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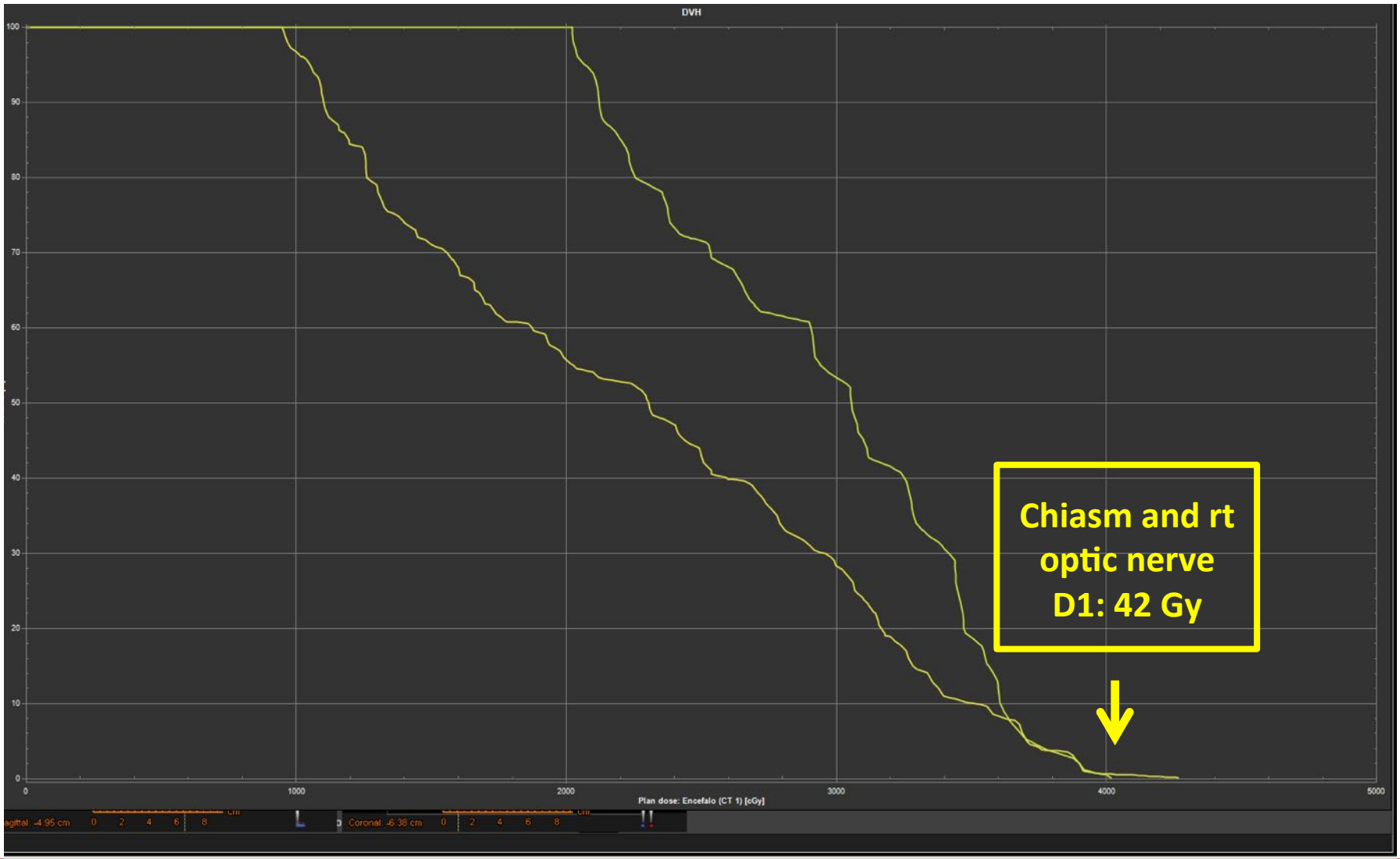
Adroterapia: nuova reale opportunità?

(P. Fossati)

2 problemi preliminari alla scelta della tecnica:

- Ricostruire il trattamento precedente
- Conoscere i constraints di dose per le reirradiazioni

Previous RT file



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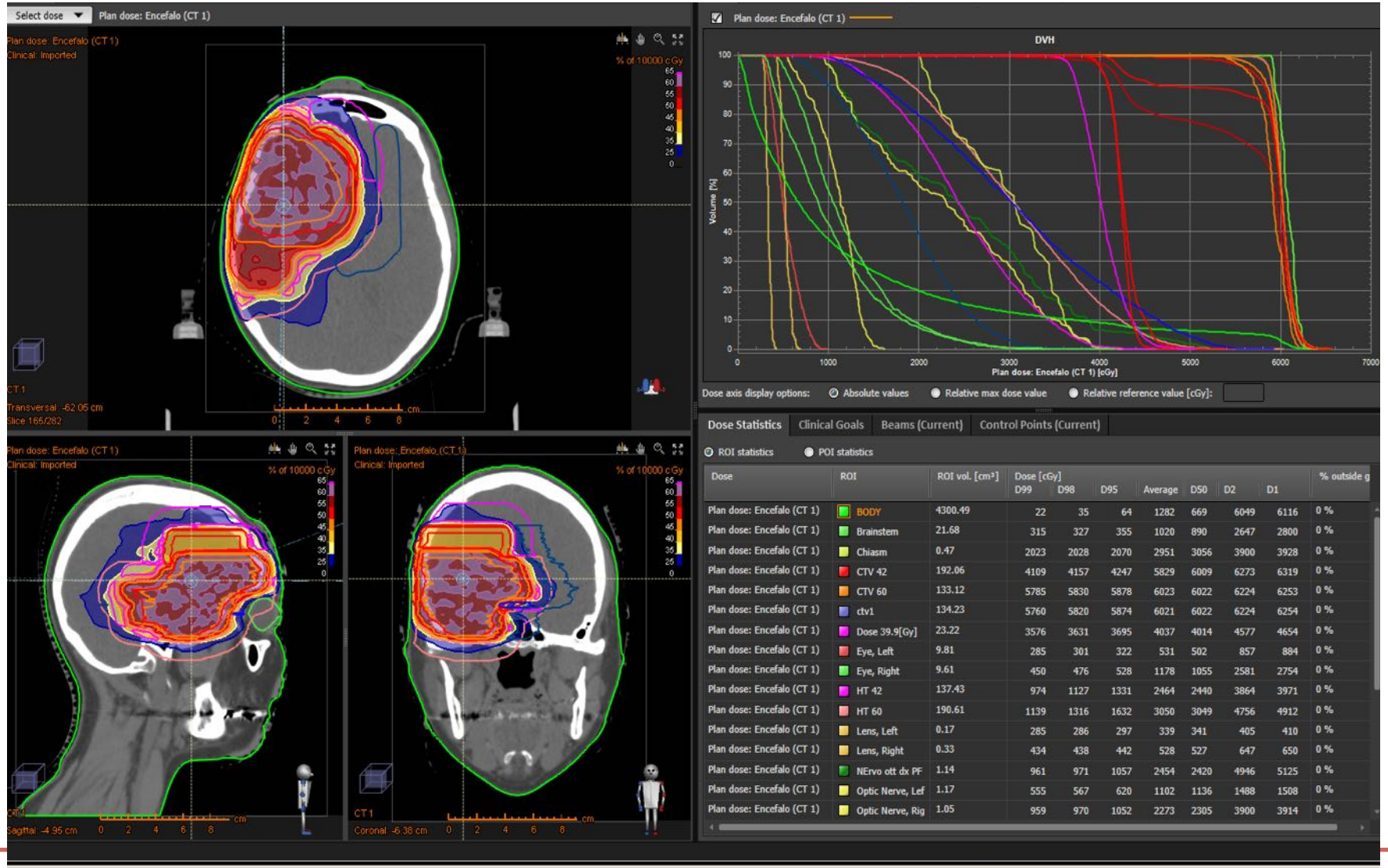
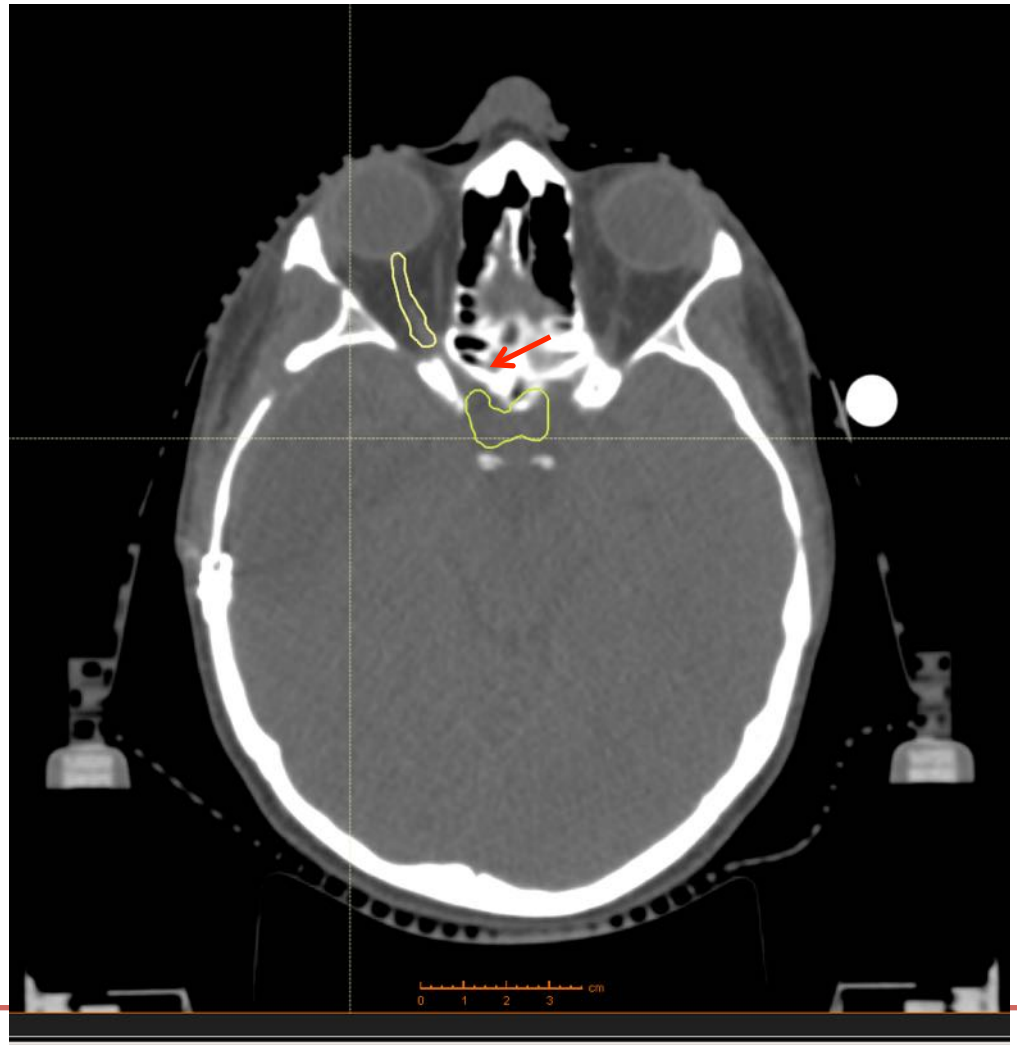
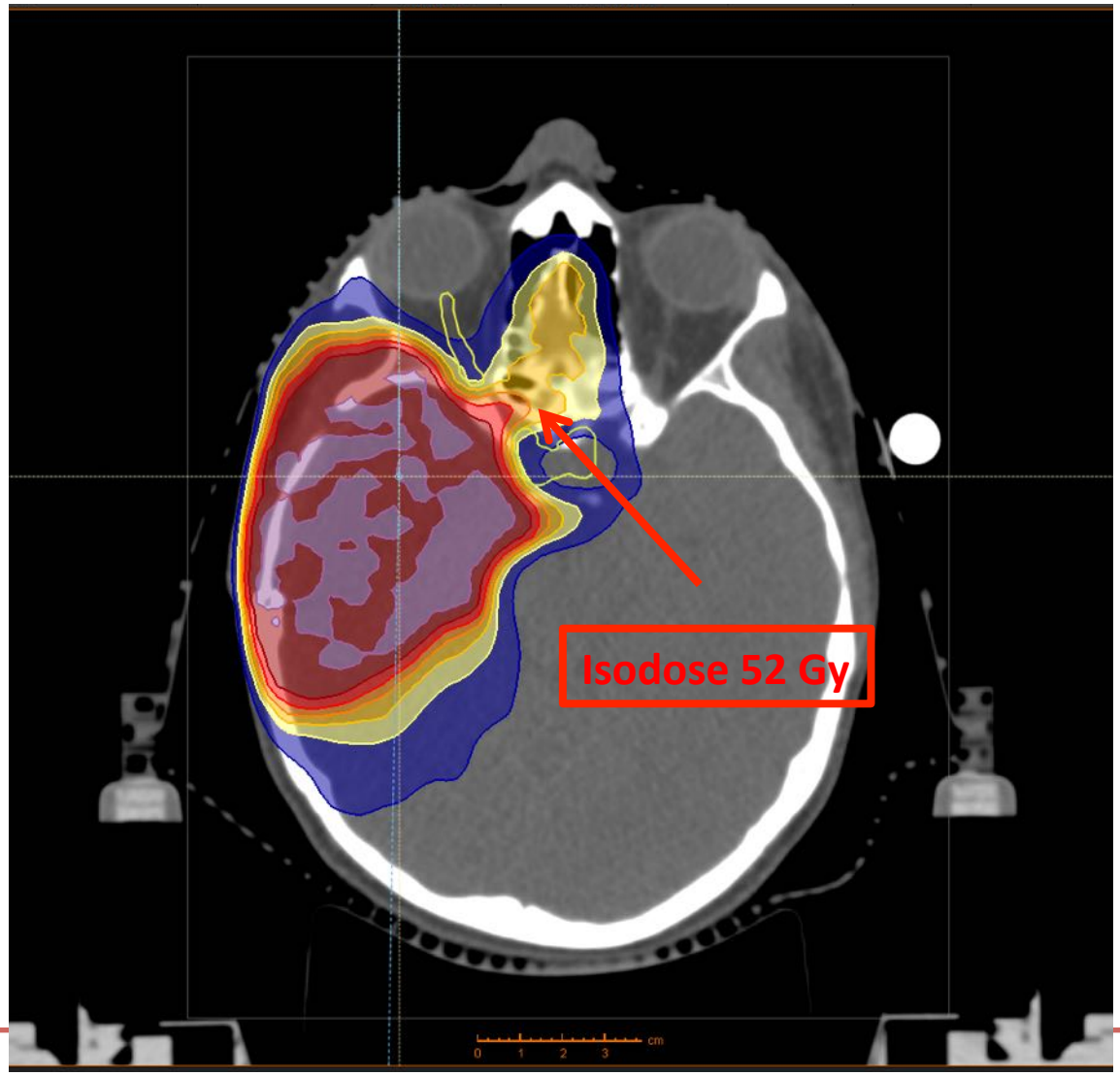


Dose	ROI	ROI vol. [cm³]	Dose [cGy] D99	D98	D95	Average	D50	D2	D1	% outside g
Plan dose: Encefalo (CT 1)	BODY	4300.49	22	35	64	1282	669	6049	6116	0 %
Plan dose: Encefalo (CT 1)	Brainstem	21.68	315	327	355	1020	890	2647	2800	0 %
Plan dose: Encefalo (CT 1)	Chiasm	0.47	2023	2028	2070	2951	3056	3900	3928	0 %
Plan dose: Encefalo (CT 1)	CTV 42	192.06	4109	4157	4247	5829	6009	6273	6319	0 %
Plan dose: Encefalo (CT 1)	CTV 60	133.12	5785	5830	5878	6023	6022	6224	6253	0 %
Plan dose: Encefalo (CT 1)	ctv1	134.23	5760	5820	5874	6021	6022	6224	6254	0 %
Plan dose: Encefalo (CT 1)	Dose 39.9[Gy]	23.22	3576	3631	3695	4037	4014	4577	4654	0 %
Plan dose: Encefalo (CT 1)	Eye, Left	9.81	285	301	322	531	502	857	884	0 %
Plan dose: Encefalo (CT 1)	Eye, Right	9.61	450	476	528	1178	1055	2581	2754	0 %
Plan dose: Encefalo (CT 1)	HT 42	137.43	974	1127	1331	2464	2440	3864	3971	0 %
Plan dose: Encefalo (CT 1)	HT 60	190.61	1139	1316	1632	3050	3049	4756	4912	0 %
Plan dose: Encefalo (CT 1)	Lens, Left	0.17	285	286	297	339	341	405	410	0 %
Plan dose: Encefalo (CT 1)	Lens, Right	0.33	434	438	442	528	527	647	650	0 %
Plan dose: Encefalo (CT 1)	NErvo ott dx PF	1.14	961	971	1057	2454	2420	4946	5125	0 %
Plan dose: Encefalo (CT 1)	Optic Nerve, Lef	1.17	555	567	620	1102	1136	1488	1508	0 %
Plan dose: Encefalo (CT 1)	Optic Nerve, Rig	1.05	959	970	1052	2273	2305	3900	3914	0 %

Previous RT file



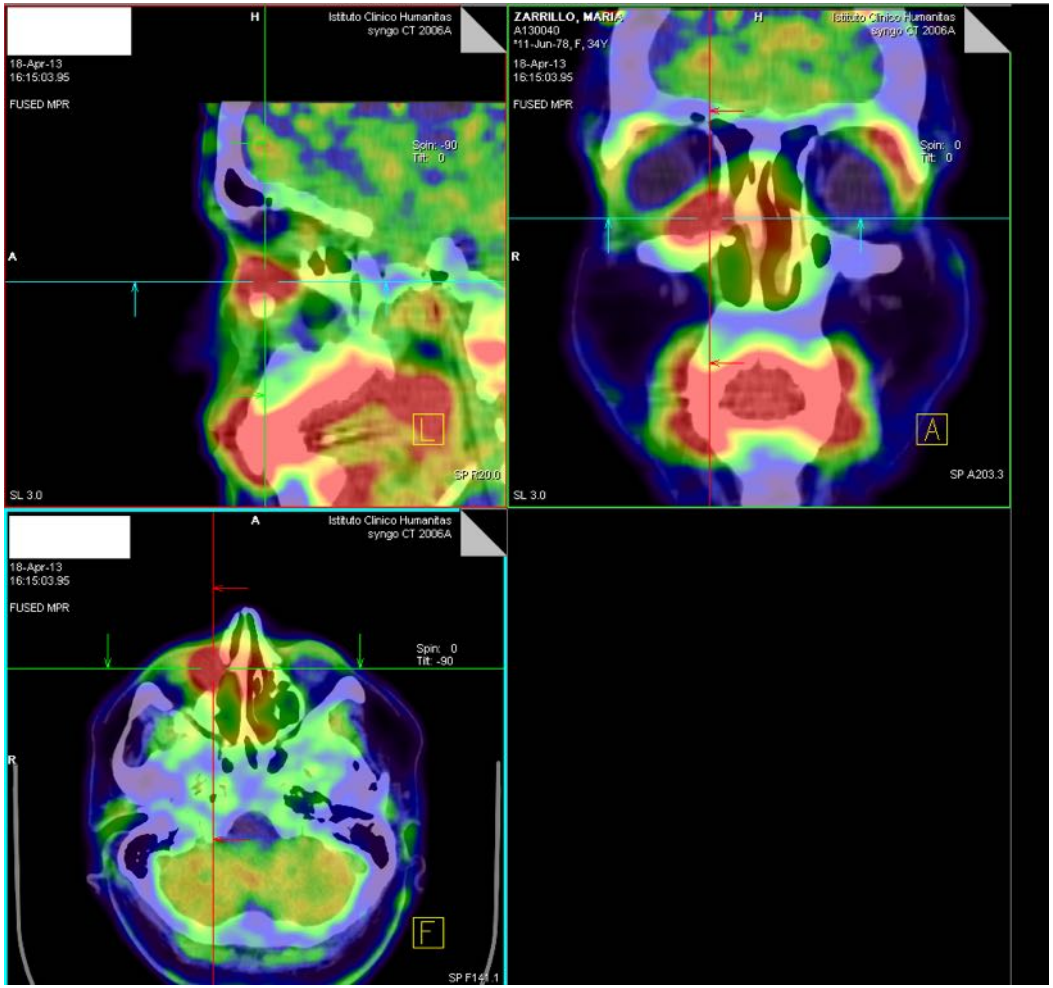
Previous RT file



CASO CLINICO

PET met pre-trattamento

recidiva di ACC seno mascellare dx
2006: chirurgia per ACC cavità nasale–rinofaringe
09/2006 al 02/11/2006 RT 50 Gy in 25 fr

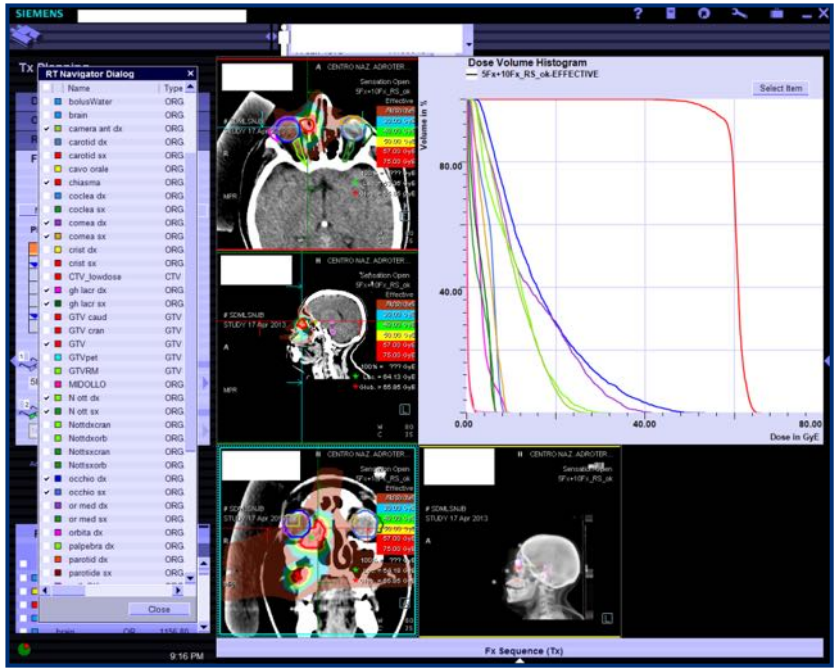


CASO CLINICO

Dose (CIRT):
60 Gy[RBE]: 4 Gy[RBE] x 15 fr

BED $_{\alpha/\beta = 2\ Gy}$ = 180 Gy

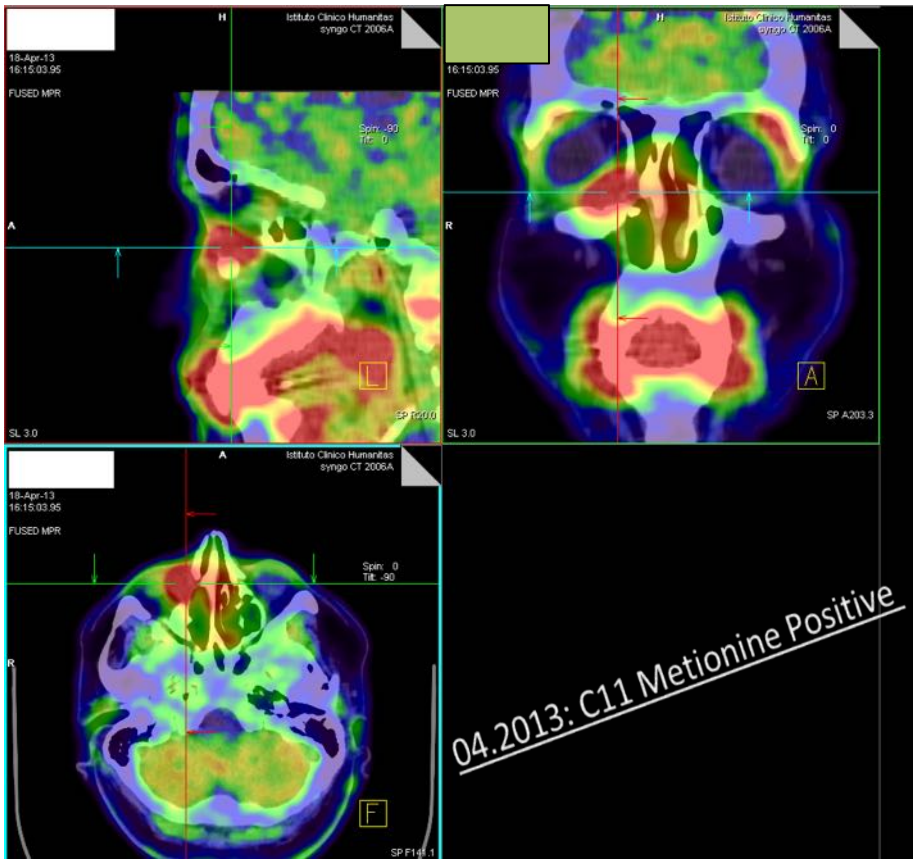
NTD $_{\alpha/\beta = 2\ Gy}$ = 90 Gy



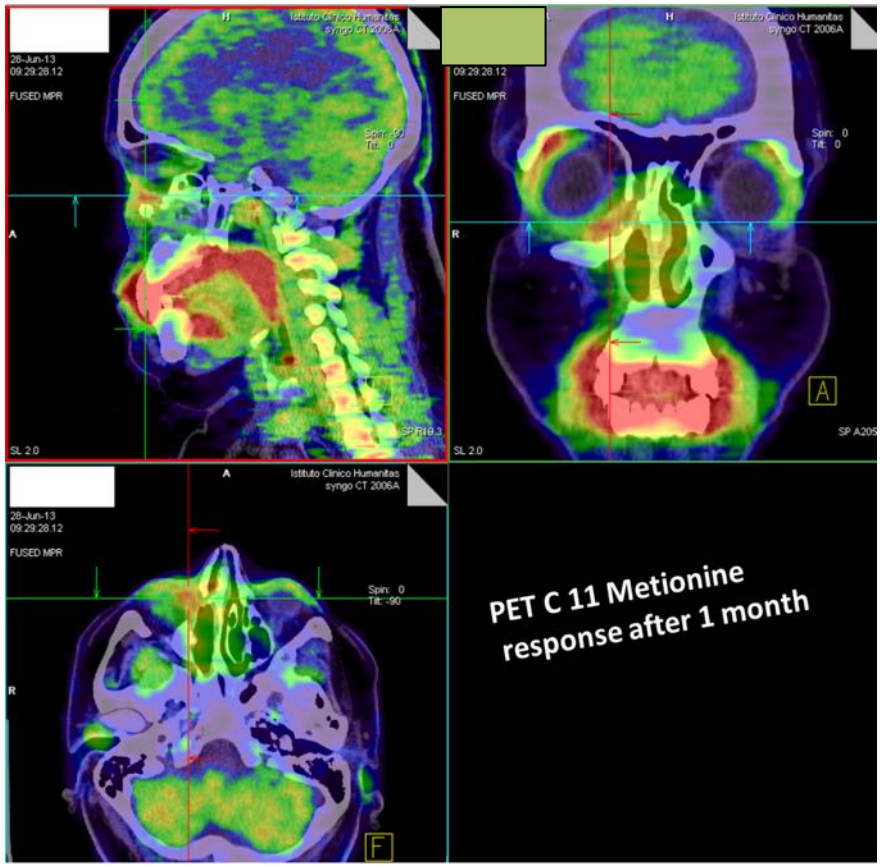
Tossicità al termine del trattamento:
Eritema G1, mucosite G2,
congiuntivite G1

CASO CLINICO

Pre-trattamento

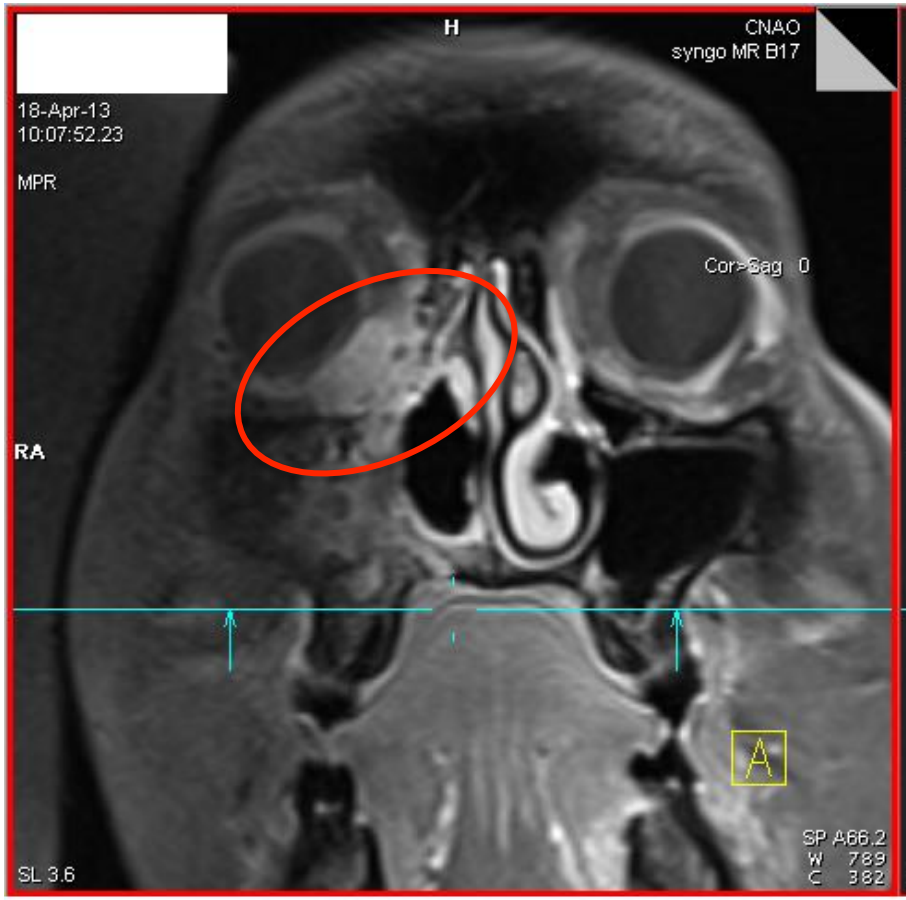


Dopo 1 mese



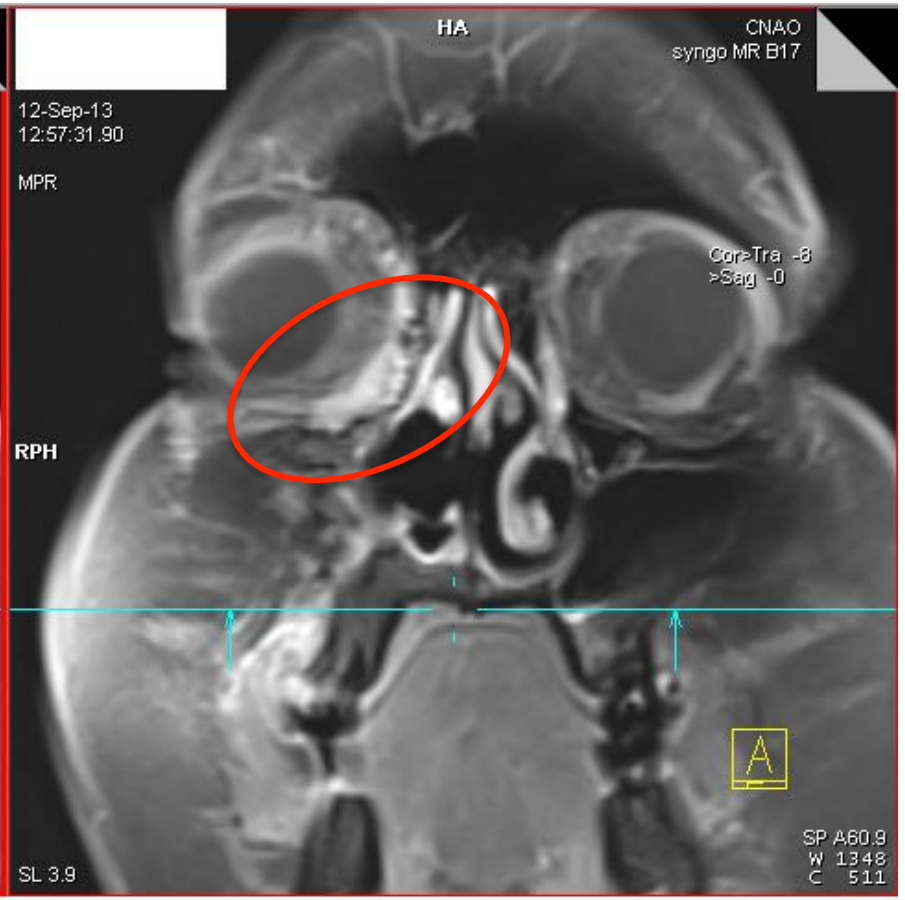
CASO CLINICO

Pre-trattamento



CC 13 mm
LL 19 mm

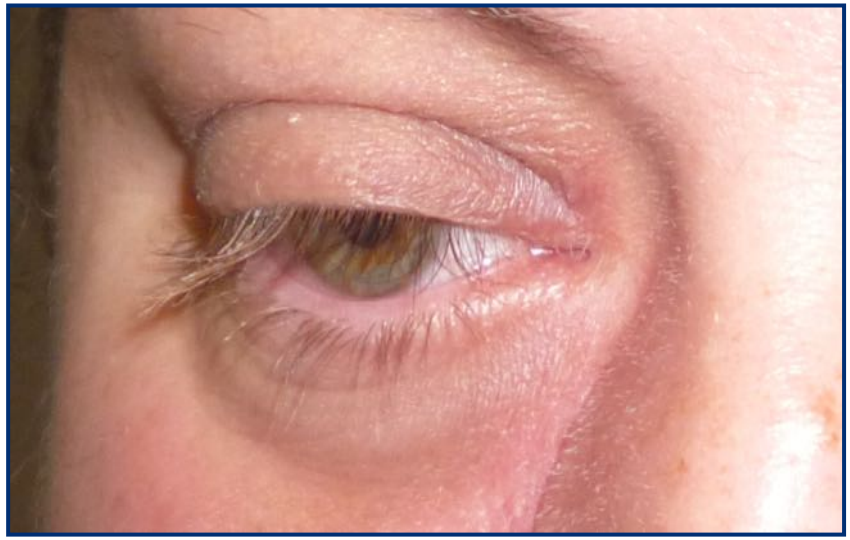
Dopo 6 mesi



CC 8 mm
LL 9 mm

CASO CLINICO

Termine trattamento:



Eritema G1, congiuntivite G1

Dopo 3 mesi:

G0

Vantaggi potenziali

Protoni e Carbonio:

- **Evitano il bagno di dosi medio basse**
  - Minor tossicità
  - Potenziale dose escalation
  - Potenziale ampliamento delle indicazioni

Carbonio:

- **Maggior efficacia contro i cloni radioresistenti**

ELSEVIER

Int. J. Radiation Oncology Biol. Phys., Vol. 57, No. 1, pp. 274–281, 2003

0360-3016/03/$–see front matter

doi:10.1016/S0360-3016(03)00529-7

BIOLOGY CONTRIBUTION

UNEXPECTED CHANGES OF RAT CERVICAL SPINAL CORD TOLERANCE CAUSED BY INHOMOGENEOUS DOSE DISTRIBUTIONS

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JACOBUS M. SCHIPPERS, PH.D.,†[1] ANTONIUS W. T. KONINGS, PH.D.,‡ AND
ALBERT J. VAN DER KOGEL, PH.D.§

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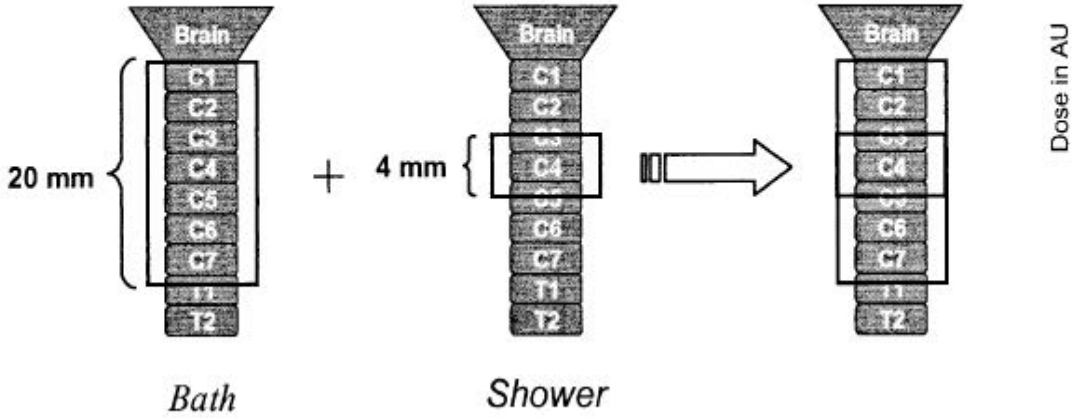
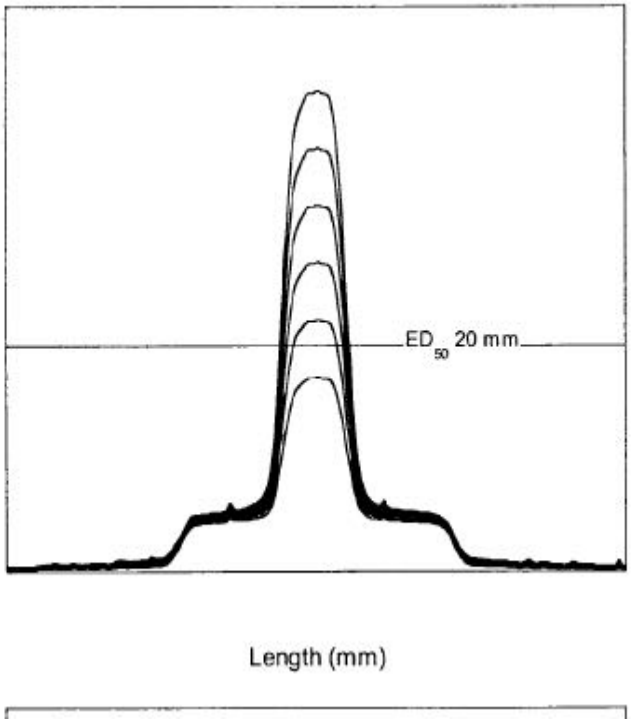


B: Symmetrical bath and shower



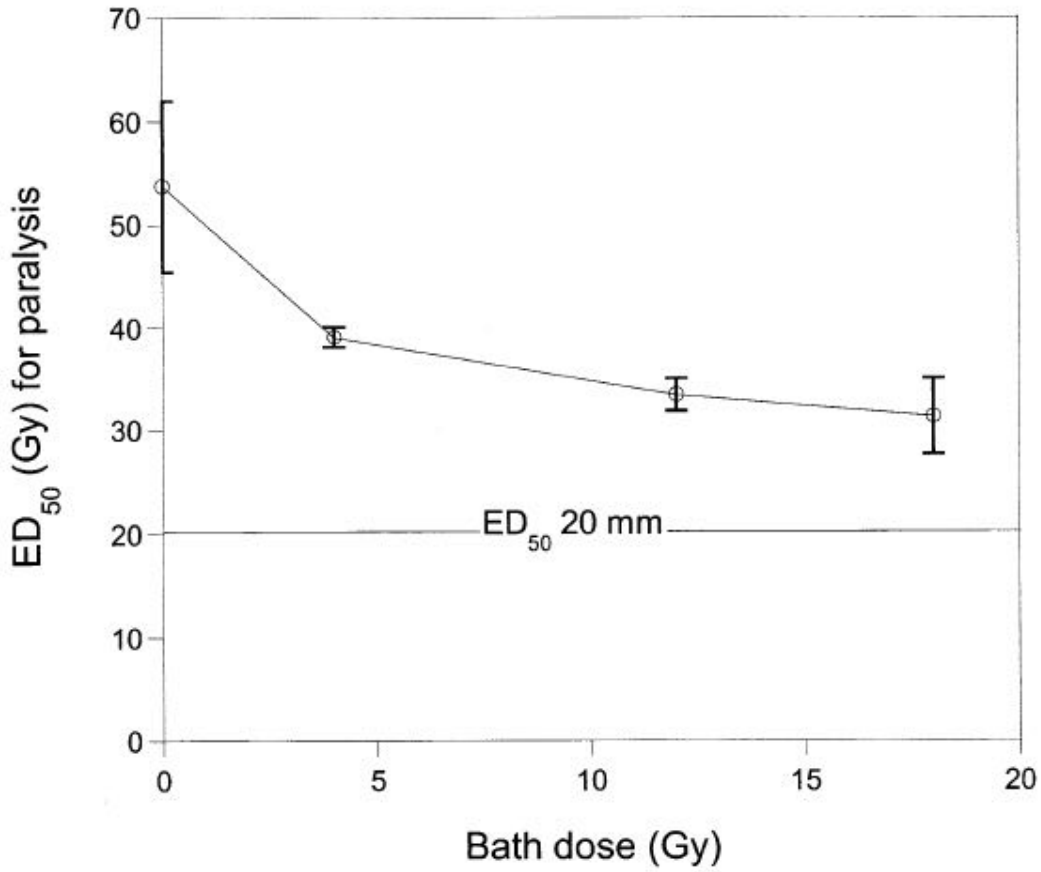


Fig. 6. ED_{50} values of the *symmetrical bath and shower* experiments. The ED_{50} value of the homogeneous single 4-mm field irradiation is set as 0 Gy bath dose. The horizontal line represents the ED_{50} value (20.4 Gy) of a homogeneous single 20-mm field irradiation. Error bars: 95% confidence intervals.

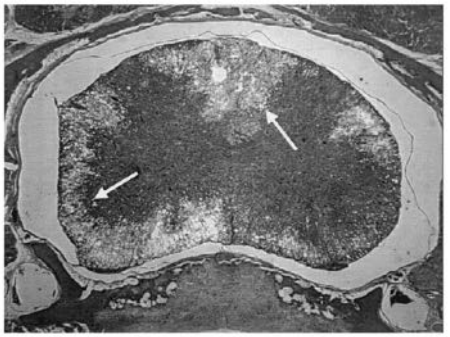


Fig. 2. Transverse section of the rat cervical spinal cord at the level of the high-dose 4-mm shower (hematoxylin and eosin stained). Extensive white matter necrosis is predominantly seen in the right ventrolateral column and dorsal tract of the white matter (see white arrows). The rat developed hind and fore limb paralysis after 163 days after irradiation with 50 Gy.

Priority Report

Radiation Damage to the Heart Enhances Early Radiation-Induced Lung Function Loss

Peter van Luijk,[1] Alena Novakova-Jiresova,[2] Hette Faber,[2] Jacobus M. Schippers,[3] Harm H. Kampinga,[2] Harm Meertens,[1] and Rob P. Coppes[1,2]

Departments of [1]Radiation Oncology and [2]Radiation and Stress Cell Biology, University Medical Center Groningen, University of Groningen, Groningen, the Netherlands and [3]Accelerator Department, Paul Scherrer Institut, Villigen, Switzerland

Cancer Res 2005; 65: (15). August 1, 2005

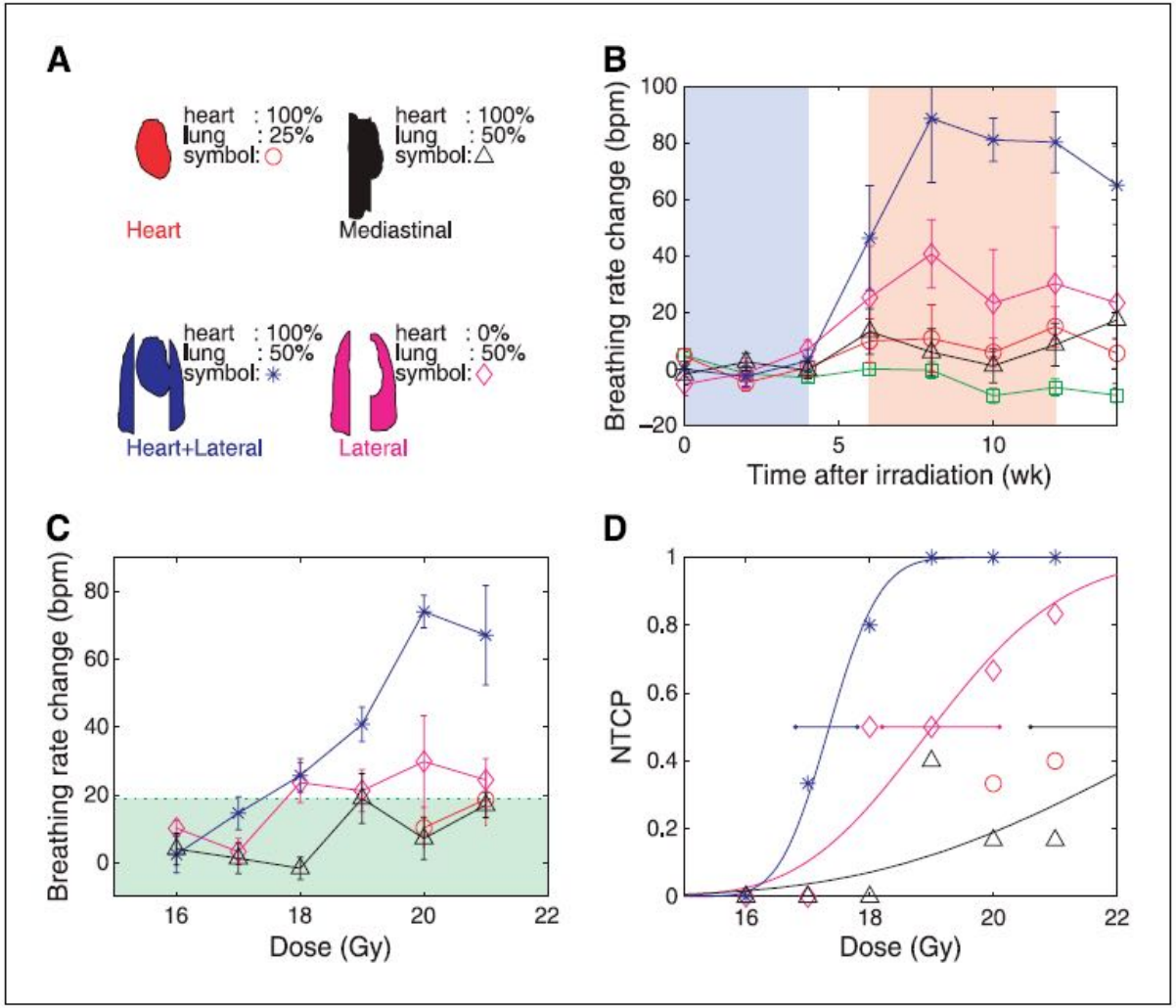


Figure 1. *B*, breathing rate as a function of time after irradiation using 20 Gy with different radiation fields shown in (*A*). The time span of the early radiation-induced function loss phase (weeks 6-12) is indicated in red. Increase in the mean breathing rate in this phase with respect to the latent phase (*blue*). An increase above the green region in (*C*) indicates pneumonitis. *D*, fraction of animals manifesting symptomatic lung function loss. *Horizontal lines*, 95% confidence limits of ED_{50}. *Bars*, SE (*B* and *C*).

Acta Oncol. 2011 January ; 50(1): 51–60. doi:10.3109/0284186X.2010.521192.

Heart irradiation as a risk factor for radiation pneumonitis

ELLEN X. HUANG[1], **ANDREW J. HOPE**[2], **PATRICIA E. LINDSAY**[2], **MARCO TROVO**[3], **ISSA EL NAQA**[1], **JOSEPH O. DEASY**[1], and **JEFFREY D. BRADLEY**[1]

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[2]*Princess Margaret Hospital, Toronto, ON, Canada*

[3]*National Cancer Institute, Aviano, Italy*

Abstract

Purpose—To investigate the potential role of incidental heart irradiation on the risk of radiation pneumonitis (RP) for patients receiving definitive radiation therapy for non-small-cell lung cancer (NSCLC).

Material and methods—Two hundred and nine patient datasets were available for this study. Heart and lung dose-volume parameters were extracted for modeling, based on Monte Carlo-based heterogeneity corrected dose distributions. Clinical variables tested included age, gender, chemotherapy, pre-treatment weight-loss, performance status, and smoking history. The risk of RP was modeled using logistic regression.

Results—The most significant univariate variables were heart related, such as heart heart V65 (percent volume receiving at least 65 Gy) (Spearman Rs = 0.245, $p < 0.001$). The best-performing logistic regression model included heart D10 (minimum dose to the hottest 10% of the heart), lung D35, and maximum lung dose (Spearman Rs = 0.268, $p < 0.0001$). When classified by predicted risk, the RP incidence ratio between the most and least risky 1/3 of treatments was 4.8. The improvement in risk modeling using lung and heart variables was better than using lung variables alone.

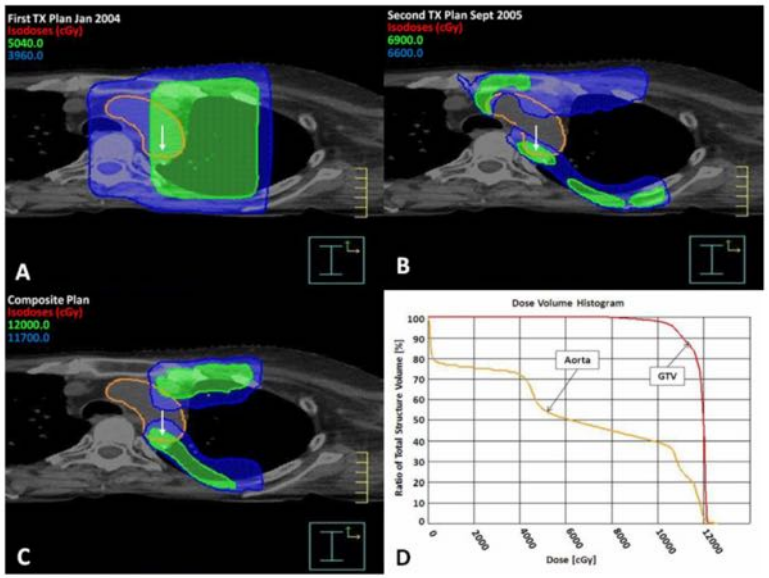
Conclusions—These results suggest a previously unsuspected role of heart irradiation in many cases of RP.

Nuovi OARs

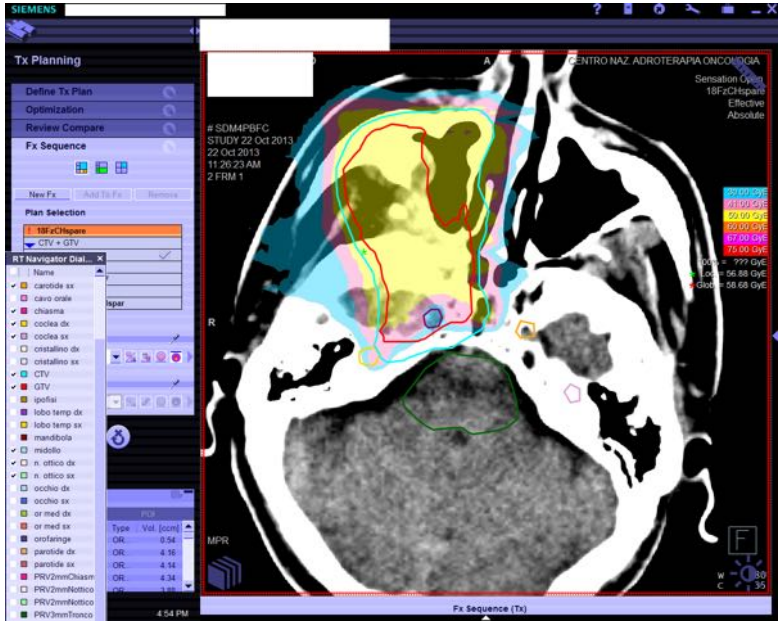
Radiother Oncol. 2013 March ; 106(3): 327–332. doi:10.1016/j.radonc.2013.02.002.

Aortic Dose Constraints when Reirradiating Thoracic Tumors

Jaden D. Evans, B.S.[*,†], Daniel R. Gomez, M.D.[*], Arya Amini, M.D.[*], Neal Rebueno, C.M.D.[*], Pamela K. Allen, Ph.D.[*], Mary K. Martel, Ph.D.[‡], Justin M. Rineer, M.D.[§], K. Kian Ang, M.D., Ph.D.[*], Sarah McAvoy, M.D.[*], James D. Cox, M.D.[*], Ritsuko Komaki, M.D.[*], and James W. Welsh, M.D.[*]



Carotide



Come decidere razionalmente ?

Maastricht University

MAASTRO

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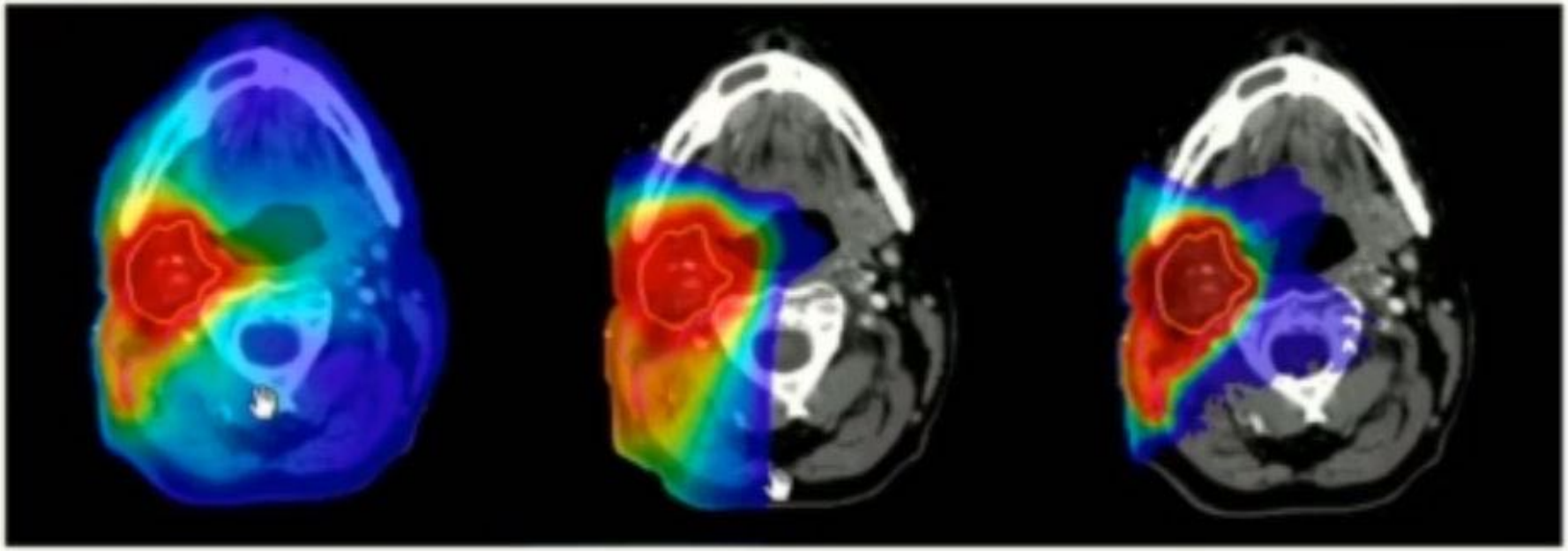
Results

ROCOCO

Radiation Oncology COllaborative COmparison



VMAT IMPT IMIT

Cortesy of Dr. **D. Eekers**

Maastricht University

MAASTRO

MAASTRO © 2015

Results

ROCOCO

Radiation Oncology COllaborative COmparison

OAR	VMAT_Dmean	IMPT_Dmean	IMIT_Dmean
BODY	5.8 (2.9)	3.9 (2.2)*	2.7 (1.7)*
Arythenoid_L	25.0 (22.2)	15.2 (20.1)*	9.8 (18.5)*
Arythenoid_R	29.2 (21.3)	17.6 (22.0)*	12.3 (18.1)*
B_of_tongue	32.9 (20.0)	26.9 (23.3)	20.0 (22.2)*
Carotid_bi	34.2 (17.7)	34.7 (19.9)	30.8 (20.4)*
Carotid_co	12.1 (8.9)	2.2 (4.6)*	0.87 (1.5)*
Brainstem	2.6 (3.2)	0.4 (0.91)*	0.2 (0.43)*
Jugular_bi	31.3 (20.9)	30.2 (23.4)	26.2 (23.8)*
Jugular_co	9.5 (6.9)	1.1 (3.3)*	0.66 (1.8)*
Larynx	34.9 (18.6)	27.8 (18.7)*	21.1 (17.8)*
Mandible	13.8 (12.0)	10.2 (11.0)*	7.2 (10.3)*

OAR	VMAT_Dmean	IMPT_Dmean	IMIT_Dmean
Oral_cavity	15.3 (15.0)	9.6 (14.1)*	8.1 (15.4)*
Parotid_bi	15.4 (15.5)	15.4 (16.4)	12.9 (14.5)*
Parotid_co	4.5 (2.3)	<0.01 (0.016)*	0.045 (0.13)*
Spinal_cord	7.1 (3.2)	1.5 (1.9)*	1.1 (0.94)*
S.C.M_R_bi	31.7 (18.0)	31.1 (21.3)	27.0 (20.9)*
S.C.M_R_co	10.2 (6.9)	1.7 (3.2)*	0.73 (1.5)*
Submnd_salv_bi	33.8 (19.9)	34.3 (20.1)	28.4 (19.0)*
Submnd_salv_co	17.8 (9.3)	0.88 (1.9)*	1 (1.3)*
Swall_muscles	32.2 (22.1)	25.8 (21.8)*	19.7 (21.3)*
Thyroid	30.6 (25.9)	29.7 (25.9)	25.7 (25.3)*
Vertebrae	18.2 (8.3)	11.2 (7.3)*	6.1 (4.8)*

Table: Mean doses at clinical relevant OARs in Gy(E) for IMPT and IMIT compared to VMAT; * is significant (P < 0.02)

- Overall mean dose benefit comparing IMPT to VMAT = **40%**
- Overall mean dose benefit comparing IMIT to VMAT = **54%**

International Journal of Radiation Oncology biology • physics

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Clinical Investigation

Definitive Reirradiation for Locoregionally Recurrent Non-Small Cell Lung Cancer With Proton Beam Therapy or Intensity Modulated Radiation Therapy: Predictors of High-Grade Toxicity and Survival Outcomes

Sarah McAvoy, MD, Katherine Ciura, CMD, Caimiao Wei, PhD, Justin Rineer, MD, Zhongxing Liao, MD, Joe Y. Chang, MD, PhD, Matthew B. Palmer, CMD, James D. Cox, MD, Ritsuko Komaki, MD, and Daniel R. Gomez, MD

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Received Jun 16, 2014, and in revised form Jul 22, 2014. Accepted for publication Jul 22, 2014.

102 pazienti

reirradiati a 60 EQD2

dopo un primo trattamento a 70 EQD2

7% esofagite G> 2

10% polmonite G>2

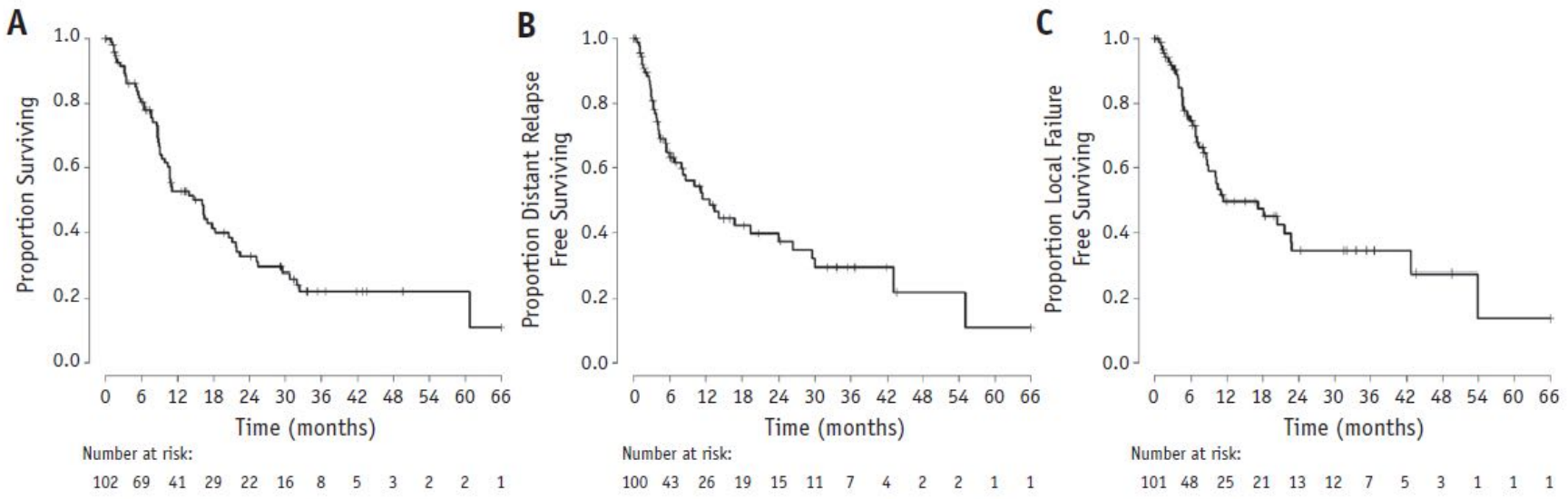


Fig. 1. (A) Overall survival, (B) distant metastasis—free survival, and (C) local failure—free survival curves for 102 patients who underwent reirradiation for recurrent non-small cell lung cancer.

VOLUME 26 · NUMBER 34 · DECEMBER 1 2008

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Randomized Trial of Postoperative Reirradiation Combined With Chemotherapy After Salvage Surgery Compared With Salvage Surgery Alone in Head and Neck Carcinoma

François Janot, Dominique de Raucourt, Ellen Benhamou, Christophe Ferron, Gilles Dolivet, René-Jean Bensadoun, Marc Hamoir, Bernard Géry, Morbize Julieron, Marine Castaing, Etienne Bardet, Vincent Grégoire, and Jean Bourhis

Fig 2. Locoregional control. Large tick marks represent the 95% CI of the point estimates. Chemoirradiation, reirradiation plus concomitant chemotherapy.

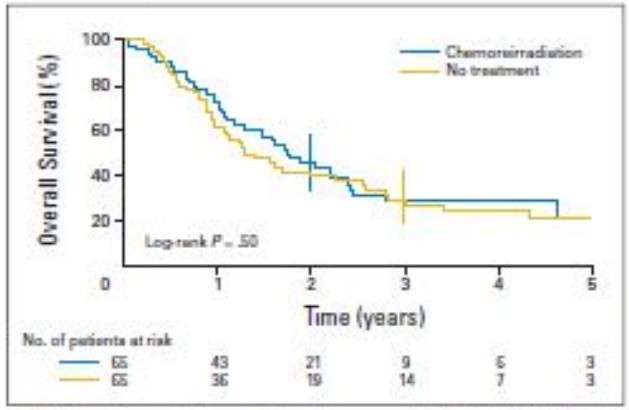
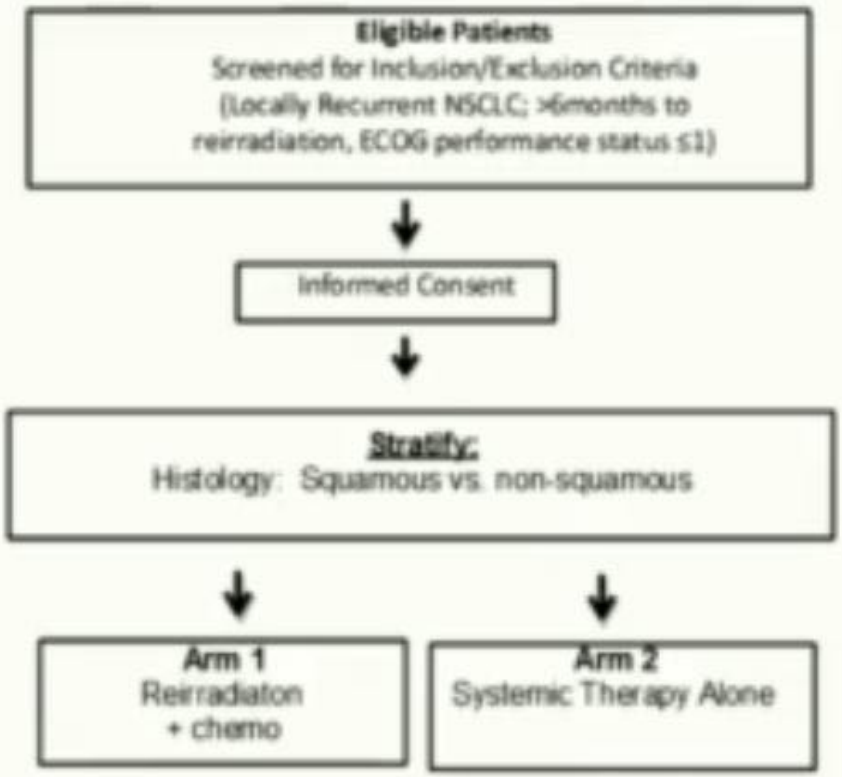


Fig 4. Overall survival. Large tick marks represent the 95% CI of the point estimates. Chemoirradiation, reirradiation plus concomitant chemotherapy.

Future Studies

MDACC Phase II



Primary Endpoint: Progression Free Survival

Penn Phase II

- Phase II trial of consolidation Pembrolizumab after concurrent chemotherapy and proton reirradiation for thoracic recurrences of non-small cell lung cancer
  - Merck sponsored
  - 35 patients, PD-1 unscreened
  - Primary Endpoint: PFS
    - 80% power to detect improvement in PFS from 6 to 10 months
  - PI: Christine Ciunci, MD

Conclusioni

- Forte razionale per l'uso dell'adroterapia nella reirradiazione
- Studi *in silico* interessanti ma da tradurre con cautela nella pratica clinica
- Studi retrospettivi iniziano ad essere disponibili
- Studi prospettici estremamente difficili
- Sarebbe auspicabile una metodologia ad hoc