2025 Multidisciplinary Cancer Update

The role of SBRT in GU cancers

Christophe Marques MD/PhD
Department of Radiation Oncology

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Disclosures

- None
- Presentation not focused on biomarkers

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Agenda

- SBRT Historical Milestones Modern Applications
- Primary Renal Cell Carcinoma
- Oligometastatic Renal Cell Carcinoma
- Primary Prostate Cancer
- Oligometastatic Prostate Cancer
- Questions
- RT specific supplemental slides

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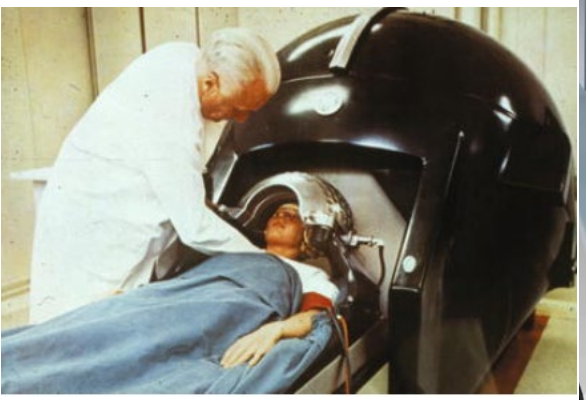
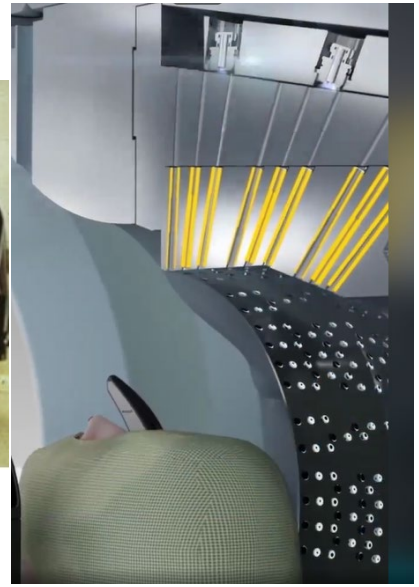
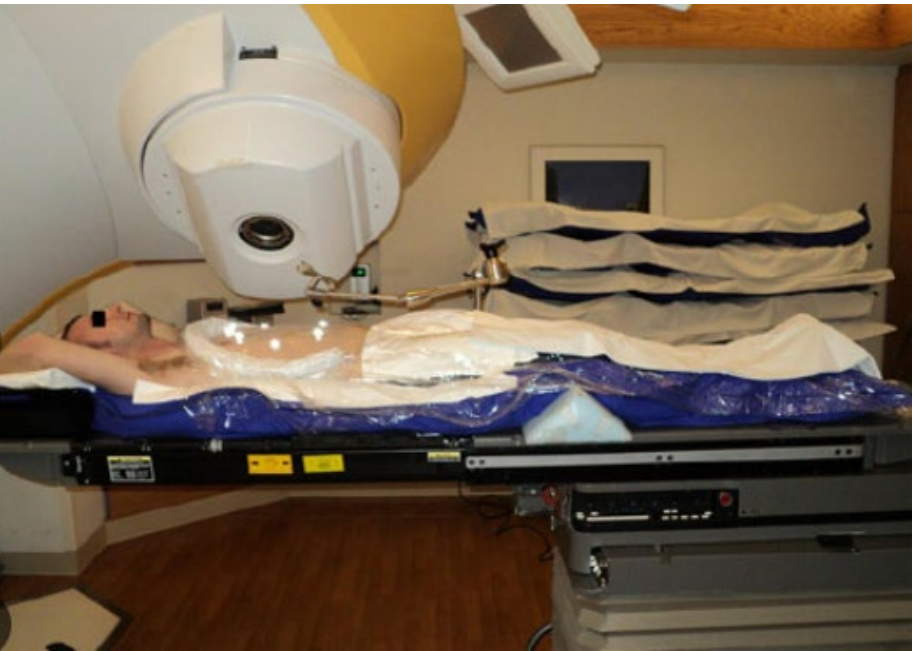
SBRT: Precision radiation beyond the cranium
Definition & Core concept







- **Stereotactic Body Radiation Therapy (SBRT)** — also called Stereotactic Ablative Radiotherapy (SABR) delivers **very high doses of radiation** to a **small, precisely defined target** in **1–5 fractions**
- Evolved from **intracranial stereotactic radiosurgery (SRS)** with the goal of achieving **ablative tumor control** in extracranial sites
- Hallmarks:
  - sub-mm accuracy with **image-guided localization**
  - **Highly conformal planning** (IMRT/VMAT, steep dose gradients)
  - **Motion management** and robust immobilization
  - **Hyperfractionation** exploiting high BED (Biologically Effective Dose)

Image courtesy of Elekta

How SBRT Began…..
Historical Milestones …… Modern Applications

- **1990s – Sweden & Japan**: Blomgren (Karolinska) & Uematsu (Tokyo) pioneer body stereotaxis for lung, liver, and spinal lesions
- **Early 2000s – Indiana University**: Timmerman et al. treat medically inoperable **Stage I NSCLC** with 54 Gy/3 fractions →
  - **Local control** >90%
  - **Overall survival** ~55%, comparable to surgery
  - acceptable toxicity when respecting proximity constraints
  - → Rapidly became **standard of care** for inoperable early-stage NSCLC
- Modern applications
  - **Primary tumors:** Early-stage NSCLC, prostate cancer (ultrahypofractionation), pancreas (selected cases)
  - **Oligometastatic disease**: Liver, lung, adrenal, bone/spine
  - **Reirradiation:** Salvage therapy where conventional fractionation is unsafe

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Primary Renal Cell Carcinoma

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2026
Kidney Cancer

NCCN Guidelines Index
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INITIAL WORKUP[a]

- History and physical (H&P)
- Complete blood count (CBC) with differential, comprehensive metabolic panel
- Urinalysis
- Abdomen ± pelvis CT[b] or MRI[b]
- CT chest[b] (preferred) or chest x-ray
- If clinically indicated
  - Bone scan
  - Brain MRI
  - Consider core needle biopsy (fine-needle aspiration [FNA] not adequate)[c]
- If urothelial carcinoma suspected (eg, central mass), consider urine cytology, ureteroscopy, or percutaneous biopsy
- If multiple renal masses, ≤46 y, or family history, consider genetic evaluation. See Hereditary Renal Cell Carcinomas (HERED-RCC-1)

Suspicious mass →

STAGE

PRIMARY TREATMENT[d,e]

Stage I (T1a) →
- Partial nephrectomy (preferred)
- or
- Percutaneous ablation
- or
- Stereotactic body radiation therapy (SBRT)
- or
- Active surveillance
- or
- Radical nephrectomy (in select patients)

Stage I (T1b) →
- Partial nephrectomy
- or
- Radical nephrectomy
- or
- Active surveillance (in select patients)
- or
- Percutaneous ablation (category 2B) (in select patients)
- or
- SBRT (in select patients)

Stage II →
- Partial nephrectomy
- or
- Radical nephrectomy
- or
- SBRT (in select patients) (category 2B)

→
- Clear cell histology: Surveillance or Adjuvant Pembrolizumab (category 1) (Grade 4 tumors with clear cell histology ± sarcomatoid features)
- Non-clear cell histology: Surveillance

Stage III[h] →
- Radical nephrectomy or Partial nephrectomy, if clinically indicated
- or
- SBRT (in select patients) (category 3)

→
- Clear cell histology: Adjuvant Pembrolizumab (category 1) or Surveillance
- Non-clear cell histology: Surveillance or clinical trial

Surveillance[f]

T1	Tumor ≤7 cm in greatest dimension, limited to the kidney
T1a	Tumor ≤4 cm in greatest dimension, limited to the kidney
T1b	Tumor >4 cm but ≤7 cm in greatest dimension, limited to the kidney
T2	Tumor >7 cm in greatest dimension, limited to the kidney
T2a	Tumor >7 cm but ≤10 cm in greatest dimension, limited to the kidney
T2b	Tumor >10 cm, limited to the kidney

Follow-up (KID-C) → Relapse or progression (KID-4)

FOLLOW-UP[g] (CATEGORY 2B)

Stereotactic ablative body radiotherapy for primary kidney cancer (TROG 15.03 FASTRACK II): a non-randomised phase 2 trial

*Shankar Siva, Mathias Bressel, Mark Sidhom, Swetha Sridharan, Ben G L Vanneste, Ryan Davey, Rebecca Montgomery, Jeremy Ruben, Farshad Foroudi, Braden Higgs, Charles Lin, Avi Raman, Nicholas Hardcastle, Michael S Hofman, Richard De Abreu Lourenco, Mark Shaw, Pascal Mancuso, Daniel Moon, Lih-Ming Wong, Nathan Lawrentschuk, Simon Wood, Nicholas R Brook, Tomas Kron, Jarad Martin, David Pryor, together with the FASTRACK II Investigator Group**

Lancet Oncol 2024; 25: 308–16

Summary

Background Stereotactic ablative body radiotherapy (SABR) is a novel non-invasive alternative for patients with

- Non-randomized, multi-center phase II *(Australia + one in Netherlands)*
- N= 70 pts (bx-confirmed RCC, single lesion) medically inoperable, high surgical risk, or declined surgery <10cm, **w/o direct contact with bowel**
- Goal Assess efficacy (local control) and safety of SABR as definitive, non-surgical therapy for primary RCC in inoperable or high-risk patients
- RT regimens
  - ≤ 4 cm lesion: 26 Gy / 1 fx
  - 4 cm - 10 cm: 42 Gy / 3 fx
- 1 EP local control (freedom from progression at 1 year)
- 2 EP toxicity, OS & CSS, distant failure, renal function changes
- mFU ~ 43 months

Siva, Lancet Onc, 2024

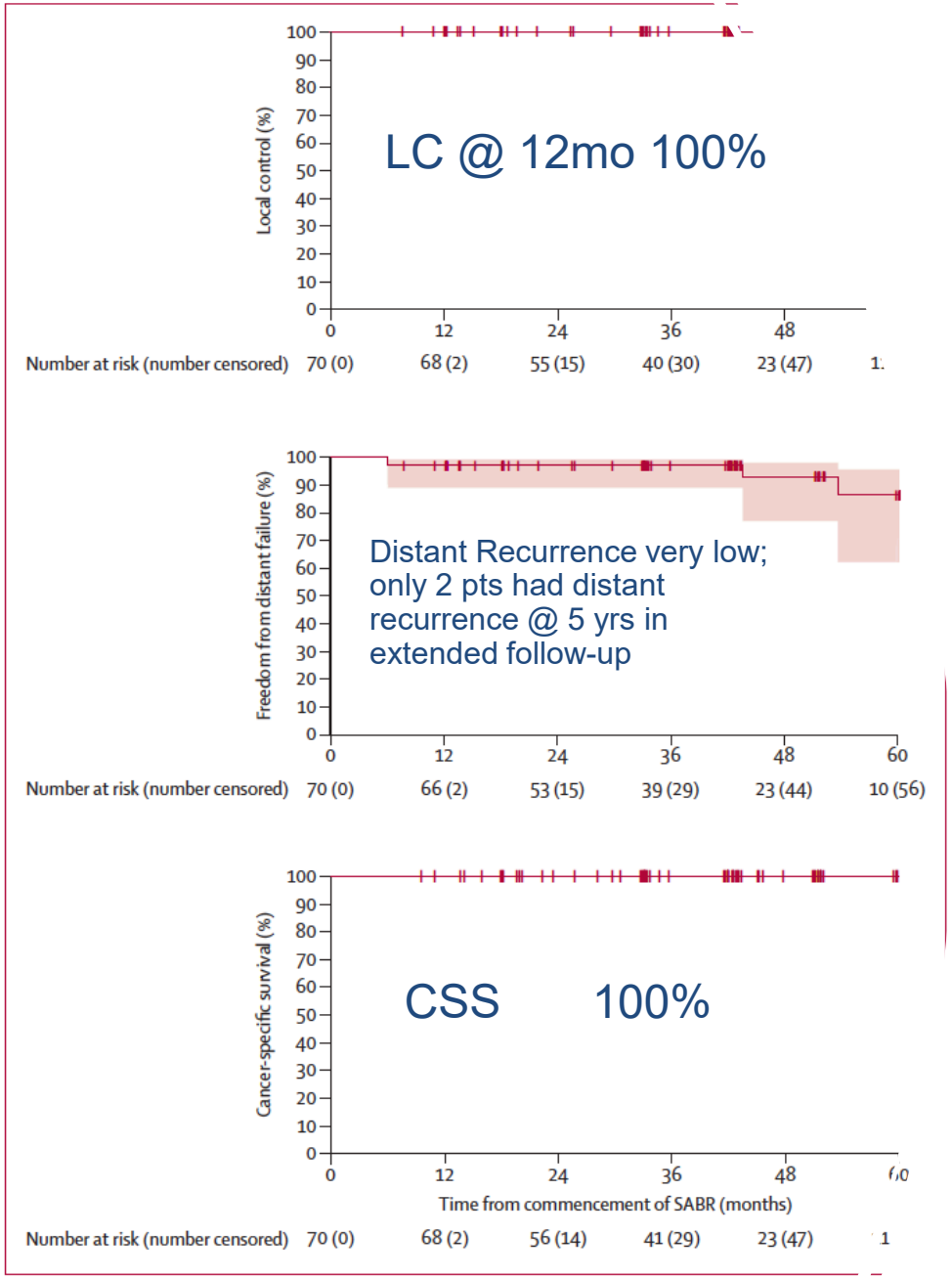


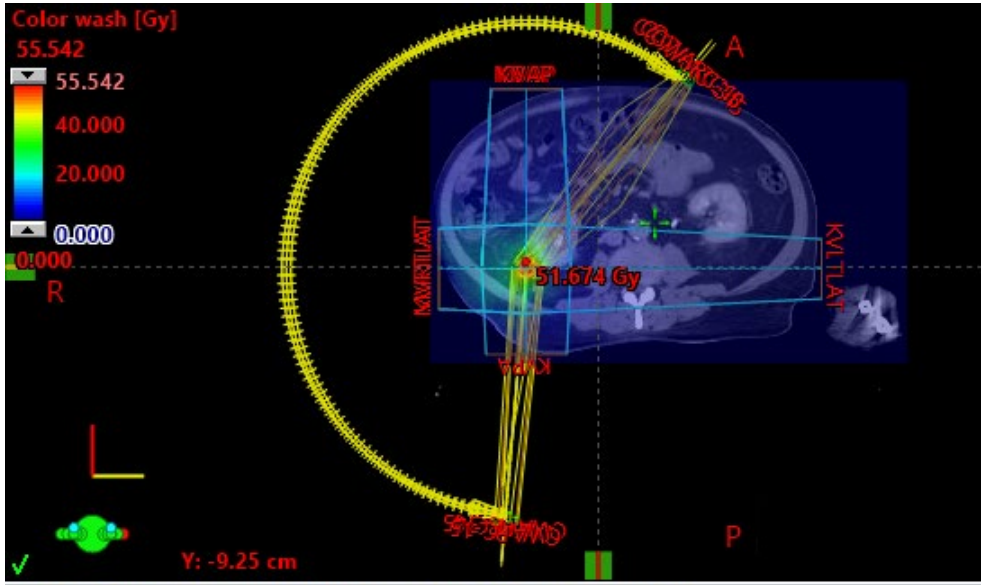
Figure 3: **Kaplan–Meier curves for local control (A), freedom from distant failure (B), and cancer-sp .if survival (C)**
Shaded areas represent 95% CIs. SABR=stereotactic ablative body radiotherapy.

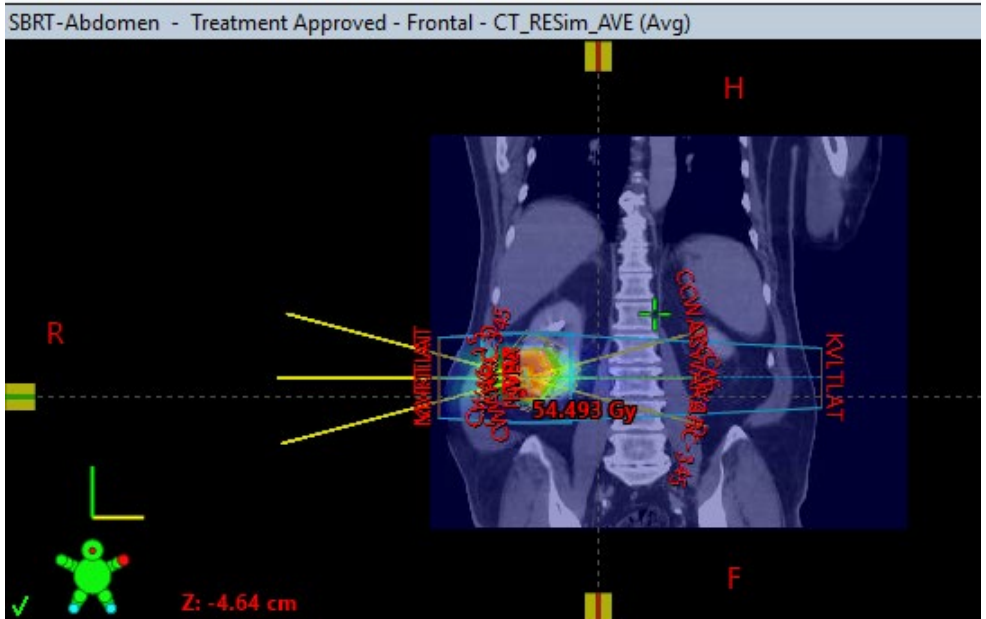
- Toxicities (Gr3) ~10% nausea/vomiting, pain, bowel obstruction, diarrhea
- Renal Function mostly stable; 1 pt required dialysis (pre-existing poor fct)

- → Trial demonstrates excellent local control and favorable safety profile of SABR for primary RCC in pts who cannot undergo surgery
- → Criticism: non-randomized and relatively small; no direct comparison to surgery or ablation
- → Patient selection matters strongly, especially regarding underlying kidney fct and tumor location

58 y.o. M with Stage I (cT1,cN0,cM0) 4.5cm right RCC s/p biopsy, s/p aborted right robotic partial nephrectomy

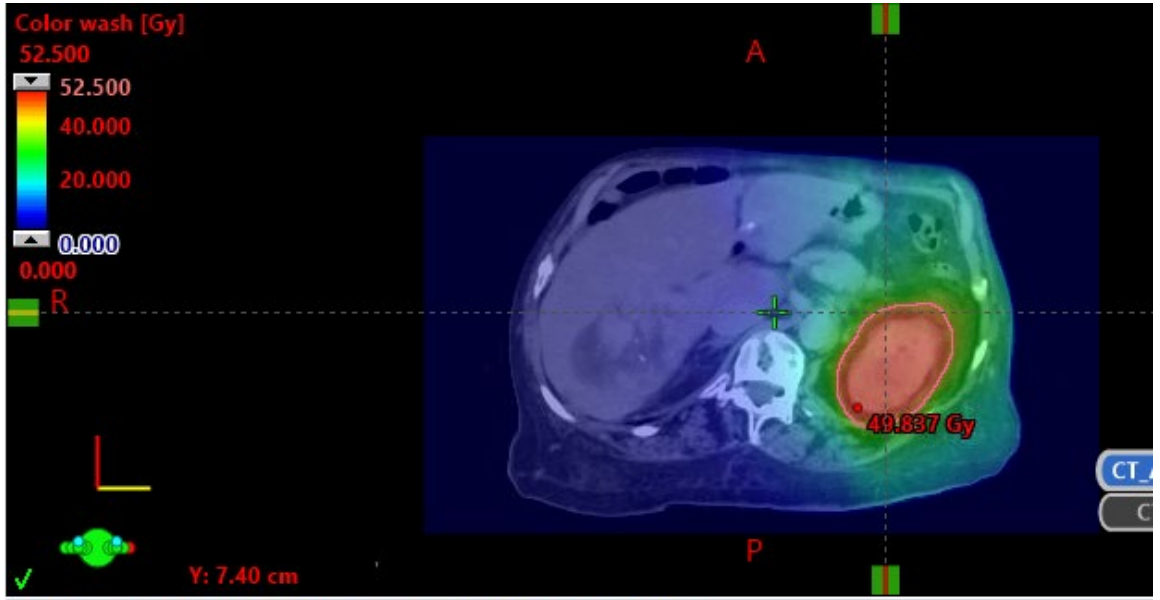
Plan 42Gy in 3 fx per TROG 15.03

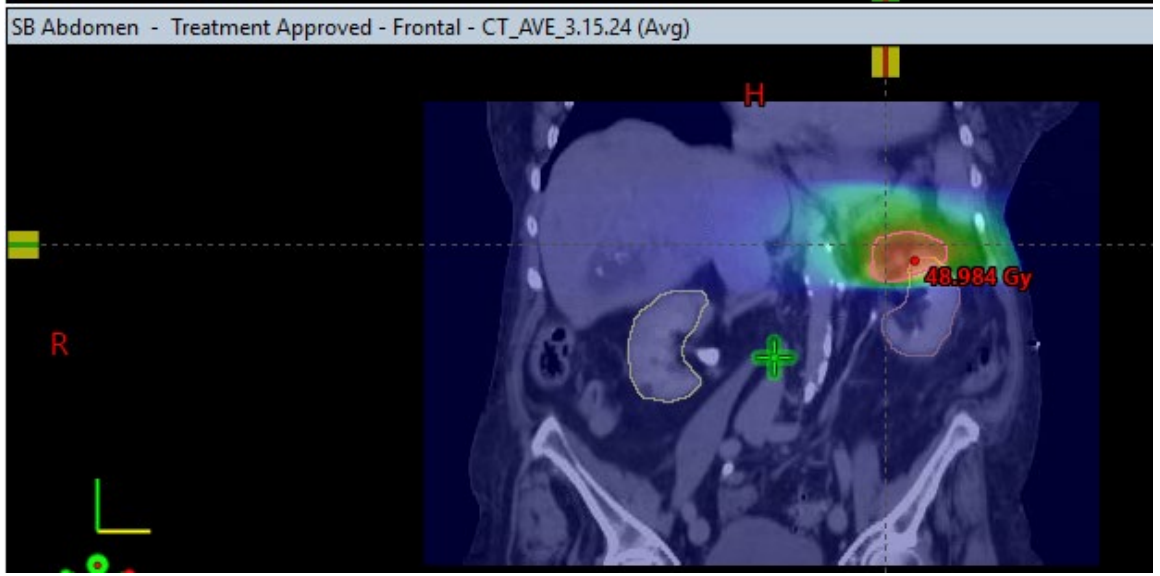




79 y.o. W with Stage I (cT1b,cN0,cM0) 5cm left RCC, s/p biopsy, PMH of SBO due to prior abdominal surgery adhesions

Plan 42Gy in 3 fx per TROG 15.03





Another prospective trials (primary RCC)

- UT Southwestern phase II Single center
  - N=16 enlarging primary RCC ≤5 cm
  - RT regimens
    - 36 Gy / 3 fx or 40 Gy / 5 fx
  - mFU 36mo
  - 1EP:
    - radiographic 1-yr LC 94% (15/16)
    - 100% non-progression by RECIST at 1 yr
  - no Gr2+ tox; modest eGFR decline (~10 mL/min at 1 yr)

EUROPEAN UROLOGY 84 (2023) 275–286

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

European Association of Urology

Platinum Priority – Kidney Cancer – Editor's Choice

Editorial by Rohann J.M. Correa, Sree Appu, Shankar Siva on pp. 287–288 of this issue

Phase 2 Trial of Stereotactic Ablative Radiotherapy for Patients with Primary Renal Cancer

Raquibul Hannan [a,b,], Mark F. McLaughlin [a], Laurentiu M. Pop [a], Ivan Pedrosa [b,c,d], Payal Kapur [b,d,e], Aurelie Garant [a,b], Chul Ahn [b,f], Alana Christie [b], James Zhu [g], Tao Wang [g], Liliana Robles [a], Deniz Durakoglugil [a], Solomon Woldu [b,d], Vitaly Margulis [b,d], Jeffrey Gahan [b,d], James Brugarolas [b,h], Robert Timmerman [a,b], Jeffrey Cadeddu [b,d]*

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(Hannan et al., Eur Urol 2023)

Radiosurgery Society Practice Guide

Practical Radiation Oncology® (2025) 15, 74–85

Special Article

Stereotactic Body Radiation Therapy for Primary Renal Cell Carcinoma: A Case-Based Radiosurgery Society Practice Guide

Andrew B. Barbour, MD, PhD,[a] Rituraj Upadhyay, MD,[b] August C. Anderson, MD,[a] Tugce Kutuk, MD,[c] Ritesh Kumar, MD,[d] Shang-Jui Wang, MD, PhD,[b] Sarah P. Psutka, MD,[e] Fatemeh Fekrmandi, MD, MSc,[f] Karin A. Skalina, MD, PhD,[g] Anna M.E. Bruynzeel, MD, PhD,[h] Rohann J.M. Correa, MD, PhD,[i] Alan Dal Pra, MD,[j] Cesar Della Biancia, PhD,[k] Raquibul Hannan, MD, PhD,[l] Alexander Louie, MD, PhD,[m] Anurag K. Singh, MD,[f] Anand Swaminath, MD,[n] Chad Tang, MD,[o] Bin S. Teh, MD,[p] Nicholas G. Zaorsky, MD, MS,[q] Simon S. Lo, MD,[a,*] and Shankar Siva, MBBS, PhD[r]

https://www.practicalradonc.org/article/S1879-8500(24)00156-5/abstract

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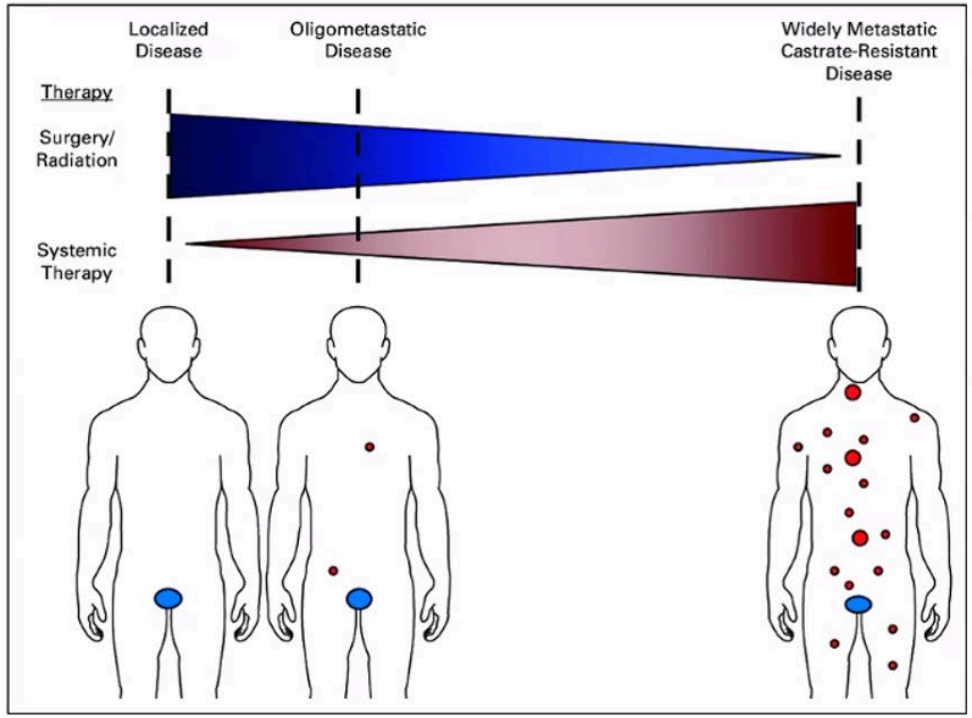
Barbour, PRO 2025

Oligometastatic Cancer

Metastatic solid tumors are generally considered incurable with treatments largely designed to palliate and extend life but not cure.



ADENOCARCINOMA OF THE KIDNEY WITH METASTASIS TO THE LUNG

CURED BY NEPHRECTOMY AND LOBECTOMY[1]

J. DELLINGER BARNEY AND EDWARD J. CHURCHILL

From the Surgical Services of the Massachusetts General Hospital

Adenocarcinoma of the kidney (hypernephroma) is a neoplasm that on occasion may be treated by removal of the primary growth and an apparently single metastasis. The following case history relates the course of a patient in whom x-ray evidence of a metastatic nodule in the lung was the first sign of disease. A nephrectomy was performed 5 months later, and 15 months following the nephrectomy the pulmonary metastasis was excised by sub-total lobectomy. The patient is surviving 5 years later in good health, without evidence of disease.

[1] Read at the annual meeting of the American Association of Genito-Urinary Surgeons, Absecon, New Jersey, May 2, 1938.

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Courtesy of Dr Chad Tang MDACC GU retreat 2025

Oligometastatic Renal Cell Carcinoma

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2026
Kidney Cancer

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STAGE IV OR RELAPSED DISEASE

	TREATMENT		DISEASE PROGRESSION
Clear cell histology	Clinical trial or First-Line Therapy (KID-D, 1 of 3) or Metastasectomy or SBRT[j] or percutaneous ablation for oligometastatic disease or Metastasectomy with complete resection of disease, followed by adjuvant Pembrolizumab within 1 year of nephrectomy and Best supportive care[k]	Follow-up (KID-C)	Clinical trial or Subsequent Therapy for Clear Cell Histology (KID-D, 2 of 3) or Metastasectomy or SBRT[j] or percutaneous ablation for oligometastatic disease and Best supportive care[k]
Non-clear cell histology	Clinical trial (preferred) or Systemic Therapy (KID-D, 3 of 3) or Metastasectomy or SBRT[j] or percutaneous ablation for oligometastatic disease and Best supportive care[k]	Follow-up (KID-C)	Clinical trial or Systemic Therapy for Non-Clear Cell Histology (KID-D, 3 of 3) or Metastasectomy or SBRT[j] or percutaneous ablation for oligometastatic disease and Best supportive care[k]

Rini Lancet Onc 2016, set comparison for future trials

- N=48, Ph II , 2008-2013
- mFU 38 mo
- 1EP: time on surveillance (i.e until systemic therapy starts

Active surveillance in metastatic renal-cell carcinoma: a prospective, phase 2 trial

Brian I Rini, Tanya B Dorff, Paul Elson, Cristina Suarez Rodriguez, Dale Shepard, Laura Wood, Jordi Humbert, Linda Pyle, Yu-Ning Wong, James H Finke, Patricia A Rayman, James M G Larkin, Jorge A Garcia, Elizabeth R Plimack

Summary

Background A subset of patients with metastatic renal-cell carcinoma show indolent growth of metastases. Because of the toxicity and non-curative nature of systemic therapy, some of these patients could benefit from initial active surveillance. We aimed to characterise the time to initiation of systemic therapy in patients with metastatic renal-cell carcinoma under active surveillance.

Methods In this prospective phase 2 trial, we enrolled patients with treatment-naive, asymptomatic, metastatic renal-cell carcinoma from five hospitals in the USA, Spain, and the UK. Patients were radiographically assessed at baseline, every 3 months for year 1, every 4 months for year 2, then every 6 months thereafter. Patients continued on observation until initiation of systemic therapy for metastatic renal-cell carcinoma; a decision that was made at the discretion of the treating physician and patient. The primary endpoint of the study was time to initiation of systemic therapy in the per-protocol population. The follow-up of patients is ongoing.

Findings Between Aug 21, 2008, and June 7, 2013, we enrolled 52 patients. Median follow-up of patients in the study was 38·1 months (IQR 29·4–48·9). In the 48 patients included in analysis, median time on surveillance from registration on study until initiation of systemic therapy was 14·9 months (95% CI 10·6–25·0). Multivariate analysis showed that higher numbers of International Metastatic Database Consortium (IMDC) adverse risk factors (p=0·0403) and higher numbers of metastatic disease sites (p=0·0414) were associated with a shorter surveillance period. 22 (46%) patients died during the study period, all from metastatic renal-cell carcinoma.

Interpretation A subset of patients with metastatic renal-cell carcinoma can safely undergo surveillance before starting systemic therapy. Additional investigation is required to further define the benefits and risks of this approach.

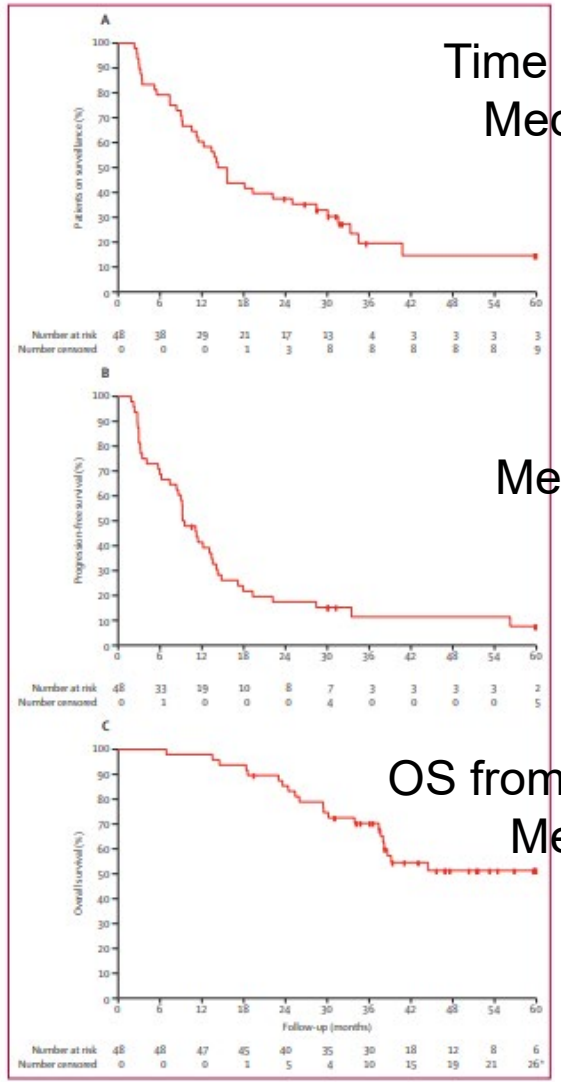
Lancet Oncol 2016; 17: 1317–24

Published Online August 3, 2016 http://dx.doi.org/10.1016/S1470-2045(16)30196-6

See Comment page 1187

See Online for podcast interview with Brian Rini

Cleveland Clinic Taussig Cancer Institute, Main Campus, Cleveland, OH, USA (Prof B I Rini MD, P Elson ScD, D Shepard MD, L Wood MSN, Prof J H Finke PhD, P A Rayman MS, J A Garcia MD); **USC Norris Comprehensive Cancer Center, Los Angeles, CA, USA** (T B Dorff MD); **Vall d'Hebron University Hospital and Institute of Oncology, Universitat Autònoma de Barcelona, Barcelona, Spain** (C Suarez Rodriguez MD, J Humbert BSc); **Royal Marsden**



Time on surveillance
Median 14.9 mo

PFS
Median 9.4 mo

OS from time of surveillance
Median 44.5 mo

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Tang, Lancet Onc, 2025

Metastasis-directed radiotherapy without systemic therapy for oligometastatic clear-cell renal-cell carcinoma: primary efficacy analysis of a single-arm, single-centre, phase 2 trial

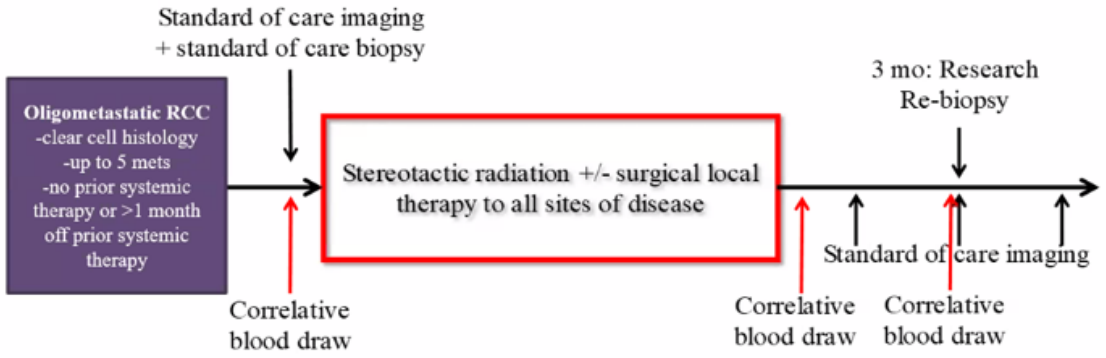
Chad Tang, Alexander D Sherry, Aaron Seo, Kieko Hara, Haesun Choi, Suyu Liu, Xiaowen Sun, Anya Montoya, Ethan B Ludmir, Amishi Y Shah, Eric Jonasch, Amado J Zurita, Craig Kovitz, Omar Alhalabi, Sangeeta Goswami, Andrew W Hahn, Matthew T Campbell, Arianna Hernandez, Kevin T Nead, Peter Van Loo, Shiqin Su, Christopher J Battey, Matthew L LaBella, Sarah Ratzel, Ashley Acevedo, Giannicola Genovese, Kanishka Sircar, Jose A Karam, Nizar M Tannir, Pavlos Msaouel

Summary

Background Select patients with metastatic clear-cell renal-cell carcinoma can be treated without systemic therapy, yet few studies have explored this population. We investigated the efficacy of metastasis-directed therapy without systemic therapy in oligometastatic clear-cell renal-cell carincoma.

Lancet Oncol 2025; 26: 1289–99
Published Online September 4, 202
https://doi.org/10.

- N=121, Ph II , 2018-2023
- RCC 1-5 mets
- mFU 38 mo
- co1EP: PFS and systemic therapy free survival
- Threshold for success > median 24mo systemic therapy free survival
- ctDNA used to determine molecular residual disease



systemic therapy free survival median 34mo

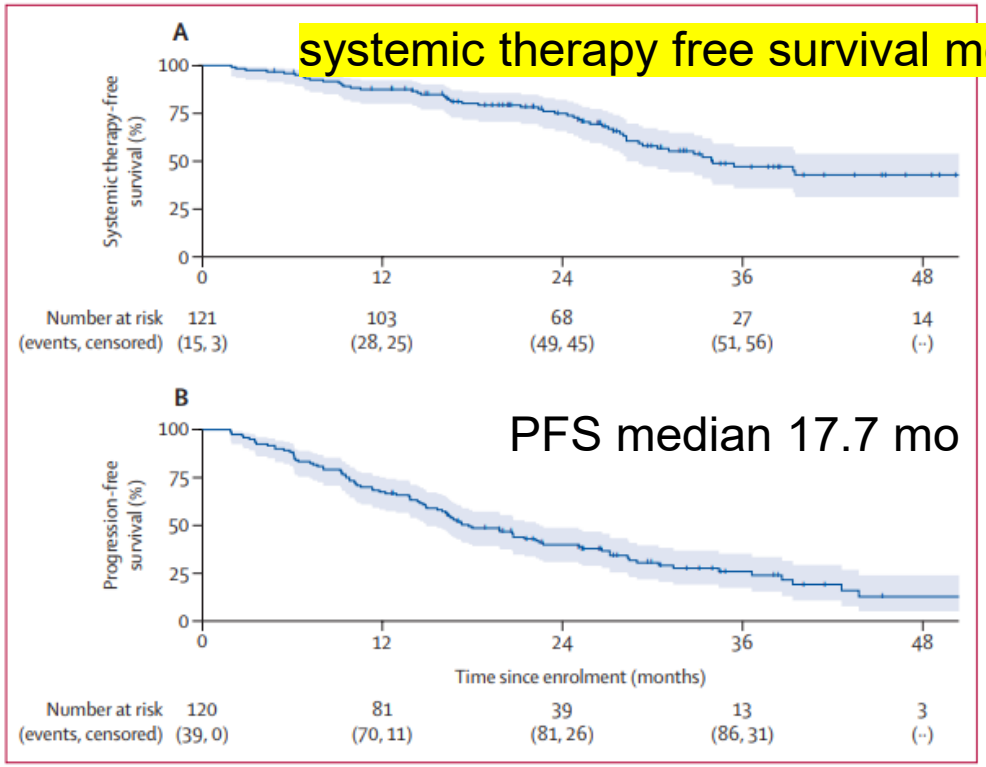


Figure 2: **Primary outcomes of systemic therapy-free survival in the intention-to-treat population (n=121; A) and progression-free survival in the per-protocol population (n=120; B)**
Vertical lines denote censored patients, and shading indicates 95% CIs.

This is the most robust RCC-only, modern dataset supporting SBRT in carefully selected patients.

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Combination with immunotherapy

- Published Ph II
  - **NIVES (phase II):** Nivolumab + SBRT in pre-treated mRCC was **safe** and produced strong **in-field responses**, but **did not improve outcomes** over nivolumab alone
  - **RADVAX-RCC (phase II, non-randomized, early data):** Nivolumab/ipilimumab + SBRT showed activity and offered feasibility signals

- Ongoing Ph III
  - **ECOG-ACRIN phase III (TPS489):** RCT comparing SABR vs upfront systemic therapy for oligometastatic RCC; co-1EP include OS

- Conclusion: for **oligometastatic** or **oligoprogressive** RCC, phase II data support SBRT for **high local control** and **meaningful delays in systemic therapy** for select patients (good PS, limited mets, non-brain/bone predominance)

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Primary Prostate Cancer

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NCCN Guidelines Version 2.2026
Prostate Cancer

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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 treatment pages and Principles of ADT (PROS-G) for other recommendations, including recommendations for neoadjuvant/concomitant/adjuvant ADT.

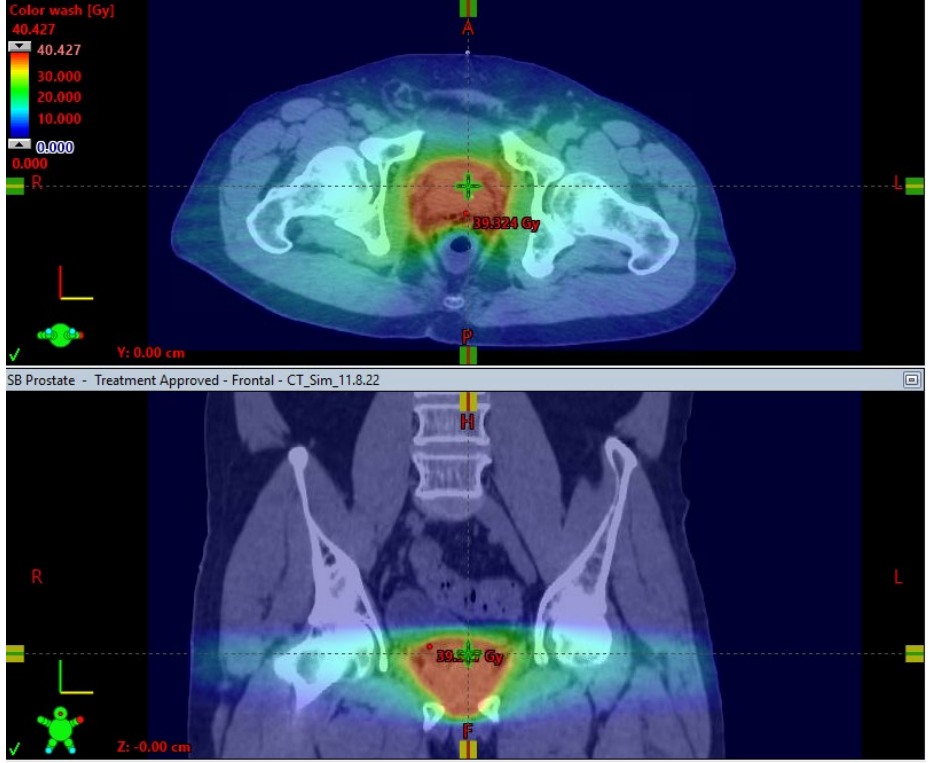
EBRT Regimen	Preferred Dose/Fraction	Definitive RT						Post-Treatment RT			Advanced Disease	
								Post-RP		Post-RT	Primary Tumor	Metastases
		Low	FIR	UIR	High	Very-High	Regional	aRT	sRT	sRT	mCSPC M0 CRPC mCRPC	MDT
Conventional	1.8–2 Gy x 37–45 fx			☼	☼	✓	✓				☼	
	1.8–2 Gy x 30–39 fx							✓	✓		☼	
Moderate Hypofractionation	3 Gy x 20 fx (preferred)[a] 2.7 Gy x 26 fx 2.5 Gy x 28 fx	☼	✓	✓	✓	✓	✓			☼	☼	☼
	2.63–2.75 Gy x 20 fx 2.5 Gy x 25 fx							✓	✓	☼	✓	☼
Ultra Hypofractionation (SBRT)	9.5 Gy x 4 fx 7.25–8 Gy x 5 fx 6 Gy x 6 fx 6.1 Gy x 7 fx	☼	✓	✓	✓	☼	☼		☼	✓	✓	✓
	9–10 Gy x 3 fx 12 Gy x 2 fx 16–24 Gy x 1 fx											✓
	6.2–6.4 Gy x 5 fx								☼			
EBRT Boost Techniques												
EBRT with simultaneous integrated boost	See footnote b.		☼	✓	✓	☼	☼		☼	☼	☼	
EBRT with sequential SBRT boost	*Prostate:* 1.8 Gy x 23–28 fx *Boost:* 6 Gy x 3 fx 9.5 Gy x 2 fx			☼	☼	☼						

(✓ Preferred; ☼ Acceptable based on clinical and medical need; Regimens shaded gray are not recommended)

Och Hea

Practice-guideline synthesis

AUA/ASTRO/ASCO (2022 update)



30. Clinicians should offer moderate hypofractionated EBRT for patients with low- or intermediate-risk prostate cancer who elect EBRT. (Strong Recommendation; Evidence Level: Grade A)

31. Clinicians may offer ultra hypofractionated EBRT for patients with low- or intermediate risk prostate cancer who elect EBRT. (Conditional Recommendation; Evidence Level: Grade B)

32. In patients with low- or favorable intermediate-risk prostate cancer electing radiation therapy, clinicians should offer dose-escalated hypofractionated EBRT (moderate or ultra), permanent low-dose rate (LDR) seed implant, or temporary high-dose rate (HDR) prostate implant as equivalent forms of treatment. (Strong Recommendation; Evidence Level: Grade B)

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Eastham, journal of urol, 2022

ASTRO 2025: QOL Results from NRG-GU005: Phase III Trial of SBRT vs. Hypofractionated IMRT for Localized Intermediate Risk Prostate Cancer

Study Design: NRG GU005 Randomized Phase III Trial

N=698 intermediate-risk prostate cancer patients (accrued 11/2017 to 6/2022)

STRATIFY

Risk Group
1.Gleason score 7(3+4) with PSA <10 ng/mL
2.Gleason score 7(3+4) with 10 ng/mL <= PSA < 20 ng/mL
3.Gleason score 6(3+3) with 10 ng/mL < PSA < 20 ng/mL

Use of Rectal Manipulation
1. No
2. Rectal balloon
3. SpaceOAR
4. SpaceOAR and rectal balloon

IMRT Standard Arm
1) 70 Gy in 28 fractions
2) 60 Gy in 20 fractions

RANDOMIZE

Arm 1: IMRT
70 Gy in 28 fractions of 2.5 Gy to the prostate
or 60 Gy in 20 fractions of 3 Gy
+/- proximal 1cm of seminal vesicles

Minimal Margins:
8 mm uniform in expansion,
5 mm posteriorly

Arm 2: SBRT
36.25 Gy in 5 fractions of 7.25 Gy to the prostate +/- proximal 1 cm of seminal vesicles

Minimal Margins:
5 mm superior inferior & laterally,
3 mm anterior & posterior

Secondary Patient Reported Outcomes 1-year post-treatment

EPIC Minimal Clinically Important Difference at Year 1

	IMRT (n=345)	SBRT (n=353)	p-value*	
Bowel domain ≥ 4 point decline from baseline	117 (46%)	98 (33%)	0.002	Favors SBRT
Urinary irritation domain ≥ 5 point decline from baseline	94 (37%)	105 (36%)	0.77	
Urinary incontinence domain ≥ 6 point decline from baseline	87 (34%)	80 (27%)	0.054	
Sexual domain ≥ 10 point decline from baseline	107 (44%)	94 (34%)	0.03	Favors SBRT
Hormonal domain ≥ 4 point decline from baseline	82 (33%)	73 (26%)	0.09	

*p-values from two-sided chi-square test

Regarding disease-free survival, 88.6% of patients in the SBRT group were free from disease progression after three years, compared to 92.1% receiving longer courses of radiation. The difference was driven mainly by higher rates of biochemical failure, or rising PSA after treatment, in the SBRT arm (7.8% vs. 4.2%, p=0.037).

"The PSA findings require careful interpretation," noted Dr. Ellis. "With treatments involving larger doses per fraction, patients can experience temporary PSA elevations, or 'benign bounces,' that resolve over time. We need five-year follow-up to determine whether these elevations translate into actual disease progression."

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SBRT/Ultrahypofx in IR Prostate Cancer

Name	Population	Dose/Fx	ADT use	1EP	Results	Conclusion
Scand HYPO-RT-PC (Ph III; Widmark et al., Lancet 2019; 10-yr update 2024)	**89% IR** 11% HR N =1,200	**Ultra-hypo:**42.7 Gy/7 fx vs **Conv:**78 Gy/39 fx	**No ADT**	**Failure-free survival (non-inferiority)**	**Non-inferior FFS** at 5 & 10 yrs similar late GU/GI tox higher **acute** GU/GI with ultra-hypo	oncologic non-inferiority of **very short-course RT** in IR safety acceptable
PACE-B (Ph III ; van As et al.; acute tox 2019, 5-yr updates 2023–2024)	**8% LR** **92% FIR** N=874	**SBRT:** 36.25 Gy/5 fx vs **SOC EBRT:**CF/MH (78–80 Gy/39–40 fx or 62 Gy/20 fx)	**No ADT**	**Biochemical/clinical failure (non-inferiority)**; safety	**SBRT non-inferior** for control at 5 yrs; acceptable late toxicity; higher transient acute GU with SBRT; PROs broadly similar.	**5-fx SBRT is** alternative to CF/MH in FIR
NRG-GU005 (Ph III; 2025 interim PRO & efficacy reports)	**Intermediate-risk** (FIR & UIR) N=698	**SBRT:** 36.25 Gy/5 fx vs **MH-IMRT:**70 Gy/28 fx	**ADT per protocol standard for UIR allowed**	Co1EP **DFS** and **bowel QOL** (EPIC)	3 yrs: **DFS superiority not met** (more PSA BF in SBRT arm); **bowel QOL favored SBRT**(fewer declines), ans less urinary incontinence at 2 yrs longer follow-up pending	comparable disease control to MH-IMRT **better bowel (and some urinary) PRO** → supports SBRT as a preferred RT schedule option
Guidelines (AUA/ASTRO/ASCO 2022 summary)	**LR & IR**		**FIR no ADT** **UIR ADT (4–6 mo)**		clinicians **may offer ultrahypofractionated EBRT** for LR/IR; (see ADT guidance)	

SBRT/Ultrahypofx in HR Prostate Cancer

Name	Design & Setting	Population	Dose/Fx	ADT use	1EP	Notes
HYPO-RT-PC (Widmark et al., 2019; long-term updates)	Ph III	**89% IR** **11% HR**	**42.7 Gy/7 fx** vs **78 Gy/39 fx** (no ENI)	**No ADT**	**Non-inferior 5-yr failure-free survival** late GU/GI similar; higher *acute*GU/GI with ultra-hypo	Only randomized evidence including some HR pts
PACE-C (Tree et al., early toxicity 2025)	Phase III RCT: **UIR + limited HR**	65% IR **35% HR**	**SBRT 36.25 Gy/5 fx** vs **MHRT ~60–70 Gy/20–28 fx (ENI per protocol)**	**ADT in both arms**(per protocol)	**Early results:similar early GI**; **higher GU grade ≥2 at 2 yrs with SBRT**; oncologic endpoints pending.	First RTC **designed** to test SBRT with ADT in HR patients

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SBRT in the Post-Prostatectomy Salvage Setting

Study / Year	Study type	indication	SBRT Regimen	ADT Use	Outcomes	Toxicity	Notes
Ballas et al., Red J 2019	Ph I dose-escalation, N=24	Biochemical recurrence post-RP	**32.5 Gy / 5 fx → 35.5 Gy / 5 fx** (dose escalation)	Optional (~40%)	2-yr bRFS ~73%	Grade 3 GU 0%, GI 0%	First dose-finding trial showing feasibility and tolerability
SBRT-SOPRANO (NCT05099414)*(on going)*	Phase II multicenter RCT	Post-RP, early salvage	**32.5–35 Gy / 5 fx**vs standard 66 Gy / 33 fx	Per protocol			Ongoing (results ~2026/2027)

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Tang JAMA Onc 2023

JAMA Oncology | Original Investigation

Addition of Metastasis-Directed Therapy to Intermittent Hormone Therapy for Oligometastatic Prostate Cancer
The EXTEND Phase 2 Randomized Clinical Trial

Chad Tang, MD; Alexander D. Sherry, MD; Cara Haymaker, PhD; Tharakeswara Bathala, MD; Suyu Liu, PhD; Bryan Fellman, MS; Lorenzo Cohen, PhD; Ana Aparicio, MD; Amado J. Zurita, MD; Alexandre Reuben, PhD; Enrica Marmonti, PhD; Stephen G. Chun, MD; Jay P. Reddy, MD, PhD; Amol Ghia, MD; Sean McGuire, MD, PhD; Eleni Efstathiou, MD; Jennifer Wang, MD; Jianbo Wang, MD; Patrick Pilie, MD; Craig Kovitz, MD; Weiliang Du, PhD; Samantha J. Simiele, PhD; Rachit Kumar, MD; Yerko Borghero, MD; Zheng Shi, MD, PhD; Brian Chapin, MD; Daniel Gomez, MD; Ignacio Wistuba, MD; Paul G. Corn, MD, PhD

IMPORTANCE Despite evidence demonstrating an overall survival benefit with up-front hormone therapy in addition to established synergy between hormone therapy and radiation, the addition of metastasis-directed therapy (MDT) to hormone therapy for oligometastatic prostate cancer, to date, has not been evaluated in a randomized clinical trial.

OBJECTIVE To determine in men with oligometastatic prostate cancer whether the addition of MDT to intermittent hormone therapy improves oncologic outcomes and preserves time with eugonadal testosterone compared with intermittent hormone therapy alone.

DESIGN, SETTING, PARTICIPANTS The External Beam Radiation to Eliminate Nominal Metastatic Disease (EXTEND) trial is a phase 2, basket randomized clinical trial for multiple solid tumors testing the addition of MDT to standard-of-care systemic therapy. Men aged 18 years or older with oligometastatic prostate cancer who had 5 or fewer metastases and were treated with hormone therapy for 2 or more months were enrolled to the prostate intermittent hormone therapy basket at multicenter tertiary cancer centers from September 2018 to November 2020. The cutoff date for the primary analysis was January 7, 2022.

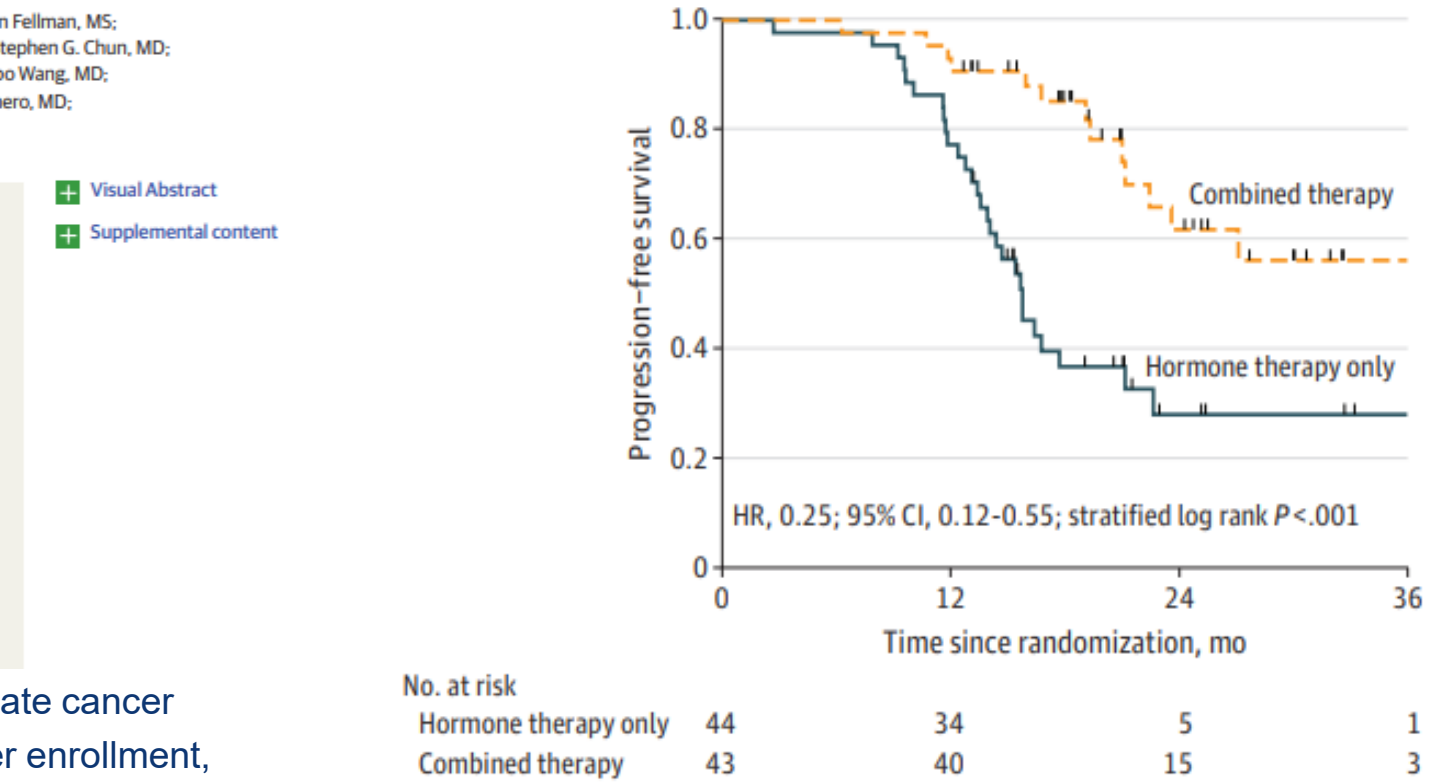
Visual Abstract

Supplemental content

- Ph II extend Trial, 1-5 mets, 87 men with stage 4 prostate cancer
- A planned break in hormone tx occurred 6 months after enrollment, after which hormone tx was withheld until **progression**.
- 1EP PFS
- mFU 22 mo

PFS median not reached (combined) vs 15.8 mo

A Progression-free survival by randomization arm



No. at risk				
Hormone therapy only	44	34	5	1
Combined therapy	43	40	15	3

- EXTEND trial iADT basket shows benefit of MDT to prolong time w/o ADT (hormone holiday)

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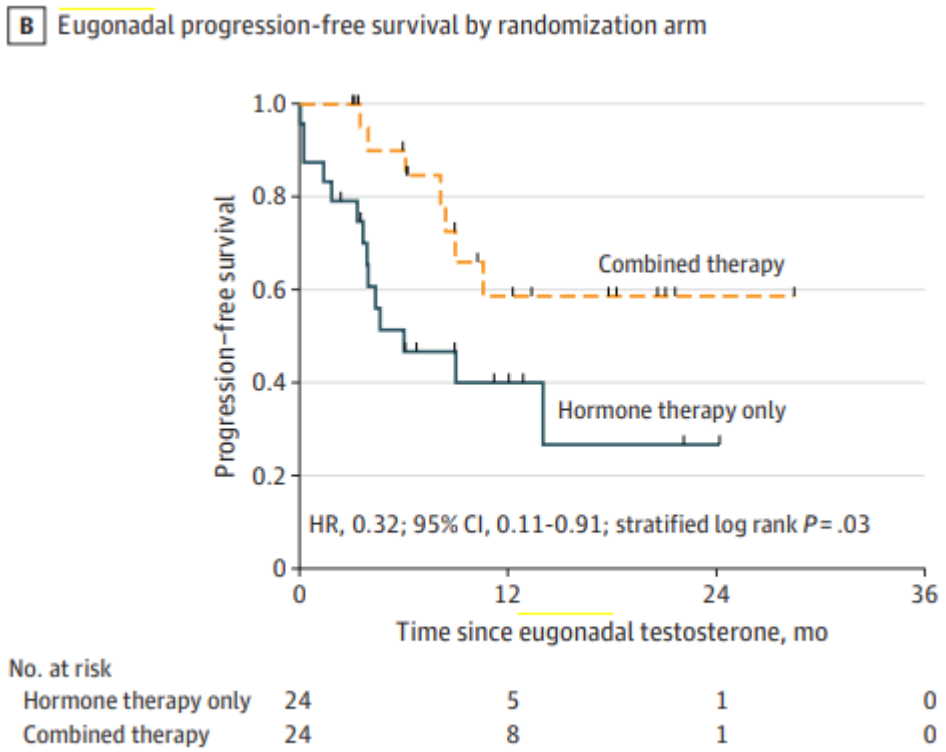
2nary endpoint eugonadal (PFS) = time from achieving a eugonadal testosterone level (>=150 ng/dL) until progression



Eugonadal PFS median not reached (combined) vs 6.1 mo

- Eugonadal PFS significantly improved using combination of MDT + hormone therapy vs hormone therapy alone

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Sherry, Eur Urol 2025 (article in press)

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

European Association of Urology

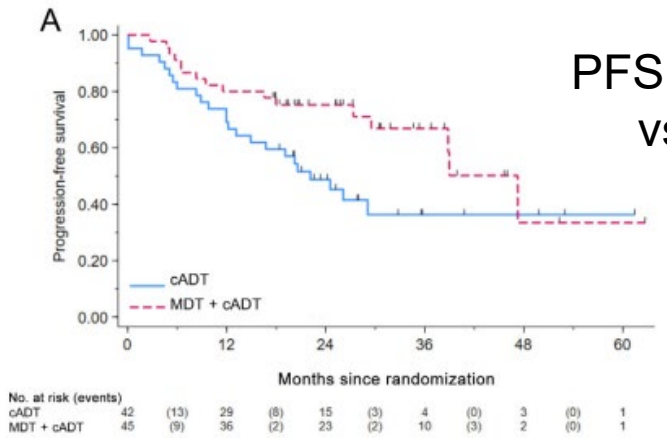
Original Article

Continuous Androgen Deprivation Therapy with or Without Metastasis-directed Therapy for Oligometastatic Prostate Cancer: The Multicenter Phase 2 Randomized EXTEND Trial

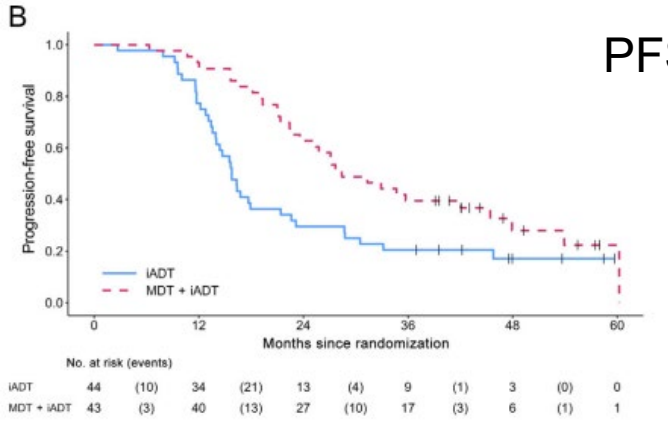
Alexander D. Sherry [a,j,†], Bilal A. Siddiqui [b,†], Cara Haymaker [c], Bryan M. Fellman [d], Marina N. Medina-Rosales [c], Tharakeswara K. Bathala [e], Shuqi Wang [d], Suyu Liu [d], Aaron Seo [a], Kieko Hara [c], Hsinyi Lu [c], Patricia Troncoso [f], Stephen G. Chun [a], Chul S. Ha [g], Lauren L. Mayo [a], Henry Mok [h], Ryan J. Park [h], Brian F. Chapin [i], Ryan M. Phillips [j], Matthew P. Deek [k], Craig A. Kovitz [l], Ana Aparicio [b], Amado J. Zurita [b], Patrick G. Pilie [b], Lorenzo Cohen [m,n], Seungtaek L. Choi [h], Alexandre Reuben [o], Phuoc T. Tran [p], Paul G. Corn [b], Sumit K. Subudhi [b,], Chad Tang [c,h,q,*]*

[a] Department of Radiation Oncology, Division of Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [b] Department of Genitourinary Medical Oncology, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [c] Department of

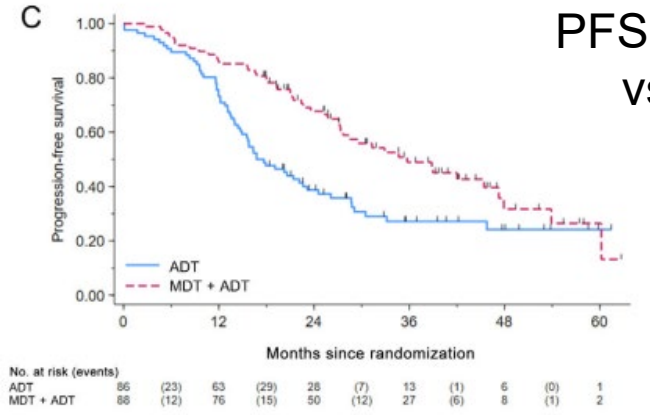
- Ph II extend Trial, 1-5 mets, 174 men with stage 4 prostate cancer, 2018-2022
- included a subset of patients with castration-resistant disease
- 2 independent powered baskets: cADT and iADT
- 1EP PFS
- mFU 42 mo for combined analysis



PFS median 47 mo (MDT+cADT)
vs 22 mo (cADT)



PFS median 28 mo (MDT+iADT)
vs 16 mo (iADT)

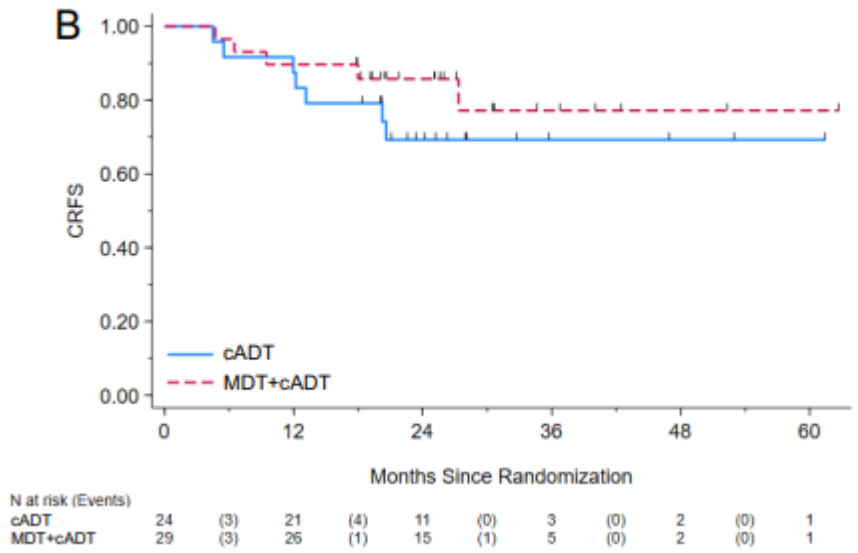


PFS median 36 mo (MDT+ADT)
vs 17 mo (ADT)

- EXTEND trial cADT basket MDT shows PFS benefit

Novel outcome: castration resistance–free survival (CRFS)

- in patients with hormone-sensitive disease, MDT + ADT was associated with superior CRFS – a novel discovery



CRFS HR 0.40 p=0.01

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Significance

- Level II RCT evidence (STOMP, ORIOLE): MDT/SBRT **delays progression and defers ADT** in metachronous castration-sensitive oligo-recurrence, with low toxicity
- Level II RCT evidence (EXTEND): When systemic therapy is indicated (intermittent or continuous), **adding MDT extends PFS** (and **eugonadal PFS** with iADT)
- Imaging is important: outcomes are best when **all PSMA-avid sites are ablated** (per ORIOLE consolidation analysis)

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Conclusion

- SBRT is now standard for localized prostate cancer
- → Multiple Ph III trials (PACE-B, HYPO-RT-PC, NRG-GU005)
- Metastasis-Directed Therapy (MDT) improves PFS in oligometastatic prostate cancer
- → ORIOLE, STOMP show delayed systemic therapy and improved PFS
- → EXTEND shows that adding MDT to ADT improves PFS
- Primary RCC
- → SBRT as an ablative alternative for inoperable or high-risk surgical candidates (FASTRACK II)
- Oligometastatic RCC
- → Tang et al showed that MDT w/o systemic therapy yields median systemic therapy free survival of ≈34 mo

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QUESTIONS

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Salvage SBRT for Local Recurrence After Prior EBRT — Key Prospective & Systematic Evidence

Study / Year	Design & N	Setting	SBRT Regimen	ADT Use	Outcomes	Toxicity	Notes
Ekanger et al., JCO 2024	Prospective single-arm, n≈100	Biopsy-proven local recurrence post-EBRT	Focal re-irradiation (mostly **30–36.25 Gy / 5 fx**)	Optional (~30–40%)	**7-yr bRFS ~60%**, local control >85%	Late grade ≥3 GU ~3–5%, GI ~2%	Longest follow-up prospective series; supports durable control with focal SBRT.
Patel et al., Red J 2023–2024	Phase I dose-escalation	Post-EBRT focal recurrence	**32.5–40 Gy / 5 fx** (escalation)	Optional	Early bRFS >70% at 2 yrs; defines MTD **~36–37.5 Gy / 5 fx**	No dose-limiting toxicity; mostly grade 1–2 GU	First prospective dose-finding trial defining safe SBRT doses after EBRT.
MRgRT Salvage Registry 2025	Prospective registry	Local recurrence post-EBRT	Adaptive MR-guided SBRT (commonly **30–35 Gy / 5 fx**)	Optional	Biochemical control ~65% at 3 yrs; LC ~90%	Grade ≥3 GU <3%, GI <2%	Confirms feasibility and safety with adaptive SBRT.
MASTER Meta-analysis, Eur Urol 2021	Systematic review / meta-analysis, 39 studies	Local recurrence after EBRT	SBRT / focal EBRT cohorts included	Mixed	Pooled 2- to 3-yr bRFS ~55–70%; LC ~80–90%	Grade ≥3 GU 3–5%, GI 1–3%	SBRT outcomes comparable to brachytherapy, cryo, HIFU, with lower morbidity.
Multi-institution series (2019–2023)	Retrospective, multi-center	Local recurrence post-EBRT	**30–36.25 Gy / 5 fx** (focal)	Mixed	bRFS ~50–70% at 3 yrs; LC >85%	Grade ≥3 GU ≤5%, GI ≤3%	Largest datasets mirror prospective results; focal SBRT clearly feasible.

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SCINTIX THERAPY TRANSFORMS TUMORS INTO CONTINUOUSLY IDENTIFIABLE TARGETS

BY USING INJECTED RADIOPHARMACEUTICALS TO LIGHT UP CANCER

1

Positron emissions generated by the radiopharmaceutical accumulate in tumors

2

RefleXion X1 machine detects the emissions from all tumors

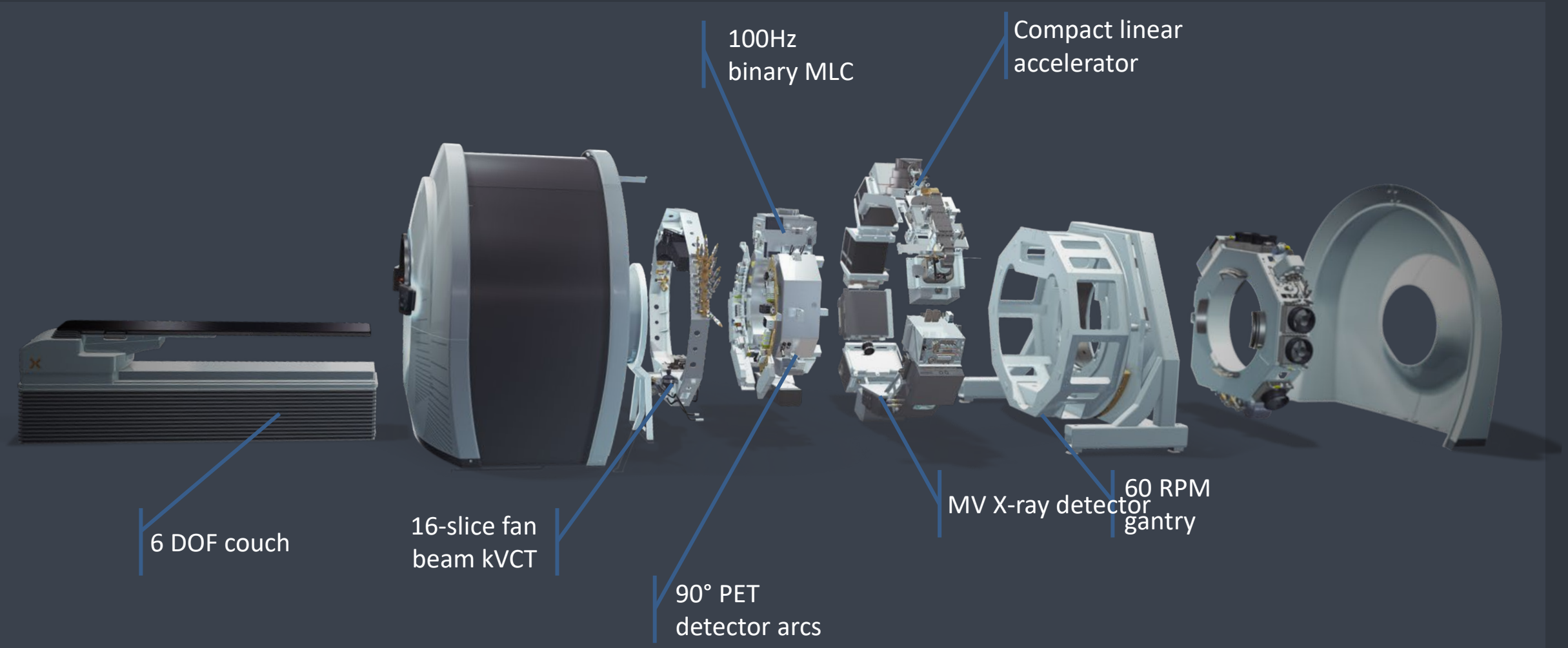
3

Algorithms use these emissions to maintain a continuous lock on tumors regardless of motion

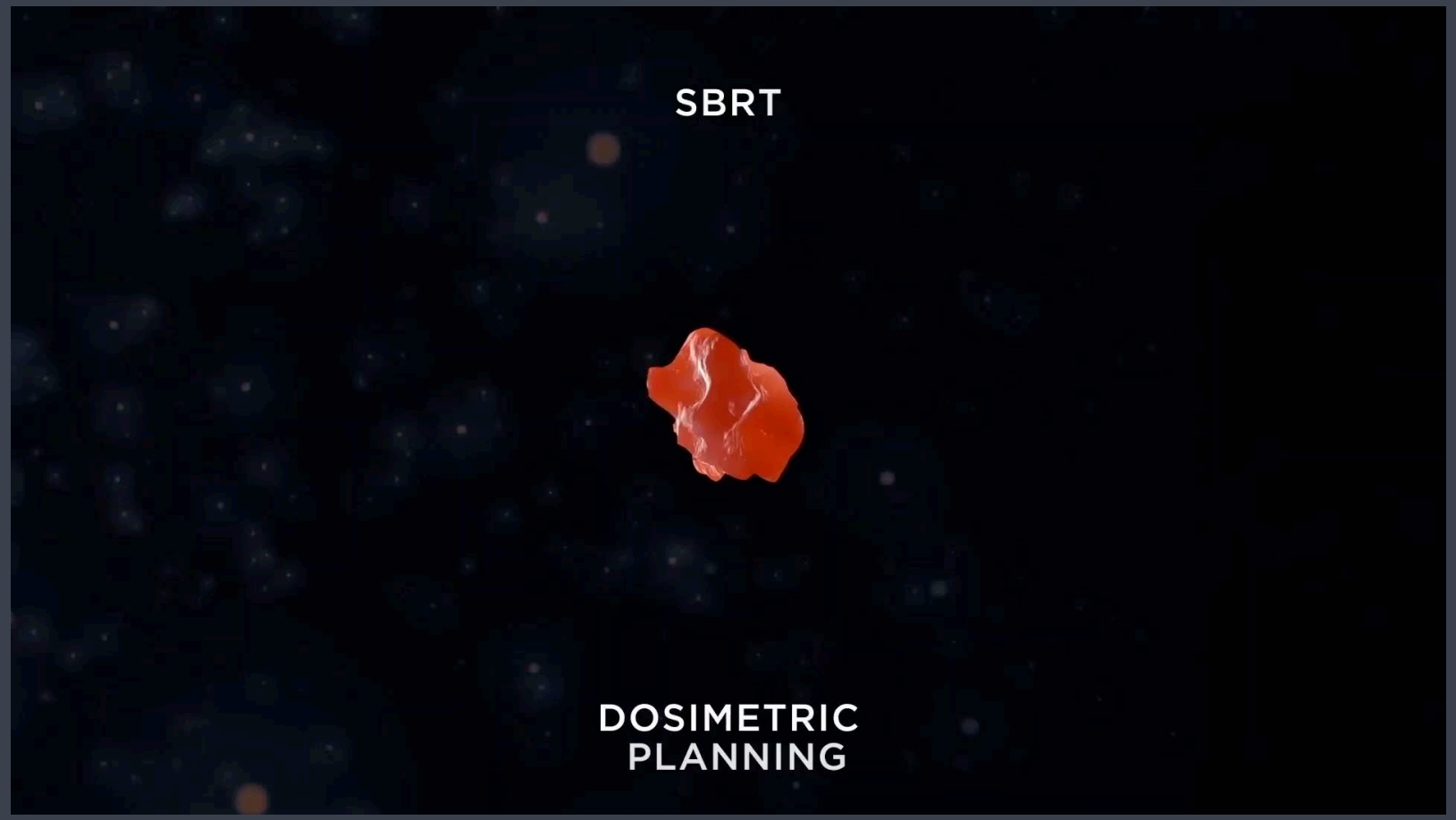
4

The X1 adjusts to continuous emissions 100 times/sec during treatment to autonomously deliver radiotherapy

REFLEXION X1 RADIOTHERAPY MACHINE: LINAC, PET, KVCT ON A ROTATING GANTRY



SCINTIX THERAPY IMPROVES THERAPEUTIC RATIO COMPARED TO SBRT



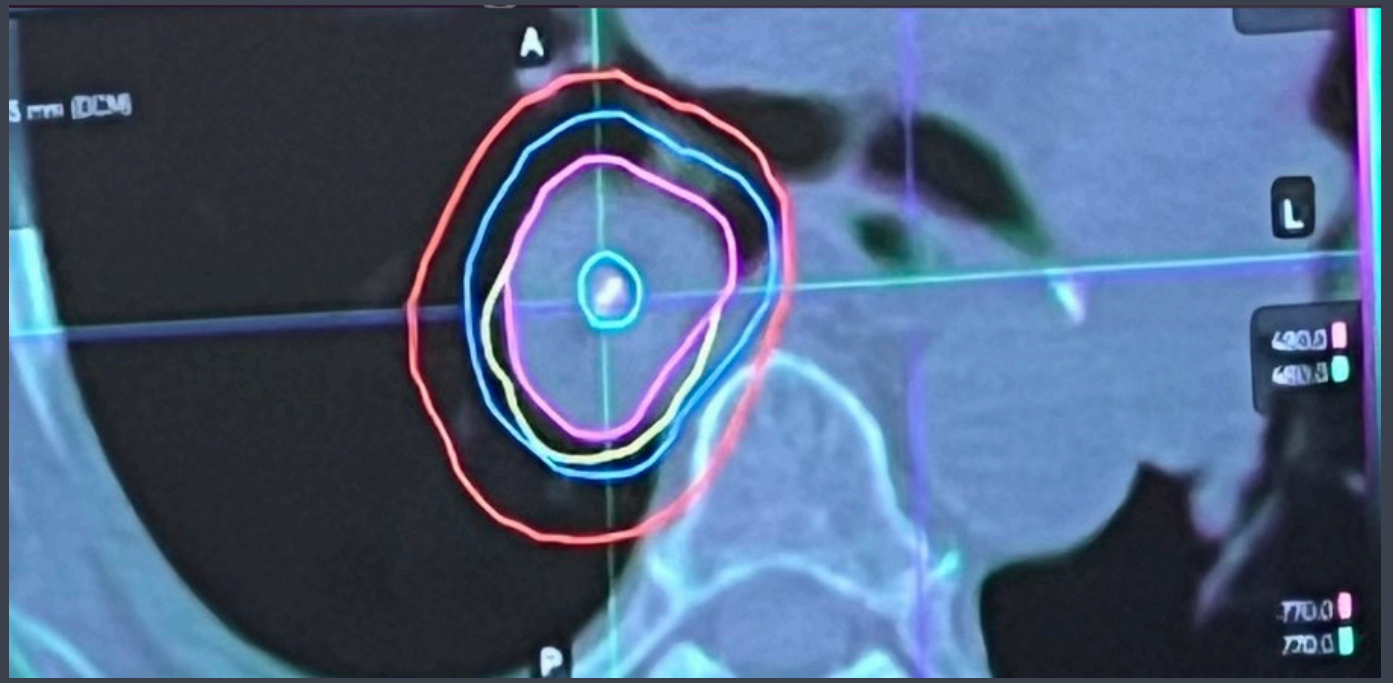
SCINTIX

- Delivers a tracked-dose to achieve a high therapeutic ratio
- Reduces the PTV and moves the dose with the motion of the target
- Ensures coverage by concentrating the dose on a moving target
- Improves therapeutic ratio compared to conventional RT and SBRT

CLINICAL CASE

ULTRACENTRAL LUNG TUMORS DEMONSTRATE INCREASING CONFIDENCE BY USERS

SCINTIX therapy safely delivered to an ultracental lung tumor within 2 cm of main bronchus/carina



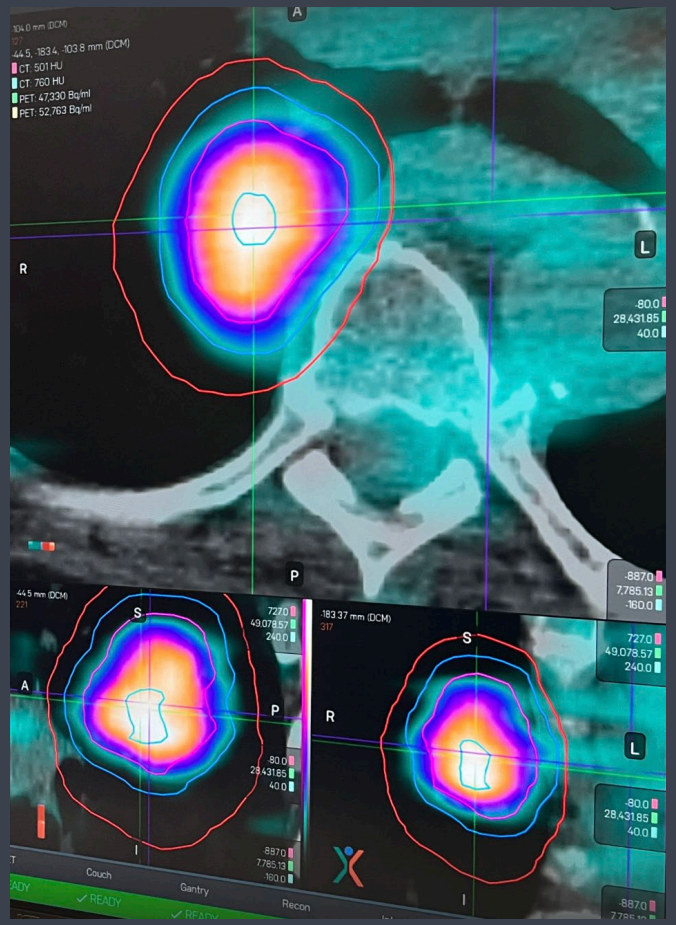
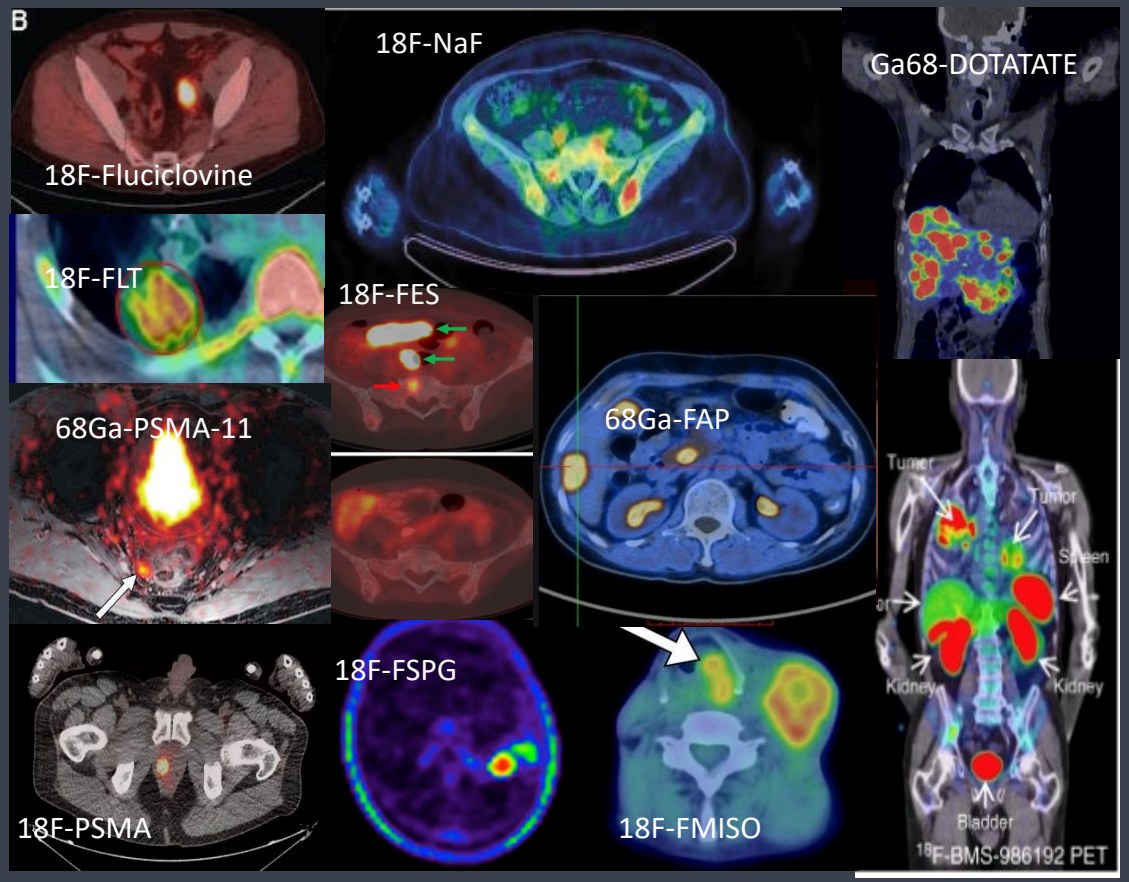


Image courtesy of Stanford Healthcare

REFLEXION'S PET TRACER PROGRAMS ENCOMPASS NOVEL RADIOTRACERS



- FDG is a well validated baseline
- Non-FDG tracers enable BgRT clinical applications in which FDG performs poorly (e.g., prostate cancer, liver metastases)
- PET tracer serves as
  - Biological fiducial for real-time treatment guidance
  - Biology sensor for treatment selection and/or response assessment
- Collect on-treatment imaging data for radiomics analyses