Nuovi aspetti radioprotezionistici in Radioterapia:

Deterministic Risk Volume vs Stochastic Risk Volume

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Strahlenschutzkommission

Geschäftsstelle der
Strahlenschutzkommission
Postfach 12 06 29
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Radiation Hygiene Requirements for Highly Conformal Radiation Therapy

Statement by the German Commission on Radiological Protection

Radiation Hygiene Requirements for IGRT (Image Guided Radiotherapy)

Recommendation by the German Commission on Radiological Protection

Target volume definitions in radiotherapy as set out by The International Commission on Radiation Units and Measurements (ICRU)

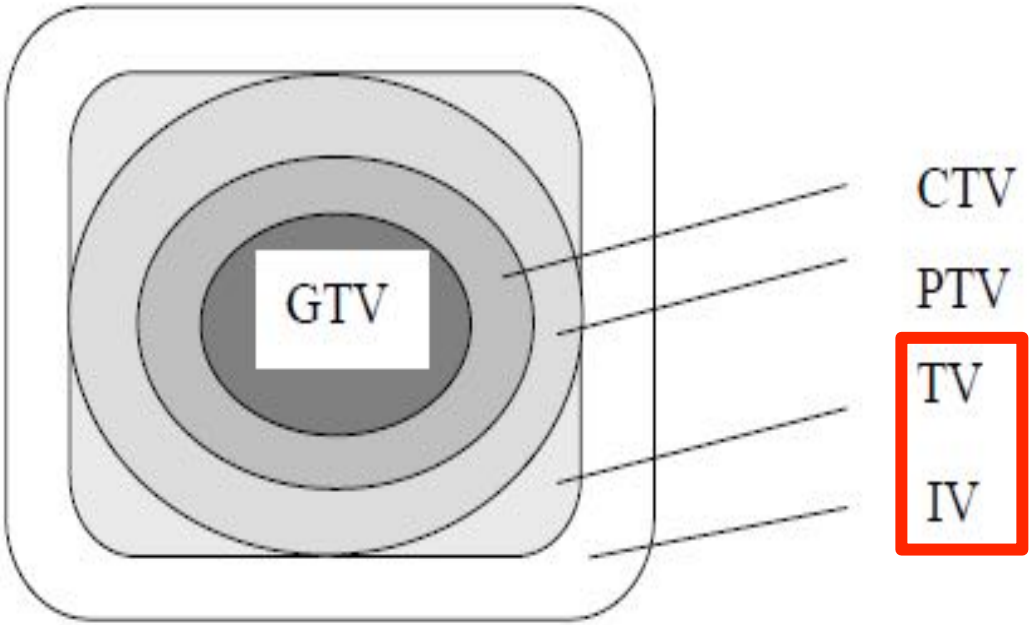
GTV: Gross tumour volume, i.e. detectable volume

CTV: Clinical target volume, i.e. GTV plus volume with suspicious (subclinical) affliction, e.g. safety margin

PTV: Planning target volume, i.e. CTV plus safety margin for movement or changes to the shape of the CTV as well as position changes and technical inaccuracy

TV: Treatment volume to be irradiated with the prescribed dose

IV: Irradiated volume, i.e. volume to be exposed to a significant dose in relation to normal tissue tolerance



ICRU 62- 71

Deterministic Risk Volume (DRV)

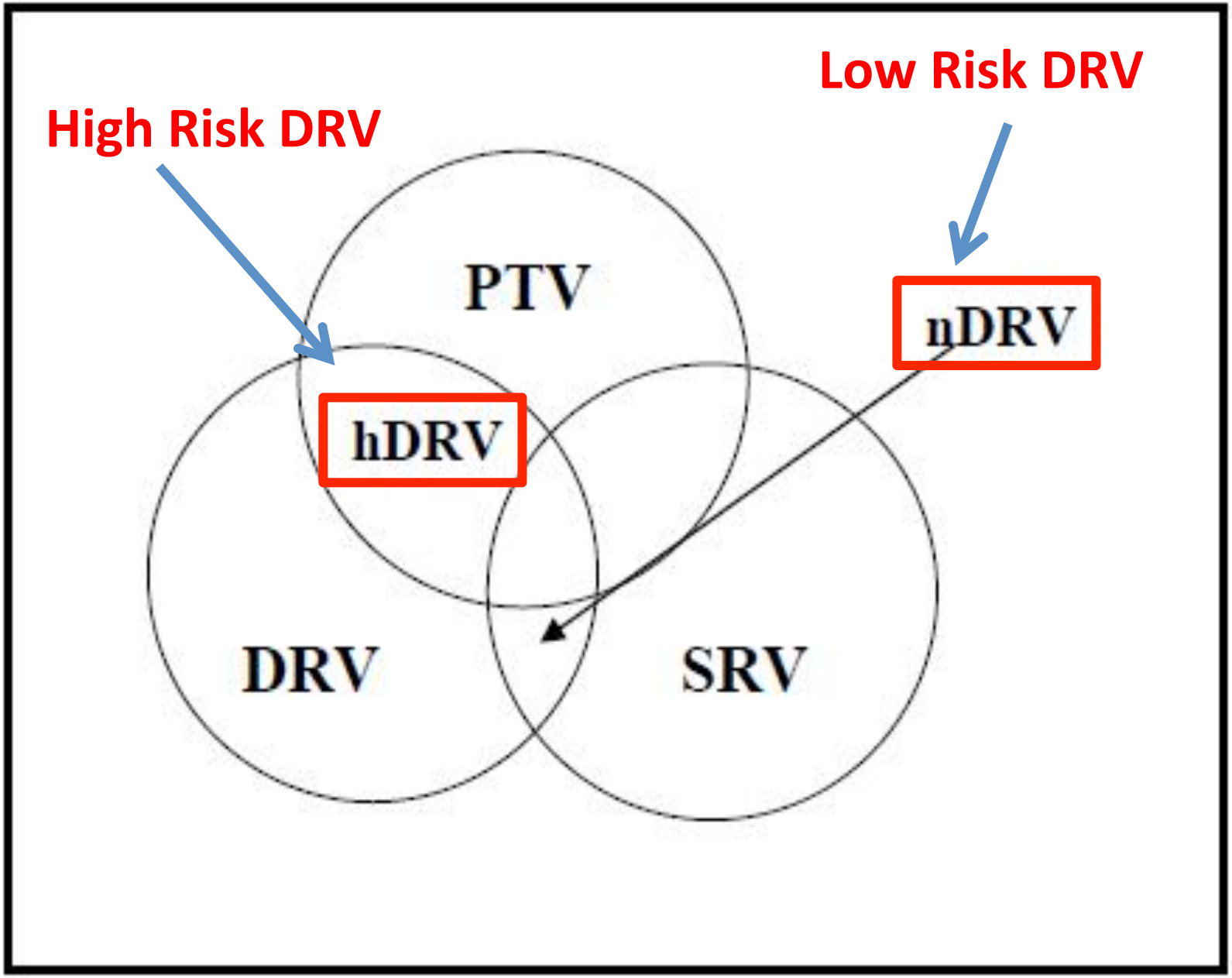
Volume che include i tessuti sani esposti ad una dose che eccede la tolleranza (supera la soglia) tessuto o organo specifica provocando effetti sintomatici o asintomatici

→il DRV include i tessuti sani ricompresi nei:

CTV – PTV

Treated Volume (dose di prescrizione)

Irradiated Volume (inclusi gli OARs)


High Risk DRV
Low Risk DRV
PTV
hDRV
nDRV
DRV
SRV

DRV

High Risk DRV

Volumi inclusi nel PTV o TV

Esempi:

- parete rettale anteriore nel PTV per ca.prostatico
- mucosa orale nel PTV del ca.rino-orofaringeo
- nervo ottico nel PTV di tumore orbitario
- midollo spinale nel PTV di una oligometastasi ossea

Low risk DRV

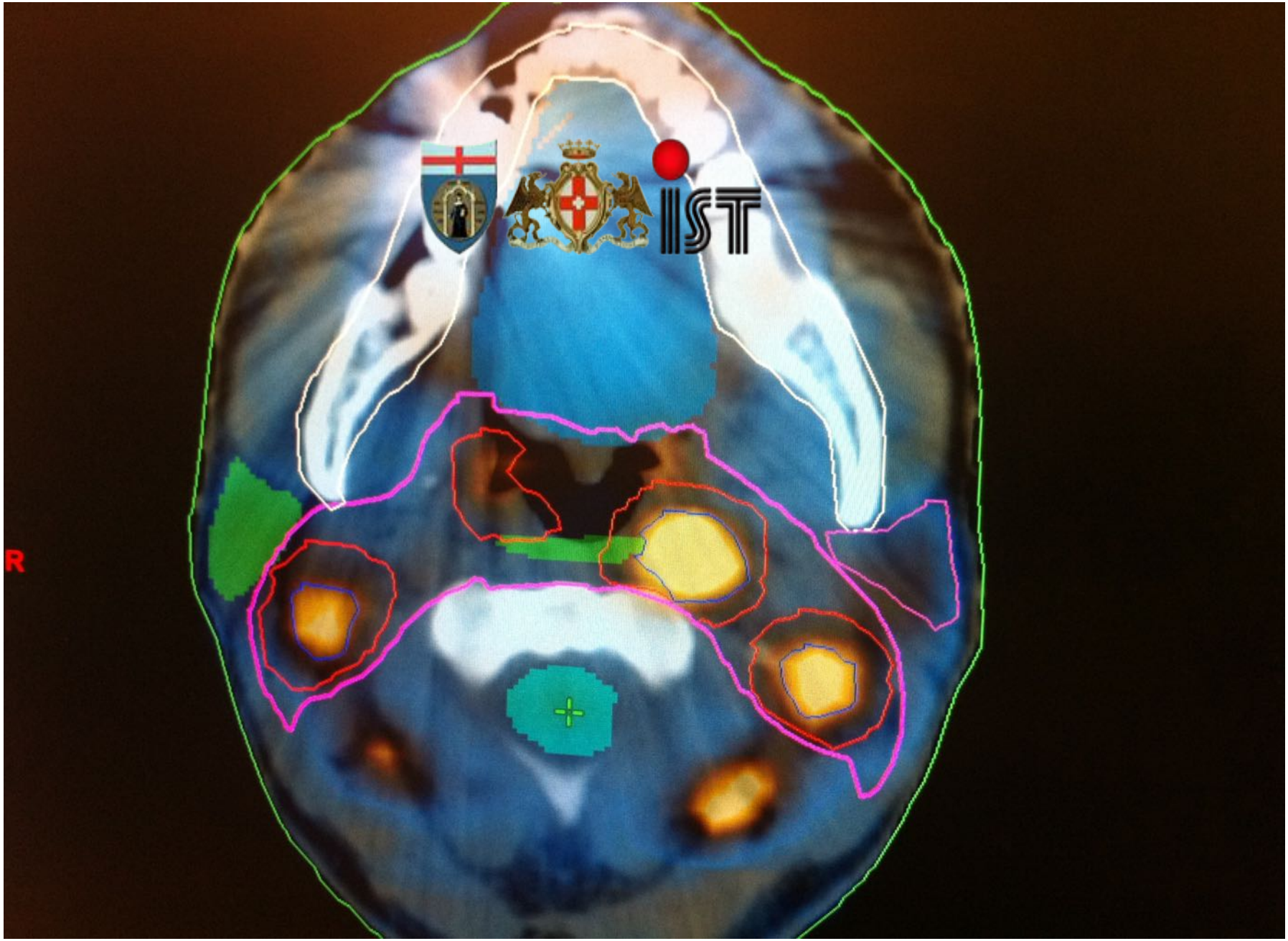
Volumi inclusi nel IV

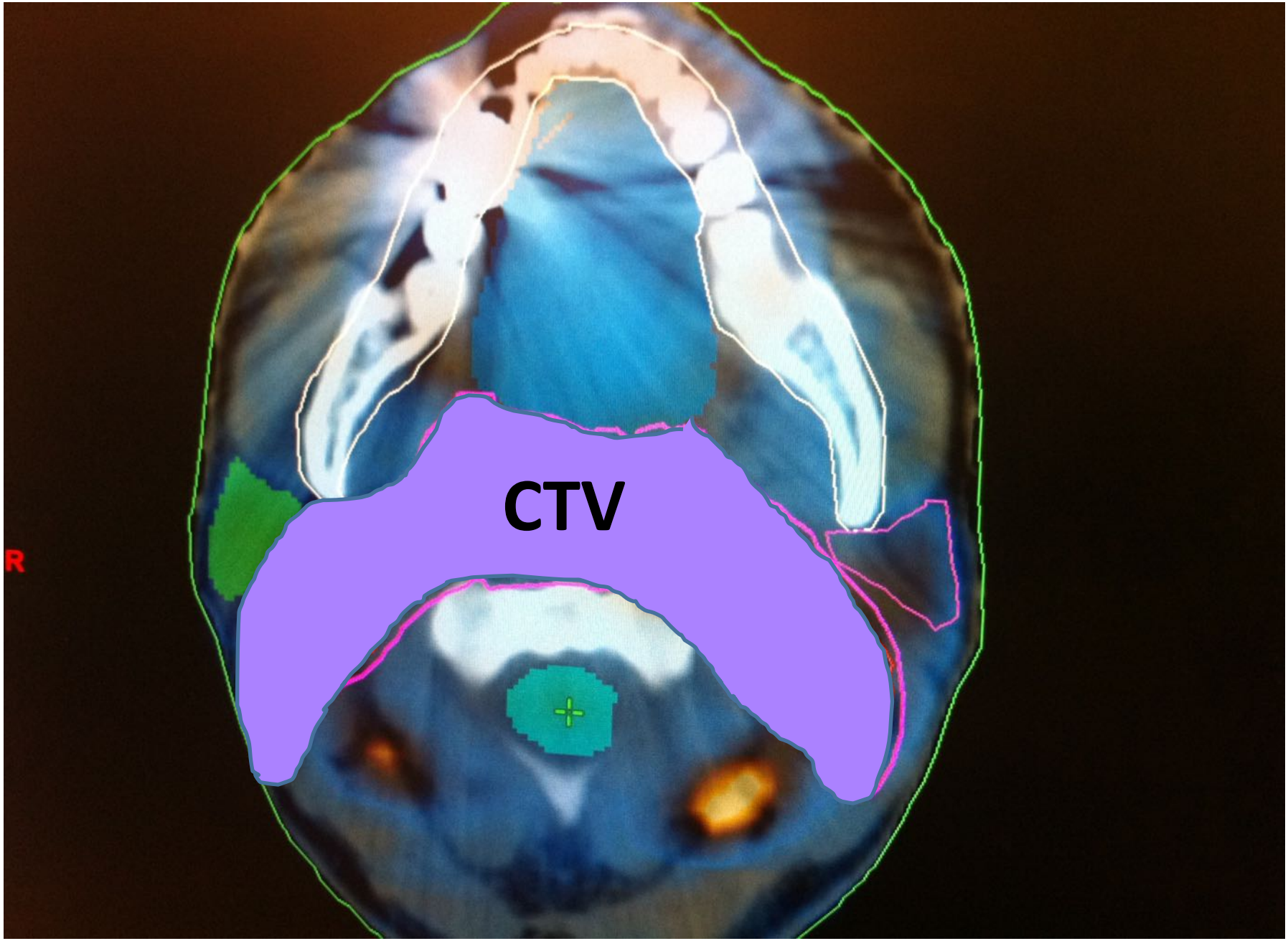
Esempi:

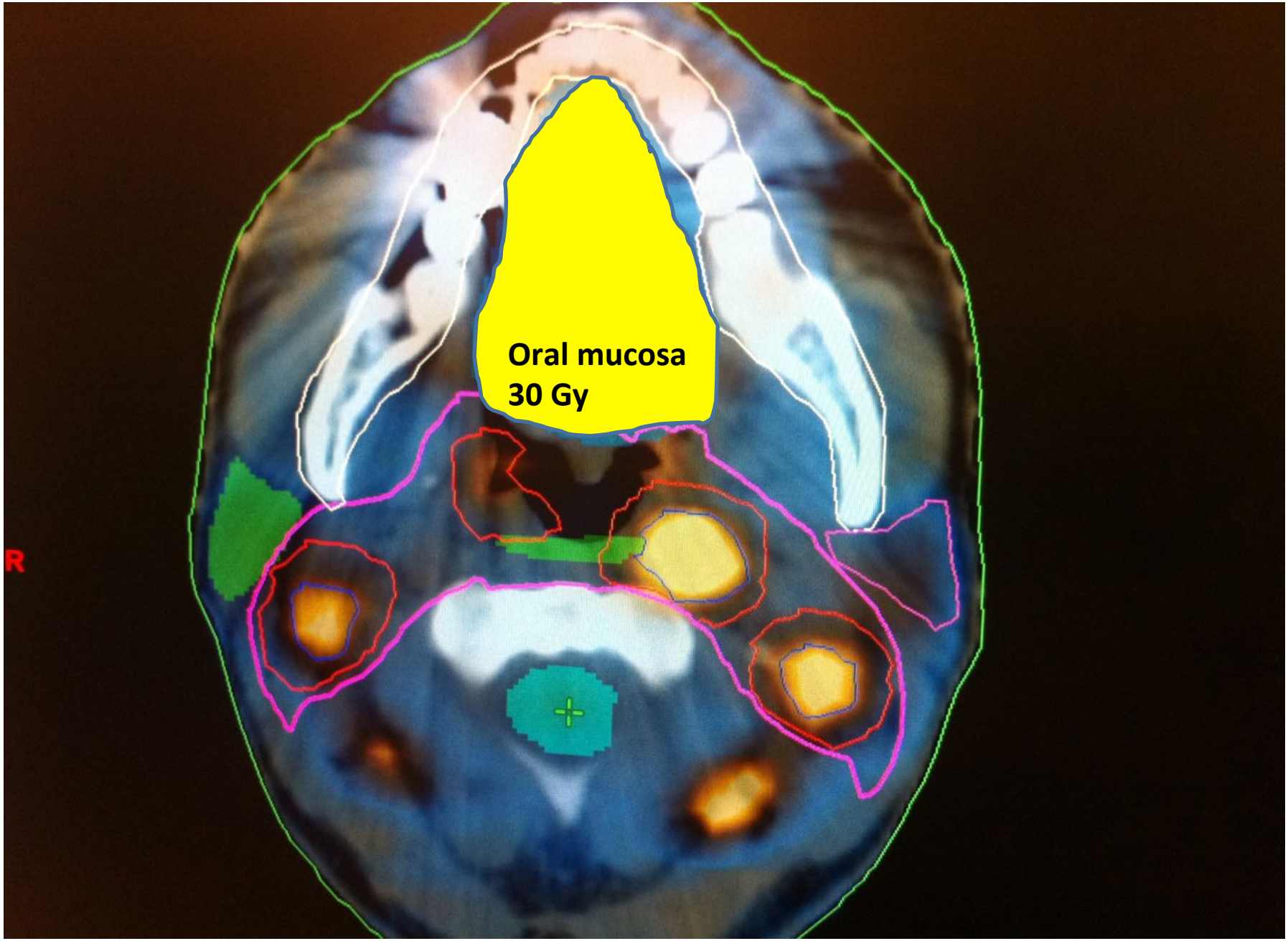
- mucosa orale / parotidi nella IMRT H&N
- intestino tenue nella IMRT pelvica
- parenchima polmonare nella RT stereotassica polmonare

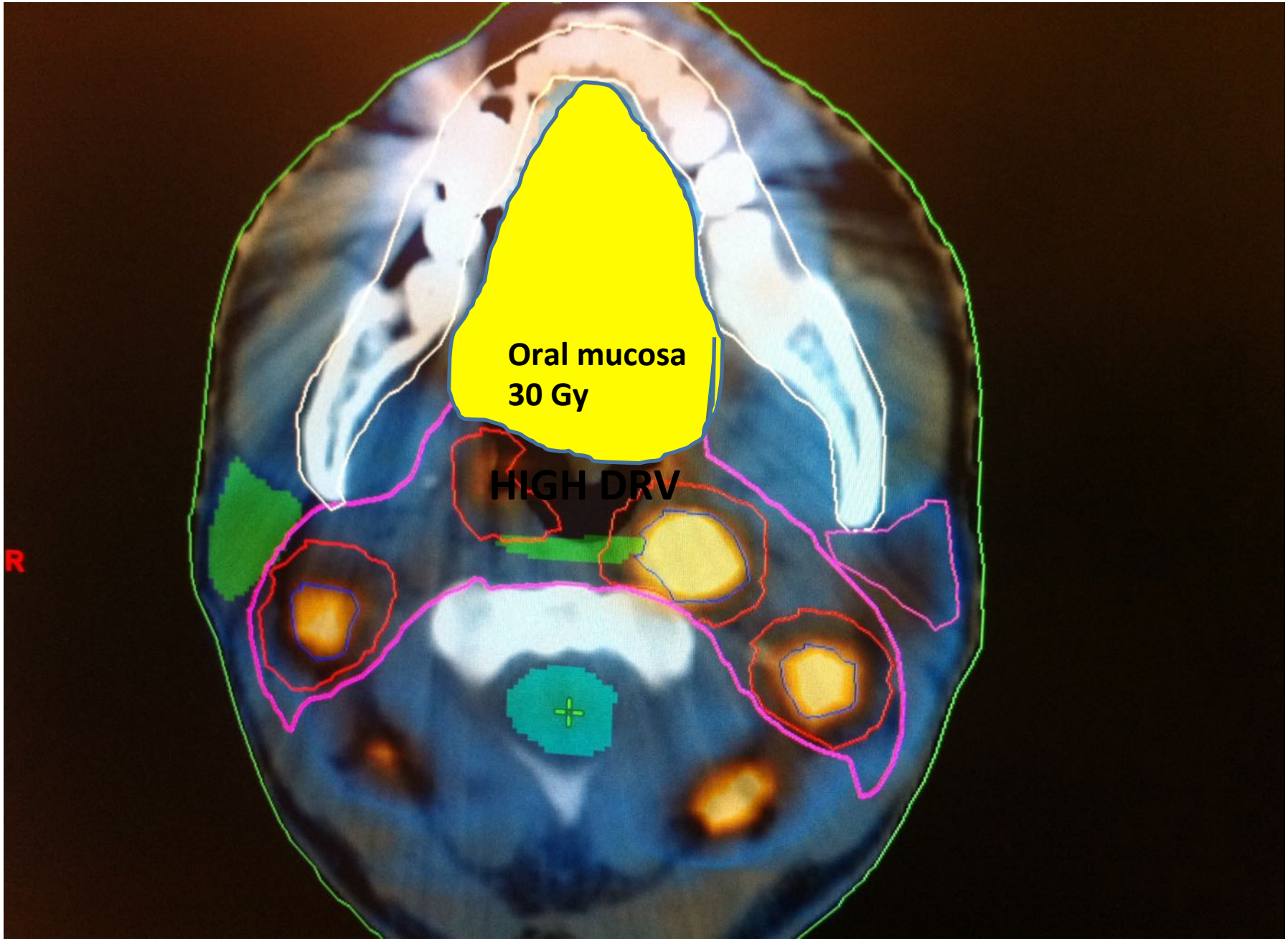
Effetti deterministici: sottostima delle dosi- soglie

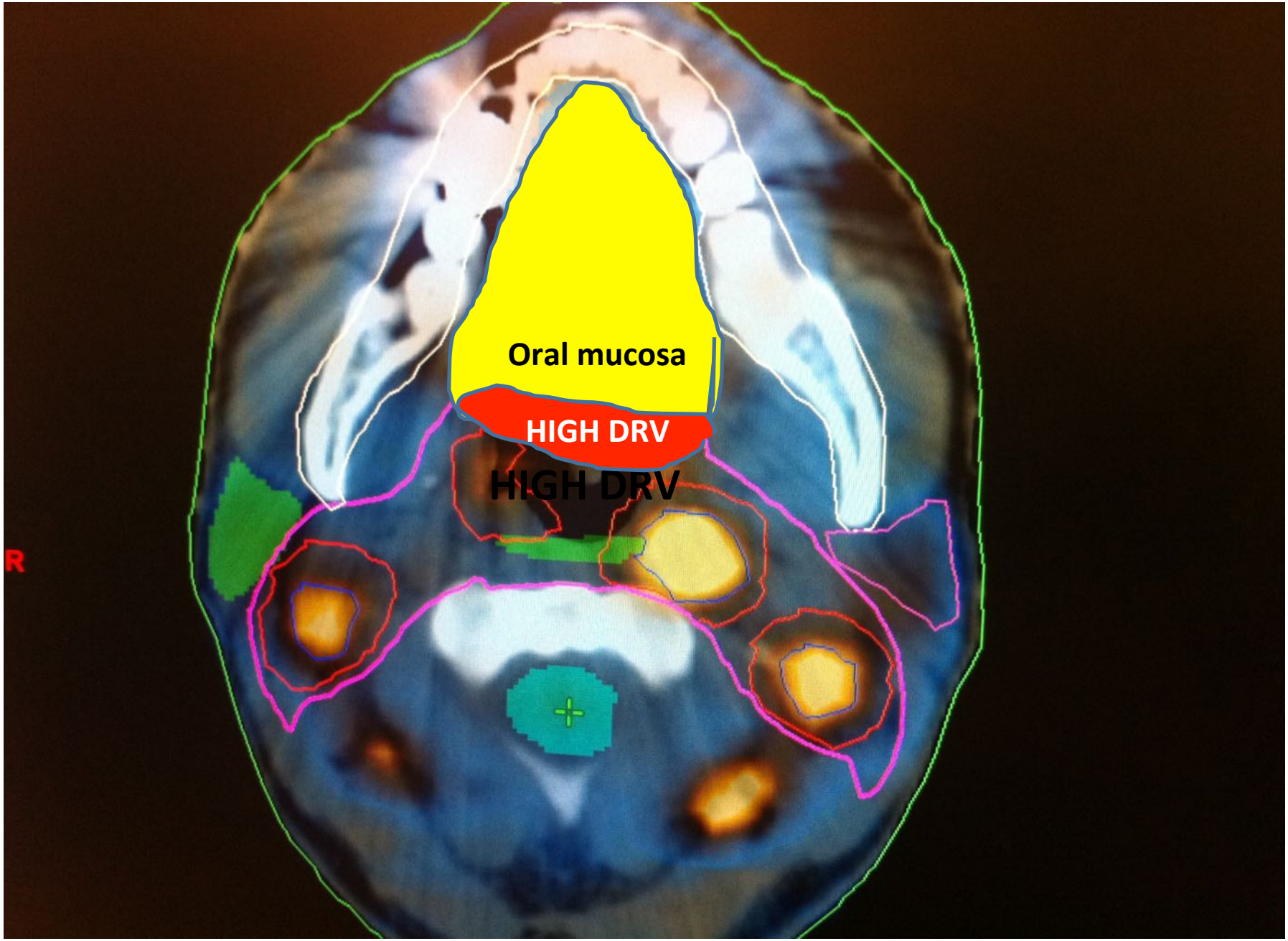
Organo/tessuto	Dose soglia	Effetto
Cristallino	0.8 Gy	opacità
Testicolo	0.1 Gy	riduzione spermatogenesi
Ovaie	2.5 Gy	sterilità transitoria
Midollo osseo	0.5 Gy	effetti mielosoppressivi
Mucosa intestinale	5- 12 Gy	malassorbimento
Mucosa orale	15-30 Gy	enantema- mucosite

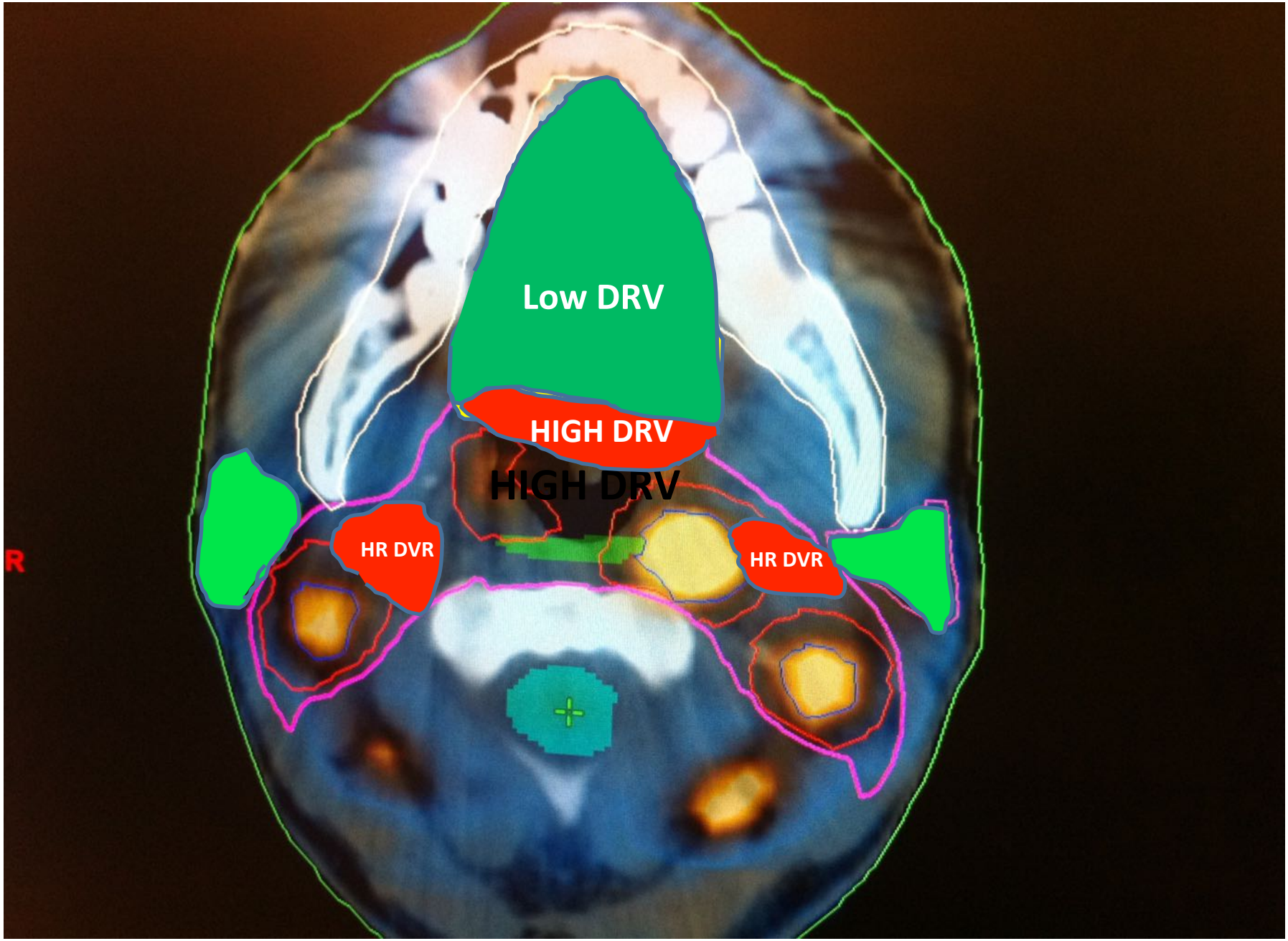

R

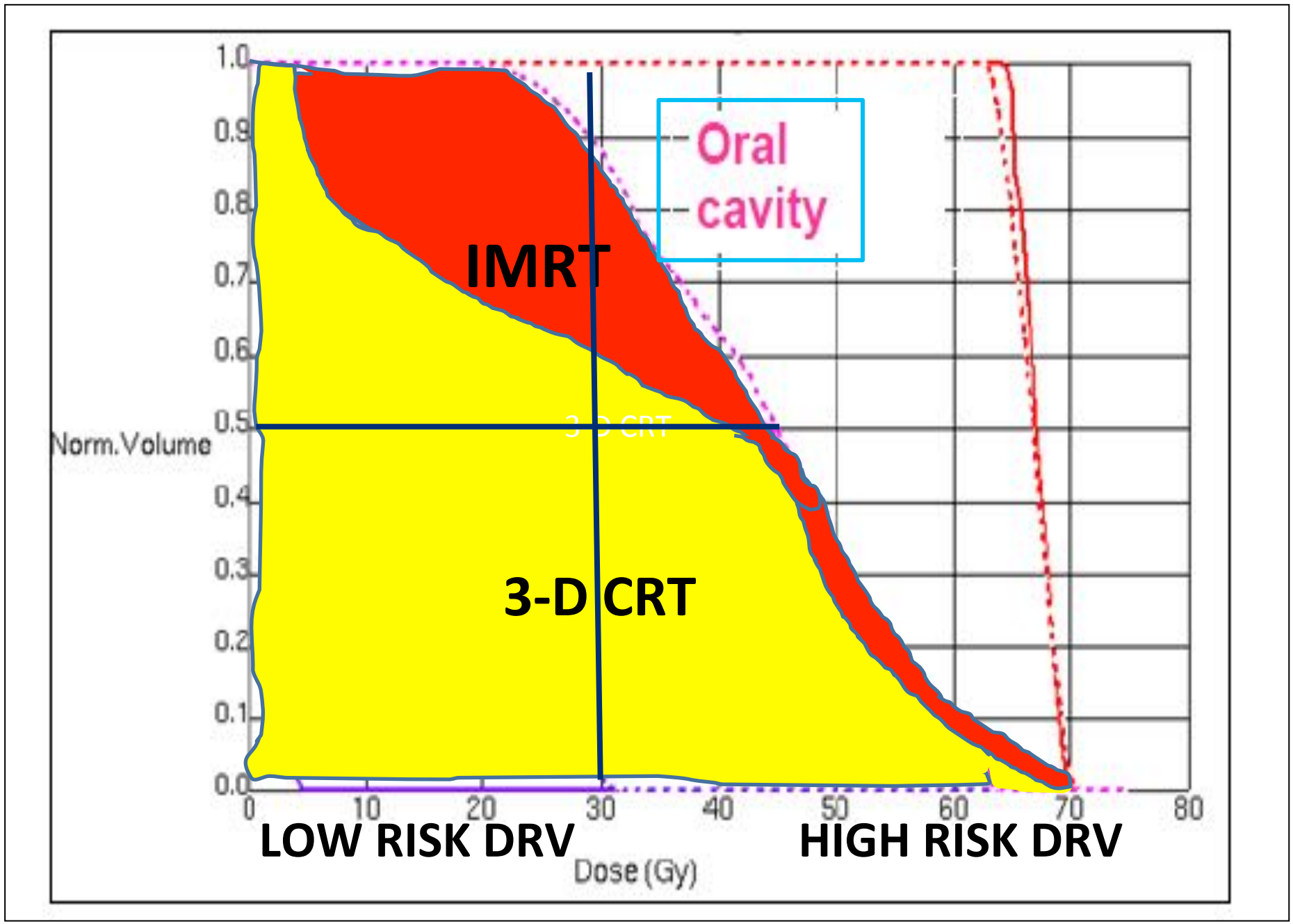

CTV
R


Oral mucosa
30 Gy
R


Oral mucosa
30 Gy
HIGH DRV
R

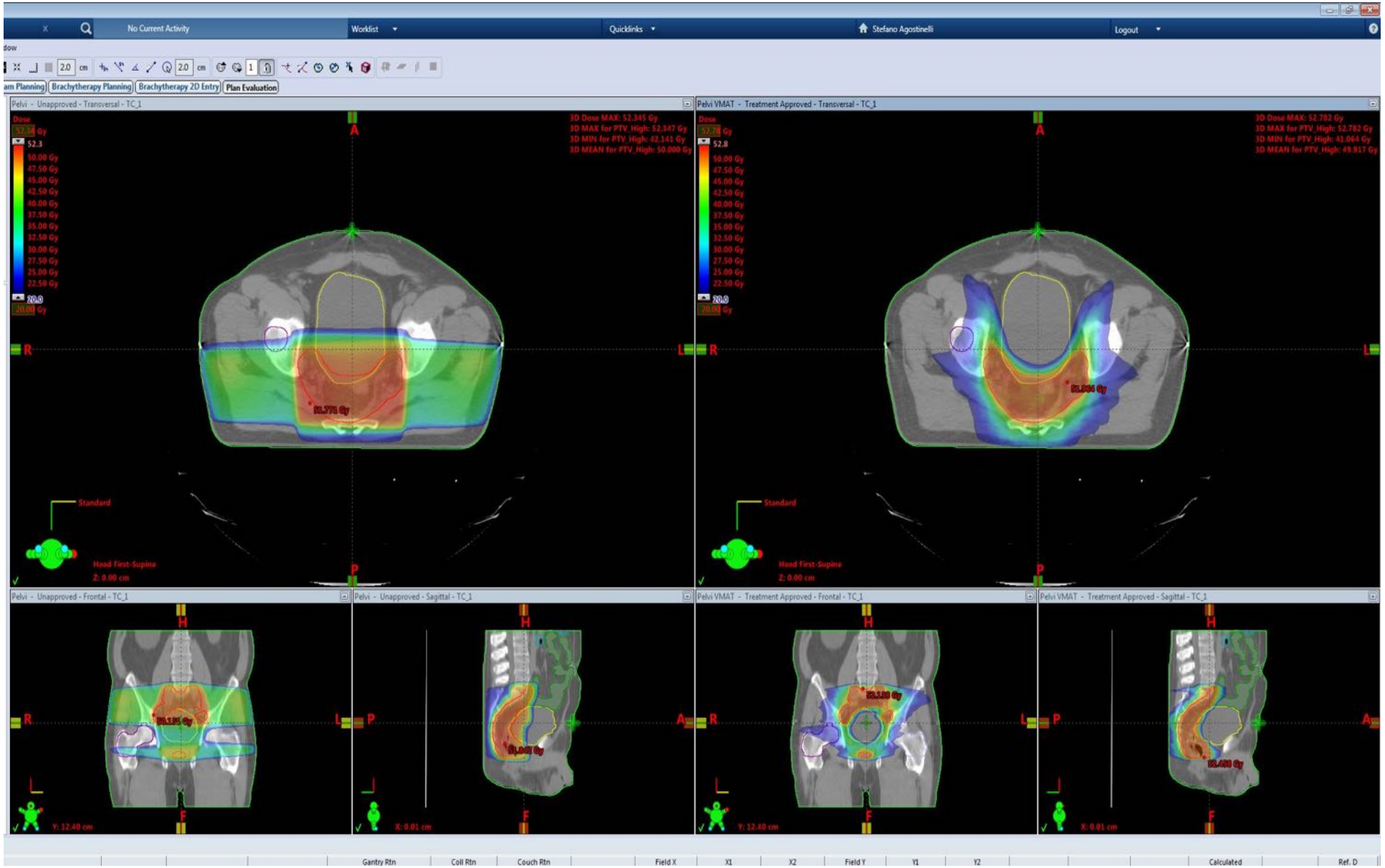

Oral mucosa
HIGH DRV
HIGH DRV
R


Low DRV
HIGH DRV
HIGH DRV
HR DVR
HR DVR
R


Oral cavity
IMRT
3-D CRT
Norm.Volume
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
0
10
20
30
40
50
60
70
80
LOW RISK DRV
HIGH RISK DRV
Dose (Gy)

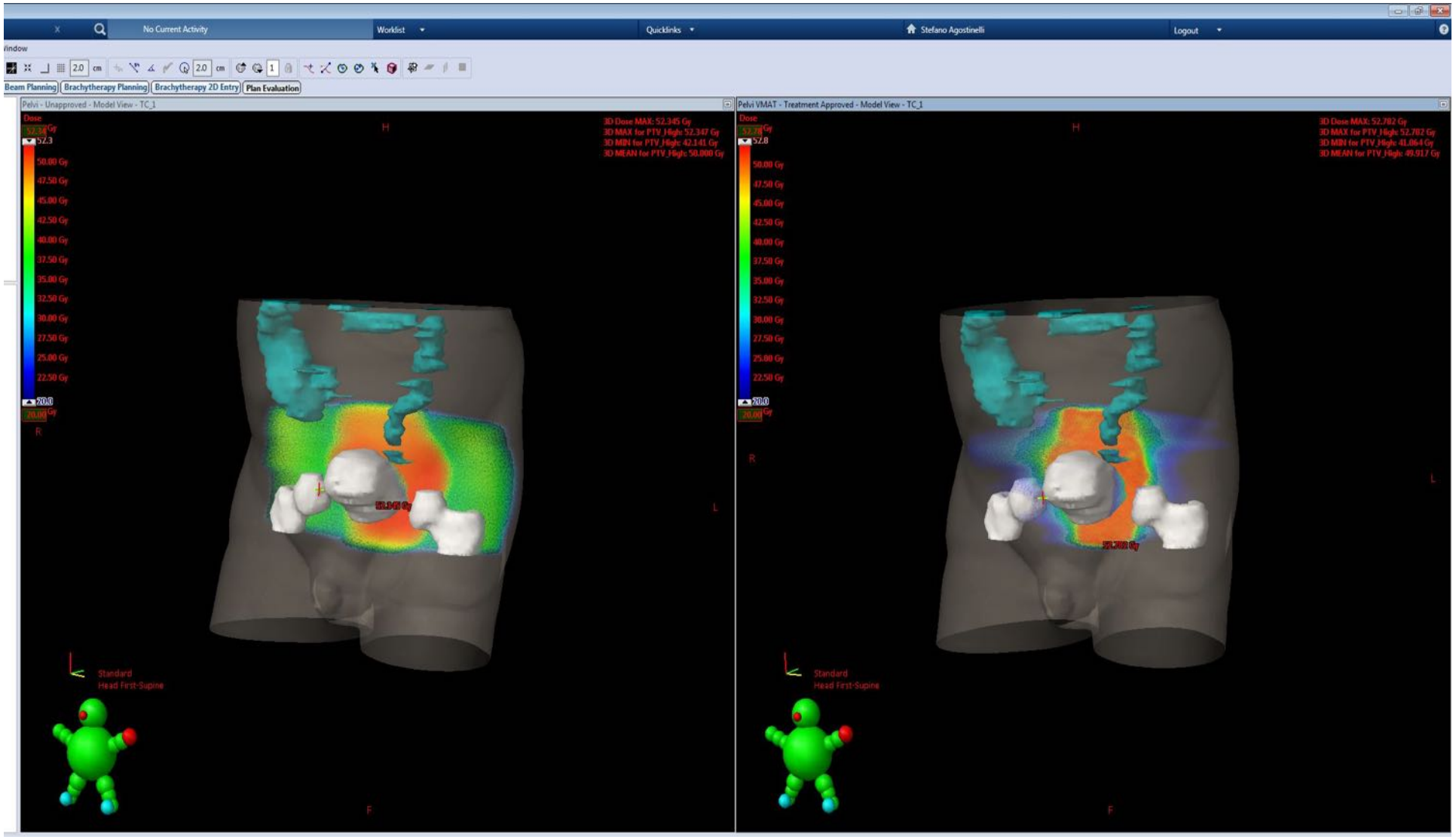
Carcinoma rettale

3-D CRT vs VMAT



Carcinoma rettale 3-D

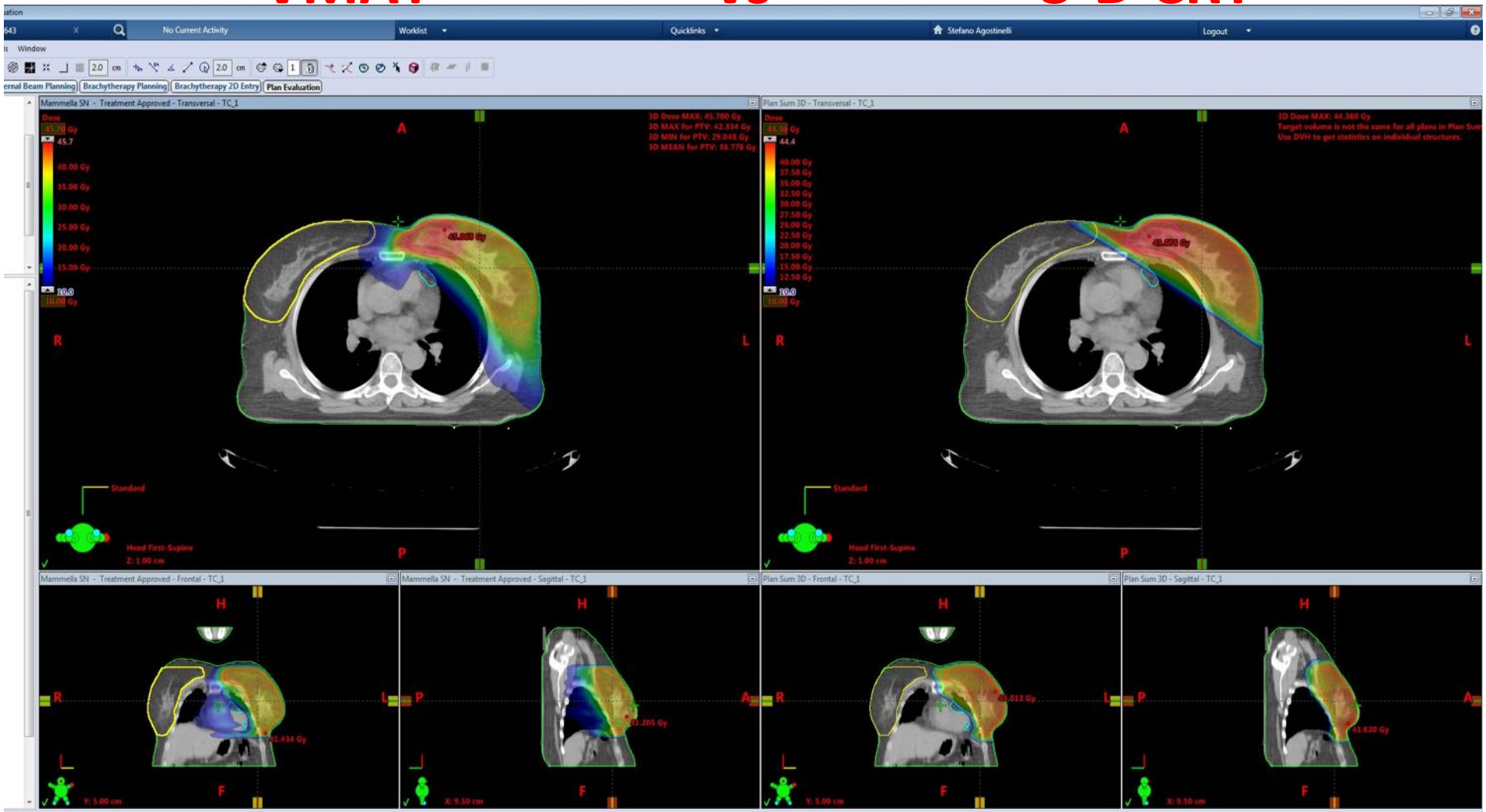
3-D CRT vs VMAT



Machine/Energy	MLC	Field Weight	Scale	Gantry Rtn [deg]	Coll Rtn [deg]	Couch Rtn [deg]	Wedge	Field X [cm]	X1 [cm]	X2 [cm]	Field Y [cm]	Y1 [cm]	Y2 [cm]	X [cm]	Y [cm]	Z [cm]	Calculated SSD [cm]	MU	Ref. D [Gy]
TrilogySN5997 - 6X	VMAT	1.757	Varian IEC	181.0 CW 179.0	30.0	0.0	None	19.6	+8.6	+11.0	20.8	+9.6	+11.2	0.00	17.00	0.00	94.2	351	
TrilogySN5997 - 6X	VMAT	1.964	Varian IEC	179.0 CCW 181.0	330.0	0.0	None	19.6	+11.0	+8.6	20.8	+9.6	+11.2	0.00	17.00	0.00	94.2	393	

Carcinoma mammario

VMAT vs 3-D CRT



Machine/Energy	MLC	Field Weight	Scale	Gantry Rtn [deg]	Coll Rtn [deg]	Couch Rtn [deg]	Wedge	Field X [cm]	X1 [cm]	X2 [cm]	Field Y [cm]	Y1 [cm]	Y2 [cm]	X [cm]	Y [cm]	Z [cm]	Calculated SSD [cm]	MU	Ref. D [Gy]
TrilogySN5997 - 6X	VMAT	0.944	Varian IEC	303.0 CW 150.0	30.0	0.0	None	21.9	+11.5	+10.5	20.8	+9.6	+11.2	9.50	5.00	1.00	91.0	283	
TrilogySN5997 - 6X	VMAT	0.983	Varian IEC	150.0 CCW 303.0	330.0	0.0	None	21.5	+11.7	+9.9	20.9	+10.5	+10.4	9.50	5.00	1.00	85.4	295	
TrilogySN5997 - 6X	VMAT	0.914	Varian IEC	303.0 CW 150.0	0.0	0.0	None	20.8	+11.3	+9.5	17.3	+8.6	+8.6	9.50	5.00	1.00	91.0	274	
TrilogySN5997 - 6X		0.000	Varian IEC	0.0	0.0	0.0	None	10.0	+5.0	+5.0	10.0	+5.0	+5.0	9.50	5.00	1.00	94.9		
TrilogySN5997 - 6X		0.000	Varian IEC	90.0	0.0	0.0	None	10.0	+5.0	+5.0	10.0	+5.0	+5.0	9.50	5.00	1.00	93.8		
TrilogySN5997 - 6X		0.000	Varian IEC	0.0	0.0	0.0	None	10.0	+5.0	+5.0	10.0	+5.0	+5.0	9.50	5.00	1.00	94.9		

DRV: come dovrebbe essere studiato

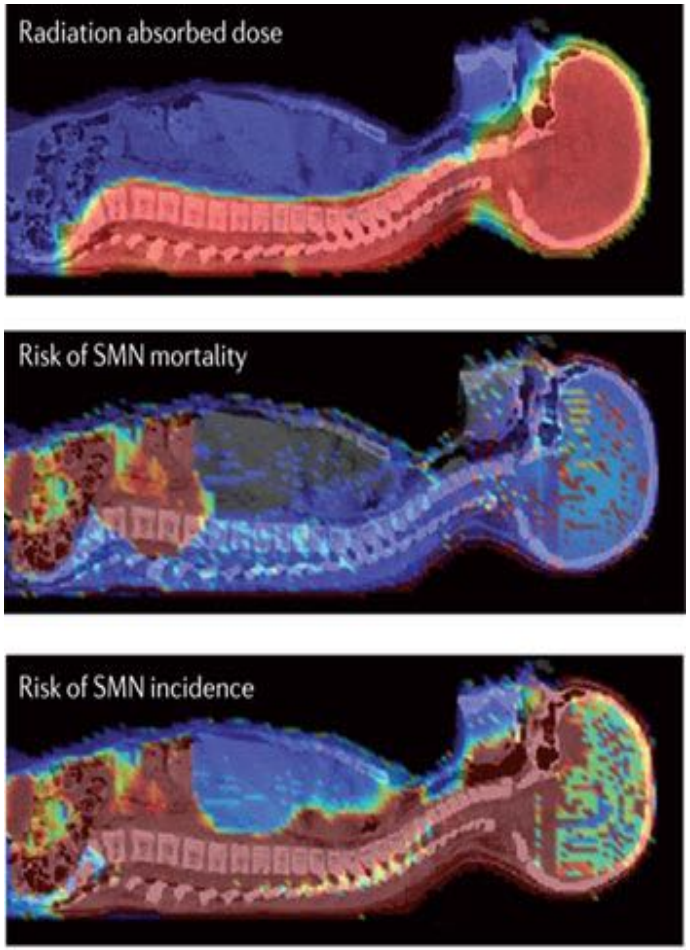
- **Steps per il contouring:**
- **1. GTV**
- **2. OARs e VOIs**
- **3. CTV → PTV**

- **Organi a risposta seriale o parallela inclusi nel PTV rientrano nel high risk DRV e devono essere evidenziati nell'Istogramma Dose-Volume**

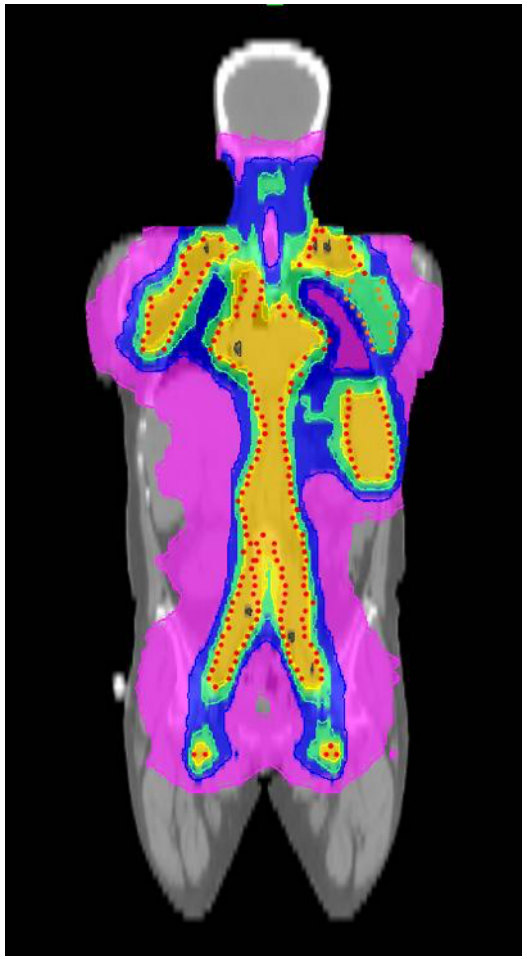
- **La dose ai tessuti inclusi nel low risk DRV può impattare sulla Quality of Life del paziente**

Prevedere il rischio di secondi tumori in pazienti irradiati e guariti con moderna tecnologia

(bassa dose ad ampi settori corporei)



Nature Reviews | Cancer



Stochastic Risk Volume (SRV)

È il volume che comprende gli organi e i tessuti che possono essere a potenziale rischio di secondi tumori radioindotti.

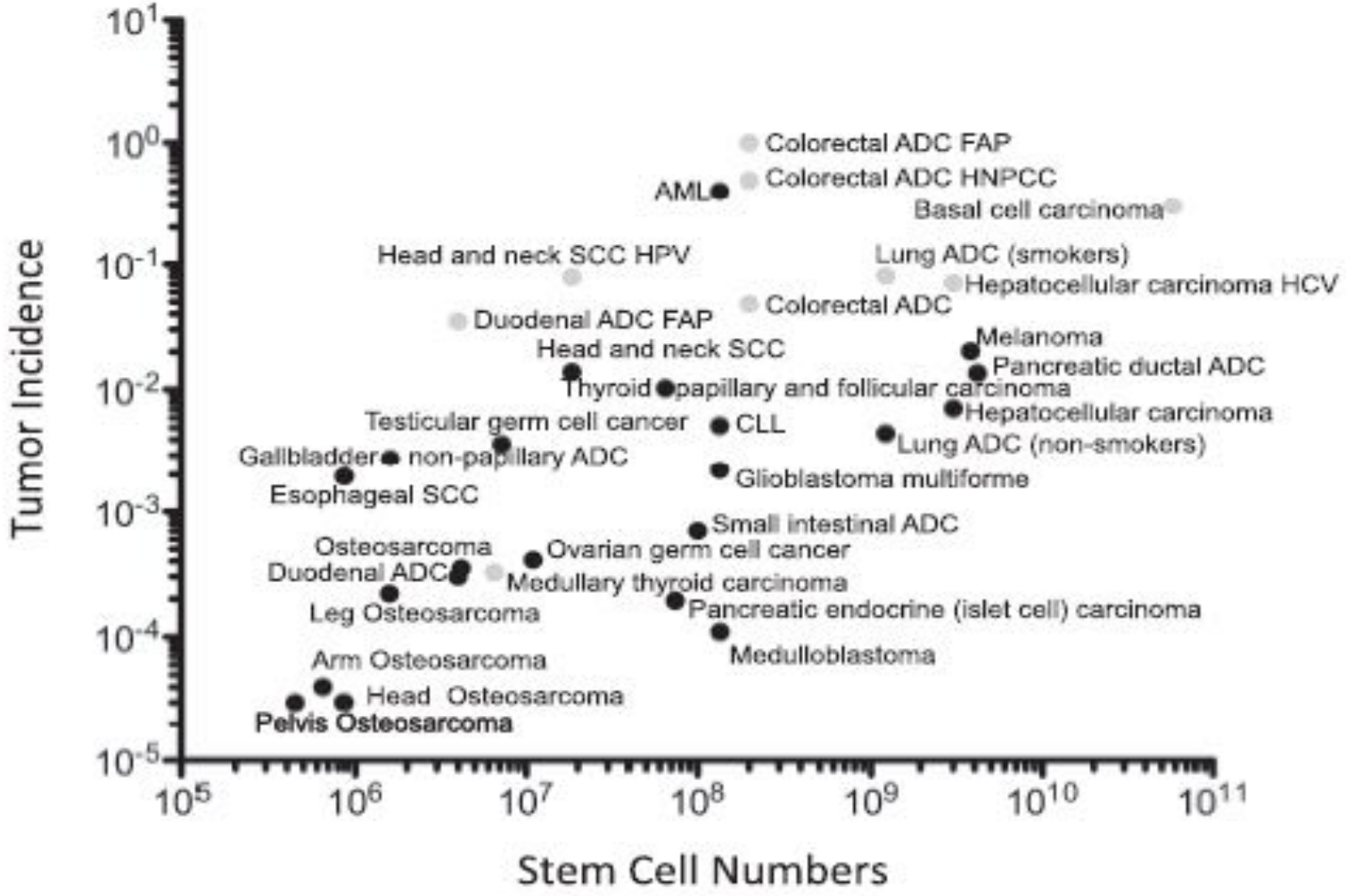
- **Il SRV include i tessuti ricompresi:**
  - **nel PTV, nel DRV e il volume corporeo esposto a IGRT**
  - **è correlato a energia (MV), radiation leakage e scattering, neutron generation**

JNCI J Natl Cancer Inst (2015) 107(10): djv213

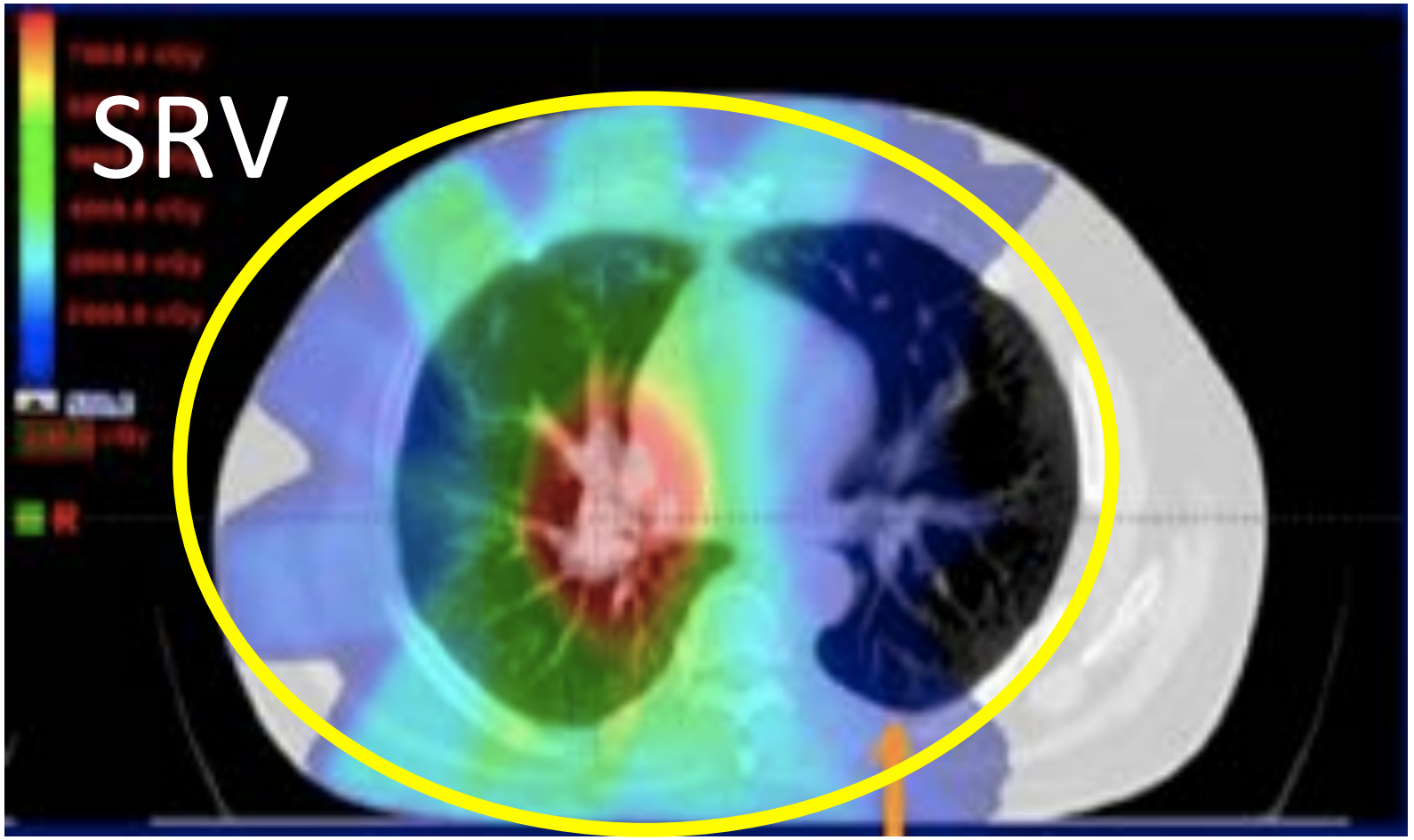
doi:10.1093/jnci/djv213
First published online August 4, 2015
Commentary

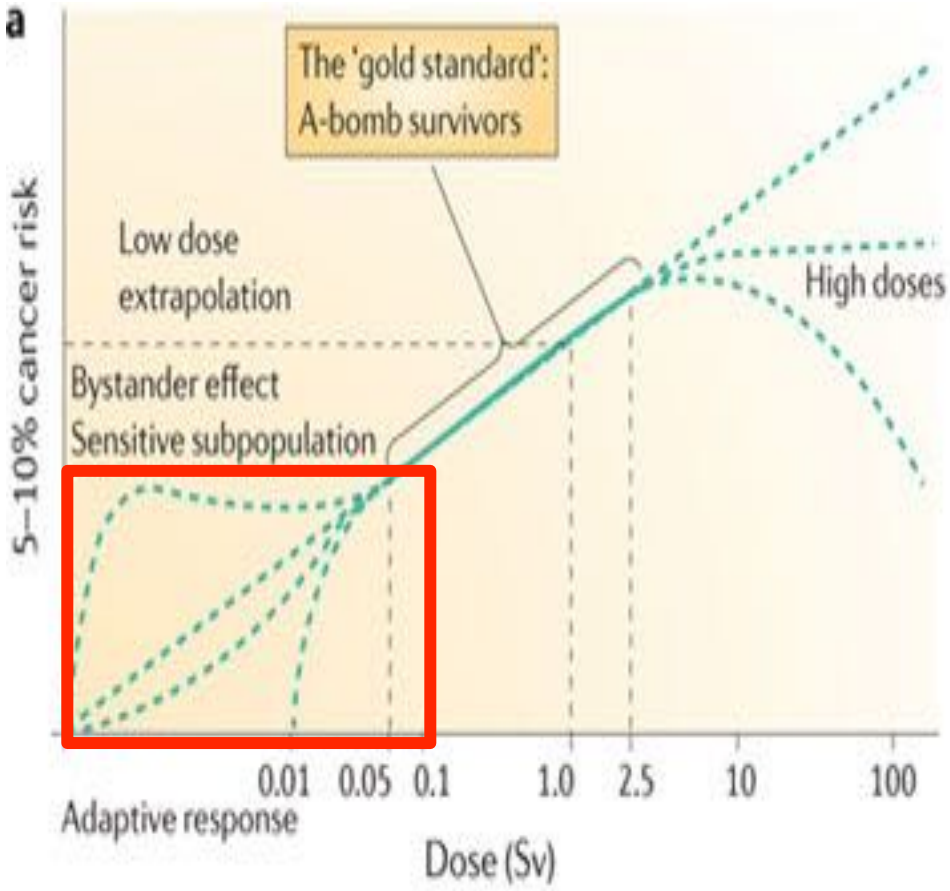
Strategies to Prevent "Bad Luck" in Cancer

Adriana Albini, Silvio Cavuto, Giovanni Apolone, Douglas M. Noonan



Risk enhancers:
promuovono la cancerogenesi nel SRV





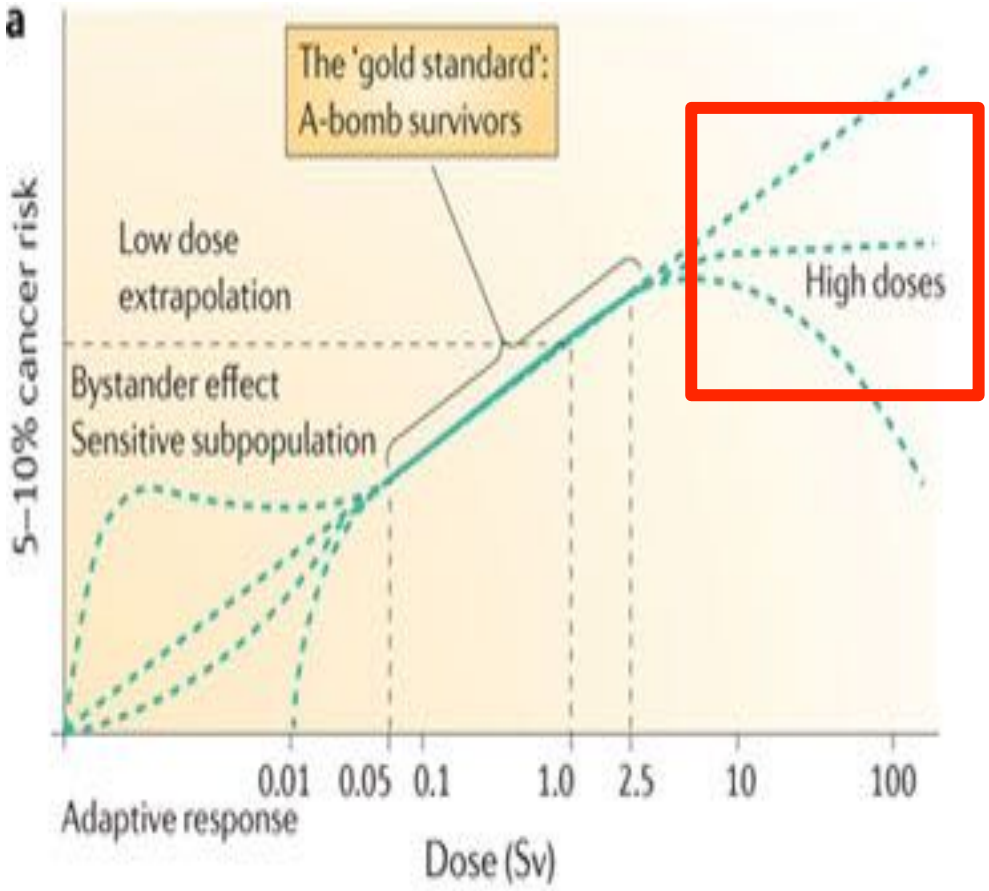
Sotto l'esposizione di 100 mSv in dose singola o 600 mSv frazionata possono intervenire 4 probabilità di effetto:

- **estrapolazione lineare del rischio**
- **risposta adattativa alle basse dosi**
- **effetto by-stander**
- **rischio nullo**

Probabilmente esiste una sovrastima del rischio stocastico con dosi < 2.5 Gy

Da E.J Hall, Columbia University, USA

Nature Reviews | Cancer



Sopra l'esposizione di 3-10 Sv possono intervenire 3 probabilità di effetto:

- **estrapolazione lineare (LEXP) del rischio**
- **Fino a 75-80 Gy (o dosi equivalenti)**

- **un plateau di rischio (LPLA) – c'e' necessità di cofattori promotori**

- **un rischio decrescente per morte cellulare radioindotta**

Probabilmente esiste una sottostima del rischio stocastico con dosi > 3 -10 Gy

-

Da E.J Hall, Columbia University, USA

Nature Reviews | Cancer

Potenziale rischio di secondo tumore radioindotto in accordo alle dosi soglia e al frazionamento

Rischio	Range delle dose soglia	esposizione	note
minimo	<0.05 - 0.1 Gy (50-100 mSv)	singola	effetti biologici
minimo	0.2-0.6 Gy (200-600 mSv)	frazionata	effetti biologici
basso	> 0.6 Gy < 3 Gy	singola o frazionata	effetti biologici
intermedio	>3.0 Gy - >10 Gy	singola o frazionata	potenziale cancerogenesi
elevato	40-45 Gy	frazionata	cancerogenesi ai margini del PTV
molto elevato	> 70 Gy	frazionata	cancerogenesi nel PTV
		Tubiana M.	Radioth Oncol 2009

Stochastic Risk Volume (SRV)

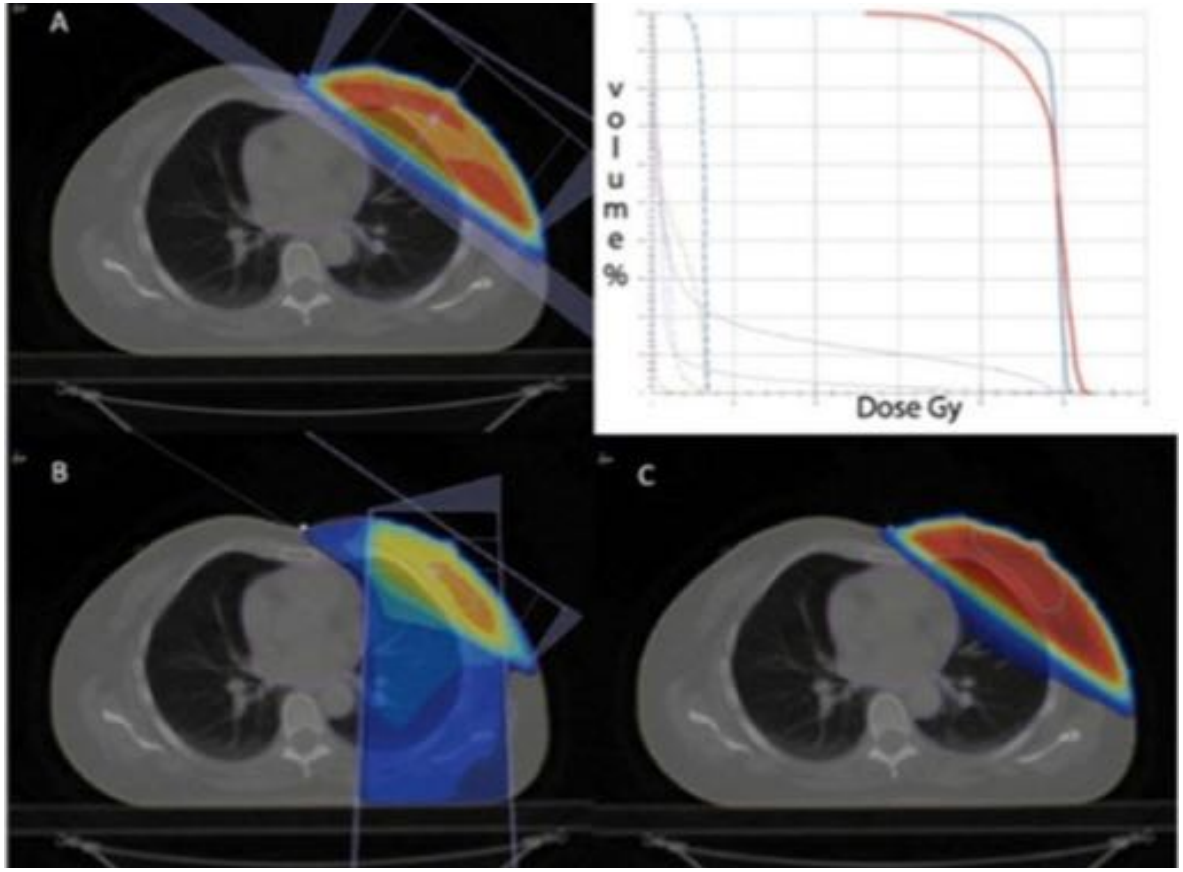
→ definizioni di «**iso-risk gradient dose**» :

- volumi a **rischio intermedio** che ricevono **3 Gy** (es. ricompresi nell'isodose 5% della dose prescritta di 60 Gy/30 fx) o **10 Gy**

- volumi a **rischio basso** che ricevono almeno **0.6 Gy** (es. ricompresi nell'isodose 1% della dose prescritta di 60 Gy/30 fx)

SRV con

3-D CRT

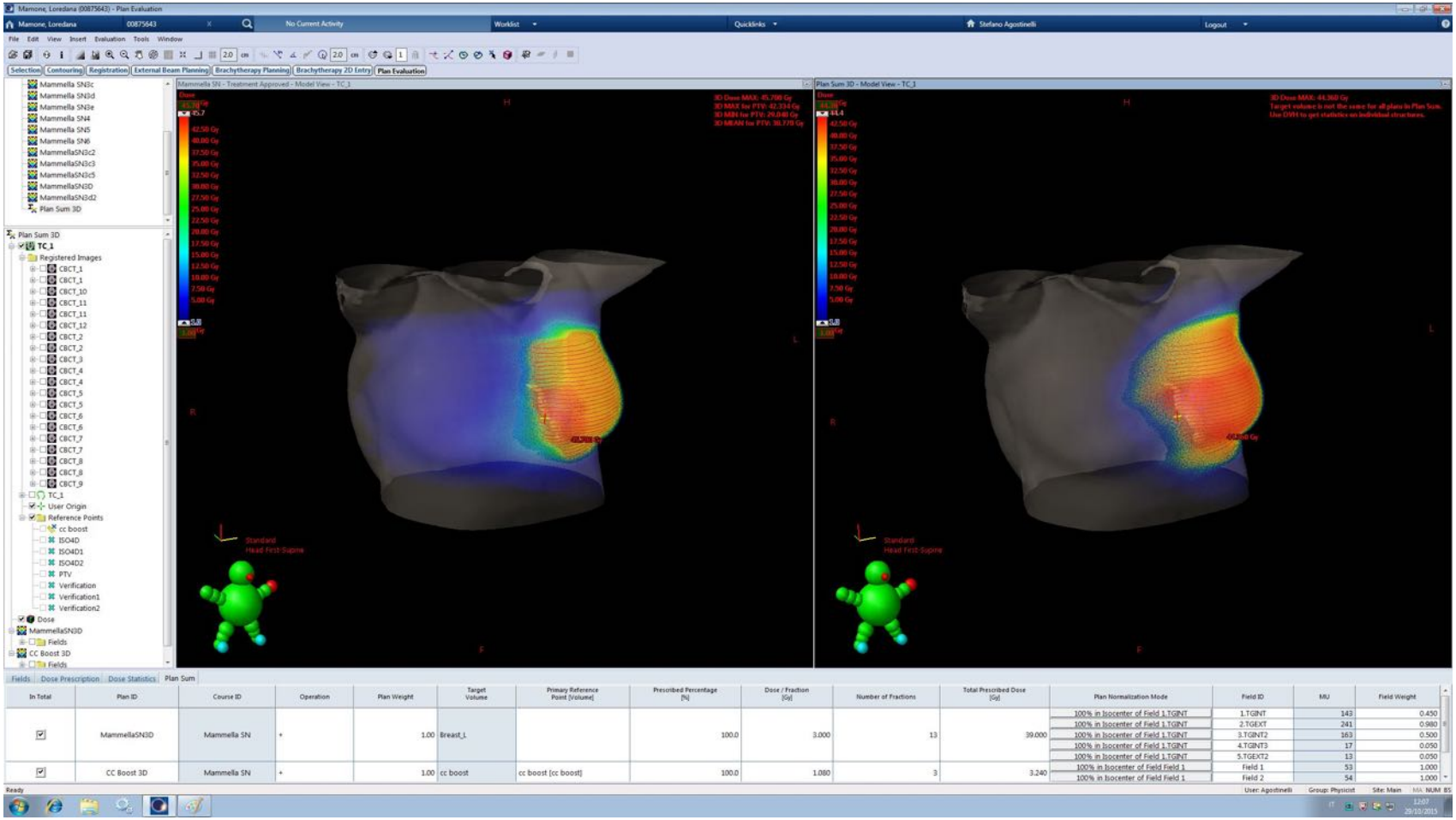


A biologically competitive 21 days hypofractionation scheme with weekly concomitant boost in breast cancer radiotherapy feasibility acute sub-acute and short term late effects.

Guenzi M, Vagge S, Azinwi NC, D'Alonzo A, Belgioia L, Garelli S, Gusinu M, Corvò R - Radiat Oncol (2010)

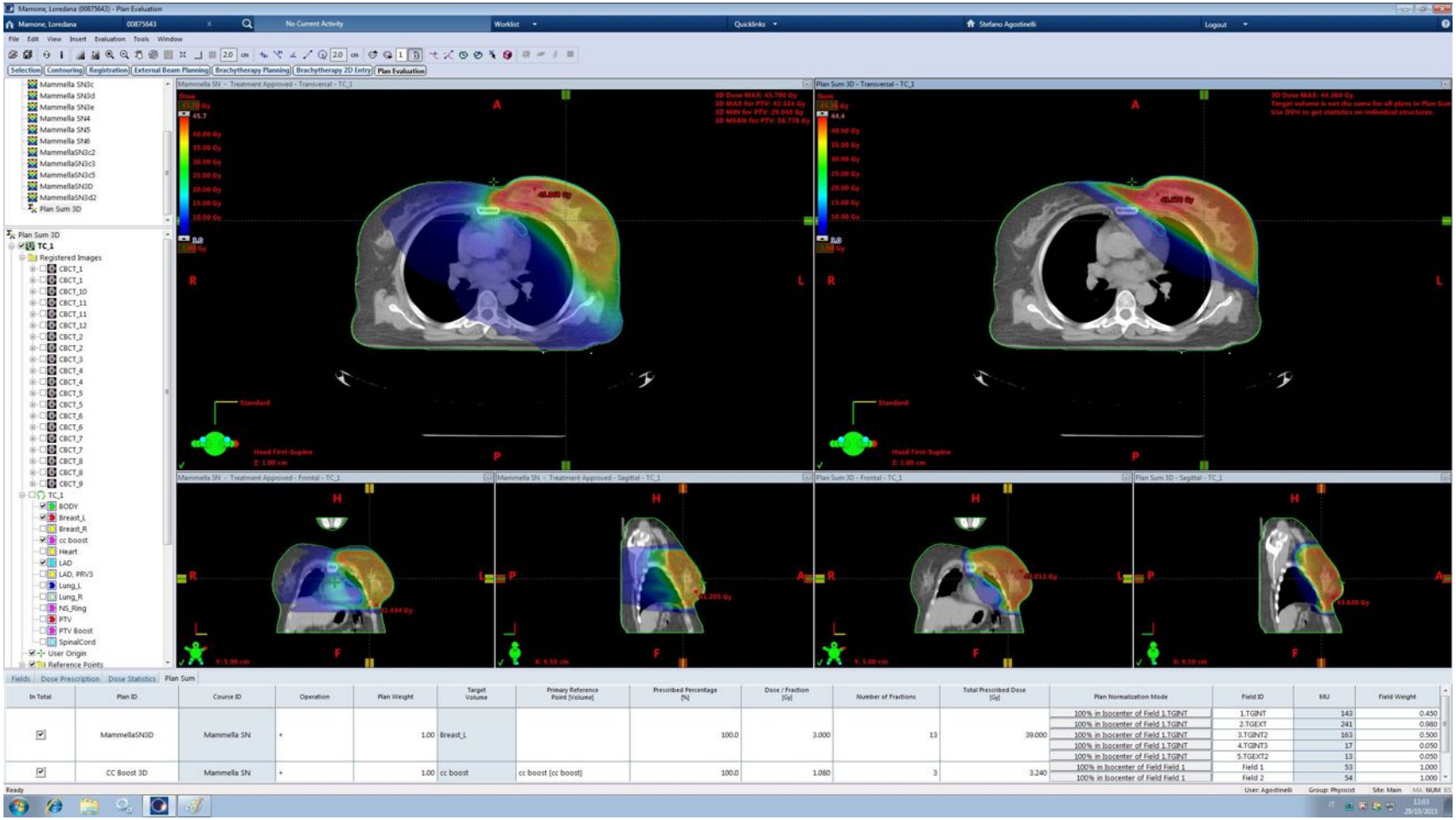
SRV (10 Gy) nel trattamento mammario

VMAT (240°) 3-D CRT



SRV(10 Gy) nel trattamento mammario

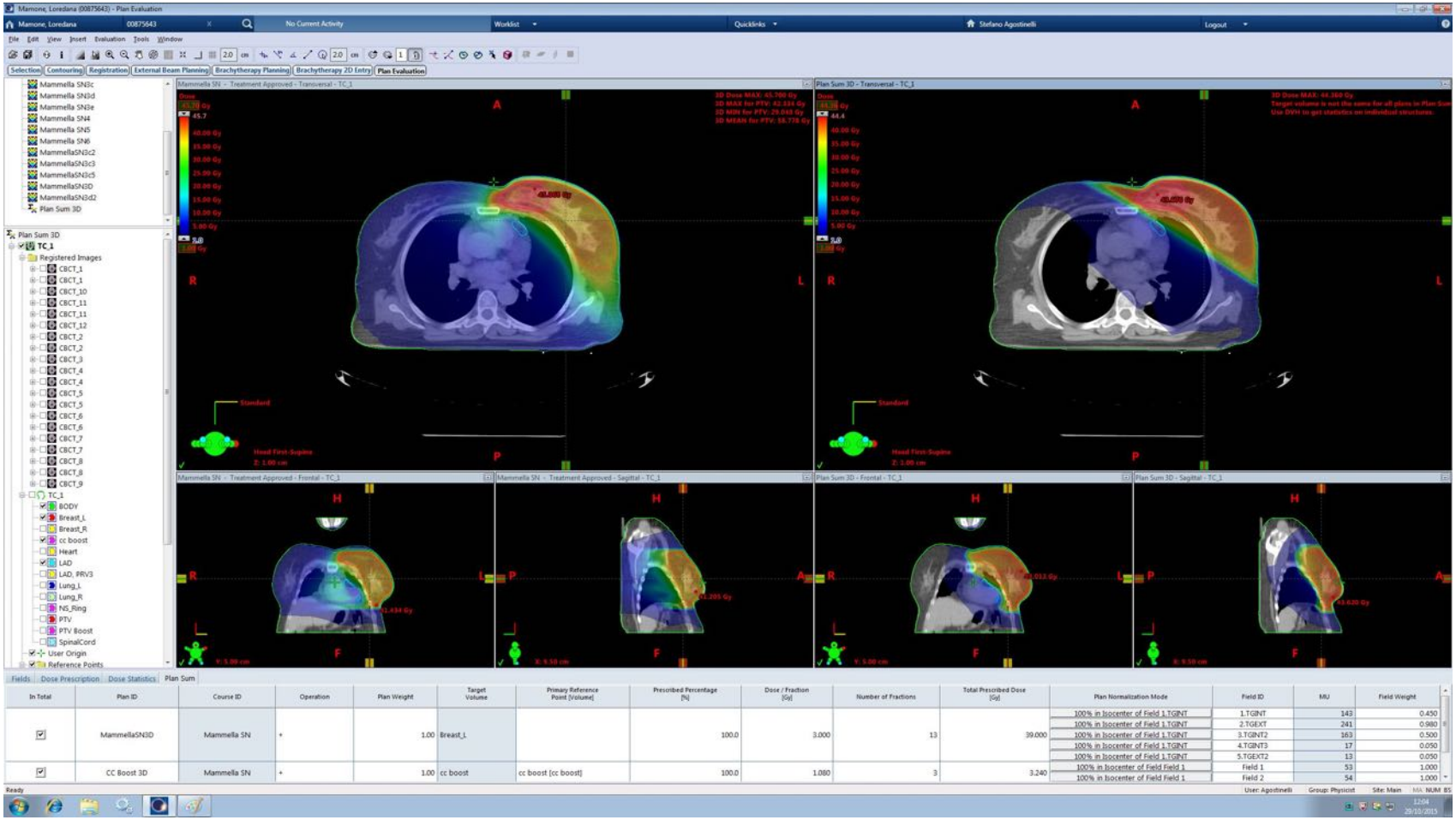
VMAT (240°) 3-D CRT



Breast cancer - Hypofractionation 42 Gy/13 fx

SRV (3 Gy) nel trattamento mammario

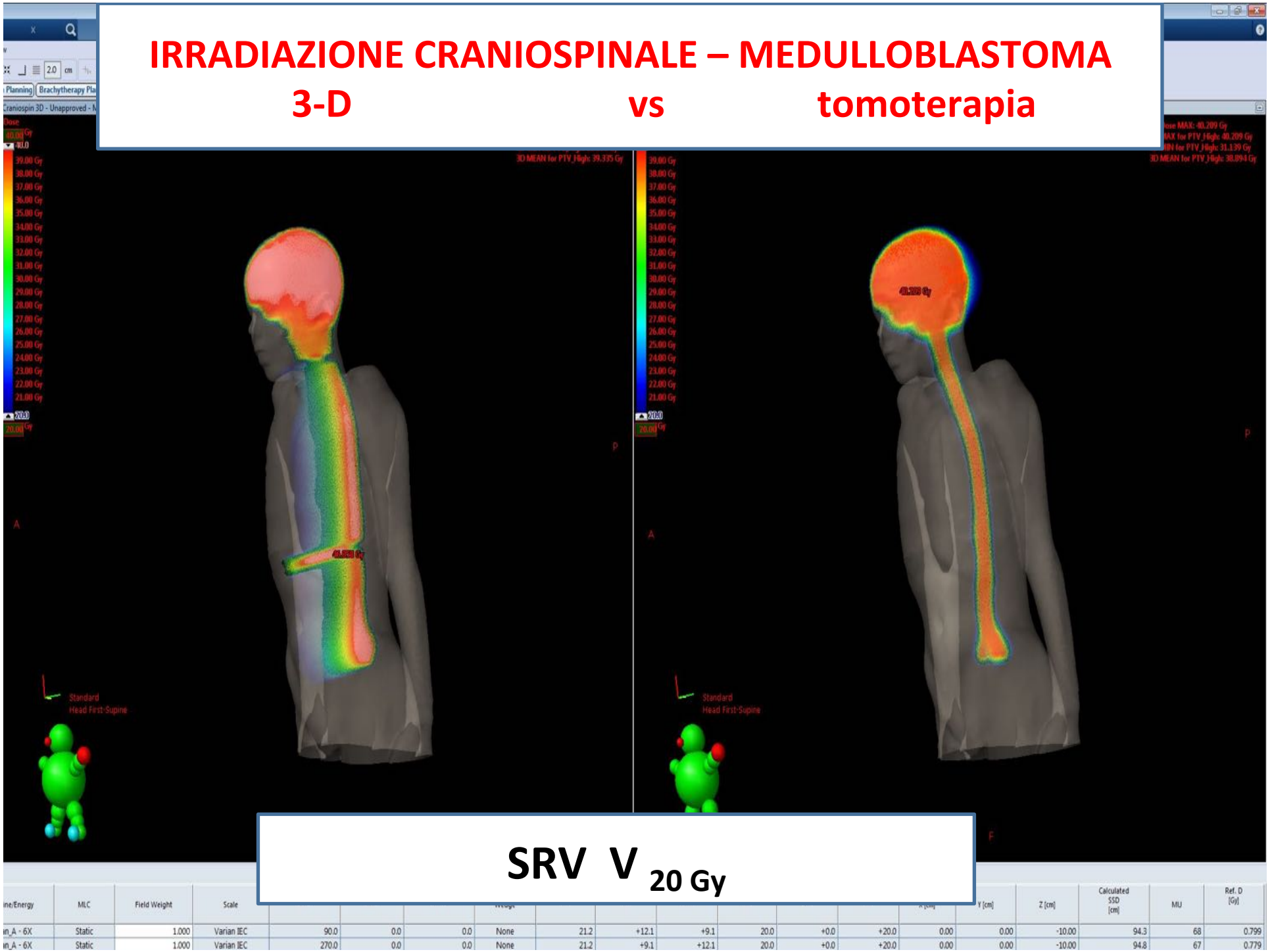
VMAT 3-D CRT



Breast Cancer- Hypofractionation 42 Gy/13 fx

IRRADIAZIONE CRANIOSPINALE – MEDULLOBLASTOMA

3-D vs tomoterapia

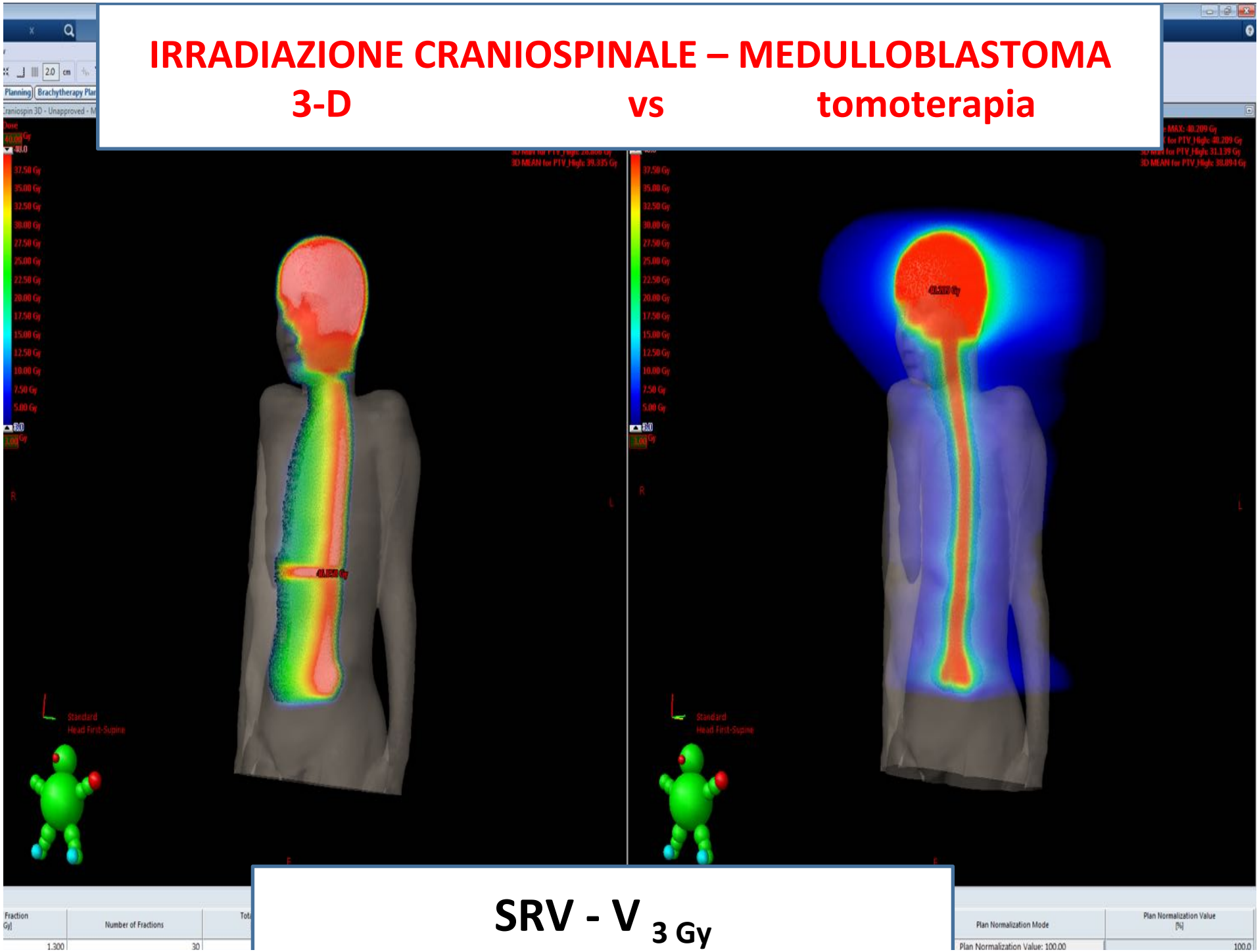


SRV $V_{20\ Gy}$

ine/Energy	MLC	Field Weight	Scale												Y [cm]	Z [cm]	Calculated SSD [cm]	MU	Ref. D [Gy]
n_A - 6X	Static	1.000	Varian IEC	90.0	0.0	0.0	None	21.2	+12.1	+9.1	20.0	+0.0	+20.0	0.00	0.00	-10.00	94.3	68	0.799
n_A - 6X	Static	1.000	Varian IEC	270.0	0.0	0.0	None	21.2	+9.1	+12.1	20.0	+0.0	+20.0	0.00	0.00	-10.00	94.8	67	0.779

IRRADIAZIONE CRANIOSPINALE – MEDULLOBLASTOMA

3-D vs tomoterapia



SRV - V $_{3\ Gy}$

SRV
dovrebbe essere studiato nei pazienti affetti da:

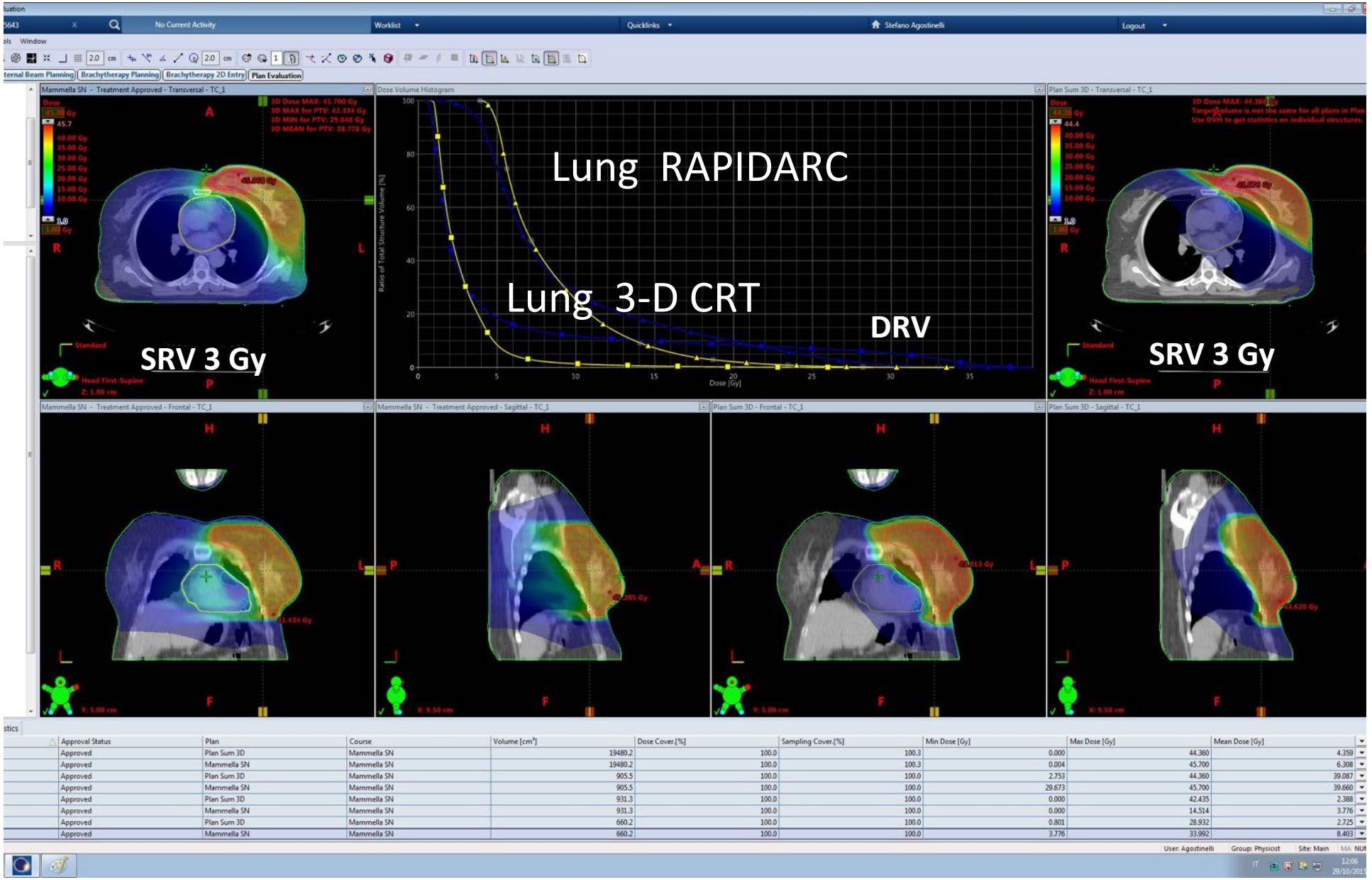
- da tumori pediatrici altamente guaribili
- da carcinoma mammario insorto prima dei 50 anni e fumatrici
- da linfoma a buona prognosi se irradiati con ampi volumi o IMRT
- da ca.prostatico se irradiati prima dei 60-65 anni
- da tumori polmonari «early» avviati a RT stereotassica

Essential tools for radiotherapy planning

- TNM staging
- Primary tumor site
- Histology
- Imaging CT/PET/MR
- Co-morbidity
- Age
- Biological markers

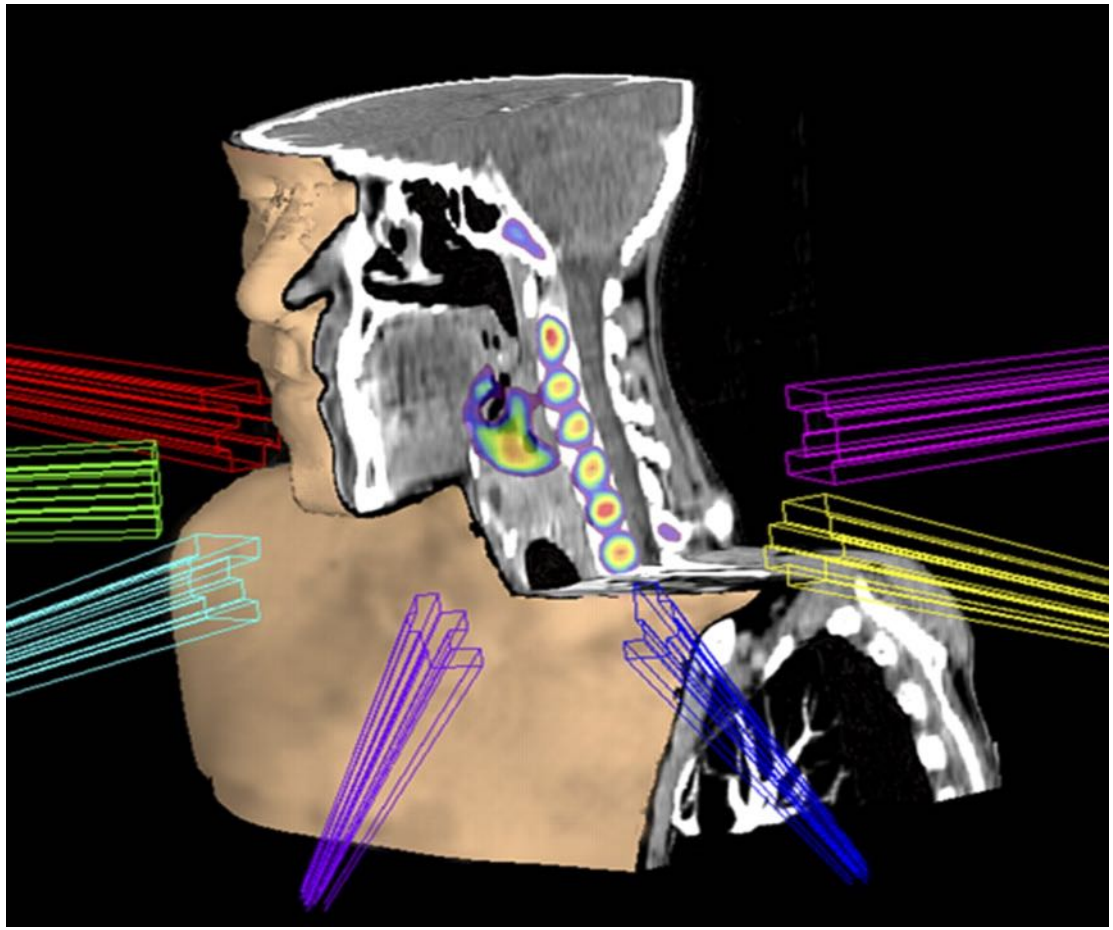
- Dose distribution
- DVH
- Dose Constraints- OARs (Quantec, 2010)
- Deterministic Risk Volume
- Stochastich Risk Volume

SRV VMAT DRV LUNG SRV 3-D RT



Approval Status	Plan	Course	Volume [cm³]	Dose Cover.[%]	Sampling Cover.[%]	Min Dose [Gy]	Max Dose [Gy]	Mean Dose [Gy]
Approved	Plan Sum 3D	Mammella SN	19480.2	100.0	100.3	0.000	44.360	4.359
Approved	Mammella SN	Mammella SN	19480.2	100.0	100.3	0.004	45.700	6.308
Approved	Plan Sum 3D	Mammella SN	905.5	100.0	100.0	2.753	44.360	39.087
Approved	Mammella SN	Mammella SN	905.5	100.0	100.0	29.673	45.700	39.660
Approved	Plan Sum 3D	Mammella SN	931.3	100.0	100.0	0.000	42.435	2.388
Approved	Mammella SN	Mammella SN	931.3	100.0	100.0	0.000	14.514	3.776
Approved	Plan Sum 3D	Mammella SN	660.2	100.0	100.0	0.801	28.932	2.725
Approved	Mammella SN	Mammella SN	660.2	100.0	100.0	3.776	33.992	8.403

grazie per l’attenzione



Visualization of risk of radiogenic second cancer in the organs and tissues of the human body

Zhang R et al, Radiat Oncol, 10: 107 , 2015

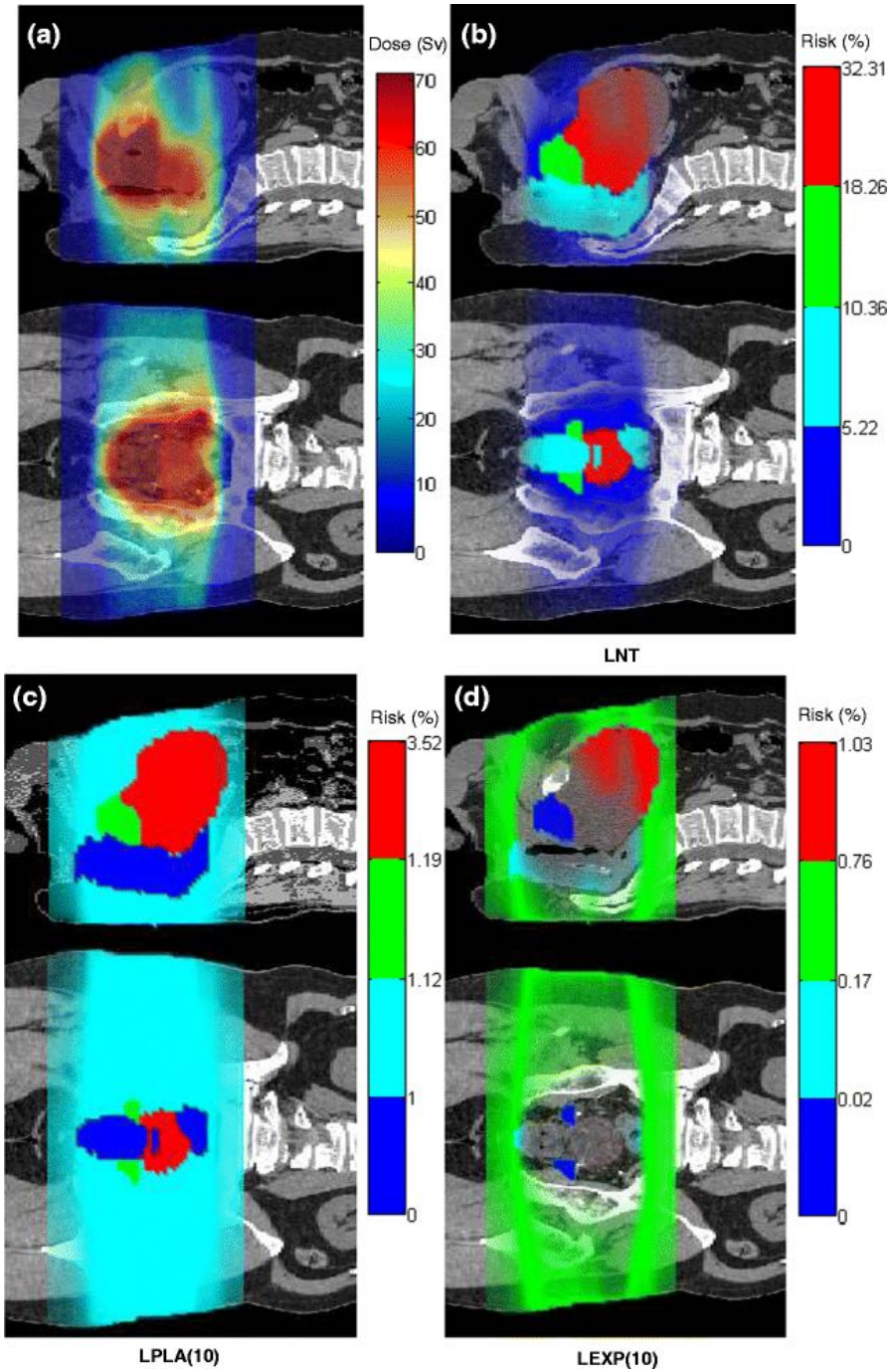
67-year old man with prostate cancer treated with photon VMAT

Lifetime risks of incidence of second cancer according to different dose-risk relationships:

LNT

LPLA (10 Sv)

LEXP (10 Sv)



Visualization of risk of radiogenic second cancer in the organs and tissues of the human body

Zhang R et al, Radiat Oncol, 10: 107 , 2015

13-year old girl with medulloblastoma treated with proton craniospinal Irradiation

Lifetime risks of incidence of second cancer according to different dose-risk relationships:

LNT
LPLA (10 Sv)
LEXP (10 Sv)