the right mandibular canal. Additionally, linear contrast enhancement is noted along the course of the **great petrosal nerve**, with a solid mass measuring 5-6 millimeters at the internal auditory canal indicative of further perineural disease extension. Faint contrast enhancement is also recognized along the course of the facial nerve in the corresponding canal, possibly of similar nature.

Chest CT-scan: multiple polmonar parenchymal subcentimetric nodules

May 2021

CNAO First evaluation

KPS 90
Paralysis of the right VII cranial nerve
Trigeminal paraesthesia

Required:

- Previous RT-plan

Base line exams

- Eye examination
- Color-Doppler Ultrasound of the neck
- Odontoiatric evaluation
- Audiometric test



Base line exams

- Audiometric test: hearing impairment G1



Tumor board discussion



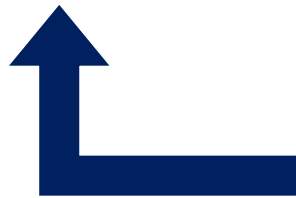
Salivary duct carcinoma rcT4b cN0 cM1, HR>95%

Re-irradiation



Systemic treatment

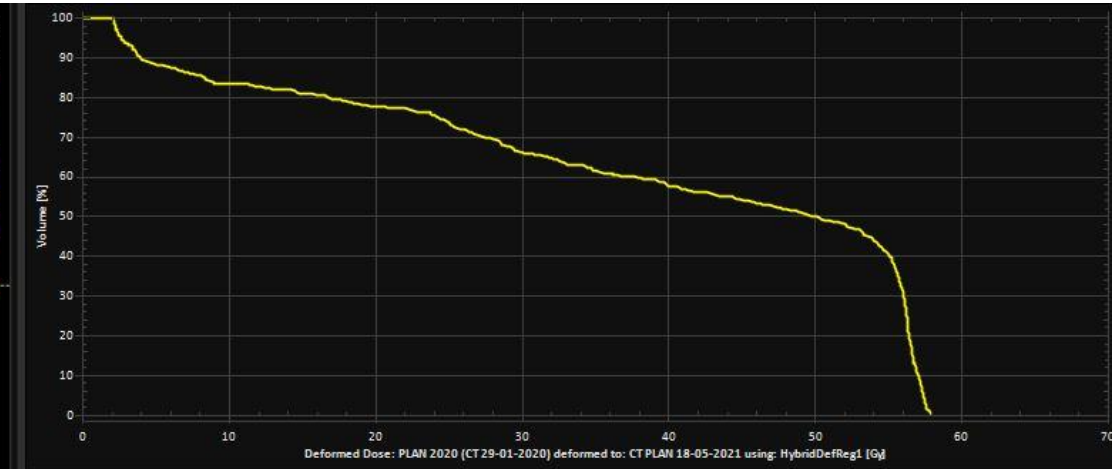
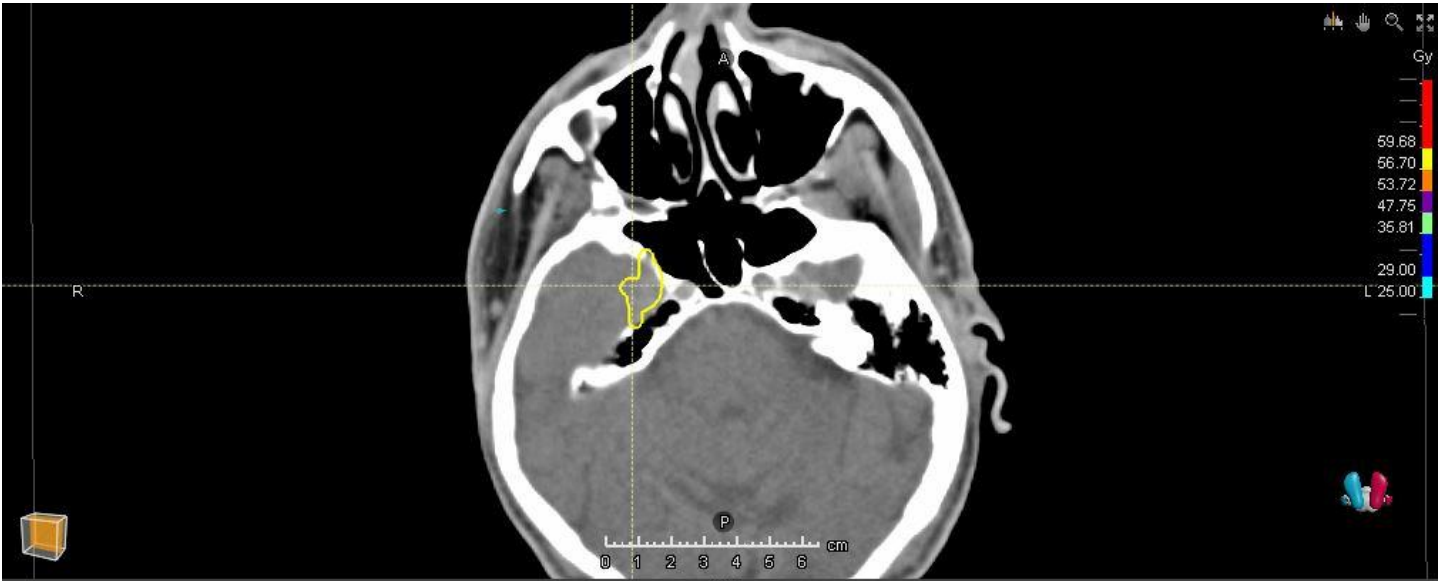
ADT → Androgenic deprivation therapy



Due to:

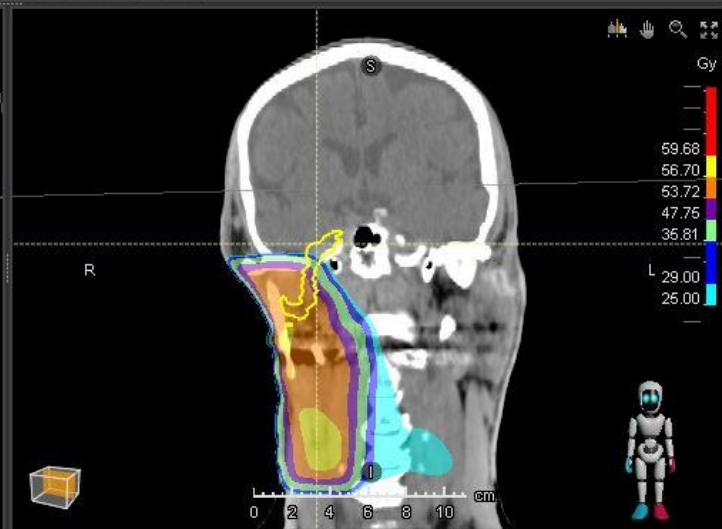
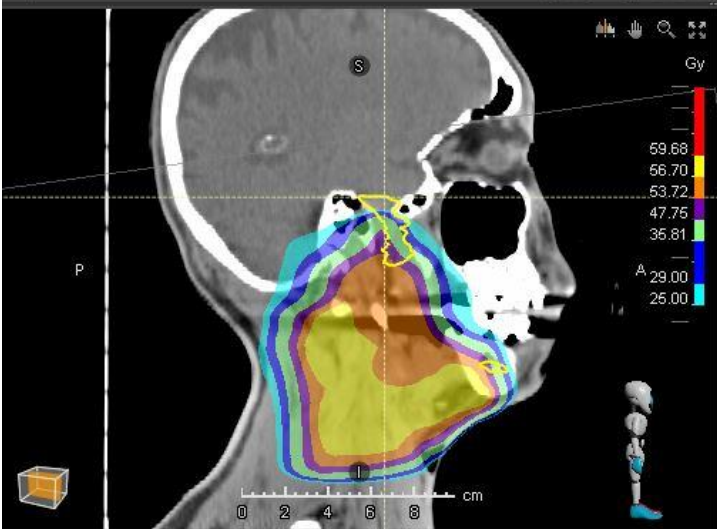
- Low burden pulmonary disease
- the symptoms reported
- patient's wishes

Planning



Dose axis: Absolute Relative max Relative dose [Gy]:

Volume axis: Relative Absolute



Dose statistics Clinical goals Biological resp... Plan fraction s... Beams (Current) Control points... BEV (Current)

ROI statistics POI statistics

Name	ROI	ROI vol. [cm ³]	Dose [Gy]						
			D99	D98	D95	Average	D50	D2	D1
Deformed Dose: PLAN...	■ GTV 2021	9.57	2.17	2.23	2.63	38.97	49.78	57.59	57.77

Original Article

Reirradiation of salivary gland tumors with carbon ion radiotherapy at CNAO

B. Vischioni^{a,*}, B. Dhanireddy^{a,b}, C. Severo^{a,c}, M. Bonora^a, S. Ronchi^a, V. Vitolo^a, M.R Fiore^a, E. D'Ippolito^a, R. Petrucci^a, A. Barcellini^a, E. Ciurlia^{a,d}, A. Iannalfi^a, A. Hasegawa^{a,e}, S. Molinelli^{a,e}, A. Mirandola^{a,e}, F. Valvo^a, R. Orecchia^{a,f}

^aRadiation Oncology Clinical Department, National Center for Oncological Hadrontherapy (CNAO), Pavia, Italy; ^bRadiation Medicine, Albert B. Chandler Hospital, University of Kentucky, USA; ^cSection of Radiological Sciences, University of Messina; ^dRadiation Oncology Department, Vito Fazzi Hospital, Lecce, Italy; ^eRadiation Oncology Department, Osaka Heavy Ion Therapy Center, Japan; and ^fDepartment of Radiotherapy, European Institute of Oncology, Milan, Italy

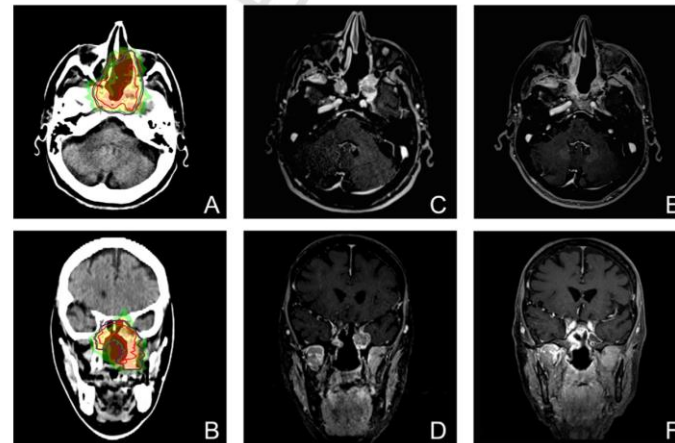
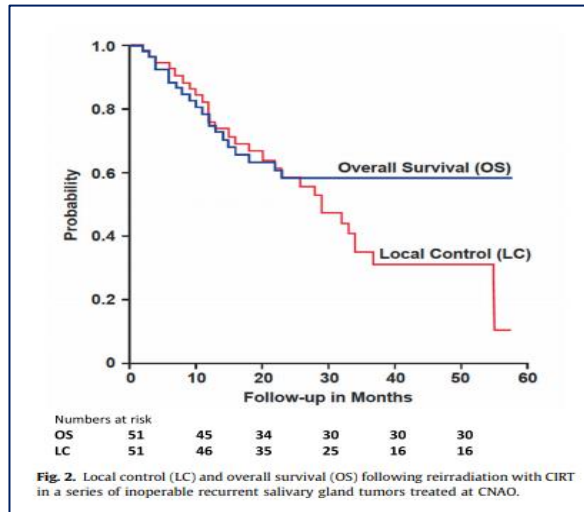


Table 4
Acute and late toxicity at last follow up.

	ACUTE TOXICITY N (%)	LATE TOXICITY N (%)
G0	11 (21.5)	14 (27.5)
G1	19 (37.3)	9 (18)
G2	19 (37.3)	19 (37)
G3	2 (3.9)	9 (17.5)

- November-2013-September2016
- 51 pts
- Median CIRT dose 60 Gy[RBE]/ 3Gy - 5[RBE] FS (range 45 - 68.8 Gy)
- Median follow-up: 18 months

PFS 1y/2y: 71.7% e 52.2%

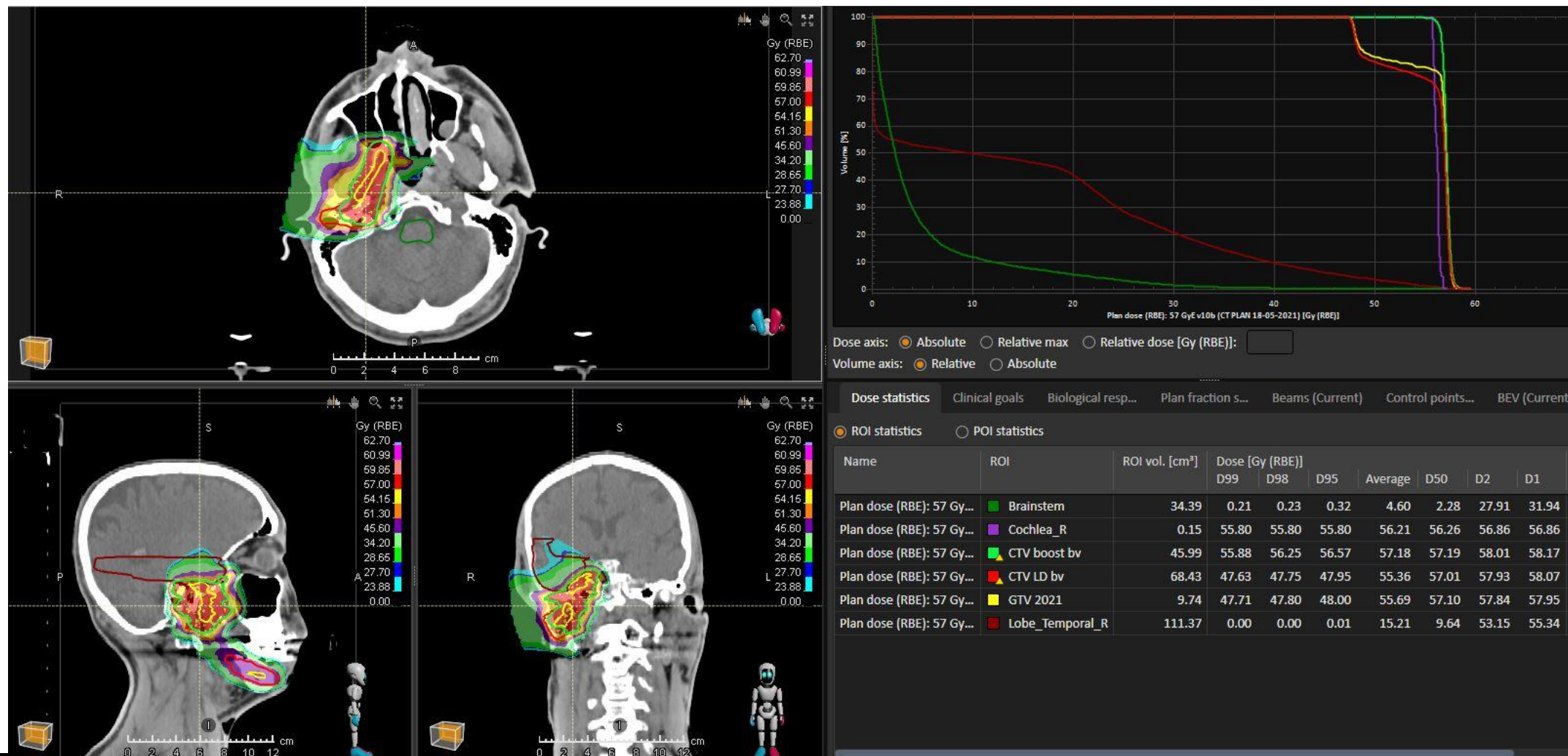
OS 1y/2y: 90.2% e 64%

From 31/05/2021 to 25/06/2021

Carbon Ions RT with a total dose of 57 Gy (RBE) in 19 fractions, 3 Gy (RBE)/fr:

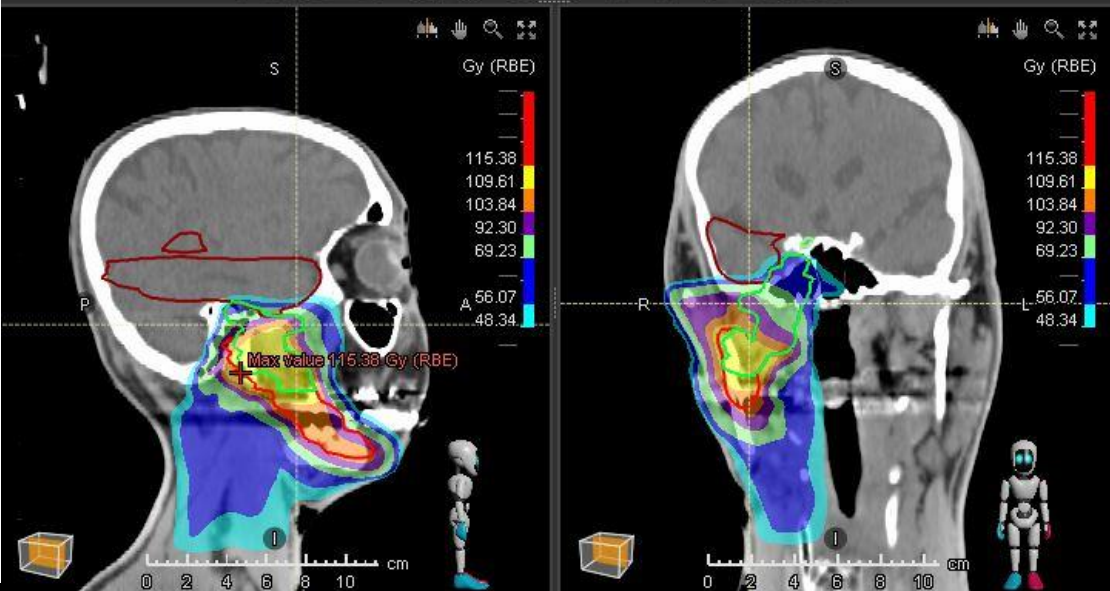
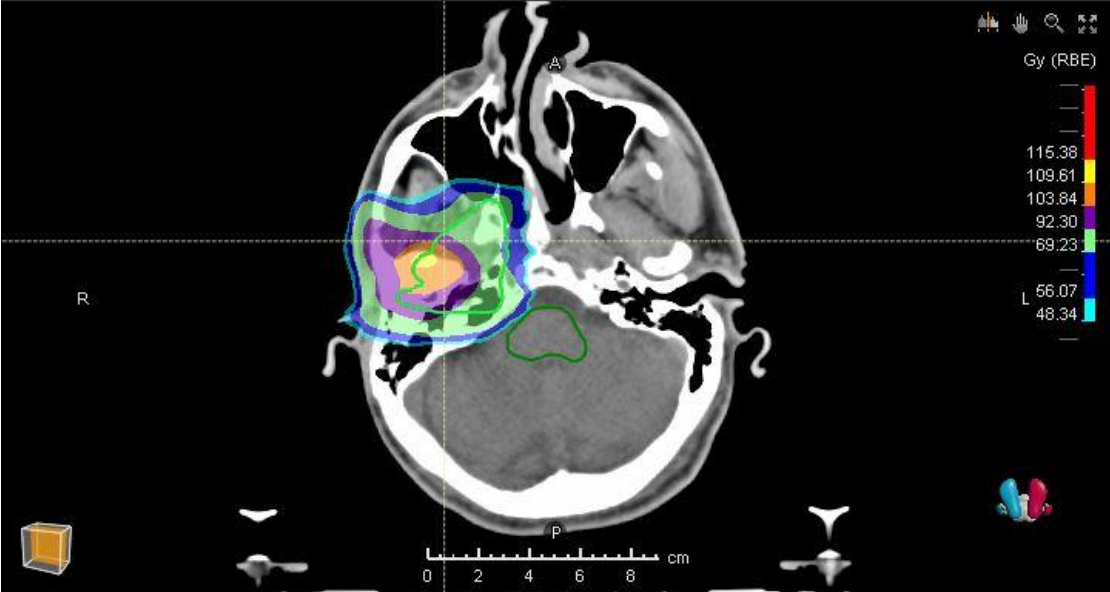
Low Dose- CTV: 48 Gy(RBE) in 16 fr, 3 Gy(RBE)/fr.

High Dose- CTV (boost): 9 Gy(RBE) in 3 fr, 3 Gy(RBE)/fr (on the cranial part of the target out of field of the previous RT volume)



Planning

Sum Plan



ROI statistics POI statistics

Name	ROI	ROI vol. [cm³]	Dose [Gy (RBE)]						
			D99	D98	D95	Average	D50	D2	D1
Summed Dose (RBE): F...	Brainstem	34.38	1.19	1.40	1.59	13.00	8.60	38.80	43.7
Summed Dose (RBE): F...	Cochlea_R	0.16	66.38	66.43	67.38	77.44	76.93	91.26	92.53
Summed Dose (RBE): F...	CTV boost bv	45.94	57.94	58.71	59.48	89.10	89.26	113.66	113.91
Summed Dose (RBE): F...	CTV LD bv	68.36	58.30	59.09	59.97	94.19	102.15	113.98	114.30
Summed Dose (RBE): F...	Lobe_Temporal_R	111.21	0.01	0.02	0.04	16.77	10.38	58.61	64.8
Summed Dose (RBE): F...	OpticNrv_R	0.55	2.05	2.10	2.29	12.07	11.33	28.70	29.56

Cumulative Dose at OARs

Constraints

Brainstem → D1% 43,72

D1% < 54

Coclea_R → Dmed < 77

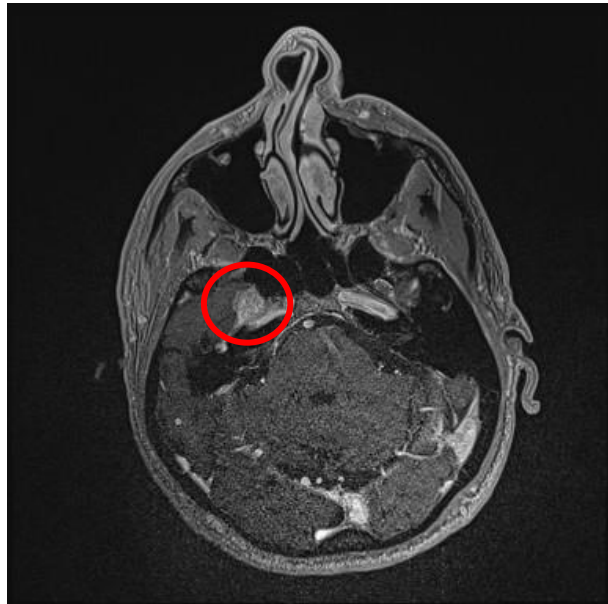
Dmed < 45

Temporal Lobe_R → D1% < 64,8

D1% < 68

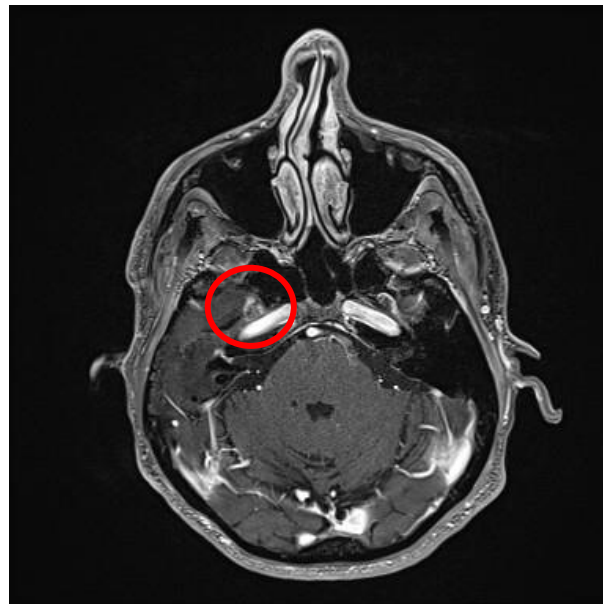
After treatment patients start HT:
Bicalutamide 50 mg 1 cp/die + Enantone 3.75 q28

Baseline



3 months

PR: local and systemic
Toxicity: Hearing loss G2



Local and
systemic
stable disease

16 months
October 2022

- ✓ Ear pain with purulent secretions
- ✓ Dermatitis and edema
- ✓ Worsening trismus
- ✓ Subcutaneous crackles in the right pre-auricular region

14/10/22 CE-MRI: area suggestive of **tissue necrosis** is observed, associated with an **infection** centred in the **deep soft tissues of the right parotid compartment**, causing occlusion of the proximal portion of the internal jugular vein with upstream thrombosis. The sigmoid sinus on the same side is affected, wrapping around the ipsilateral styloid process and extending cranially to involve the lower part of the mastoid until reaching the external auditory canal. Without sure signs of disease





WHAT'S
NEXT?

Tumor board discussion



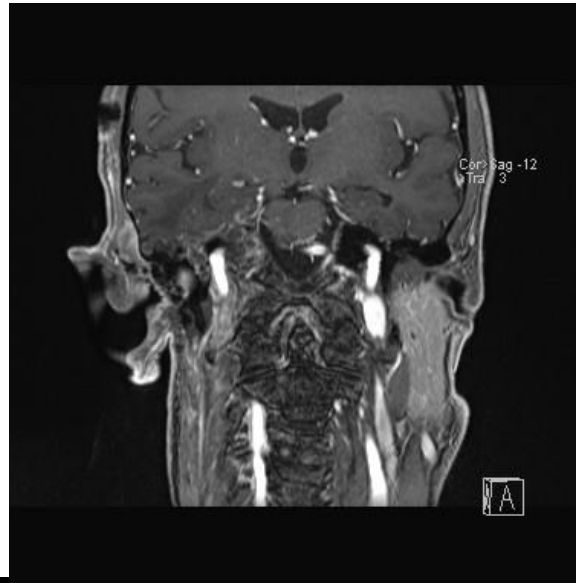
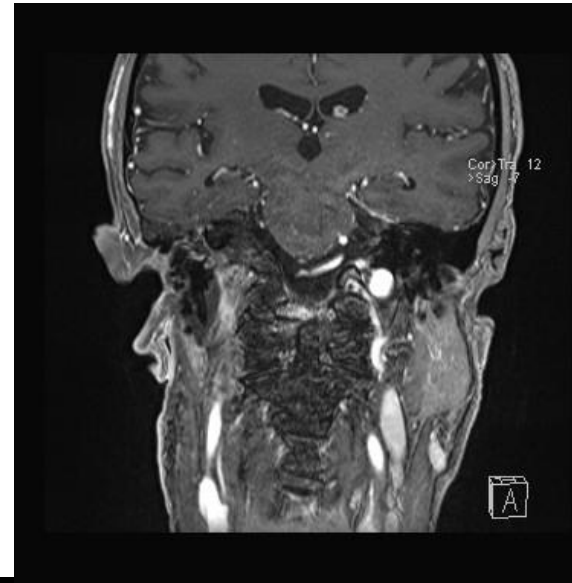
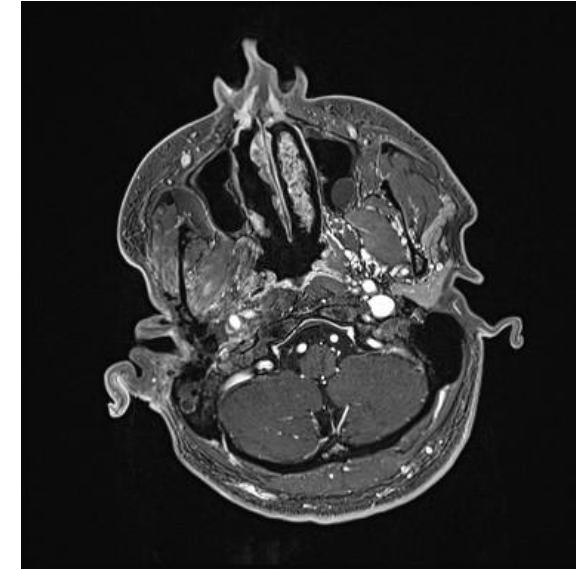
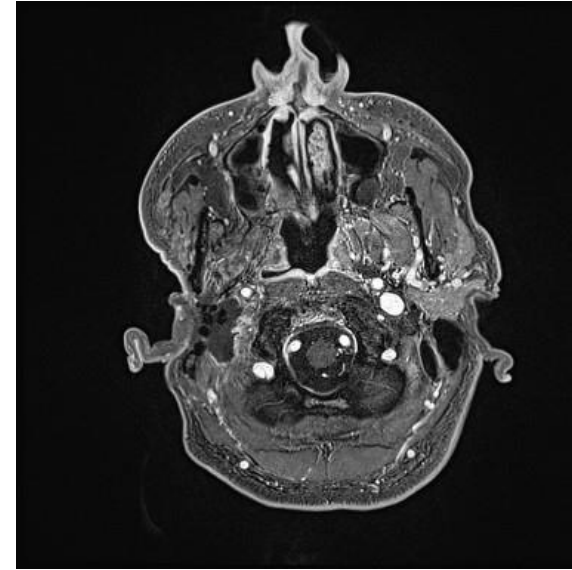
- ✓ CT angiography
- ✓ Antibiotic after swab and antibiogram
- ✓ STOP HT (Hormone Therapy)
- ✓ Reevaluation with MRI at 2 months
- ✓ And CT-scan

18 months

- Improvement of clinical condition
- CT angiography: No deficit carotid hemodynamically significant
- MRI stability of necrosis area
- Chest CT-scan: stable disease

MRI: dimensional reduction of the necrosis area without sure signs of residual disease.

24 months





WHAT'S
NEXT?

- Patients follows his follow-up program every 3 months with MRI and Chest CT-scan in order to monitoring pulmonary micro metastasis
- He didn't restart HT yet
- He makes periodically Otolaryngologist visits in order to control the onset of new infections of the external auditory canal that may worsening the necrosis.
- In case of infection suspicious he periodically perform a swab and starting a specific antibiotics therapy

THANK YOU

