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Tratamiento radioterápico de las masas renales: ¿es la SBRT un nuevo estándar?

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1. INTRODUCTION
   - Renal tumors and radiotherapy

2. EVIDENCE
   - Primary tumors
   - Metastatic renal cell carcinoma (mRCC)
   - Metastases in the kidney

3. TREATMENT WITH SBRT
   - Technique
   - Challenges

4. CONCLUSIONS

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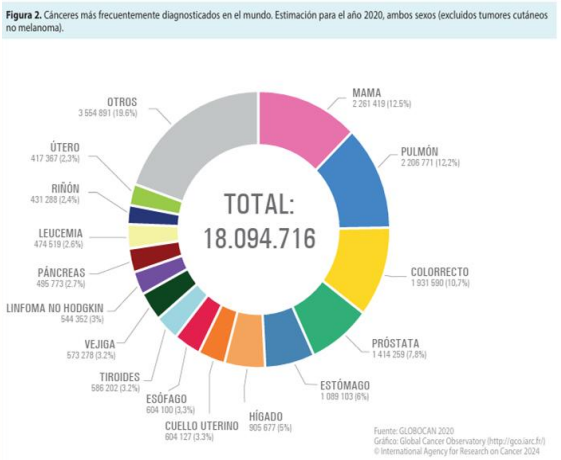
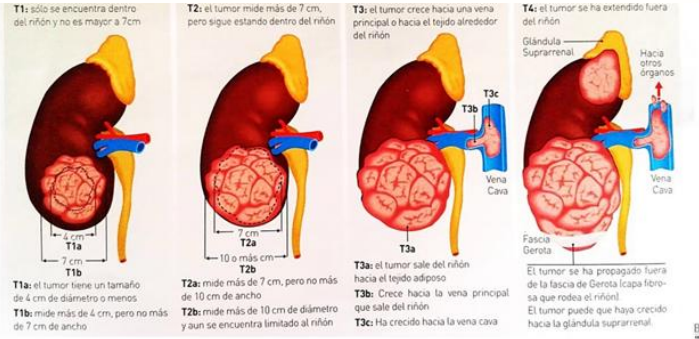
INTRODUCTION

Renal Masses	Treatment	Limitations
Primary renal tumor (80% clear cell carcinoma)	**Total or partial nephrectomy**	• Age and/or comorbidities • Renal insufficiency/single-kidney
	Ablative techniques (thermal ablation, radiofrequency, cryoablation, etc.)	• Size (< 3-4 cm) • Location (>1 cm from anatomical structures) • Technique
Metastases from other tumors (melanoma and other solid tumors)	Systemic treatment	



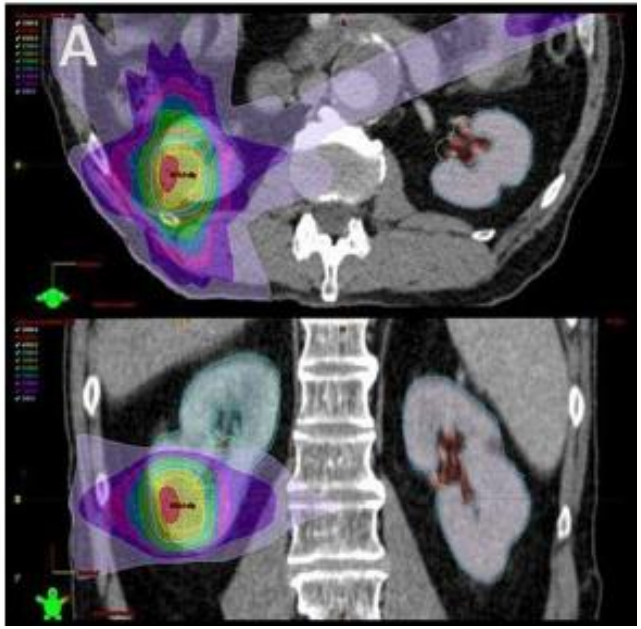


RADIOTHERAPY

- Palliative or symptomatic control (pain, bleeding, etc.)
- Is it a radioresistant tumor?
    - Low vs. high doses per fraction
    - Preclinical models: Ablative doses may overcome radioresistance mechanisms linked to HIF-1α activation, which promotes endothelial cell survival.

SBRT (Stereotactic Body Radiotherapy)

- High-dose fractions in a limited number of sessions (1-5)
- Highly conformal dose distribution
- Non-invasive
- Effective and convenient treatment for tumors:
    - With complex anatomical locations or challenging growth patterns (endophytic and/or centrally located in the kidney)
    - Larger than 3-4 cm
    - In elderly patients and/or those with comorbidities
    - In single-kidney patients
- Provides good local control and high tolerability

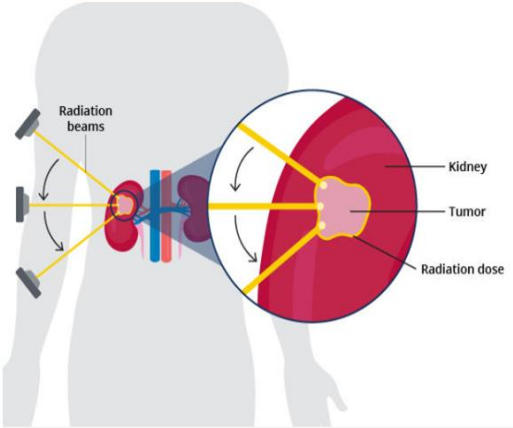


Yang et al., 2024

SBRT:

- NCCN Guidelines Version 3.2025, EAU and ESMO:

"SBRT is considered an ablative therapy and may be considered for non-optimal surgical candidates with stage I (category 2B), II, or III (both category 3) kidney cancer".



In stereotactic body radiotherapy (SBRT) for localized kidney cancer, imaging is used to precisely map the tumor, which radiation oncologists then use to create a treatment plan for directly targeting it with multiple radiation beams.
Credit: National Cancer Institute

ASTRO 2024
SBRT Effective Option for Kidney Cancer - NCI, n.d.

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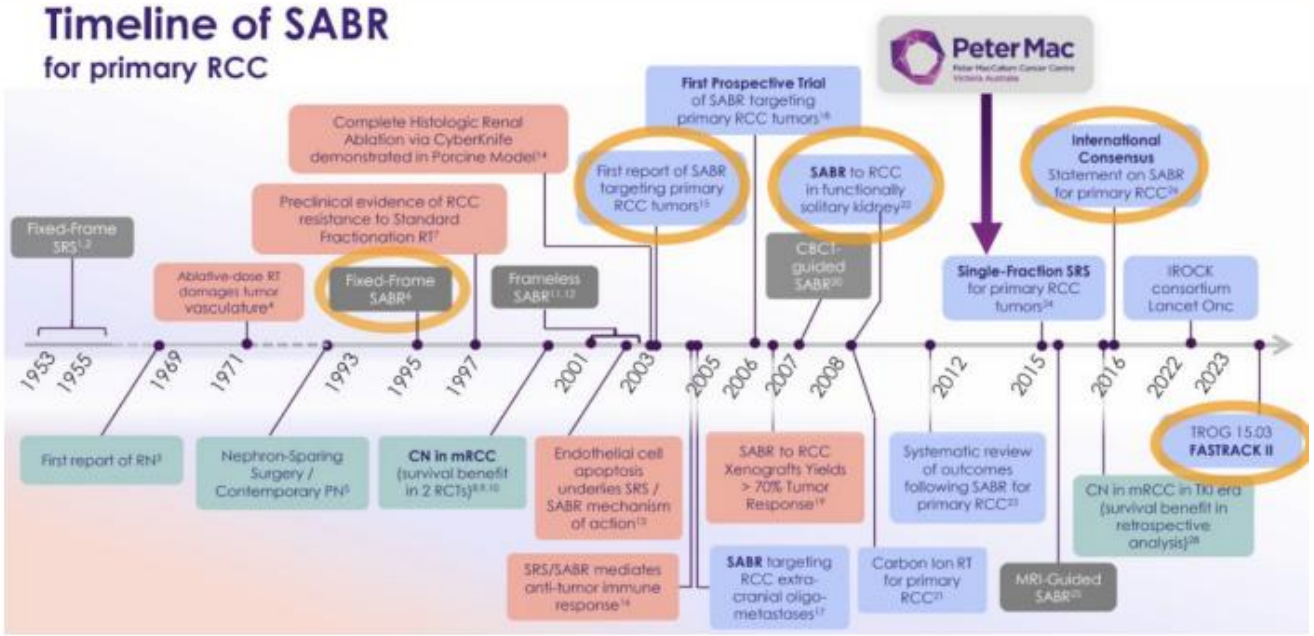
EVIDENCE

1. PRIMARY RENAL TUMOR (RCC)



1st Author, Year	Patients	Tumor Size (median, cm; unless stated)	Dose & Fractions	Local Control (%)	Change in eGFR (mLs/min)
Svedman, 2006	5	NR	30-45Gy in 2-4 fractions	80	NR
McBride, 2013	15	3.4	21-48Gy in 3	80	-18
Staehler, 2015	29	33.7 cm^3	26Gy in 1	100	-6.5
Ponsky, 2015	19	57.9 cm^3	24-48Gy in 4	100	NR
Siva, 2017	33	4.8	26Gy in 1 or 42Gy in 3	97	-11
Singh, 2017*	14	NR	15Gy in 1	*	*
Correa, 2018	12	8.7	25-35Gy in 5	100	-9.9
Kasuya, 2019	8	4.3	66-72Gy in 12 (CIRT)	100	-10.8
Funayama, 2019	13	2.28	60 or 70 Gy in 10	92.3	-16.7
Grubb, 2021	11	3.7	48,54,60Gy in 3	90	-7
Kirste, 2022	7	2.8	50Gy in 5 (1 pt had 60Gy in 8)	100	-7.1
Lapierre, 2023	13	3.3	32, 40 or 48 Gy in 4, or 40Gy in 5	100	-5.9
Hannan, 2023	16	3.2	36 Gy in 3 (63%) OR 40Gy in 5	94	-12.1

ASTRO 2024

Phase 2 Trial of Stereotactic Ablative Radiotherapy for Patients with Primary Renal Cancer (Hannan et al. European Urology 2023):

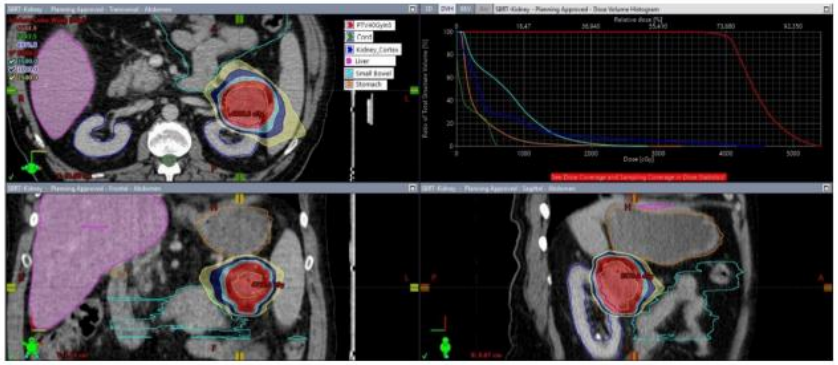


Fig. 1 – Representative patient treatment plan depicting axial (top left), coronal (bottom left), and sagittal (bottom right) views, along with a dose volume histogram (top right). The 40 Gy in five fractions PTV is shown in red, kidney in blue, small bowel in cyan, stomach in orange, and liver in magenta. Dose color wash values are 40 Gy (red), 35 Gy (cyan), 30 Gy (blue), and 25 Gy (yellow). PTV = planning treatment volume.

Design:

- Prospective trial RCC ≤5 cm mass. 16 patients (2014-2019)
- 36 Gy/3 or 40 Gy/5 fractions

Outcomes:

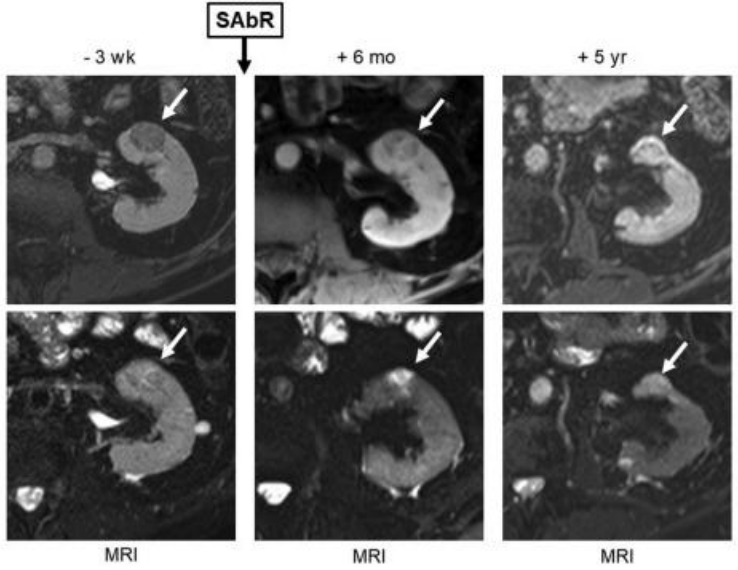
- Median f/u of 3 years
- **95% LC at 1 year** (primary endpoint). By RECIST 100%
- OS at 3 years was 79%

Toxicity:

- No grade ≥2 acute or late toxicity
- eGFR declined from 65.6 to 55.4 mL/min at 1 yr (p0.004).

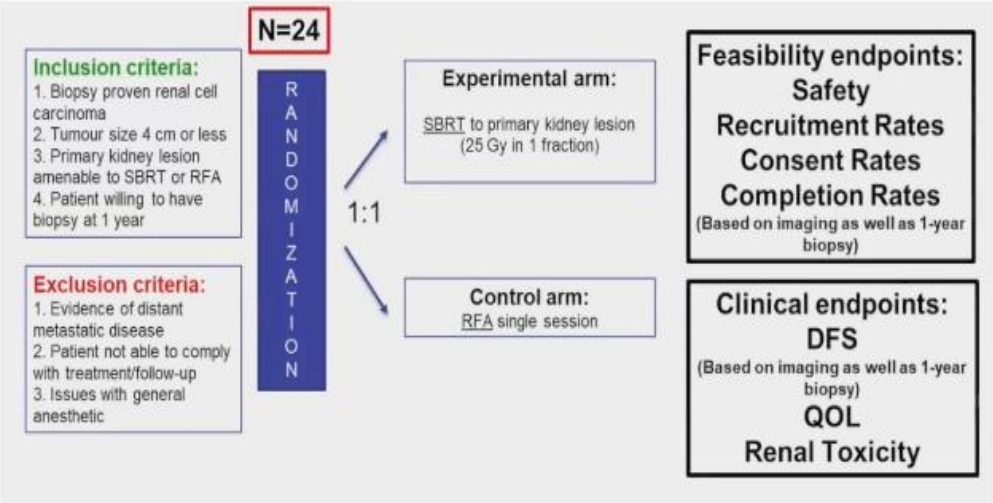
Other findings:

- Tumor viability decreased from 4.6% to 0.7% at 1 yr (p0.003).
- **Pathologic evidence:** hyalinization, necrosis, and reduced tumor cellularity.
- **Radiation induced cellular senescence**



Final Results from a Prospective Randomized Pilot Trial of Stereotactic Body Radiation Therapy vs. Radiofrequency Ablation for the Management of Small Renal Masses (RADSTER) (Abstract only) (Swaminath et al. ASTRO 2023):

Pilot randomized trial



Outcomes:

- No radiographic (RECIST) local failure in 1 year for both groups
- RFA tumors, more likely lose arterial enhancement
- **1-y post-treatment biopsies (complete response)**:
  - RFA (7/7)
  - SBRT (4/13)
- No patients developed distant disease or died from RCC

Toxicity:

- Only one grade 2 acute pain flare (SBRT patient)
- No late toxicity in 1 year for both groups
- No difference in mean eGFR reduction
(RFA: −3 mL/min; SBRT: −5.3 mL/min; p = 0.07)

Stereotactic ablative body radiotherapy for primary kidney cancer (TROG 15.03 FASTRACK II): a non-randomised phase 2 Trial (Siva et al. Lancet Oncol 2024):

- 70 patients between July 2016 and Feb 2020
- **26 Gy/1fx for tumours ≤4 cm or 42 Gy/3fx for tumours > 4 cm to 10 cm**
- Primary endpoint was local control
  (defined as no progression of the primary renal cell cancer - RECIST v.1.1)

Key inclusion criteria	• Age ≥ 18 years old • All patients must have a biopsy confirmed diagnosis of RCC with no more than a single lesion within a kidney (bilateral RCC is allowable) • ECOG performance of 0-2 inclusive • Life expectancy > 9 months • Either medically inoperable, technically high risk for surgery or decline surgery • Multidisciplinary decision for active treatment
Key exclusion criteria	• Pre-treatment estimated glomerular filtration (eGFR) rate < 30 mls/min • Prior systemic therapies for RCC • Previous high-dose radiotherapy to an overlapping region • Tumours of larger than 10cm in size • Direct contact of the target tumour with bowel • Untreated prior malignancy, or prior malignancy within 2 years of screening • Visceral / Bony metastatic disease • Horseshoe kidney

	Single-fraction 26 Gy group (n=23)	Three-fraction 42 Gy group (n=47)
Age, years	73 (66–80)	78 (71–82)
Sex		
Male	14 (61%)	35 (74%)
Female	9 (39%)	12 (26%)
ECOG performance status		
0	7 (30%)	19 (40%)
1	9 (39%)	22 (47%)
2	7 (30%)	6 (13%)
Tumour location		
Left	12 (52%)	19 (40%)
Right	11 (48%)	28 (60%)
Tumour maximal dimension, cm	3·3 (3·0–3·6)	5·3 (4·6–6·0)
Tumour volume, mL	16 (11–19)	58 (42–88)
RENAL score	7 (6–8)	9 (8–10)
RENAL complexity group		
Low	4 (17%)	17 (36%)
Moderate	9 (39%)	4 (9%)
High	10 (43%)	26 (55%)
Charlson comorbidity index	6 (5–6)	8 (6–9)

Data are median (IQR) or n (%). ECOG=Eastern Cooperative Oncology Group. SABR=stereotactic ablative radiotherapy.

Table 1: **Baseline patient characteristics, displayed per SABR treatment**

RENAL Nephrometry Score
https://www.mdcalc.com/calc/3908/renal-nephrometry-score

- Size (cm)
- Exophytic/endophytic
- Distance to the collecting system
- Location/contact in relation to the renal hilum/vascularization

Outcomes:

- Median follow-up was 43 months (IQR 38–60).
- Local control at 12 months 100% (p<0·0001).
- Seven (10%) patients had grade 3 treatment-related adverse events.

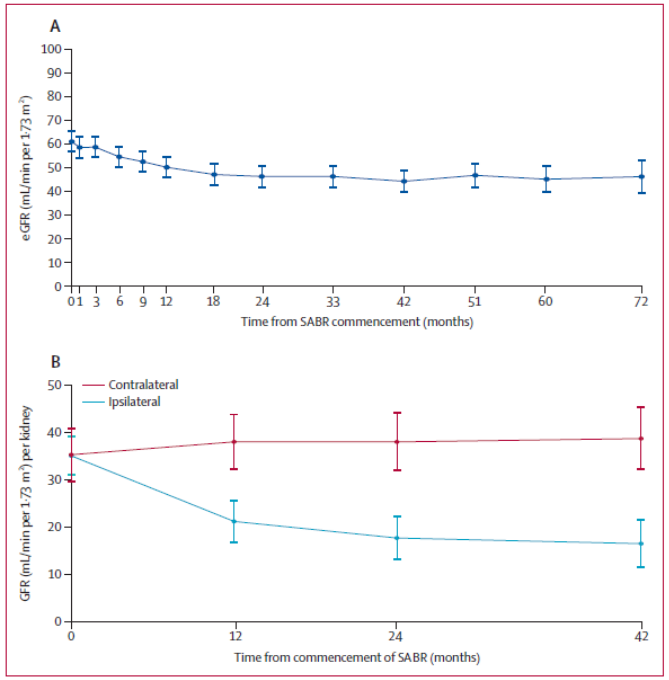
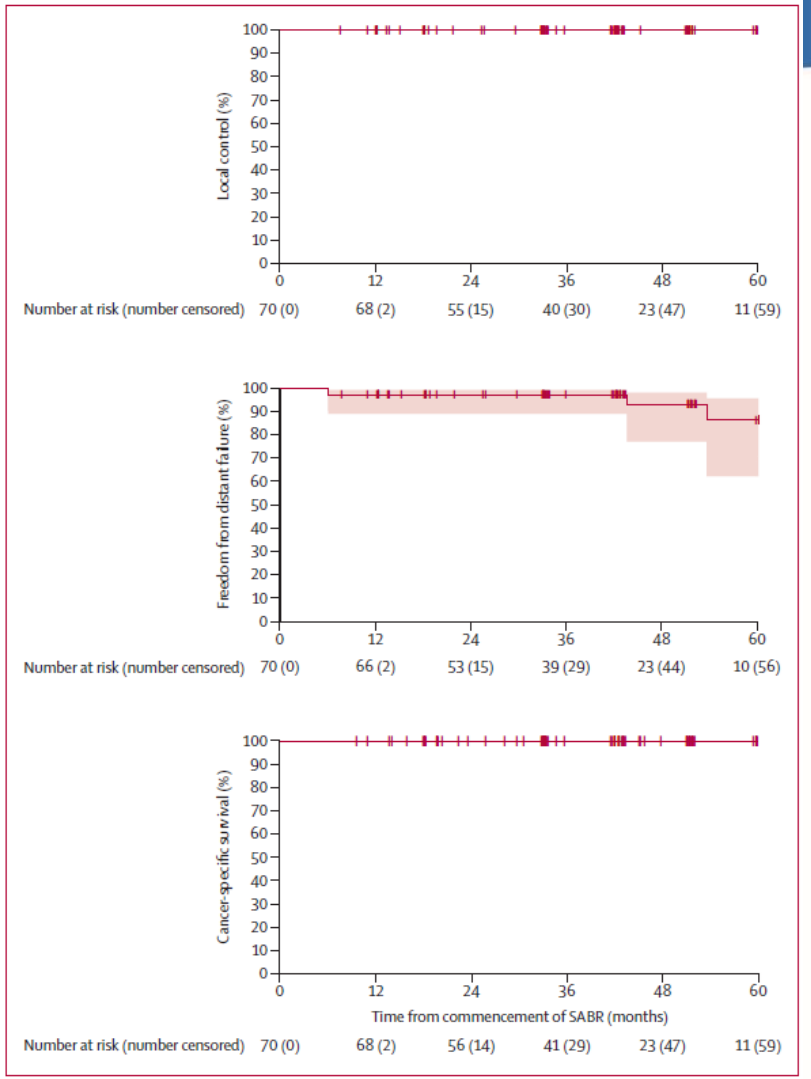


Figure 4: Renal function outcomes

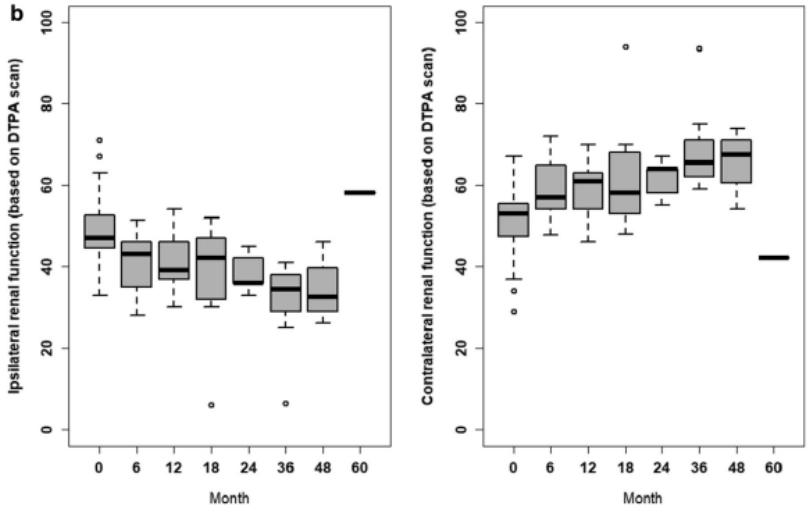


Patient-reported quality of life following stereotactic body radiation therapy for primary kidney cancer - results from a prospective cohort study (AQuOS-RCC) (Swaminath et al. Clinical Oncology 2021):

- Multi-institutional prospective trial. 28 patients.
- 30 - 42 Gy/3.5 fractions.
- **QoL assessment:**
  - No significant reduction in any QoL metric was observed
  - A trend to reduce QoL at 1 week, with improvement over time.

Stereotactic Body Radiotherapy for Renal Cell Carcinoma: Oncological and Renal Function Outcomes (Glicksman et al. Clinical Oncology 2023):

- Mixed prospective and retrospective institutional database. 74 patients.
- Median follow-up 27.8 m (IQ 17.6-41.7).
- 1, 2 and 4-y LF was 5.85, 7.77 and 7.77% (significantly associated with PTV volume)
- 2-y distant metastasis 4.24%.
- The median change in global eGFR: -7.0 (IQ -14.5 to -1.0) at 1-y and -11.5 (-19.5 to -4.0) at 2-y (significantly **associated with higher volume of uninvolved renal cortex)**



Tumor size and baseline eGFR were associated with an eGFR decline

(Tan et al. European Urology Oncology, 2024)

The Emerging Role of Stereotactic Ablative Radiotherapy for Primary Renal Cell Carcinoma: A Systematic Review and Meta-Analysis (Correa et al, European Urology Focus, 2019):

- 26 studies (11 prospective trials).
- 383 tumors in **372 patients**
  - Median age 70.4 (62–83) years
  - Mean tumor size 4.6 (2.3–9.5) cm
  - 26 Gy/1 fraction and 40 Gy/5 fractions

- Median follow-up 28.0 (5.8–79.2) months
- **Local control 97.2%** (95% confidence interval [CI]: 93.9–99.5%)
- **Grade 3–4 toxicity 1.5%** (95% CI: 0–4.3%)
- Post-SABR eGFR change–7.7 ml/min (95% CI: –12.5 to –2.8).

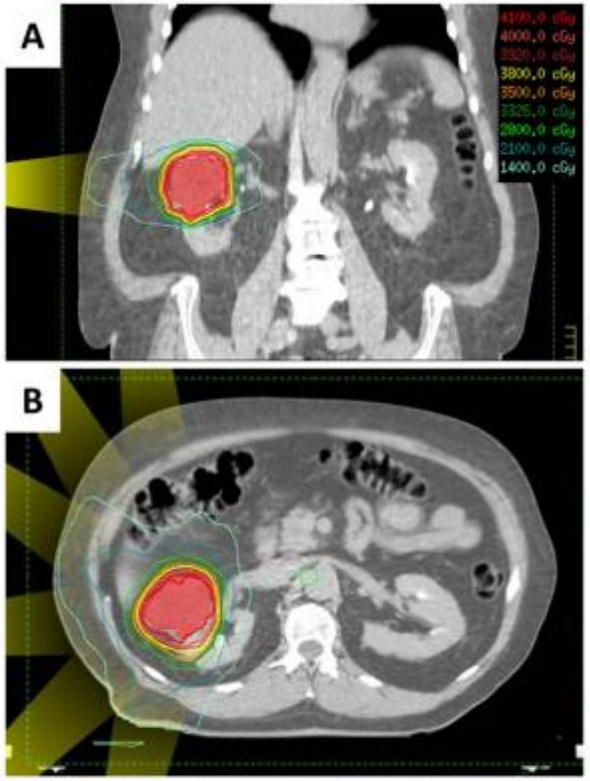


Fig. 1 – Stereotactic ablative radiotherapy for primary renal cell carcinoma (RCC). A representative radiotherapy plan treating a 6.5 cm right-sided RCC with 40 Gy in five fractions is shown in (A) axial and (B) coronal planes.

5-year outcome meta-analysis from IROCK (the International Radiosurgery Consortium of the Kidney) (Siva et al. Lancet Oncol 2022):

- **190 patients** (2007-2018).
- Median follow-up was **5 years** (IQR 3.4–6.8).
- **Local failure 5.5%** (95% CI 2.8–9.5).
- eGFR decreased by 14.2 mL/min (IQR 5.4–22.5). 4% dialysis.

	All patients (n=190)	Single-fraction SABR (n=81)	Multifraction SABR (n=109)
Any toxic effects			
Grade 1–2	70 (37%)	29 (36%)	41 (38%)
Grade 4	1 (1%)	0	1 (1%)
Fatigue			
Grade 1–2	51 (27%)	17 (21%)	34 (31%)
Nausea			
Grade 1–2	25 (13%)	16 (20%)	9 (8%)
Chest wall pain			
Grade 1–2	12 (6%)	5 (6%)	7 (6%)
Skin-related toxic effects			
Grade 1–2	3 (2%)	2 (2%)	1 (1%)
Gastritis			
Grade 1–2	3 (2%)	1 (1%)	2 (2%)
Grade 4	1 (1%)	0	1 (1%)
Bowel-related toxic effects			
Grade 1–2	3 (2%)	1 (1%)	2 (2%)
Grade 4	1 (1%)	0	1 (1%)

Data are n (%). There were no grade 3 toxic effects and no treatment-related deaths. SABR=stereotactic ablative body radiotherapy.

Table 2: **Toxic effects summary for all patients and by single-fraction versus multifraction SABR (n=190)**

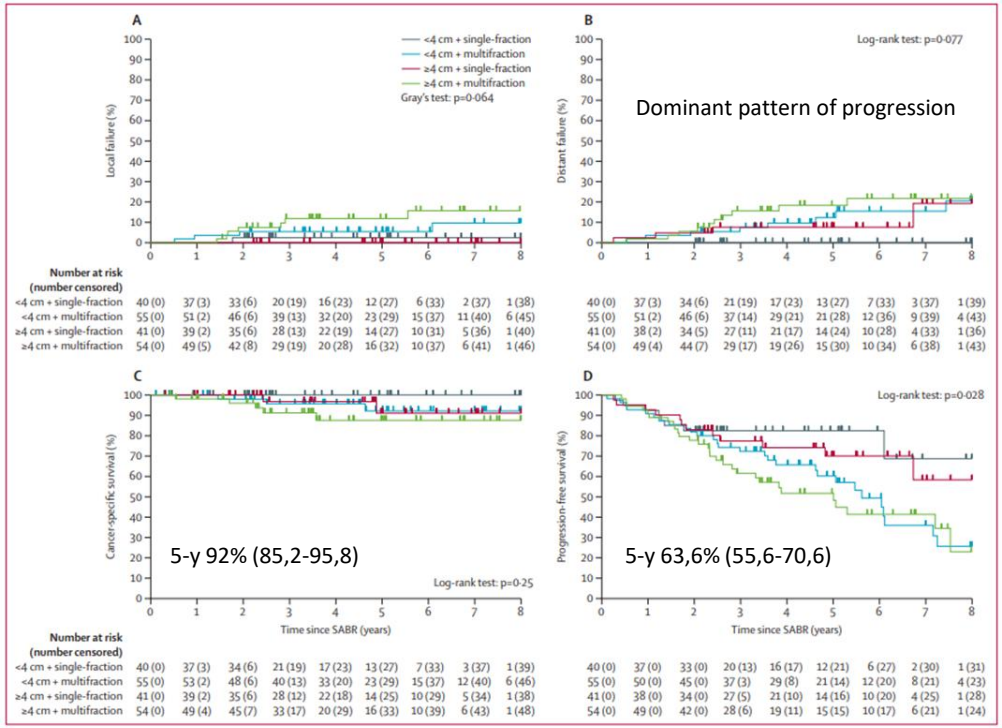


Figure 2: **Kaplan-Meier plots stratified by maximum tumour dimension (<4 cm *vs* ≥4 cm) and single-fraction versus multifraction SABR**
Plots are shown for local failure (A), distant failure (B), cancer-specific survival (C), and progression-free survival (D). Local and distant failure based on cumulative incidence function and competing risk model with death as competing event. Vertical dashes denote censored patients. SABR=stereotactic ablative body radiotherapy.

Siva et al. Lancet Oncol 2022

Results of Stereotactic Body Radiation Therapy for Primary Renal Cell Carcinoma in a Large Multicenter Series (Abancourt et al. European Oncology, 2025):

- **144 patients** (2008-2020).
- 42 Gy/3fx and 26 Gy/1fx.

- Median f-up of 43 mo (IQR 24.0–81.2).
- **5-y LC 96%** (95% CI, 92–99).
- The median OS was 58 mo.
- 5-y cancer-related deaths was 8% (95% CI, 3–15).
- Toxicity: G-1 (32%), G-2 (14%), G-3 (1%). G-4 (dialysis -1%). eGFR loss –7 ml/min (IQR, –17; 0).

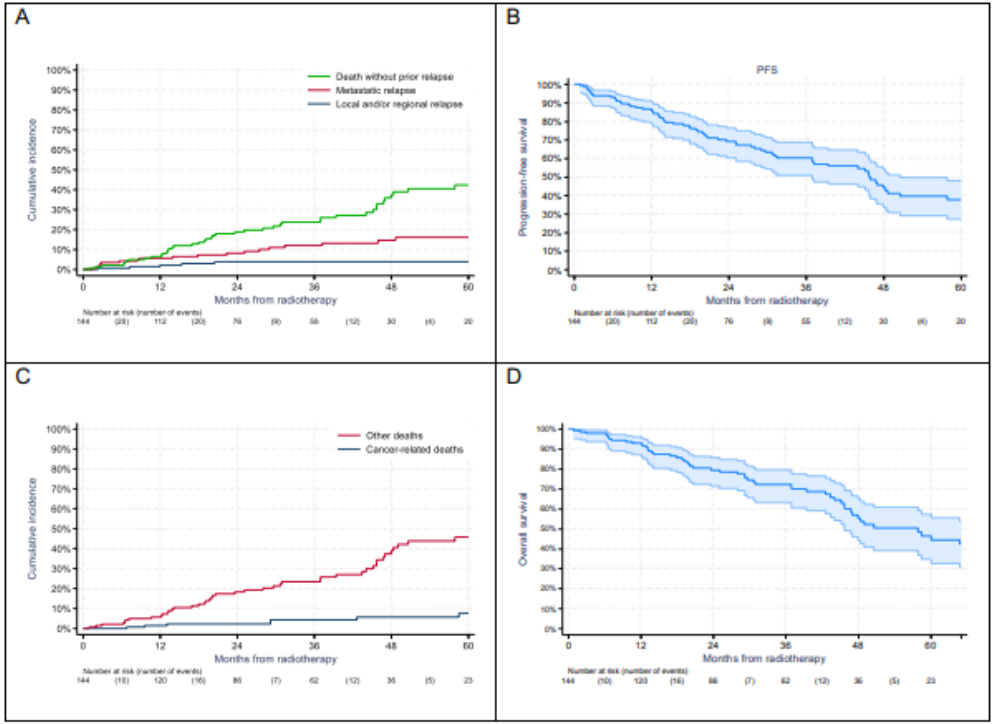


Fig. 1 – *Oncological outcomes*: (A) cumulative incidence of local and/or regional relapse, and cumulative incidence of the other competing events, and (B) progression-free survival. Kaplan-Meier estimates: (C) cumulative incidence of cancer-related deaths and cumulative incidence of deaths other than cancer-related death, and (D) overall survival.

Comparative efficacy and safety of ablative therapies in the management of primary localised renal cell carcinoma: a systematic review and meta-analysis (Huang et al. Lancet Oncol 2025):

- 133 studies and **8910 patients** (2000-2024)
- Low rate of grade 3-4 toxicity:
  - SBRT 2% (11/612)
  - Radiofrequency ablation 2% (39/2503)
  - Microwave ablation 1% (22/2069)
  - Cryoablation 3% (121/3726)

<u>Multidisciplinary discussions and individualise treatments.</u>

	SBRT (N=612)	Radiofrequency ablation (N=2503)	Microwave ablation (N=2069)	Cryoablation (N=3726)
Local control (primary endpoint)				
Overall				
1 year	99% (97–100; I^2=6%)	96% (94–98; I^2=73%)	97% (95–99; I^2=74%)	95% (93–96; I^2=61%)
2 years	97% (95–99; I^2=0%)	95% (92–98; I^2=77%)	95% (92–98; I^2=77%)	94% (91–96; I^2=69%)
5 years	95% (89–98; I^2=42%)	92% (88–96; I^2=78%)	86% (75–94; I^2=66%)	90% (87–93; I^2=74%)
Tumour size <4 cm				
1 year	98% (93–100; I^2=0%)	97% (94–98; I^2=74%)	97% (95–99; I^2=77%)	96% (95–97; I^2=48%)
2 years	95% (90–99; I^2=0%)	96% (93–98; I^2=77%)	96% (93–98; I^2=79%)	95% (93–97; I^2=62%)
5 years	98% (91–100; I^2=0%)	95% (91–97; I^2=65%)	92% (72–100; I^2=61%)	91% (88–94; I^2=75%)
Tumour size ≥4 cm				
1 year	99% (97–100; I^2=26%)	91% (86–95; I^2=0%)	94% (91–97; I^2=0%)	88% (82–94; I^2=59%)
2 years	98% (96–99; I^2=0%)	88% (83–93; I^2=0%)	92% (87–96; I^2=15%)	86% (80–92; I^2=52%)
5 years	93% (85–98; I^2=59%)	79% (64–91; I^2=83%)	82% (65–94; I^2=78%)	85% (76–93; I^2=60%)
Cancer-specific survival (secondary endpoint)				
Overall				
1 year	100% (98–100; I^2=0%)	100% (98–100; I^2=30%)	100% (98–100; I^2=57%)	100% (100–100; I^2=0%)
2 years	97% (94–99; I^2=0%)	99% (97–100; I^2=64%)	99% (96–100; I^2=56%)	100% (99–100; I^2=52%)
5 years	95% (92–98; I^2=0%)	100% (98–100; I^2=0%)	98% (94–100; I^2=22%)	97% (94–99; I^2=79%)
Tumour size <4 cm				
1 year	100% (95–100; I^2=0%)	100% (98–100; I^2=39%)	100% (98–100; I^2=65%)	100% (100–100; I^2=0%)
2 years	100% (77–100; I^2=0%)	99% (96–100; I^2=69%)	98% (94–100; I^2=66%)	100% (100–100; I^2=0%)
5 years	100% (77–100; I^2=0%)	100% (98–100; I^2=0%)	97% (91–100; I^2=0%)	98% (95–100; I^2=83%)
Tumour size ≥4 cm				
1 year	100% (98–100; I^2=23%)	100% (92–100; I^2=0%)	100% (98–100; I^2=0%)	99% (95–100; I^2=43%)
2 years	96% (93–99; I^2=0%)	100% (92–100; I^2=0%)	100% (98–100; I^2=0%)	94% (90–97; I^2=0%)
5 years	95% (91–98; I^2=0%)	–*	100% (96–100; I^2=0%)	94% (89–98; I^2=0%)

Data in parentheses are 95% CIs and I^2. SBRT=stereotactic body radiotherapy. *No studies reported on ≥4 cm tumours treated with radiofrequency ablation.

Table 2: **Local control (primary endpoint) and cancer-specific survival (select secondary endpoint) across treatment types, overall and stratified by tumour size**

Stereotactic body radiotherapy for primary renal cell carcinoma: a systematic review and practice guideline from the International Society of Stereotactic Radiosurgery (ISRS)(Siva et al. Lancet Oncol 2024):

- 36 studies (13 prospective trials) and **822 patients**
- Outcomes:
  - Median follow-up was 31,2 months
  - Median **local control rate was 94,1%** (range 70·0–100)
  - 5-year progression-free survival was 80,5% (95% CI 72–92)
  - 5-year overall survival was 77,2% (95% CI 65–89).

	Level of evidence	Strength of recommendation	Citation
Optimal dose regimens for SBRT in patients with primary renal cell carcinoma include 26 Gy in one fraction if the tumour is ≤4–5 cm and 42–48 Gy in three fractions if the tumour is >4–5 cm, or potentially 40 Gy in five fractions if the dose constraints for organs-at-risk cannot be met for three fractions	IV	Moderate	8, 9, 17, 20, 26, 29, 36, 44, 45
A routine post-SBRT biopsy should not be performed to evaluate response and is only recommended in patients with imaging findings concerning for disease progression	IIb	Strong	24, 36, 44
For patients with a solitary kidney, SBRT is an approach associated with both excellent local control and acceptable renal function preservation (except in patients with stages 4 and 5 chronic kidney disease); technical approaches to reduce the volume of irradiated kidney, particularly in the intermediate dose-wash region, is recommended	IIIa	Strong	16, 46, 47
Optimal post-treatment follow-up schedule after SBRT for primary renal cell carcinoma includes cross-axial imaging of the abdomen, including both kidneys and adrenals every 6 months and surveillance scans including chest imaging at a minimum	IIb	Moderate	48–52

Level of evidence derived using Oxford Centre for Evidence-Based Medicine: Levels of Evidence.[54] Strength of recommendation derived using GRADE consensus methodology.[55] RCC=renal cell carcinoma. SBRT=stereotactic body radiotherapy.

Table 3: **ISRS recommendations for patients with primary renal cell carcinoma receiving SBRT**

2. METASTATIC RENAL CELL CARCINOMA (mRCC)

- 20–30% present de novo metastases.
- 12–30% will develop metastases after local treatment (lung, lymph nodes, and bone).
- Metastatic patient survival: 15% at 5 years.

- <u>SBRT:</u>
  - Local control rates above 80%.
  - Low moderate or severe toxicity (0–10%).
  - Progression-free survival at 1 year of 60–83%.
  - **Delay the need to start or change systemic therapies.**

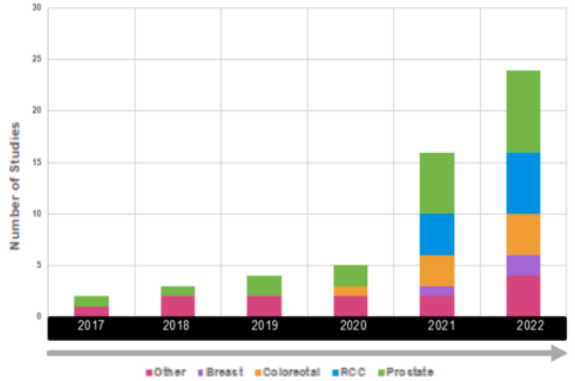


Fig. 2. Number of studies in stereotactic ablative radiotherapy in oligoprogressive disease by year from 2017 to 2022 stratified by cancer primary.

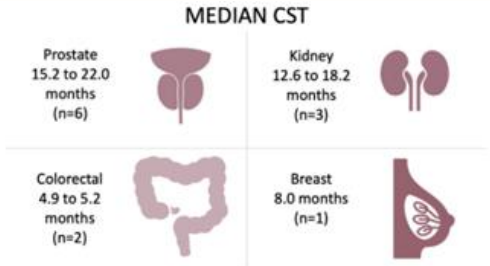


Fig. 5. Median change in systemic therapy (CST) infographic stratified by histology.

Villafuerte and Swaminath. Cancers, 2024
Tan et al. Radiotherapy and Oncology 2024

Study/Author,y	Metastasic disease	N, inclusion criteria	SBRT	Median f-u	Outcomes	Toxicity
RADVAX pase II (Hammers, 2020)	High metastatic volumen.	25 pt. Prior TKI and IL2.	50Gy/5 fx		56% response rate of non-irradiated lesions	8% G2 (pneumonitis)
Phase II (Tang, 2021)	Metachronous OMD (<5)	30 pt. Systemic therapy and sequential SBRT	5fx >7Gy/fx 60-70Gy/10fx 52-67.5Gy/15fx	17.5 m	1-y LC 97% 1-y PFS 64% 1-y OS 100% 1-y FF new lesions 67% 1-y Next treatment 82%	2 had grade 3 (back pain and muscle weakness) 1 had a grade 4 (hyperglycemia)
Phase II (Hannan, 2022)	Metachronous and synchronous OMD (<3)	23 pt. Systemic therapy and sequential SBRT	20–25 Gy/1fx 36–39 Gy/3 fx 35–40 Gy/5 fx	21.7 m	1-year LC 100% 1-year PFS 82.6% 1-year OS 95.7% 1-y FF next tx 91.3%	one grade 2 one grade 5 (immune-related colitis)
RAPPORT phase I,II (Siva, 2022)	OMD (<5)	**30 pt.** **SBRT followed by 8C of Pembrolizumab**	20 Gy/1 fx (77%) 30 Gy/10 fx	28 m	2-y FF local progression 92% **Disease control 83%** 1-2 yr OS 90% and 74% 1-2 yr PFS 60 and 45%	13% grade 3 AEs (pneumonitis, dyspnea, high ALK/ALT)
Phase II (Cheung, 2021)	OPD (<5)	37 pt. > 3m on TKI	40Gy/5 fx	1.8 m	1-yr LC rate 93% 1-yr Next tx 47% Median PFS 9.3 m Median time Next tx 12.6 m	No grade 3–5 toxicities
Phase II (Hannan, 2022)	OPD (<3)	20 pt. Systemic therapy and sequential SBRT	≥25 Gy/1 ≥36 Gy/3 ≥40 Gy/5	10.4 m	LC 100% SBRTextended systemic tx by >6m: 70% Median PFS 24.4 m Median time to next tx/death 11.1 m	One (5%) had grade 3 toxicity No grade 4–5 toxicity

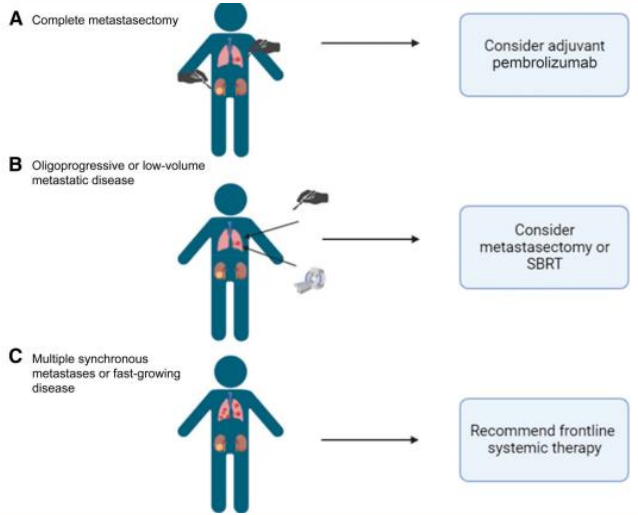
Ongoing trials

Study design	NRG-GU012 (SAMURAI),[21] phase 2	CYTOSHRINK,[22] phase 2	ECOG-ACRIN-8211 (SOAR),[23] phase 3	SWOG-S1931 (PROBE),[24] phase 3
ClinicalTrials.gov identifier	NCT05327686	NCT04090710	NCT05863351	NCT04510597
Patient population	• De novo mRCC • ≥ 1 IMDC risk factor • Primary lesion ≤ 8 cm in anterior-posterior dimension • Nonsurgical candidate	• De novo mRCC • Primary lesion ≤ 20 cm • Intermediate- or poor-risk IMDC criteria	• mRCC • 2-5 metastatic lesions (oligometastatic) • Primary site status postsurgery • Intracranial metastasis • Favorable- or intermediate-risk IMDC criteria	• De novo mRCC • Intermediate- or high-risk IMDC criteria
Study objective	Role of SBRT/SABR to intact primary disease	Role of SBRT/SABR to intact primary disease	Role of SBRT/SABR in oligometastatic RCC	Role of CN in patients with mRCC undergoing standard of care: ICI-based combination therapy
Random assignment	Combination systemic therapy (doublet IO or IO in combination with VEGF inhibitor) ± SBRT/ SABR (42 Gy/3 Fx) to the primary	Doublet IO (nivolumab/ ipilimumab) ± SBRT/ SABR (30-40 Gy/5 Fx) to the primary	Standard-of-care systemic therapy alone vs sequential SABR to all metastasis followed by systemic therapy at time of progression	All patients start with ICI-based combination therapy for 12 weeks, then randomly assigned 1:1 to receive CN followed by systemic therapy vs continuing on systemic therapy alone
Primary endpoint	PFS	PFS	OS and average AE	OS

ASCO 2023

Cytoreductive SBRT in mRCC:

- Cytoreductive nephrectomy and metastasectomy are considered in mRCC.
- **Prospective studies** on the use of SBRT in a similar manner.
- **Advantages:**
    1. Potentially reduce the number of active cancer cells.
    2. Address a possible source of additional metastases.
    3. Enhance the immune response → "abscopal effect": reduction in size of both target and non-target lesions."



Trial Name	Radiation Dose	Timing of RT	Systemic Therapy	Primary Objective
Cytoshrink NCT04090710	30–40 Gy/5	SBRT in between first and second cycles	Ipilimumab + Nivolumab	- PFS
Samurai [1] NCT05327686	42 Gy/3	SBRT prior to cycle 1	(1) Ipilimumab + Nivolumab (2) Pembrolizumab + Axitinib (3) Avelumab + Axitinib (4) Pembrolizumab + Lenvatinib	- Nephrectomy and radiographic PFS

[1] includes node-positive unresectable cases. PFS—progression-free survival; RT—radiotherapy; SBRT—stereotactic body radiotherapy.

Villafuerte and Swaminath, Cancers 2024.
Dason et al. ASCO EDUCATIONAL BOOK, 2023.

3. METASTASIS IN THE KIDNEY:

- Rare.
- Current management is based on the **extrapolation of SBRT in primary tumors**.
- Palliative purposes or definitive therapy in oligometastatic disease.
- Limited toxicities and high local control rates (delay systemic therapy, improve progression-free survival, or potentially overall survival).

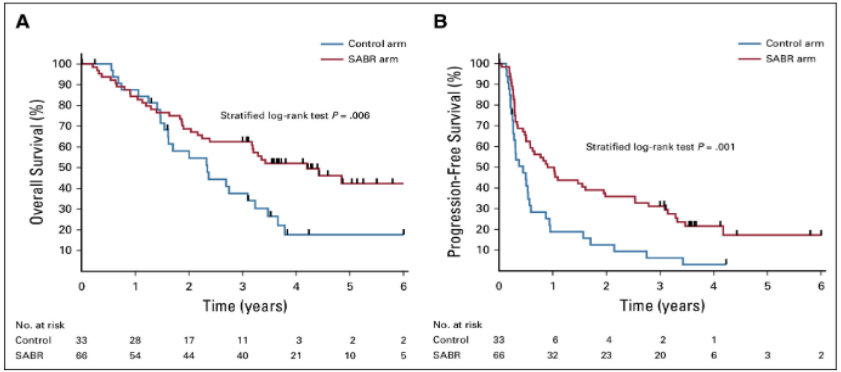


Fig 2. Kaplan-Meier plots for (A) overall survival and (B) progression-free survival. SABR, stereotactic ablative radiotherapy.

Verma & Simone, 2017;
Palma et al., 2020

1. INTRODUCTION
   - Renal tumors and radiotherapy

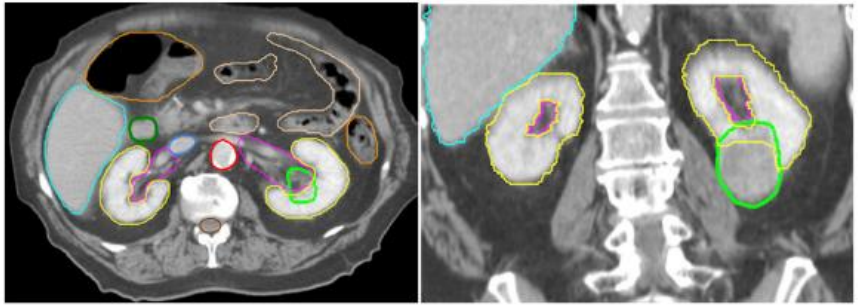
2. EVIDENCE
   - Primary tumors
   - Metastatic renal cell carcinoma (mRCC)
   - Metastases in the kidney

3. TREATMENT WITH SBRT
   - Technique
   - Challenges

4. CONCLUSIONS

Renal SBRT:

- Consider referral to a high volume center with specialized expertise.
- T1 tumors (<7 cm in diameter).
- **Biologically effective dose (BED) to >72 - 80 Gy** assuming an α/β 10 in 1–5 fractions on consecutive or non-consecutive days:
    - 26 Gy in 1 fraction
    - 42–48 Gy in 3–4 fractions
    - 40–50 Gy in 5 fractions



Treatment technique:

- **4D-CT and fusion with a renal protocol CT and/or renal MRI**.

- Internal target volume (ITV) and/or motion management with respiratory gating.

- Use of daily pretreatment imaging (MRI or cone-beam CT).

- OAR should be contoured to include a 3-mm planning OAR volume (PRV) and to account for motion on 4D-CT.

Challenges with SBRT:

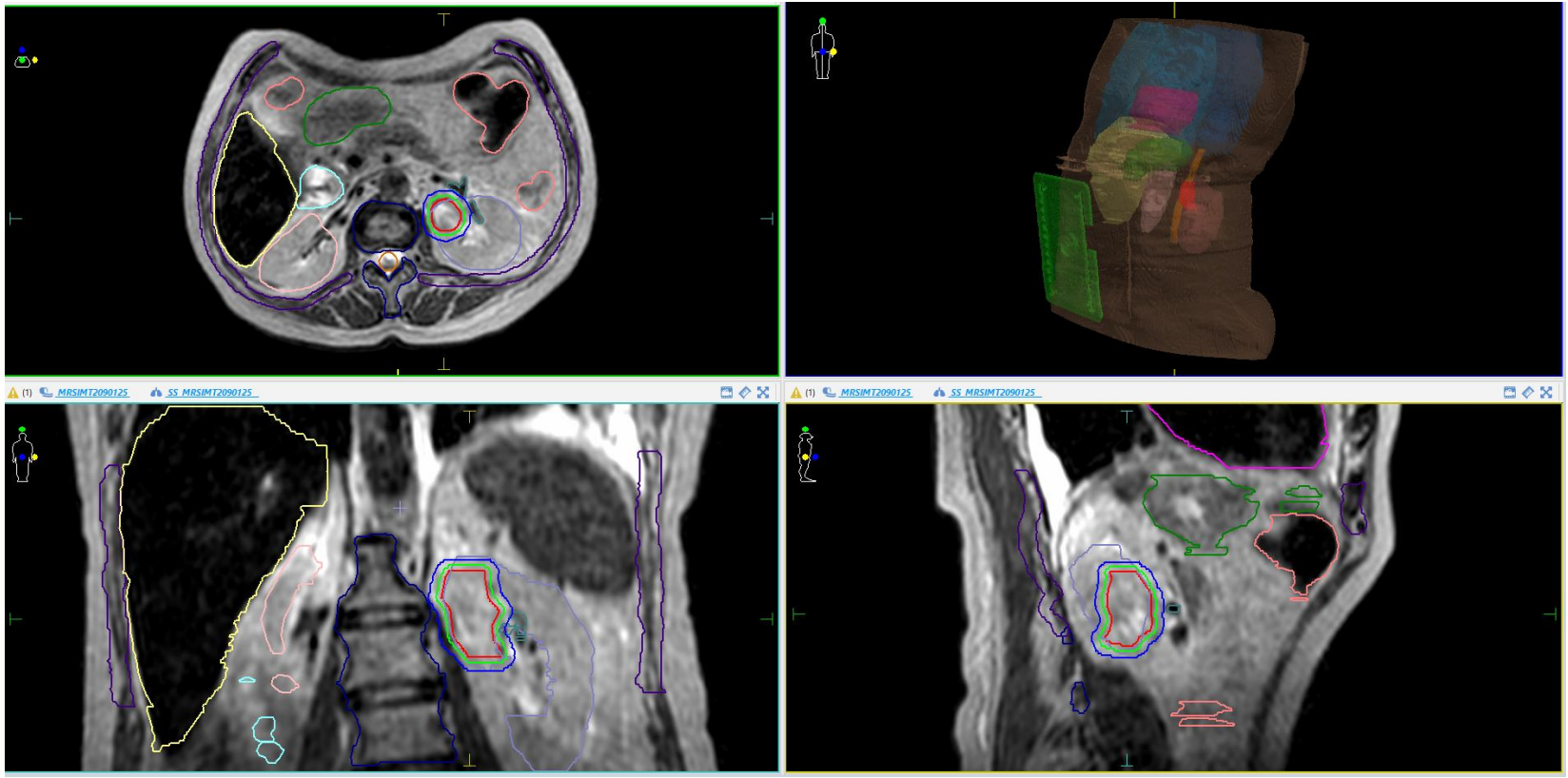
- Motion management
- Insertion of fiducials (risk of hemorrhage in highly vascular tumors)
- Tumors that have broad contact with the bowel
- Response assessment

Recommendations:

- Potential role for MRI-based SABR to improve tumor visualization/tracking (real-time online monitoring)
- Adaptive radiation: improve conformality, avoid high dose in OAR

Follow-up:

- Late response:
  - DNA damage: loss of proliferative capacity and the progressive development of cell death over time → slow reduction in tumor size and - persistence of enhancement for months or even years. It is not dose-dependent.
  - Slow-growing tumor, so a gradual radiographic response to treatment is expected.
  - "Pseudoprogression" (inflammation and edema induced by treatment).
  - Definition of local control = disease stability.
- RECIST criteria.
- Future research with MRI and PET (early changes in diffusion and perfusion as biomarkers).
- Biopsy is not recommended in routine clinical practice.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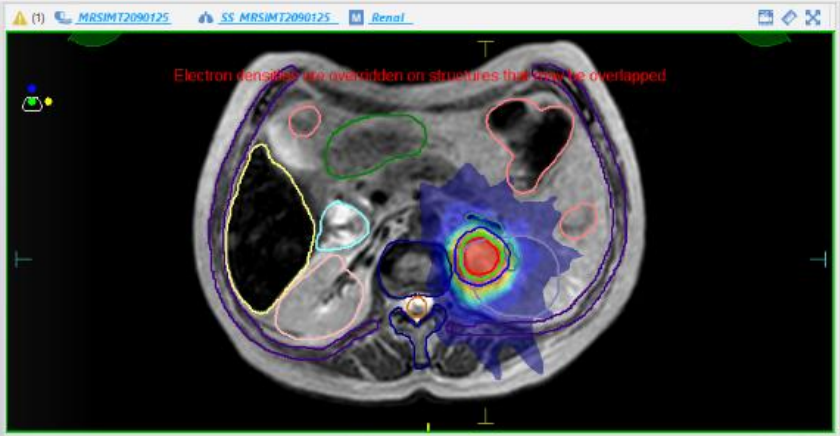
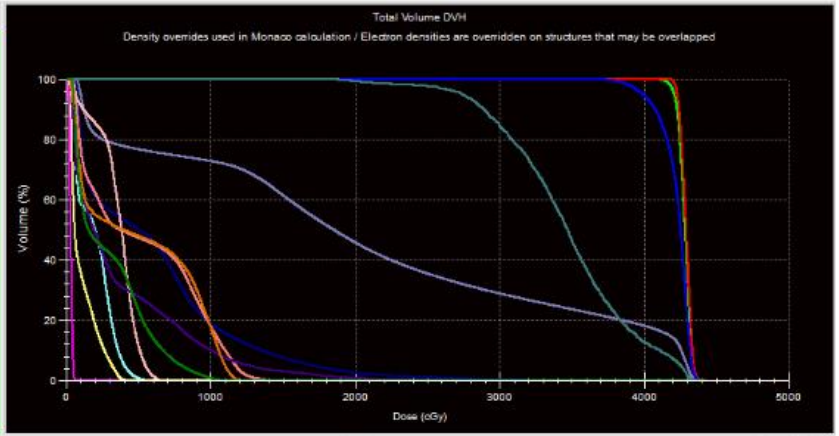
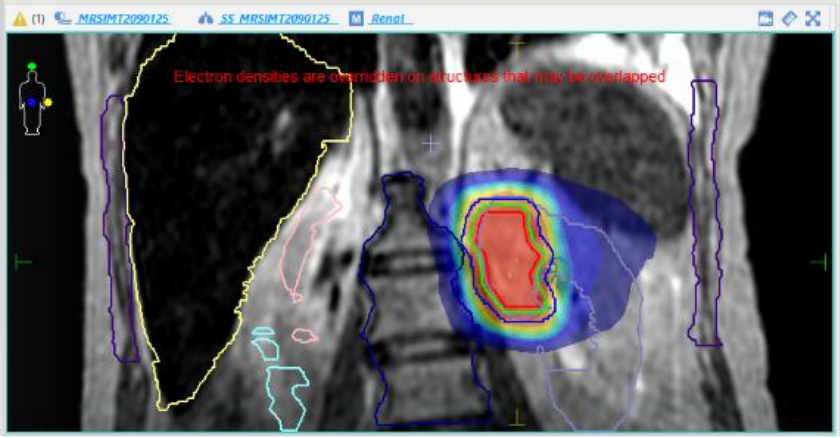

(1) MRSIMT2090125 SS MRSIMT2090125 Renal
Electron densities are overridden on structures that may be overlapped


Total Volume DVH
Density overrides used in Monaco calculation / Electron densities are overridden on structures that may be overlapped
Volume (%)
Dose (cGy)
0
20
40
60
80
100
1000
2000
3000
4000
5000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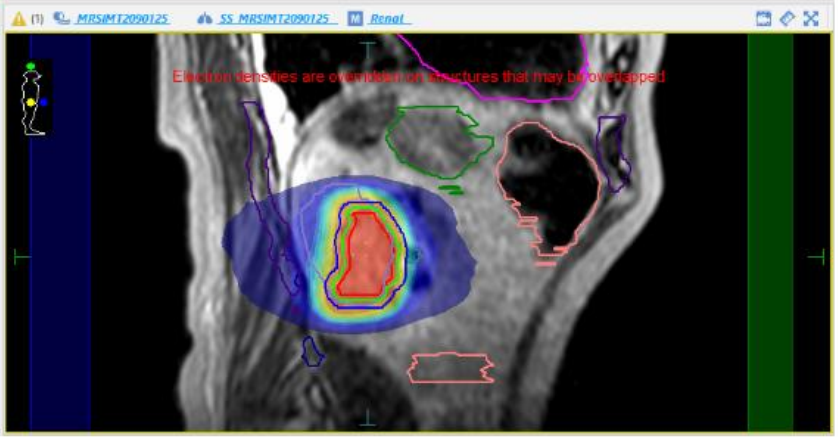
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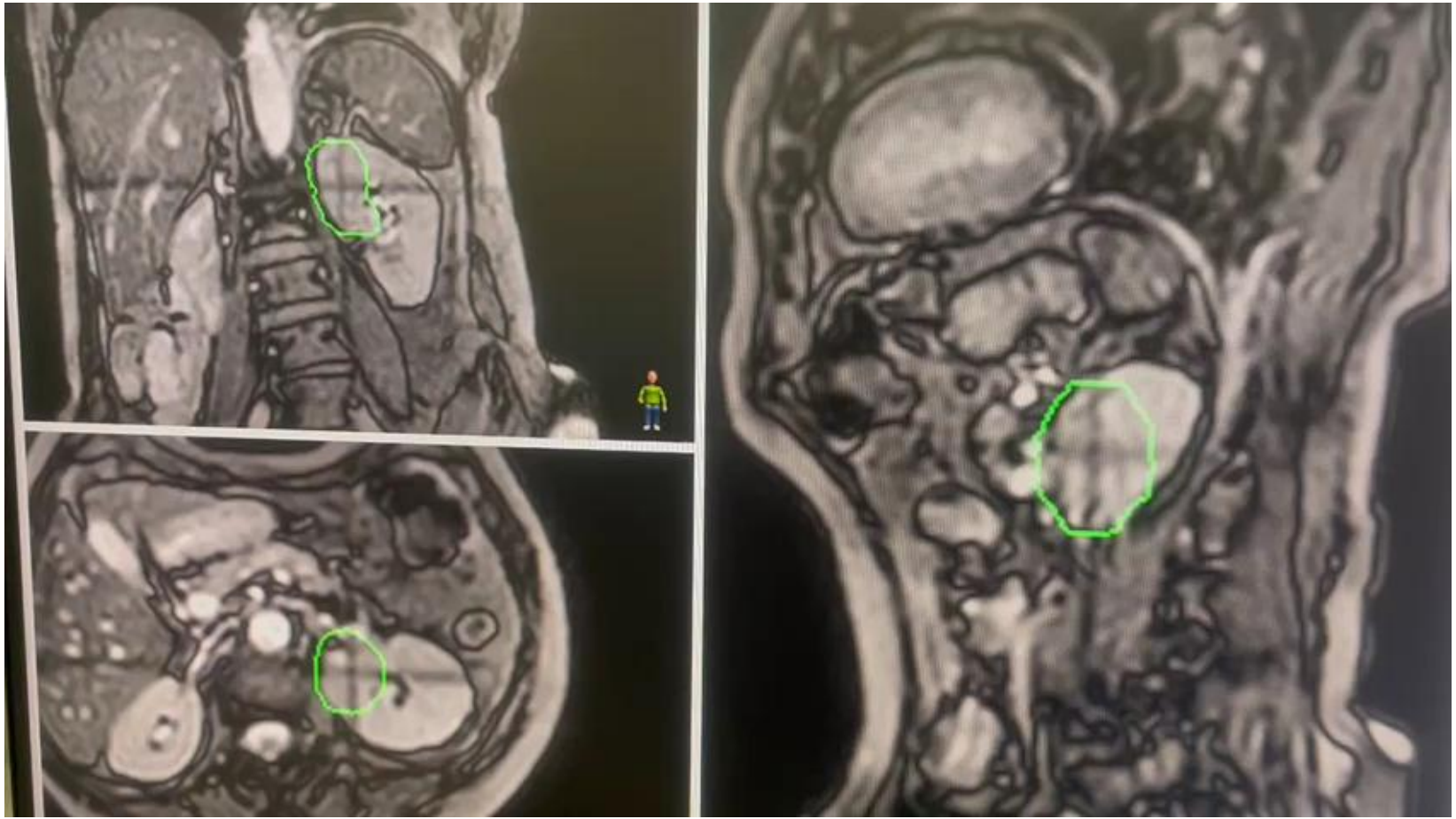

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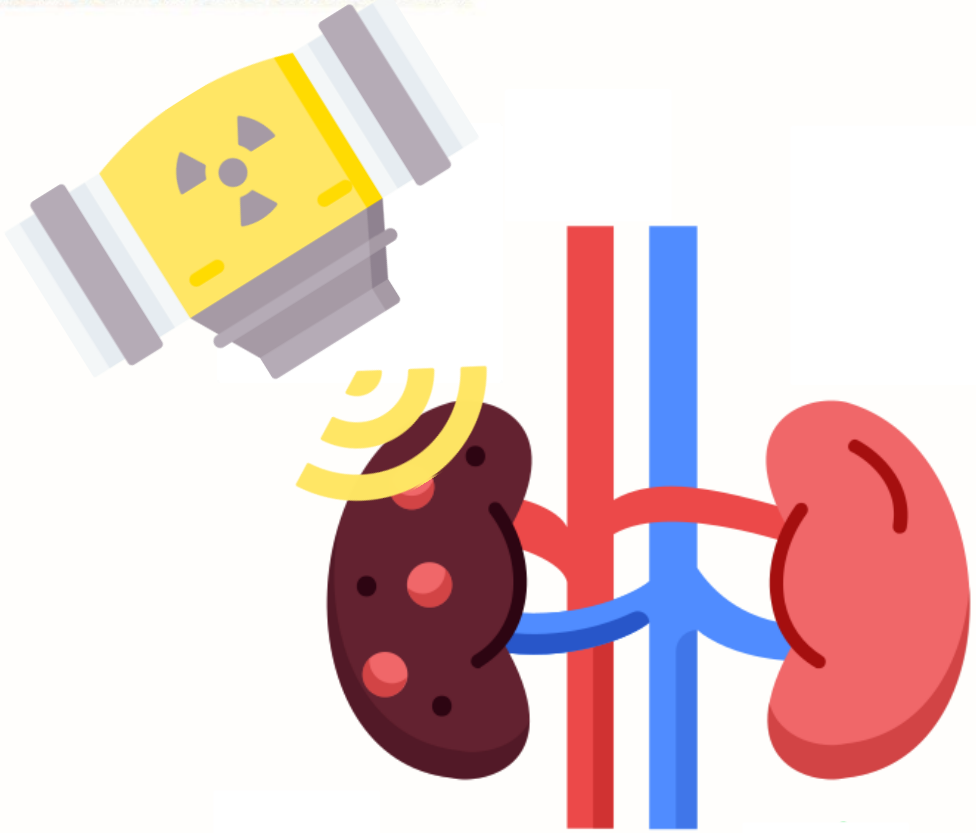
Conclusions:

1. SBRT is an effective and safe option for patients with inoperable localized RCC.
2. SBRT in the oligometastatic/progressive disease setting provides high local control and can delay the need for systemic therapies for approximately 1 year.
3. Novel clinical trials exploring SBRT with systemic therapy hold promising potential for patients with mRCC.
4. MRgRT provides high-definition soft-tissue contrast which permits direct visualization of tumors and adjacent radiosensitive OAR.



Thank you.

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