Sistema Socio Sanitario
Regione Lombardia
ASST Lecco

Sabato 27 Novembre 2021

RADIOTERAPIA OGGI E DOMANI,
20 (+1) anni della
U.O.C. di Radioterapia dell'Ospedale Manzoni di Lecco

Politecnico di Milano – Polo Territoriale di Lecco – Aula Magna
Via G. Previati 1/c—Lecco

Stato dell'arte, problematiche attuali e prospettive future RADIOTERAPIA STEREOTASSICA

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Istituto Europeo di Oncologia IRCCS, Milano
Università degli Studi di Milano

UNIVERSITÀ DEGLI STUDI DI MILANO
IEO Istituto Europeo di Oncologia
Fondazione Umberto Veronesi – per il progresso delle scienze
CORE FACULTY
Fondazione IEO·CCM RICERCA ONCOLOGICA E CARDIOVASCOLARE
AIRC

DISCLOSURES

ALL OUTSIDE THE CURRENT LECTURE:

Research funding:

AIRC Italian Association for Cancer Research (institutional grants),

FIEO-CCM & FUV (institutional grants)

Accuray (institutional grant)

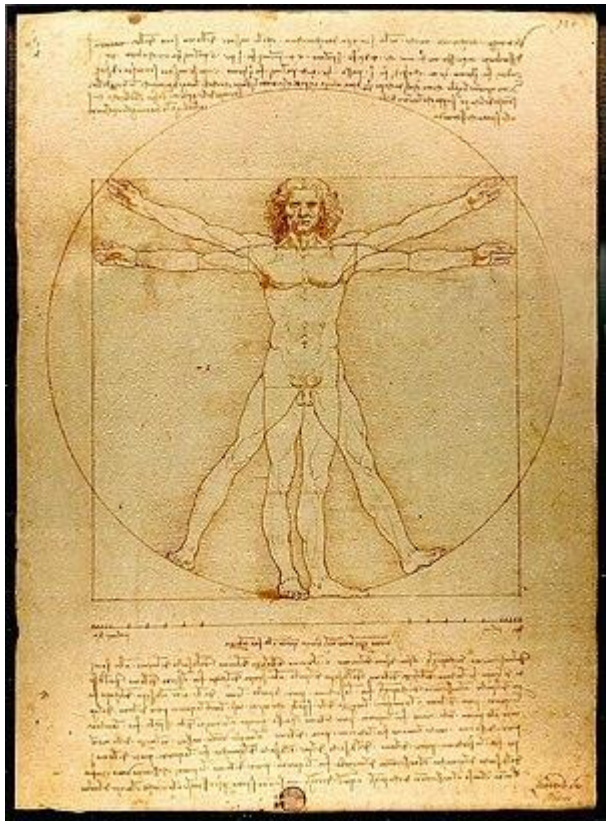
Travel expenses or speaker fees:

Janssen, Ferring, Bayer, Roche, Astellas, Elekta, Carl Zeiss, Ipsen, Accuray, IBA

AGENDA

- SBRT and SRS
- Brain
- Thorax
- Abdomen/pelvi
- Particular scenarios:

  oligometastases, re-irradiation



https://en.wikipedia.org/wiki/Vitruvian_Man#/media/File:Da_Vinci_Vitruve_Luc_Viatour.jpg

Game changer

https://www.cuf.pt/en/cuf-services/international-cuf/medical-offer
https://commons.wikimedia.org/wiki/File:Gamma-knife-cuf.jpg

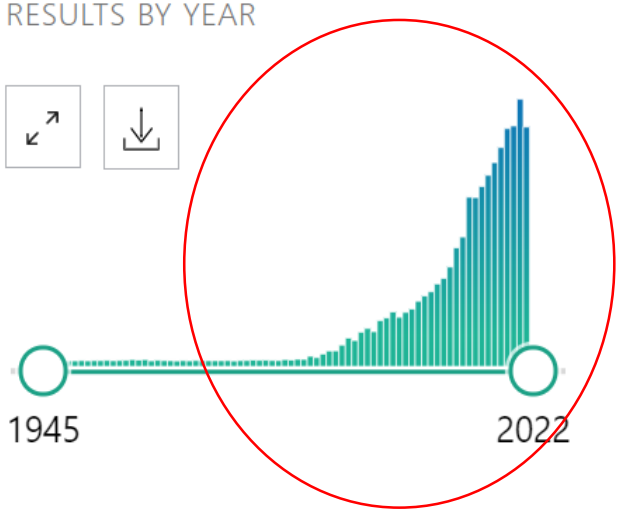
Game changer

MY NCBI FILTERS

27,139 results

Page 1 of 2,714

RESULTS BY YEAR



TEXT AVAILABILITY

1

Cite

Share

Operating procedures, risk management and challenges during implementation of adaptive and non-adaptive MR-guided **radiotherapy**: 1-year single-center experience.

Garcia Schüler HI, Pavic M, Mayinger M, Weitkamp N, Chamberlain M, Reiner C, Linsenmeier C, Balermpas P, Krayenbühl J, Guckenberger M, Baumgartl M, Wilke L, Tanadini-Lang S, Andratschke N.

Radiat Oncol. 2021 Nov 14;16(1):217. doi: 10.1186/s13014-021-01945-9.

PMID: 34775998

BACKGROUND: Main purpose was to describe procedures and identify challenges in the implementation process of adaptive and non-adaptive MR-guided **radiotherapy** (MRgRT), especially new risks in workflow due to the new technique. RESULTS: A summary of the processes on the M

15 th Nov 2021

La radiologia medica (2019) 124:315–322
https://doi.org/10.1007/s11547-018-0972-6

RADIOTHERAPY

Radiotherapy for oligometastatic cancer: a survey among radiation oncologists of Lombardy (AIRO-Lombardy), Italy

Barbara Alicja Jereczek-Fossa[1,2] · Barbara Bortolato[3] · Marianna Alessandra Gerardi[1] · Samantha Dicuonzo[1] · Virginia Maria Arienti[3] · Stefania Berlinghieri[4] · Stefano Bracelli[5] · Michela Buglione[6] · Mariangela Caputo[7] · Gianpiero Catalano[8] · Luigi Franco Cazzaniga[9] · Luigi De Cicco[5] · Nadia Di Muzio[10] · Francesco Romeo Filippone[9] · Andrei Fodor[10] · Davide Franceschini[11] · Paolo Frata[4] · Stefania Gottardo[2,15] · Giovanni Battista Ivaldi[12] · Antonio Laudati[13] · Stefano Maria Magrini[6] · Elisa Mantero[7] · Ilaria Meaglia[12] · Sara Morlino[7] · Mauro Palazzi[3] · Fabio Piccoli[9] · Paola Romanelli[1] · Marta Scorsetti[11,14] · Flavia Serafini[13] · Luciano Scandolaro[13] · Riccardo Valdagni[2,7,16] · Roberto Orecchia[2,17] · Paolo Antognoni[15] · the Lombardy Section of the Italian Society of Oncological Radiotherapy (Associazione Italiana di Radioterapia Oncologica-Lombardia, AIRO-L)

Oligometastatic cancer: 7-15% of all RT patients

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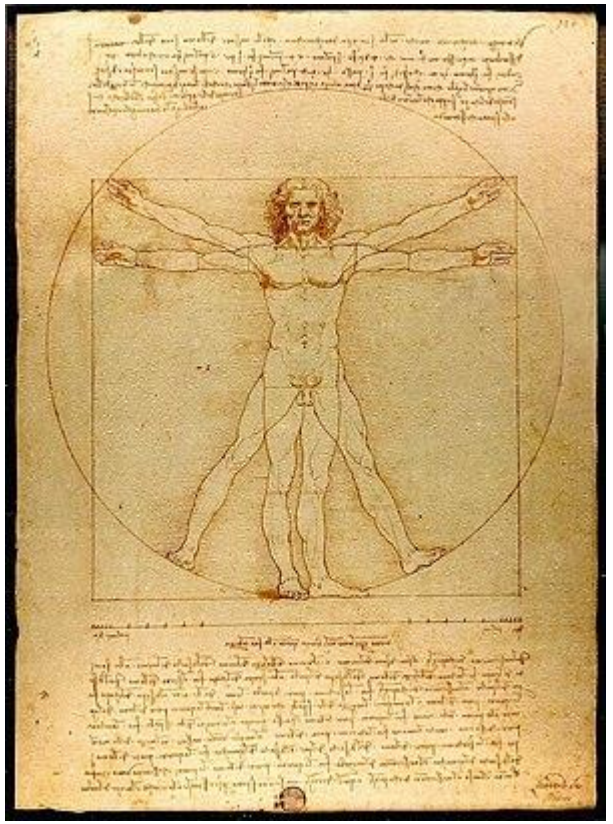
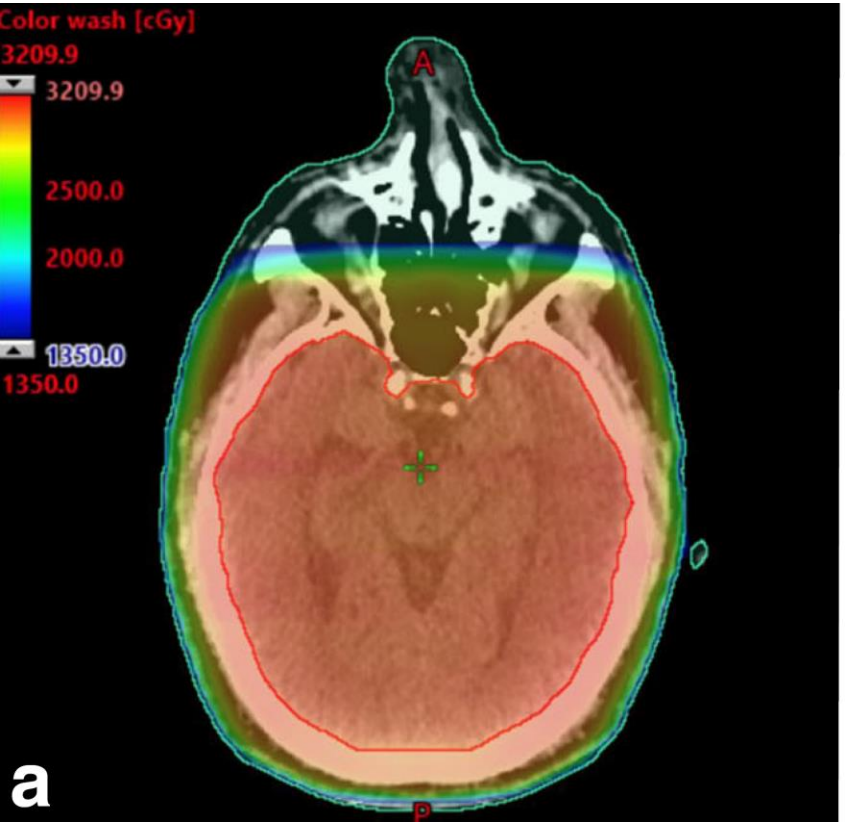
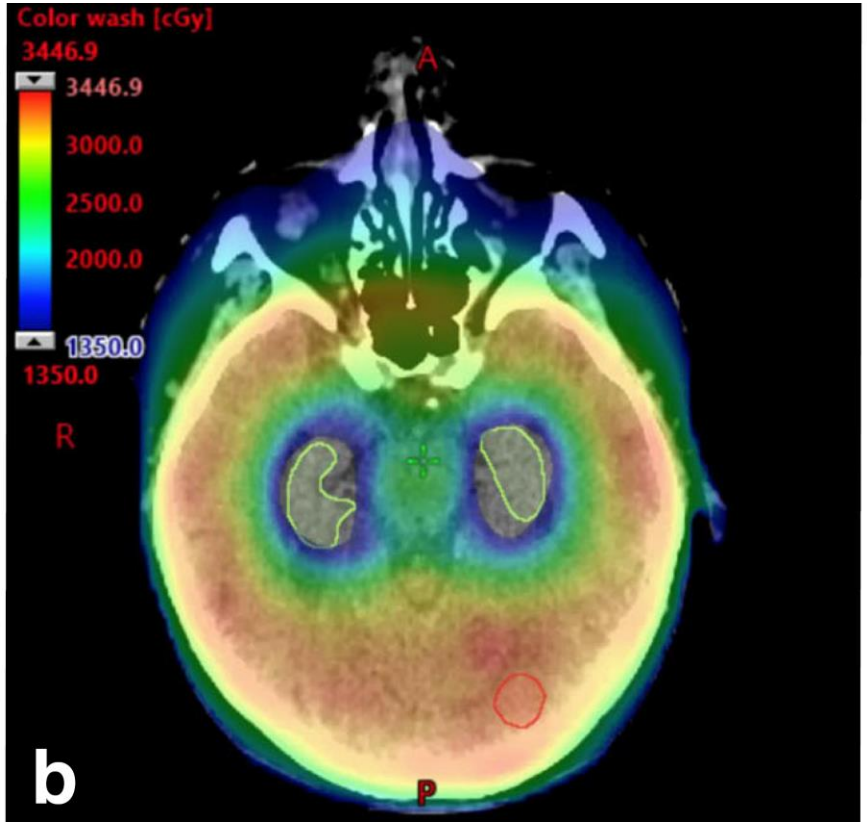
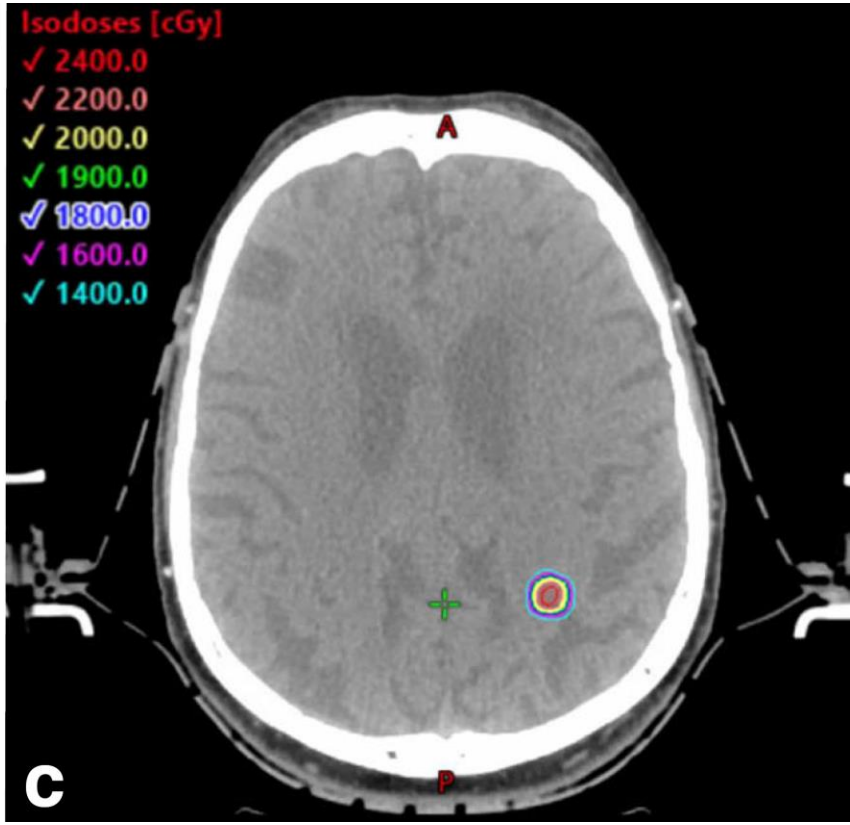


https://en.wikipedia.org/wiki/Vitruvian_Man#/media/File:Da_Vinci_Vitruve_Luc_Viatour.jpg

RT for brain metastasis







Whole brain RT

WBRT

Hippocampal avoidance (sparing) WBRT

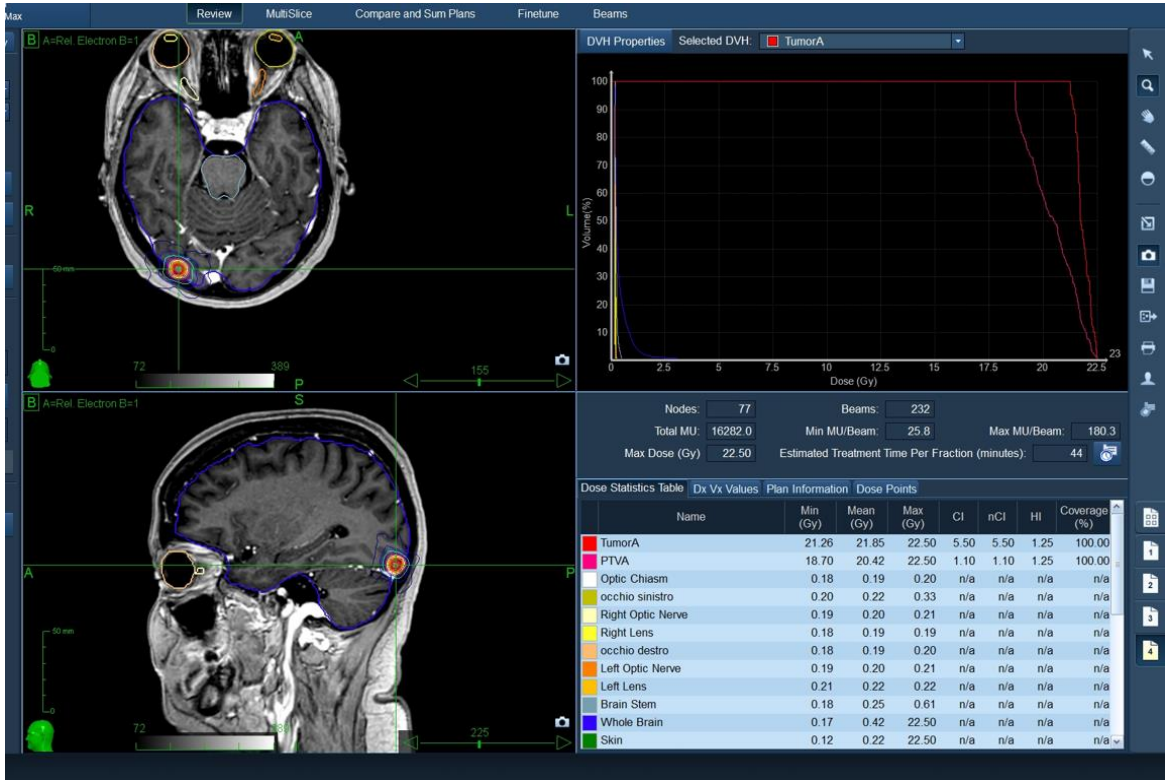
HS-WBRT (IMRT)

Stereotactic radiosurgery

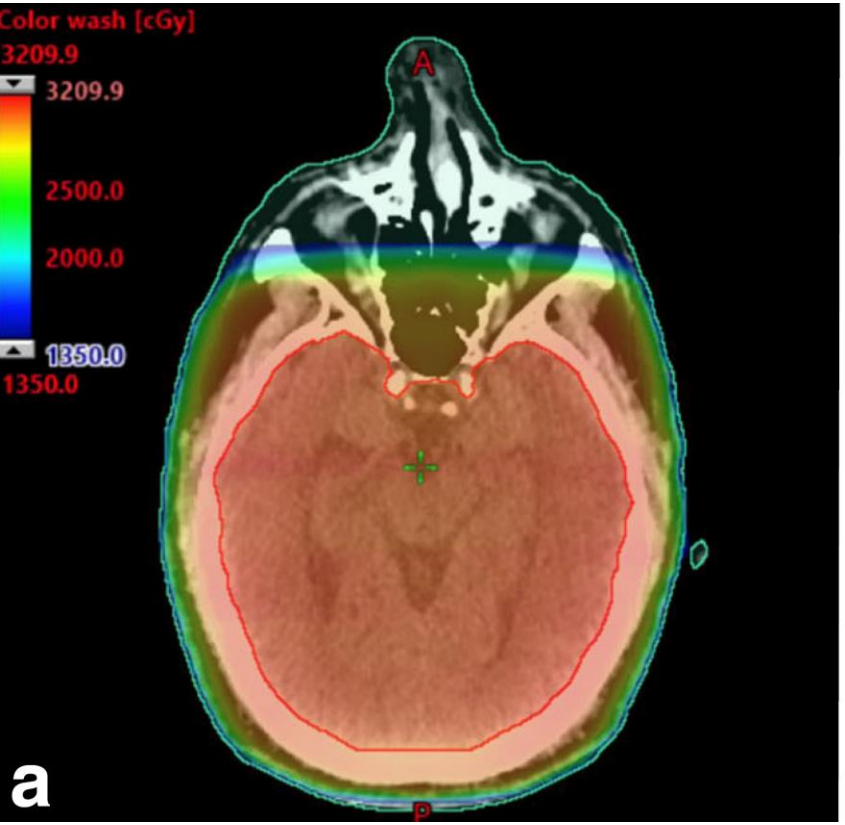
SRS

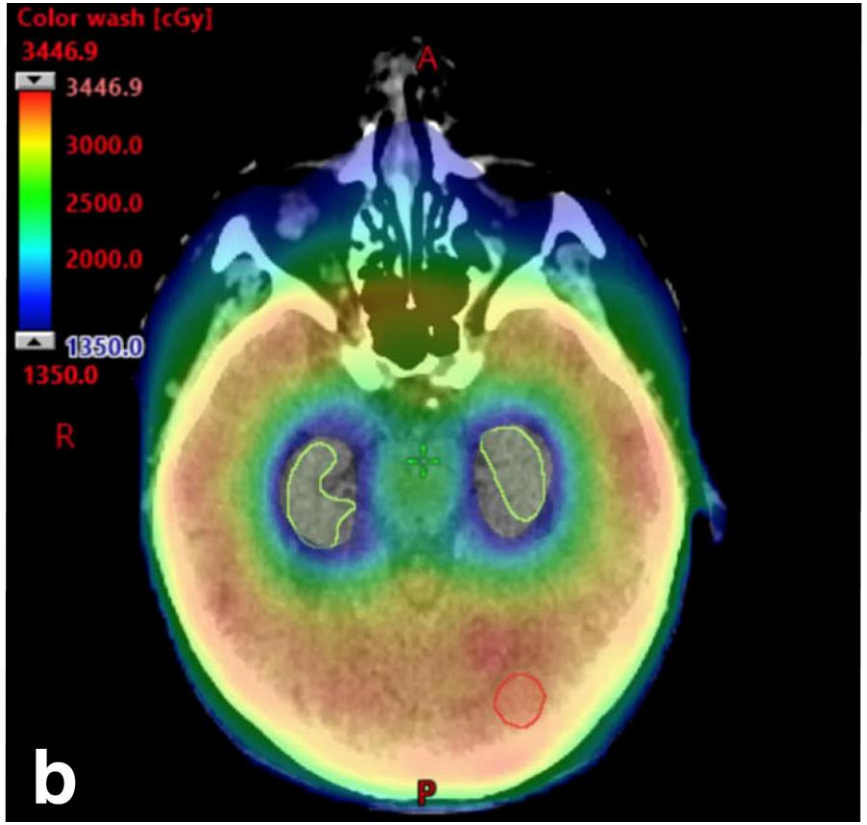
Tanguturi S, Warren LEG, Current Oncology Reports (2019) 21: 50, doi.org/10.1007/s11912-019-0803-5

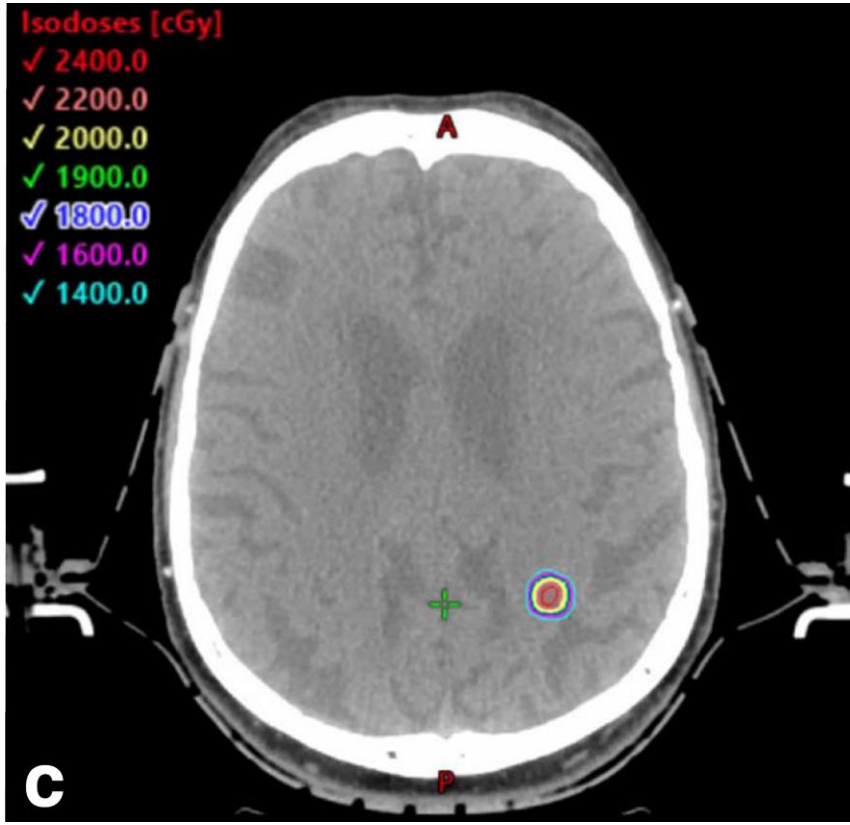
Any site can be treated, with favorable DVHs



RT for brain metastasis







Whole brain RT

Hippocampal avoidance (sparing) WBRT

Stereotactic radiosurgery

IEO: **15 patients/2020**

40 patients/2020

215 patients/2020

Tanguturi S, Warren LEG, Current Oncology Reports (2019) 21: 50, doi.org/10.1007/s11912-019-0803-5

SRS in > 10 mts

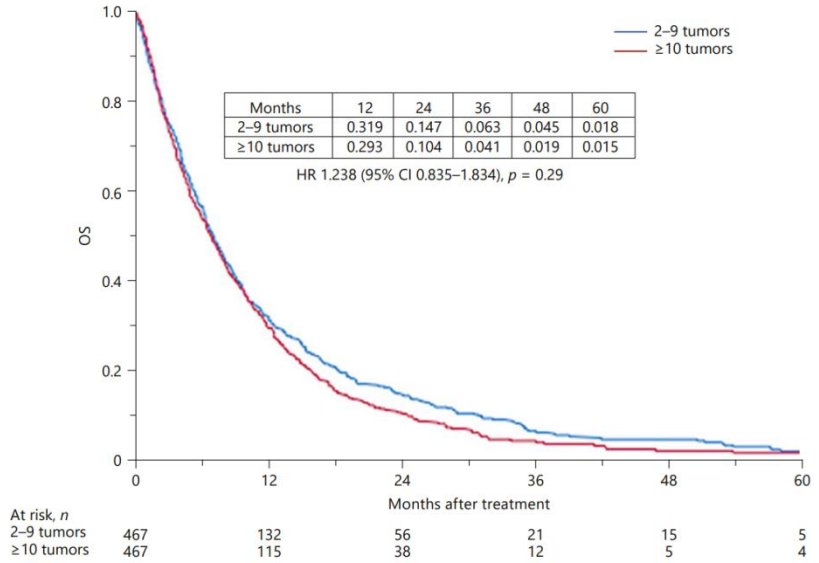
Tumor Radiosurgery

Niranjan A, Lunsford LD, Kano H (eds): Leksell Radiosurgery.
Prog Neurol Surg. Basel, Karger, 2019, vol 34, pp 110–124 (DOI: 10.1159/000493056)

Stereotactic Radiosurgery for Patients with 10 or More Brain Metastases

Masaaki Yamamoto[a, b] Yoshinori Higuchi[e] Yasunori Sato[c, d]
Hidetoshi Aiyama[a, e] Hidetoshi Kasuya[b] Bierta E. Barfod[a]

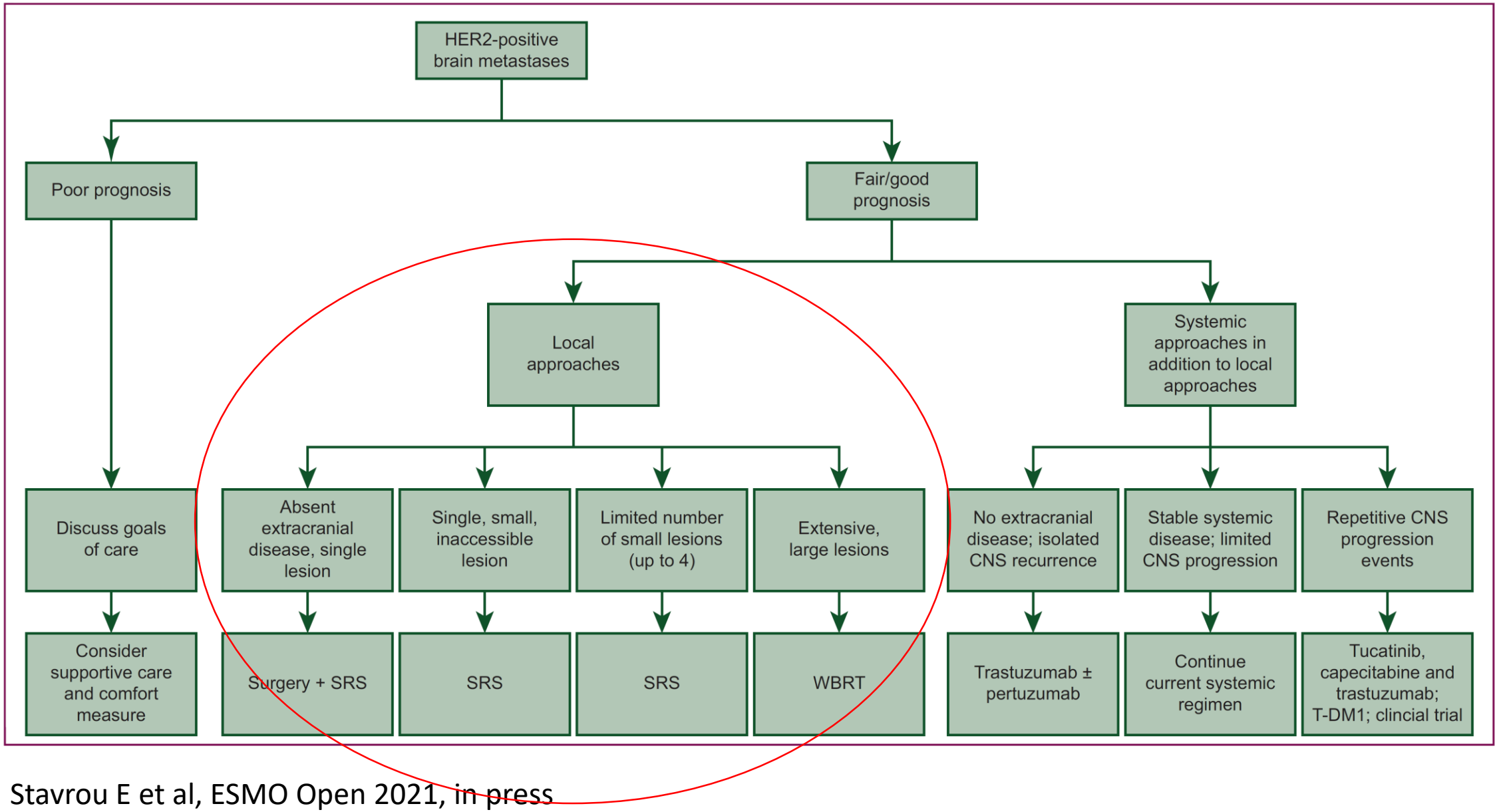
[a]Katsuta Hospital Mito Gamma House, Hitachinaka, Japan; [b]Department of Neurosurgery, Tokyo Women's Medical University Medical Center East, Tokyo, Japan; [c]Department of Neurosurgery, Chiba University Graduate School of Medicine, Chiba, Japan; [d]Department of Global Clinical Research, Chiba University Graduate School of Medicine, Chiba, Japan; [e]Department of Neurosurgery, Faculty of Medicine, University of Tsukuba, Tsukuba, Japan



Months	12	24	36	48	60
2–9 tumors	0.319	0.147	0.063	0.045	0.018
≥10 tumors	0.293	0.104	0.041	0.019	0.015

OS did not differ between patients with 2 to 4 metastases and those with 5–10 (median OS 10.8 months in both groups)

Boston algorythm for HER2-positive brain mets



Stavrou E et al, ESMO Open 2021, in press

SRT re-irradiation is feasible… (review 13 studies)

cancers

MDPI

Systematic Review

Efficacy and Safety of a Second Course of Stereotactic Radiation Therapy for Locally Recurrent Brain Metastases: A Systematic Review

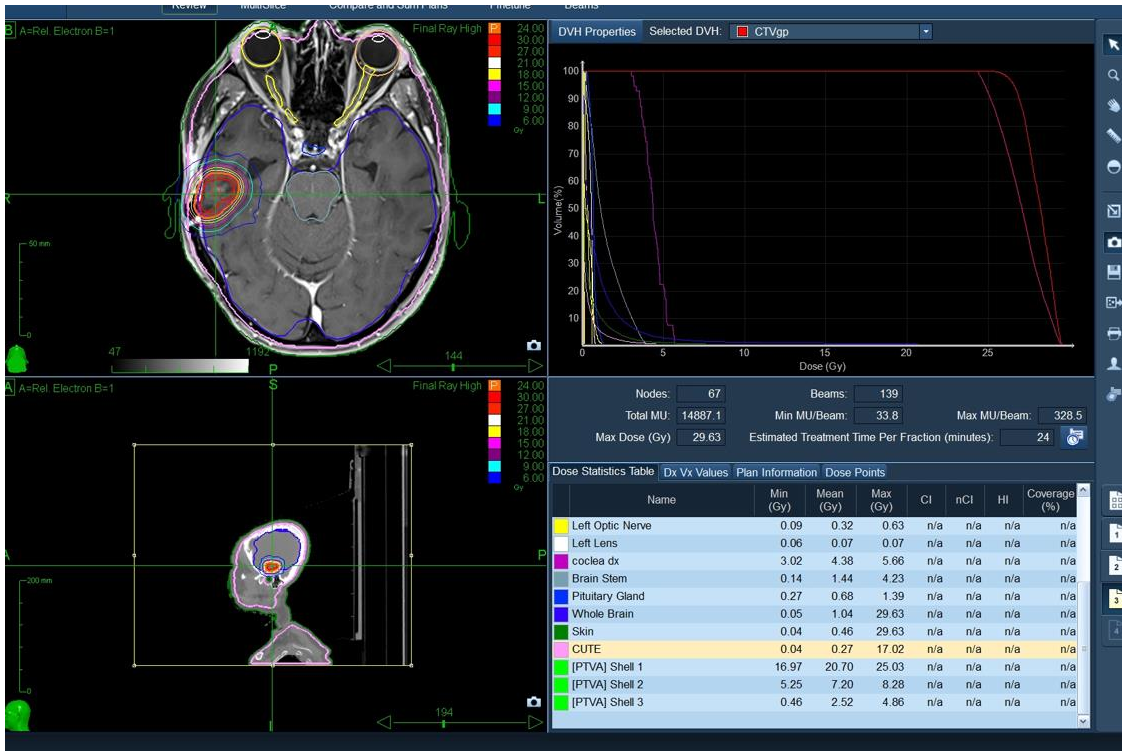
François Lucia [1,*], Ruben Touati [1], Nicolae Crainic [2], Gurvan Dissaux [1], Olivier Pradier [1], Vincent Bourbonne [1] and Ulrike Schick [1]

For patients with a limited number of BM, SRS/SRT achieves
favorable **tumor control rates of 80–90% at 12 months**
while sparing normal brain tissue, with a **radionecrosis (RN) rate of 3 to 5%**

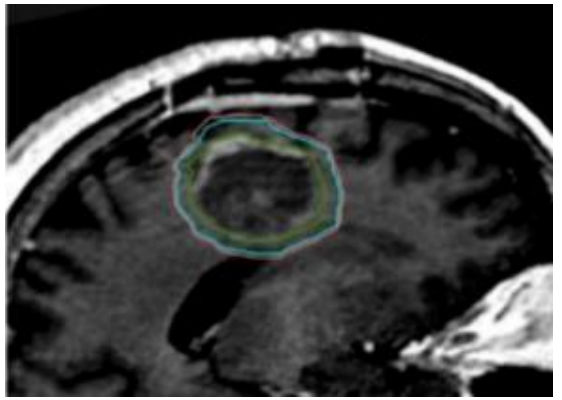
Cancers **2021**, 13, 4929. https://doi.org/10.3390/cancers13194929

Postoperative RT for brain mets

1. No RT
2. Whole brain RT
3. **Stereotactic RT (SRT, SRS)**



SRS to surgical cavity (tumor bed)

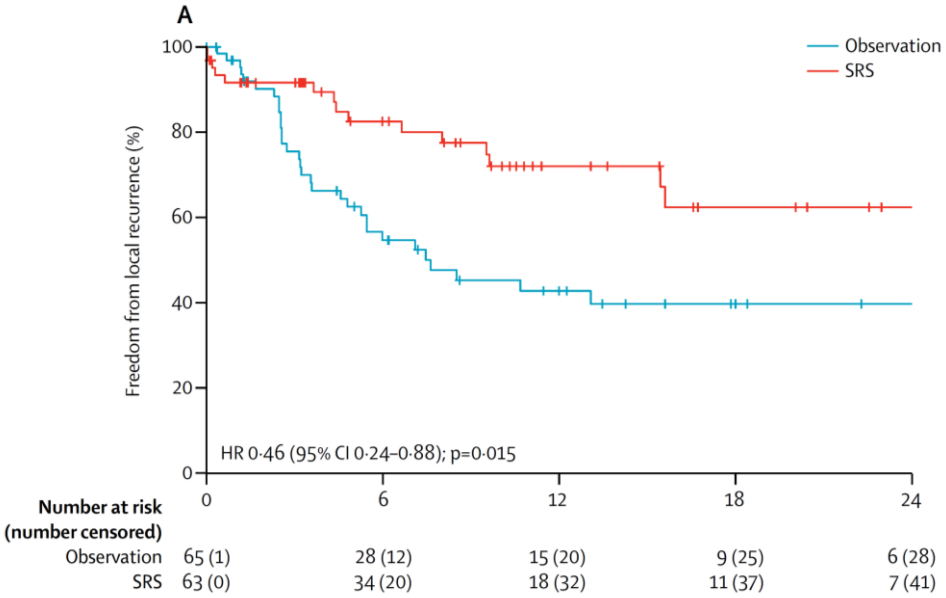


Post-operative stereotactic radiosurgery versus observation for completely resected brain metastases: a single-centre, randomised, controlled, phase 3 trial

Lancet Oncol 2017; 18: 1040–48

El Shafie et al Cancers **2019**, 11(3), 294;

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

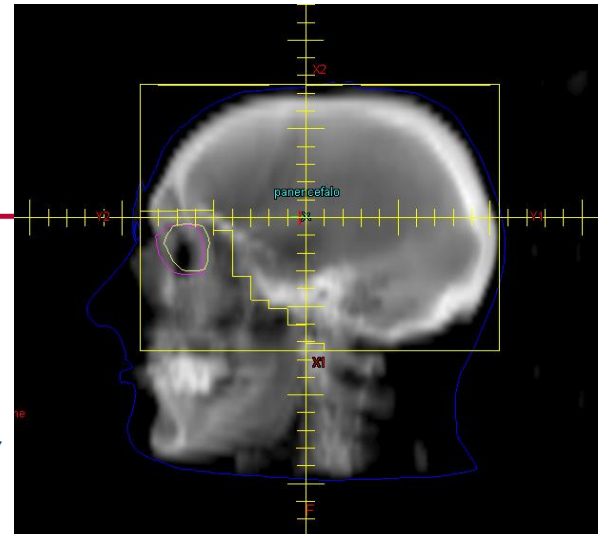


SRS improved the 1-year freedom from local failure

72% vs. 43%

P = 0.015

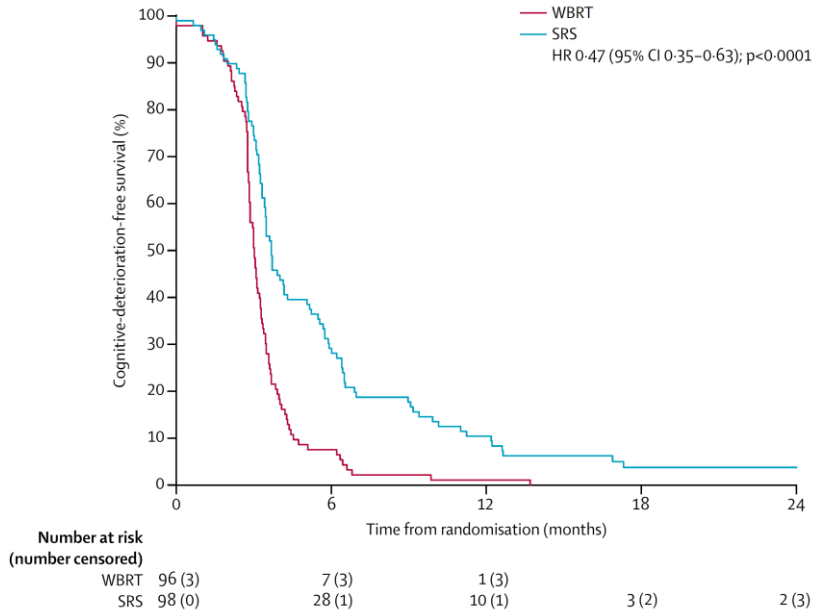
SRS or WBRT after surgery



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

Lancet Oncol 2017; 18: 1049–60

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



- **Decline in cognitive function - more frequent with WBRT than with SRS**
- No difference in overall survival
- SRS should be considered one of the standards of care as a less toxic alternative to WBRT

Critical Review

Stereotactic Radiosurgery for Postoperative Metastatic Surgical Cavities: A Critical Review and International Stereotactic Radiosurgery Society (ISRS) Practice Guidelines

Kristin J. Redmond, MD, MPH,* Antonio A.F. De Salles, MD, PhD,† Laura Fariselli, MD,‡ Marc Levivier, MD, PhD,§,‖ Lijun Ma, PhD,¶ Ian Paddick, MSc,# Bruce E. Pollock, MD,** Jean Regis, MD,†† Jason Sheehan, MD, PhD,‡‡ John Suh, MD,§§ Shoji Yomo, MD,‖‖ and Arjun Sahgal, MD¶¶

- 8 retrospective series, 1 phase 2 prospective study, 3 randomized controlled trials, and 1 consensus contouring paper
- Local control: 80.5%
- Randomized data suggest improved local control with single-fraction SRS compared with observation and improved cognitive outcomes compared with WBRT
- The toxicity of SRS/SRT in the postoperative setting was limited

Int J Radiation Oncol Biol Phys, Vol. 111, No. 1, pp. 68−80, 2021

Table 4 ISRS summary recommendations

Recommendation	Level of evidence
After surgery for a brain metastasis, postoperative SRS is preferred over observation due to superior local control	I
For patients with 1 resected brain metastasis, ECOG performance status of 0-2, and a resection cavity measuring <5 cm, postoperative SRS to the resection cavity is recommended to minimize cognitive toxicity compared with whole brain radiation therapy	I
Target volume should include the resection cavity and entire surgical tract with consideration to expand the clinical target volume to include a 5-10 mm expansion beyond the preoperative tumor location along bone flap in those tumors contacting the dura preoperatively, while respecting anatomic barriers, and a 1-5 mm expansion along sinuses for tumors contacting a sinus preoperatively. In addition, a 2-3 mm radial expansion to PTV should be considered.	III
Prescription doses of approximately 30-50 Gy $EQD2_{10}$, 50-70 $EQD2_5$, and 70-90 $EQD2_2$ have been associated with reasonable local control, but formal comparative studies are warranted. Emerging data suggest single-fraction treatment without dose de-escalation is appropriate in cavities <2 cm in size and that fractionated regimens may provide superior local control compared with single-fraction SRS in patients with large metastases greater than 2.5-3 cm.	III
The consent process for brain metastases surgery should include a discussion of the risk of surgical dissemination of tumor manifesting as leptomeningeal disease.	III

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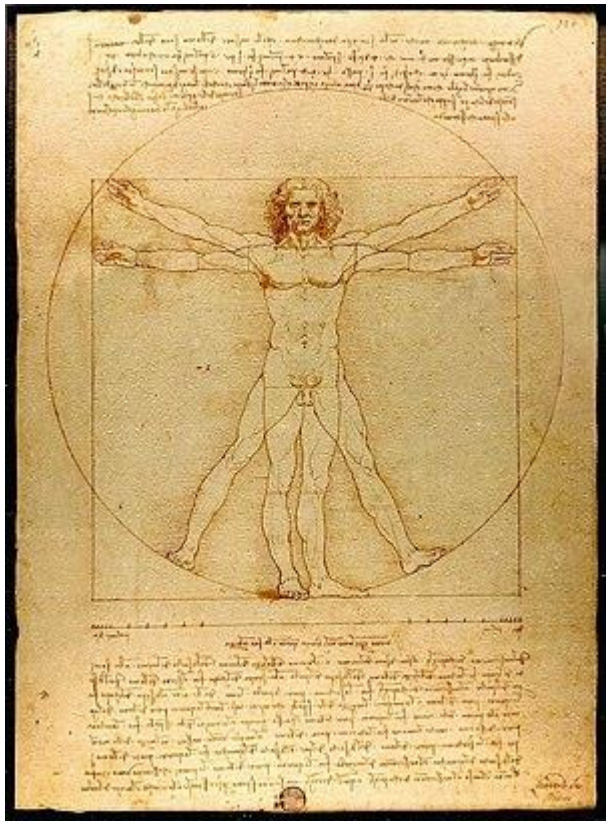
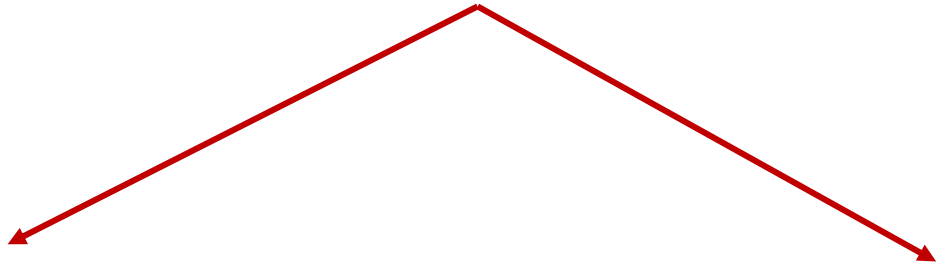


https://en.wikipedia.org/wiki/Vitruvian_Man#/media/File:Da_Vinci_Vitruve_Luc_Viatour.jpg

STAGE I NSCLC: SBRT vs RT TROG 09.02 CHISEL

Ball D. et al. Lancet Oncol 2019; 20: 494–503
Stereotactic ablative radiotherapy versus standard radiotherapy in stage 1 non-small-cell lung cancer (TROG 09.02 CHISEL): a phase 3, open-label, randomized controlled trial

101 patients : biopsy-confirmed stage 1 (T1–T2aN0M0) NSCLC
FDG-PET staged
medically inoperable or had refused surgery
ECOG 0-1
peripherally located tumor



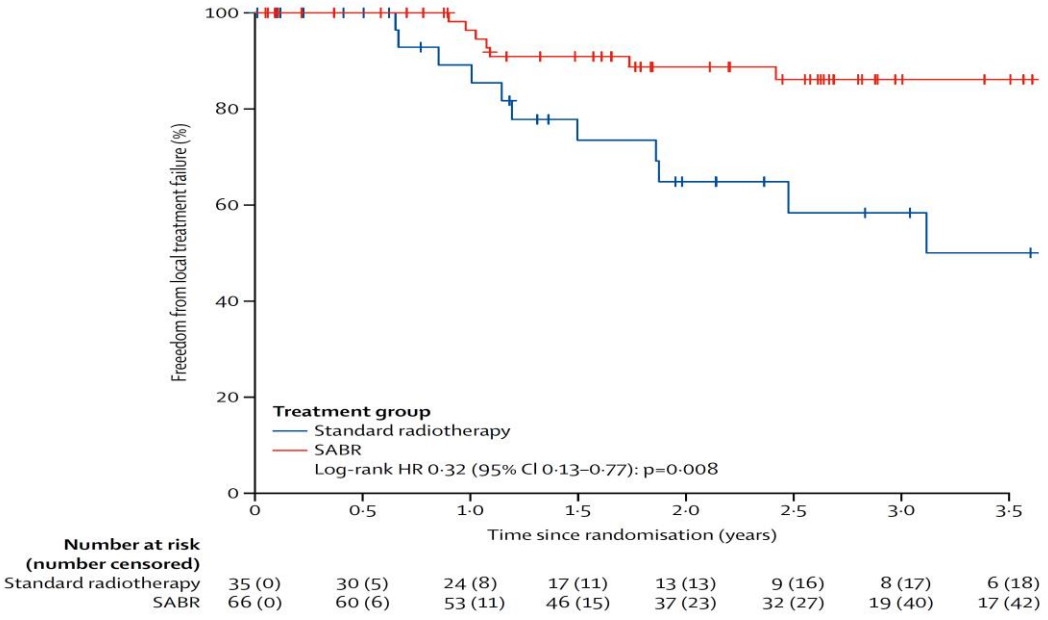
SABR
54 Gy/3 fr of 18 Gy
48 Gy/4 fr of 12 Gy

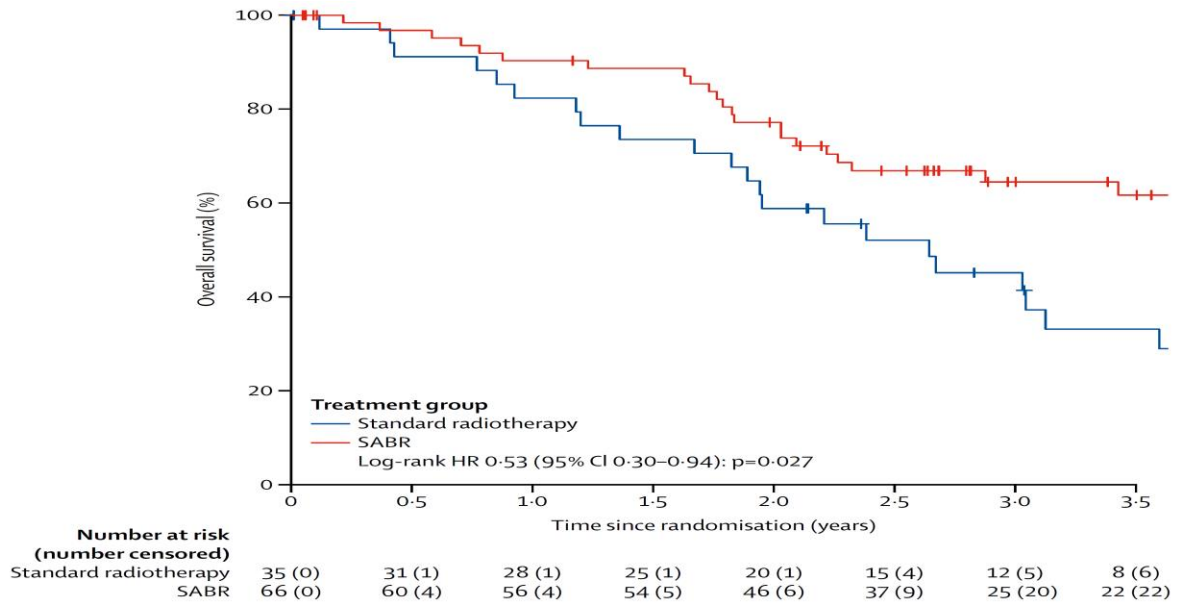
standard RT
66 Gy/33 fr of 2 Gy
50 Gy/20 fr of 2.5 Gy

STAGE I NSCLC: SBRT vs RT TROG 09.02 CHISEL

Ball D. et al. Lancet Oncol 2019; 20: 494–503

Stereotactic ablative radiotherapy versus standard radiotherapy in stage 1 non-small-cell lung cancer (TROG 09.02 CHISEL): a phase 3, open-label, randomized controlled trial





SABR: superior local control and OS without an increase in major toxicity

SABR should be the treatment of choice for this patient group

SBRT as alternative to surgery

SABRTooth: a randomised controlled feasibility study of stereotactic ablative radiotherapy (SABR) with surgery in patients with peripheral stage I nonsmall cell lung cancer considered to be at higher risk of complications from surgical resection

Kevin N. Franks[1,2,13], Lucy McParland[3,13], Joanne Webster[3], David R. Baldwin[4], David Sebag-Montefiore[1,2,3], Matthew Evison[5], Richard Booton[5], Corinne Faivre-Finn[6], Babu Naidu[7], Jonathan Ferguson[8], Clive Peedell[8], Matthew E.J. Callister[9], Martyn Kennedy[9], Jenny Hewison[10], Janine Bestall[10], Walter M. Gregory[3], Peter Hall[11], Fiona Collinson[3], Catherine Olivier[3], Rachel Naylor[3], Sue Bell[3], Peter Allen[12], Andrew Sloss[12] and Michael Snee[1]

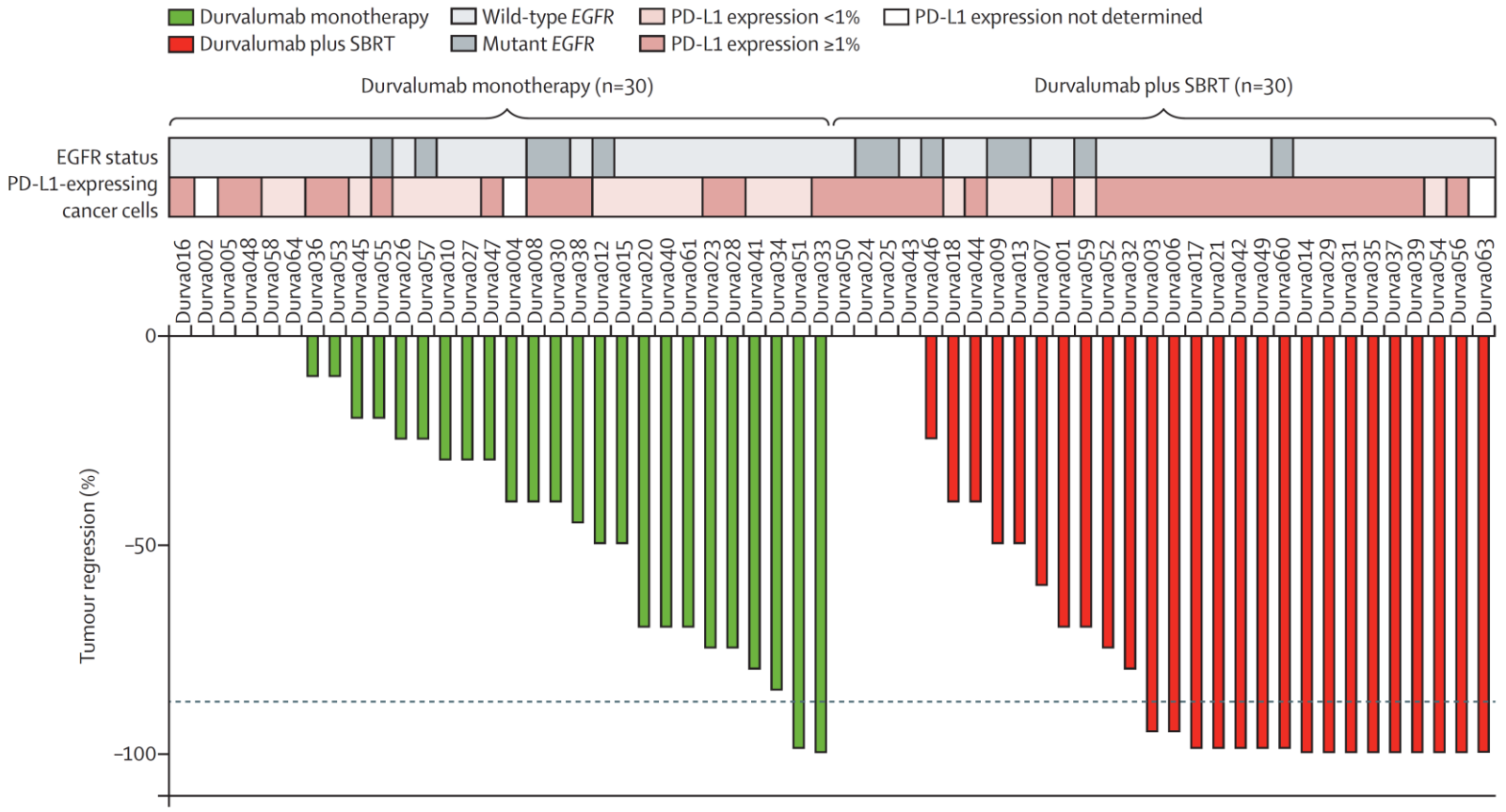
- A phase III RCT randomising higher risk patients between SABR and surgery is not feasible in the National Health Service.
- Patients have pre-existing treatment preferences, which was a barrier to recruitment.
- **A significant proportion of patients randomised to the surgical group declined and chose SABR.**

Eur Respir J 2020; 56: 2000118
https://doi.org/10.1183/13993003.00118-2020

Neoadjuvant durvalumab with or without stereotactic body radiotherapy in patients with early-stage non-small-cell lung cancer: a single-centre, randomised phase 2 trial

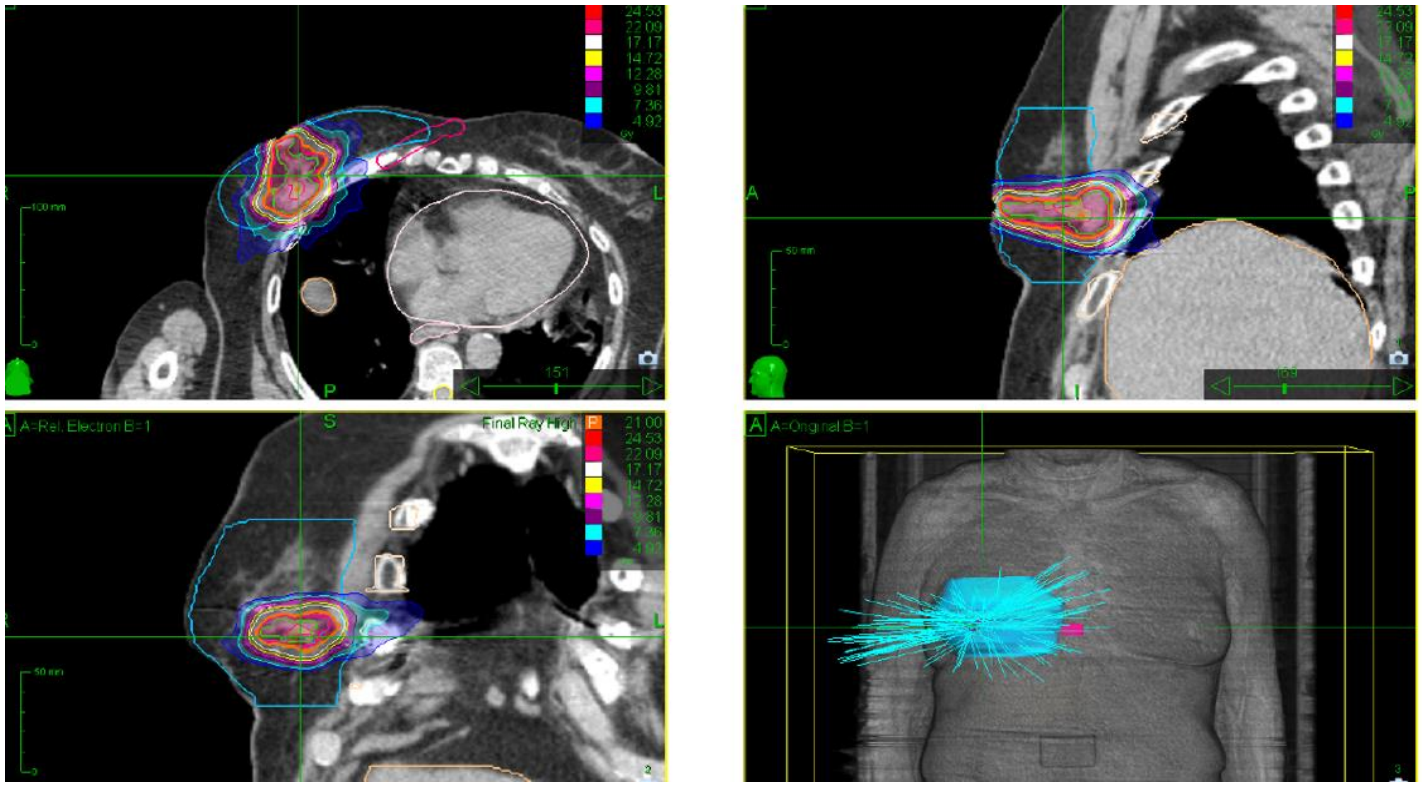
Nasser K Altorki, Timothy E McGraw, Alain C Borczuk, Ashish Saxena, Jeffrey L Port, Brendon M Stiles, Benjamin E Lee, Nicholas J Sanfilippo, Ronald J Scheff, Bradley B Pua, James F Gruden, Paul J Christos, Cathy Spinelli, Joyce Gakuria, Manik Uppal, Bhavneet Binder, Olivier Elemento, Karla V Ballman, Silvia C Formenti

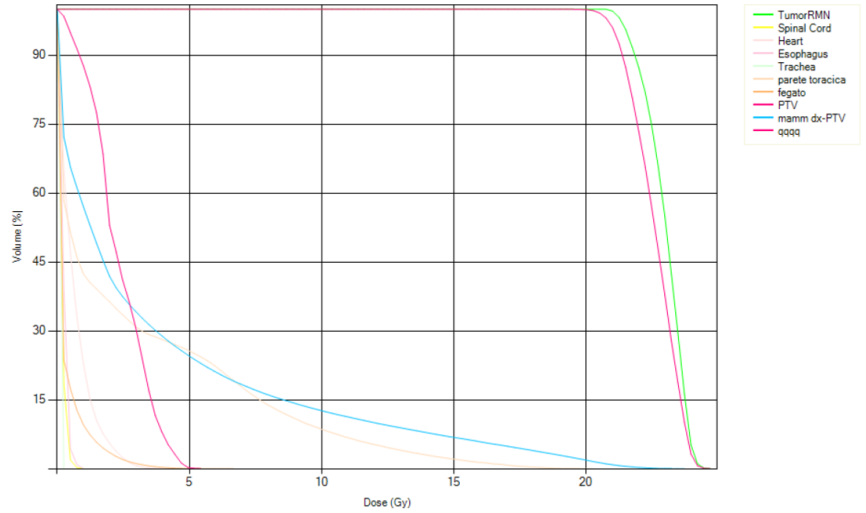
IT vs IT + SBRT



Lancet Oncol 2021; 22: 824–35

Breast cancer SBRT





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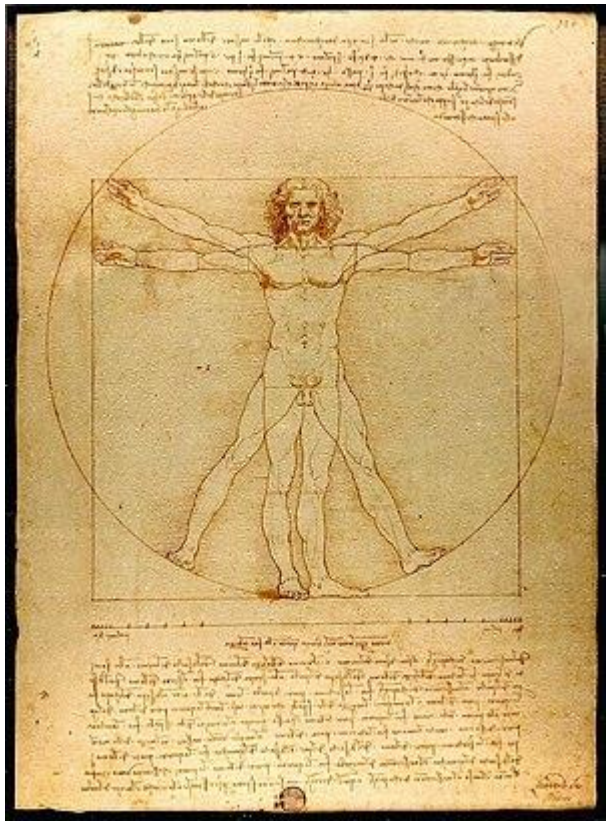
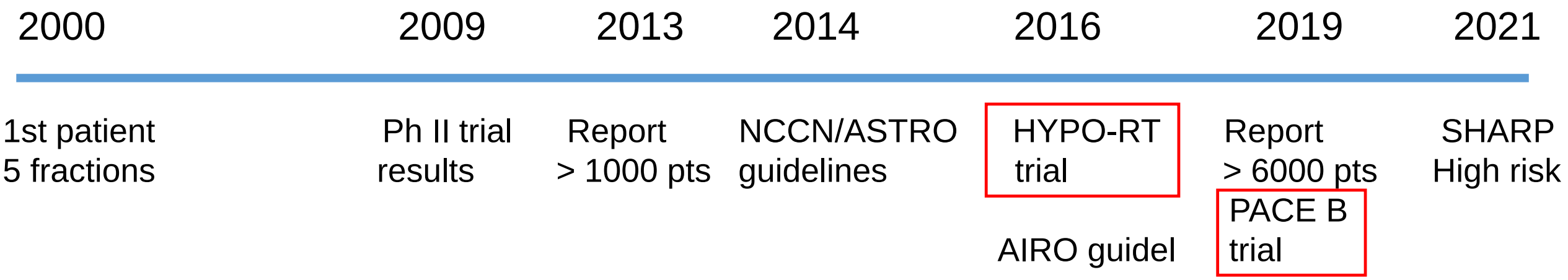


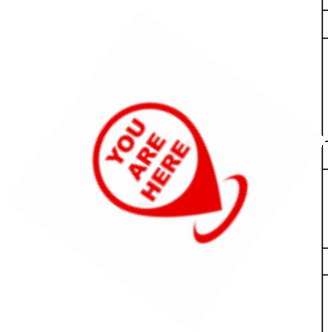
https://en.wikipedia.org/wiki/Vitruvian_Man#/media/File:Da_Vinci_Vitruve_Luc_Viatour.jpg

PROSTATE EXTREME HYPOFRACTIONATION



Courtesy of Thomas Zilli, ESTRO 2021

Where are we?



National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2021
Prostate Cancer

NCCN Guidelines Index
Table of Contents
Discussion

PRINCIPLES OF RADIATION THERAPY

Table 1: Below are examples of regimens that have shown acceptable efficacy and toxicity. The optimal regimen for an individual patient warrants evaluation of comorbid conditions, voiding symptoms and toxicity of therapy. Additional fractionation schemes may be used as long as sound oncologic principles and appropriate estimate of BED are considered.

See PROS-3, PROS-4, PROS-5, PROS-6, PROS-7, PROS-9, PROS-13, and PROS-G for other recommendations, including recommendations for neoadjuvant/concomitant/adjuvant ADT.

Regimen	Preferred Dose/Fractionation	NCCN Risk Group (✓ indicates an appropriate regimen option if radiation therapy is given)					
		Very Low and Low	Favorable Intermediate	Unfavorable Intermediate	High and Very High	Regional N1	Low Volume M1[a]
EBRT							
Moderate Hypofractionation (Preferred)	3 Gy x 20 fx 2.7 Gy x 26 fx 2.5 Gy x 28 fx	✓	✓	✓	✓	✓	
	2.75 Gy x 20 fx						✓
Conventional Fractionation	1.8–2 Gy x 37–45 fx	✓	✓	✓	✓	✓	
Ultra-Hypofractionation	7.25–8 Gy x 5 fx 6.1 Gy x 7 fx	✓	✓	✓	✓		
	6 Gy x 6 fx						✓
Brachytherapy Monotherapy							
LDR Iodine 125 Palladium 103 Cesium 131	145 Gy 125 Gy 115 Gy	✓	✓				
HDR Iridium-192	13.5 Gy x 2 implants 9.5 Gy BID x 2 implants	✓	✓				
EBRT and Brachytherapy (combined with 45–50.4 Gy x 25–28 fx or 37.5 Gy x 15 fx)							
LDR Iodine 125 Palladium 103 Cesium 131	110–115 Gy 90–100 Gy 85 Gy			✓	✓		
HDR Iridium-192	15 Gy x 1 fx 10.75 Gy x 2 fx			✓	✓		

[a] High-volume disease is differentiated from low-volume disease by visceral metastases and/or 4 or more bone metastases, with at least one metastasis beyond the pelvis vertebral column. Patients with low-volume disease have less certain benefit from early treatment with docetaxel combined with ADT.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

NCCN, ASTRO and AIRO guidelines

have included

ultrahypofractionation (SBRT)

as an option for Pca

in centers with technology&clinical expertise

EUROPEAN UROLOGY 79 (2021) 243–262

available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

Review – Prostate Cancer

EAU-EANM-ESTRO-ESUR-SIOG Guidelines on Prostate Cancer—2020 Update. Part 1: Screening, Diagnosis, and Local Treatment with Curative Intent

Nicolas Mottet [a,], Roderick C.N. van den Bergh [b], Erik Briers [c], Thomas Van den Broeck [d],*

Caution in high risk…


WHAT'S
NEXT

High risk Pca? Pelvis?

Focal boosting of the DIL

Shorter schedules

Courtesy of Giulia Marvaso, ESTRO 2021

Less than 5 fractions: 3? 2? 1?

Original Article

Two versus five stereotactic ablative radiotherapy treatments for localized prostate cancer: A quality of life analysis of two prospective clinical trials

Yasir Alayed [a,b,c], Harvey Quon [d], Patrick Cheung [a,b], William Chu [a,b], Hans T. Chung [a,b], Danny Vesprini [a,b], Aldrich Ong [e], Amit Chowdhury [e], Dilip Panjwani [f], Joelle Helou [g], Geordi Pang [a,b], Renee Korol [a,b], Melanie Davidson [a,b], Ananth Ravi [a,b], Boyd McCurdy [e], Liying Zhang [a], Alexandre Mamedov [a], Andrea Deabreu [a], Angela Commisso [a], Kristina Commisso [h], Andrew Loblaw [a,b,*]

[a] Odette Cancer Centre, Sunnybrook Health Sciences Centre, Toronto; [b] Department of Radiation Oncology, University of Toronto, Canada; [c] Division of Radiation Oncology, College of Medicine, King Saud University, Riyadh, Saudi Arabia; [d] Department of Radiation Oncology, Tom Baker Cancer Centre, Calgary; [e] CancerCare Manitoba, Winnipeg, Canada; [f] Compassionate Cancer Centers, India; [g] Department of Radiation Oncology, University of Toronto, Princess Margaret Cancer Centre; and [h] University Health Network, Toronto, Canada

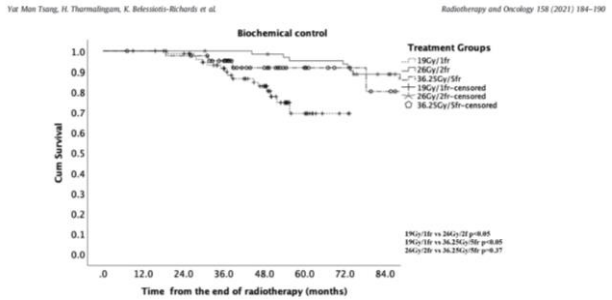
International Journal of Radiation Oncology biology • physics
www.redjournal.org

40Gy/3 fr

Clinical Investigation

Toxicity at 1 Year After Stereotactic Body Radiation Therapy in 3 Fractions for Localized Prostate Cancer

Alessandro Magli, MD,* Alessia Farneti, MD,† Adriana Faiella, MD,† Mariaconsiglia Ferriero, MD,‡ Valeria Landoni, PhD,§ Diana Giannarelli, PhD,‖ Eugenia Moretti, PhD,¶ Ugo de Paula, MD,# Sara Gomellini, MD,# and Giuseppe Sanguineti, MD†



JAMA Oncology | Original Investigation

Safety and Efficacy of Virtual Prostatectomy With Single-Dose Radiotherapy in Patients With Intermediate-Risk Prostate Cancer
Results From the PROSINT Phase 2 Randomized Clinical Trial

Carlo Greco, MD; Oriol Pares, MD; Nuno Pimentel, MD; Vasco Louro, MD; Inês Santiago, MD; Sandra Vieira, PhD; Joep Stroom, PhD; Dalila Mateus; Ana Soares; João Marques; Elda Freitas; Graça Coelho; Manuela Seixas; Antonio Lopez-Beltran, MD; Zvi Fuks, MD

24Gy/1fr

19Gy/1fr

19Gy/1fr
26Gy/2fr
36.25Gy/5fr

Radiotherapy and Oncology 159 (2021) 67–74
Contents lists available at ScienceDirect
Radiotherapy and Oncology
journal homepage: www.thegreenjournal.com

Original Article

Single dose high-dose-rate brachytherapy with focal dose escalation for prostate cancer: Mature results of a phase 2 clinical trial

Shreya Armstrong [a,b,*], Stephanie Brown [a], May Stancliffe [c,d], Peter Ostler [a], Robert Hughes [a], Peter Hoskin [a], Roberto Alonzi [a]

Radiotherapy and Oncology 158 (2021) 184–190
Contents lists available at ScienceDirect
Radiotherapy and Oncology
journal homepage: www.thegreenjournal.com

Original Article

Ultra-hypofractionated radiotherapy for low- and intermediate risk prostate cancer: High-dose-rate brachytherapy vs stereotactic ablative radiotherapy

Yat Man Tsang [a,*], Hannah Tharmalingam [a], Katherine Belessiotis-Richards [a], Shreya Armstrong [a], Peter Ostler [a], Robert Hughes [a], Roberto Alonzi [a], Peter J Hoskin [a,b]

Radiotherapy and Oncology 139 (2019) 83–86
Contents lists available at ScienceDirect
Radiotherapy and Oncology
journal homepage: www.thegreenjournal.com

Short Communication

Single fraction urethra-sparing prostate cancer SBRT: Phase I results of the ONE SHOT trial

Thomas Zilli [a,b,*], Ciro Franzese [d], Marta Bottero [a], Niccolò Giaj-Levra [g], Robert Förster [f], Daniel Zwahlen [e], Nikolaos Koutsouvelis [a], Aurelie Bertaut [h], Julie Blanc [h], Giuseppe Roberto D'agostino [d], Filippo Alongi [g,i], Matthias Guckenberger [f], Marta Scorsetti [c,d], Raymond Miralbell [a,b]

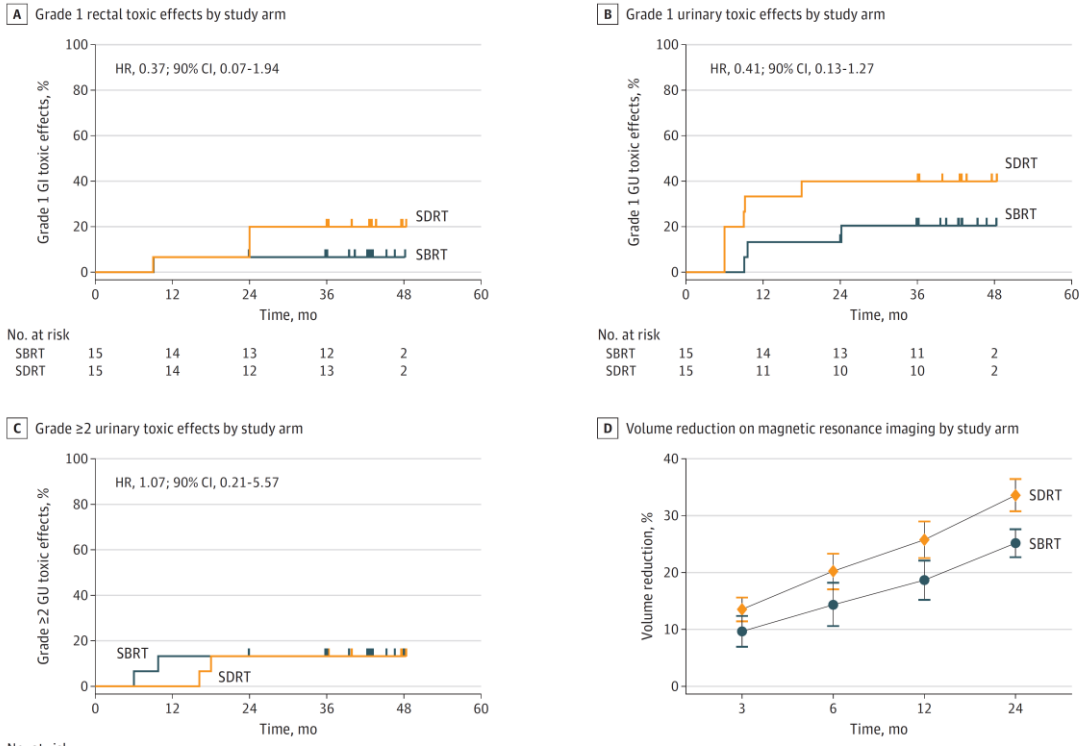
JAMA Oncology | Original Investigation

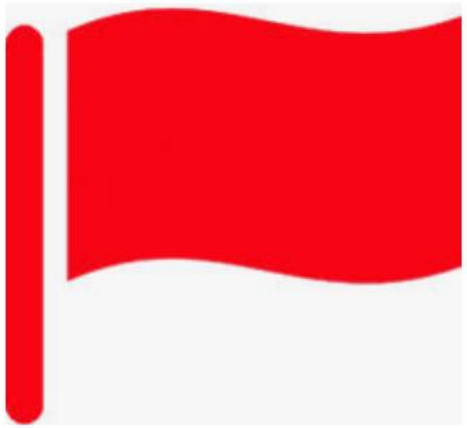
Safety and Efficacy of Virtual Prostatectomy With Single-Dose Radiotherapy in Patients With Intermediate-Risk Prostate Cancer

Results From the PROSINT Phase 2 Randomized Clinical Trial

Carlo Greco, MD; Oriol Pares, MD; Nuno Pimentel, MD; Vasco Louro, MD; Inês Santiago, MD; Sandra Vieira, PhD; Joep Stroom, PhD; Dalila Mateus; Ana Soares; João Marques; Elda Freitas; Graça Coelho; Manuela Seixas; Antonio Lopez-Beltran, MD; Zvi Fuks, MD

ground- breaking





PROSTATE CANCER

Single dose prostate radiotherapy — a step too far?

Alison C. Tree and Nicholas J. van As

LOCAL SALVAGE APPROACH

1. Surgery
2. HIFU
3. Cryotherapy
4. BRT


available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

Review – Prostate Cancer

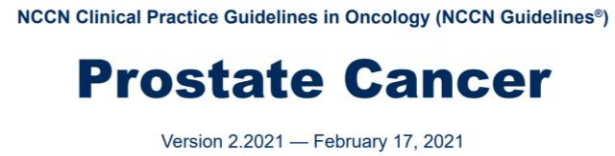
EAU-EANM-ESTRO-ESUR-SIOG Guidelines on Prostate Cancer. Part II—2020 Update: Treatment of Relapsing and Metastatic Prostate Cancer


ESMO

ANNALS OF ONCOLOGY

SPECIAL ARTICLE

Prostate cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†


NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Prostate Cancer

Version 2.2021 — February 17, 2021

SBRT


Radiotherapy and Oncology 129 (2018) 377–386

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Guidelines

Radiotherapy for recurrent prostate cancer: 2018 Recommendations of the Australian and New Zealand Radiation Oncology Genito-Urinary group

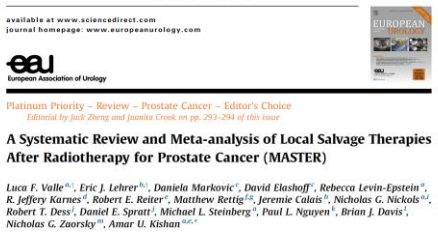
Hester Lieng, Amy J. Hayden, David R.H. Christie, Brian J. Davis, Thomas N. Eade, Louise Emmett, Tanya Holt, George Hruby, David Pryor, Thomas P. Shakespeare, Mark Sidhom, Marketa Skala, Kirsty Wiltshire, John Yaxley, Andrew Kneebone

.

Cornford P et al**. EAU-ESTRO-SIOG Guidelines on Prostate Cancer** Eur Urol. 2021;79:263-282.
Parker C, et al. Prostate cancer: **ESMO Clinical Practice Guidelines.** Ann Oncol 2020;31:1119-34
NCCN Clinical practice guidelines in Oncology 2021
Lieng H et al. Radioth Oncol 2018;129:377–386

Finally 2021

Meta-analyses	MASTER, Valle LF et al. Eur Urol. 2021 Sep;80(3):280-292 Corkum MT et al., Adv Radiat Oncol . 2020;5:965-977 Ingrosso G et al., Eur Urol Oncol 2020;3:183-197
Systematic Reviews and Reviews	Munoz F et al., Cancer Treat Rev 2021;95:102176 Baty M et al. Cancer/Radiotherapie 2019;23:541-558 Philippou Y et al. Eur Urol Focus 2016;2:158-171 Tetreault-Laflamme A et al. Semin Radiat Oncol 2016
ESTRO ACROP Consensus	Jereczek-Fossa BA et al. Cancer Treat Rev 2021;98:102206



EUROPEAN UROLOGY 80 (2021) 280–292

available at www.sciencedirect.com
journal homepage: www.europeanurology.com

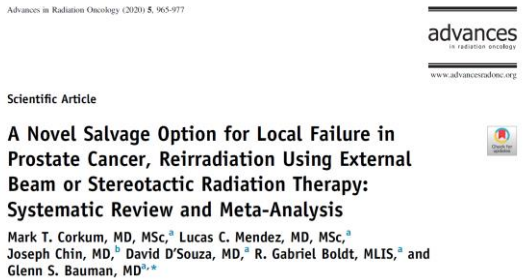
European Association of Urology

Platinum Priority – Review – Prostate Cancer – Editor's Choice

Editorial by Jack Zheng and Juanita Crook on pp. 293–294 of this issue

A Systematic Review and Meta-analysis of Local Salvage Therapies After Radiotherapy for Prostate Cancer (MASTER)

Luca F. Valle, Eric J. Lehrer, Daniela Markovic, David Elashoff, Rebecca Levin-Epstein, R. Jeffery Karnes, Robert E. Reiter, Matthew Rettig, Jeremie Calais, Nicholas G. Nickols, Robert T. Dess, Daniel E. Spratt, Michael L. Steinberg, Paul L. Nguyen, Brian J. Davis, Nicholas G. Zaorsky, Amar U. Kishan



Advances in Radiation Oncology (2020) 5, 965-977

advances in radiation oncology

www.advancesradonc.org

Scientific Article

A Novel Salvage Option for Local Failure in Prostate Cancer, Reirradiation Using External Beam or Stereotactic Radiation Therapy: Systematic Review and Meta-Analysis

Mark T. Corkum, MD, MSc,[a] Lucas C. Mendez, MD, MSc,[a] Joseph Chin, MD,[b] David D'Souza, MD,[a] R. Gabriel Boldt, MLIS,[a] and Glenn S. Bauman, MD[a,*]

Cancer Treatment Reviews 95 (2021) 102176

Contents lists available at ScienceDirect

Cancer Treatment Reviews

journal homepage: www.elsevier.com/locate/ctrv

Systematic or Meta-analysis Studies

Outcomes and toxicities of re-irradiation for prostate cancer: A systematic review on behalf of the Re-Irradiation Working Group of the Italian Association of Radiotherapy and Clinical Oncology (AIRO)

Fernando Munoz, Francesco Fiorica, Luciana Caravatta, Consuelo Rosa, Letizia Ferella, Luca Boldrini, Bruno Fionda, Anna Rita Alitto, Alessia Nardangeli, Francesco Dionisi, Stefano Arcangeli, Alessandro Di Marzo, Antonio Pontoriero, Vittorio Donato, Mariangela Massaccesi

Cancer Treatment Reviews 98 (2021) 102206

Contents lists available at ScienceDirect

Cancer Treatment Reviews

journal homepage: www.elsevier.com/locate/ctrv

Hot Topic

Salvage stereotactic body radiotherapy (SBRT) for intraprostatic relapse after prostate cancer radiotherapy: An ESTRO ACROP Delphi consensus

Barbara A. Jereczek-Fossa, Giulia Marvaso, Mattia Zaffaroni, Simone Giovanni Gugliandolo, Dario Zerini, Federica Corso, Sara Gandini, Filippo Alongi, Alberto Bossi, Philip Cornford, Berardino De Bari, Valérie Fonteyne, Peter Hoskin, Bradley R. Pieters, Alison C. Tree, Stefano Arcangeli, Donald B. Fuller, Ciro Franzese, Jean-Michel Hannoun-Levi, Guillaume Janoray, Linda Kerkmeijer, Young Kwok, Lorenzo Livi, Mauro Loi, Raymond Miralbell, David Pasquier, Michael Pinkawa, Nathaliel Scher, Marta Scorsetti, Mohamed Shelan, Alain Toledano, Nicholas van As, Andrea Vavassori, Thomas Zilli, Matteo Pepa, Piet Ost, on the behalf of the European Society for Radiotherapy, Oncology Advisory Committee on Radiation Oncology Practice (ESTRO ACROP)

The best option?

Invasive RP

Less invasive HIFU, cryo, BRT

Non invasive SBRT

Salvage therapy	5y biochemical control	GU tox (G3-4)	GI tox (G3-G4)
Prostatectomy	37-65%	15-65%	5-10%
HIFU	45-54%	10-40%	0.5-6%
Cryotherapy	50% (23-70%)	3-19%	2%-14%
Brachytherapy	50% (34-77%)	10-20%	2%-6%
SBRT	**35-50%**	**0-5%**	**0-2%**

Tetreault-Laflamme A, Crook J Semin Radiat Oncol 2016;27:67-78

A Systematic Review and Meta-analysis of Local Salvage Therapies After Radiotherapy for Prostate Cancer (MASTER)

Luca F. Valle[a,†], *Eric J. Lehrer*[b,†], *Daniela Markovic*[c], *David Elashoff*[c], *Rebecca Levin-Epstein*[a], *R. Jeffery Karnes*[d], *Robert E. Reiter*[e], *Matthew Rettig*[f,g], *Jeremie Calais*[h], *Nicholas G. Nickols*[a,i], *Robert T. Dess*[j], *Daniel E. Spratt*[j], *Michael L. Steinberg*[a], *Paul L. Nguyen*[k], *Brian J. Davis*[l], *Nicholas G. Zaorsky*[m], *Amar U. Kishan*[a,e,*]

Table 1 – Summary of patient and treatment characteristics for local salvage modalities

	Age (yr)	Whole-gland salvage (%)	Biopsy-proven recurrence (%)	Presalvage PSA (ng/mL)	Perisalvage ADT use (%)	Interval from initial treatment to recurrence or salvage (mo)	Median follow-up (mo)	Number of studies (*n*)	Number of patients (*n*)
RP	65	100	99	6.0	16	50	47	52	2686
Cryotherapy	66	93	99	5.8	35	63	32	32	5153
HIFU	69	86	100	5.0	18	63	33	20	1783
SBRT	72	61	81	4.0	37	89	26	8	261
HDR	71	85	94	4.5	43	61	40	16	586
LDR	69	92	95	5.5	37	67	52	32	853

ADT = androgen deprivation therapy; HDR = high-dose-rate brachytherapy; HIFU = high-intensity focused ultrasound; LDR = low-dose-rate brachytherapy; PSA = prostate-specific antigen; RP = radical prostatectomy; SBRT = stereotactic body radiotherapy.

Eur Urol 2020 Dec 10;S0302-2838(20)30874-5

150 studies were included for analysis.

Invasive:

Radical prostatectomy

=

Less invasive:

Cryo
HIFU
BRT

=

Non Invasive:

SBRT

Tumor control

Valle L et al. Eur Urol 2020 Dec 10;S0302-2838(20)30874-5

150 studies were included for analysis.

Invasive:

Radical
prostatectomy
HIFU

=

Less
invasive:

Cryo
BRT

=

Non
Invasive
SBRT

GU toxicity

Valle L et al. Eur Urol 2020 Dec 10;S0302-2838(20)30874-5

150 studies were included for analysis.

Invasive:

Radical prostatectomy
Cryo
HIFU

=

BRT

=

SBRT

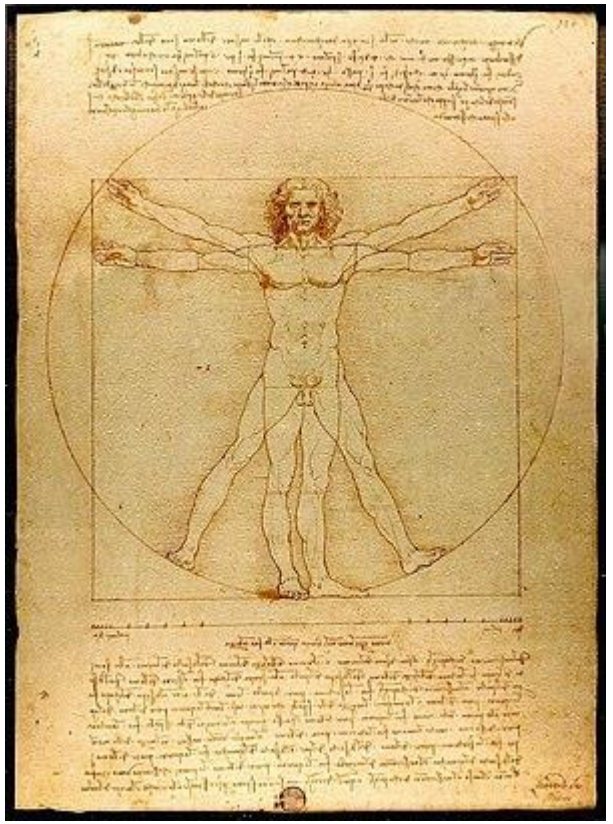
GI Toxicity

Valle L et al. Eur Urol 2020 Dec 10;S0302-2838(20)30874-5

AGENDA

- ❑ SBRT and SRS
- ❑ Brain
- ❑ Thorax
- ❑ Abdomen/pelvi
- ❑ **Particular scenarios:**

oligometastases, re-irradiation



https://en.wikipedia.org/wiki/Vitruvian_Man#/media/File:Da_Vinci_Vitruve_Luc_Viatour.jpg

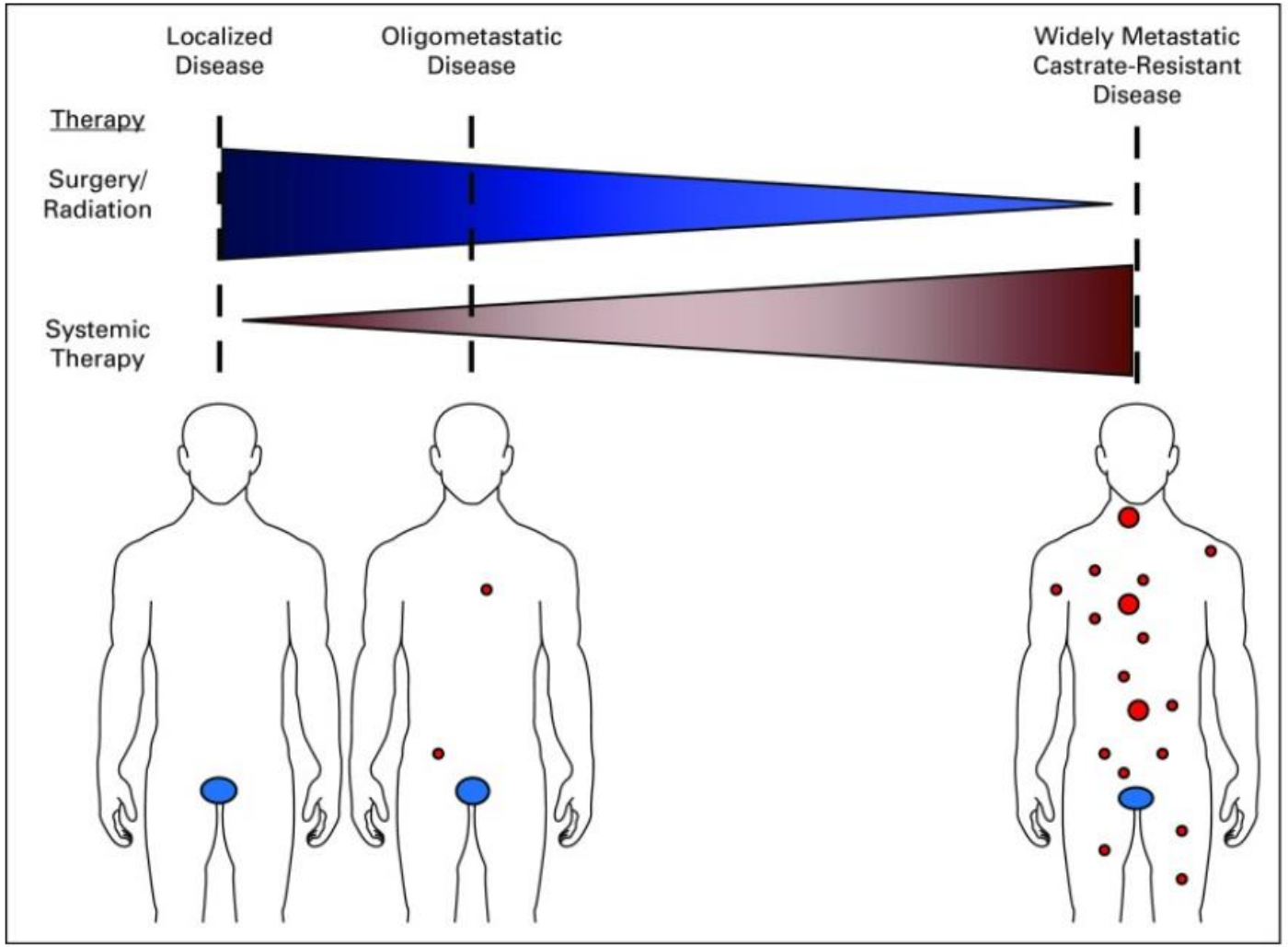
DEFINITION

1. Nr of mets

DEFINITION

1. Nr of mets
2. Volume of mets
3. Nr of organs
4. Type of organs (lymph nodes, bone, visceral organs)
5. Primary tumor
6. Time to occurrence

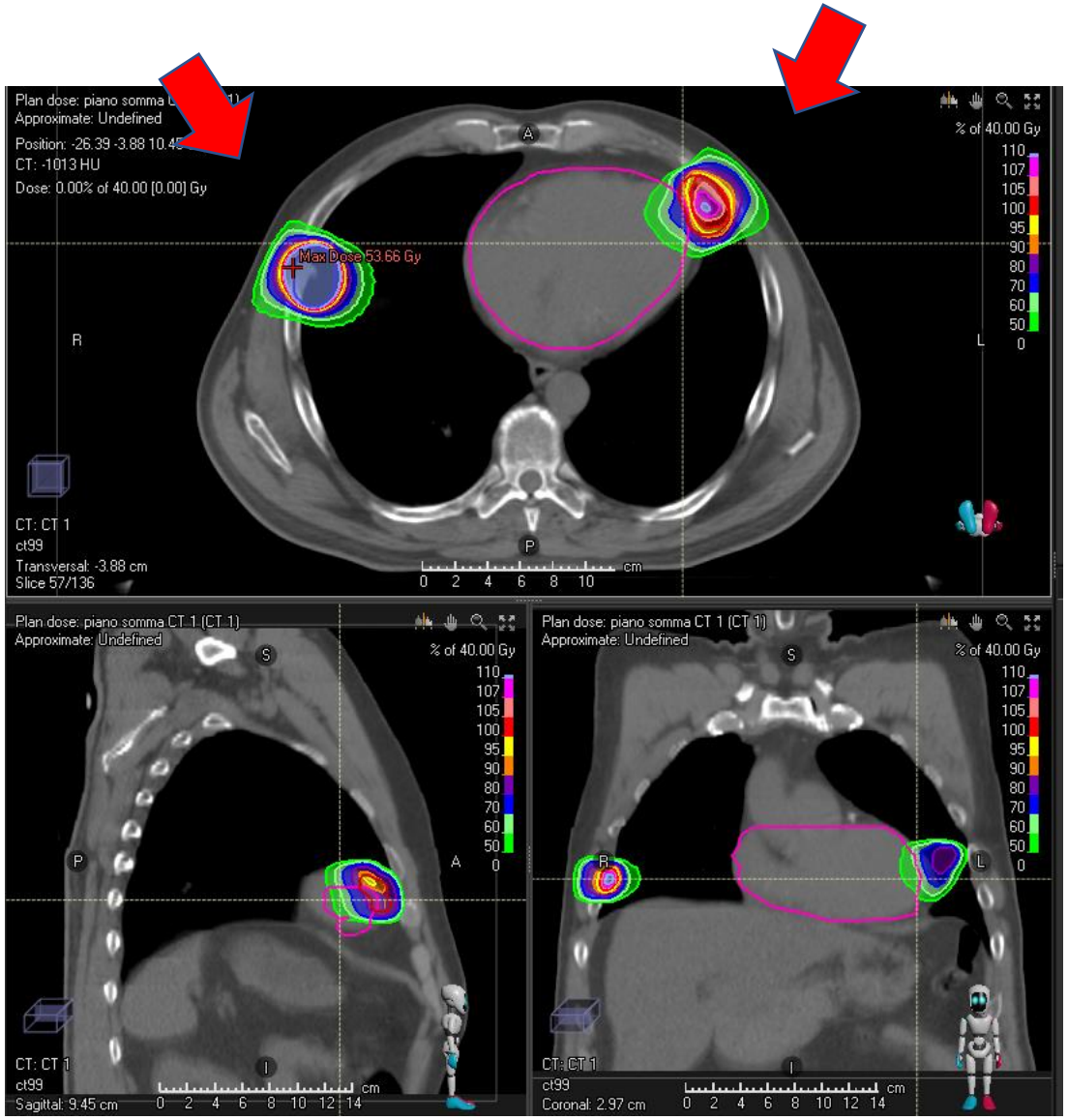
Altering the natural history of oligometastatic cancer



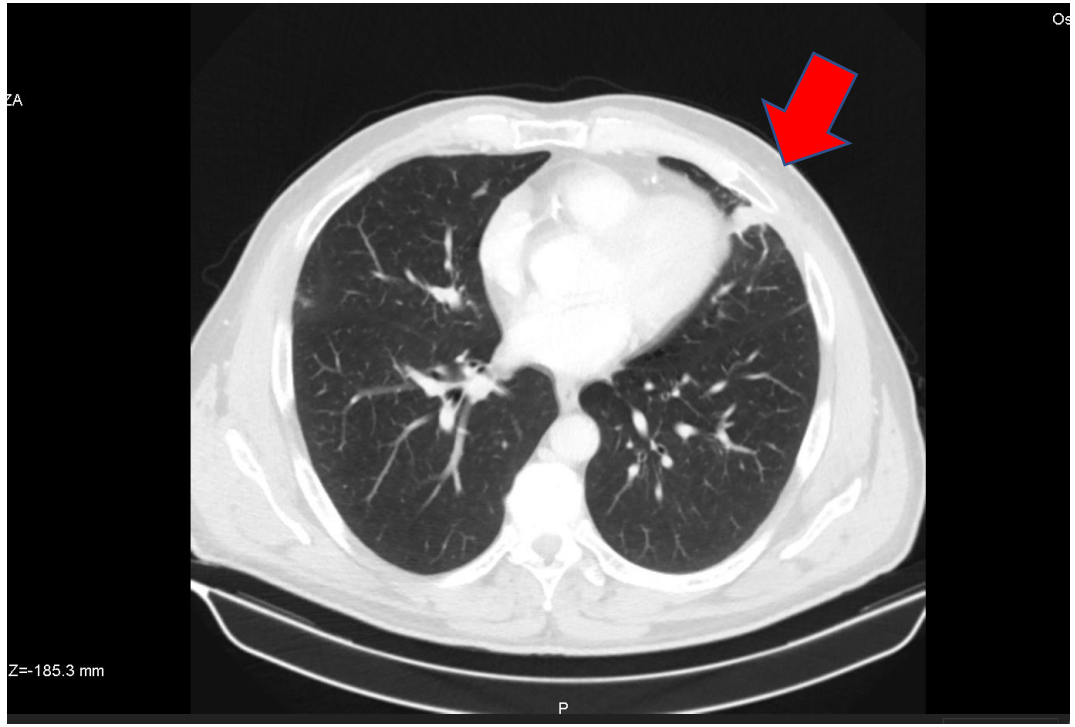
Tran PT, Antonarakis ES, Journal of Oncology Practice, 03 Jan 2017, 13(1):21-24
DOI: 10.1200/jop.2016.018846

SBRT: 50 Gy in 5 fractions

SBRT: 40 Gy in 5 fractions

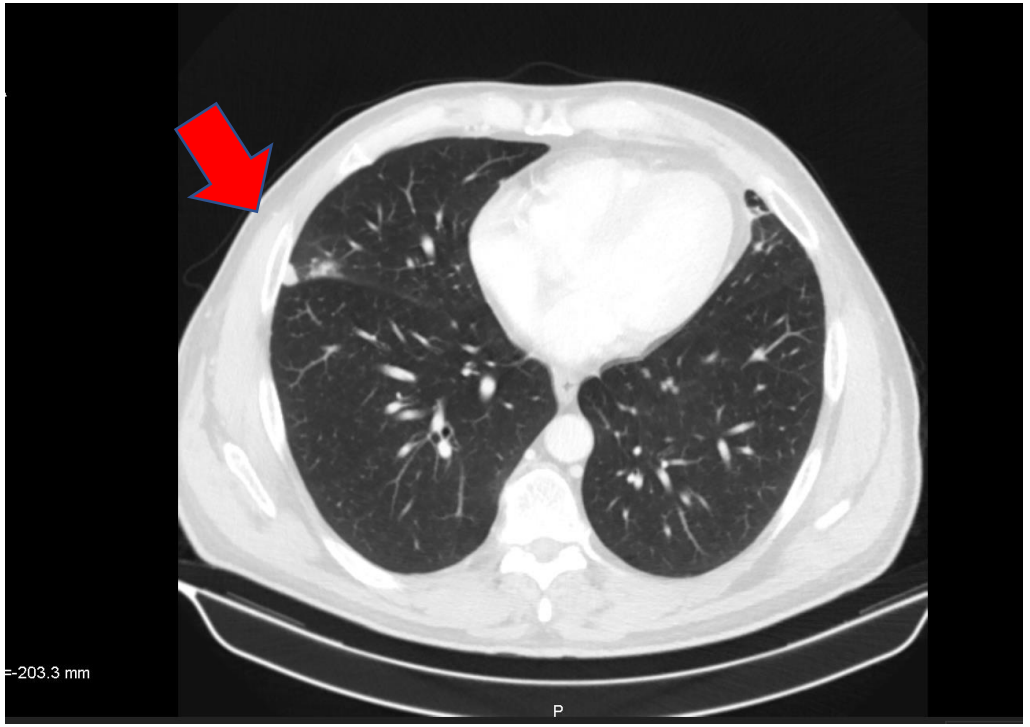


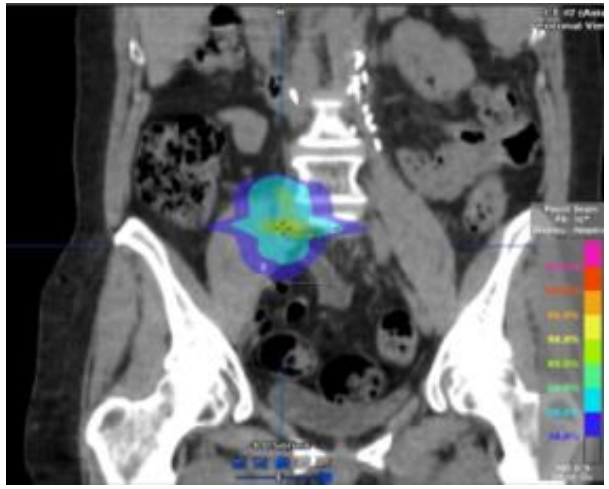
Radioterapia ablativa Stereotassica



TC di controllo

Da 2.5 anni
senza terapia
attiva
(drug holiday)





Local Consolidative Therapy Vs. Maintenance Therapy or Observation for Patients With Oligometastatic Non–Small-Cell Lung Cancer: Long-Term Results of a Multi-Institutional, Phase II, Randomized Study

Gomez D et al published at jco.org on May 8, 2019: DOI https://doi.org/10.1200/JCO.19.00201

- Early trial closure after 49 patients (a significant PFS benefit in the LCT arm)
- With an updated median follow-up time of 38.8 months:

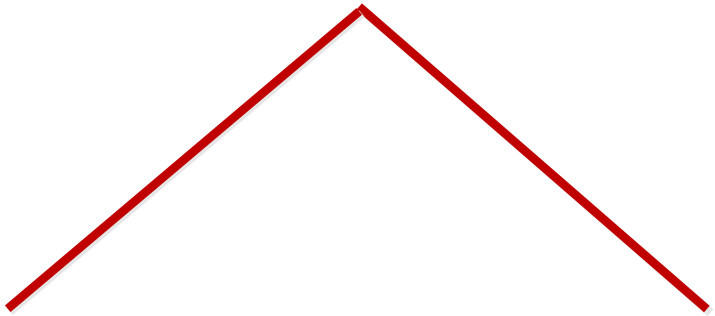
	LCT	MT/O	
PFS	14.2m	4.4m	P=0.022
OS	41.2m	17m	P=0.017

tripling PFS
nearly tripling OS

- No additional grade 3 or greater toxicities were observed.

SABR-COMET study

Oligometastatic breast, colon, prostate, lung cancer



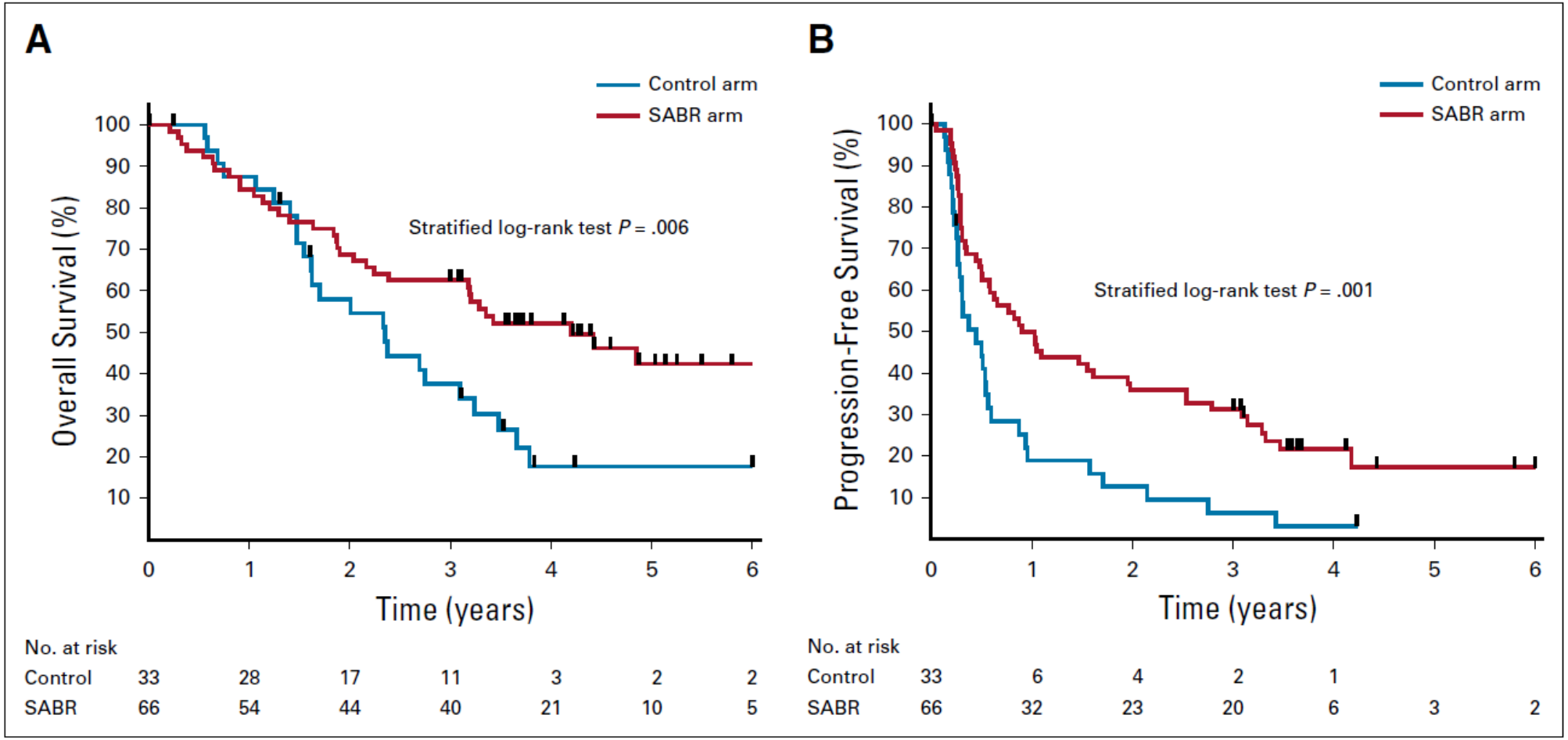
Standard of care

Standard of care
+ SBRT

Palma DA et al. J Clin Oncol 38:2830-2838.

Benefit in OS: **22 m**

Absolute benefit at 5 years: **24.6%**



Palma DA et al. J Clin Oncol 38:2830-2838.

Palma et al. BMC Cancer (2019) 19:816
https://doi.org/10.1186/s12885-019-5977-6

BMC Cancer

STUDY PROTOCOL Open Access

Stereotactic ablative radiotherapy for the comprehensive treatment of 4–10 oligometastatic tumors (SABR-COMET-10): study protocol for a randomized phase III trial

David A. Palma[1*], Robert Olson[2], Stephen Harrow[3], Rohann J. M. Correa[1], Famke Schneiders[4], Cornelis J. A. Haasbeek[4], George B. Rodrigues[1], Michael Lock[1], Brian P. Yaremko[1], Glenn S. Bauman[1], Belal Ahmad[1], Devin Schellenberg[2], Mitchell Liu[2], Stewart Gaede[1], Joanna Laba[1], Liam Mulroy[5], Sashendra Senthi[6], Alexander V. Louie[7], Anand Swaminath[8], Anthony Chalmers[9], Andrew Warner[1], Ben J. Slotman[4], Tanja D. de Gruijl[4], Alison Allan[1] and Suresh Senan[4]

New histologies: TCC

1. Patel V, et al. (2017) Survival after metastasectomy for metastatic urothelial carcinoma: a systematic review and meta-analysis Bl Cancer 3(2) 121–132

2. Shah S, et al (2017) Consolidative radiotherapy in metastatic urothelial cancer Clin Genitourin Cancer 15(6) 685–688

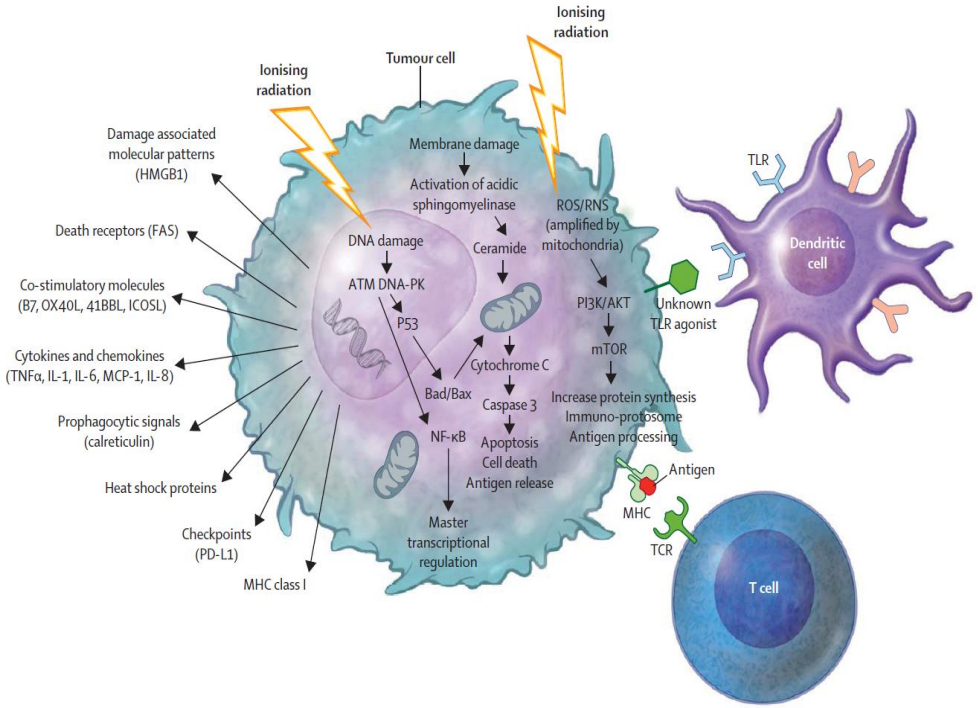
3. Manig L, et al (2016) Predicting survival after irradiation of metastases from transitional carcinoma of the bladder Anticancer Res 36(12) 6663–6665

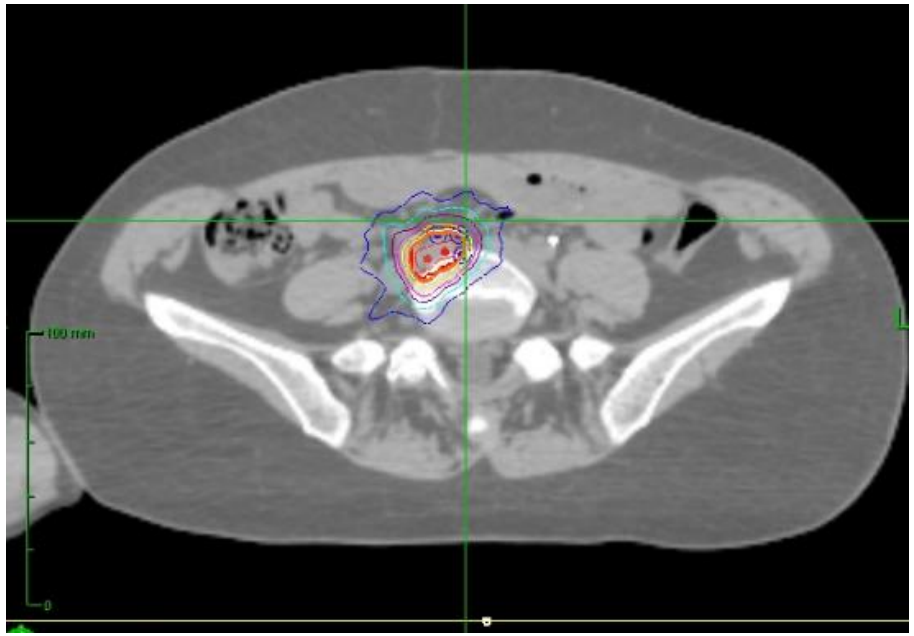
4. Augugliaro M, et al (2019) Recurrent oligometastatic transitional cell bladder carcinoma: is there room for radiotherapy? Neoplasma 66(1) 160–165

5. Leonetti A, et al (2018) Radiotherapy for the treatment of distant nodes metastases from oligometastatic urothelial cancer: a retrospective case series Int J Urol 25(10) 879–886 https://doi.org/10.1111/iju.13773 PMID: 30103254

6. Francese C et al. Stereotactic Body Radiation Therapy in the Management of Oligometastatic and Oligoprogressive Bladder Cancer and Other Urothelial Malignancies Clin Oncol (R Coll Radiol). 2021 Jan;33(1):50-56.

Sundahl N, et al. : Randomized phase 1 trial of pembrolizumab with sequential versus concomitant stereotactic body radiotherapy in metastatic urothelial carcinoma
Eur Urol 2019, 75(5) 707–711





Sharabi A, et al. Lancet Oncol 2015;16:e498-509.
Finkelstein et al. Clin Dev Immunol 2011;439752

EUROPEAN UROLOGY OPEN SCIENCE 27 (2021) 19–28

available at www.sciencedirect.com
journal homepage: www.eu-openscience.europeanurology.com

European Association of Urology

Review – Prostate Cancer

Oligorecurrent Prostate Cancer and Stereotactic Body Radiotherapy: Where Are We Now? A Systematic Review and Meta-analysis of Prospective Studies

Giulia Marvaso [a,b,†], *Stefania Volpe* [a,b,†,‡], *Matteo Pepa* [a,*], *Matteo Augugliaro* [a], *Giulia Corrao* [a,b], *Annalisa Biffi* [c,d], *Mattia Zaffaroni* [a], *Luca Bergamaschi* [a,b], *Francesco Maria La Fauci* [a,e], *Francesco Alessandro Mistretta* [f], *Stefano Luzzago* [b,f], *Federica Cattani* [e], *Gennaro Musi* [b,f], *Giuseppe Petralia* [b,g], *Gabriella Pravettoni* [b,h], *Ottavio De Cobelli* [b,f], *Roberto Orecchia* [i], *Barbara Alicja Jereczek-Fossa* [a,b]

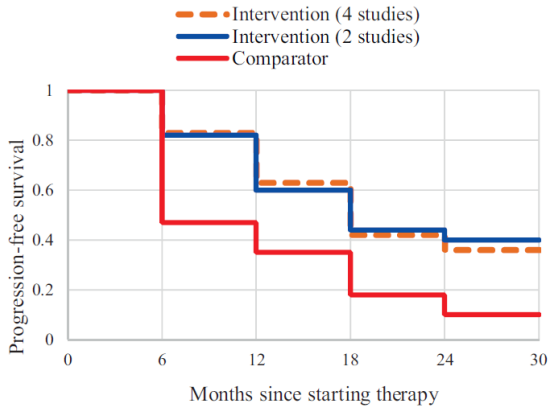


Fig. 2 – Kaplan-Meier survival curve for survivors to oligometastatic prostate cancer: intervention (four studies: observational studies and RCT; *n* = 323), intervention (two studies: RCT; *n* = 67), and comparison (two studies: RCT; *n* = 49). The dotted orange line represents all patients in the intervention arm (four studies). The blue line includes individuals in the intervention arm (two studies: RCT). The red line includes patients in the observation arm (two studies: RCT). RCT = randomized controlled trial.

445 pts

6 prospective studies:
- 2 randomised
- 4 observational

Almost 100% local control

PFS benefit is mantined at 2 y

Almost no toxicity

Hormone-sensitive oligometastatic prostate cancer

Clinical trial design

STOMP	ORIOLE	POPSTAR	MSKCC *
Phase II RCT Intervention arm: 31 Observation arm: 31 Oligometastatic recurrence, 1–3 metastases (PET/CT), M1a-c SABR, or all-site metastasectomy	Phase II RCT (2:1) Intervention arm: 36 Observation arm: 18 Oligometastatic recurrence, 1–3 metastases (conventional imaging), M1a-b SABR	Phase I Single arm: 33 (22 [a]) Oligometastatic recurrence, 1–3 metastases (PET/CT), M1a-b SABR	Phase I Single arm: 20 Synchronous, 1–10 metastases (conventional imaging), M1a-b CRP + PLND ± RPLND ± SABR
			

Clinical trial outcomes

STOMP	ORIOLE	POPSTAR	MSKCC *
LC: 100% 3 yr	LC: 98.9% 6 mo	LC: 97% 1 yr	NR
ADT-FS Intervention arm: 21 mo Observation arm: 13 mo (HR 0.60; 95% CI [0.40–0.90]; $p = 0.11$ [b])	**PFS** Intervention arm: *not reached* Observation arm: 31 mo (HR 0.30; 95% CI [0.11–0.81; $p = 0.02$)	**ADT-FS** 2 yr [a]: 48% (95% CI 31–75)	**PFS** (PSA ≤ 0.05 ng/ml) 12 mo: 60% (10% [c]) 20 mo: 50% (20% [c])

Connor M et al. E U R O P E A N U R O L O G Y O N C O L O G Y 3 (2 0 2 0) 5 8 2 – 5 9 3

ORIOLE: phase II randomized trial

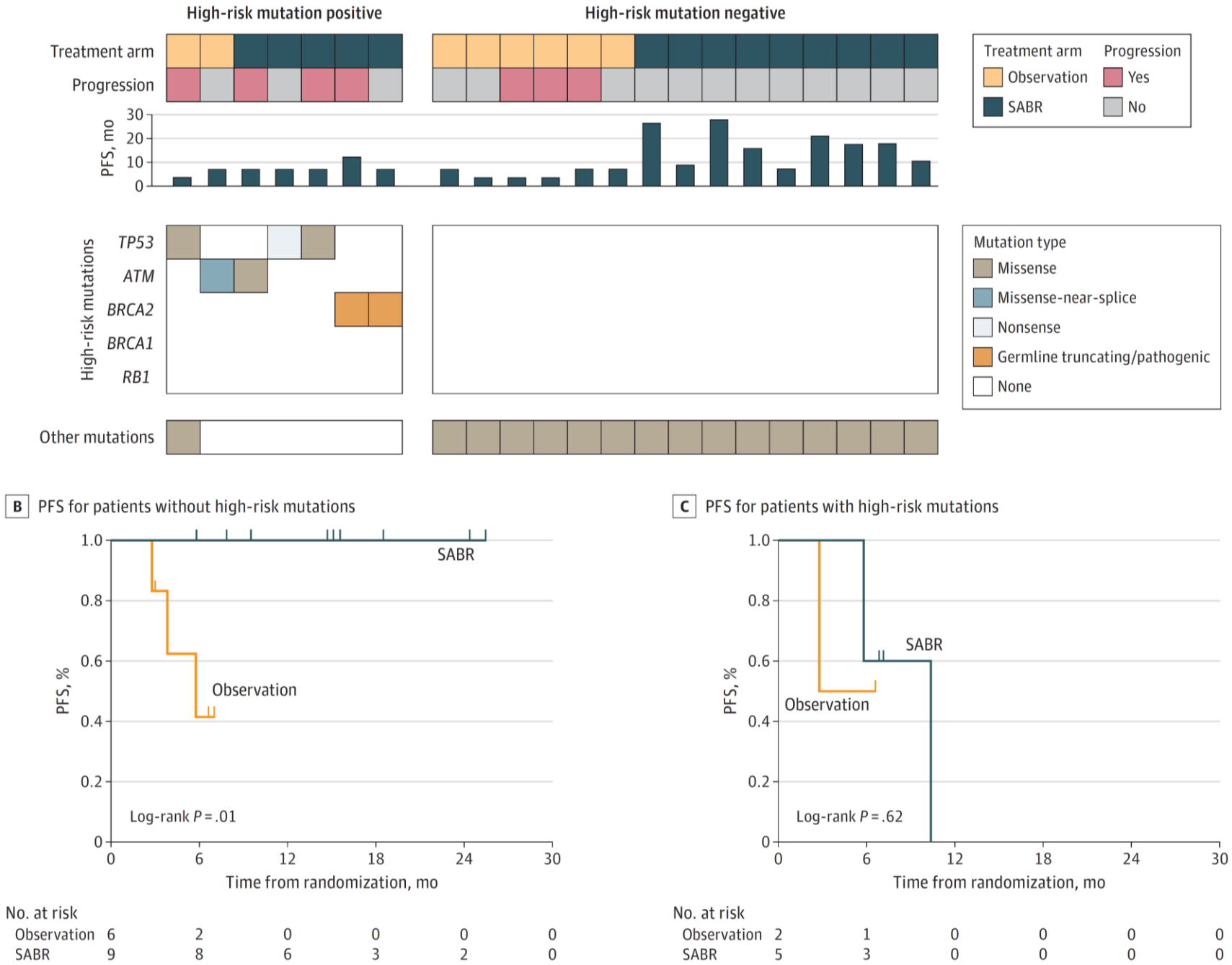
Association of tumor biology and outcome of SBRT

any oligorecurrent patient with a high-risk mutation

(mutations of key gatekeepers of genomic integrity like BRCA 1/2, ATM, TP53, or RB1)

would soon progress when managed with MDT alone

Philips R et al. JAMA Oncol. 2020;6(5):650-659.



Philips R et al. JAMA Oncol. 2020;6(5):650-659.

SBRT to oligometastatic CRPC

Retrospective studies

1. Triggiani L et al. World J Urol. 2019 Mar 11. doi: 10.1007/s00345-019-02717-7
2. Berghen C et al. Eur Urol Oncol 2019 Sep 23. pii: S2588-9311
3. Valeriani M et al. Radiation Oncology (2019) 14:205
4. Deek MP et al. Eur Urol Oncol. 2020 Jun 11:S2588-9311(20)30058-4

SBRT to oligoprogressive-mCRPca:
next-line systemic treatment free survival (NEST)

30 pts with CRPC

SBRT/surgery + 1-3 progressive mets (maintaining systemic therapy)

MAIN FINDINGS:

- **median NEST-free survival: 16 months**
- **progression-free survival: 10 months**
- **only minor radiotherapy- or surgery-related toxicity**

Berghen C et al. Eur Urol Oncol 2019 Sep 23. pii: S2588-9311

Combo trials (mCRPC and SBRT)

ClinicalTRialsgov. Name/Centre/PI	Study design	Arms
NCT03449719 ARTO/Univ of Florence, Italy	Phase II Randomized Trial: Trial Comparing Efficacy and Safety of Abiraterone and Abiraterone Associated With of Ablative Radiation Therapy in Patients With Oligometastatic CRPC	**ABI +/- SBRT**
NCT03503344 PILLAR/Univ of California, San Francisco, USA	Phase II Randomized Trial : Apalutamide With or Without Stereotactic Body Radiation Therapy in Treating Participants With CRPC	**Apalutamide +/- SBRT**
NCT01818986 University of Texas Southwestern Medical Center, USA	Phase II, Single arm Trial: Sipuleucel-T and Stereotactic Ablative Body Radiation (SABR) for Metastatic CRPC	**Sipuleucel + SBRT**
NCT02685397 Jewish General Hospital, Canada	Adaptive Phase II/III Randomized Trial: The Role of Stereotactic Body Radiotherapy in the Management of CRPC Cancer With Oligometastases:	**Enzalutamide +/- SBRT**
NCT04070209 Jewish General Hospital, Canada	A Pilot Phase II Trial: The Role of Therapeutic Layering of Stereotactic Body Radiotherapy on Darolutamide in the Management of Oligoprogressive CRPC	**Darolutamide + SBRT**

PSMA-PET guided RT trials

Oligometastatic disease					
NCT03569241	2	MDT + ADT vs MDT + whole-pelvis RT + ADT (6 mo total)	Nodal relapse after RP or RT, identified on choline, PSMA, or FACBC PET/CT with ≤3 nodes avid	178	2-yr metastasis free survival
NCT03298087	2	RP + leuprolide + apalutamide + abiraterone + SBRT (6 mo ADT total)	De novo M1a or M1b with ≤5 metastases that would be classified as M1a or M1b	28	Percentage of patients with PSA < 0.05 ng/mL at 6 mo after testosterone recovery
NCT03902951	2	Leuprolide + apalutamide + abiraterone + SBRT (6 mo ADT total)	Recurrence after RP with ≤5 metastases that would be classified as M1a or M1b	28	Percentage of patients with PSA < 0.05 ng/mL at 6 mo after testosterone recovery
NCT03503344	2	Apalutamide + SBRT vs apalutamide alone	Castrate-resistant disease (3 PSA > 0.05 ng/mL on continuous antiandrogen therapy) with ≤5 lesions on PSMA PET/CT	60	Proportion of patients with PSA < 0.2 ng/mL at 18 mo
NCT04222634	2	MDT	≤3 extracranial oligoprogressive lesions; ^{18}F-PSMA PET/CT used as part of the investigational study, not to define the number of lesions	18	Next-line systemic treatment–free survival and PSMA PET/CT accuracy and predictive value
NCT03525288	2	RT to 1–5 lesions found on ^{18}F-DCFPyL-PSMA PET/CT vs standard RT	≤5 lesions on conventional imaging (including N1 lesions by echelon by 1 lesions and with ≤3 non-bone lesions) or selected NCCN high risk or biochemical recurrence (after RP [PSA ≥ 0.2 ng/mL] or RT [PSA ≥ nadir +2 ng/mL])	130	Failure-free survival

Kishan A et al. Eur Urol Focus. 2020 Oct 10:S2405-4569(20)30283-2.

EURURO-9491; No. of Pages 10
ARTICLE IN PRESS
EUROPEAN UROLOGY XXX (2021) XXX–XXX

available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

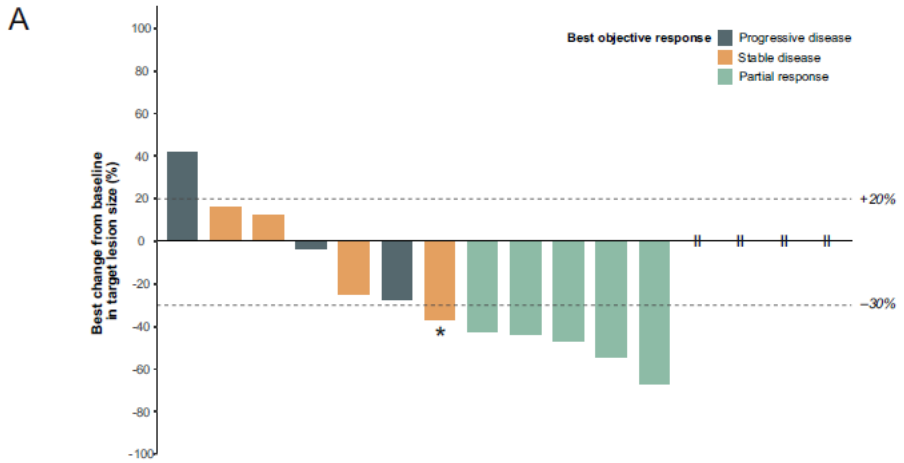
Platinum Priority – Prostate Cancer

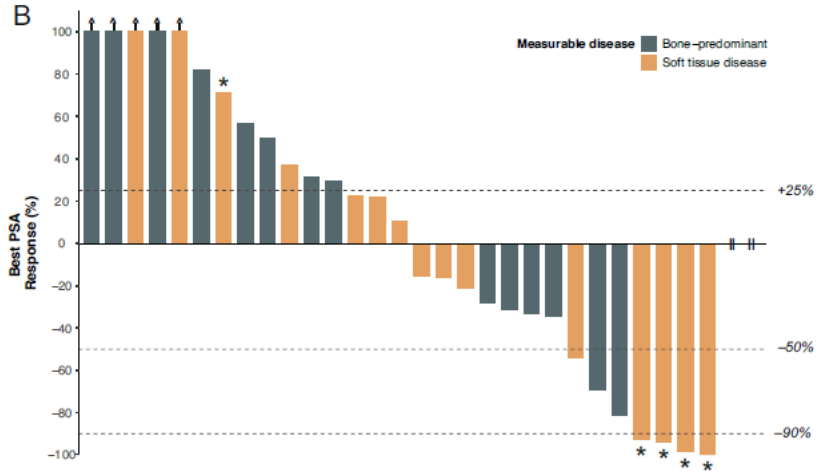
Editorial by XXX on pp. x–y of this issue

Avelumab Combined with Stereotactic Ablative Body Radiotherapy in Metastatic Castration-resistant Prostate Cancer: The Phase 2 ICE-PAC Clinical Trial

Edmond M. Kwan [a,b], Lavinia Spain [c,d,e], Angelyn Anton [d,e,f], Chun L. Gan [b], Linda Garrett [b], Deborah Chang [b], Elizabeth Liow [b], Caitlin Bennett [e], Tiantian Zheng [g], Jianjun Yu [g], Chao Dai [g], Pan Du [g], Shidong Jia [g], Heidi Fettke [h,i], Claire Abou-Seif [j], Gargi Kothari [k], Mark Shaw [i,k], Phillip Parente [d,e], Carmel Pezaro [d,e], Ben Tran [c,f,i], Shankar Siva [i,k], Arun A. Azad [a,c,i,]*

- Advanced and heavily pretreated prostate cancer (CRPC)
- SBRT + avelumab was safe
- in nearly half of patients: cancer control for 6 months or longer
- SBRT may improve the effectiveness of immunotherapy in prostate cancer.





GOOD NEWS FOR OUR PATIENTS

1. Local control 90-100%
2. Almost no toxicity
3. Median 2-3 years of
   DRUG HOLIDAY

Chronic curable patients

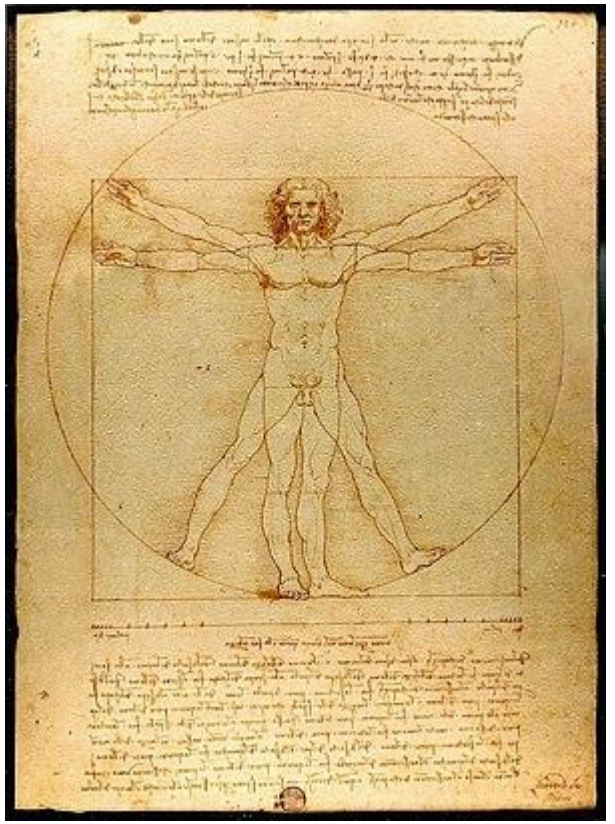
Meta-static -> meta-stable disease

AGENDA

- ❑ SBRT and SRS
- ❑ Brain
- ❑ Thorax
- ❑ Abdomen/pelvi
- ❑ Particular scenarios:

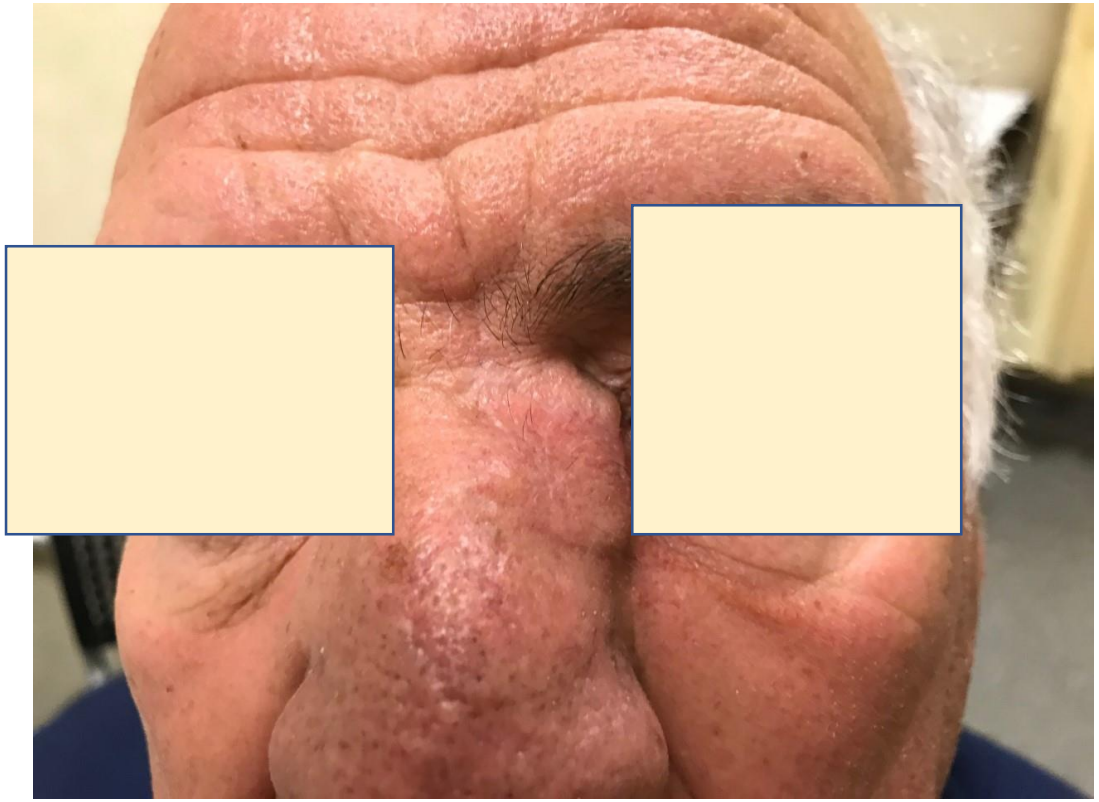
  oligometastases, re-irradiation,

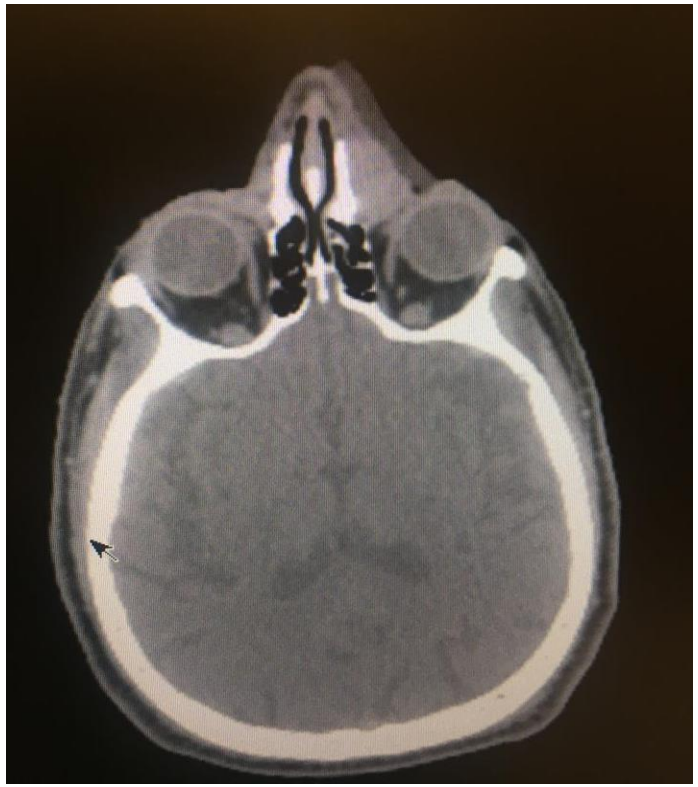
  difficult sites

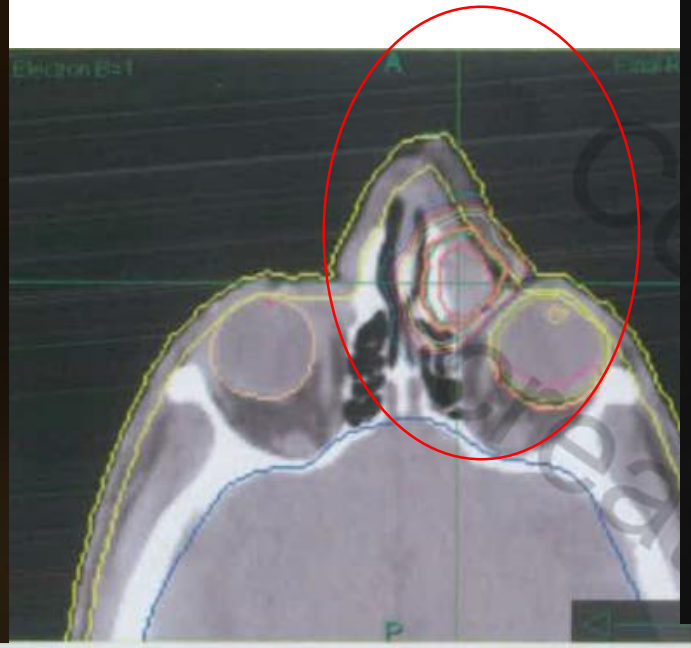


https://en.wikipedia.org/wiki/Vitruvian_Man#/media/File:Da_Vinci_Vitruve_Luc_Viatour.jpg

RT in Squamous Cell Carcinoma



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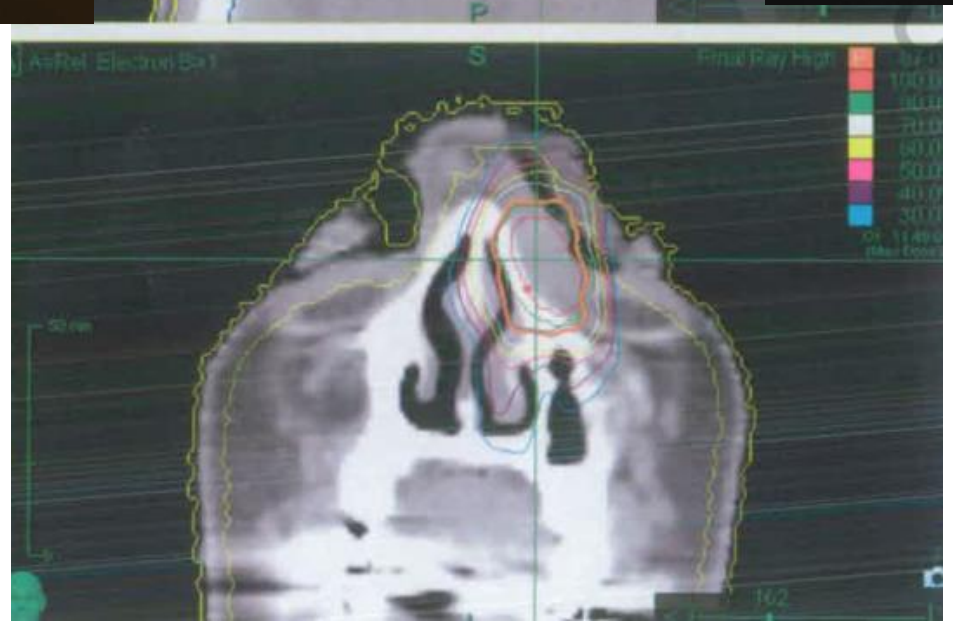
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EJO European Journal of Ophthalmology

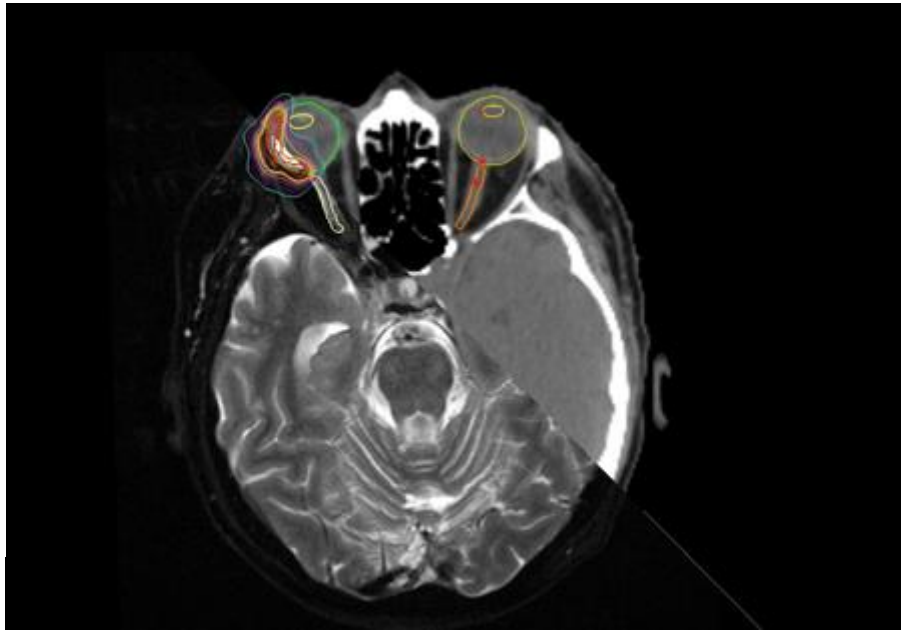
Original research article

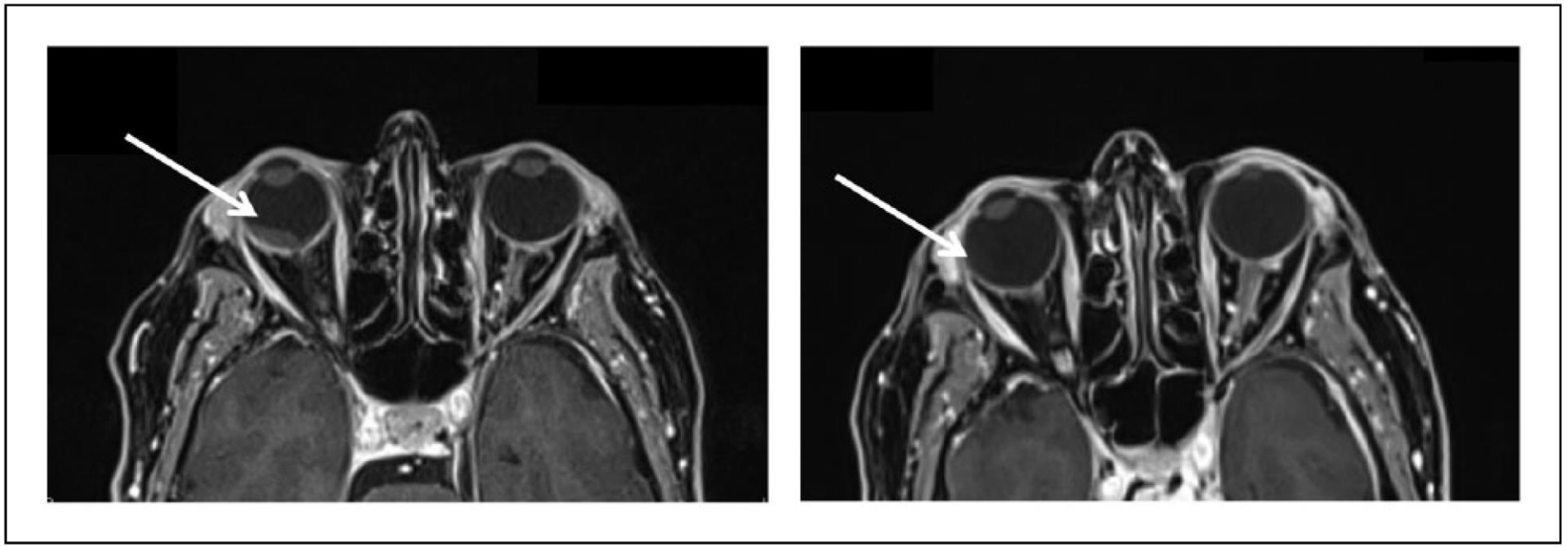
CyberKnife radiotherapy for orbital metastases: A single-center experience on 24 lesions

European Journal of Ophthalmology
2019, Vol. 29(1) 61–68

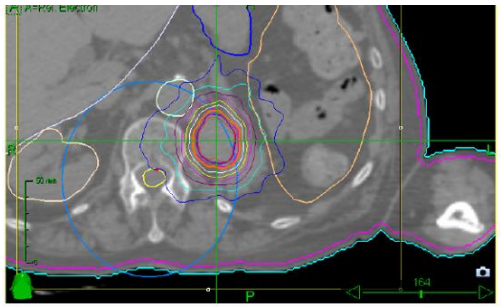
DOI: 10.1177/1120672118761728
journals.sagepub.com/home/ejo
SAGE

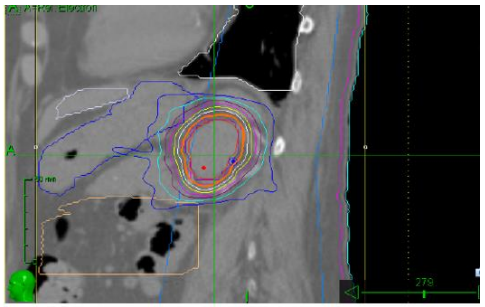
Giulia Riva[1,2], Matteo Augugliaro[1,2], Gaia Piperno[2], Annamaria Ferrari[2], Elena Rondi[3], Sabrina Vigorito[3], Delia Ciardo[2], Roberto Orecchia[4] and Barbara Alicja Jereczek-Fossa[1,2]

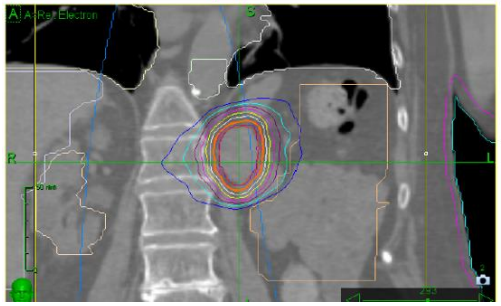


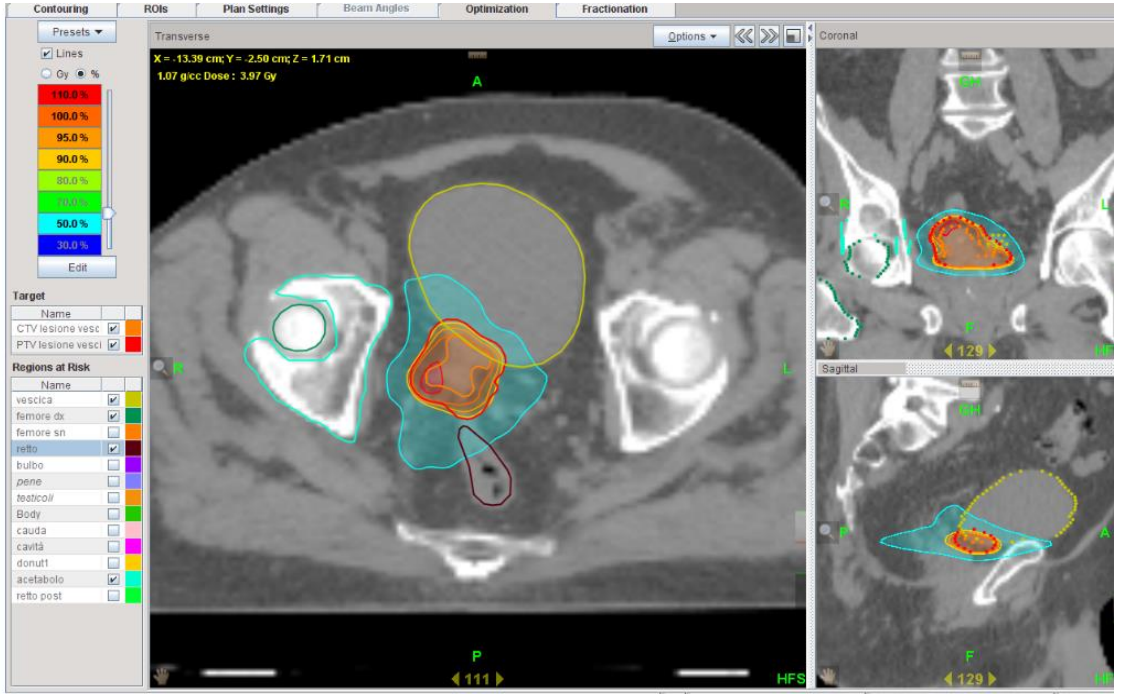


VIRTUAL SURGERY:
Small primary or recurrent tumors in inoperable patients









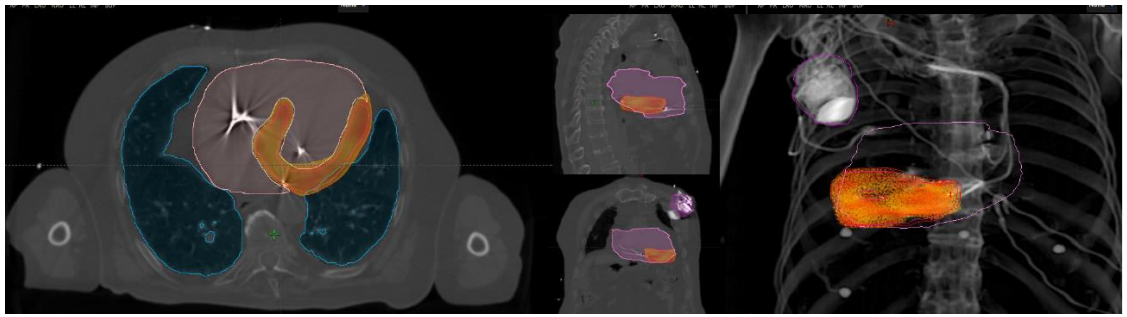
Heart radioablation

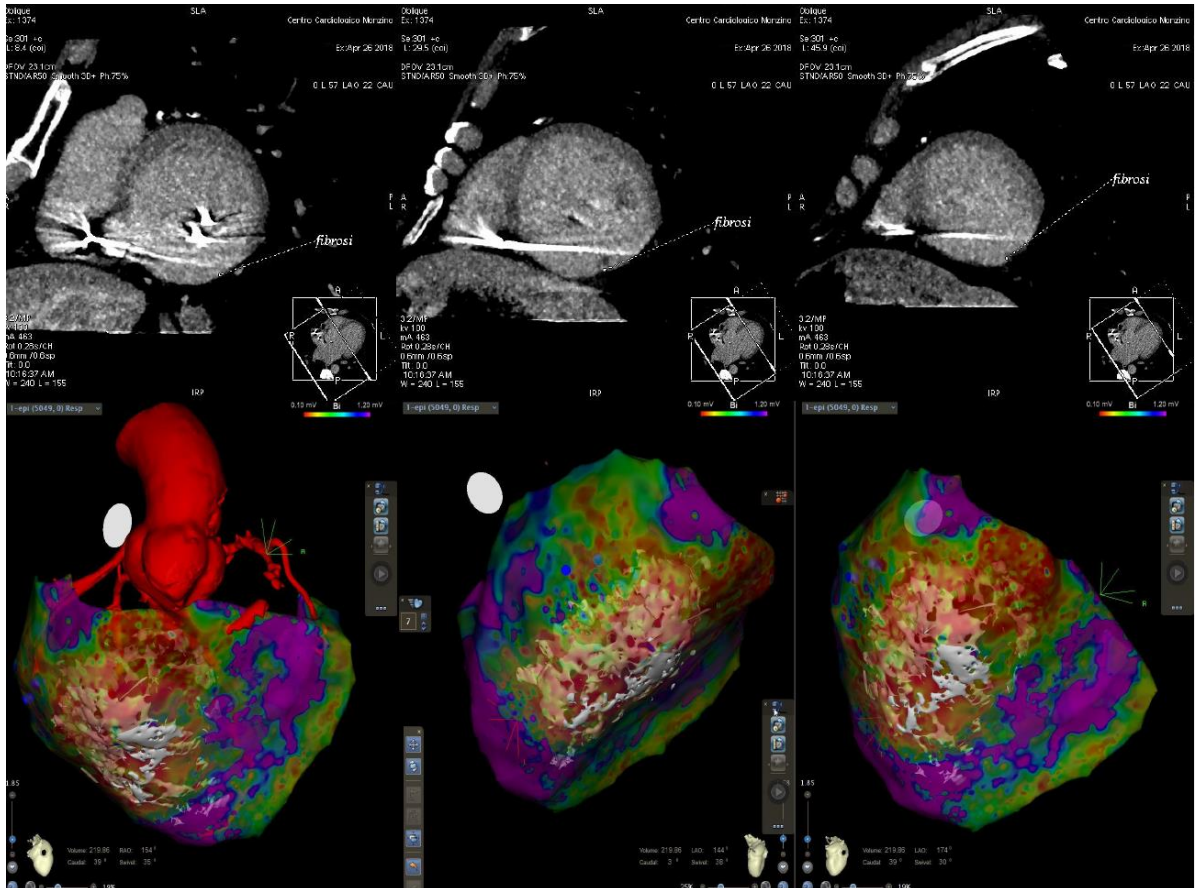
J Interv Card Electrophysiol. 2020 Aug 27. doi: 10.1007/s10840-020-00855-2. Online ahead of print.

STRA-MI-VT (STereotactic RadioAblation by Multimodal Imaging for Ventricular Tachycardia): rationale and design of an Italian experimental prospective study

C Carbucicchio [1], B A Jereczek-Fossa [2 3], D Andreini [4 5], V Catto [6], G Piperno [3], E Conte [4], F Cattani [7], E Rondi [7], S Vigorito [7], C Piccolo [7 8], A Bonomi [9], A Gorini [2 10], M Pepa [3], S Mushtaq [4], G Fassini [6], M Moltrasio [6], F Tundo [6], G Marvaso [2 3], F Veglia [9], R Orecchia [11], E Tremoli [12], C Tondo [6 5]

phase Ib/II, open-label study [Clinical trials gov NCT04066517]



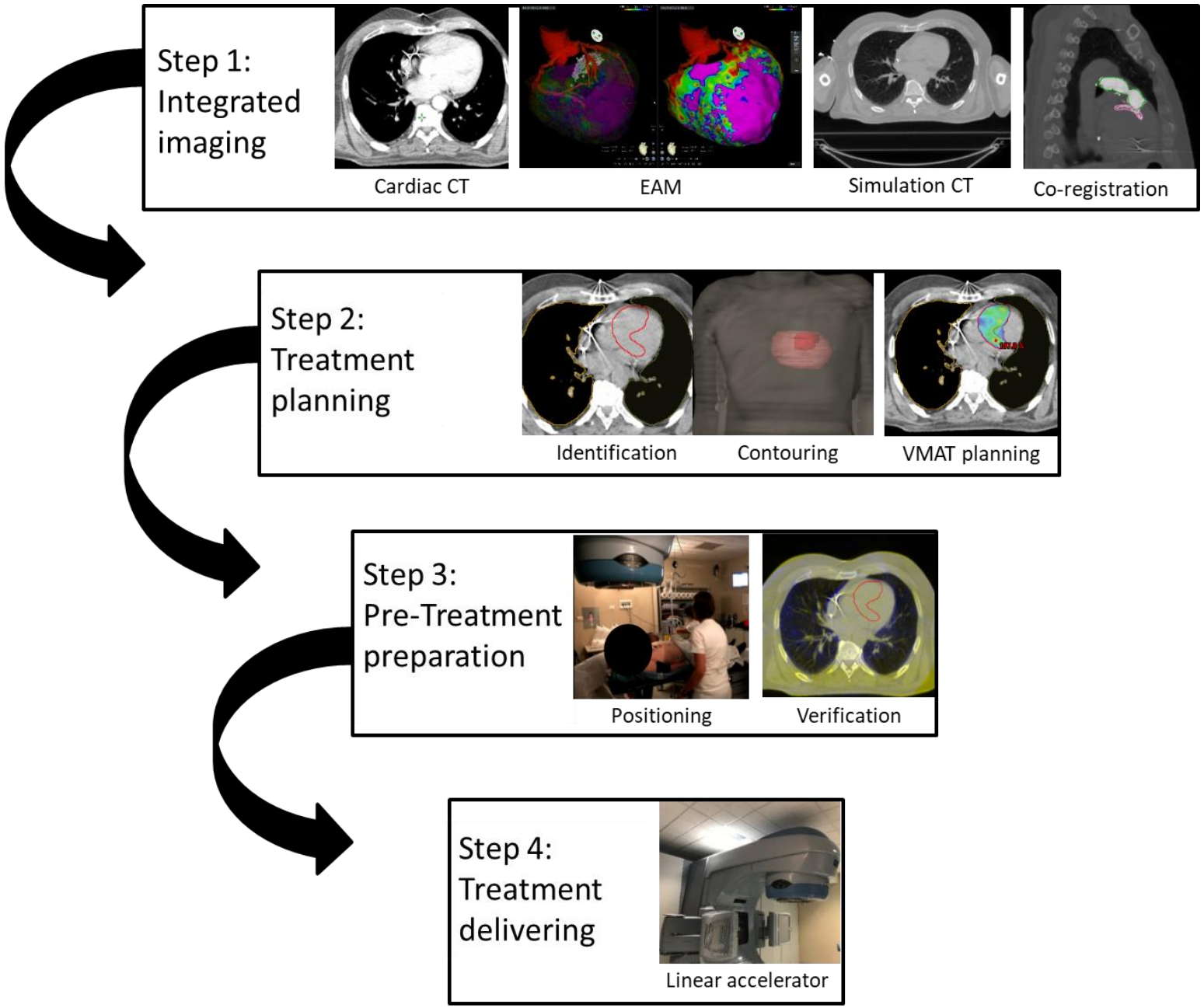


IEO Istituto Europeo di Oncologia

Centro Cardiologico Monzino

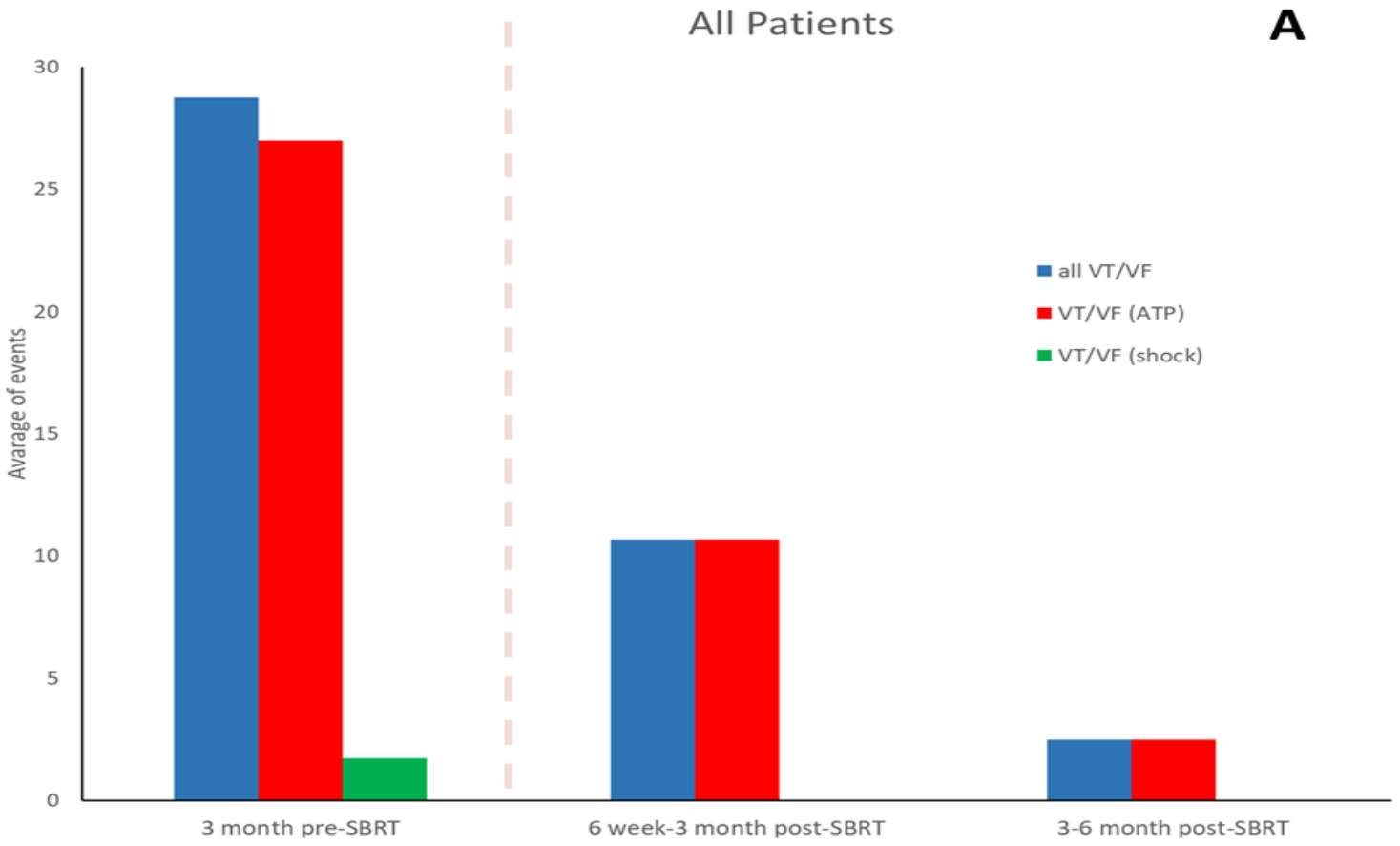
IEO Istituto Europeo di Oncologia

WORKFLOW



Carbucicchio C, Jereczek-Fossa BA submitted

PRELIMINARY RESULTS: radioablation for VT (IEO-CCM)



Journal of Interventional Cardiac Electrophysiology (2021) 62:427–439
https://doi.org/10.1007/s10840-021-01060-5

Check for updates

Stereotactic radioablation for the treatment of ventricular tachycardia: preliminary data and insights from the STRA-MI-VT phase Ib/II study

Corrado Carbucicchio[1] · Daniele Andreini[2,3] · Gaia Piperno[4] · Valentina Catto[1] · Edoardo Conte[2] · Federica Cattani[5] · Alice Bonomi[6] · Elena Rondi[5] · Consiglia Piccolo[5] · Sabrina Vigorito[5] · Annamaria Ferrari[4] · Matteo Pepa[4] · Mattia Giuliani[7] · Saima Mushtaq[2] · Antonio Scarà[8] · Leonardo Calò[8] · Alessandra Gorini[7,9] · Fabrizio Veglia[6] · Gianluca Pontone[2] · Mauro Pepi[10] · Elena Tremoli[11] · Roberto Orecchia[12] · Giulio Pompilio[13,14] · Claudio Tondo[1,14] · Barbara Alicja Jereczek-Fossa[4,9]

Received: 21 May 2021 / Accepted: 2 September 2021 / Published online: 5 October 2021

Carbucicchio C, Jereczek-Fossa BA in press

HOW T O DO IT SAFELY?

Table 13.1 Systems for documentation of side-effects, with examples for oral mucositis

Grade	General	RTOG/EORTC	CTCAE v3	WHO
0	No change	No change	No change	No change
1	Mild	Erythema, mild soreness, painless erosions	Erythema; normal diet	Soreness, erythema
2	Moderate/clear	Painful erythema, oedema or ulcers; can eat	Patchy ulceration; can eat and swallow modified diet	Erythema, ulcers; can eat solids
3	Severe/significant	Painful erythema, oedema or ulcers; cannot eat	Confluent ulcerations, bleeding with minor trauma; unable to adequately aliment or hydrate orally	Ulcers; requires liquid diet only
4	Life-threatening	Requires parenteral or enteral support	Tissue necrosis; significant spontaneous bleeding	Alimentation not possible
5	Death owing to side-effects	Death owing to side-effects	Death owing to side-effects	Death owing to side-effects

RTOG/EORTC, Radiation Therapy and Oncology Group and the European Organisation for Research and Treatment of Cancer; CTCAE v3, the Common Terminology Criteria for Adverse Events, version 3; WHO, World Health Organization.

Joiner M, Van der Kogel A, Basic Clinical Radiobiology 4° ed.

CTCAE: Higher rate of G1 and G2 urinary toxicity
Yoshida K et a.: Anticancer Res 2014;34:2015-2018.

Do it safely….

Practical Radiation Oncology® (2021) 11, e355–e365

Topic Discussion

Organ at Risk Dose Constraints in SABR: A Systematic Review of Active Clinical Trials

Serenna G. Gerhard, BHSc (candidate),[a] David A. Palma, MD, PhD,[a,*] Andrew J. Arifin, MD,[a] Alexander V. Louie, MD, PhD,[b] George J. Li, HBSc,[c] Faiez Al-Shafa, MD,[d] Patrick Cheung, MD,[b] George B. Rodrigues, MD, PhD,[a] Carol W. Bassim, DMD, MSc, MHSc,[e] and Mark T. Corkum, MD, MSc[b]

Constraints review from 85 trials using:

Timermann et al
UK SABR Hanna et al
AAPM
Hy-TEC etc

Practical Radiation Oncology® (2021) 11, e355–e365

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Topic Discussion

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53 of 85 eligible clinical trials contributed OAR constraints
Constraints 1-8 fractions
33 OARs

RESULTS:

- substantial variability in OAR dose constraints (dose, volumes, optional vs mandatory)
- OARs displaying the most variability were the rectum, penile bulb, and chest wall and ribs

Do it safely….

Constraints review from 85 trials…

Practical Radiation Oncology® (2021) 11, e355–e365

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Topic Discussion

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Table 1 Dose constraints from selected OARs for SABR delivered in 1 fraction

Parameter	No. studies reporting	Modal dose constraint (Gy)	Median dose constraint (Gy)	Interquartile range (Gy)	Minimum dose constraint (Gy)	Maximum dose constraint (Gy)
Spinal cord						
D_{max} (≤0.1 cm^3)	18	14	14	14-14	14	15
D0.35 cm^3	13	10	10	10-10	10	10

Table 2 Dose constraints from selected OARs for SABR delivered in 3 fractions

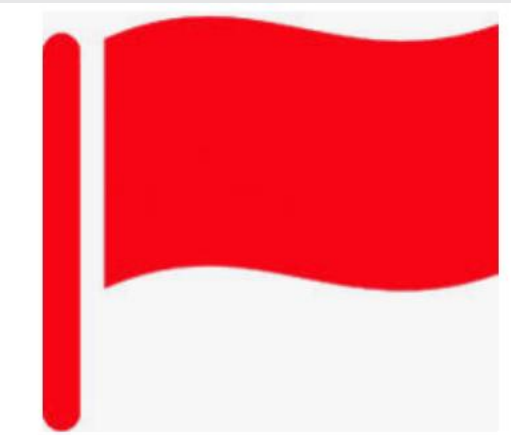
Parameter	No. studies reporting	Modal dose constraint (Gy)	Median dose constraint (Gy)	Interquartile range (Gy)	Minimum dose constraint (Gy)	Maximum dose constraint (Gy)

Table 3 Dose constraints from selected OARs for SABR delivered in 5 fractions

Parameter	No. studies reporting	Modal dose constraint (Gy)	Median dose constraint (Gy)	Interquartile range (Gy)	Minimum dose constraint (Gy)	Maximum dose constraint (Gy)

Table 5 Comparison of modal 5 fraction dose constraints included in our study with AAPM-TG 101, Timmerman, NRG-BR001, and the UK Consensus Guidelines

Organ	Parameter	Mode of included studies Volume dose (Gy)	AAPM-TG 101 Volume dose (Gy)	Timmerman Volume dose (Gy)	NRG-BR001 Volume dose (Gy)	UK Consensus Volume dose (Gy)
Colon	D_{max} (<0.1 cm^3)	38	38	38	40	
	D0.5 cm^3	32				
	D20 cm^3	25	25	25	28.5	
Rectum	D_{max} (<0.1 cm^3)	38	38	38	55	
	D0.5 cm^3	30, 32				
	D3.5 cm^3	50			50	
	D20 cm^3	25	25	25	32.5	
Bladder wall	D_{max} (<0.1 cm^3)	38	50	38	38	
	D0.5 cm^3					
	D15 cm^3					
Ureter	D_{max} (<0.1 cm^3)					
	D0.5 cm^3					
Penile bulb	D_{max} (<0.1 cm^3)					
	D0.5 cm^3					
	D3 cm^3					
Femoral heads	D10 cm^3					

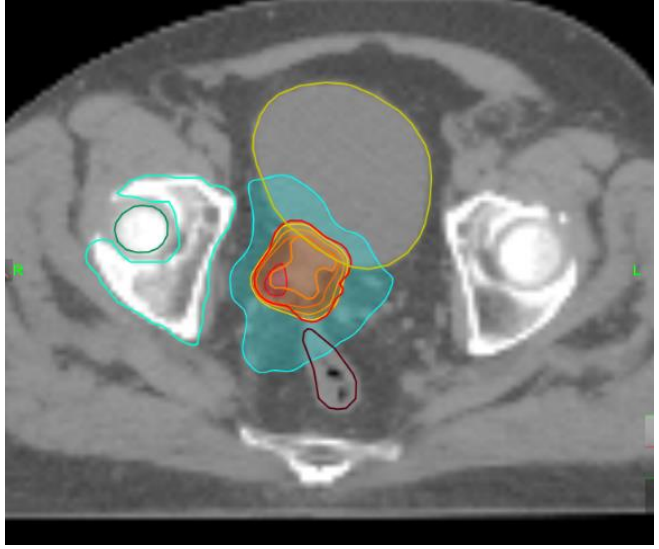


WARNING:

1. **No clinical data matched with constraints**
2. **Patterns of practice study**
3. **Readers should exercise prudence when reviewing and referencing such constraints.**

Gerhard S et al. Pract Radiat Oncol 2021;11:e355-e365.

TAKE HOME MESSAGES



- SBRT/SRS is widely employed in oncology
- Higher level evidence is becoming available
- High quality planning and delivery are essential
- Scrupulous data collection is warranted in order to establish safety constraints for routine use (standardisation)

Thank you!