Radioterapia con fraccionamiento espacial (SFRT): cómo y cuándo aplicar Lattice, PATHY y Core Boost

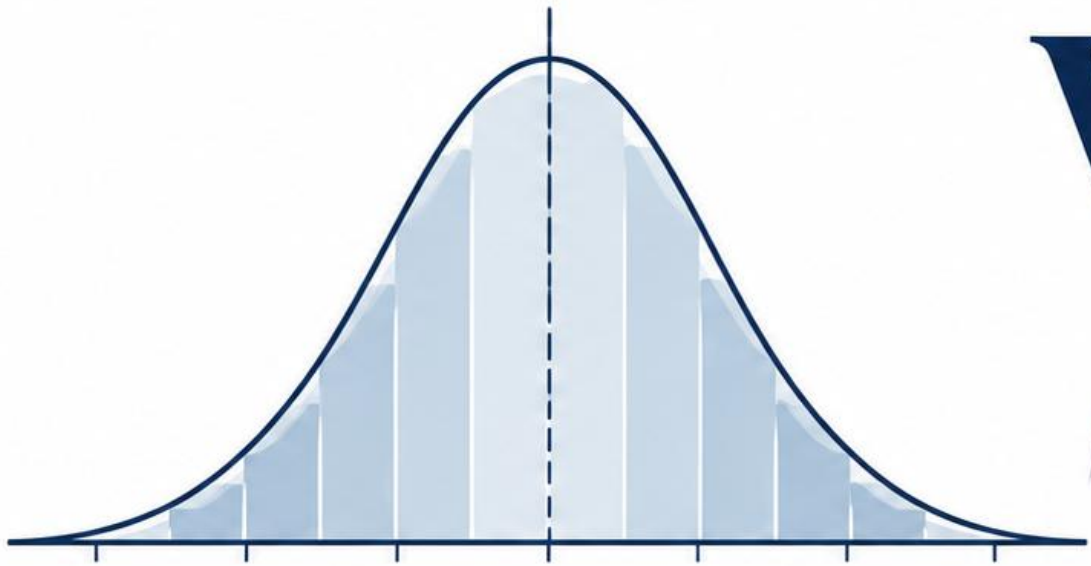
Santiago Velázquez



Declaración sobre el uso de IA:
La inteligencia artificial no se ha utilizado para generar, seleccionar ni definir contenidos. Su uso se ha limitado exclusivamente a la mejora de recursos gráficos e imágenes

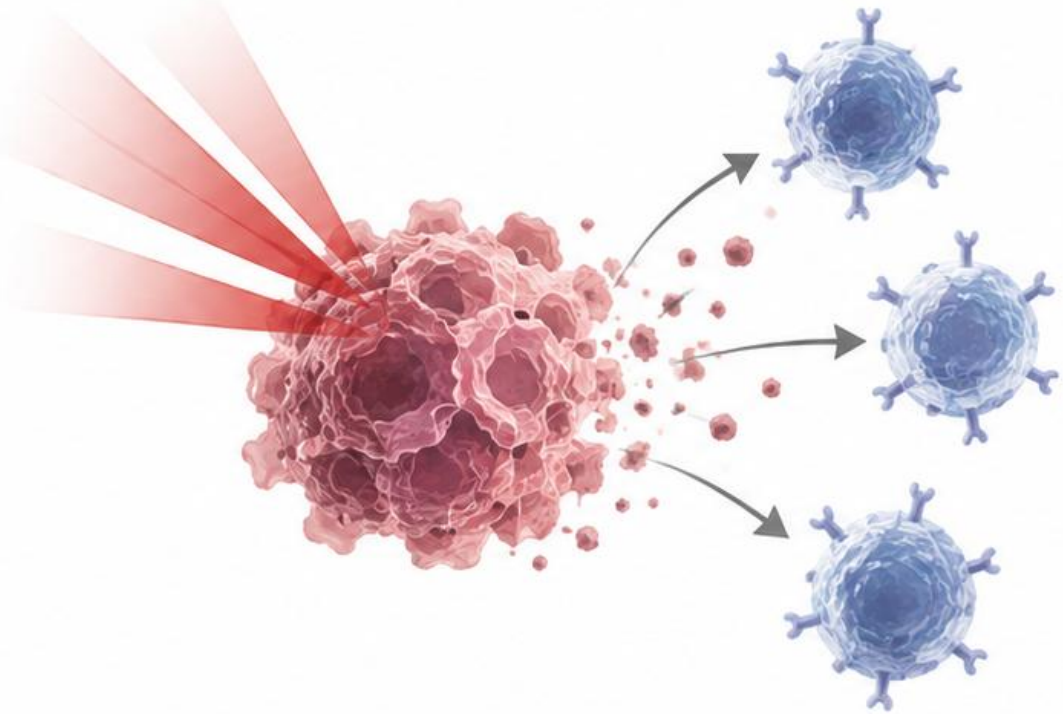


RT binomial



VS

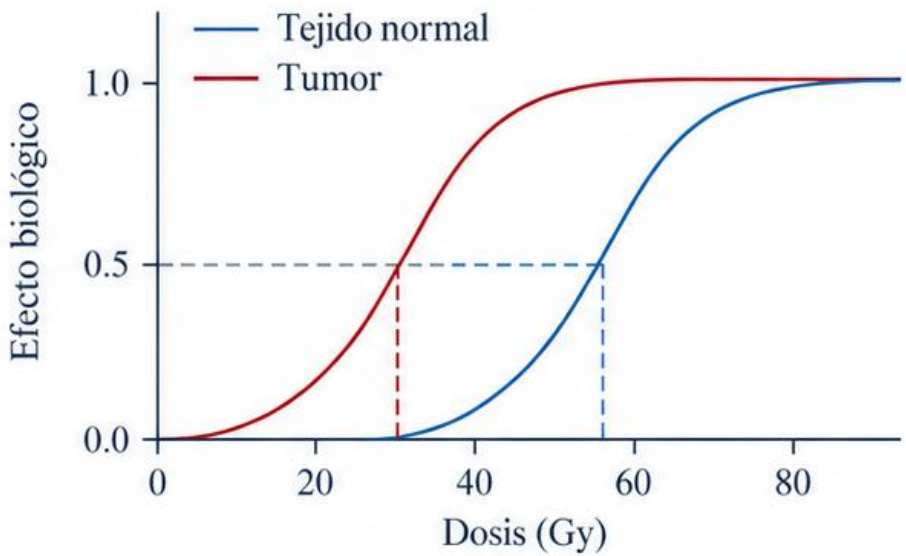
Radio-inmunoestimulación



Modelo LQ

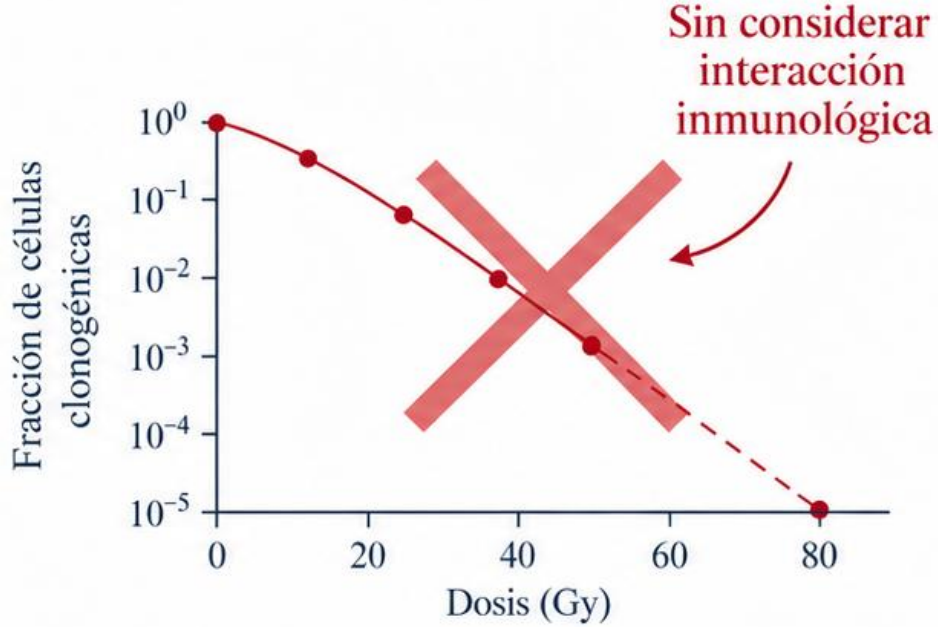
Útil para limitar toxicidad

Insuficiente para definir control tumoral



Toxicidad

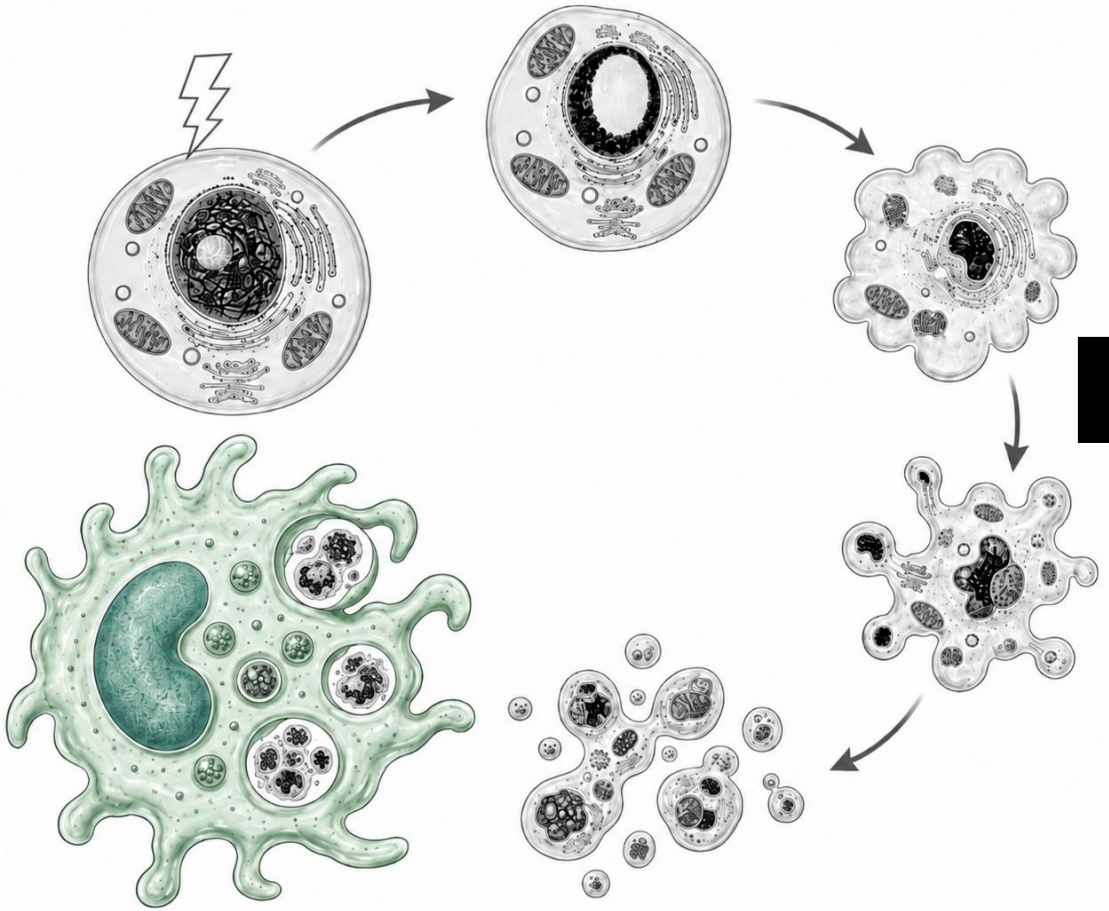
$$S = e^{-(\alpha D + \beta D^2)}$$



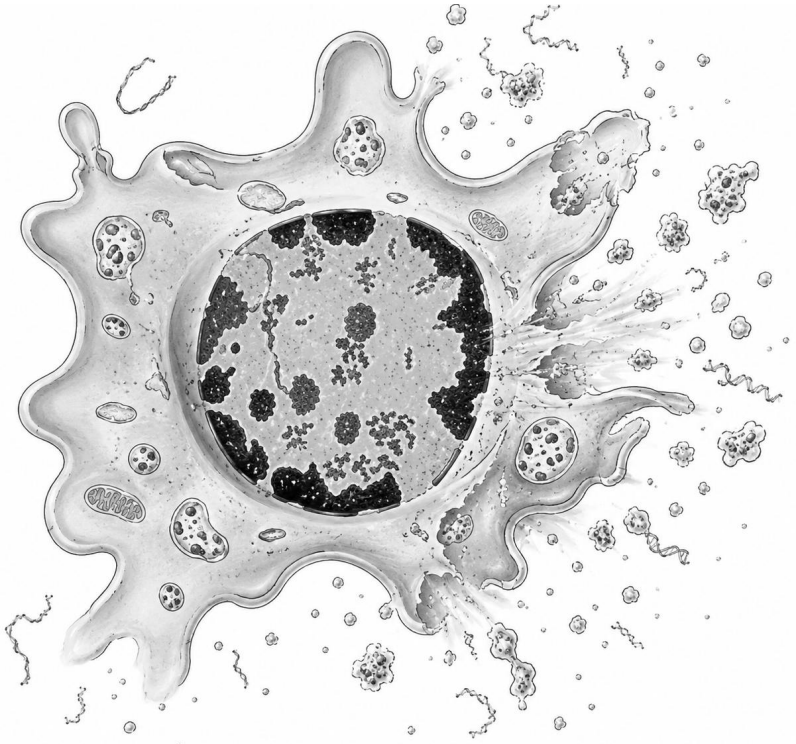
Control tumoral

La seguridad no equivale al control tumoral

TESIS DOCTORAL



La RT induce mayoritariamente apoptosis (p53 funcional), catástrofe mitótica (alta proliferación), autofagia (hipoxia) y senescencia.
- CHEN, H., et al. Radiotherapy modulates tumor cell fate decisions: A review. Radiation Oncology. 2022, vol. 16, no. 6, p. 946..



La SABR-SFRT induce mayoritariamente Necrosis.
- Garcia-Barros M, Paris F, Cordon-Cardo C, Lyden D, Rafii S, Haimovitz-Friedman A, et al.
Tumor response to radiotherapy regulated by endothelial cell apoptosis. *Science*. 2003 Aug 15;300(5622):1155–9.
- Dutta PR, Siva S, Chu W, Chander S, Pham D, Lau E, et al. Stereotactic Body Radiation Therapy (SBRT) for Renal Cell Carcinoma: A Review. *Cancers (Basel)*. 2024 Mar;16(6):946.

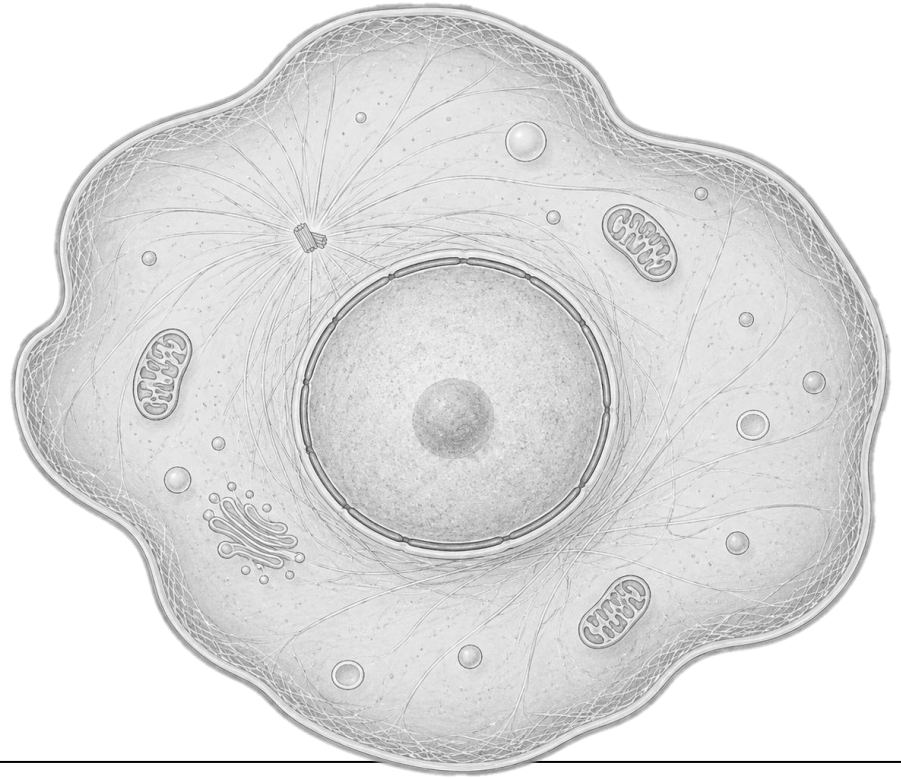


1. Citoquinas proinflamatorias
2. Presentación de antígenos
3. Citoquinas apoptóticas

BERNSTEIN, Michael B., et al. Immunotherapy and stereotactic ablative radiotherapy (ISABR): a curative approach? *Nature reviews Clinical oncology*, 2016 vol. 13, no 8, p. 516-524.
WANG, Xuehuan, et al. Reframing the Paradigm: SBRT as an Engineer of the Tumor Immune Microenvironment vol. 17, p. 1754669.*Frontiers in Immunology*, 31 March 2026

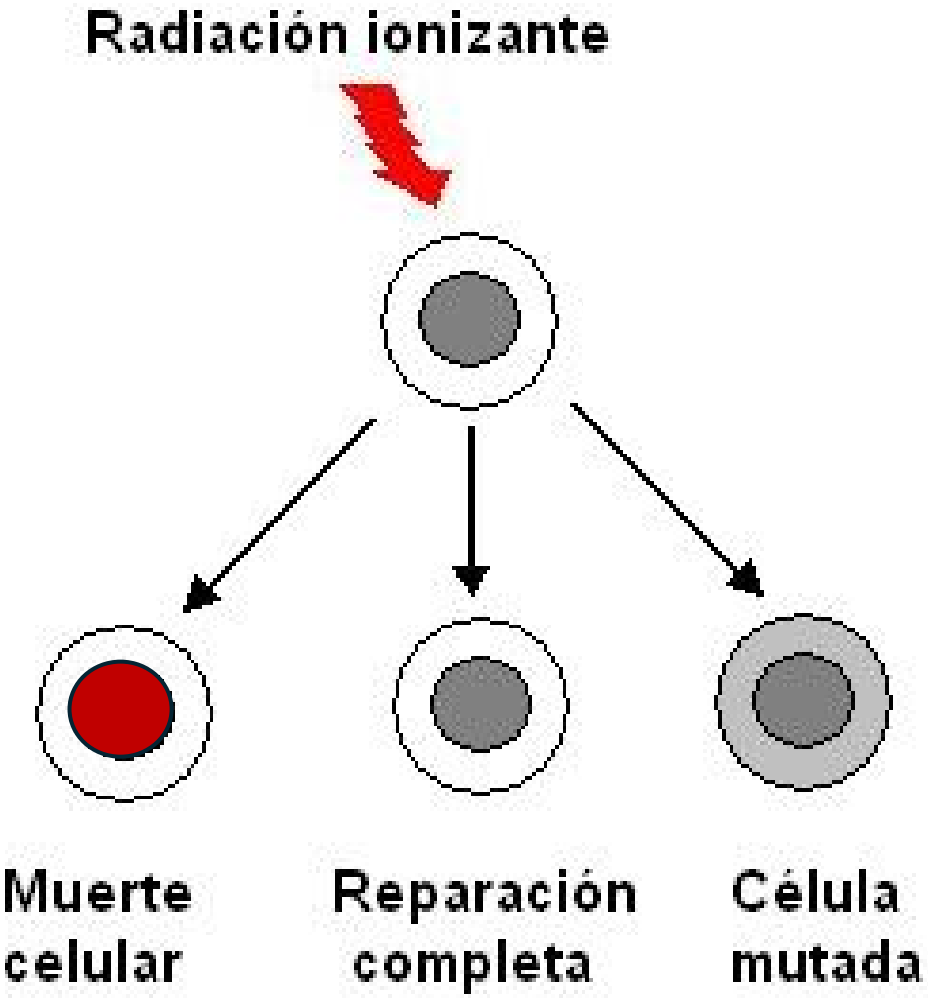
TESIS DOCTORAL

d>> y t<< ➡ ↑ Hydrólisis ➡ Estrés oxidativo





FORMENTI, DEMARIA
Radiation Therapy to Convert de Tumor into a in situ Vaccine.
International Journal of Radiation Oncology, Biology, Physics 84: 879-880 , 2012



CHEN, Xinyi, et al. Molecular mechanisms underlying the abscopal effect induced by radiotherapy and its synergistic translational potential with immunotherapy *Therapeutic Advances in Medical Oncology*, 2025, vol. 17, p. 17588359251387534.

SABR:

d>12Gy

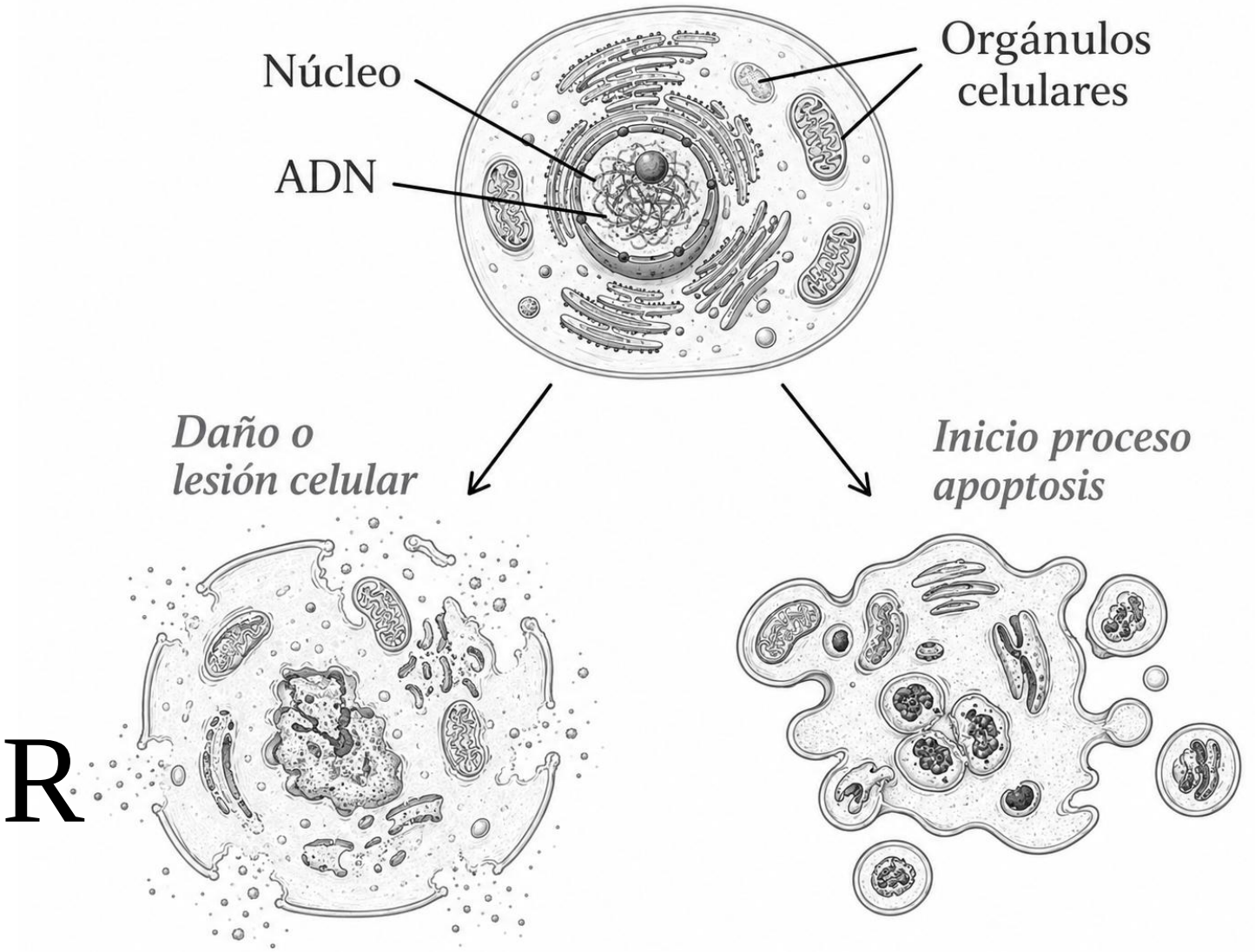
t< 6 min

BED_{10}>100Gy

Robustness-t-Complexity

t≠Beam-on time
t=Elapsed Tx time

Elkin 1960
Belli 1966
Ang 1987
Hall 1991
Benedict 1997
Garcia-Barros 2003
Fowler 2004
Dieterich S 2006
Murphy 2007
Ling 2010
Stieb 2015
Santiago 2016
Saberi 2017
Tabrizi 2018
Hirai 2021
Lucchini R 2023
Li F 2025


Núcleo
ADN
Orgánulos celulares
Daño o lesión celular
Inicio proceso apoptosis

SABR RT






60
5
10
15
20
25
30
35
40
45
50
55

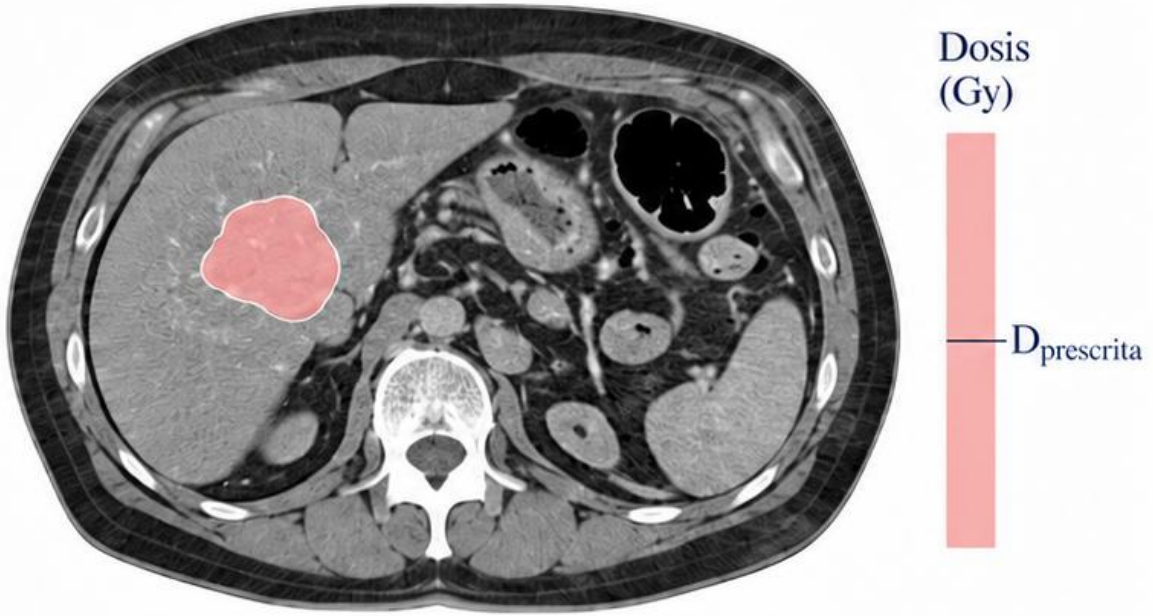
¿Qué papel tiene el gradiente de dosis?

ΔTCP · Beatriz Sánchez-Nieto

Sánchez-Nieto B, Nahum AE. The delta-TCP concept. IJROBP 1999;44;369–380.

ICRU 50 (1992)

Homogeneidad del PTV



Estandarización clínica

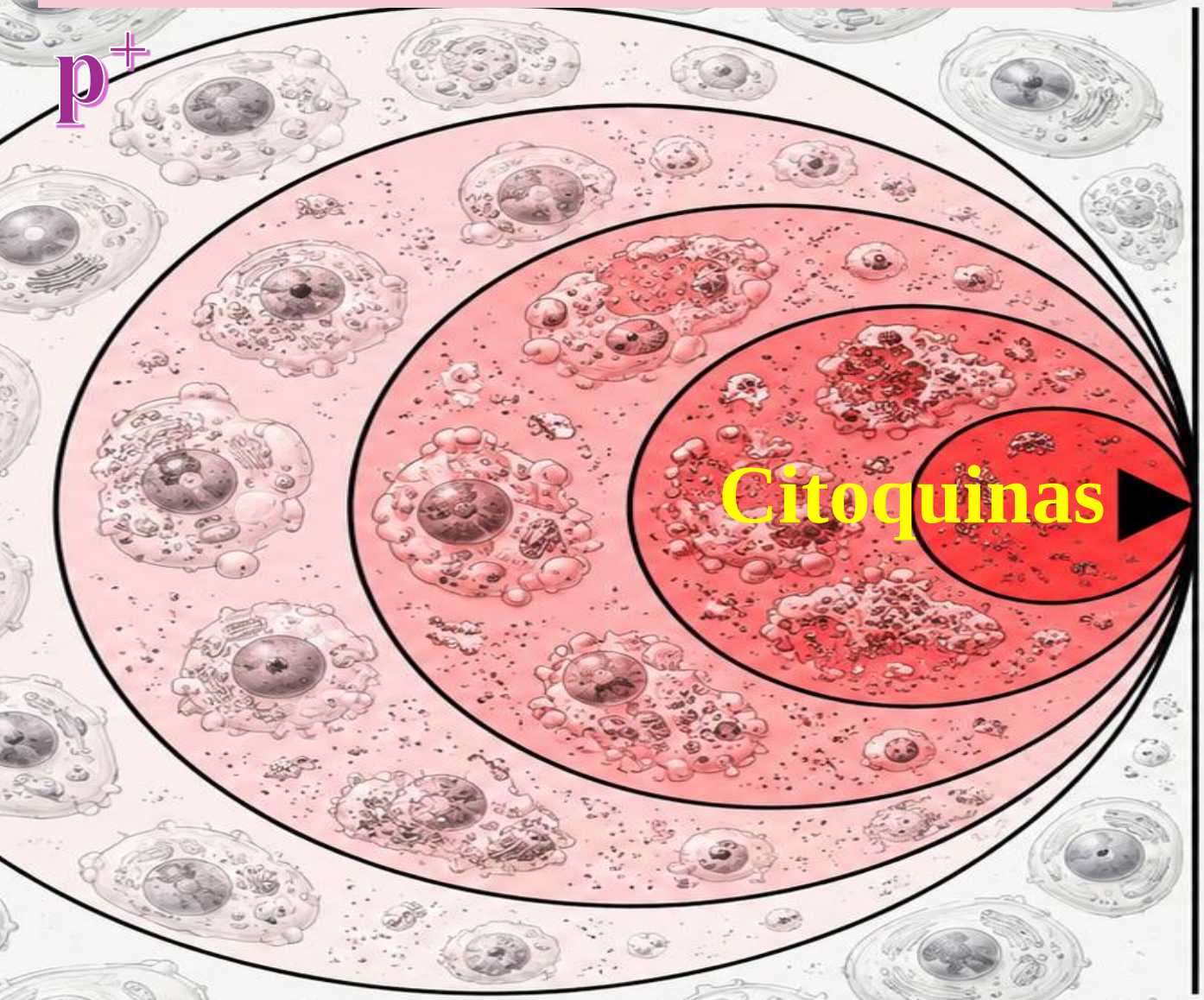
ΔTCP

Control tumoral ≠ uniformidad ciega



Distribución biológicamente optimizada

La homogeneidad facilita comparar resultados;
no define por sí sola la mejor distribución intratumoral.



Distancia paracrina

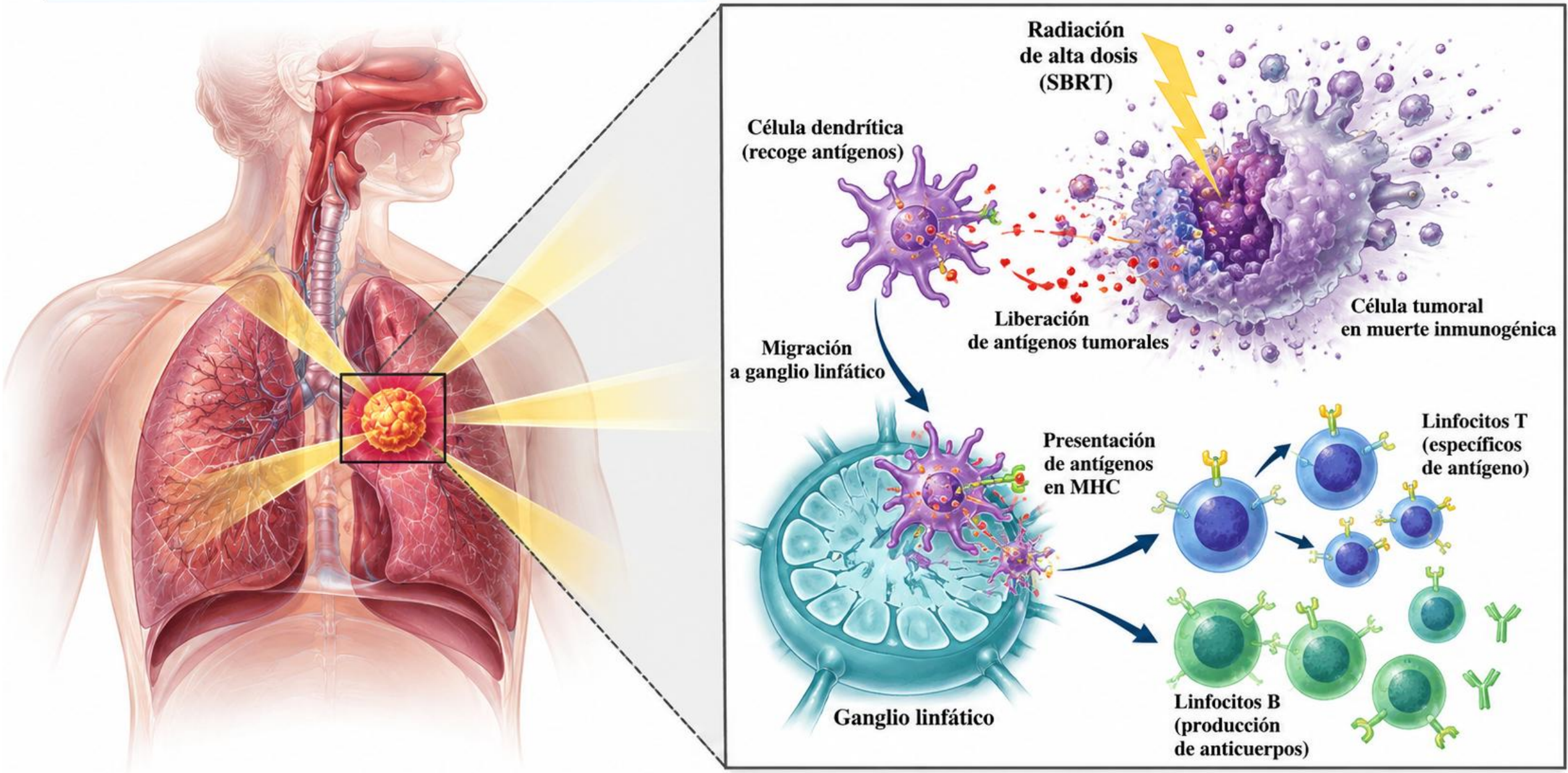
0Gy

CASCADA Citoquinas

TUBIN, Slavisa, et al. Shifting the immune-suppressive to predominant immune-stimulatory radiation effects by SBRT-PArtial tumor irradiation targeting HYpoxic segment Cancers, 2020, vol. 13, no 1, p. 50.

AMENDOLA, Beatriz E., et al. Safety and efficacy of lattice radiotherapy in voluminous non-small cell lung cancer. *Cureus*, 2019, vol. 11, no 3.

EFECTO VACUNA DE LA SBRT



Abscopal effects of radiation therapy: A clinical review for the radiobiologist

Shankar Siva [a,b,*], Michael P. MacManus [a,b], Roger F. Martin [b,c], Olga A. Martin [a,b,c,*]

[a] Division of Radiation Oncology and Cancer Imaging, Peter MacCallum Cancer Centre, Melbourne, VIC, Australia
[b] Sir Peter MacCallum Department of Oncology, The University of Melbourne, Melbourne, VIC, Australia
[c] Molecular Radiation Biology Laboratory, Research Division, Peter MacCallum Cancer Centre, The University of Melbourne, VIC, Australia

. As lymphocytes are exquisitely sensitive to irradiation, repetitive daily delivery of cytotoxic doses of radiation can deplete migrating immune effector cells. However, work from our institution identified that single dose (12 Gy) radiotherapy did not deplete established tumors of effector cells ($CD8^+$ T, $CD4^+$ T and NK cells) critical to the curative activity of radiotherapy when used in combination with immuno-therapy.

CV

CV

CV

THE LANCET Oncology

Volume 6, Issue 7, July 2005, Pages 520–528



Review

New insights on cell death from radiation exposure

Dr Kevin M Prise, PhD[a], , , Giuseppe Schettino, Kathryn D Held, PhD[b]

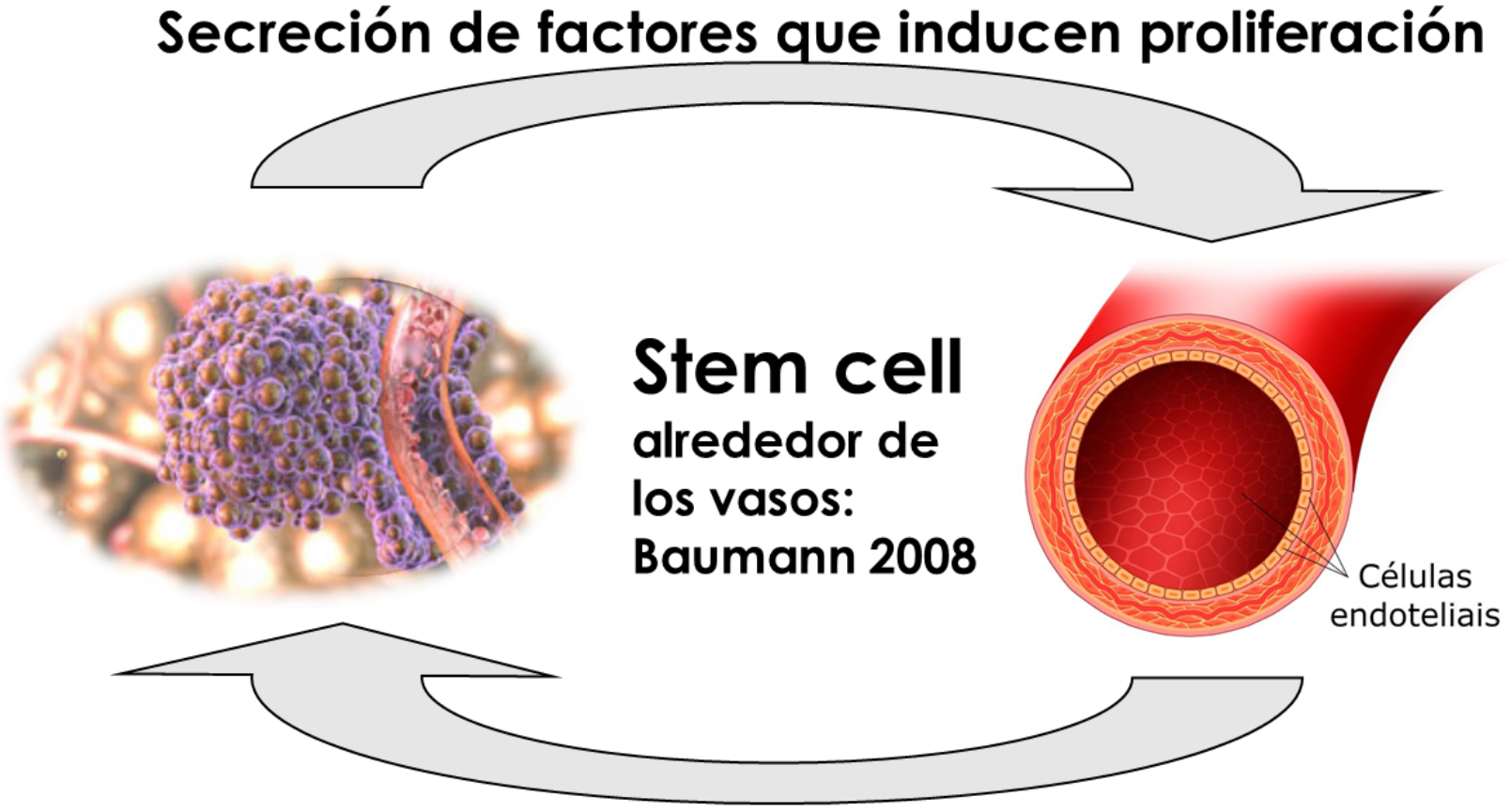
Even over 12 Gy, in a **short time** administration, an "eat-me" signal that is thought to be required for dendritic cell recognition and engulfment of dying tumor cells



Vascular endothelial injury

11 Gy

TESIS DOCTORAL



Garcia-Barros M, Friedman A, et al. Tumor response to radiotherapy regulated by endothelia cell apoptosis.
Science. (2003) 300:1155–9. doi: 10.1126/science.1082504

Park HJ.Radiation-induced vascular damage in tumors: implications of vascular damage in ablative hypofractionated radiotherapy (SBRT and SRS). Radiat Res. (2012) 177:311–27. doi: 10.1667/RR2773.1

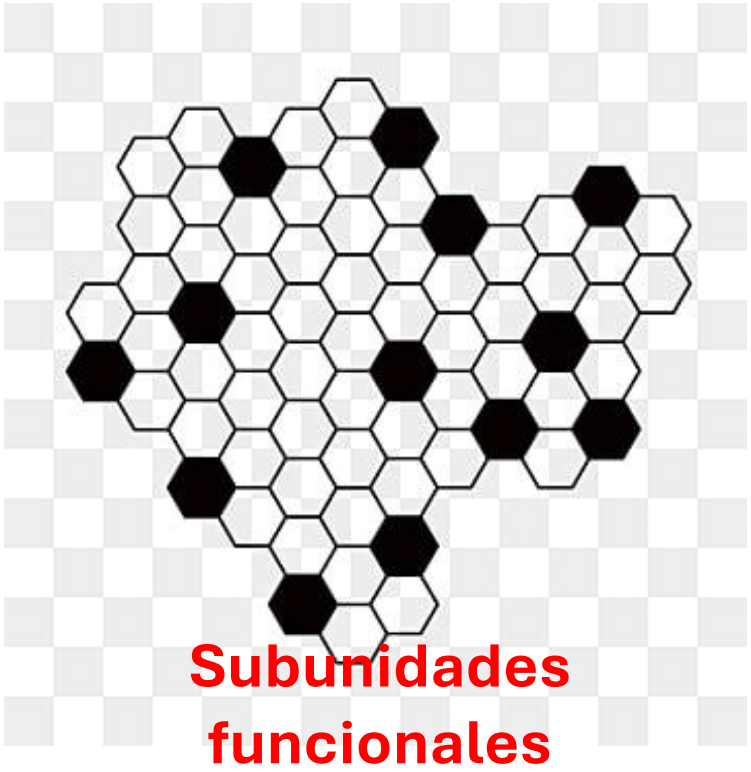
Song C et al. Real-time tumor oxygenation changes after single high-dose radiation therapy in orthotopic and subcutaneous lung cancer in mice: clinical implication for stereotactic ablative radiation therapy schedule optimization.
Int J Radiat Oncol Biol Phys. (2016) 95:1022–31. doi: 10.1016/j.ijrobp.2016. 01.064

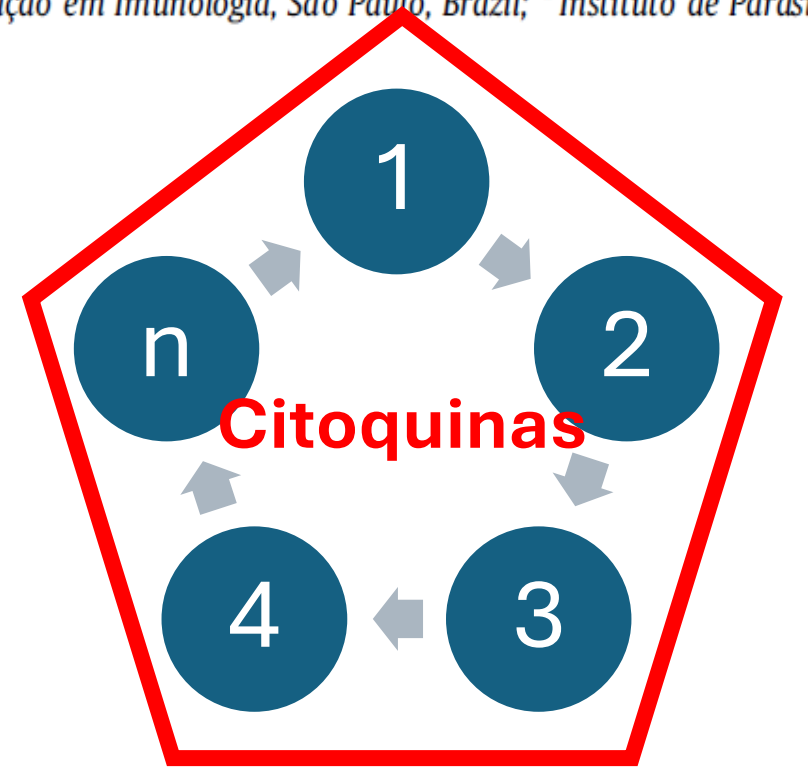
The importance of bystander effects in radiation therapy in melanoma skin-cancer cells and umbilical-cord stromal stem cells

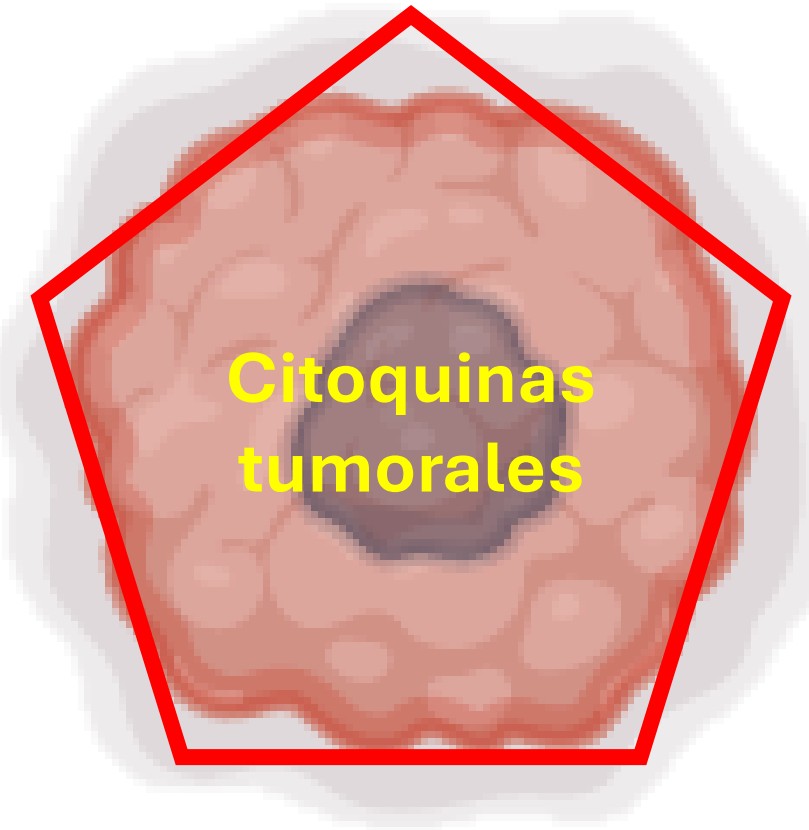


Jaime Gómez-Millán [b,1], Iana Suly Santos Katz [c,1], Virgínea de Araujo Farias [a], Jose-Luis Linares-Jesús López-Peñalver [a], Gustavo Ortiz-Ferrón [a], Carmen Ruiz-Ruiz [a], Francisco Javier Oliver [d], José Mariano Ruiz de Almodóvar [a,e,*]

[a] *Instituto de Biopatología y Medicina Regenerativa, Universidad de Granada, Spain;* [b] *Hospital Universitario Virgen de la Victoria, Unidad de Gestión Clínica de Oncología, Málaga, Spain;* [c] *Instituto Butantan, Centro de Pesquisa e Formação em Imunologia, São Paulo, Brazil;* [d] *Instituto de Parasitología y Biomedicina López-Neyra; and* [e] *Hospital Universitario San Cecilio, Granada, Spain*





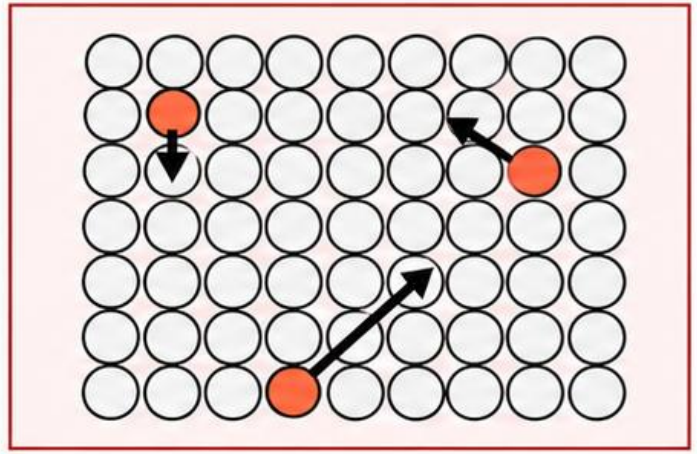


Bystander

Se establece a través de comunicaciones **PARACRINAS**

De célula irradiada a célula NO irradiada

Blyth BJ, Sykes PJ. Radiation-induced bystander effects: what are they, and how relevant are they to human radiation exposures? *Radiation Research.* 2011;176(2):139–157.

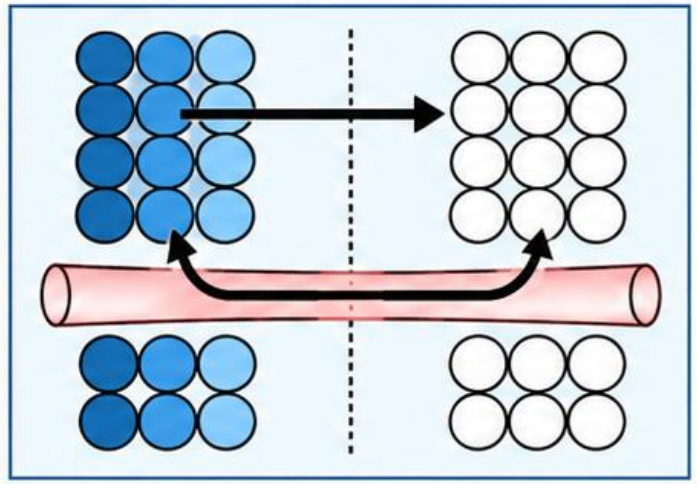


Abscopal

Se establece a través de comunicaciones **"ENDOCRINAS"**

De tejido irradiado a tejido NO irradiado

Demaria S. Ionizing radiation inhibition of distant untreated tumors (abscopal effect) is immune mediated. *International Journal of Radiation Oncology Biology Physics.* 2004;58(3):862–870.

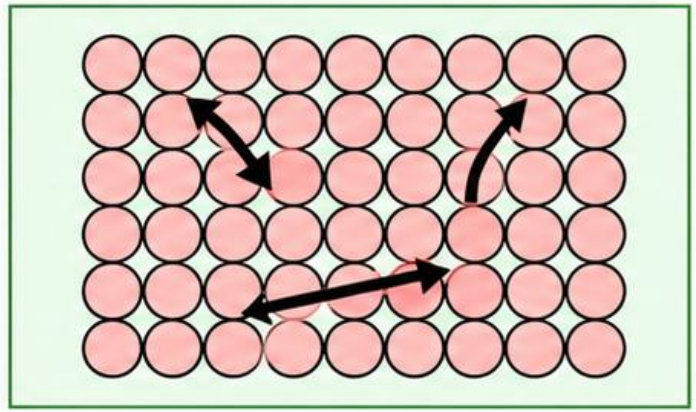


Cohortes

Se establece a través de comunicaciones **YUXTACRINAS**

De "célula irradiada" a "célula irradiada"

Blyth BJ, Sykes PJ. *Radiation Research.* 2011;176(2):139–157.







Immunosuppressive therapies!

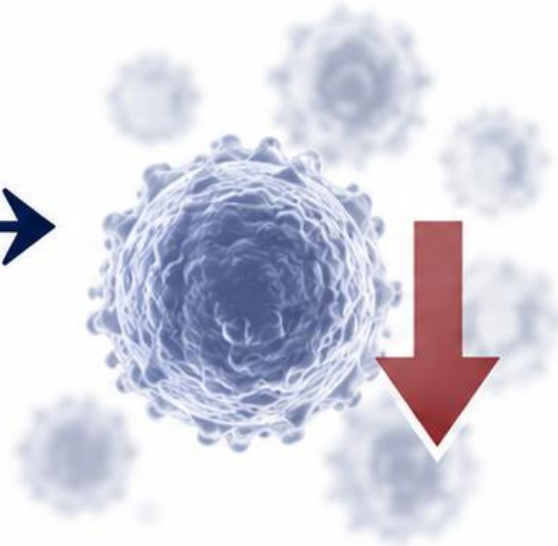
Inmunodepresores sistémicos



Corticoides

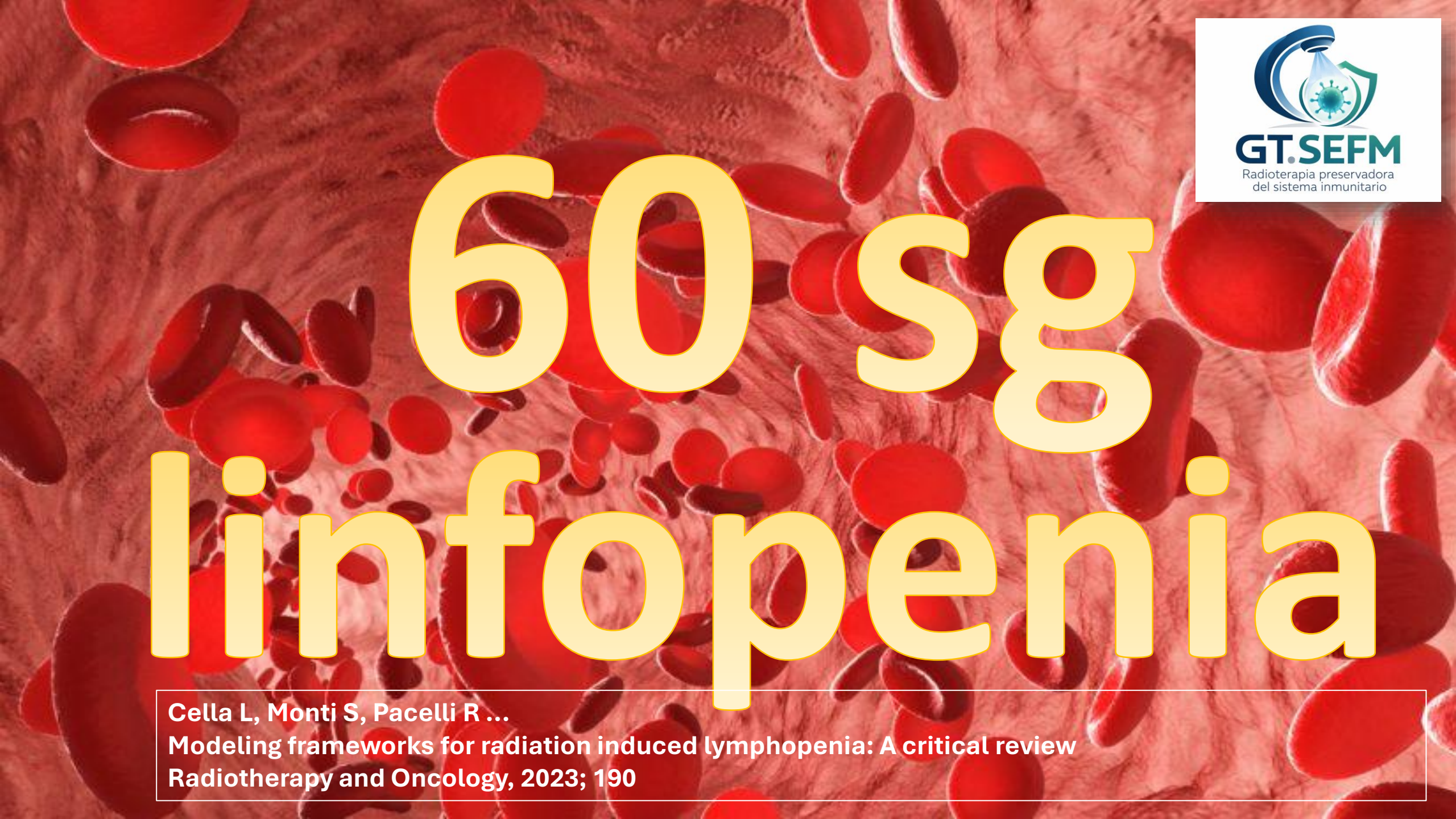


Quimioterapia



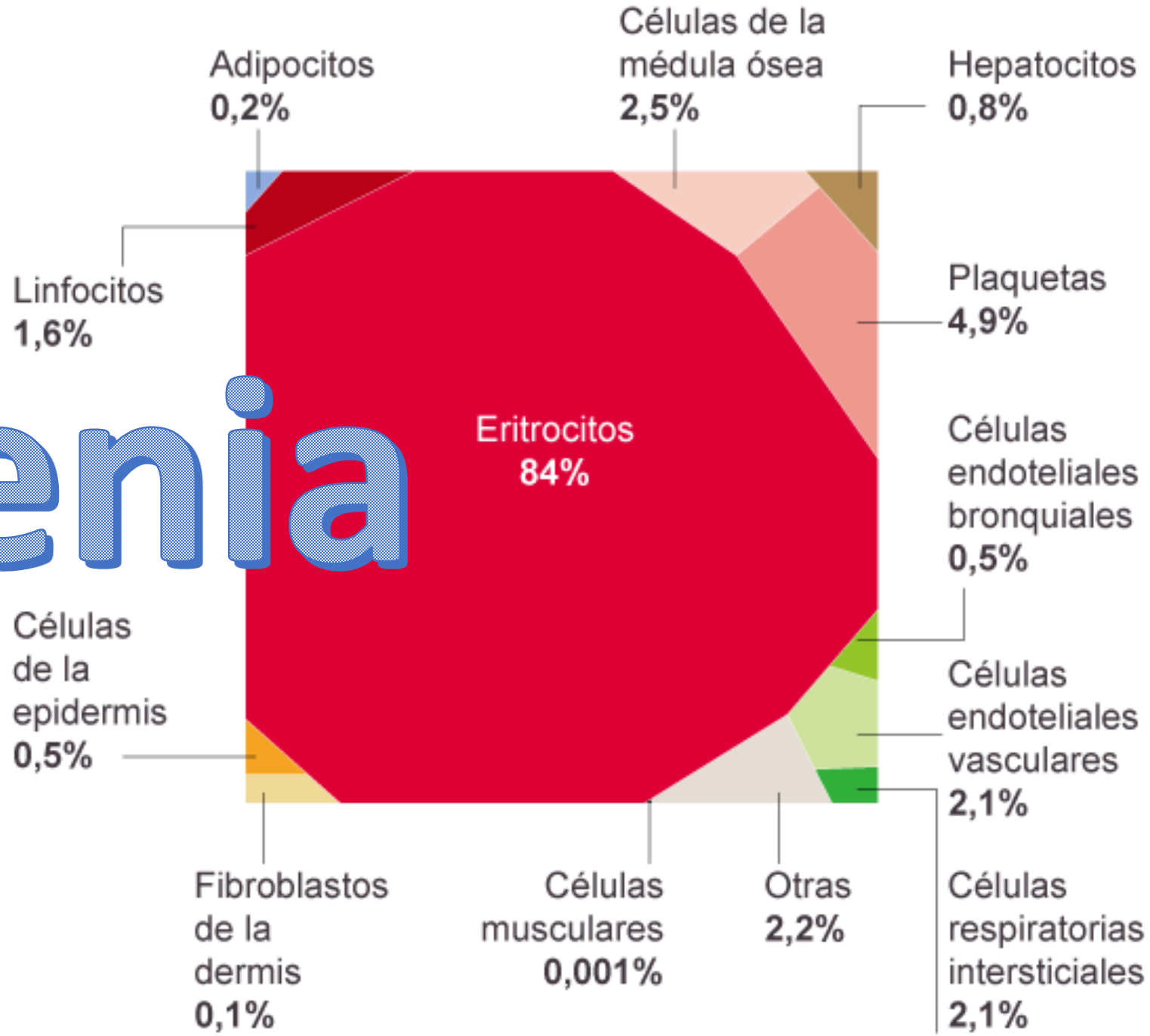
↓ respuesta inmune

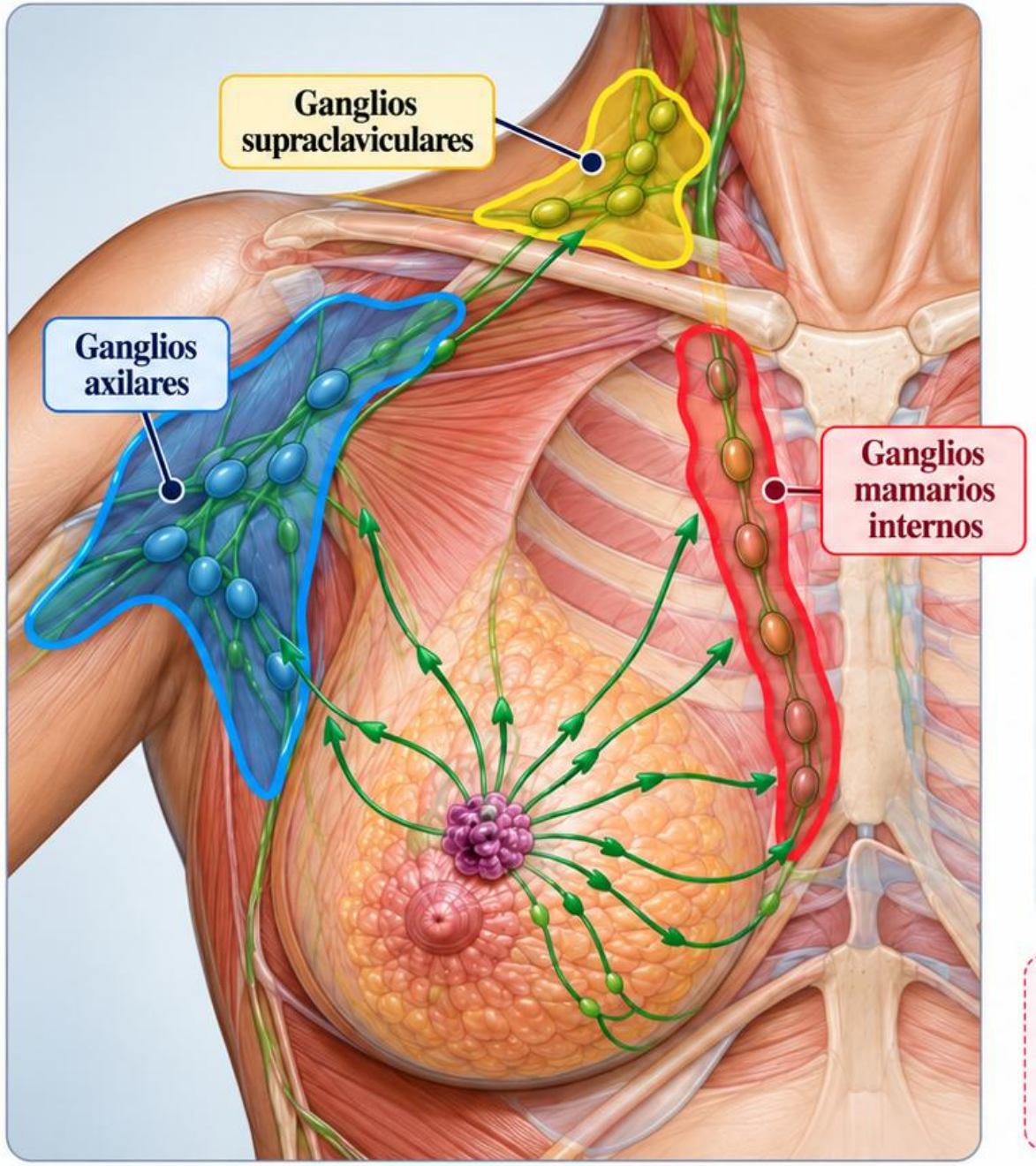
↓ linfocitos



Cella L, Monti S, Pacelli R ...
Modeling frameworks for radiation induced lymphopenia: A critical review
Radiotherapy and Oncology, 2023; 190

Astenia


Adipocitos
0,2%
Células de la médula ósea
2,5%
Hepatocitos
0,8%
Linfocitos
1,6%
Plaquetas
4,9%
Eritrocitos
84%
Células endoteliales bronquiales
0,5%
Células de la epidermis
0,5%
Células endoteliales vasculares
2,1%
Fibroblastos de la dermis
0,1%
Células musculares
0,001%
Otras
2,2%
Células respiratorias intersticiales
2,1%



VanguaRT-26

Irradiación nodal selectiva

¿inmunodepresión?

1. Los ganglios de drenaje tumoral son **órganos inmunológicos clave.**
2. La irradiación nodal electiva puede reducir **presentación antigénica, primado de linfocitos T y aumentar la linfopenia.**
3. En la era de la inmunoterapia, su indicación merece **reevaluación individualizada.**

Tratado en VanguaRT26

- **Ángela Matías Pérez:** ganglios de drenaje tumoral e inmunidad.
- **David Vicente Baz:** integración de terapias sistémicas con radioterapia.

¿Qué condiciona el efecto sistémico de la SABR/SFRT?

1 **Tiempo de irradiación**
1ª UM → última UM

2 **Tamaño de la dosis**

3 **Gradiente de dosis**
interno y externo

4 **Estado inmunológico**

5 **Complejidad del plan**

6 **Cascada mecanística**

↓ ITV + ↓ PTV + ↓ fluencia → ↓ tiempo de irradiación → ↓ linfopenia | ↓ interplay

7 **Decisiones técnicas**

Forward | FFF | tasa máxima | partícula | sobreescritura de densidad

- Galluzzi L. et al. *Nat Rev Clin Oncol.* 2023;20:543–557.
- Jenkins SV et al. *Semin Radiat Oncol.* 2024;34:284–291.

III ROTACIÓN
ONCOLOGÍA RADIOTERÁPICA

SEOR
SOCIEDAD ESPAÑOLA DE ONCOLOGÍA RADIOTERÁPICA

Before, the systemic effects seen in studies were less than 1%. But recently, we've seen more case reports. While SABR is great for local control and disease-free time, even stage IV cases were included.



¿Por qué algunos hospitales todavía están en porcentajes tan bajos?



Factores de planificación y selección que favorecen la inmunodepresión asociada a RT-QT

01

Terapias inmunodepresoras previas o simultáneas

QT · RT-INS · corticoides



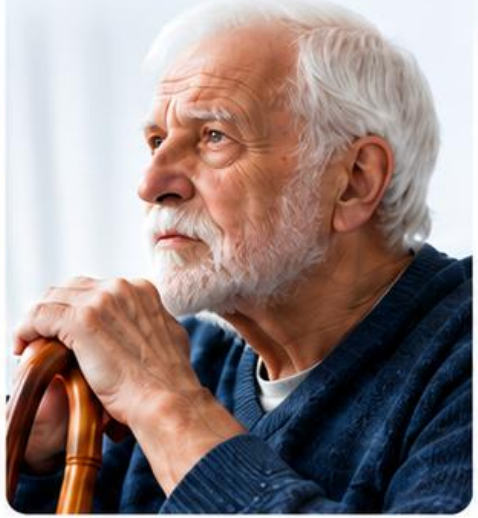
02

Dosis por fracción insuficientes



03

Selección de pacientes añosos



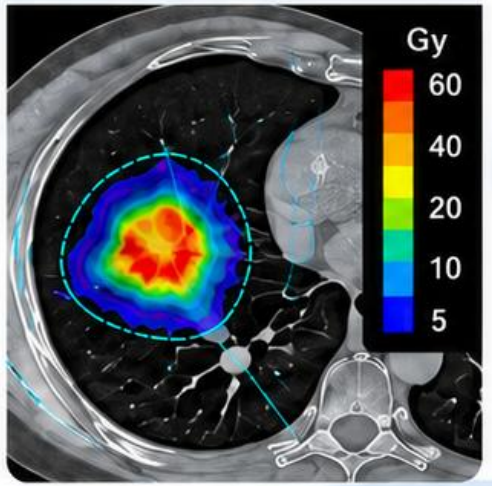
04

Tiempos prolongados de irradiación



05

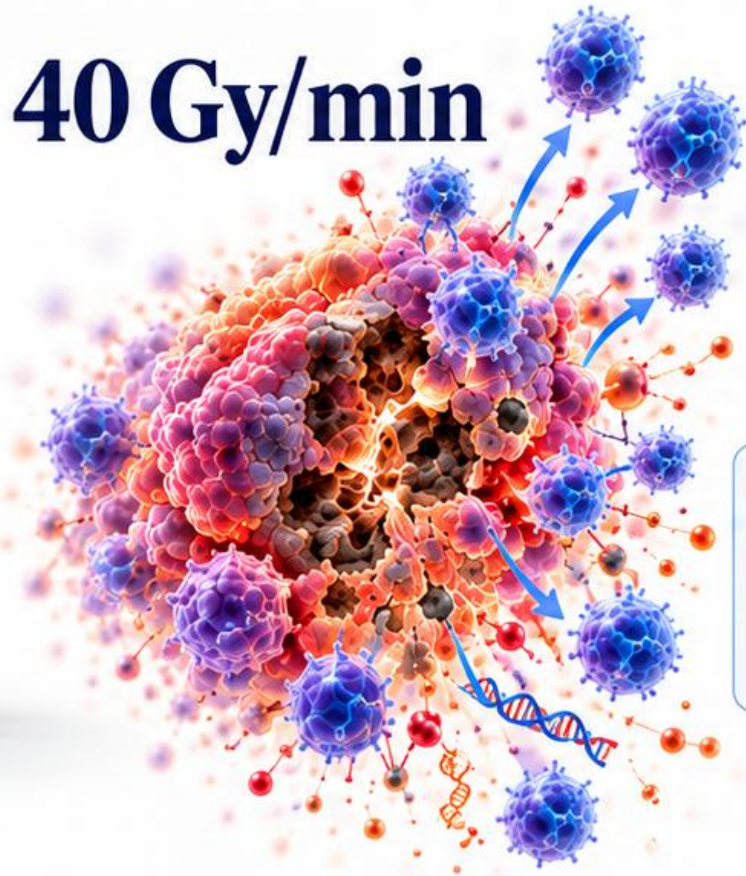
Grandes gradientes de dosis (dentro y fuera del PTV)



ACCELA: VELOCIDAD Y POTENCIAL INMUNOESTIMULADOR



40 Gy/min



↓ Elapsed Tx time
40 Gy/min · hojas 6,5 cm/s · gantry 2,5 rpm

1 ↑ rotura de membrana y necrosis directa

2 ↓ linfopenia radioinducida

3 ↑ estrés oxidativo

ROS

A. ↑ detritus ADN / ARN tumoral → antígenos

B. ↑ citoquinas proinflamatorias → infiltración linfocítica

↑ mensajería apoptótica entre células tumorales

↑ NTE

Hipótesis inmunobiológica relevante

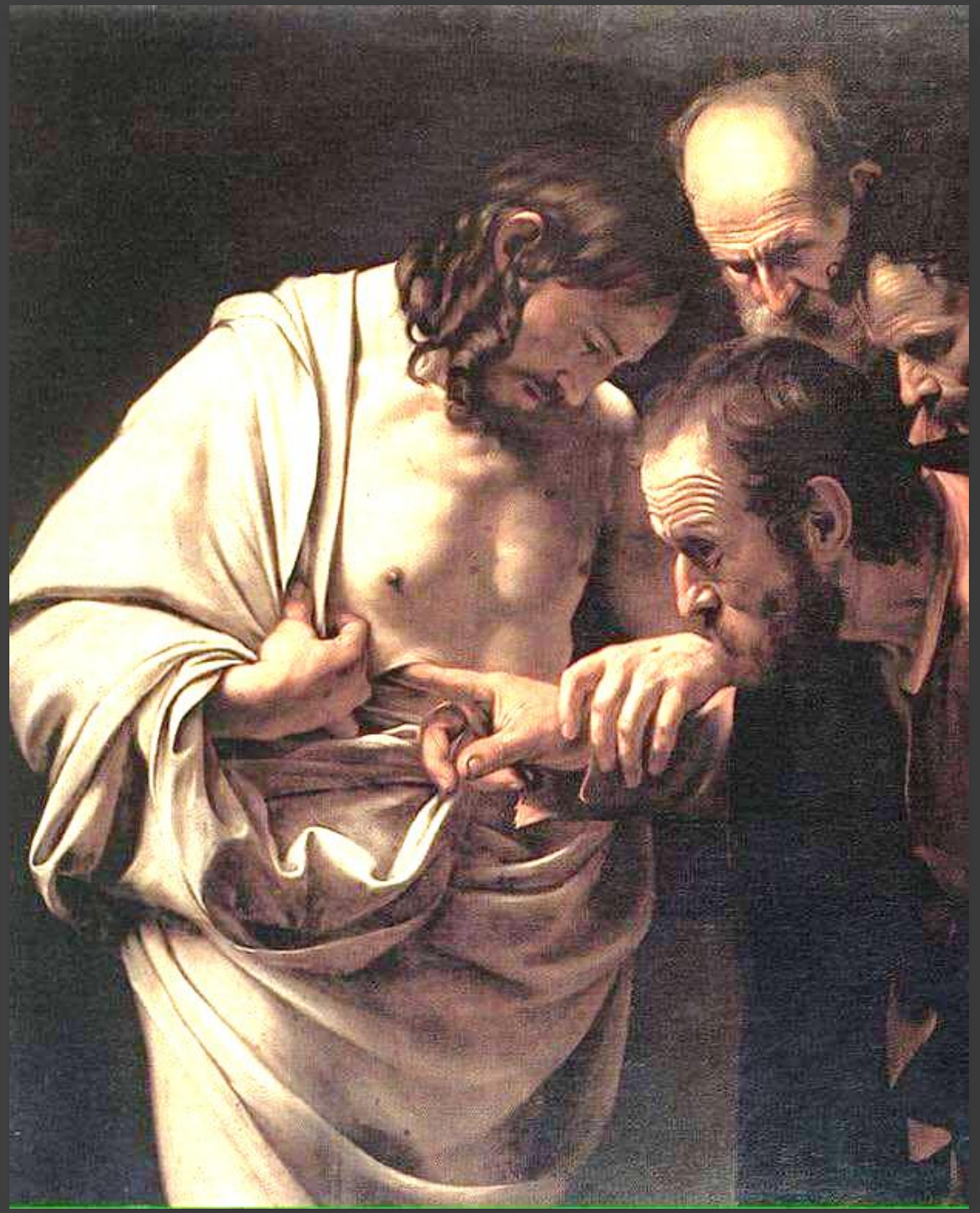
III ROTACIÓN
ONCOLOGÍA RADIOTERÁPICA

SEOR
SOCIEDAD ESPAÑOLA DE ONCOLOGÍA RADIOTERÁPICA

La disciplina que estudia la combinación adecuada de **inmunoterapia** y **SABR** se denomina



La inmunoterapia junto a SABR no solo **potencia el efecto sistémico deseado**, sino que también puede ayudar a **compensar prácticas menos óptimas** con SABR.

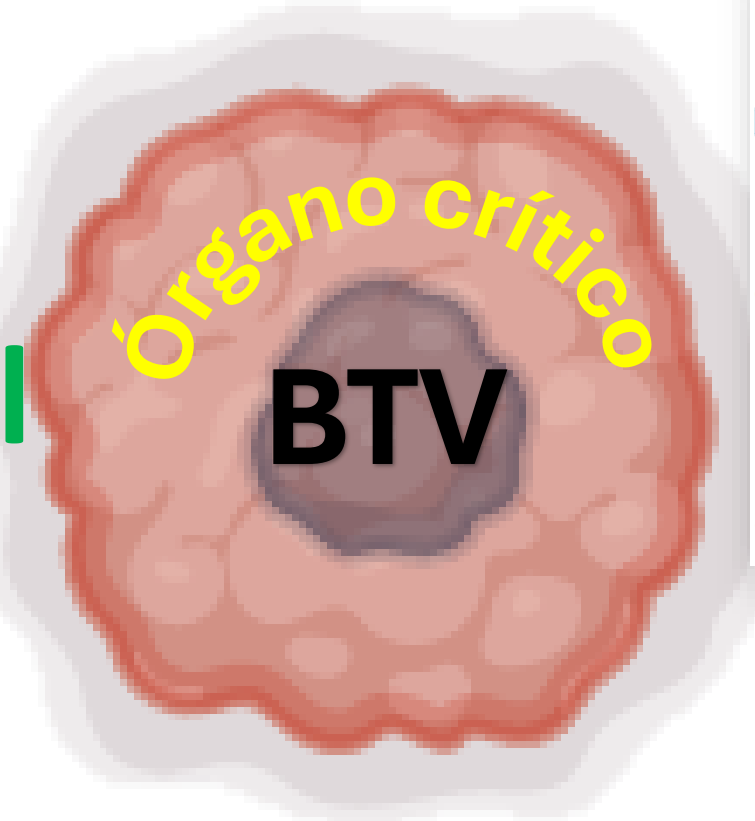


PATHY = SBRT(hipoxia)+~~RT~~

Control local

Bystander

Abscopal



Tubin *et al. Radiation Oncology* (2019) 14:21
https://doi.org/10.1186/s13014-019-1227-y

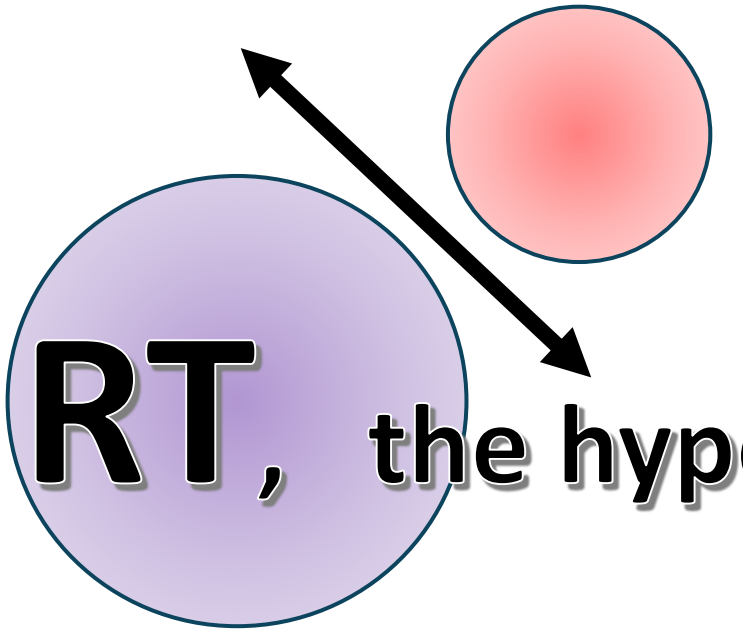
Radiation Oncology

METHODOLOGY Open Access

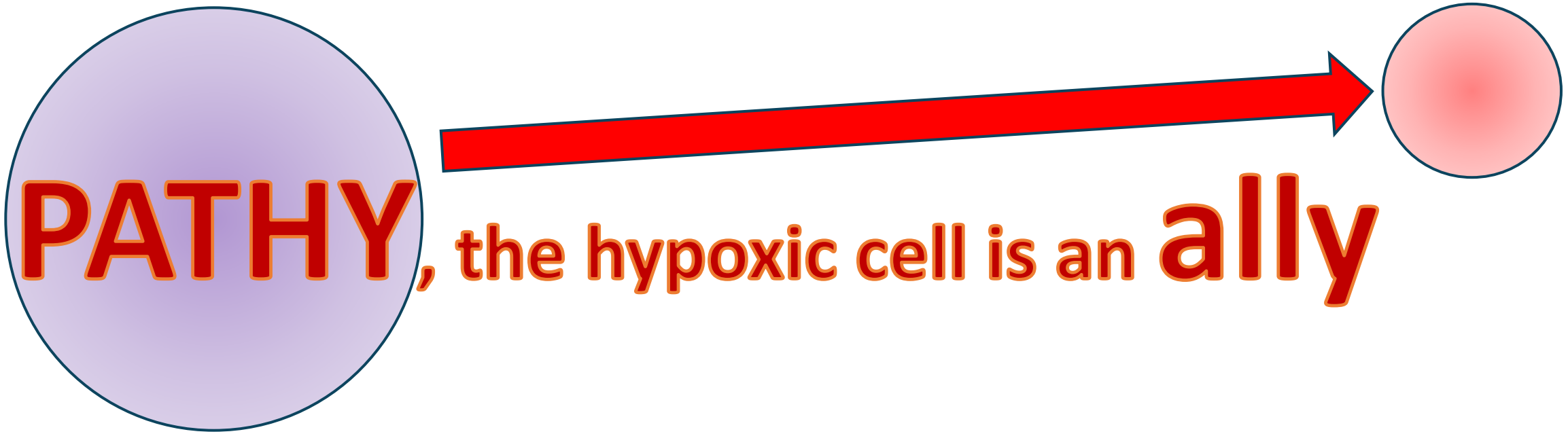
Novel stereotactic body radiation therapy (SBRT)-based partial tumor irradiation targeting hypoxic segment of bulky tumors (SBRT-PATHY): improvement of the radiotherapy outcome by exploiting the bystander and abscopal effects

Slavisa Tubin[1*], Helmut H. Popper[2] and Luka Brcic[2]

2019



For RT, the hypoxic cell is an enemy



For PATHY, the hypoxic cell is an ally







This was a challenging and aggressive case of squamous cell carcinoma that invaded the skull, filled the cranial fossae, and displaced the ocular orbits, compressing the optic nerves and causing blindness. We used SFRT instead of conventional radiotherapy over six alternate sessions. This image captures what we encountered before starting the third session

Dra. Quintana

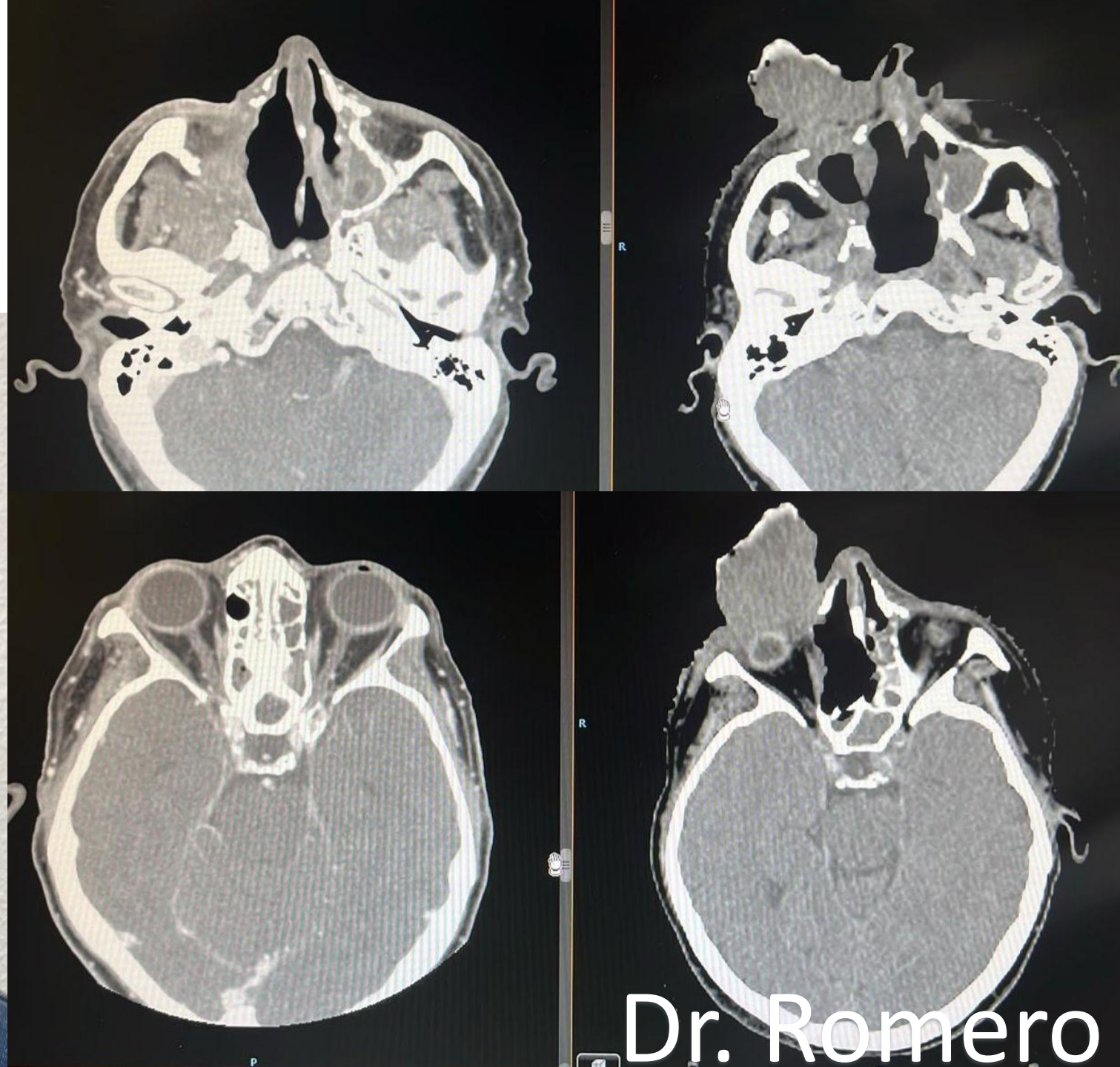




26 July 2024, 6 months later the patient is able to see perfectly

Mujer de 59 años con carcinoma epidermoide previamente tratado con radioterapia externa hasta una dosis total de 67,5 Gy en 30 fracciones, que presenta una recidiva local de comportamiento biológico altamente agresivo



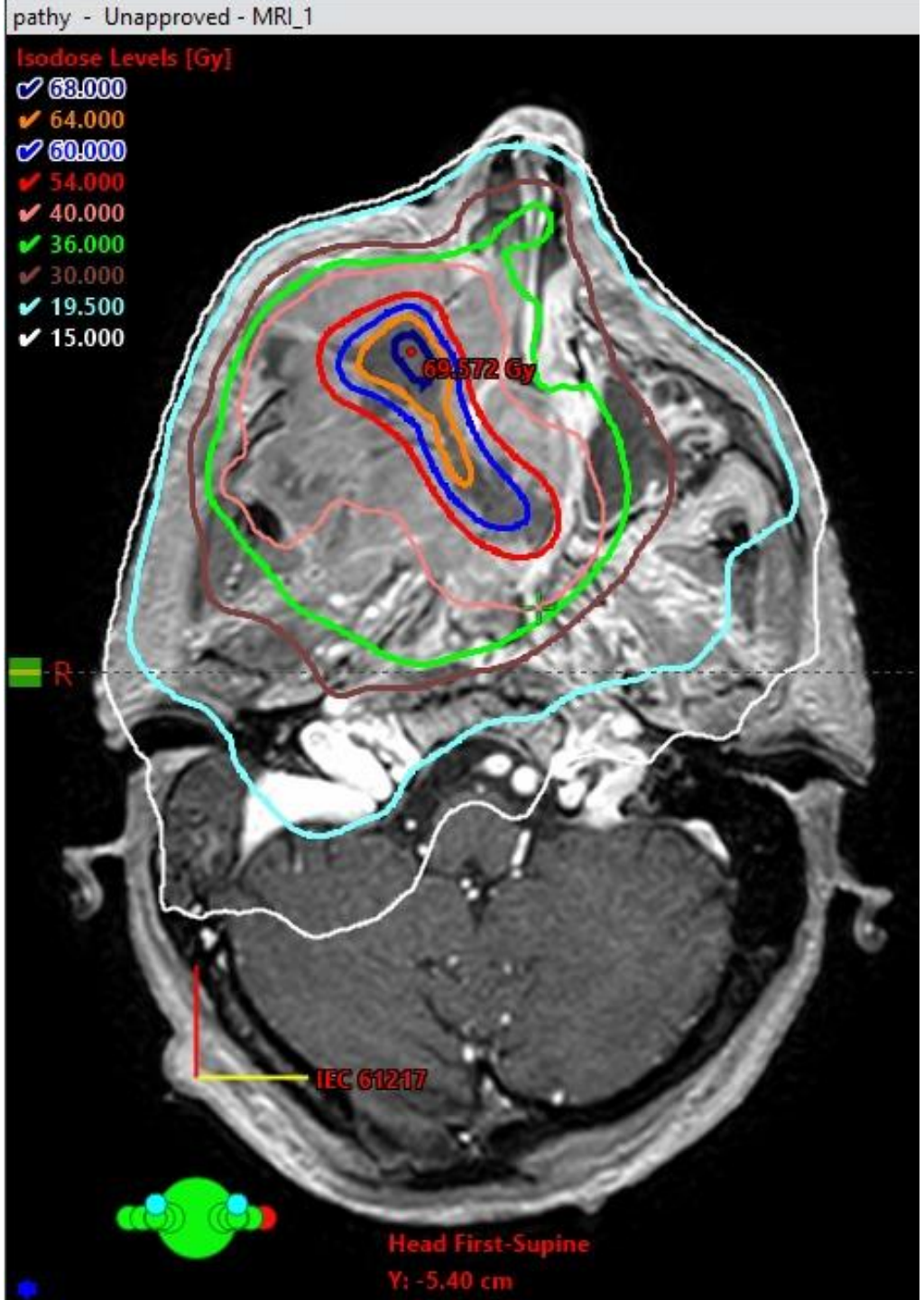


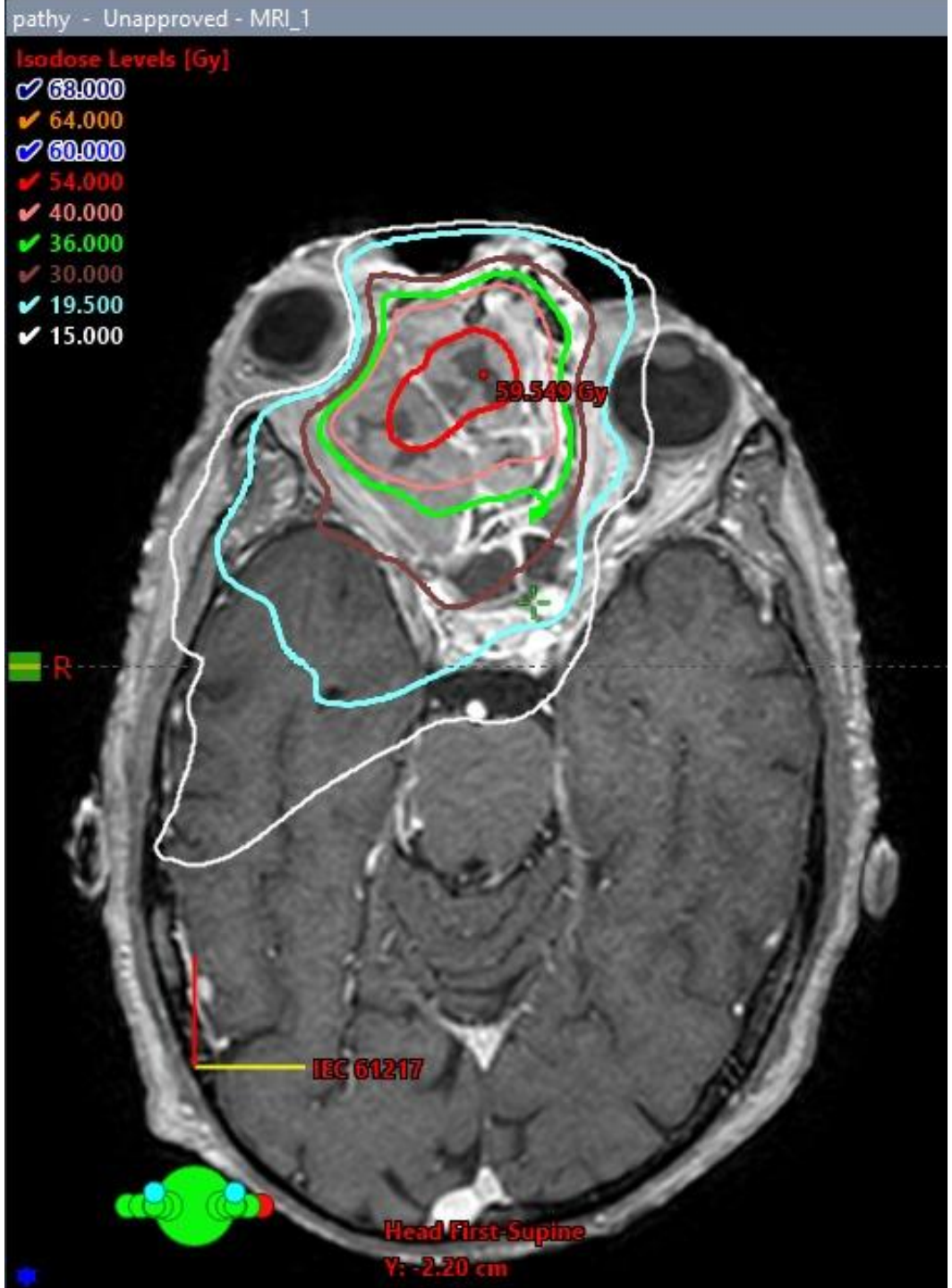
Dr. Romero

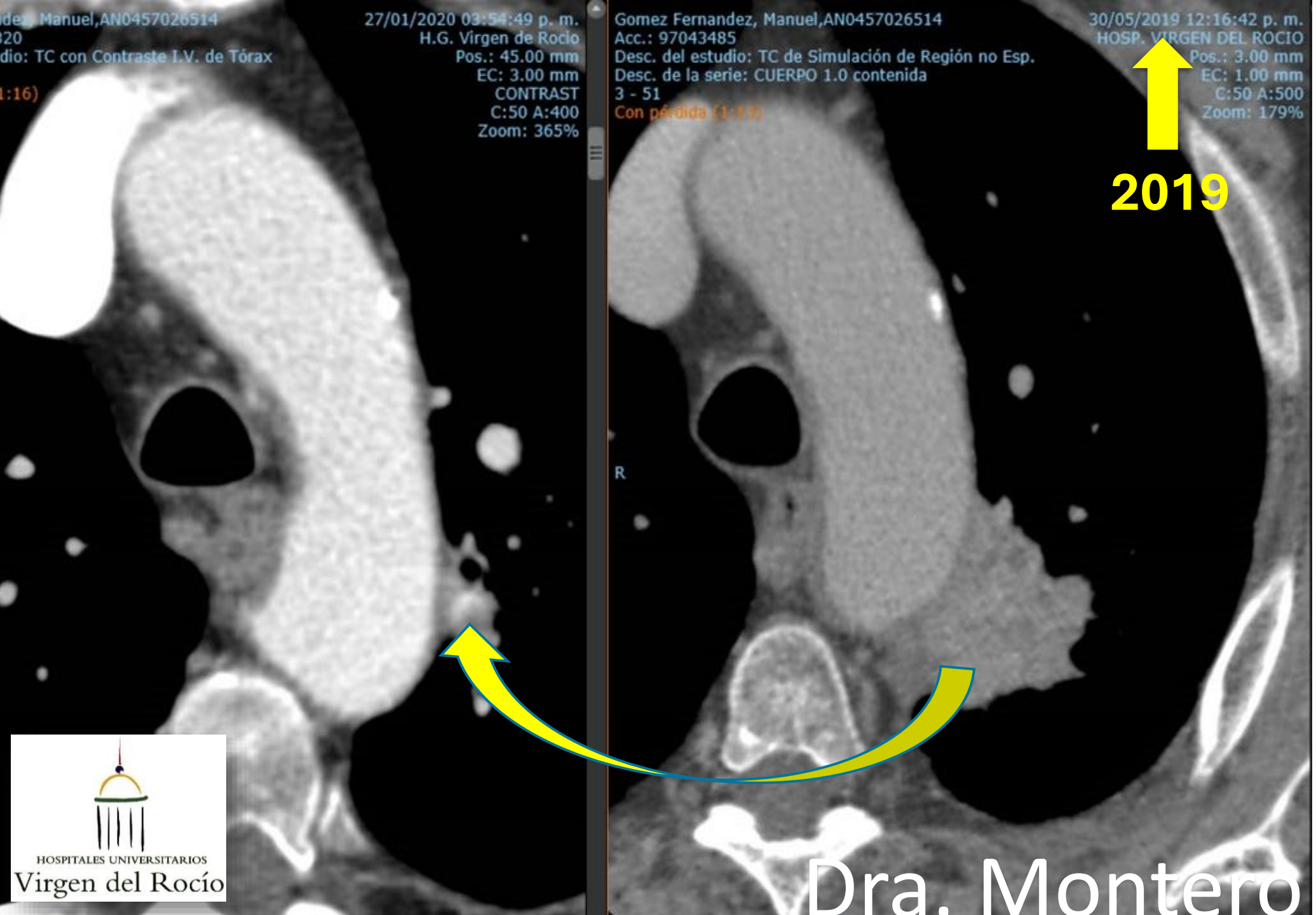


Paciente de 51 años con neurofibromatosis tipo I y un sarcoma maxilar derecho de alto grado irresecable (T4N0MxG3). El tumor invadía la órbita, la cavidad nasal, los etmoides y el espacio masticador.
Tras radioterapia adaptada al concepto PATHY después de tratamiento de primera línea con doxorrubicina, el paciente presentó una mejoría radiológica sostenida, recuperación visual parcial, control completo del dolor y un estado funcional ECOG 0 en el seguimiento a los ocho meses.

Dr. Romero


pathy - Unapproved - MRI_1
Isodose Levels [Gy]
68.000
64.000
60.000
54.000
40.000
36.000
30.000
19.500
15.000
69.572 Gy
R
IEC 61217
Head First-Supine
Y: -5.40 cm


pathy - Unapproved - MRI_1
Isodose Levels [Gy]
68.000
64.000
60.000
54.000
40.000
36.000
30.000
19.500
15.000
59.549 Gy
R
IEC 61217
Head First-Supine
Y: -2.20 cm

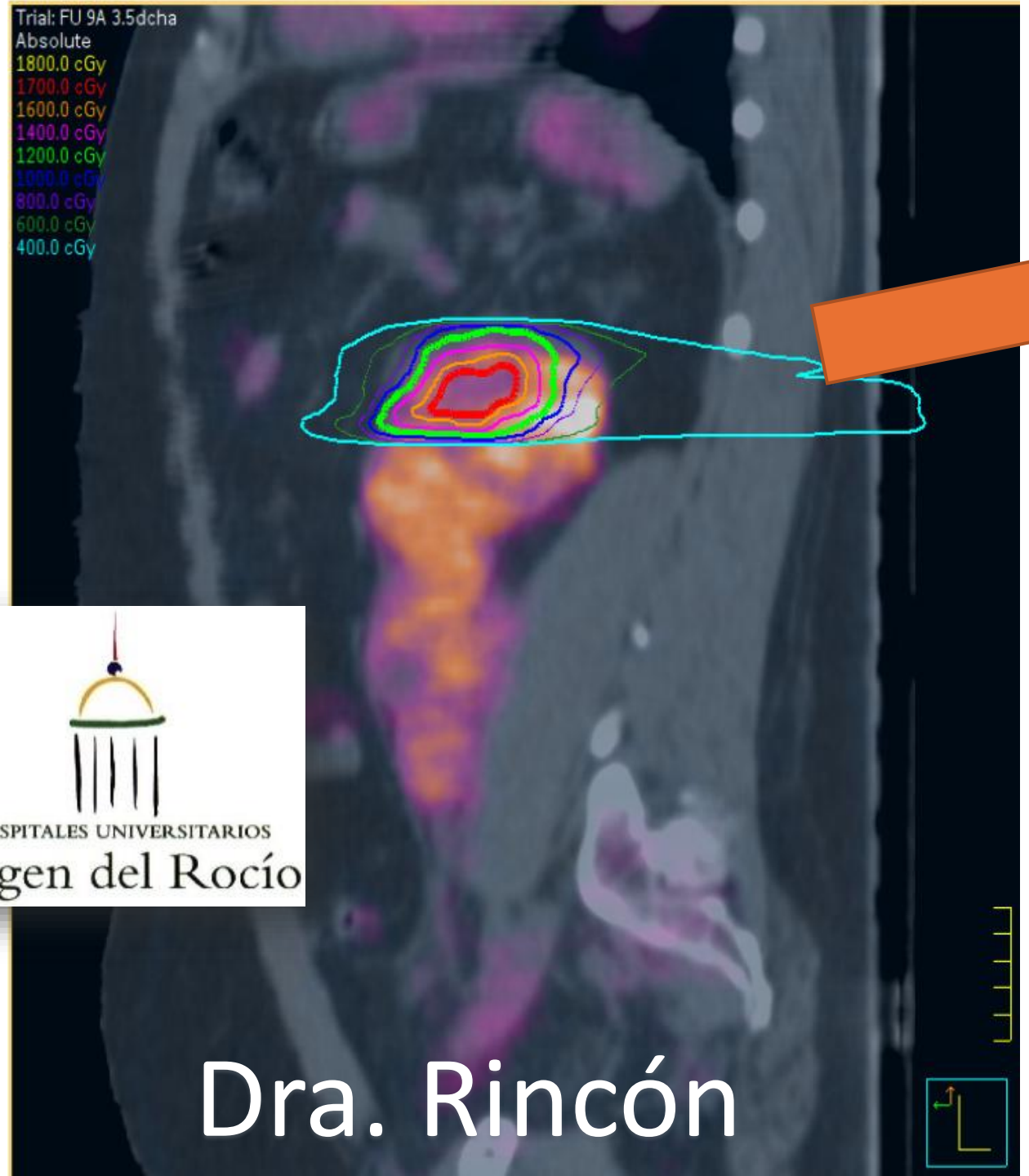


HOSPITALES UNIVERSITARIOS
Virgen del Rocío

Dra. Montero

After irradiating only one-fifth of the volume, the tumor had disappeared

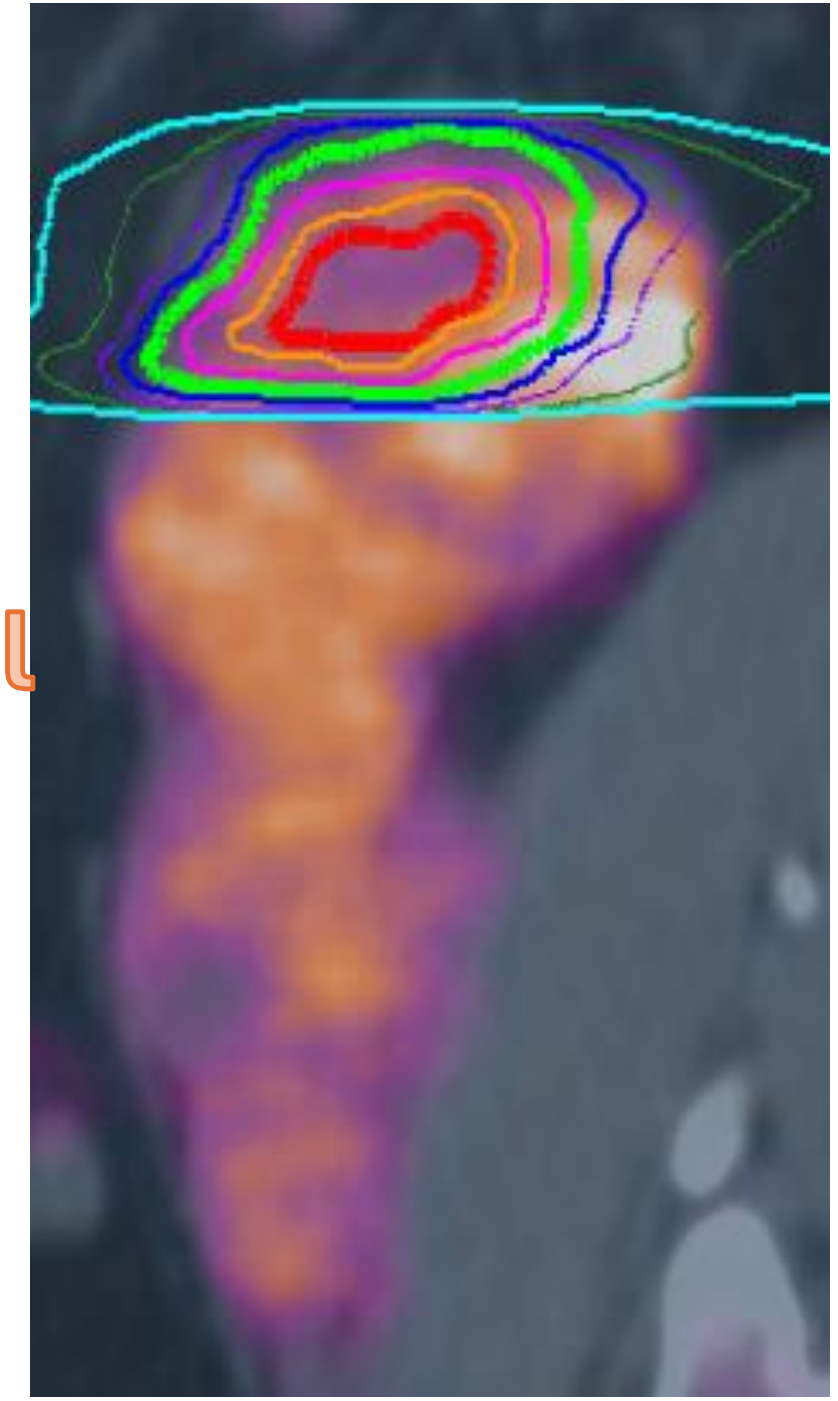
by 8 months



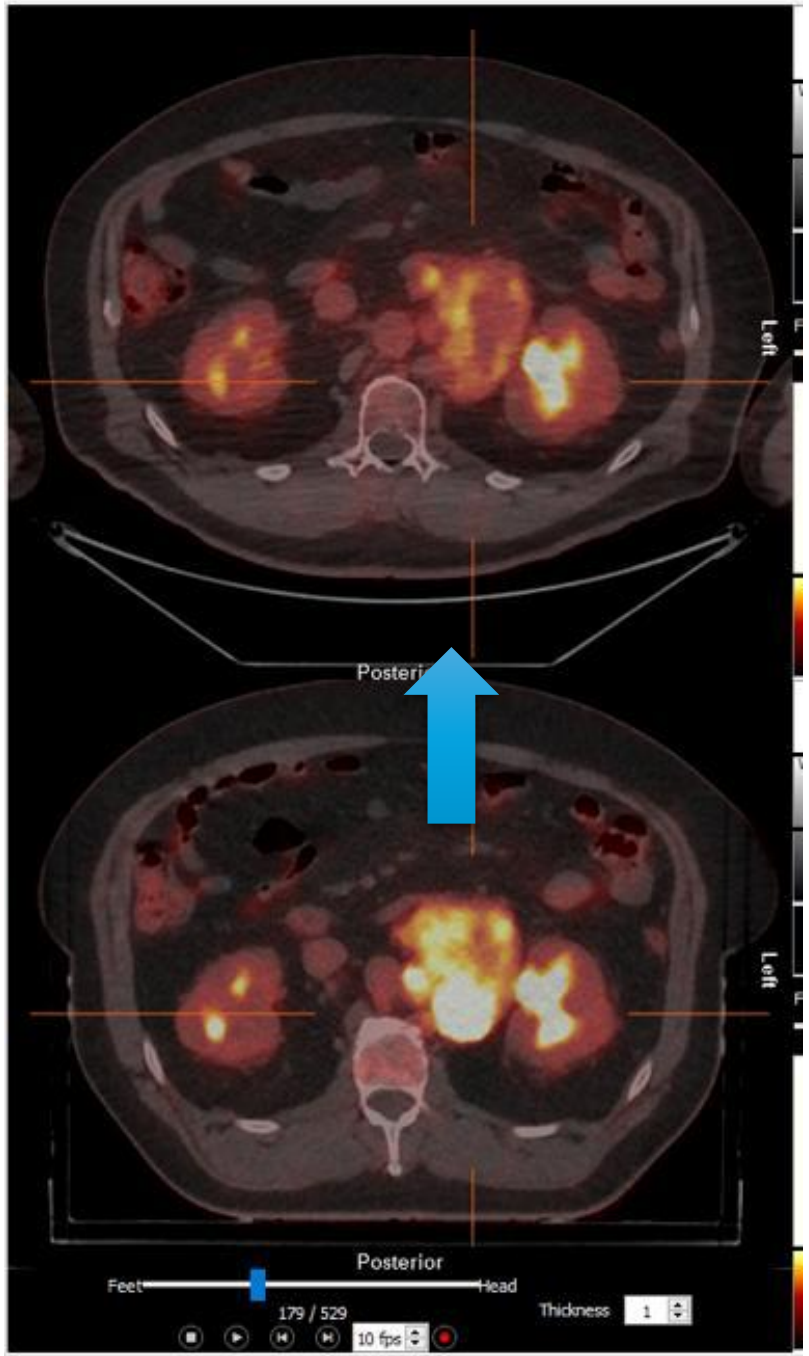
HOSPITALES UNIVERSITARIOS
Virgen del Rocío

Dra. Rincón

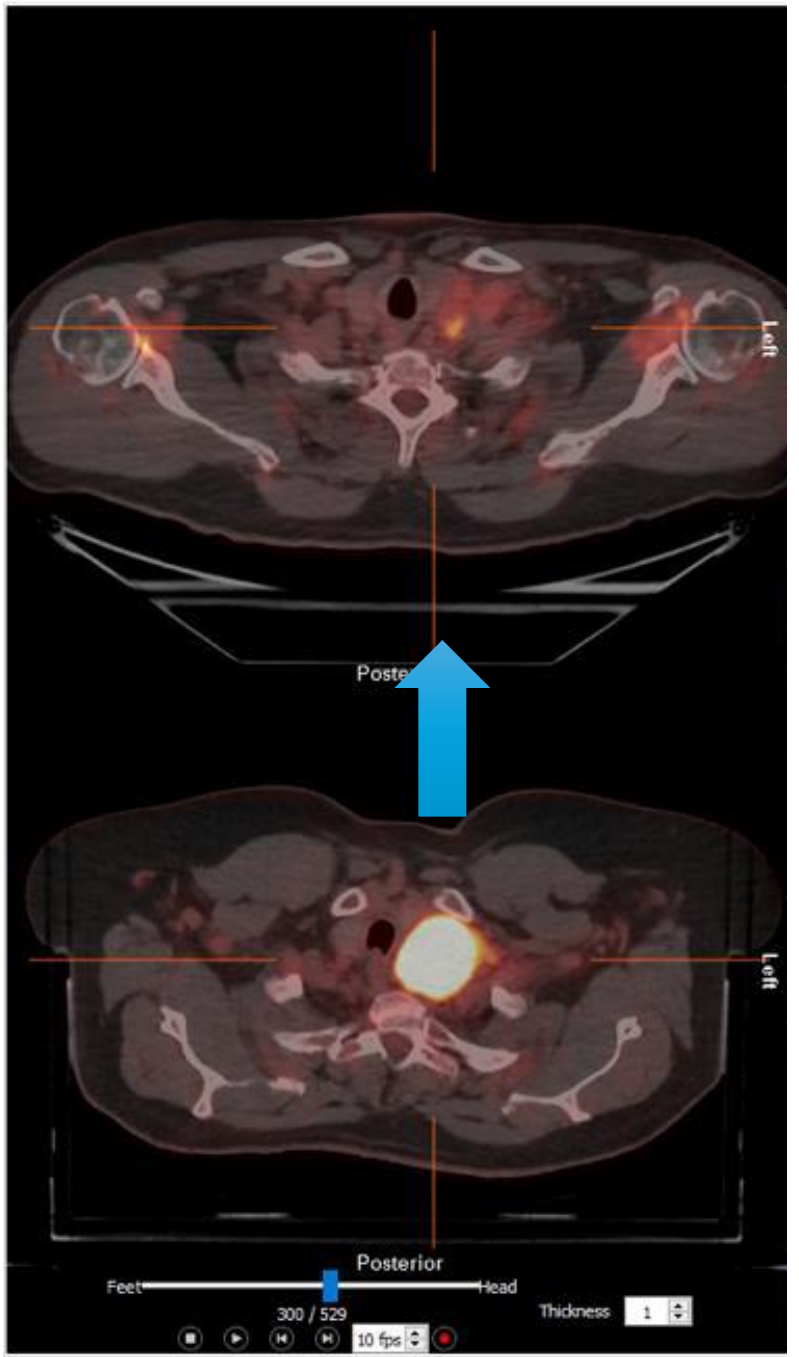
8%Vol



Study Date: April 12 2023 11:39:05
Study ID: 13851

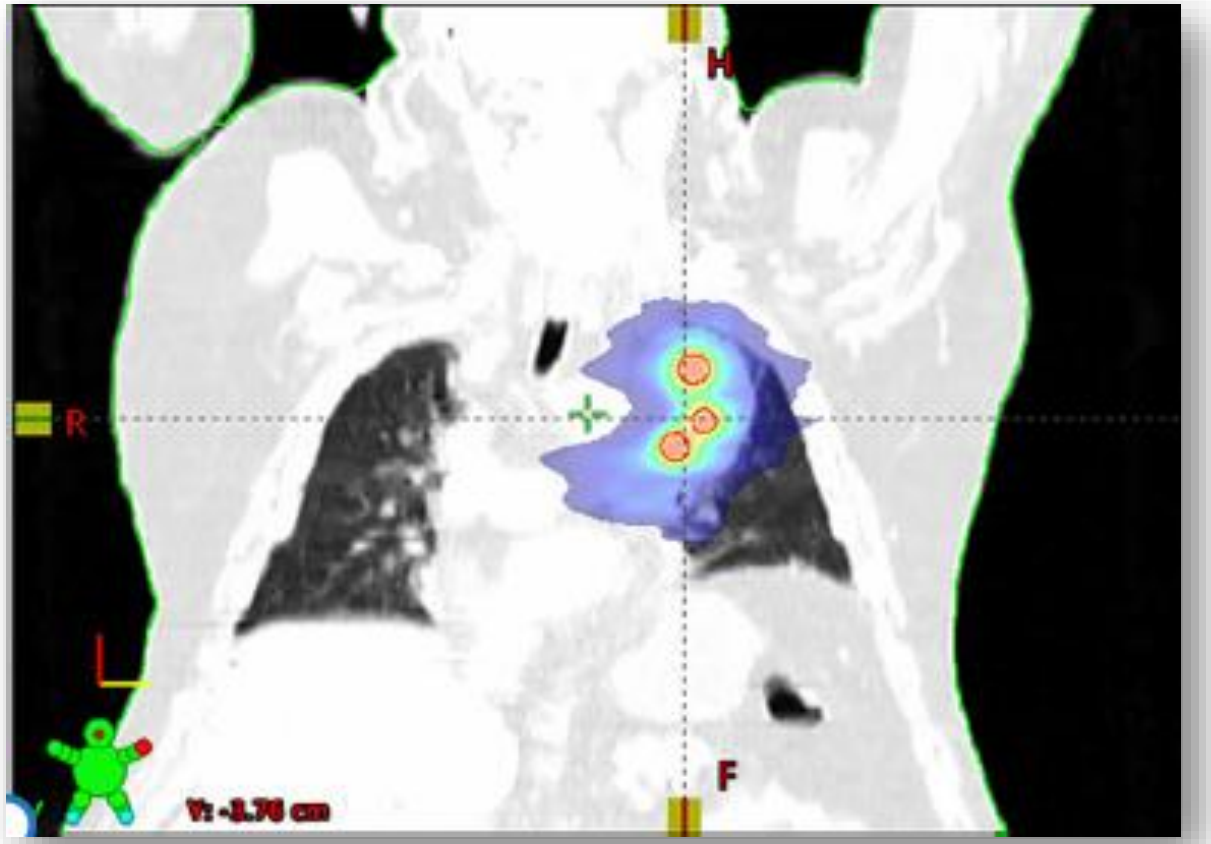


AN0546213970
Study Date: April 12 2023 11:39:05
Study ID: 13851



HOSPITALES UNIVERSITARIOS
Virgen del Rocío

Lattice = SBRT(kernel)+RT



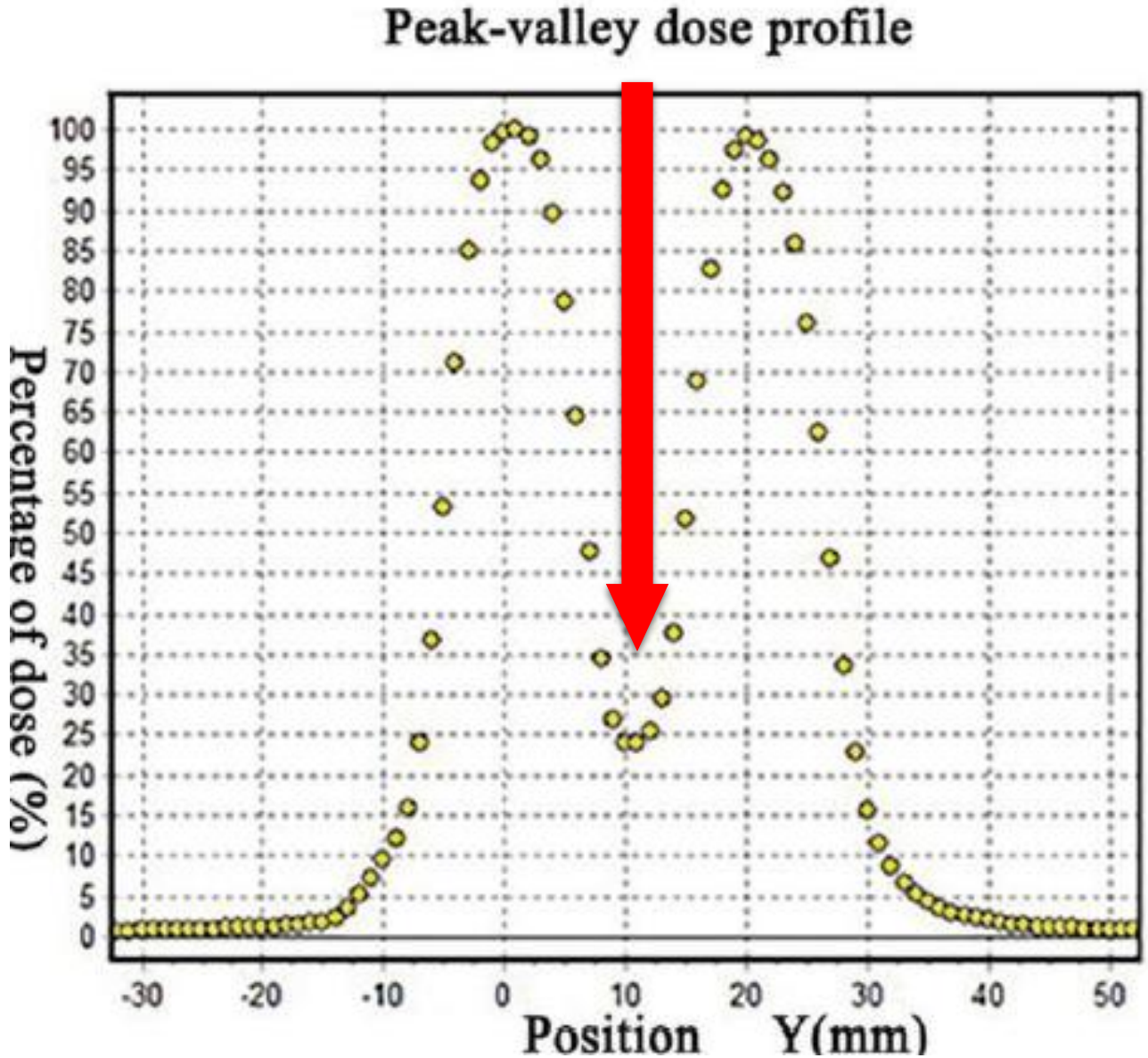


TNF-α



12Gy

20Gy

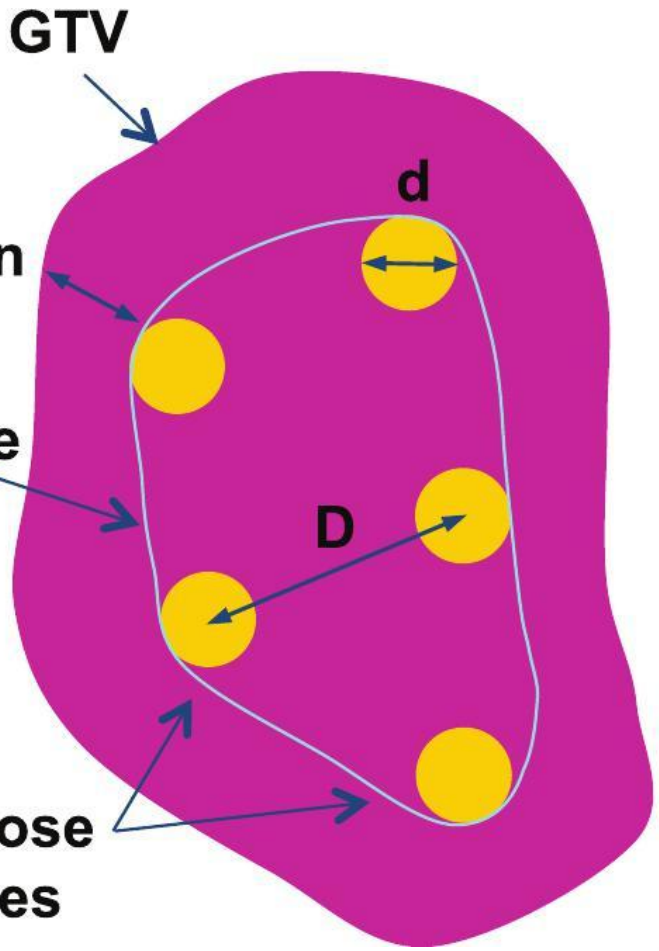


3Gy

5Gy

¿Dónde colocar los vértices de Lattice?

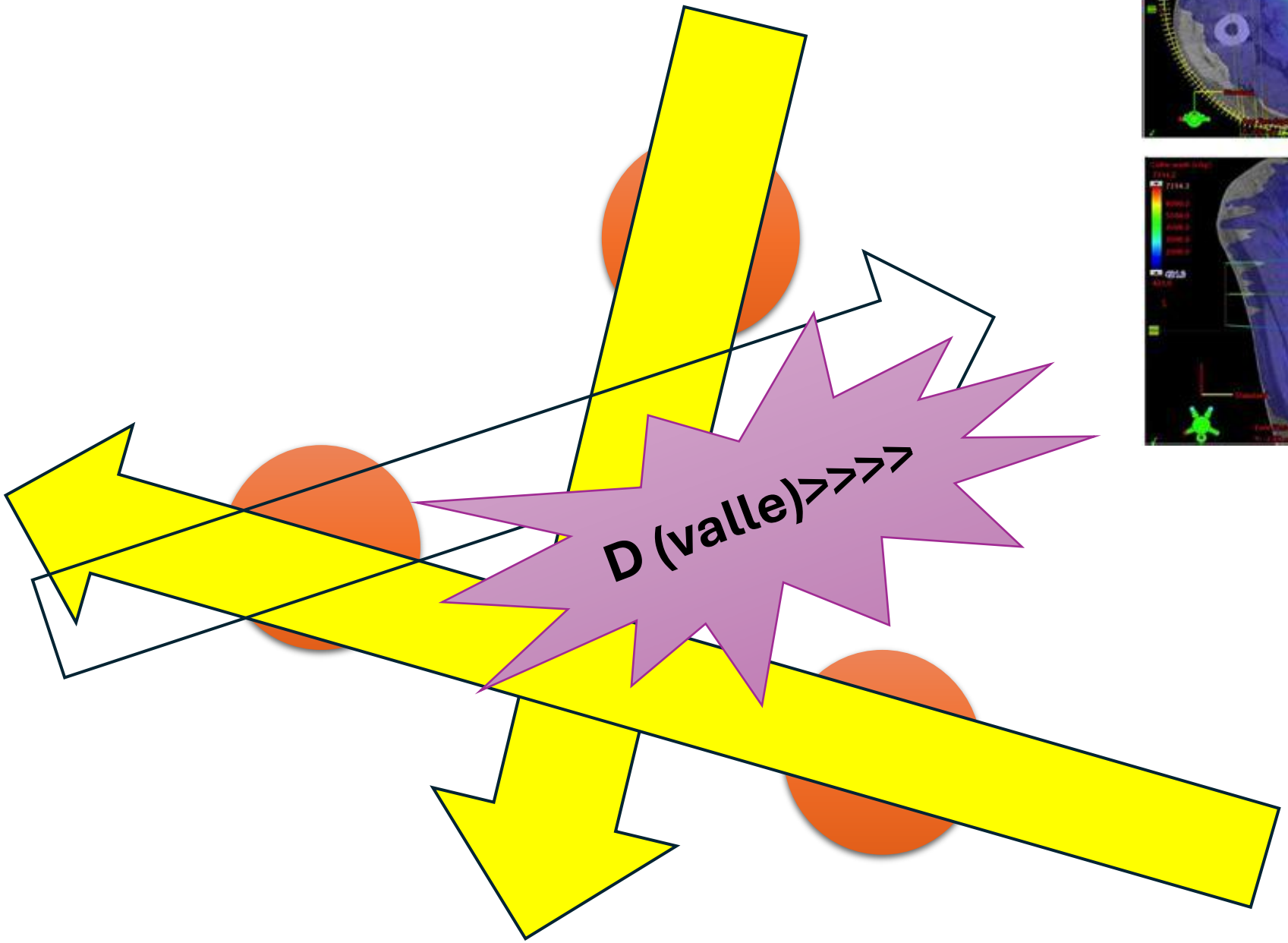


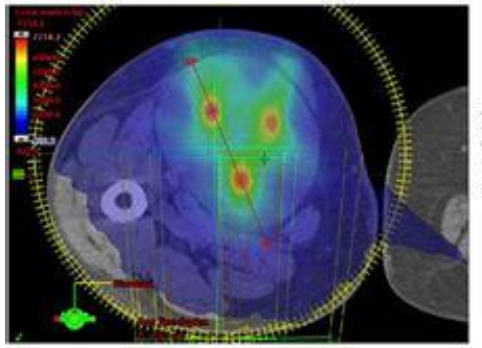


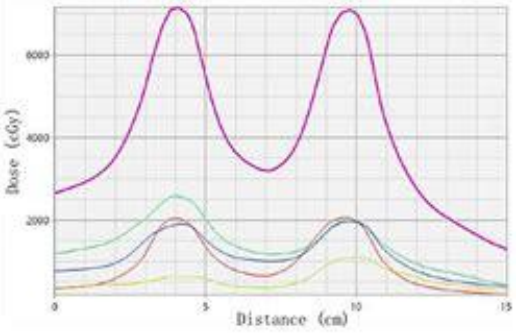


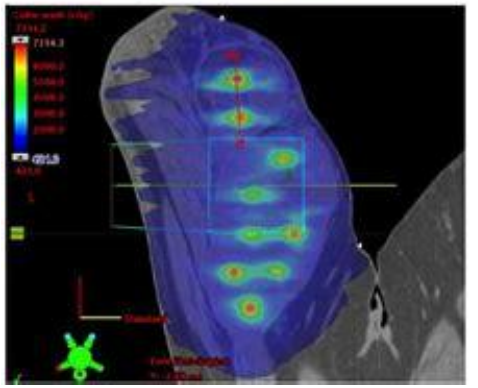
Vertex diameter d = 0.5–1.5 cm
Vertices separation D = 2.0–5.0 cm
$V_{vertices}/V_{GTV}$ (volume ratio): 1.0–10.0%
$Dose_{vertices}$: 10–25 Gy per fraction
$Dose_{valley}$: <5 Gy per fraction
$Dose_{GTV\ margin}$: 2–5 Gy
GTV: ≥50 cc

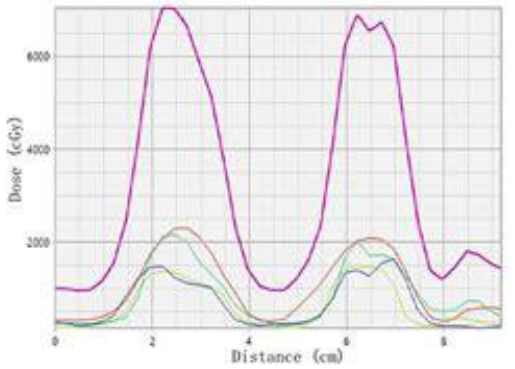
Lattice VMAT











BAJAMOS PROBABILIDAD

Agosto de 2022

cancers

MDPI

Article

Impressive Results after "Metabolism-Guided" Lattice Irradiation in Patients Submitted to Palliative Radiation Therapy: Preliminary Results of LATTICE_01 Multicenter Study

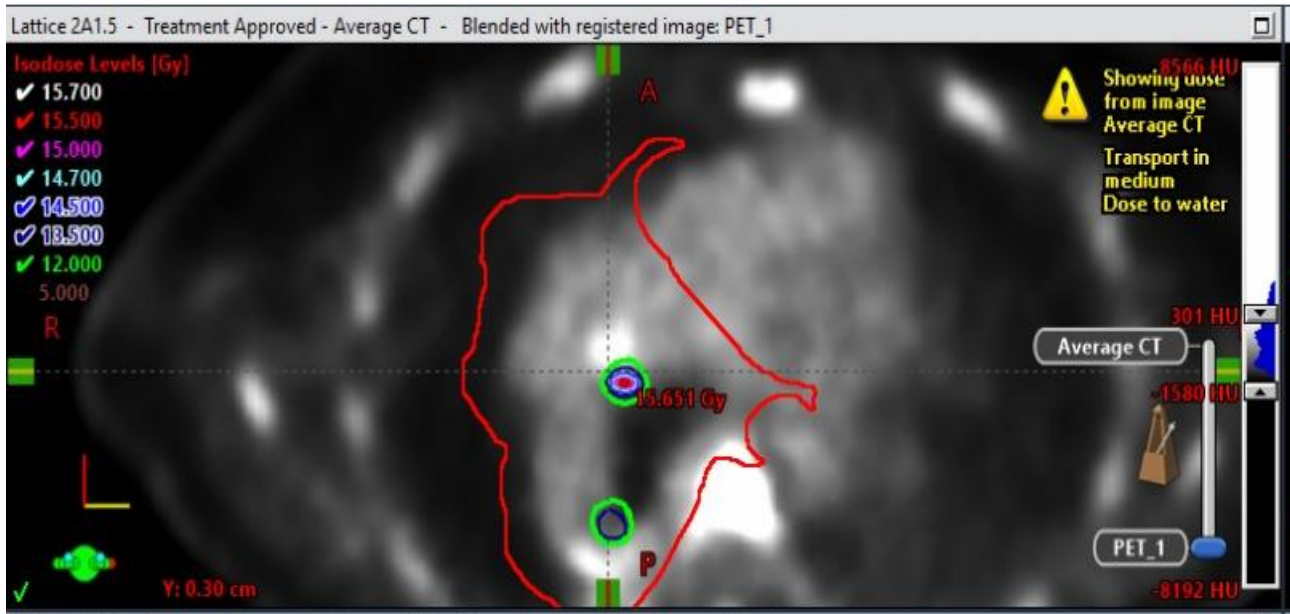
Gianluca Ferini [1,†], Silvana Parisi [2,†], Sara Lillo [2], Anna Viola [3,*], Fabio Minutoli [2], Paola Critelli [2], Vito Valenti [1], Salvatore Ivan Illari [3], Anna Brogna [4], Giuseppe Emmanuele Umana [5], Giacomo Ferrantelli [2], Gabriele Lo Giudice [2], Chiara Carrubba [2], Valentina Zagardo [2], Anna Santacaterina [6], Salvatore Leotta [6], Alberto Cacciola [2], Antonio Pontoriero [2] and Stefano Pergolizzi [2]

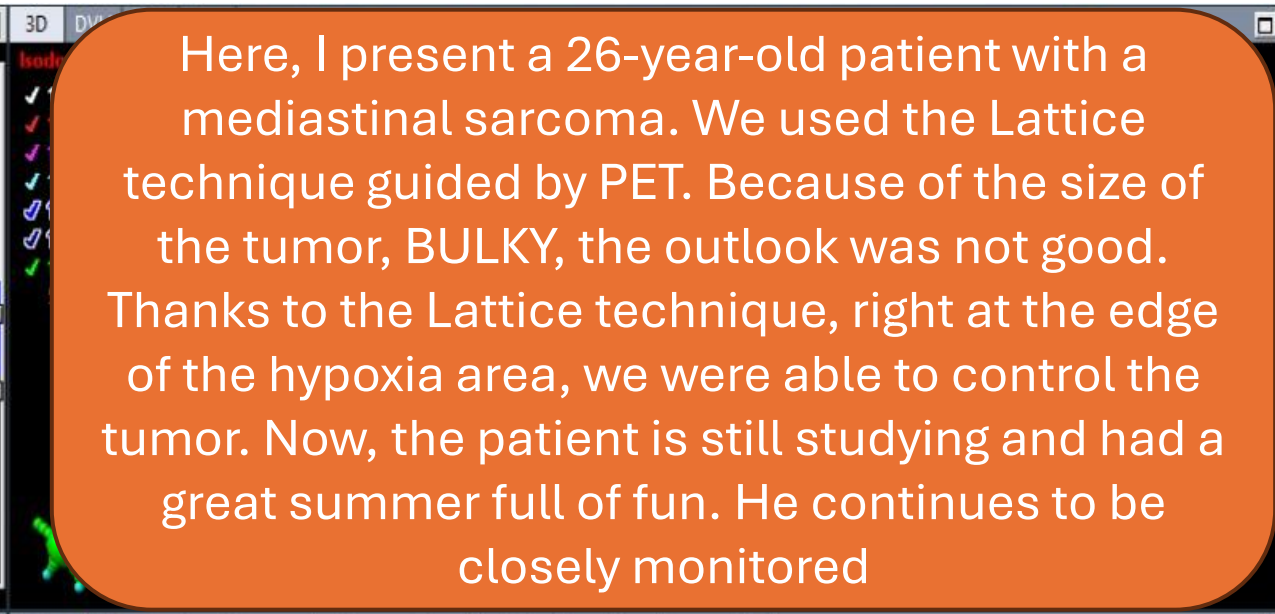
Estadíos IV- Lattice

- **The rate of symptomatic response was 100%,**
- and it was observed **immediately after lattice RT** delivery in **3/30** patients, while **27/30** patients had a symptomatic response within **8** days from the end of GTV irradiation.
- **The rate of overall clinical response was 89%,**

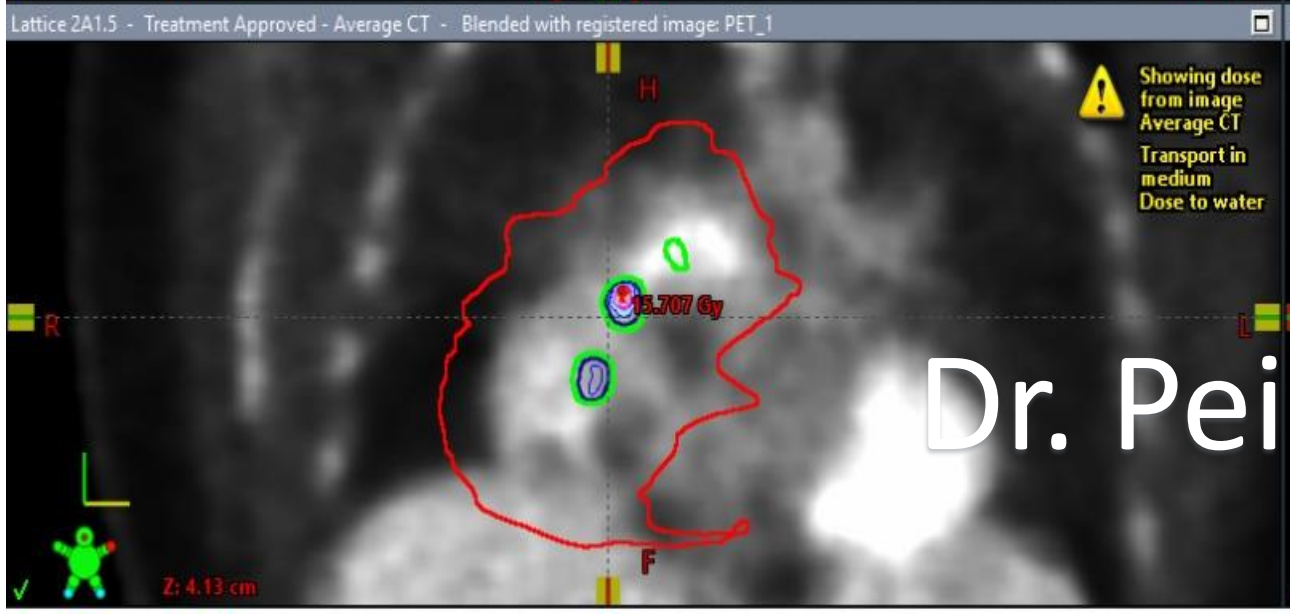
  including 23% of complete remission.
- **The 1-year overall survival rate was 86.4%**

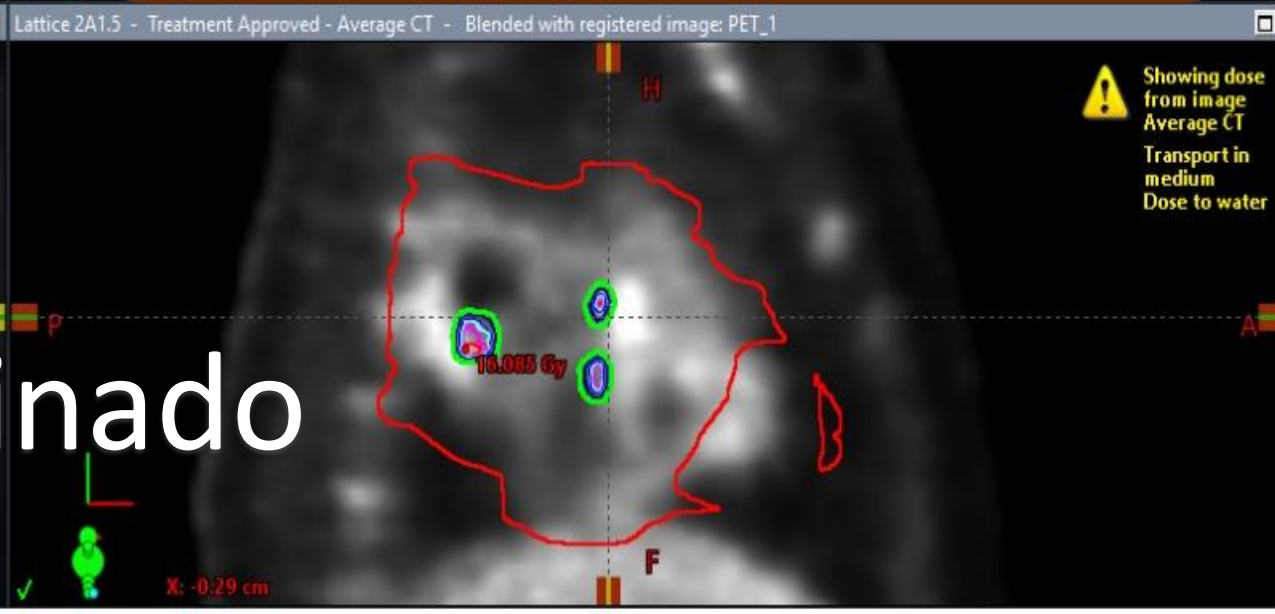
Mediastinal sarcoma 25 abril 2025





Here, I present a 26-year-old patient with a mediastinal sarcoma. We used the Lattice technique guided by PET. Because of the size of the tumor, BULKY, the outlook was not good. Thanks to the Lattice technique, right at the edge of the hypoxia area, we were able to control the tumor. Now, the patient is still studying and had a great summer full of fun. He continues to be closely monitored





Dr. Peinado

Where Should the Vertices Be Placed?

Optimizing the Geometric Distribution of Lattice Vertices to Maximize Cold Valleys Using VMAT with Negative Margins

Santiago Velazquez-Miranda, Fernando Picon-Garcia, Javier Sanchez-Esperon

Introduction

Lattice Radiotherapy (LRT) has proven to be a valuable tool for treating large tumors by creating a heterogeneous dose distribution characterized by areas of high dose (peaks) and low dose (valleys). A sine qua non condition for achieving the out-of-target biological effects of SFRT treatments is the presence of tumor areas with genuinely low doses, enabling the cells in these regions to amplify the inflammatory and apoptotic signals produced by cells in high-dose areas. However, conventional strategies based on uniform spatial criteria for vertex distribution face limitations in maximizing the dose/volume gradient in the valleys.

This study introduces a novel geometric approach that redefines vertex placement using a central helical pattern within the tumor, optimizing dose delivery with negative-margin VMAT techniques.

Junta de Andalucía
Consejería de Salud y Consumo

SUBVENCIONES PARA LA FINANCIACION DE LA I+D+i EN BIOMÉDICINA Y EN CIENCIAS DE LA SALUD EN ANDALUCÍA

AÑO 2025 *(Versión 0_15/05/2025)*

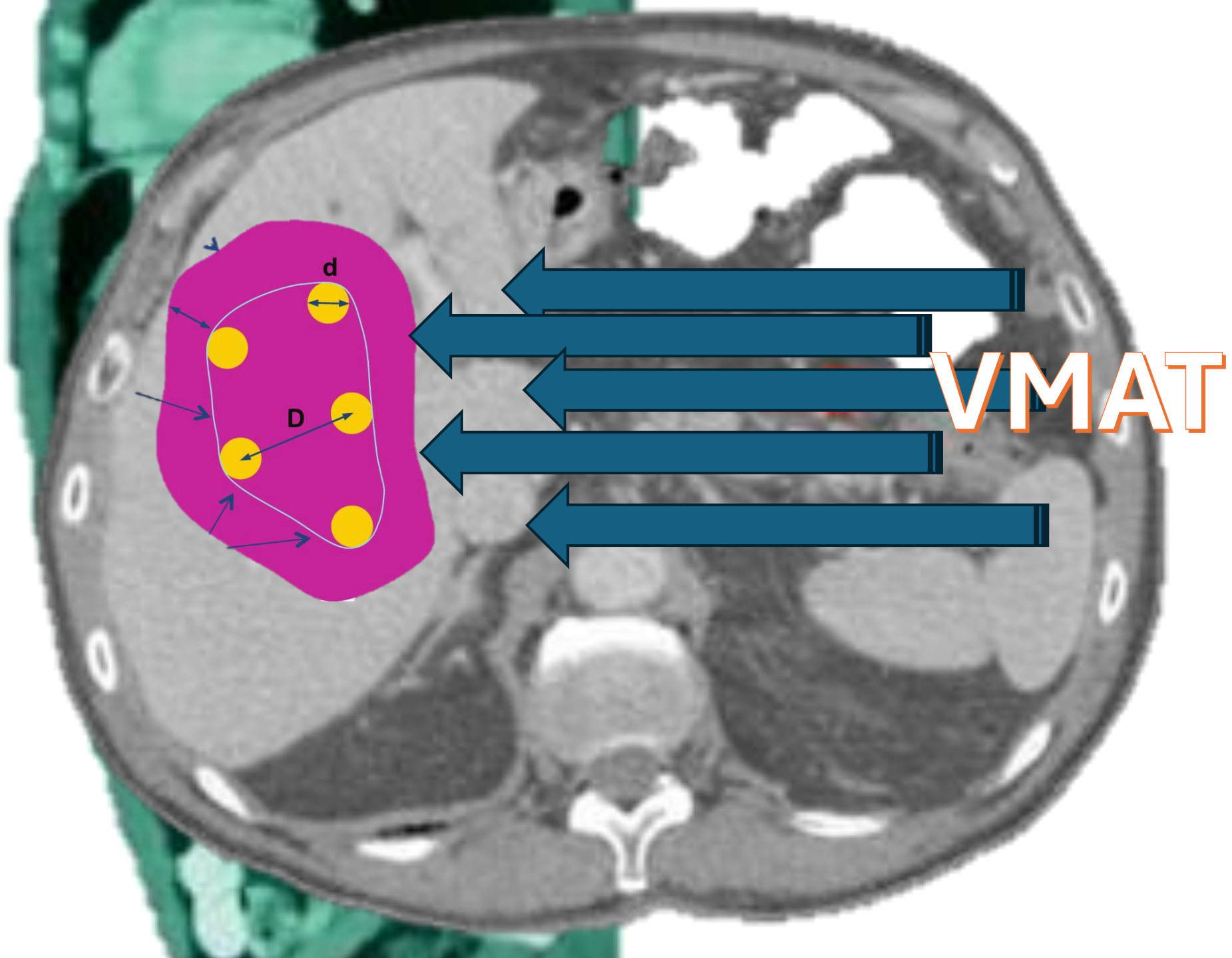
1. *Proyectos de investigación en salud temática general*
2. *Proyectos de investigación en atención primaria, hospitales comarcales y CHAREs*
3. *Proyectos de investigación e innovación colaboración público-privada*

INVESTIGADOR/ES PRINCIPAL/ES

NOMBRE Y APELLIDOS: MARÍA LUISA AGUILAR ADAME
NOMBRE Y APELLIDOS: SANTIAGO VELÁZQUEZ MIRANDA

TÍTULO DEL PROYECTO

EVALUACIÓN DEL DESESTADIAJE EN PACIENTES CON TUMORES BULKY Y ECOG ≤ 2 CON EL TRATAMIENTO LATTICE EN RADIOTERAPIA MEDIANTE EL PROCEDIMIENTO LATTICE-HELIXRAD. ESTUDIO HÉLICE

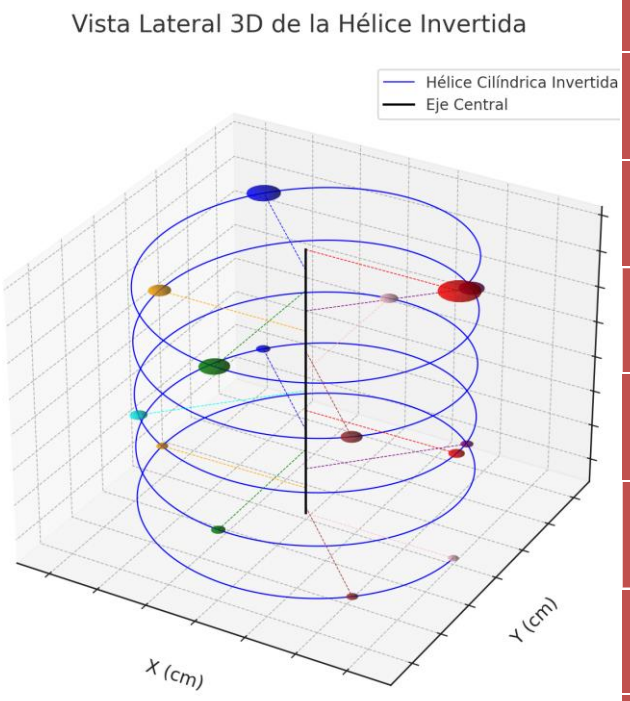

d
D
VMAT

It’s the geometry, not the dosimetry, stupid!



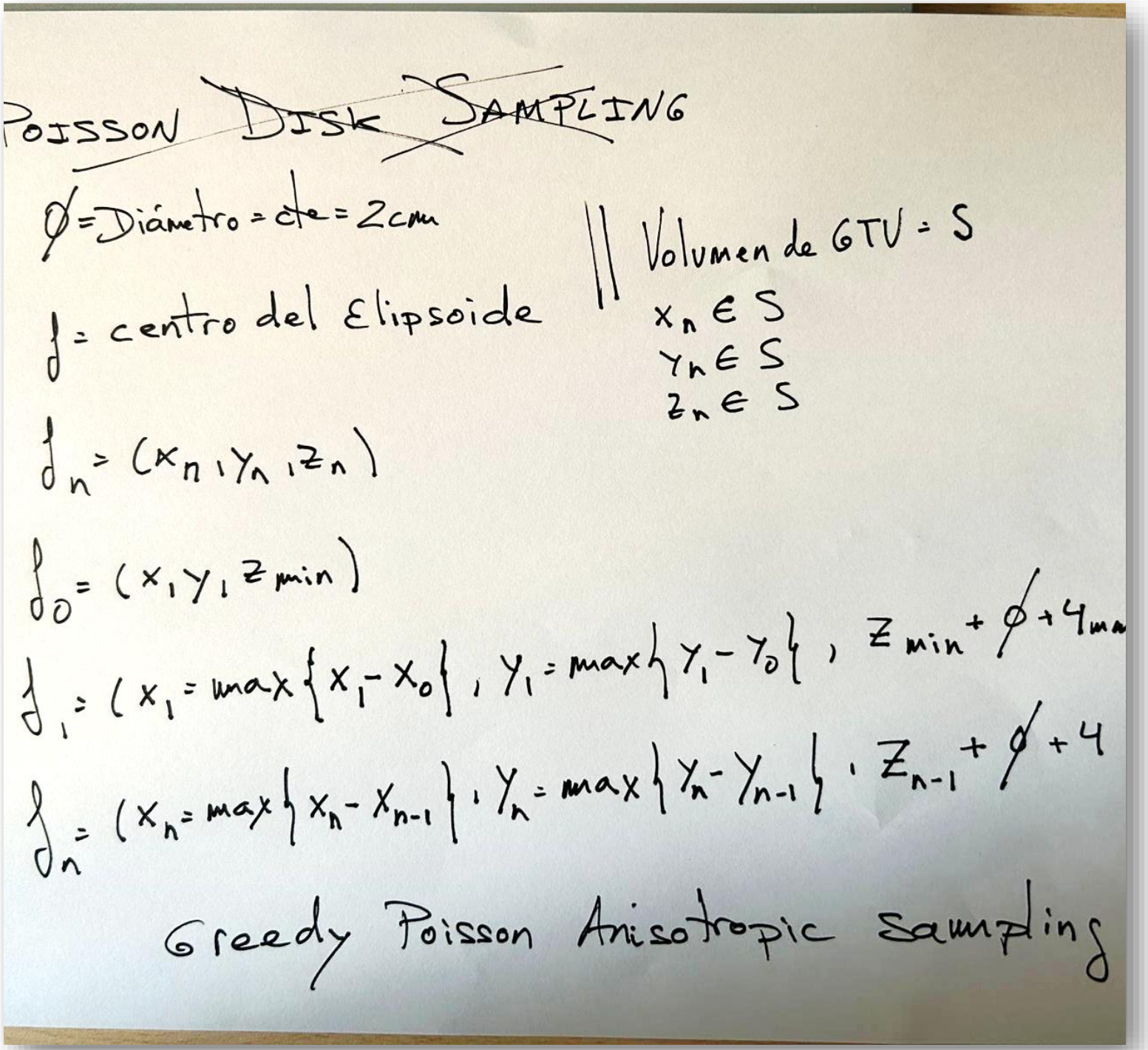
OPTIMIZAR A AMENDOLA





Elemento	Definición matemática
Volumen tumoral	${}^{T}V \subset \mathbb{R}^3$
Diámetro axial mínimo	${}^{T}\varphi_{min} = \min_z\ {}^{T}\varphi(z)$
Diámetro helicoidal local	${}^{H}\varphi(z) = {}^{T}\varphi(z) - \mathbf{1\ cm}$
Diámetro del vértice	${}^{VERTEx}\varphi$
Paso helicoidal	$p = {}^{VERTEx}\varphi + \mathbf{2\ mm}$
Rotación angular	$\boldsymbol{\theta_n = \theta_0 + n \cdot 3\pi/4}$
Índice discreto	$n \in \{0,1,\ldots,N\}$
Coordenada axial discreta	$z_n = n \cdot p$
Parametrización del vértice	$r(n) = ({}^{H}\varphi(z_n)/2\ \cos\theta_n\ ,\ {}^{H}\varphi(z_n)/2\ \sin\theta_n\ ,\ z_n)$

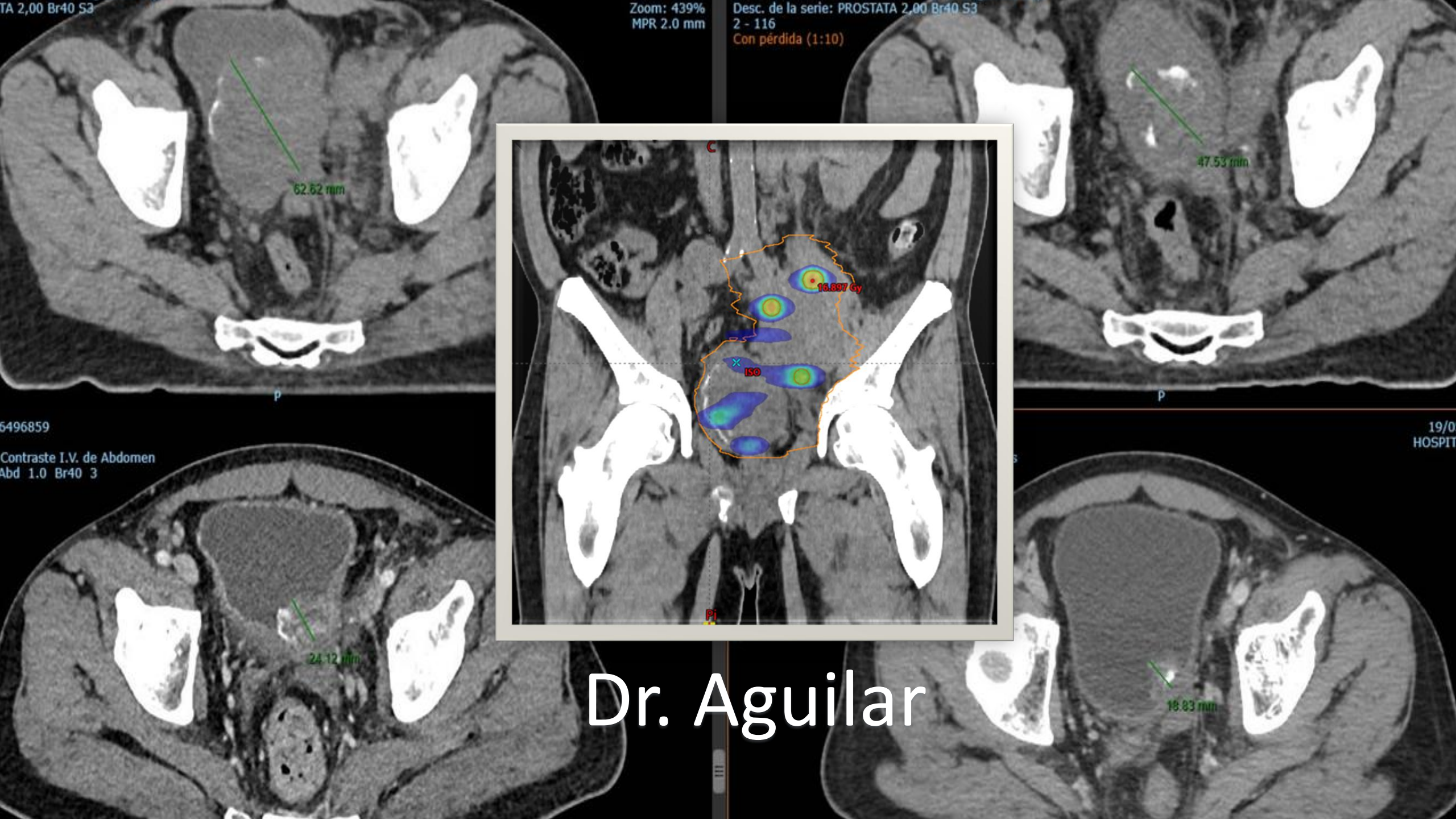
Nota: Cuando un vértice de la hélice fue considerado inadecuado por el oncólogo radioterápico, se desplazó hacia el eje de la hélice.



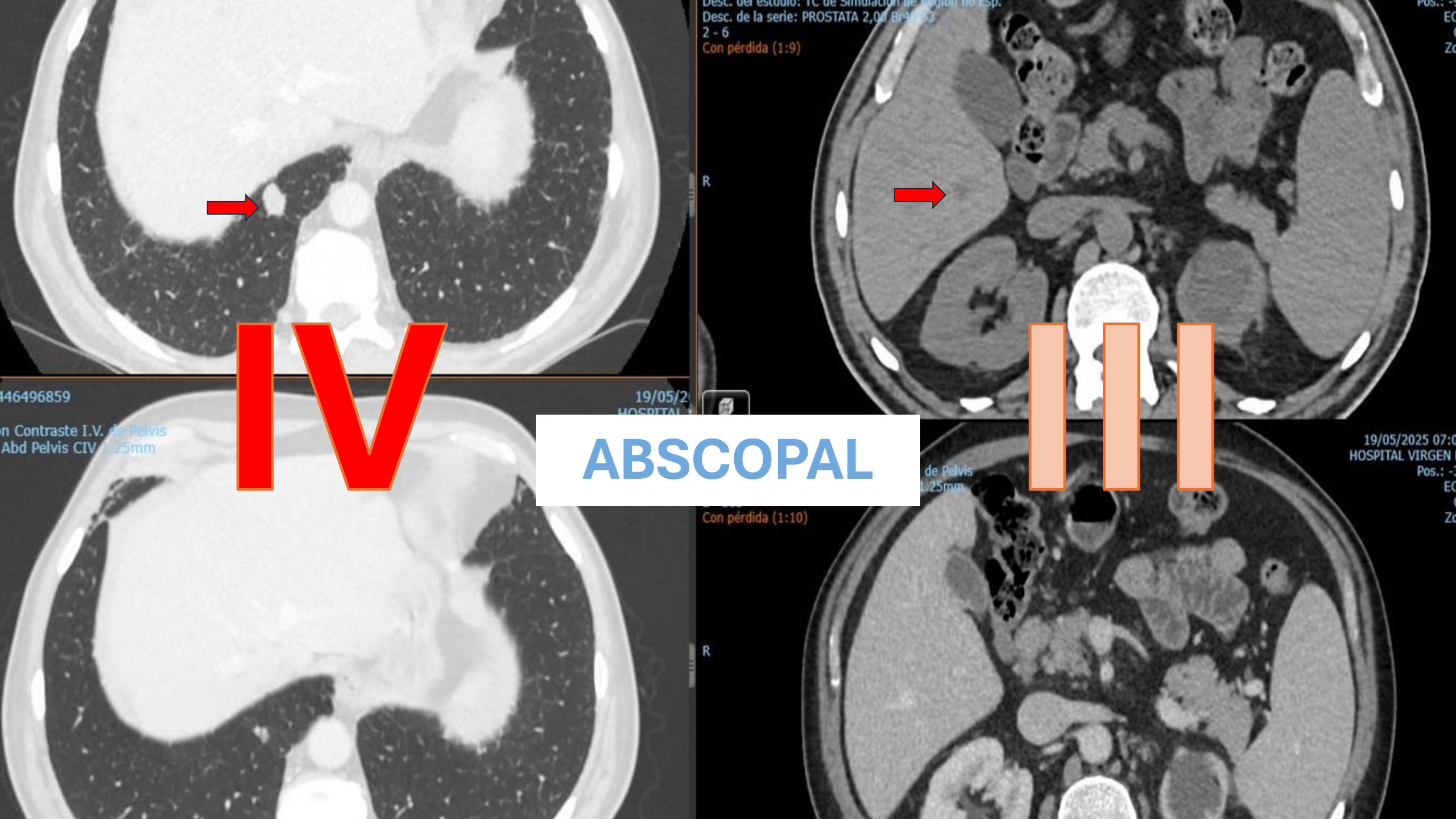
We already have an app that places vertices using an optimized helical philosophy:

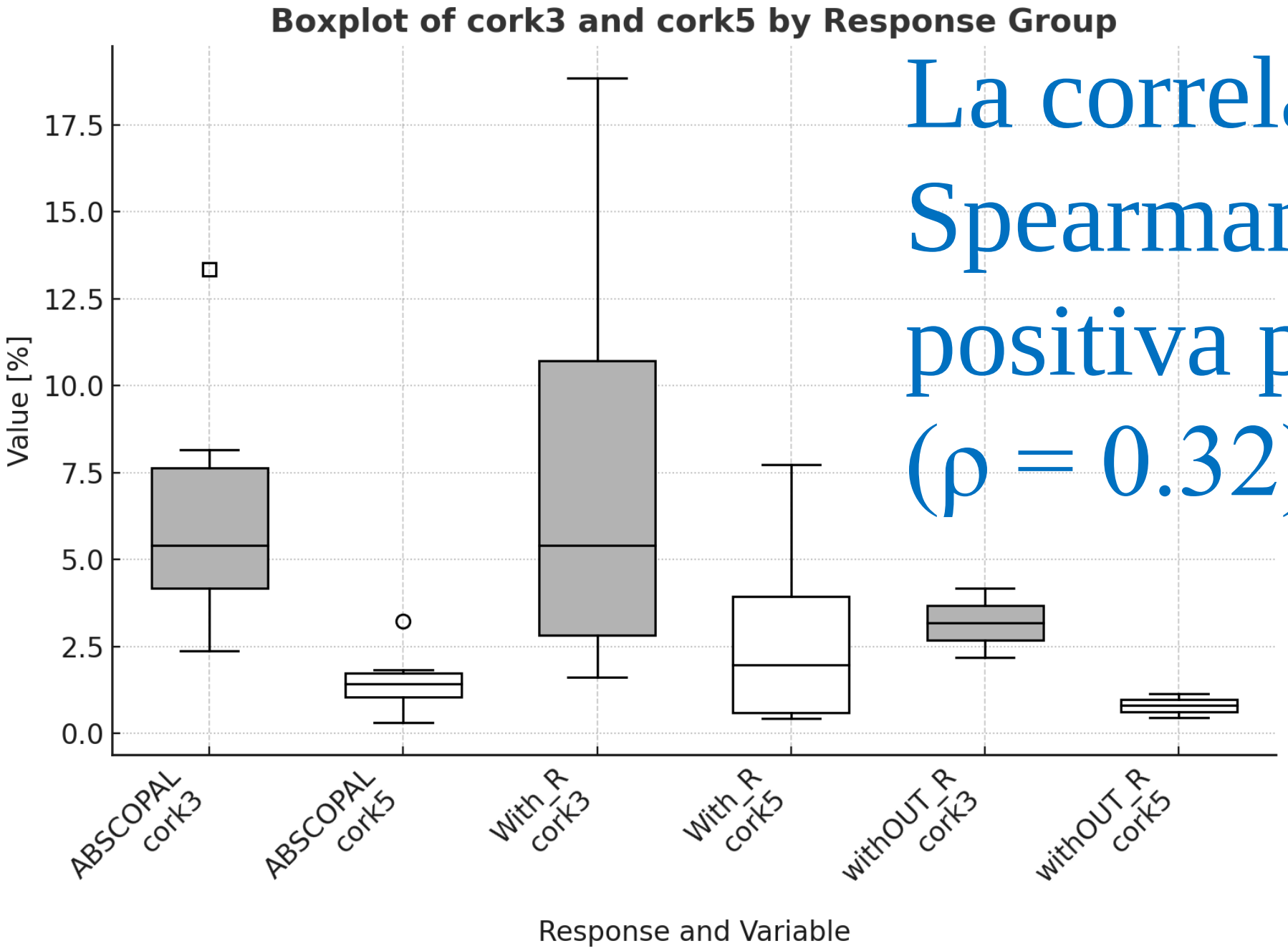
GREEDY POISSON ANISOTROPIC SAMPLING =

Helix+


TA 2,00 Br40 S3
Zoom: 439%
MPR 2.0 mm
62.62 mm
Desc. de la serie: PROSTATA 2,00 Br40 S3
2 - 116
Con pérdida (1:10)
47.53 mm
C
16.897 Gy
ISO
P
6496859
Contraste I.V. de Abdomen
Abd 1.0 Br40 3
24.12 mm
19/0
HOSPIT
16.83 mm

Dr. Aguilar


IV
ABSCOPAL
III
Desc. de la serie: PROSTATA 2,0
2 - 6
Con pérdida (1:9)
R
Con pérdida (1:10)
R
19/05/2025 07:0
HOSPITAL VIRGEN
Pos.: -3
EC
Zo



La correlación de Spearman fue positiva para **cork3** ($\rho = 0.32$) …

…indicando que

mayores volúmenes de tejido tumoral “frío”

por vértice

se asocian a mayor probabilidad de

respuesta sistémica

0680 - SFRT in the Clinic 2: Emerging Planning Concepts & International Experience (ID 41)

Session Type SFRT in the Clinic Track
Date Fri, 04.12.2026
Session Time 11:40 - 12:40
Room Auditorium II

SFRT Patients Treatments Results in China (ID 375)

Presenter Yuan Shuang Hu (China)
Lecture Time 11:40 - 12:00

New SFRT Planning Concepts: the HELIX Project and Patient Results (ID 376)

Presenter Santiago Velázquez-Miranda (Spain)
Lecture Time 12:00 - 12:20

Journal of
Personalized Medicine

MDPI

Review

Partially Ablative Radiotherapy for Bulky Tumors: A Narrative Review of a Developing Concept

Savino Cilla [1,*], Costanza Maria Donati [2], Milly Buwenge [2], Gabriella Macchia [3], Francesco Deodato [3,4], Silvia Cammelli [2,5] and Alessio Giuseppe Morganti [2,5]

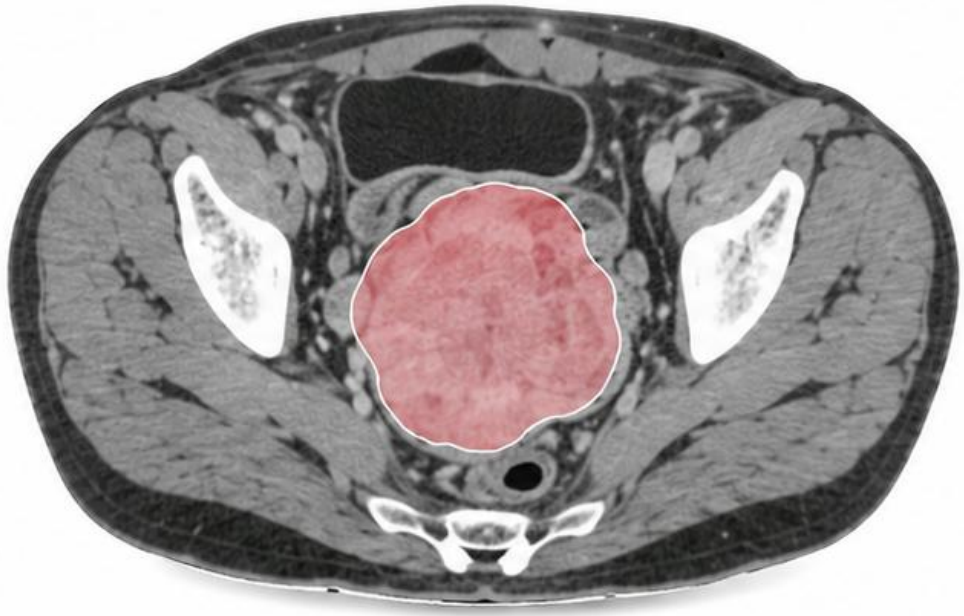
1 Medical Physics Unit, Responsible Research Hospital, 86100 Campobasso, Italy
2 Radiation Oncology Unit, Istituto di Ricovero e Cura a Carattere Scientifico Azienda Ospedaliero-Universitaria di Bologna, 40138 Bologna, Italy; milly.buwenge@unibo.it (M.B.); alessio.morganti2@unibo.it (A.G.M.)
3 Radiation Oncology Unit, Responsible Research Hospital, 86100 Campobasso, Italy; francesco.deodato@unicatt.it (F.D.)
4 Radiology Institute, Università Cattolica del Sacro Cuore, 00168 Roma, Italy
5 Department of Medical and Surgical Sciences, Alma Mater Studiorum University of Bologna, 40138 Bologna, Italy

9-10 ABRIL 2026 IV REUNIÓN NACIONAL MULTIDISCIPLINAR DE INNOVACIÓN EN CÁNCER MÁLAGA HOTEL EUROSTARS Organiza: Aedc Colaborador: quirónsalud Sec. técnica: EMIRAL

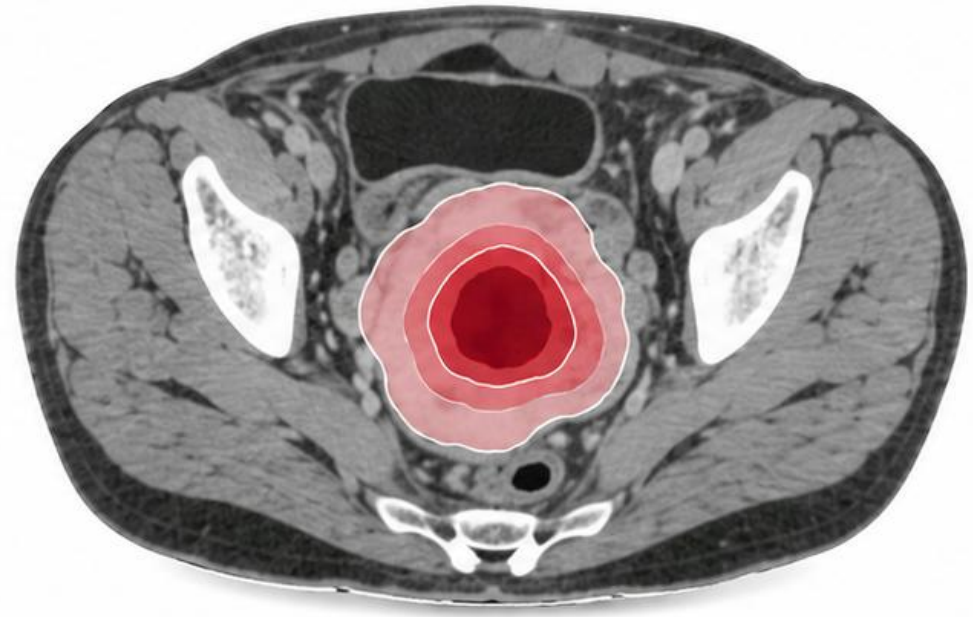
CORE Boost

Escalada intratumoral deliberada

Convencional



CORE Boost



Periferia tratada

Núcleo hiperirradiado

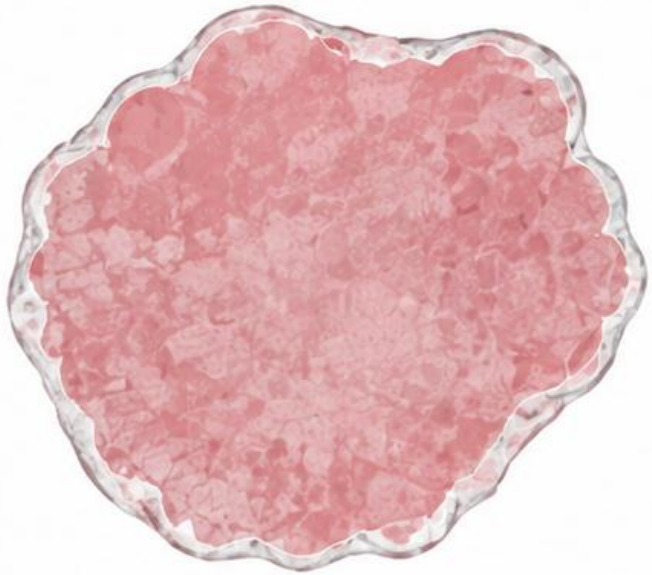
Heterogeneidad intencional

Wittenstein et al. *Strahlenther Onkol*, 2023

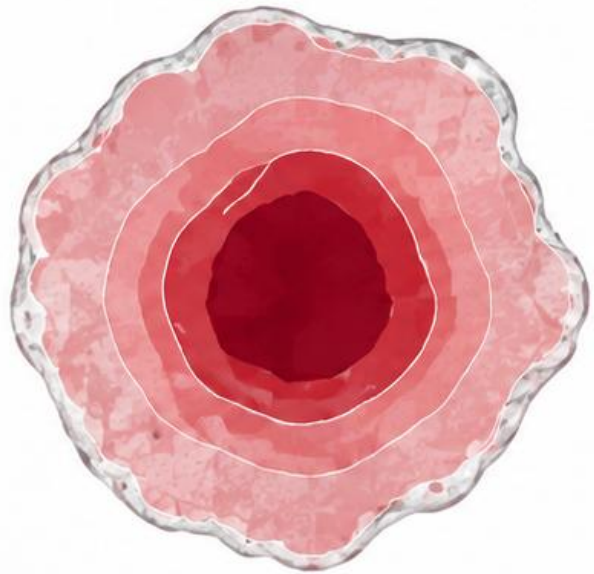
Idea central

El tumor no tiene por qué recibir la misma dosis en todas partes

Homogeneidad ciega



Heterogeneidad útil



- Más dosis donde importa
- Menos castigo periférico
- Puente hacia SFRT

CORE Boost es una forma clínica de pensar la distribución intratumoral de dosis.

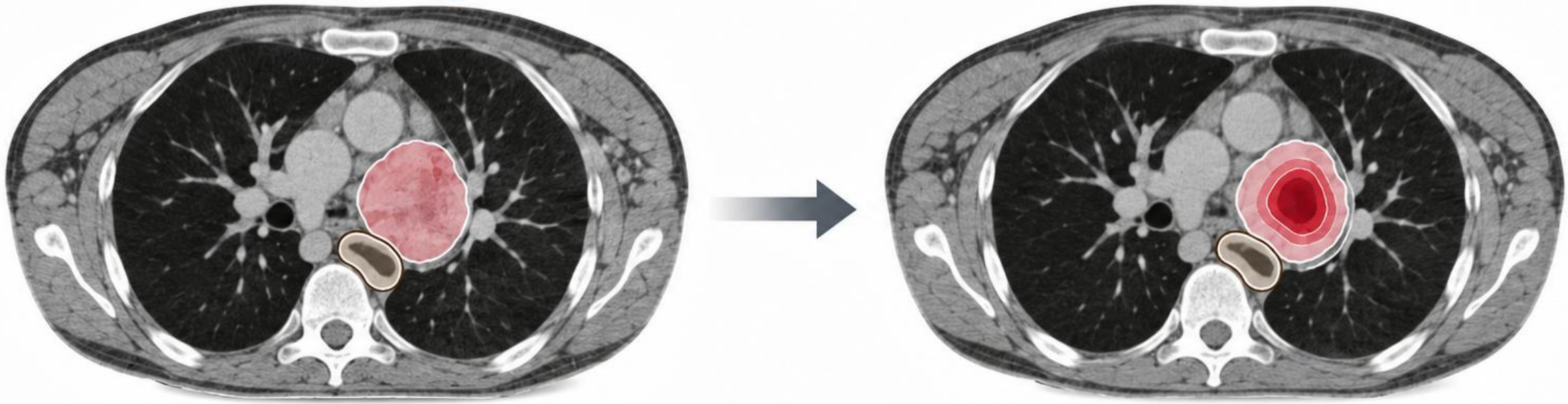
Geometría primero; biología después.

Ventaja dosimétrica

Cuando la periferia está limitada por un OAR

SBRT homogénea

Core Boost



Periferia limitada | Esófago (OAR) | Núcleo intensificado | TCP ↑ (modelo)

35 Gy periferia · 60 Gy núcleo

La heterogeneidad intencional puede aumentar el control sin violar restricciones críticas.

Suyusal et al. *Med Dosim*, 2026

Estudio original

Tumor Core Boost Study

1

21 pacientes

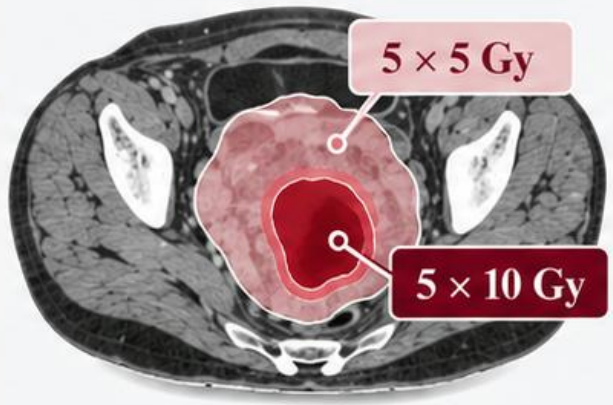
Tumores > 4 cm

2

Esquema 1

5 × 5 Gy

(tumor completo)

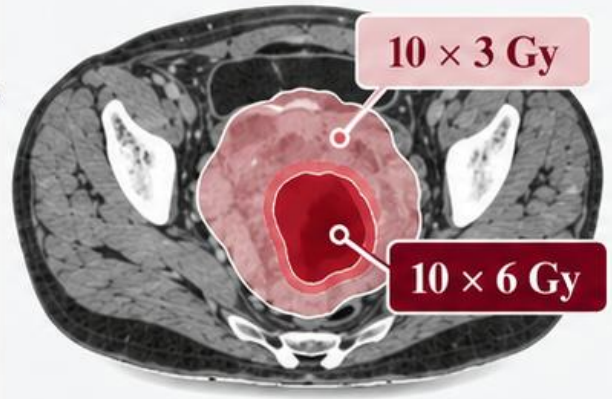


3

Esquema 2

10 × 3 Gy

(tumor completo)



4

Viable

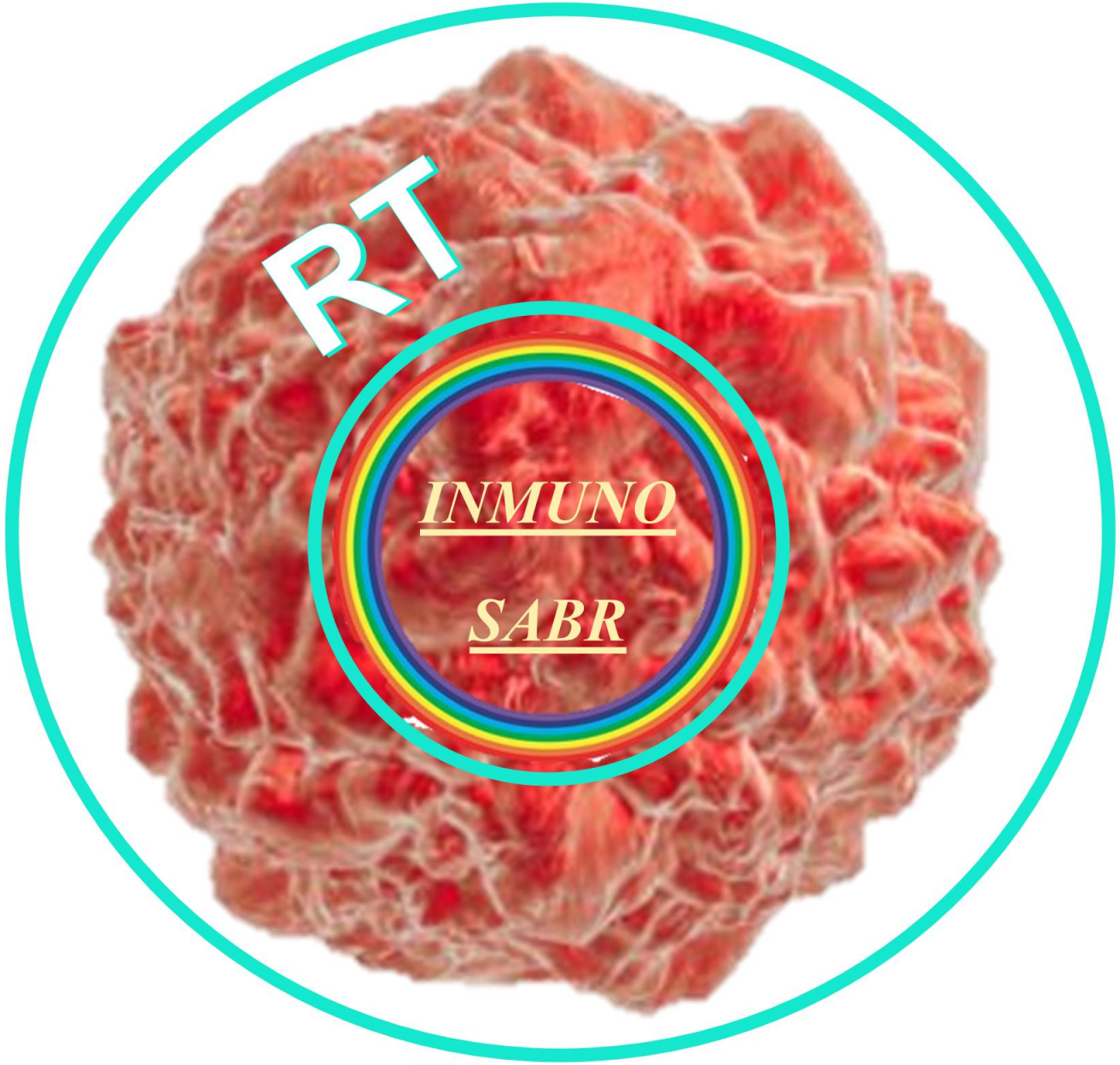
Bien tolerado

Seguimiento agudo: 42 días

Escalar el núcleo tumoral fue factible sin toxicidad aguda limitante.

Wittenstein et al. *Strahlenther Onkol*, 2023

PABR



Strahlenther Onkol (2023) 199:258–267
https://doi.org/10.1007/s00066-022-01976-5

ORIGINAL ARTICLE

The tumor core boost study: A feasibility study of radical dose escalation to the central part of large tumors with an integrated boost in the palliative treatment setting

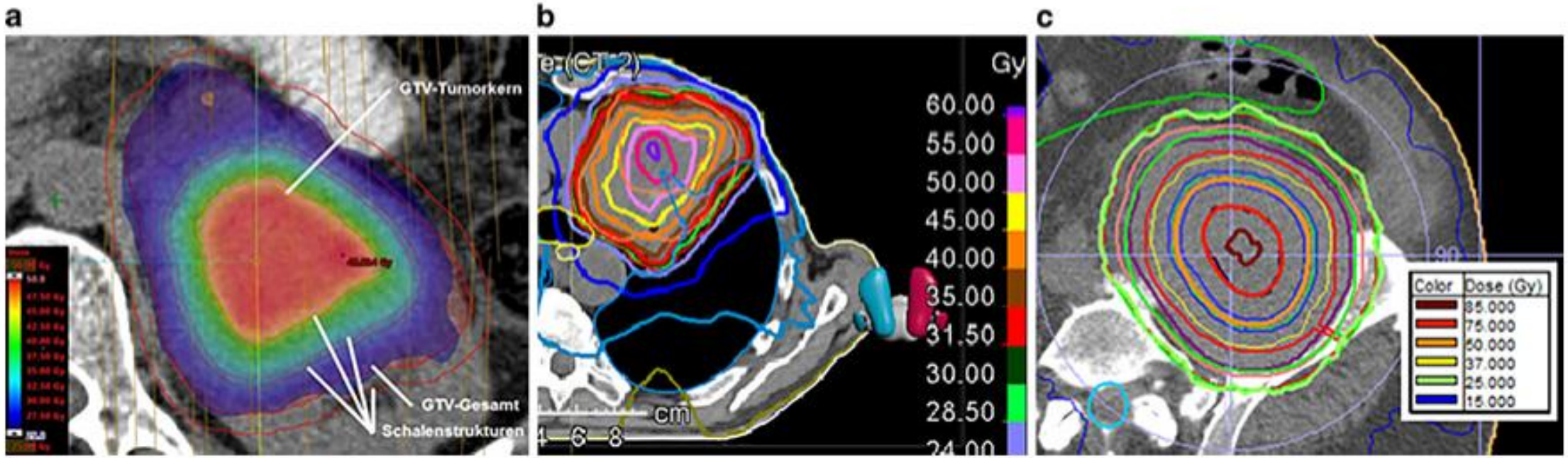
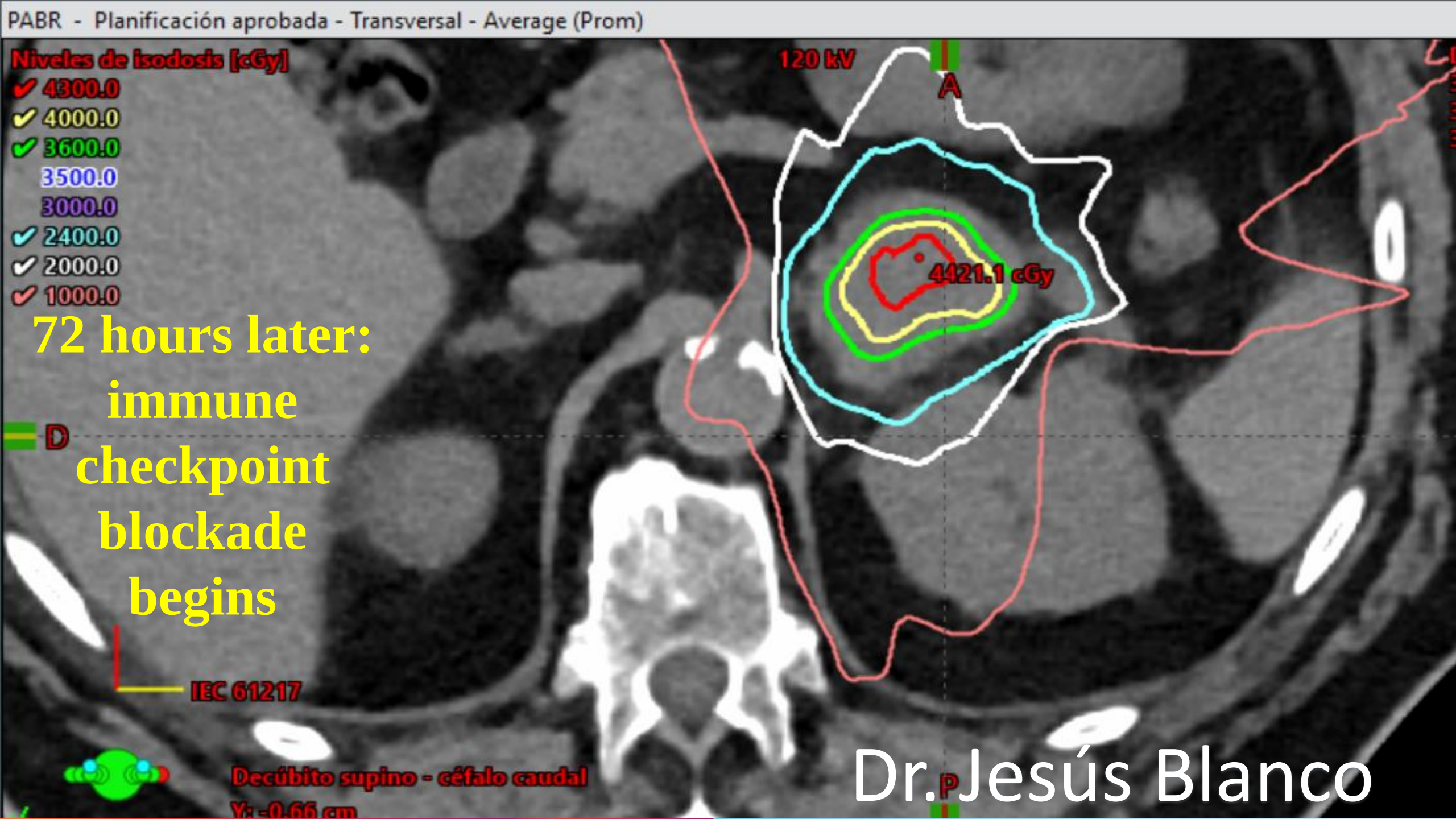


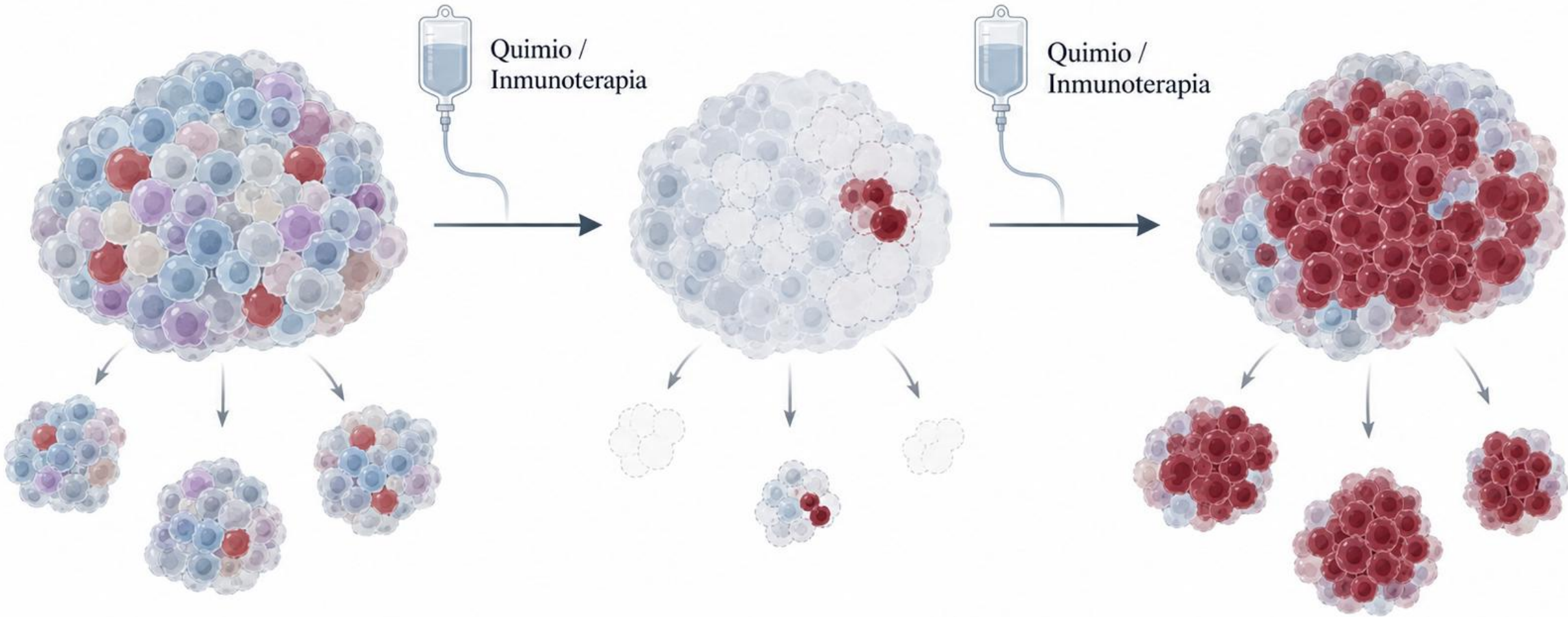
Fig. 2 Depiction of dose distribution in axial view of three different tumor core boost plans at the three different study sites with three different planning platforms: **a** Eclipse (Varian Medical Systems, Palo Alto, CA, USA), **b** RayStation (RaySearch, Stockholm, Sweden), **c** Monaco (Elekta, Stockholm, Sweden)

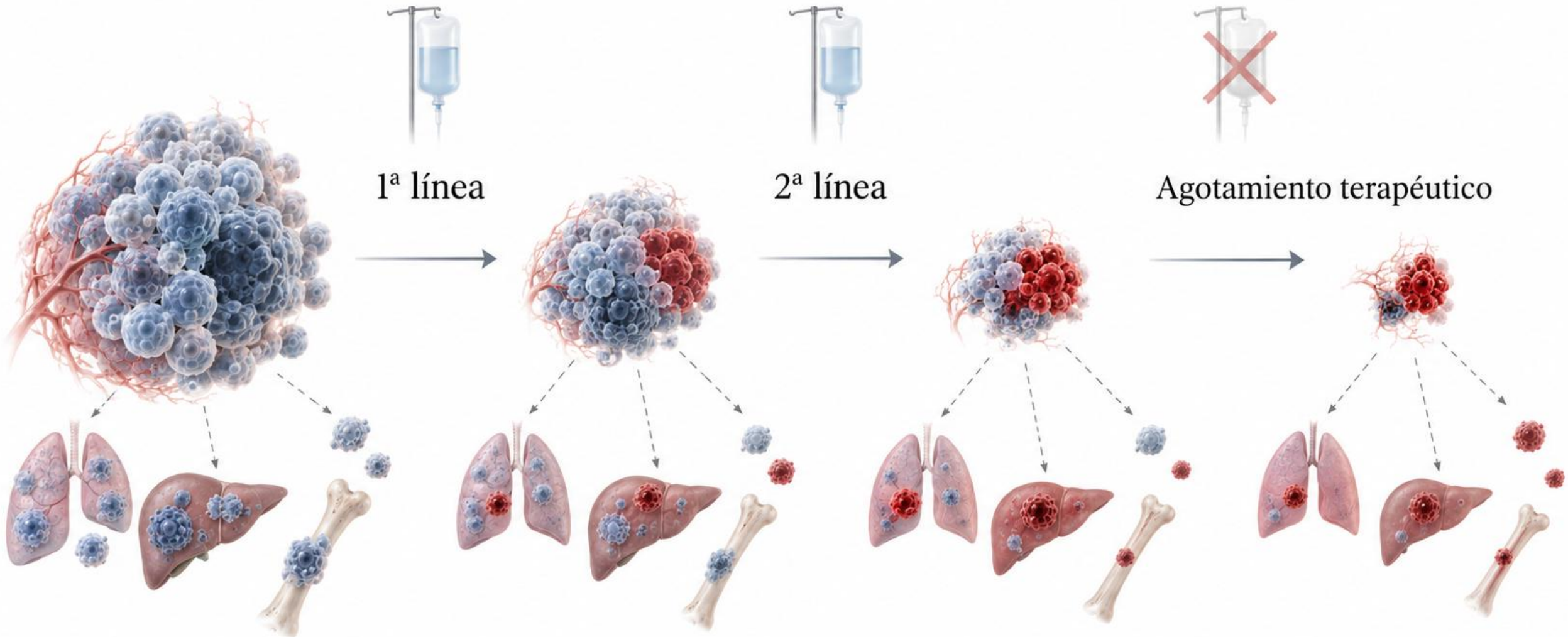

PABR - Planificación aprobada - Transversal - Average (Prom)
Niveles de isodosis [cGy]
4300.0
4000.0
3600.0
3500.0
3000.0
2400.0
2000.0
1000.0
120 kV
A
4421.1 cGy
72 hours later: immune checkpoint blockade begins
D
IEC 61217
Decúbito supino - céfalo caudal
P
Dr. Jesús Blanco

Agotamiento terapéutico prematuro

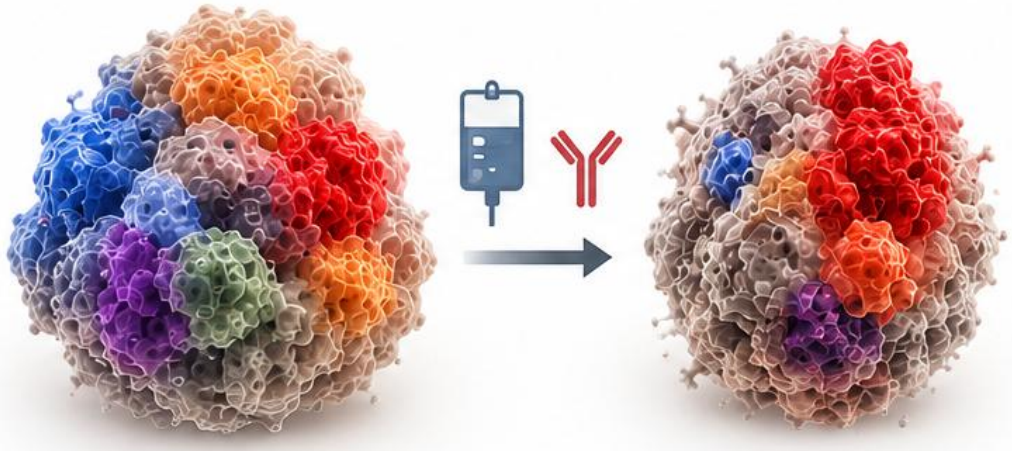
Oportunidad de rescate con SBRT / SFRT

Selección de clones resistentes

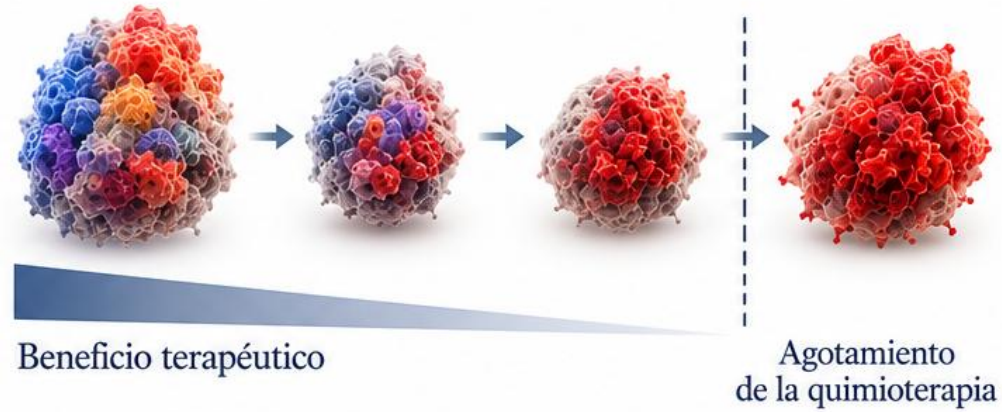



1ª línea
2ª línea
Agotamiento terapéutico

1. Quimio / inmunoterapia

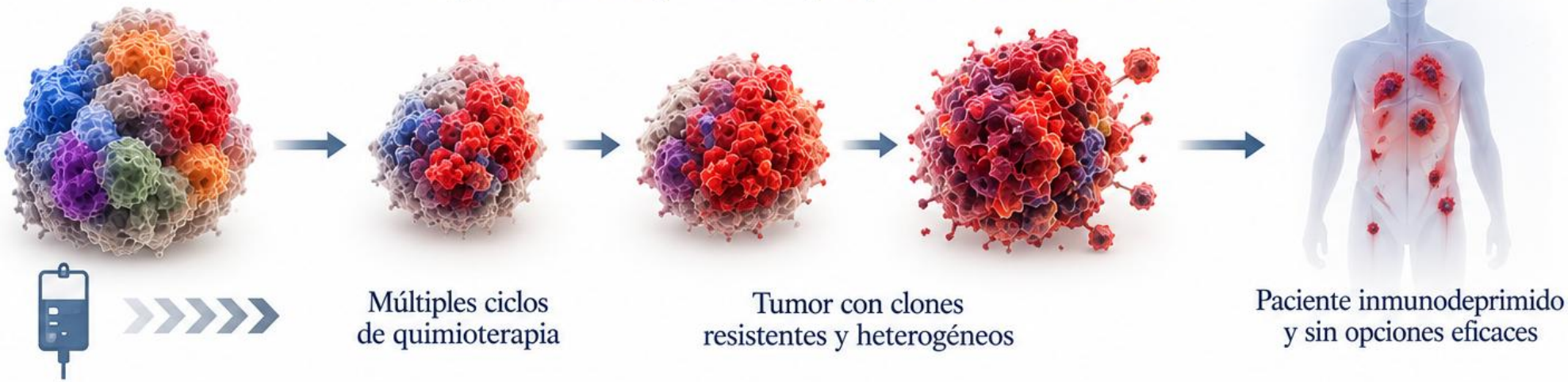


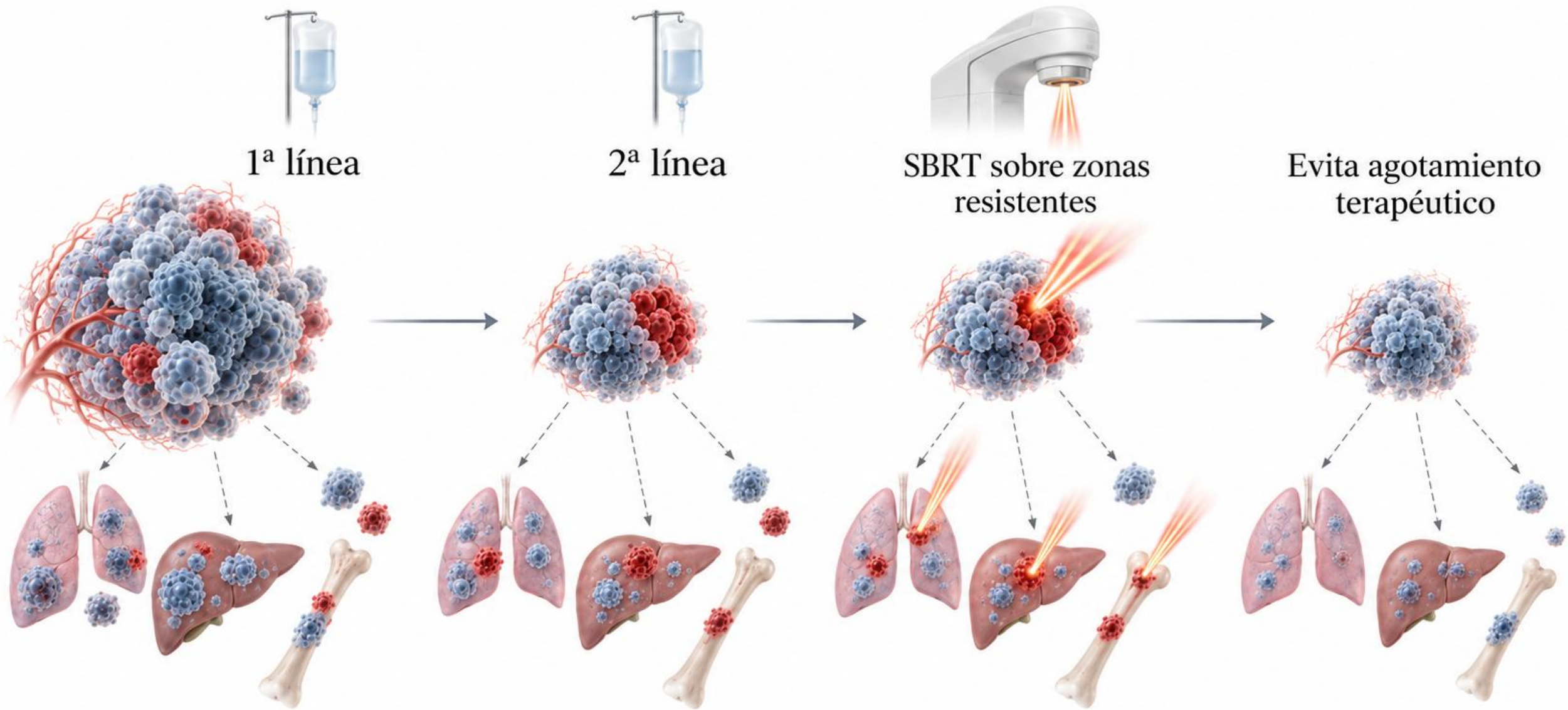
2. Agotamiento terapéutico



4. Estrategia incorrecta

Agotar toda la quimioterapia y acudir tarde a la RT

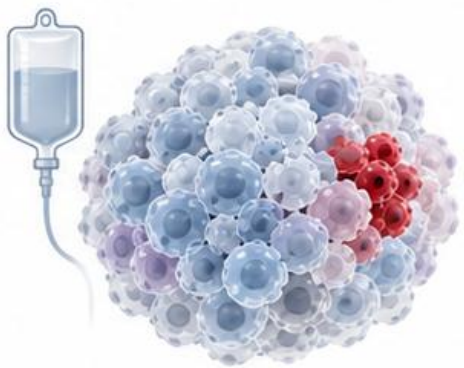



1ª línea
2ª línea
SBRT sobre zonas resistentes
Evita agotamiento terapéutico

Agotamiento terapéutico prematuro

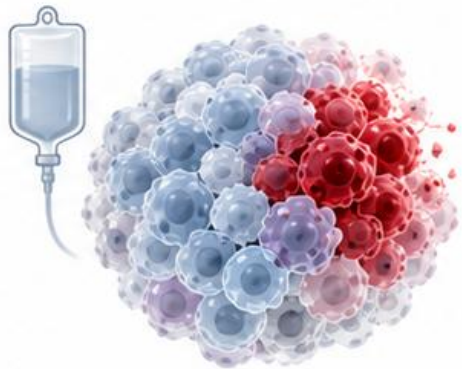
Oportunidad de rescate con SBRT / SFRT

Tratamiento sistémico activo



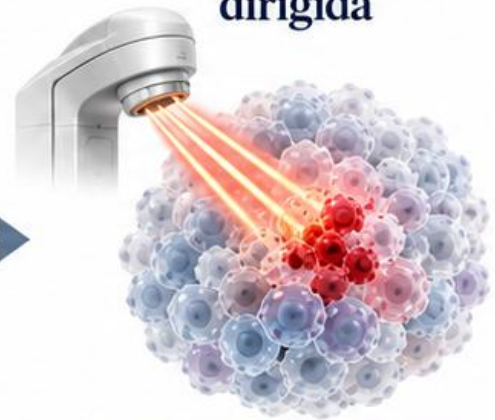
Respuesta global con clones resistentes incipientes.

Oligoprogresión focal



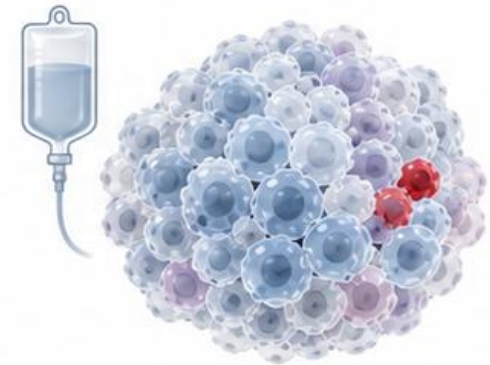
Progresión limitada en uno o pocos focos.

SBRT / SFRT dirigida



Ablación del foco resistente con SBRT / SFRT.

Prolongación del beneficio sistémico



Control de la enfermedad y preservación de la línea sistémica.

Tratar precozmente la oligoprogresión puede retrasar el cambio de línea sistémica.

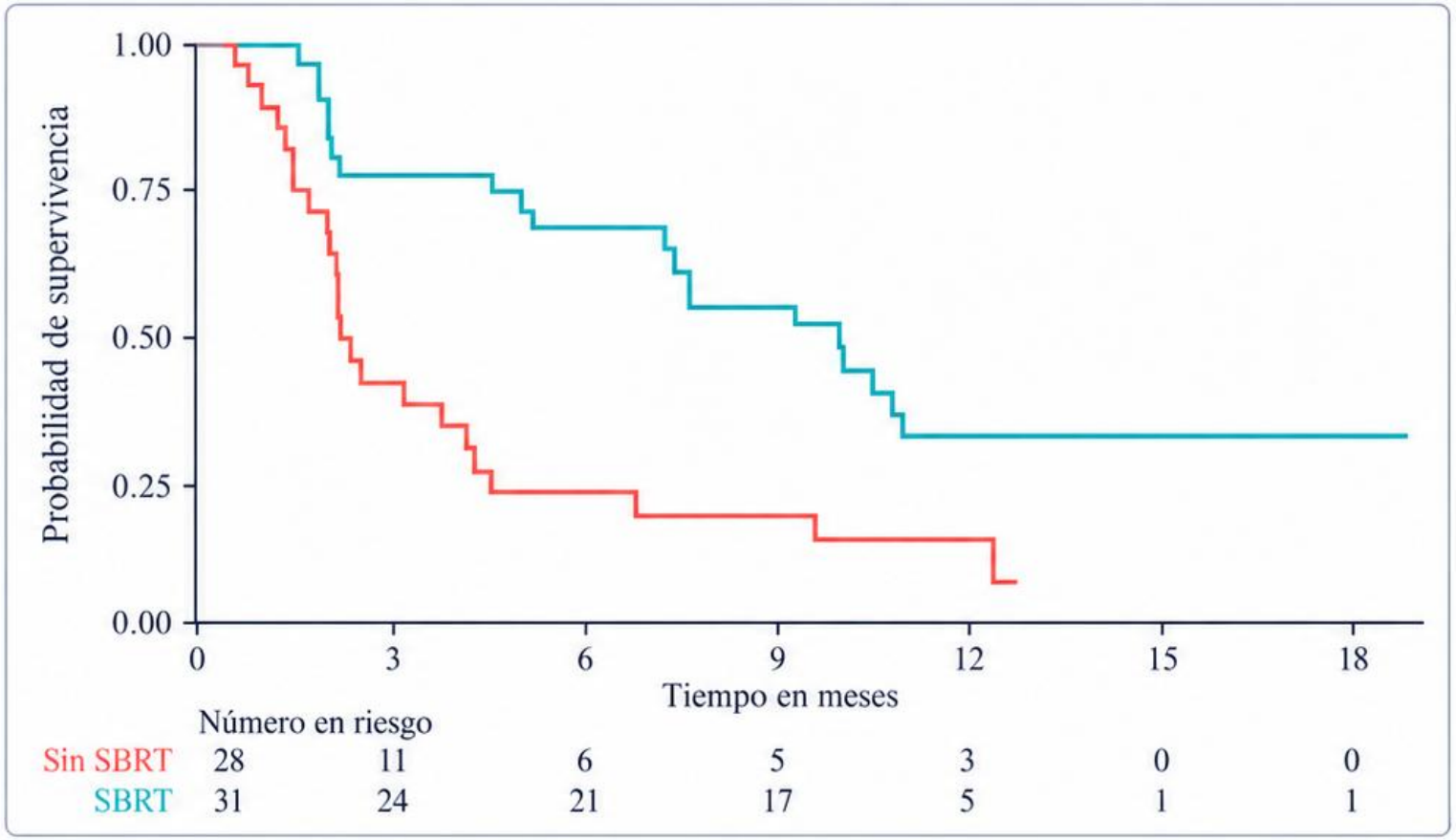
Bibliografía clave

1. Weickhardt AJ, Scheier B, Burke JM, et al. Local ablative therapy of oligoprogressive disease prolongs disease control by tyrosine kinase inhibitors in oncogene-addicted non-small-cell lung cancer. *J Thorac Oncol*. 2012;7(12):1807-1814.
2. Tsai CJ, Yang JT, Shaverdian N, et al. Standard-of-care systemic therapy with or without stereotactic body radiotherapy in patients with oligoprogressive breast cancer or non-small-cell lung cancer (CURB oligoprogression): an open-label, randomised, controlled, phase 2 study. *Lancet*. 2024;403(10422):171-182.
3. Huet C, Basse C, Knetki-Wroblewska M, et al. Outcomes Analysis of Patients Receiving Local Ablative Therapy for Oligoprogressive Metastatic NSCLC Under First-Line Immunotherapy. *Clin Lung Cancer*. 2024;25(8):e402-e410.e3.

La evidencia clínica disponible se apoya principalmente en SBRT.

Agotamiento terapéutico prematuro

Oportunidad de rescate con SBRT / SFRT



La mediana de supervivencia libre de progresión aumentó 4 veces en pacientes con cáncer de pulmón no microcítico tratados con SBRT

Datos del ensayo CURB

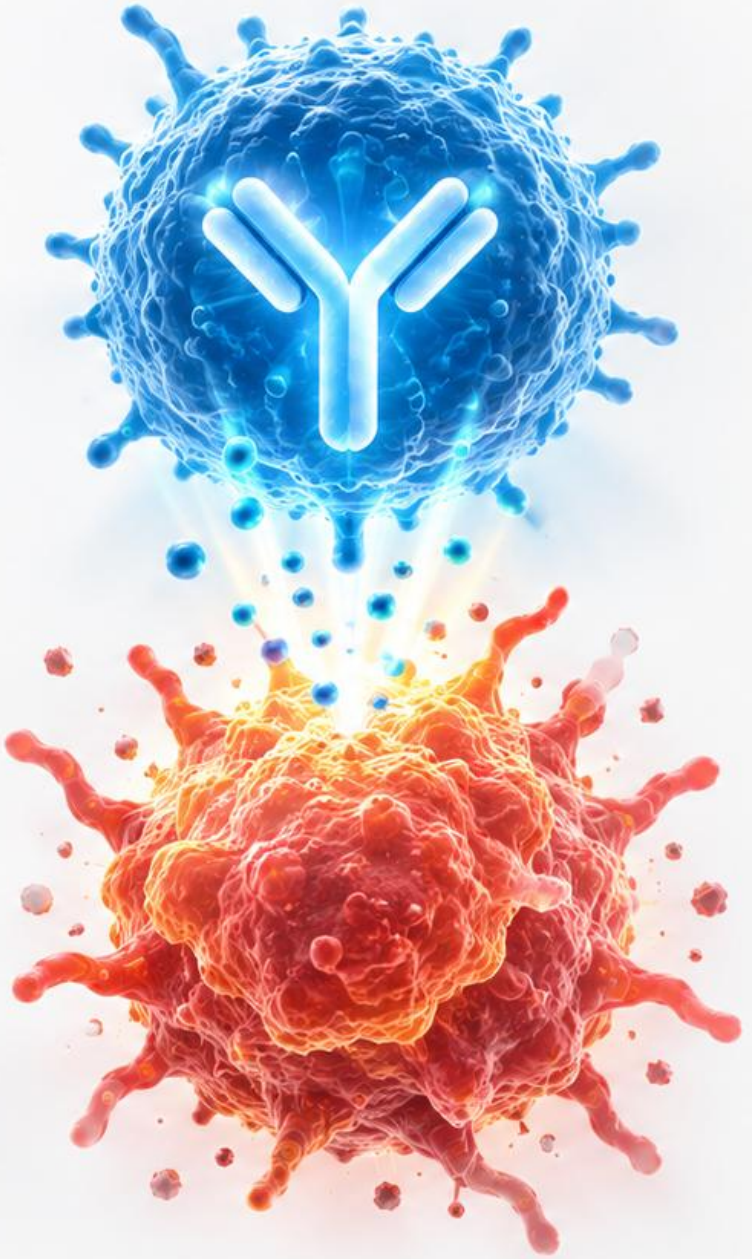
1. Tsai CJ, Yang JT, Shaverdian N, et al. Standard-of-care systemic therapy with or without stereotactic body radiotherapy in patients with oligoprogressive breast cancer or non-small-cell lung cancer (CURB oligoprogression): an open-label, randomised, controlled, phase 2 study. *Lancet*. 2024;403(10422):171–182.
2. Huet C, Basse C, Knetki-Wróblewska M, et al. Outcomes Analysis of Patients Receiving Local Ablative Therapy for Oligoprogressive Metastatic NSCLC Under First-Line Immunotherapy. *Clin Lung Cancer*. 2024;25(8):e402–e410.e3.

¿Qué ocurre con RIE + IO?

Despertador inmunológico

+

Potenciador inmunológico

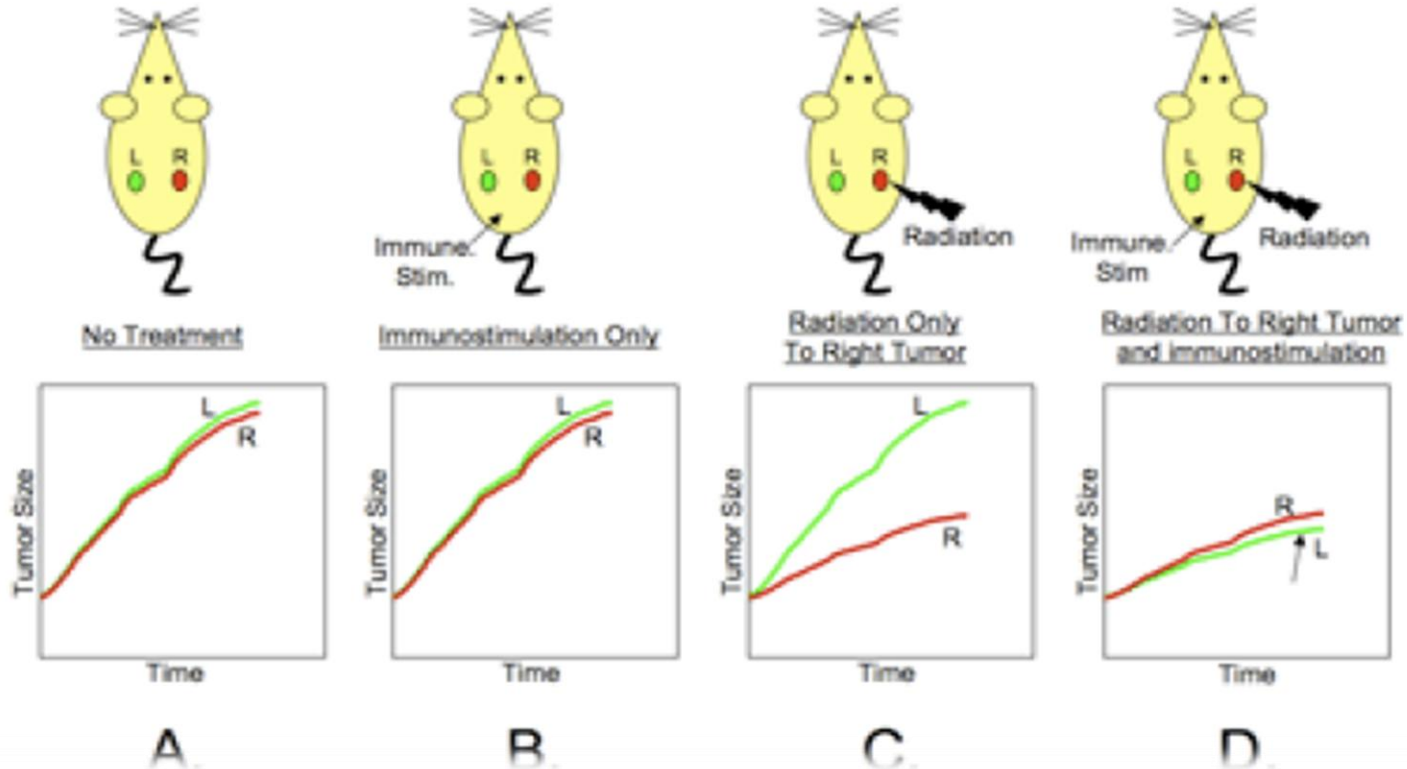


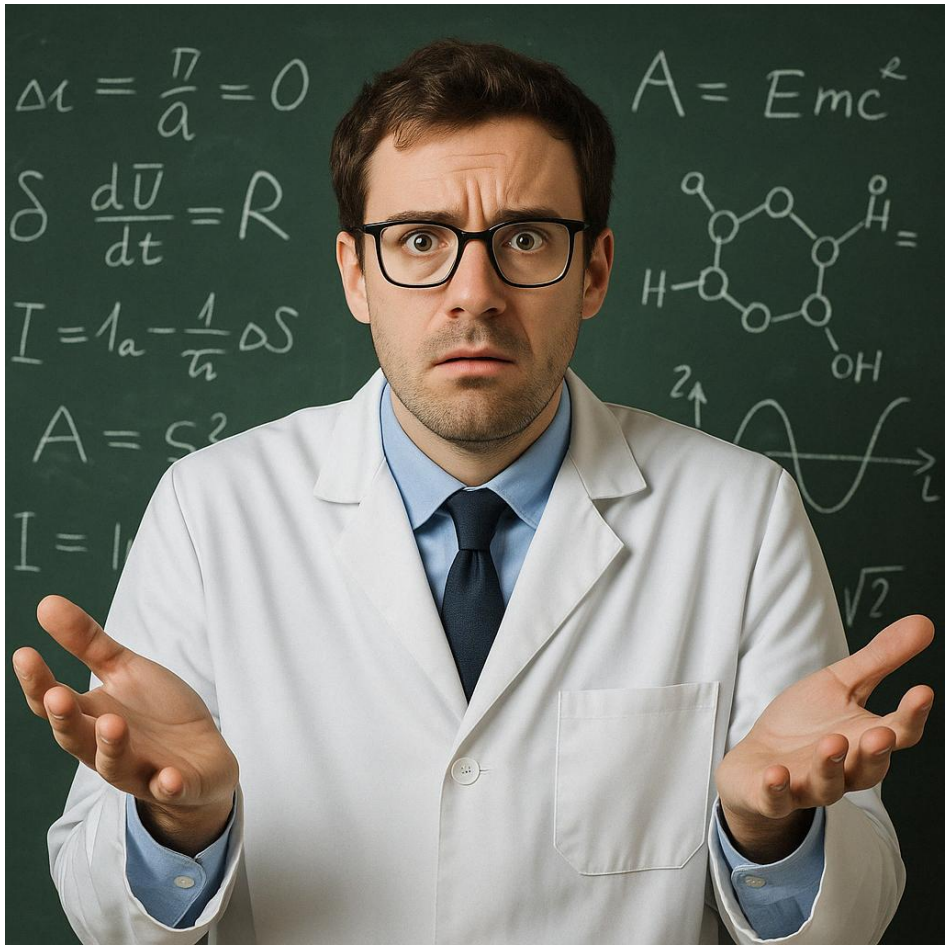
BIOLOGY CONTRIBUTION

IONIZING RADIATION INHIBITION OF DISTANT UNTREATED TUMORS (ABSCOPAL EFFECT) IS IMMUNE MEDIATED

SANDRA DEMARIA, M.D.,* BRUCE NG, M.S.,† MARY LOUISE DEVITT, A.A.S.,‡ JAMES S. BABB, PH.D.,§
NORIKO KAWASHIMA, M.S.,* LEONARD LIEBES, PH.D.,† AND SILVIA C. FORMENTI, M.D.‡

Fms-like tyrosine kinase receptor 3 ligand (Flt3-L): factor de crecimiento que estimula la producción de células dendríticas (DC)



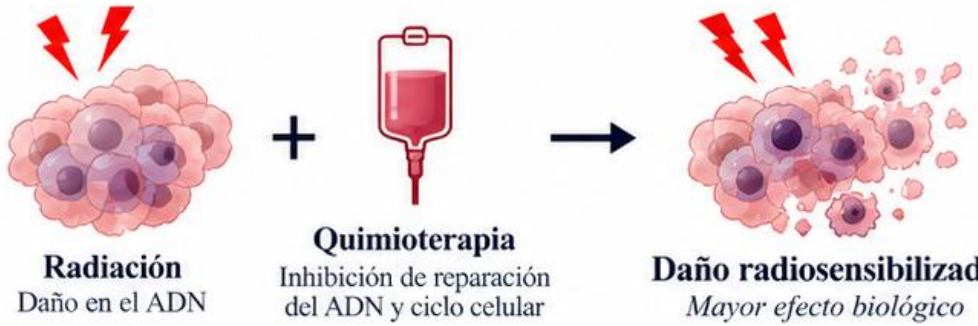


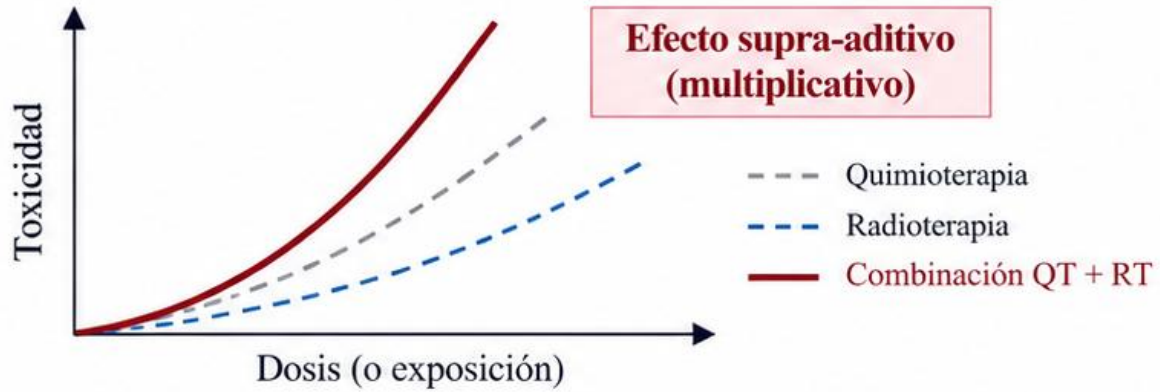
¿Por qué este enfoque terapéutico no está más difundido?

Toxicidad de las combinaciones con radioterapia

Quimioterapia + Radioterapia

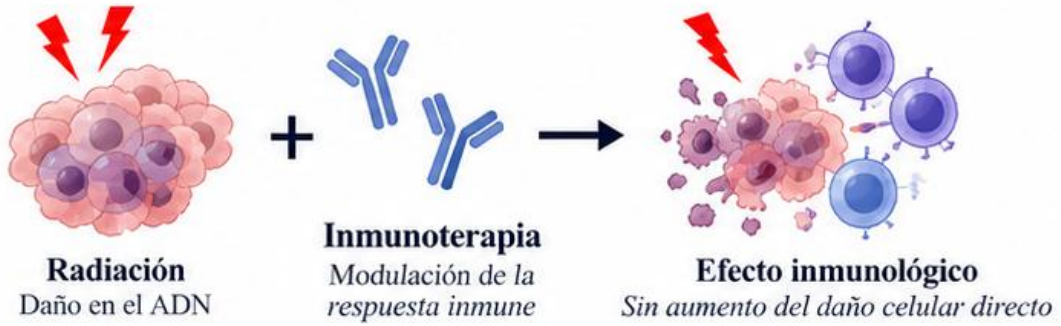
Radio-sensibilización celular

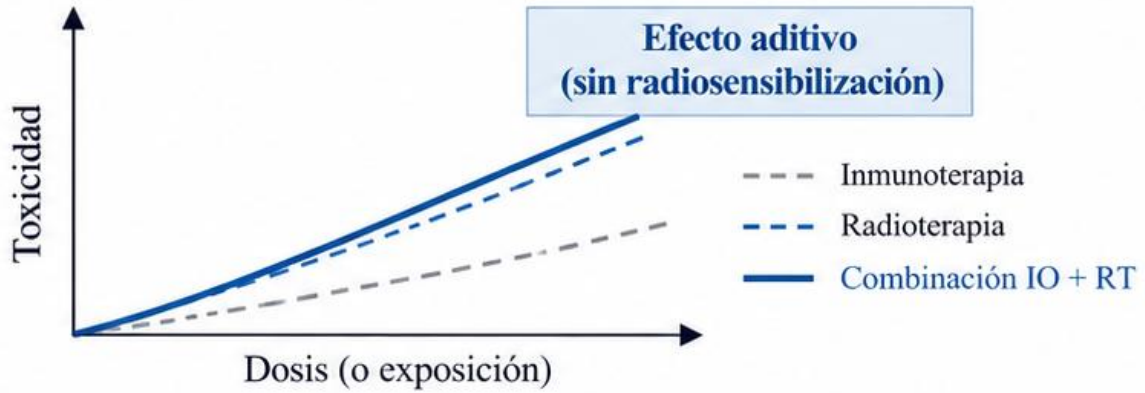




Inmunoterapia + Radioterapia

Sin radiosensibilización celular





La quimioterapia puede radiosensibilizar las células normales, aumentando de forma **multiplicativa** la **toxicidad**, mientras que la inmunoterapia no produce radiosensibilización celular y sus toxicidades se comportan de forma **aditiva**.

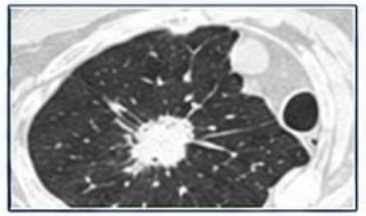
van Aken ES et al. ESMO–ESTRO consensus statements on the *safety of combining radiotherapy with immune checkpoint inhibitors, VEGF(R) inhibitors, or multitargeted tyrosine kinase inhibitors. Ann Oncol. 2023;34(6);560–577.*

Indicaciones orientativas de SABR / Lattice / PATHY



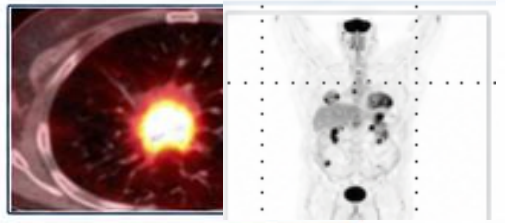
SABR

Lesiones aisladas



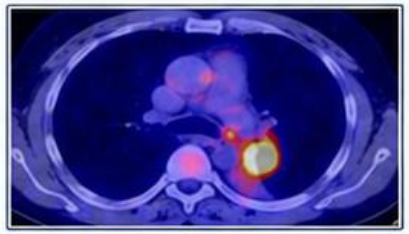
¡SABR

Lesiones hiperactivas con metástasis



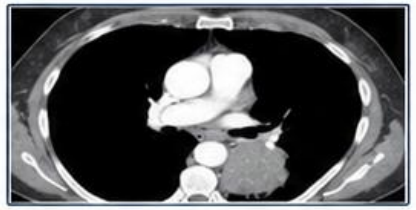
IG-Lattice

Lesiones con necrosis, reirradiación
o proximidad a órganos críticos



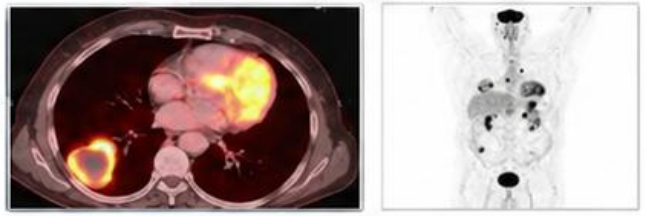
Lattice

Lesiones bulky



PATHY

Lesiones bulky necróticas metastásicas



Referencias

1. Iori F, et al. Lattice Radiation Therapy in clinical practice: A systematic review. *Clin Transl Radiat Oncol.* 2022;39:100569.
2. Tubin S. A Partial Tumor Irradiation Approach for Complex Bulky Disease. *Semin Radiat Oncol.* 2024;34(3):323-336.

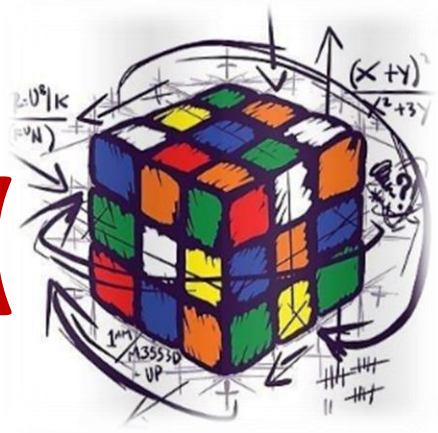
	RT	SIP	Lattice	Single Fraction	SBRT	PATHY	iSABR	FLASH	protones
Diana terapéutica	M_1	M_1-M_3	M_3	DAÑO VASCULAR	M_1-M_3	**M_3**	M_1-M_3	M_1	M_1
Tipo Muerte celular	Auto Fagia	AutoF Rotu-M	Estrés,Ro tu-M	Abla ción	Rotu-M	Estrés	Rotu-M	Abla ción	Auto Fagia
Dependencia muerte celular	indep	dep	dep	indep	dep	dep	dep	indep	indep
Ventana terapéutica	distrBD	distri-D, ∇D	∇D	∇D	∇D	∇D	∇D	tasa	distrBD
R.Inmuno	↓	↔	↑	↔	↑↑	↑	↑↑↑↑	↑↑	↓
Extensión efecto	Loco-R	Loco-R, sistémico	Sistémica	Local	Sistémica	Sistémica	Sistémica	Local	Loco-R

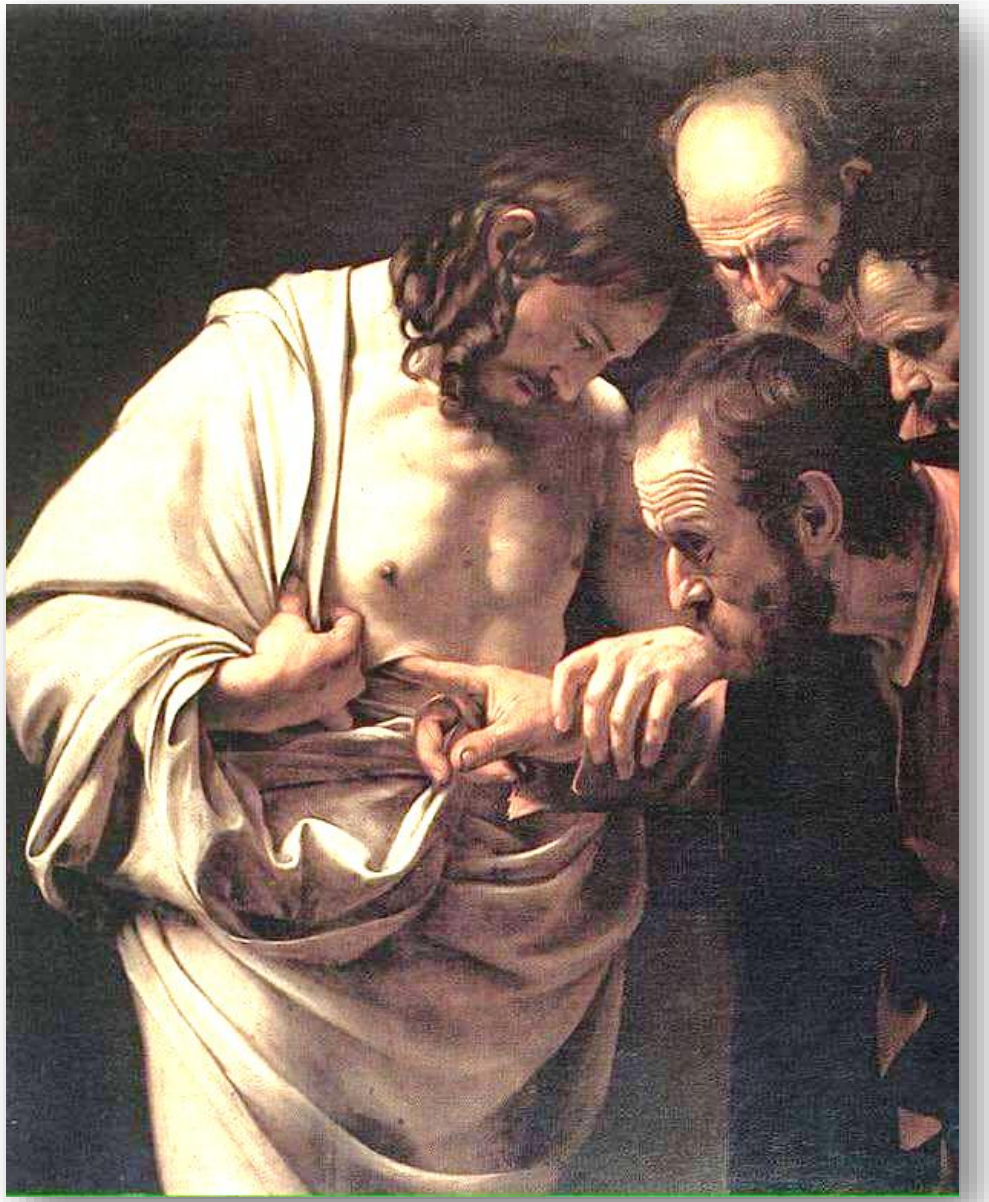
Beyond Dogma: Breaking the Barriers of Conventional Thinking

Instead of

D/d () → $\rho_c=0$

better

Dbio( **)→ ΔInmuno→$\rho_c=0$**



Cuando una cosa es nueva, la gente dice:

"No es verdad"

Más tarde, cuando su verdad se vuelve obvia, dicen:

"No es importante"

Finalmente, cuando su importancia no puede negarse, dicen:

”No es nuevo”

-William James-