IORT of brain metastases

History, challenges and perspectives

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The roots of RT

Wikipedia

Wilhelm Conrad Röntgen

1895 First description of x-rays

Wikipedia

Diagnostic X-rays

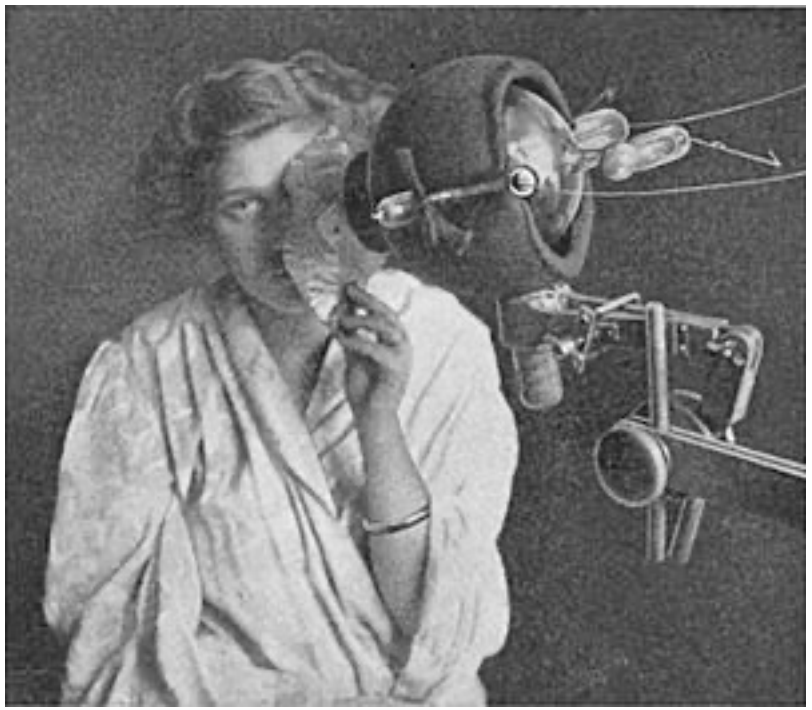
Wikipedia

Therapeutic X-rays

The roots of RT

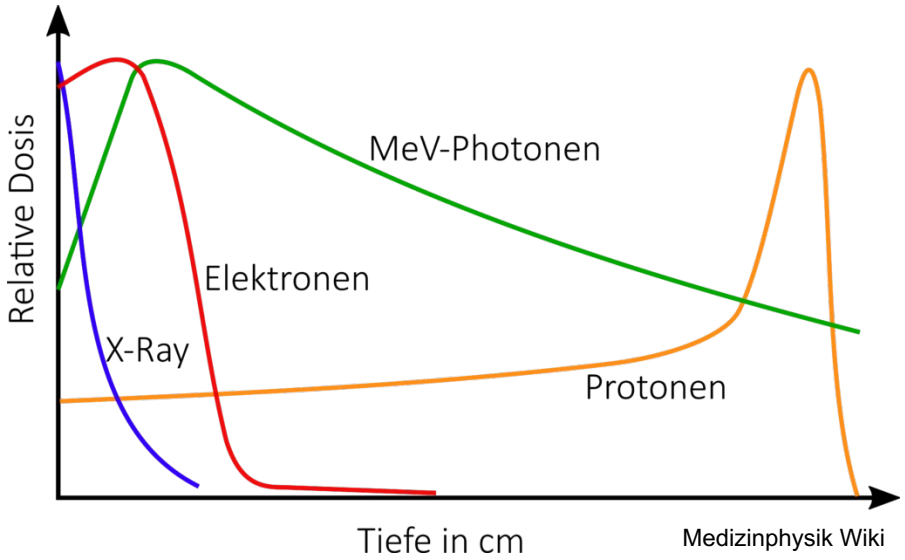
Wikipedia

Wilhelm Conrad Röntgen



Wikipedia

1915, X-ray RT of epithelioma
50-150 keV



The roots of RT

Wikipedia

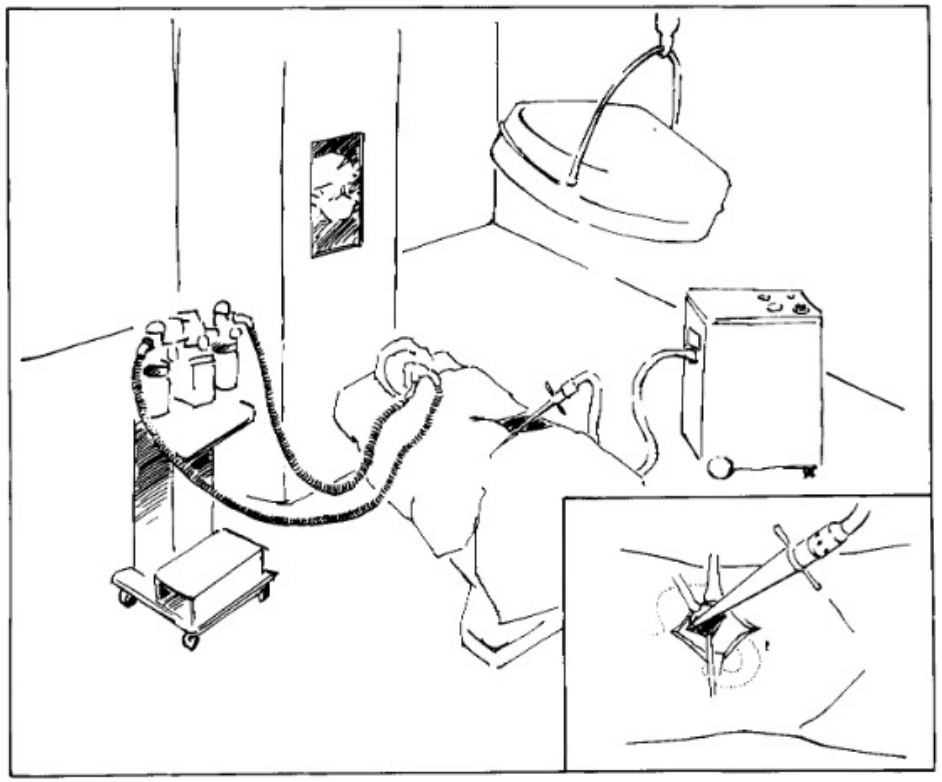
Marie Curie

1897 First description of radioactivity

Wikipedia

Radium tube therapy, 1905

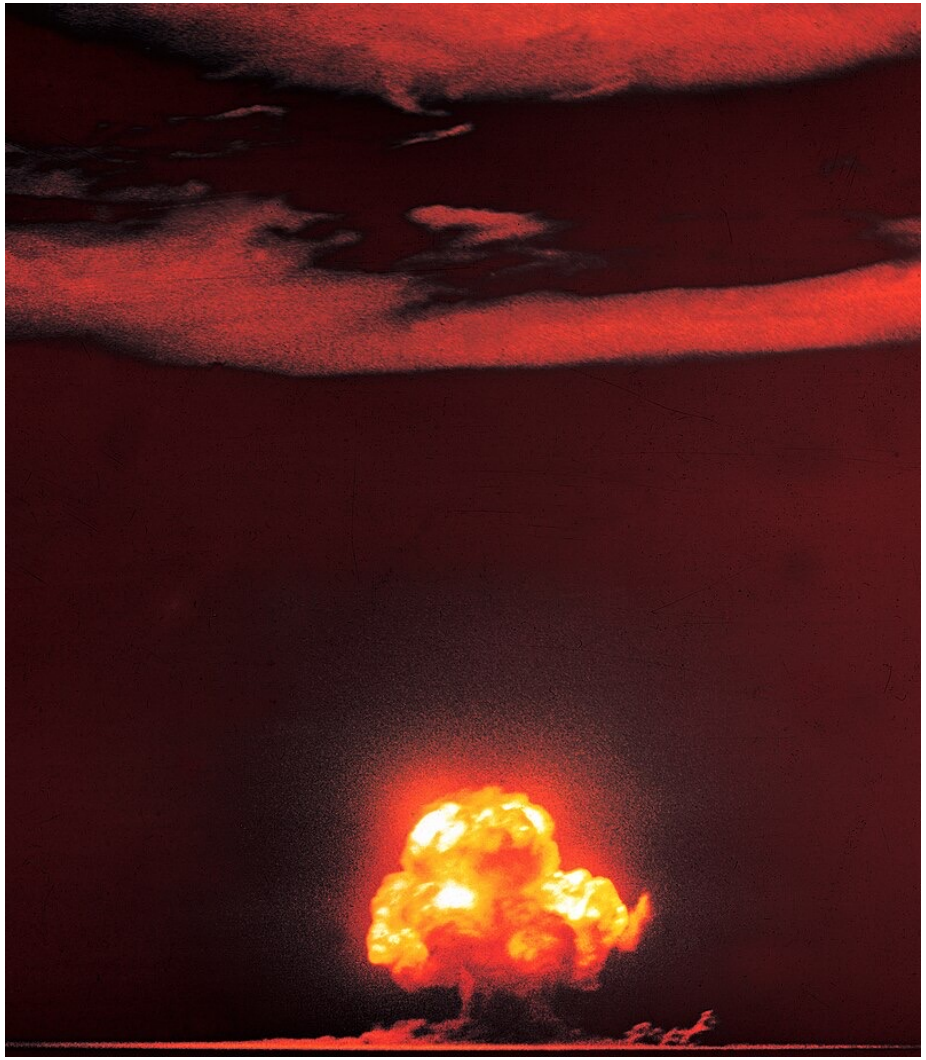
The roots of RT



Intraoperative contact roentgen therapy, 1940
Hoekstra et al., 1987

1906	First IORTs with low-energy X-rays
1930	IORT for abdominal and bladder cancer
1960s	Introduction of MV IORT
1970s	First brain tumor IORTs

The change of a paradigm



Manhattan Project

Wikipedia

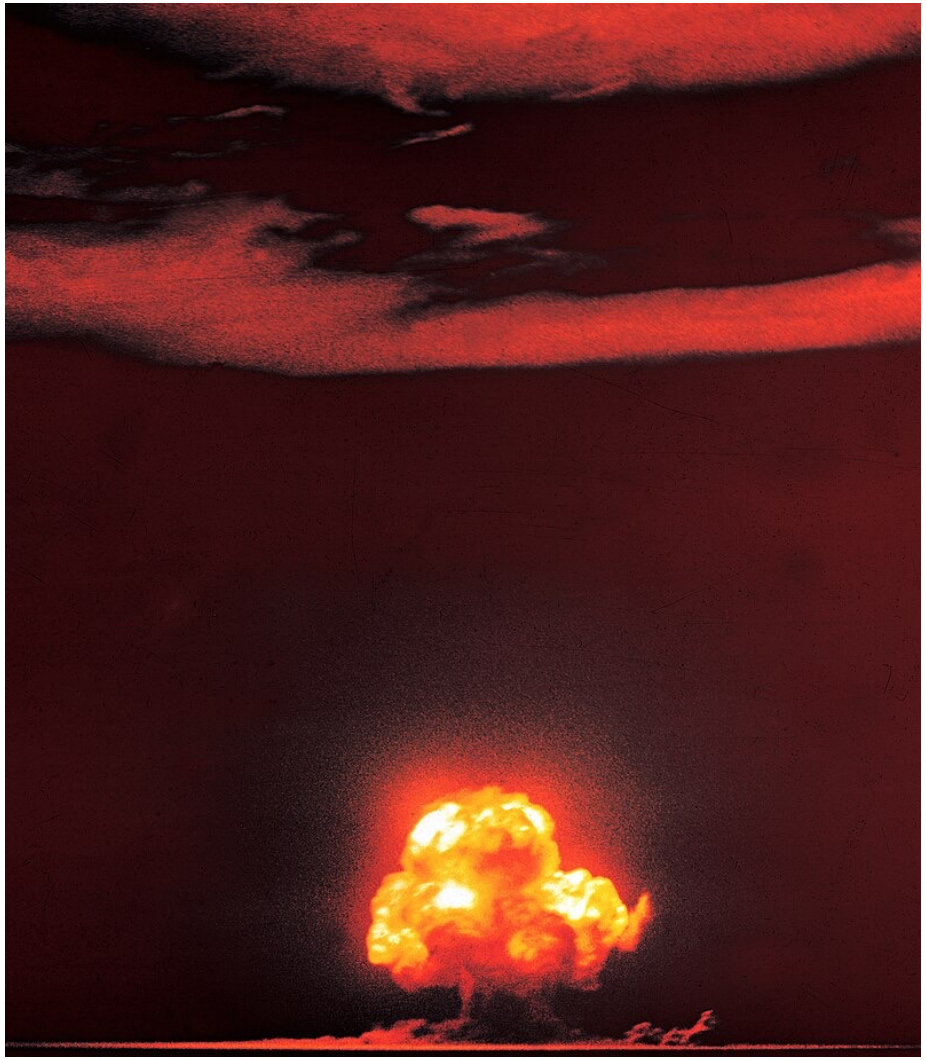
1950s Nuclear reactors producing artificial radioisotopes for RT

→ Cobalt-60

Wikipedia

Cobalt-60 linear accelerator

The change of a paradigm



Wikipedia

Manhattan Project

1960s Ascent of LINACs

Wikipedia

First US patient treated with LINAC RT in 1957

The 21st century

Automation

Digitalization

Artificial Intelligence

The 21st century

IMRT

IGRT

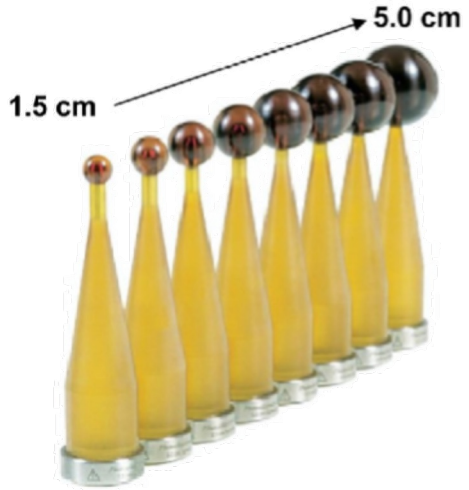
Stereotactic RT

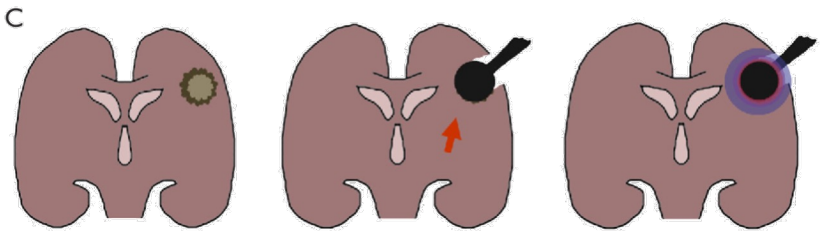
Artificial Intelligence

The alternative: IORT

INTRABEAM® (Carl Zeiss Meditech)

Low-energy X-rays (50 kV, 40 mA)
Spherical applicators (polyetherimid)

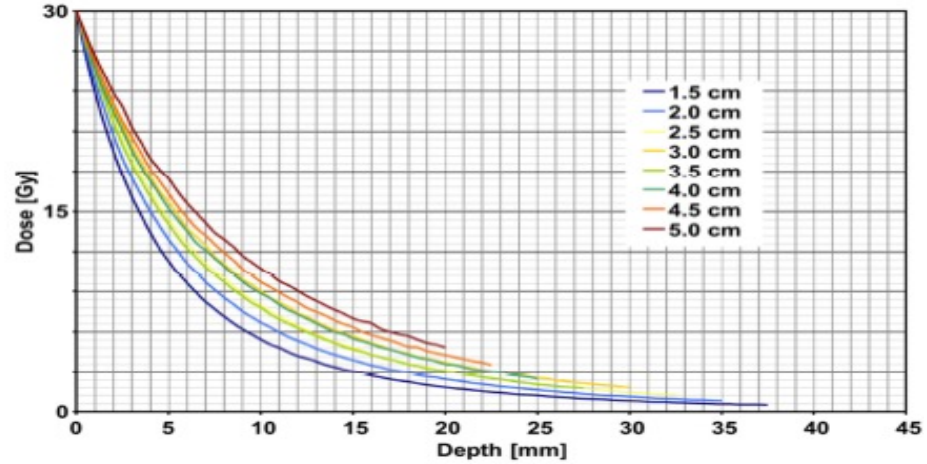




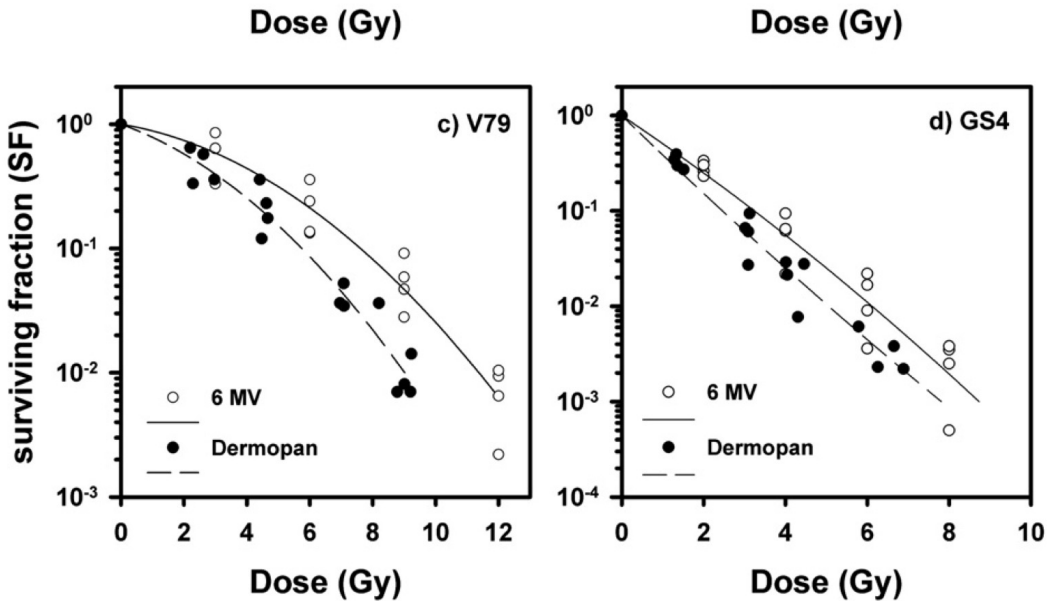
RT time 10-45 min depending on dose and applicator size

The alternative: IORT

INTRABEAM® (Carl Zeiss Meditech)



Steep dose gradient



Higher RBE

Vaidya et al. Lancet 2014
Vaidya et al. N Engl J Med 2013
Vaidya et al. Lancet 2010
Belletti et al. Clin Cancer Res 2008
Karapurakal et al. Int J Radiat Oncol Biol Phys. 2006
Liu et al., 2013

The 21st century

IMRT

Adaptive RT

Stereotactic RT

4D-CT

IGRT

Artificial Intelligence

Why would someone then still perform IORT?

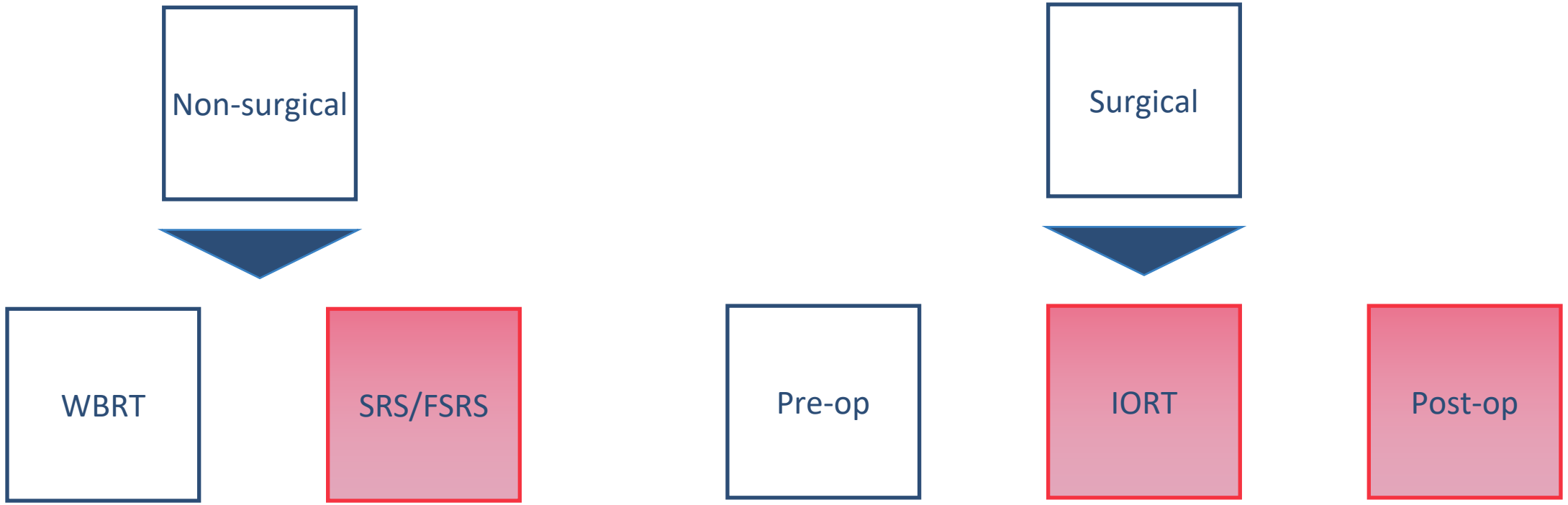
Challenges

Perspectives

Challenge 1: Achieving tumor control

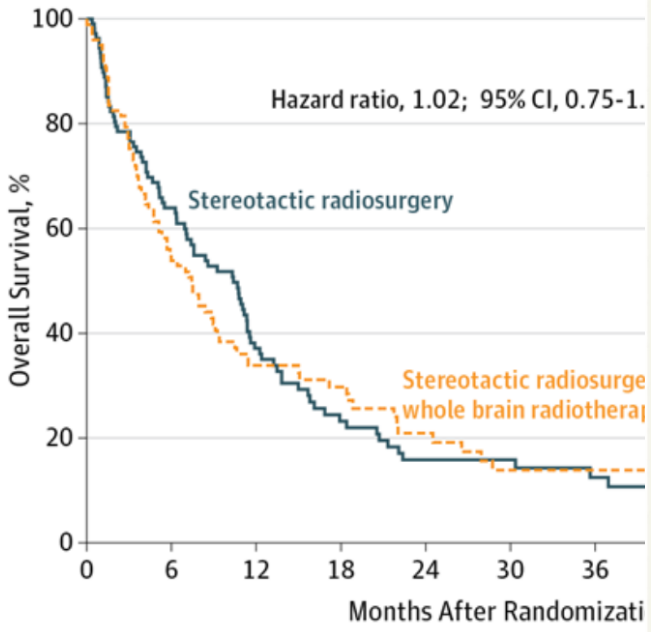
Created with Photoshop

Challenge 1: Achieving tumor control



Challenge 1: Achieving t

Figure 3. Kaplan-Meier Estimates of Overall Survival According to Tre



No. at risk

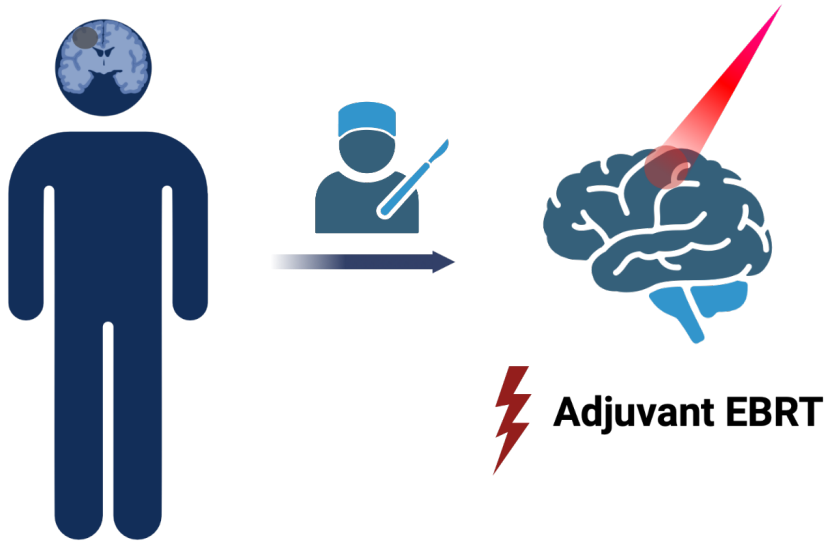
Stereotactic radiosurgery	111	64	35	19	13	10	7
Stereotactic radiosurgery plus whole brain radiotherapy	102	50	28	22	13	8	8

Brow

Table 2. Patients Who Experienced Cognitive Deterioration by 3 Months and Difference Between Groups

	No. (%) of Participants			
	SRS Alone (n = 63)	SRS Plus WBRT (n = 48)	Mean Difference, % (95% CI)	*P* Value[a]
Change from baseline[b]				
HVLT-R				
Immediate recall				
Deterioration	5 (8.2)	14 (30.4)	22.2 (5.4 to 39.1)	.004
No deterioration	56 (91.8)	32 (69.6)		
Delayed recall				
Deterioration	12 (19.7)	24 (51.1)	31.4 (12.1 to 50.7)	<.001
No deterioration	49 (80.3)	23 (48.9)		
Recognition				
Deterioration	14 (22.6)	19 (40.4)	17.8 (−1.5 to 37.2)	.06
No deterioration	48 (77.4)	28 (59.6)		
TMT-A time to complete				
Deterioration	10 (16.7)	14 (30.4)	13.8 (−4.4 to 32.0)	.11
No deterioration	50 (83.3)	32 (69.6)		
TMT-B time to complete				
Deterioration	11 (19.0)	16 (37.2)	18.2 (−1.4 to 37.9)	.07
No deterioration	47 (81.0)	27 (62.8)		
COWAT total				
Deterioration	1 (1.9)	8 (18.6)	16.7 (2.4 to 31.0)	.01
No deterioration	52 (98.1)	35 (81.4)		
GPS total seconds				
Deterioration	17 (29.3)	21 (47.7)	18.4 (−2.4 to 39.3)	.07
No deterioration	41 (70.7)	23 (52.3)		
Outcome for cognitive progression at 3 mo				
Stable	23 (36.5)	4 (8.3)	−28.2 (−44.2 to −12.2)	<.001
Progression	40 (63.5)	44 (91.7)		

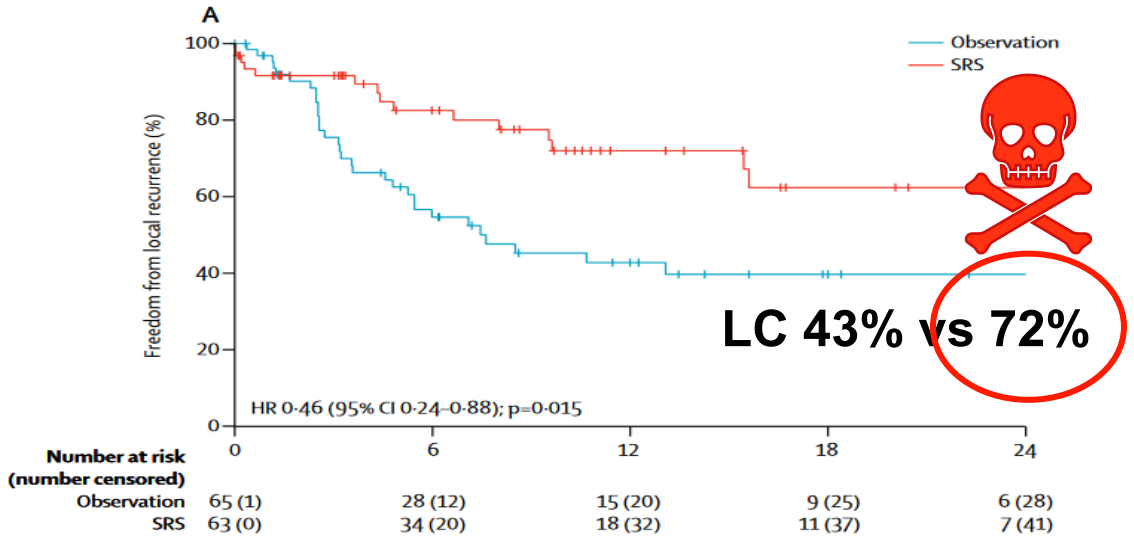
Challenge 1: Achieving tumor control

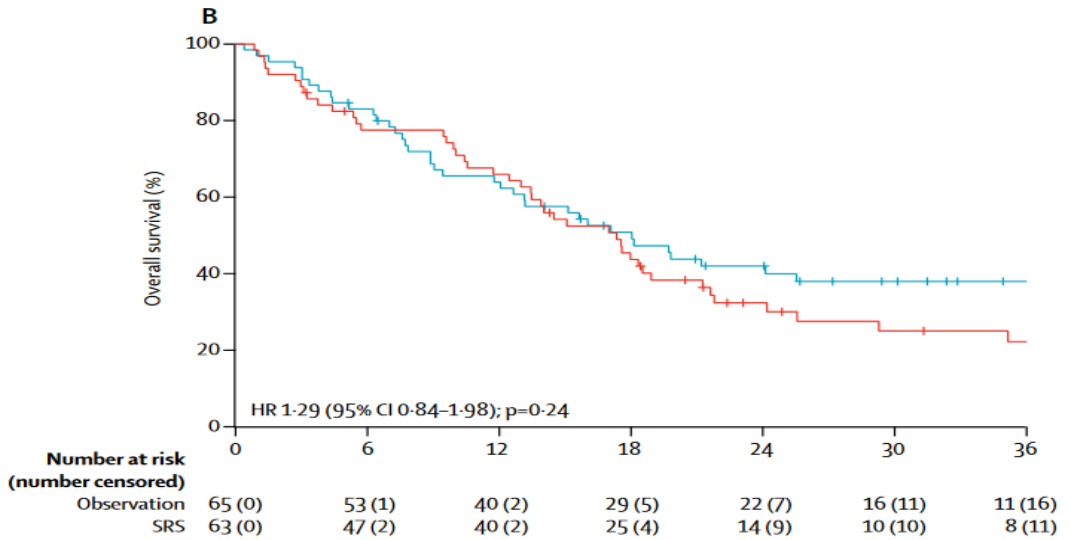


Post-operative stereotactic radiosurgery versus observation for completely resected brain metastases: a single-centre, randomised, controlled, phase 3 trial

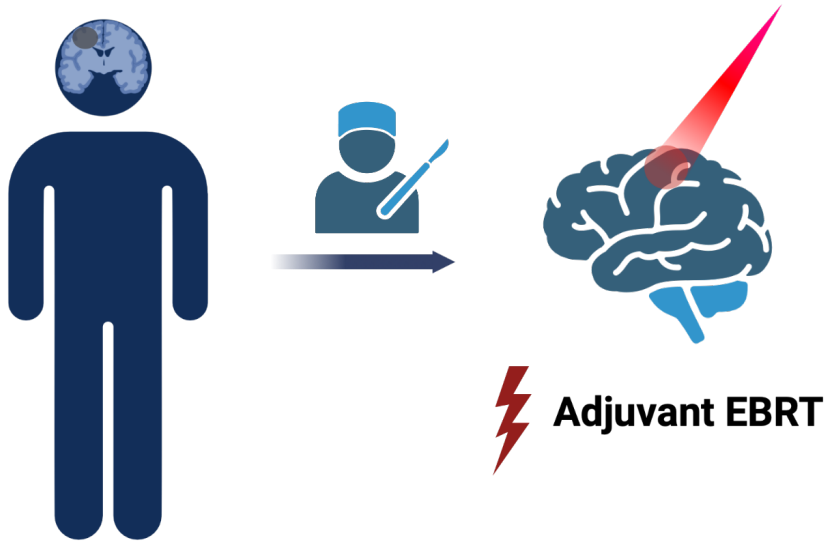
Anita Mahajan, Salmaan Ahmed, Mary Frances McAleer, Jeffrey S Weinberg, Jing Li, Paul D Brown, Stephen Settle, Sujit S Prabhu, Frederick F Lang, Nicholas Levine, Susan McGovern, Erik Sulman, Ian E McCutcheon, Syed Azeem, Daniel Cahill, Claudio Tatsui, Amy B Heimberger, Sherise Ferguson, Amol Ghia, Franco Demonte, Shaan Raza, Nandita Guha-Thakurta, James Yang, Raymond Sawaya, Kenneth R Hess, Ganesh Rao

***Lancet Oncol* 2017; 18: 1040–48**





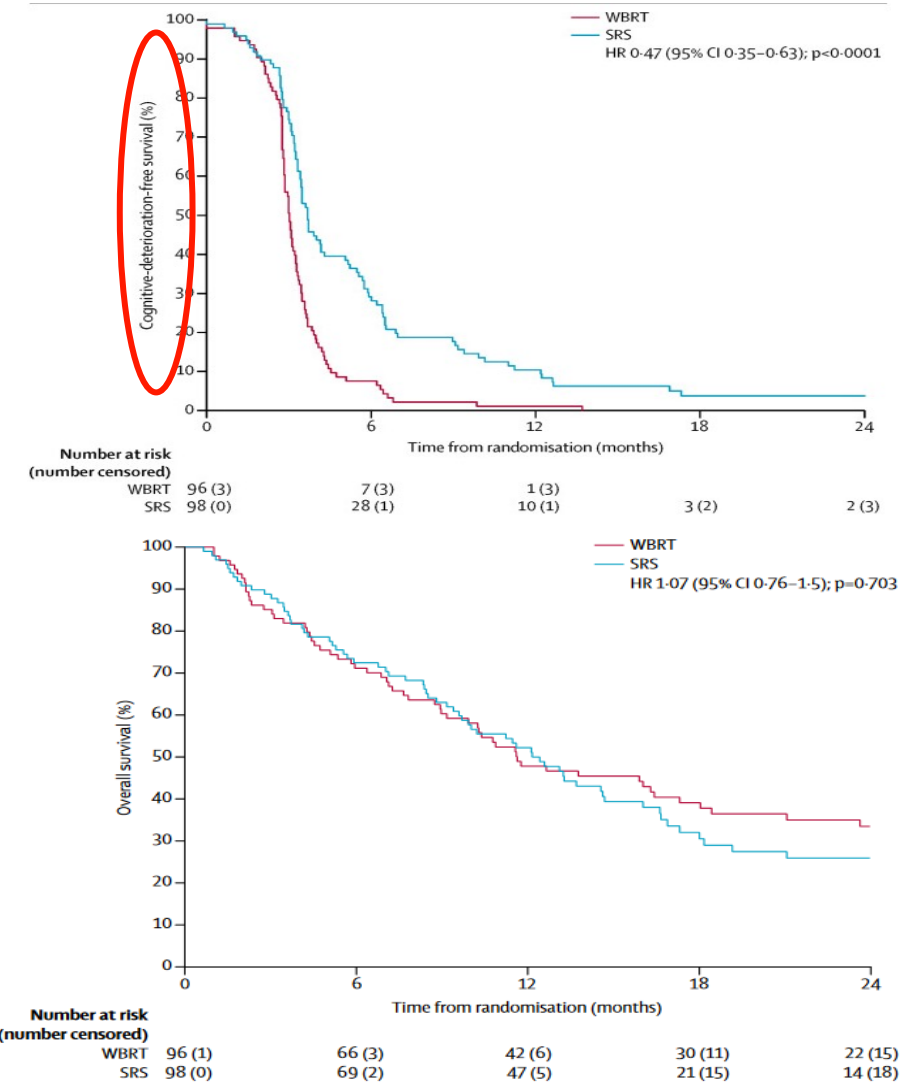
Challenge 1: Achieving tumor control



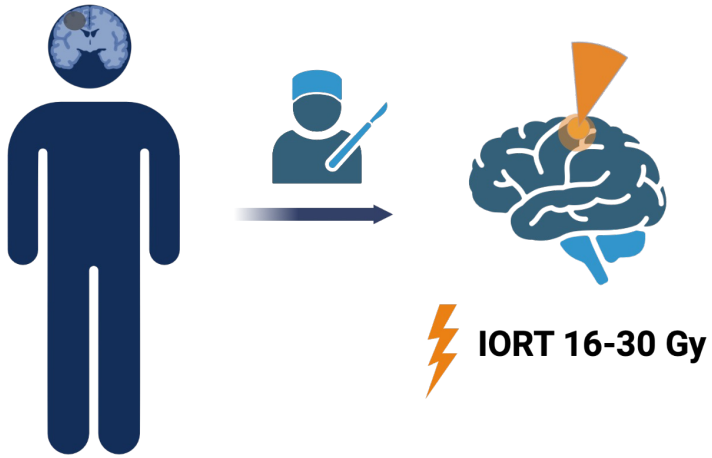
Postoperative stereotactic radiosurgery compared with whole brain radiotherapy for resected metastatic brain disease (NCCTG N107C/CEC·3): a multicentre, randomised, controlled, phase 3 trial

Paul D Brown, Karla V Ballman, Jane H Cerhan, S Keith Anderson, Xiomara W Carrero, Anthony C Whitton, Jeffrey Greenspoon, Ian F Parney, Nadia N I Laack, Jonathan B Ashman, Jean-Paul Bahary, Costas G Hadjipanayis, James J Urbanic, Fred G Barker II, Elana Farace, Deepak Khuntia, Caterina Giannini, Jan C Buckner, Evanthia Galanis, David Roberge

***Lancet Oncol* 2017; 18: 1049–60**



Challenge 1: Achieving tumor control



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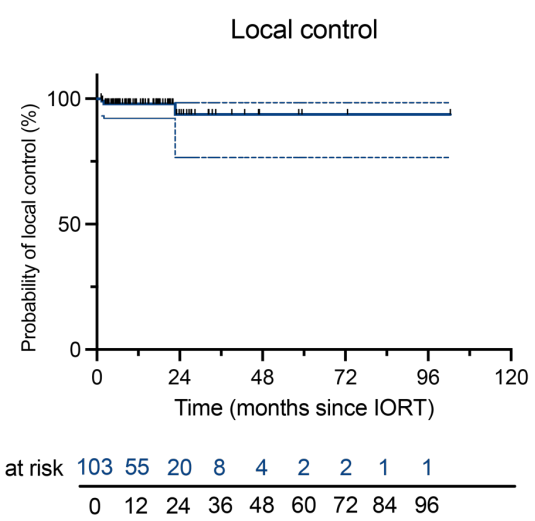
CLINICAL INVESTIGATION

Multicentric Assessment of Safety and Efficacy of Combinatorial Adjuvant Brain Metastasis Treatment by Intraoperative Radiation Therapy and Immunotherapy

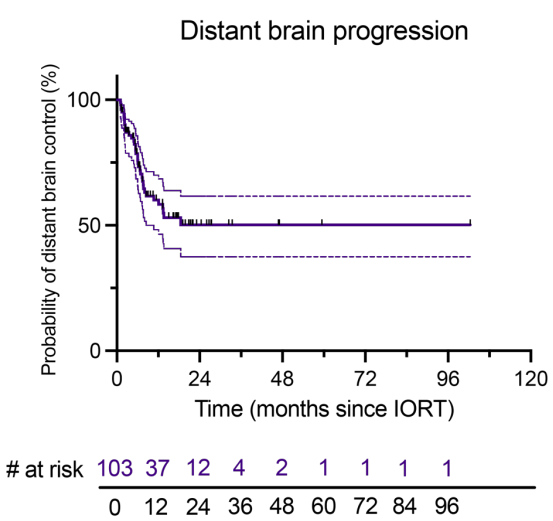
Julian P. Layer, MD,*,† Ehab Shiban, MD,‡ Stefanie Brehmer, MD,§ Christian D. Diehl, MD,‖ Douglas Guedes de Castro, MD,¶ Motaz Hamed, MD,# Cas S. Dejonckheere, MD,* Daniel T. Cifarelli, MD,** Lea L. Friker, MD,†,†† Ulrich Herrlinger, MD,‡‡ Michael Hölzel, MD,† Hartmut Vatter, MD,# Matthias Schneider, MD,# Stephanie E. Combs, MD,‖ Leonard Christopher Schmeel, MD,* Christopher P. Cifarelli, MD, PhD,** Frank A. Giordano, MD,§§,‖‖,¶¶ Gustavo R. Sarria, MD,* and Klaus-Henning Kahl, MD##

- Multiple publications since 2018, with over 300 patients
- 1-year LC: >90%
- Radionecrosis: about 5%
- No increased mortality
- No increased toxicity
- No added toxicity in combination with systemic treatments

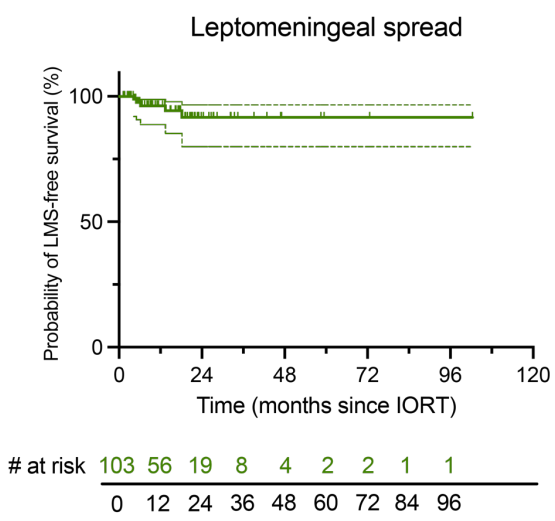
Challenge 1: Achieving tumor control



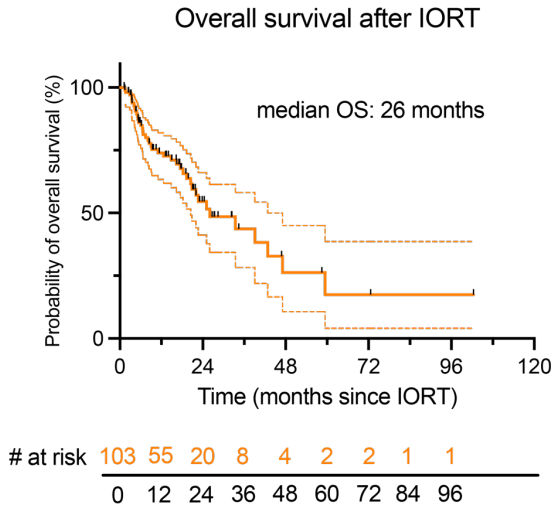
1-year-LCR 98.0%



1-year-DBP rate 40.0%



Cumulative LMS rate 4.9%



1-year OS rate 74.0%

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Challenge 2: Not obstructing the care paths

Avoid

unnecessary treatment interruptions

waiting time

restricted access to care (temporal/geographical/personal)

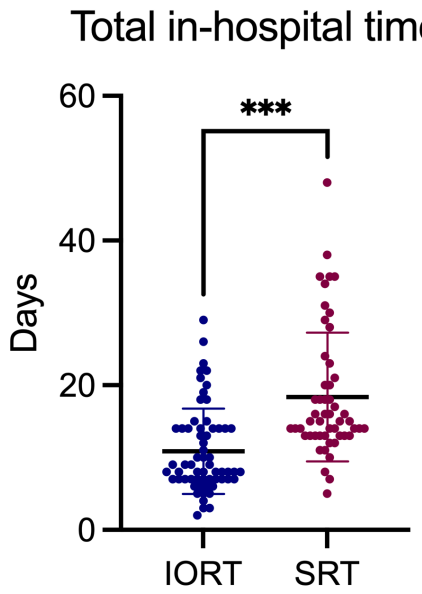
Enable

Constant flow of medical treatment

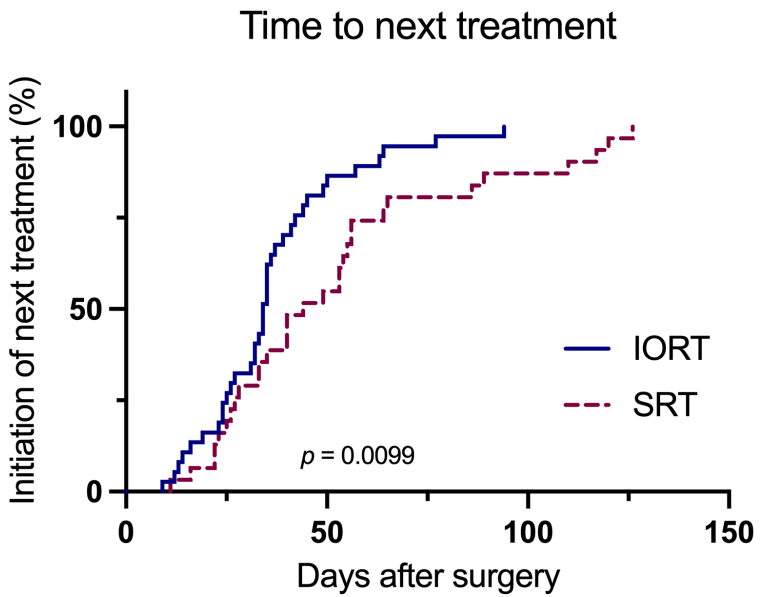
interdisciplinary treatment concepts

Challenge 2: Not obstructing the care paths

Immediate tumor cell eradication



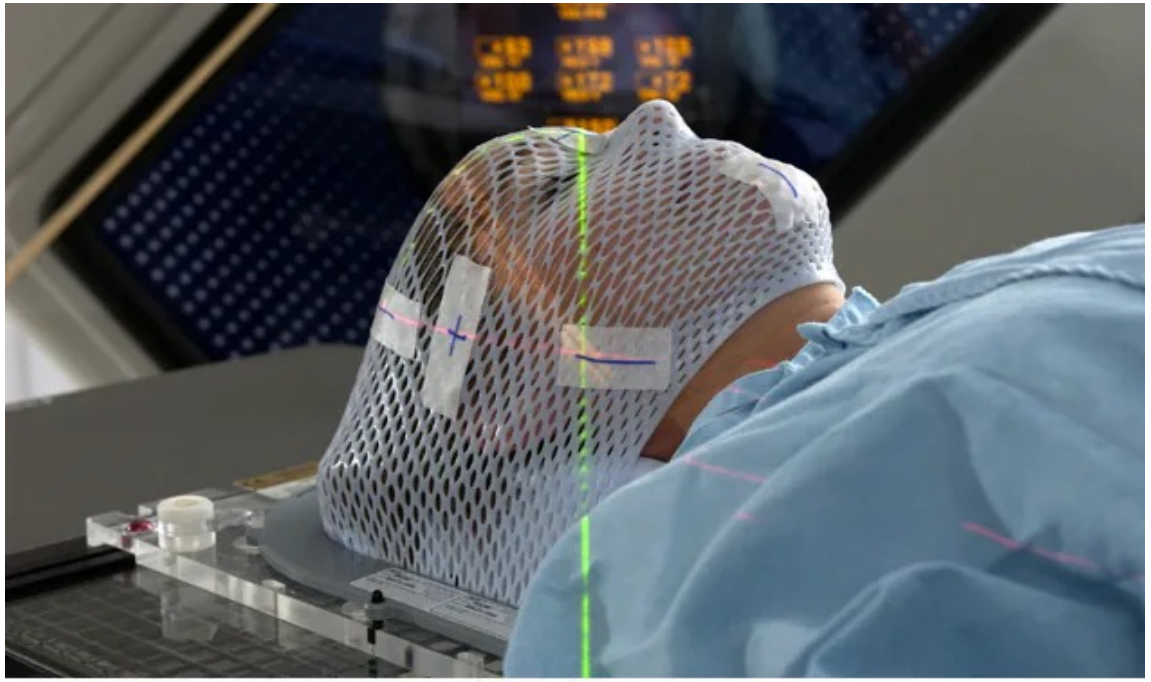
Reduced hospitalization times



Timely admission to subsequent treatments

Challenge 3: Optimizing care paths

Wikipedia



Challenge 3: Optimizing care paths

Reduced hospitalization times

Created with Photoshop

Challenge 3: Optimizing care paths

Reduced hospitalization times

Reduced treatment times

Challenge 3: Optimizing care paths

Reduced hospitalization times

Reduced treatment times

Reduced transportation times

Challenge 3: Optimizing care paths

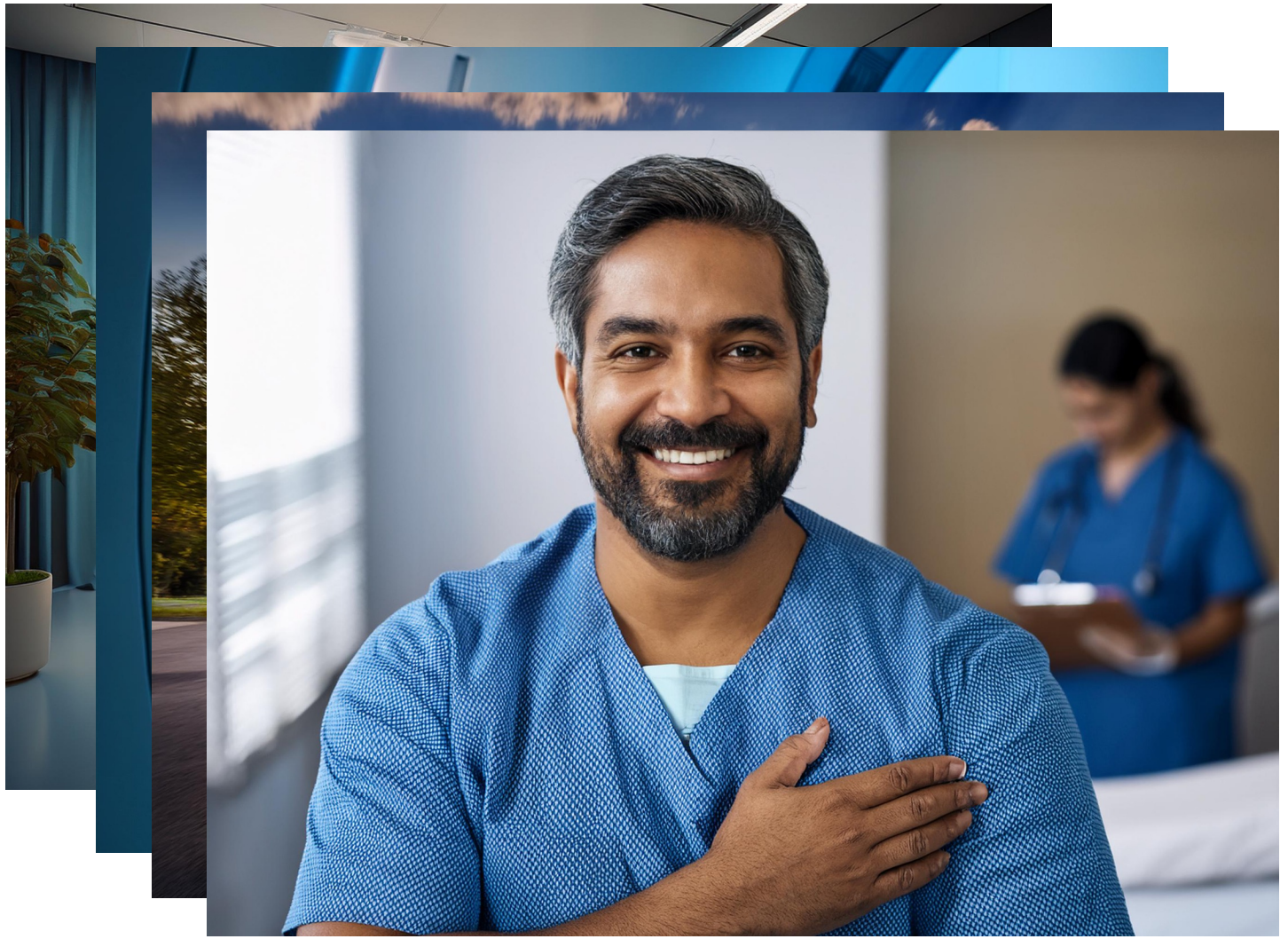
Reduced hospitalization times

Reduced treatment times

Reduced transportation times

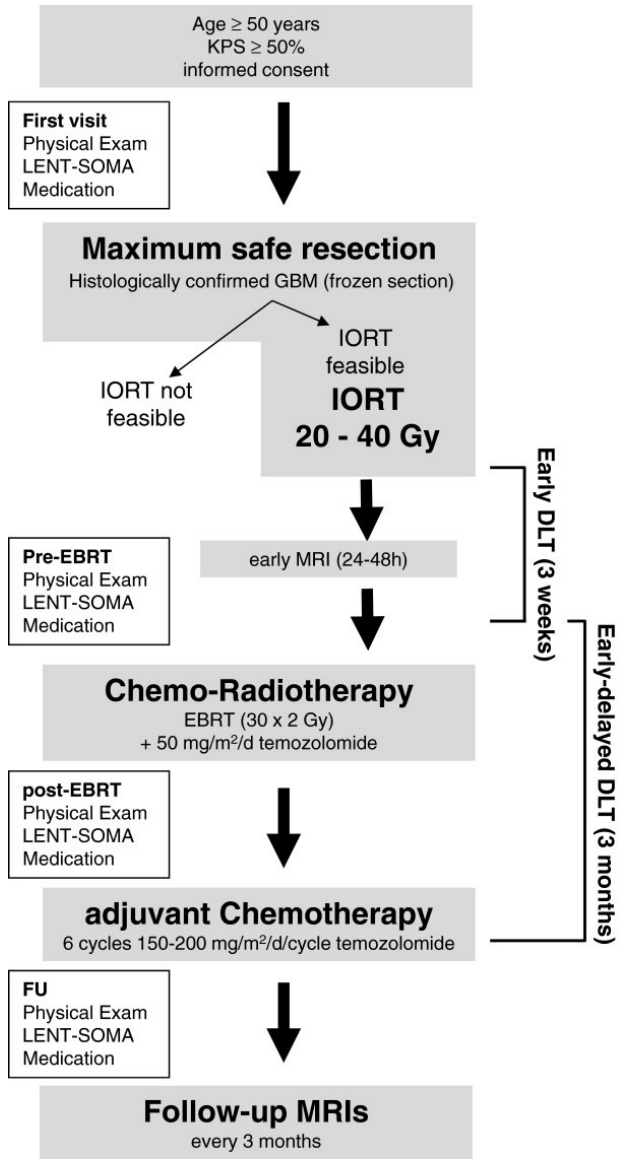
↓

Improved patient quality of life



Challenge 3: Optimizing care paths

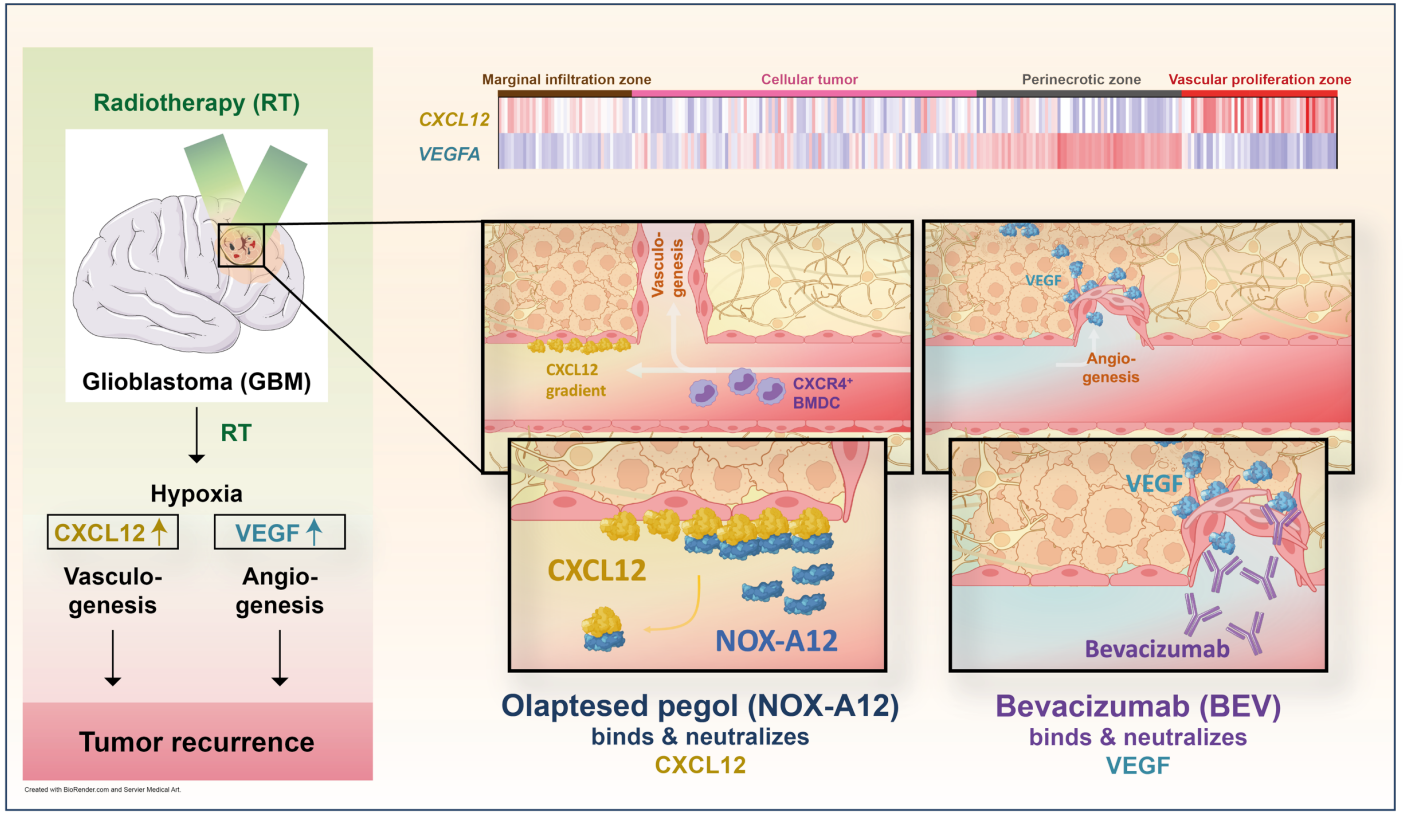
Rearrange and combine radiotherapeutic options



Giordano et al., 2014

Challenge 3: Optimizing care paths

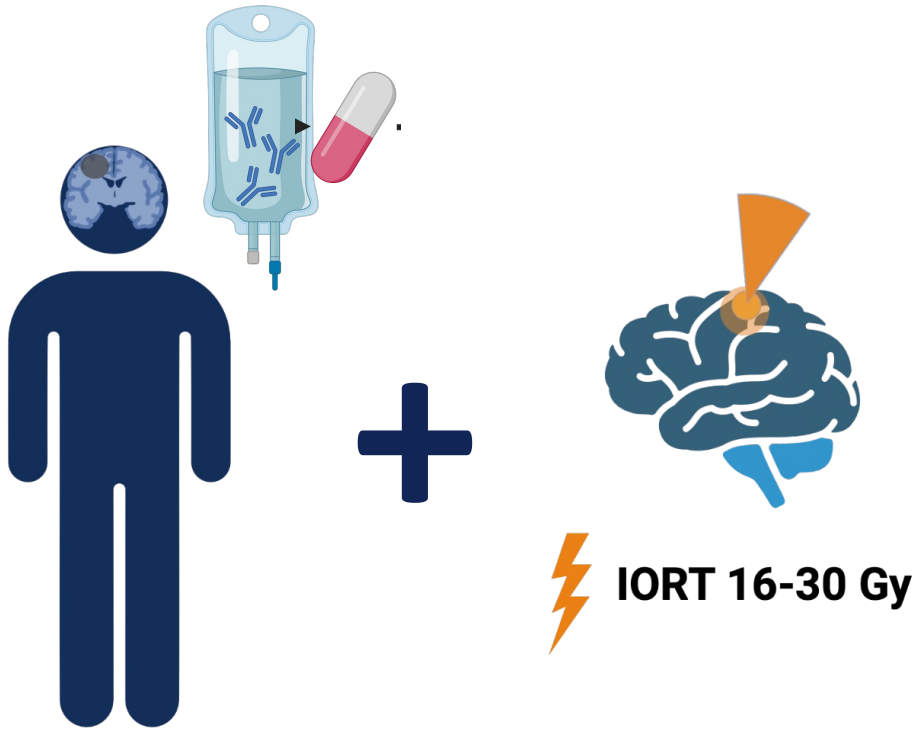
GLORIA trial



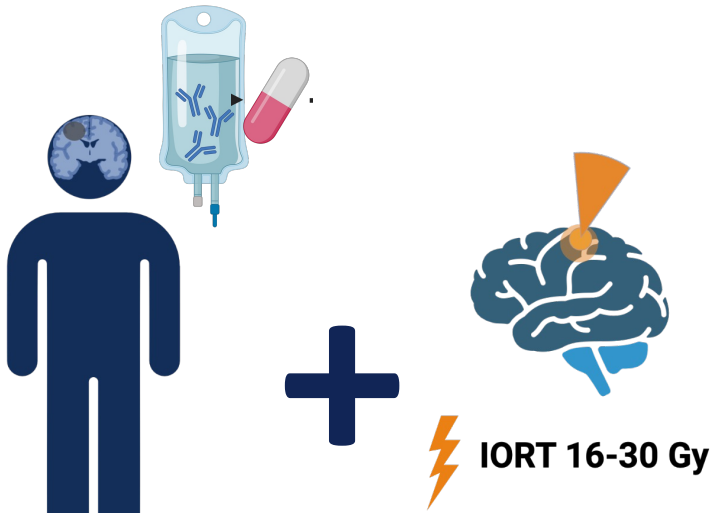
Combine RT with targeted treatment approaches

Challenge 3: Optimizing care paths

Combine RT with targeted treatment approaches



Challenge 4: Timing matters

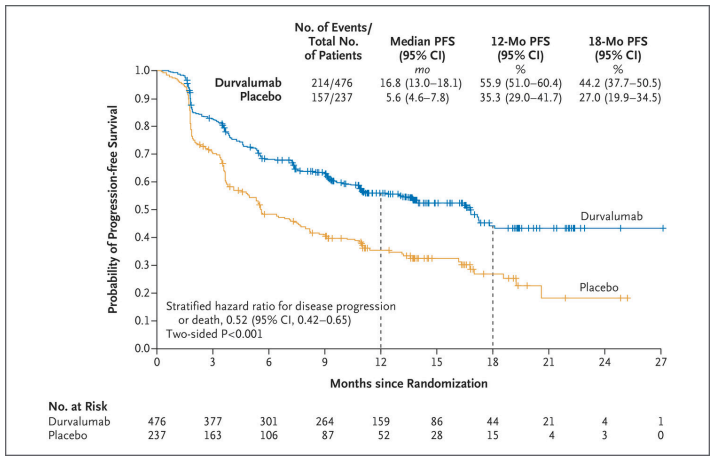


Efficacy

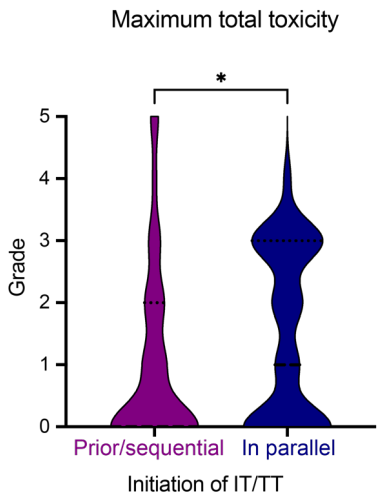
Timing

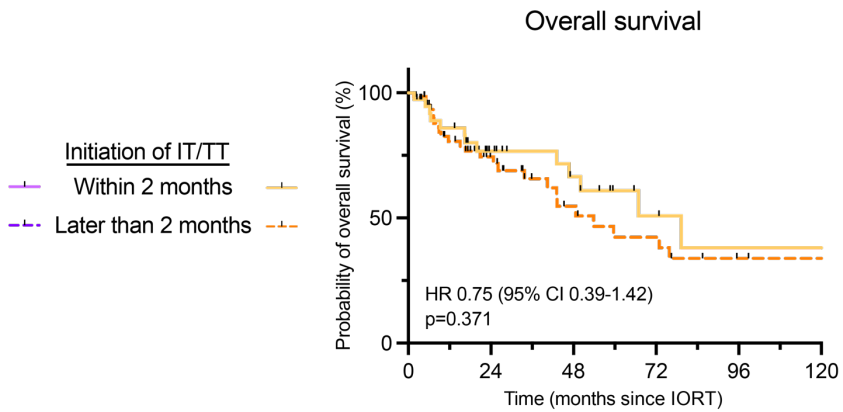
Toxicity

PACIFIC: benefit for sequential IT



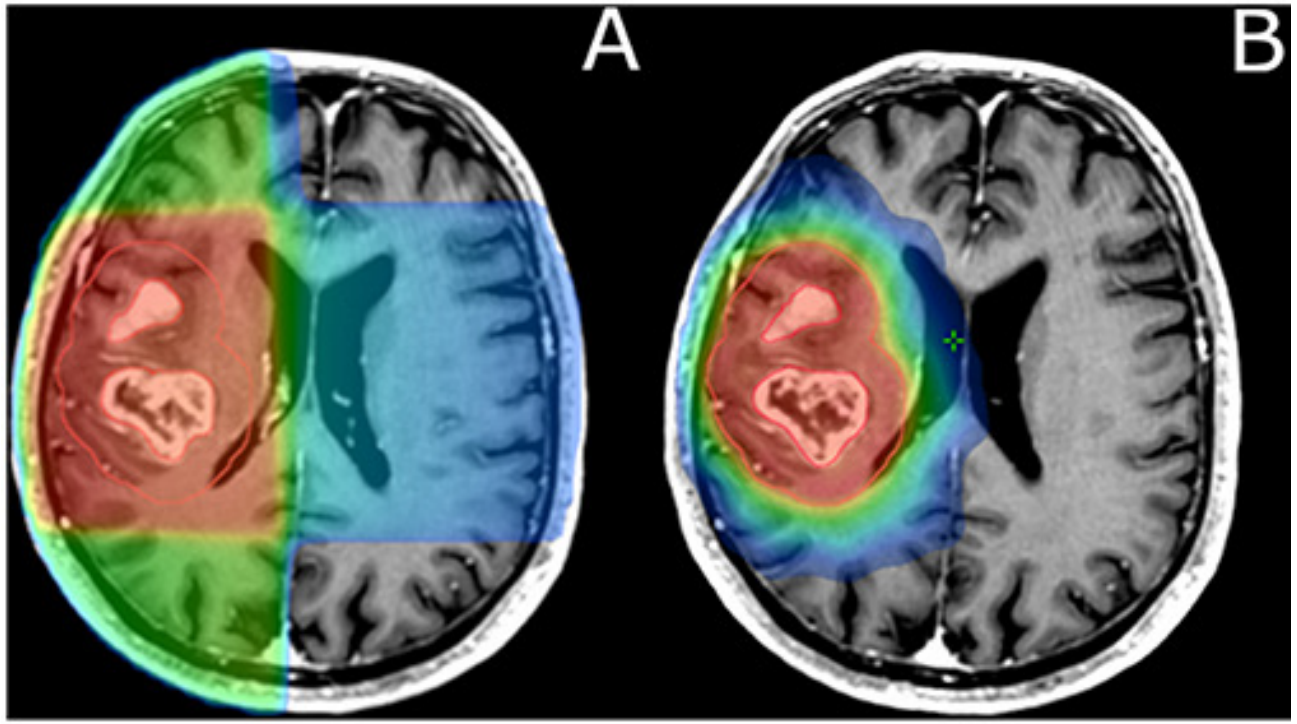
Antonia et al., 2017





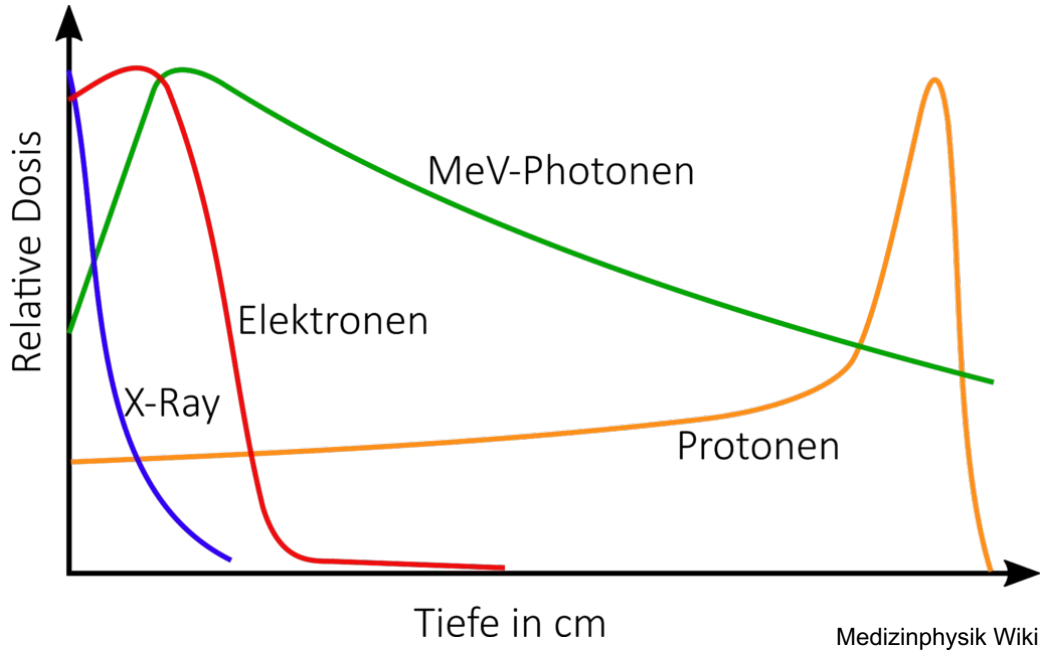
Layer et al., 2024

Challenge 5: Avoiding dose spillage

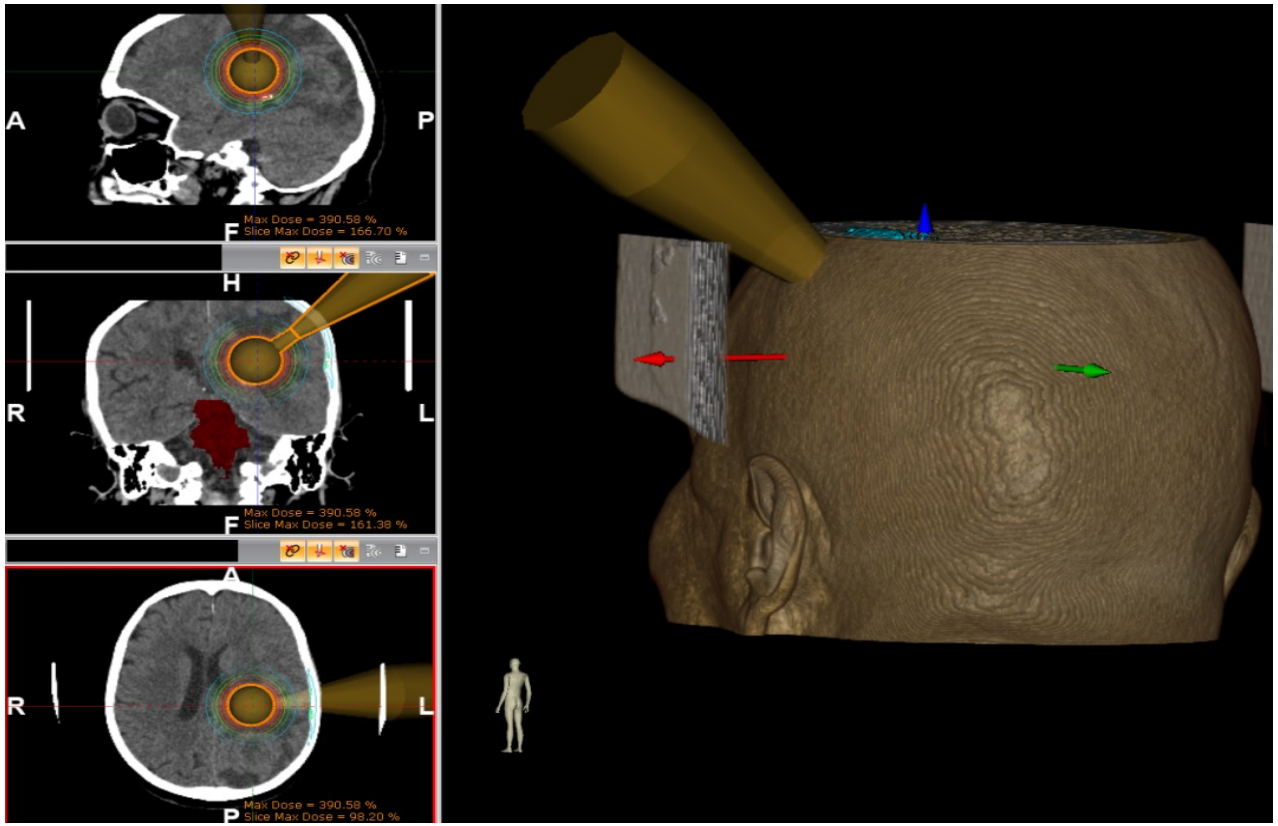


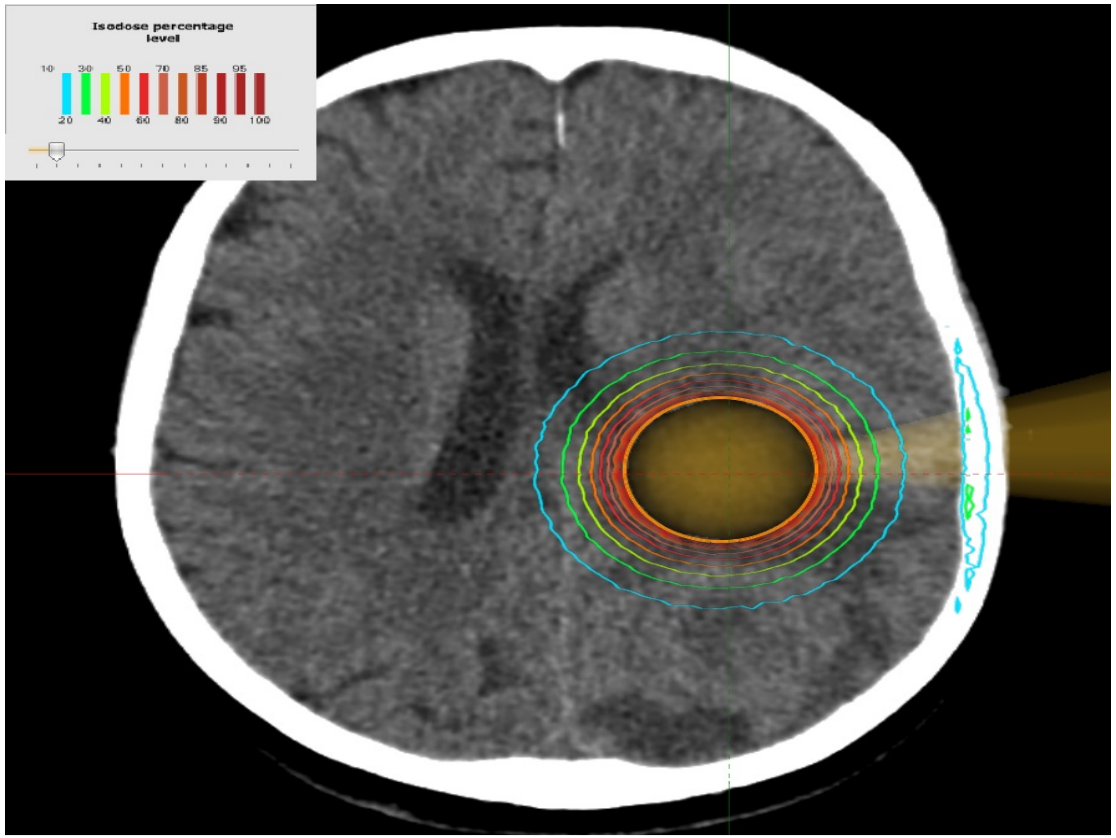
3D-CRT IMRT

Gèrard et al., 2019



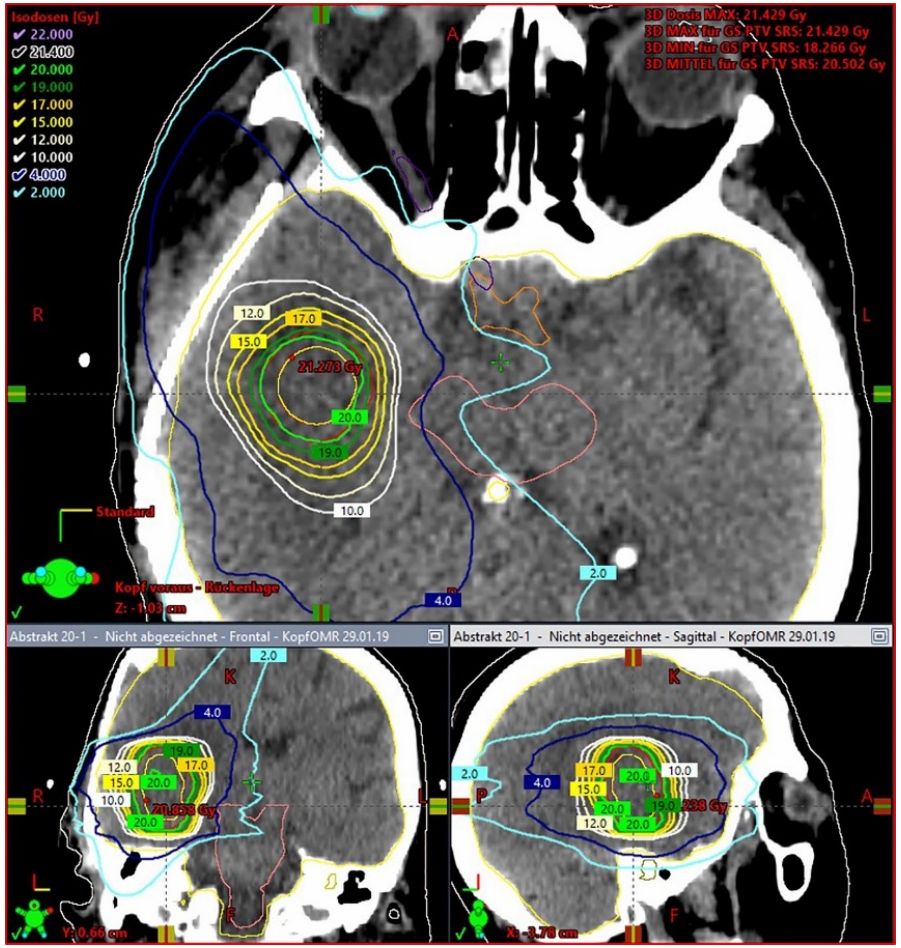
Challenge 5: Avoiding dose spillage

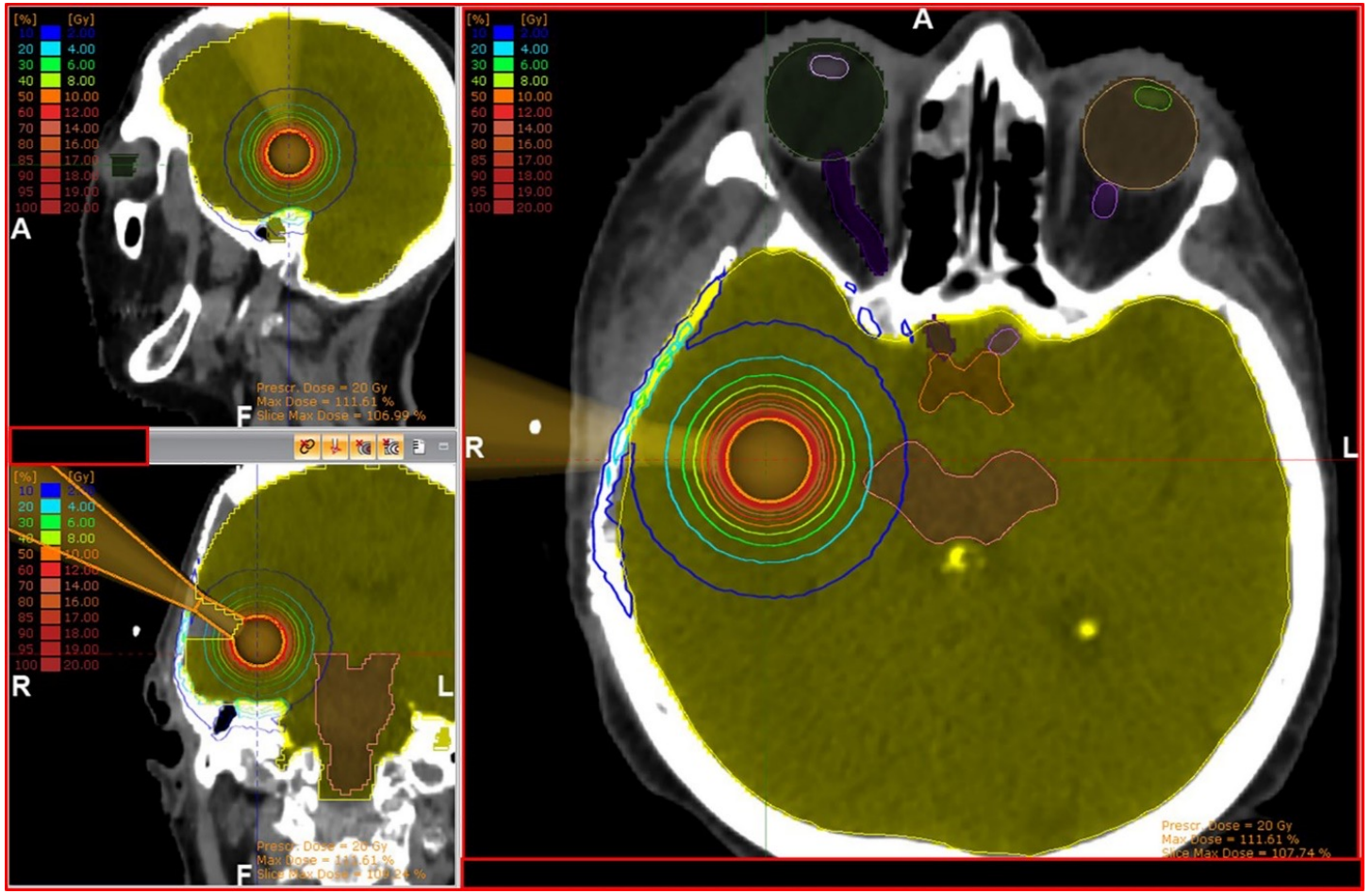




Sarria et al. 2021

Challenge 5: Avoiding dose spillage

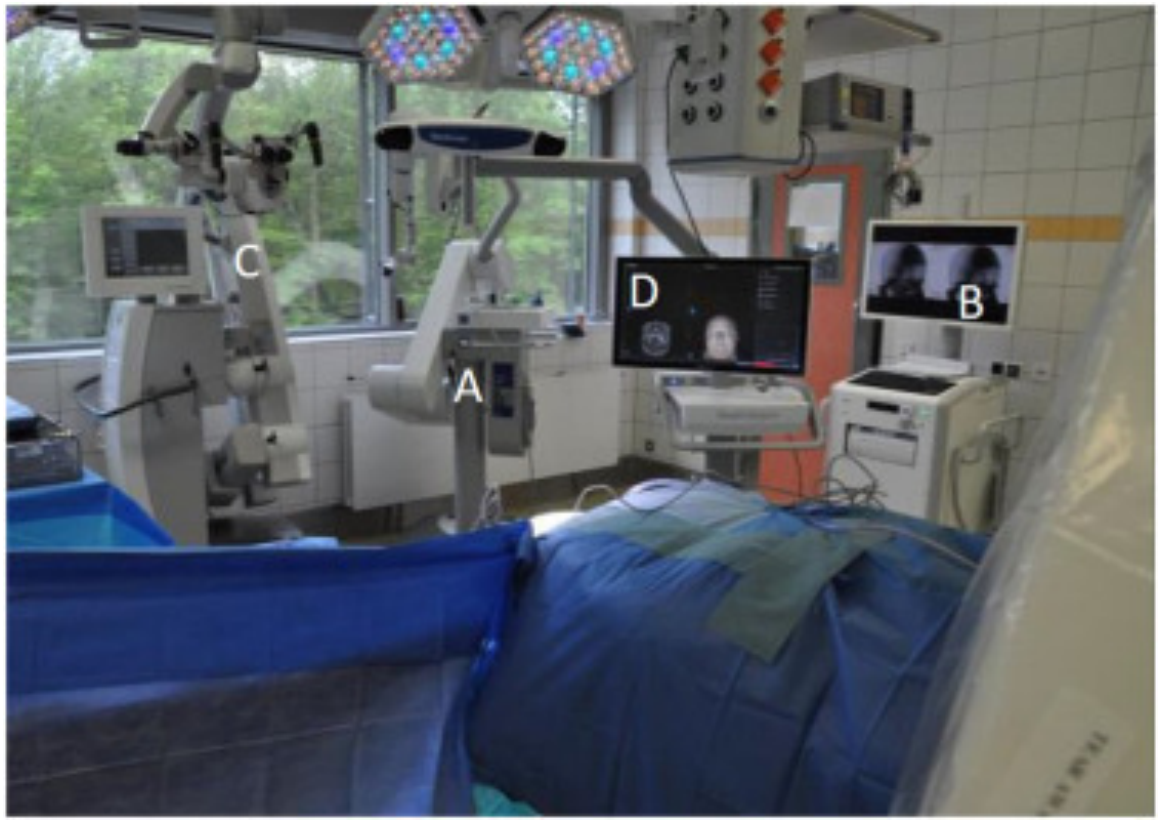




Sarria et al. 2021

Challenge 6: Ensuring precision

INTRABEAM® (Carl Zeiss Meditech)

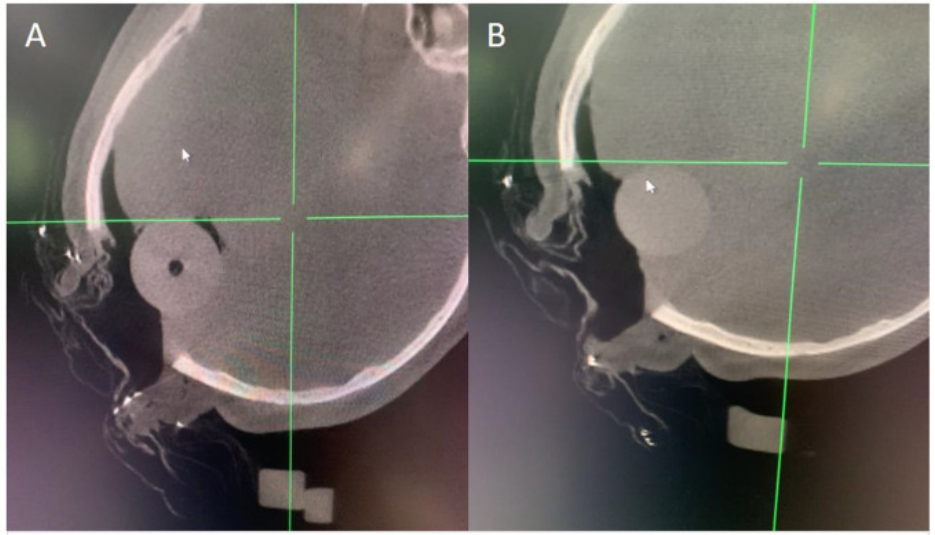


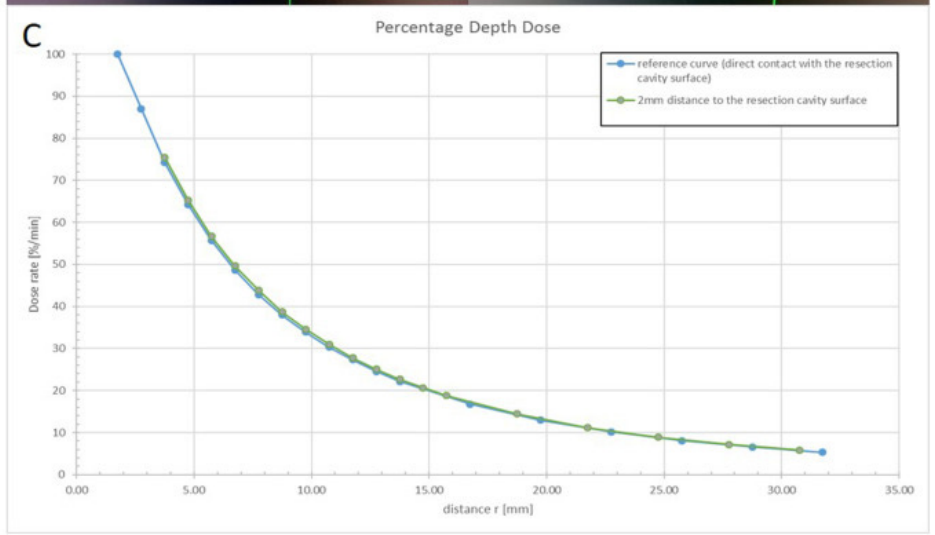
Grimmer et al. 2024

(A) kV IORT device
(B) CBCT mobile display station
(C) surgical microscope
(D) neuronavigation camera + screen

Challenge 6: Ensuring precision

O-Arm trial

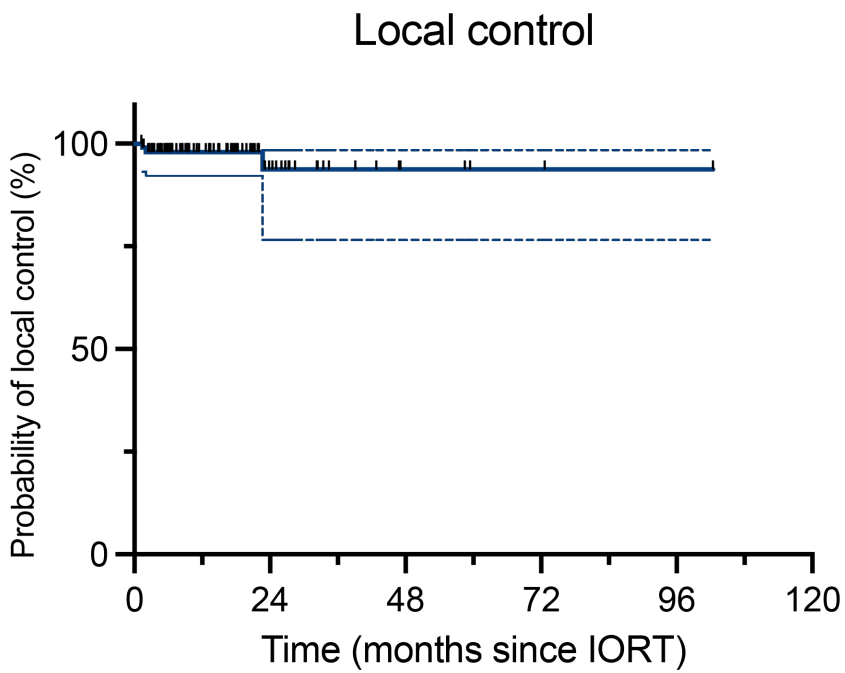




Grimmer et al. 2024

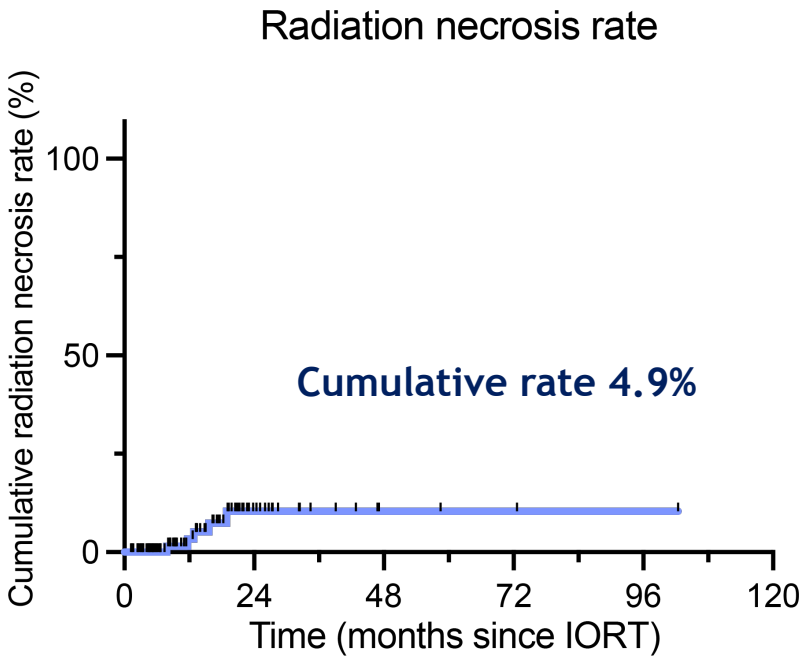
Challenge 6: Ensuring precision

O-Arm trial



# at risk	103	55	20	8	4	2	2	1	1
	0	12	24	36	48	60	72	84	96

1-year-LCR 98.0%



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The perspective of IORT

- Trend towards individualized care
- Identification of patients at risk of

  recurrence ⟷ overtreatment
- Recognition of personal patient will
- Growing number of therapeutic options

Whom do we offer IORT?

ALL patients.

Whom do we recommend IORT?

Patients with

… singular/solitary brain metastasis

… urgent follow-up procedures

… claustrophoby

… MRI contraindications

… reduced performance score

… transportation issues

… highly palliative treatment situations

Thank you very much for your attention.

2:40 PM **Brain metastases: Interim analysis of the phase II trial INTRAMET**

Miquel Macià, MD
Department of Radiation Oncology
Institut Català d'Oncologia
Barcelona University
Barcelona, Spain

3:00 PM **IORT combined with immunotherapy in brain metastases**

Julian Layer, MD
Department of Radiation Oncology
University Hospital Bonn
Germany

3:20 PM **IORT in glioblastoma: INTRAGO phase II trial update**

Frank Giordano, MD
Radiotherapy and Radiation Oncology
Professor
University Medical Center Mannheim
Germany

3:40 PM **Kyphoplasty and intraoperative radiotherapy (Kypho-IORT) for vertebral tumors**

Frederic Bludau, MD
Head of Spinal Surgery Division
University Medical Center Mannheim
Germany

4:00 PM **Abstracts session**

4:00 PM **Intraoperative or Postoperative Stereotactic Radiotherapy for Brain Metastases: Time to Systemic Treatment Onset and Other Patient-Relevant Outcomes**

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