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Teaching Case

SABR for Synchronous Bilateral Primary Renal Cell Carcinoma: A Case Report

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Introduction

Bilateral renal cell carcinoma (RCC), either synchronous or metachronous, accounts for approximately 1% to 5% of RCC cases.[1] Synchronous RCC poses a challenge for physicians as there are no standards of care, and management varies on the complexity of the individual case. Historically, surgery, either bilateral radical nephrectomy or nephron sparing surgery (NSS), has been the treatment of choice, with good long-term tumor control.[1-3] However, bilateral synchronous RCC poses a surgical challenge in balancing oncological efficacy and preserving renal function. There is no standard procedure to deal with bilateral RCC. NSS is typically the preferred treatment to preserve renal function.

Radiofrequency ablation (RFA) has been offered as an alternative to surgery in patients with unilateral small RCC. There are very limited data for its use in bilateral RCC. In one such report involving 12 patients, Zhang et al[4] reported encouraging outcomes with RFA in the treatment of bilateral RCC. It can provide adequate local tumor control and cancer specific survival compared with NSS while not affecting renal function.

One case of bilateral synchronous primary RCCs treated with proton-based stereotactic radiation therapy was reported by Frick et al.[5] The authors reported marginal decline in renal function at 1-year follow-up (baseline glomerular filtration rate of 34 mL/min/1.73 m^2, 1-year post stereotactic body radiation therapy 29 mL/min/1.73 m^2). Though there was shorter follow-up for this case, there is increasing evidence to support the use of SABR in cases of unilateral RCC.[6,7] Considering good local control and relative preservation of renal function post-SABR, it can be a good alternative to invasive procedures like radical nephrectomy, NSS, or RFA.

We report a case of a patient presenting with synchronous bilateral RCC treated with SABR at our institution.

Case Report

In line with our institutional Human Research Ethics Committee policy, ethical clearance was not required for this case report.

An 84-year-old male with Eastern Cooperative Oncology Group performance status 0 underwent a computed tomography (CT) scan when presented to a local emergency department after a fall from a ladder. CT scan was negative for any acute posttrauma findings. However, there were incidental findings of right lower pole and left upper pole renal masses measuring 5 × 5 cm and

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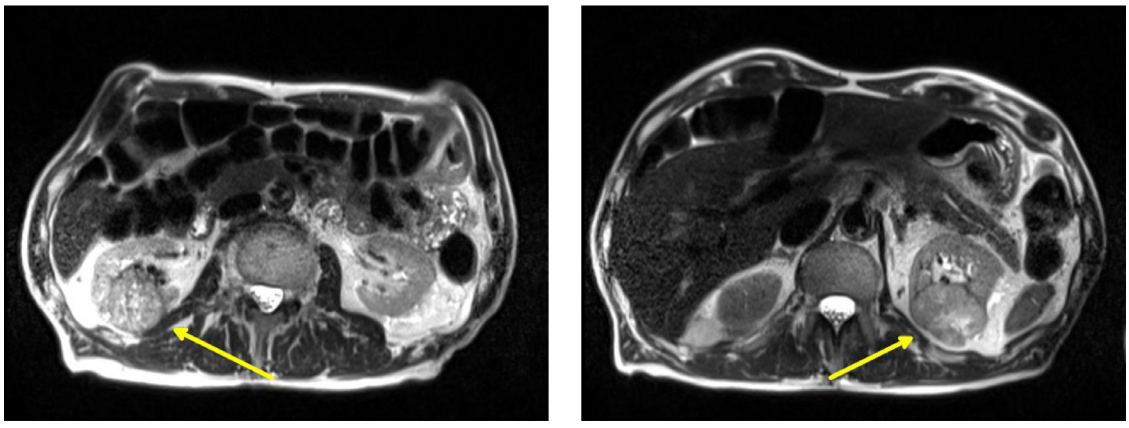

Fig. 1 Magnetic resonance images with circumscribed 55 × 35 × 52-mm mass in the mid to lower pole of right kidney (left) and 53 × 40 × 44-mm mass in the upper pole of left kidney (right).

5 × 4 cm, respectively. He had a history of hypertension. He was reviewed by a urologist as an outpatient for further workup. Further investigation with magnetic resonance imaging confirmed a well-circumscribed 55 × 35 × 52 mm mass in the right kidney mid to lower pole with involvement of the renal sinus and 53 × 40 × 44 mm mass in the left upper pole (Fig 1). Image guided true-cut biopsy confirmed bilateral clear cell renal carcinoma with Fuhrman grade 2. Baseline renal function was within normal limits with a serum creatinine of 96 micromole per liter umol/L, an estimated glomerular filtration rate (eGFR) of 62 mL/min, and a chromium-51 ethylenediaminetetraacetic acid isotopic calculated GFR of 67 mL/min. The split function on technetium-99m dimercapto succinic acid was 52%:48% left and right differential renal function, respectively.

After discussion in the local multidisciplinary meeting, he was offered a staged surgical procedure with left partial nephrectomy followed by further completion partial or radical nephrectomy for contralateral tumor. However, the patient declined. Considering his good general health, he also declined active surveillance for his cancer. He was reviewed at our department to explore the option of SABR

After discussion in our institutional urology multidisciplinary meeting, 42 Gy in 3 fractions was prescribed to both tumors. The patient was simulated with a 4-dimensional CT scan (4D-CT) in free breathing on a Brilliance Big Bore 16-slice CT scanner (Philips Medical Systems, Cleveland, OH). The BodyFix vacuum drape (Elekta, Stockholm, Sweden) was used at simulation and during treatment to reduce respiratory motion.[8] Separate internal target volumes for right and left kidney were contoured on the average intensity projection of the 4D-CT. A planning target volume was generated from an isotropic 5-mm margin expansion of each internal target volumes (Fig 2). Organs at risk (OAR) were delineated on the average intensity projection. Two plans were created, 1 for each planning target volume. Each plan consisted of 9 noncoplanar fields at 18 MV using the 3D conformal radiation therapy technique (Fig 3). Dose was optimized and calculated with the Eclipse treatment planning system (Varian Medical Systems, Palo Alto). Dose volume

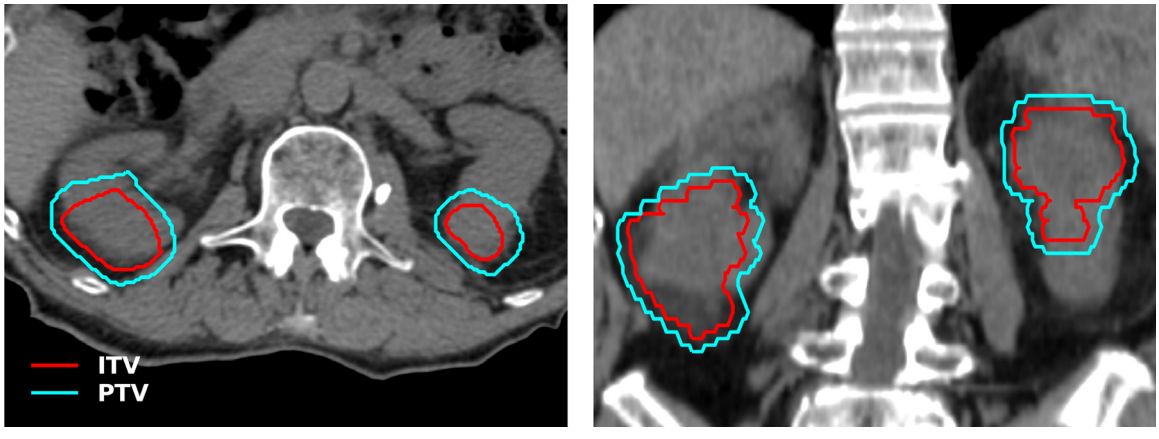

Fig. 2 Representative axial (left) and coronal (right) sections of planning computed tomography showing internal target volumes (ITVs) (red) and planning target volumes (PTVs) (cyan).

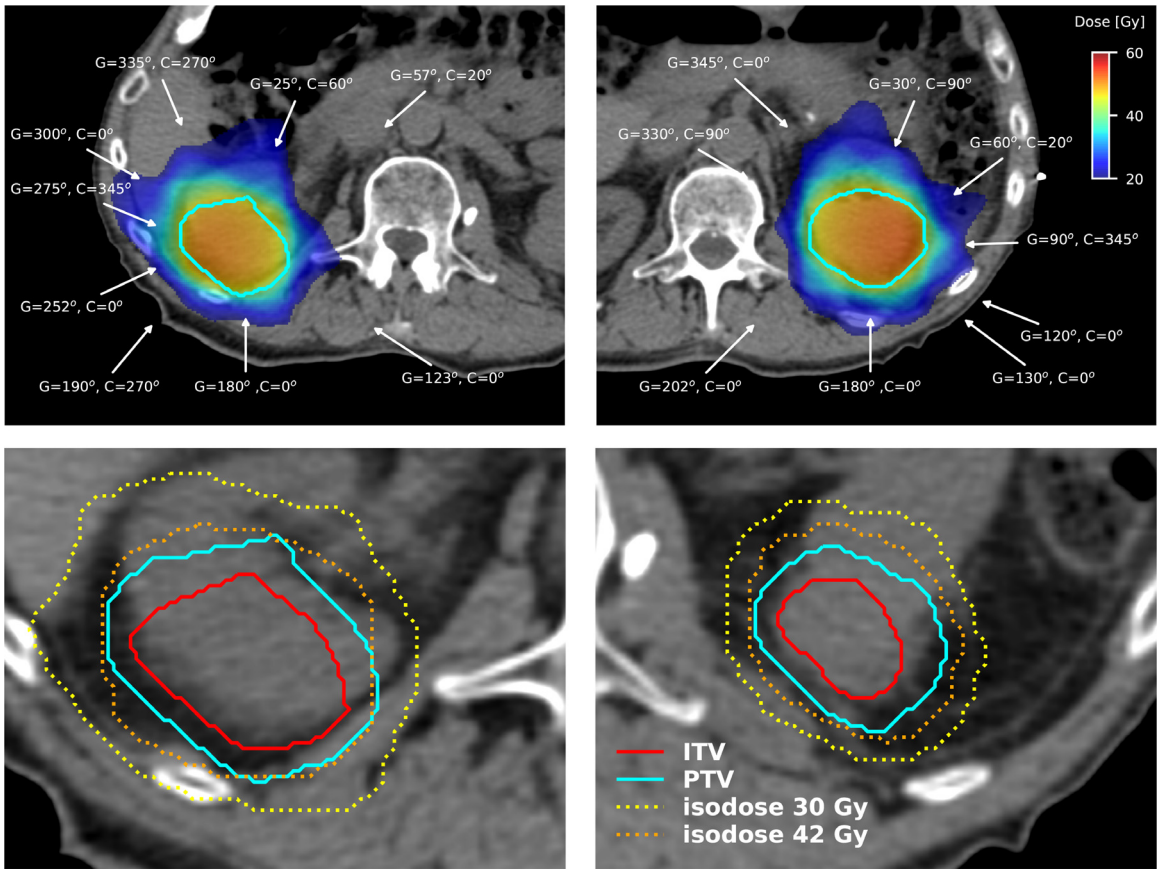

Fig. 3 Top left and right panel show filed arrangements for right and left kidney radiation plan, respectively. Gantry (G) and couch (C) angles are shown. Bottom left and right show planning target volumes (cyan) covered with prescribed dose 42 Gy isodose line (yellow) with 30 Gy isodose line (orange) washout for right and left tumors, respectively.

histograms of the tumors and OARs are shown in Figure 4. Dose metrics to OARs are summarized in Table 1. All dose limits were respected, except the large bowel near to maximum dose (large bowel D0.03 cc = 43.11 Gy > 42 Gy). Nontumor kidney volume receiving more than 50% of the prescription dose (V50%) was 178 cm^3 (61.5% of the volume) and 166 cm^3 (55.6% of the volume) for the right and left kidney, respectively.

He was able to tolerate treatment well without any significant grade 3 or 4 toxicity. He experienced grade 2 fatigue posttreatment, which settled in 3 months. There was a gradual decline in his renal function as expected postradiation therapy (Table 2). His creatinine and eGFR, 18 months posttreatment, were 143 umol/L and 37 mL/min, respectively. Last imaging investigation at 18 months was consistent with stable radiologic findings

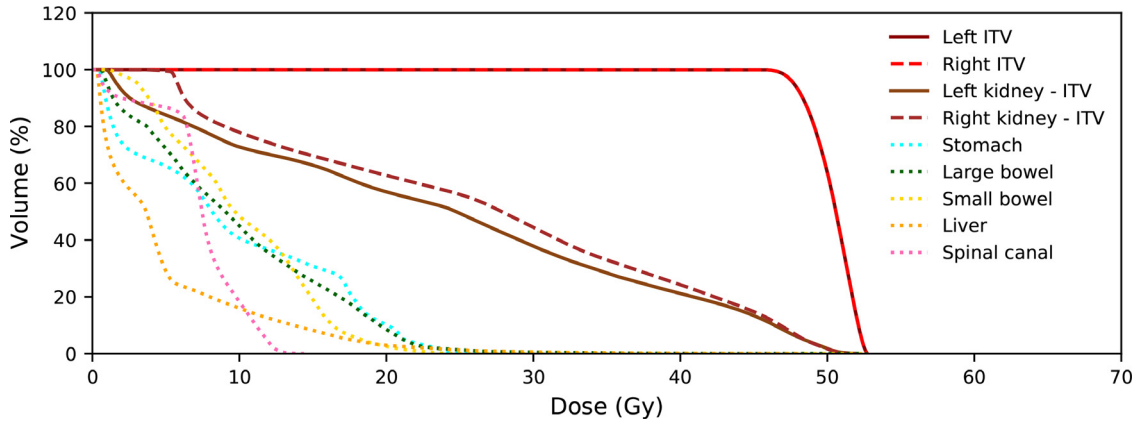

Fig. 4 Dose volume histogram (DVH) of the right and left tumors and organs at risk.

Table 1 Organ-at-risk doses

Organ at risk	Maximum dose (Gy)	Near to maximum dose (Gy)	Mean dose (Gy)
Spinal cord	14.3	13.8	7.4
Left kidney	52.8	52.7	30.4
Left kidney - ITV	52.1	51.9	24.1
Right kidney	52.7	52.6	33.3
Right kidney - ITV	51.6	51.5	26.5
Small bowel	26.2	25.5	10.2
Large bowel	44.3	43.1	9.8
Liver	48.0	46.9	5.1
Stomach	27.1	26.8	9.6

Abbreviation: ITV = internal target volume.

without any local progression or appearance of distant disease. He died due to hemorrhagic cerebrovascular stroke 2 years posttreatment unrelated to RCC or SABR.

Discussion

We report a case of synchronous bilateral RCC treated with definitive intent SABR at our institution. To our knowledge, this is the first reported case to highlight the safety of simultaneous photon-based SABR in synchronous bilateral RCCs. However, this is not the first case to be treated with radiation therapy in such a scenario. Frick et al[5] reported the safety and efficacy of proton-based stereotactic body radiation therapy in a 47-year-old female with bilateral synchronous RCCs. Our case presents some novelty due to the patient's older age, larger tumor sizes, higher delivered radiation therapy dose, and longer follow-up of 2 years.

Active surveillance with ongoing imaging was another reasonable option to manage this case, which was declined by the patient owing to good performance status and no significant comorbidity apart from hypertension. This approach risked the potential of metastatic seeding by bilateral uncontrolled primaries.

The management of synchronous bilateral RCC presents a challenge to treating surgeons. Just like the surgical recommendation for our case, most surgeons prefer a 2-step staged approach.[3,9] However, Blute et al[10] reported similar complication rates and oncological outcomes with simultaneous bilateral surgery. There are advantages to a single intervention, which include but are not limited to reduced psychological and physiological stress, single anesthesia, and a reduced hospital stay. Similarly, RFA can be delivered either simultaneously or in a step-wise procedure.[4] In the previous reported case, the proton-based radiation therapy to a dose of 30 Gy in 5 fractions delivered every other day was well tolerated without any grade >1 toxicity.[5] Similarly, our reported case had simultaneous SABR to both RCCs over 3 fractions delivered every other day without experiencing any grade 3 or 4 treatment-related toxicity.

Table 2 Renal function trend

Time line	eGFR (mL/min)	Creatinine (μmol/L)
Baseline pre-SABR	62	96
Six months post-SABR	71	89
12 months post-SABR	41	134
18 months post-SABR	37	143

Abbreviation: eGFR = estimated glomerular filtration rate.

Currently, NSS is considered as an optimal care option in localized RCCs with tumor size of less than 4 cm.[11] Considering a tumor size of 5 cm in this case, NSS, though realistically an option to preserve renal function, may have been technically challenging and may have resulted in poor oncological-related outcomes. Similarly, RFA is also associated with increased local failures in patients with endophytic and larger than 3 cm RCCs.[12,13] Our patient was free of local progression at 18 months post radiation therapy but this was a relatively short follow-up compared with other modalities. Recently, Siva et al[14] has reported encouraging results with SABR for unilateral T1b RCCs, with a local failure rate of 2.9% at 4 years.

Preservation of renal function is the utmost factor to consider while managing synchronous bilateral RCCs, which makes nephron-sparing approaches, including NSS, RFA, and SABR, more attractive options for treating physicians as well as patients. As expected, there was a decline in renal function posttreatment in our case, with a 40% reduction in eGFR from baseline. A similar or even more profound decline in renal function can be expected from a proposed surgical plan. After NSS for synchronous bilateral RCCs, there is expected decline in renal function with reported long-term haemodialysis rates of approximately

10%.[2] However, most patients selected for NSS have relatively good baseline renal function and small tumor size compared with the case presented herein.

In conclusion, this case highlighted that SABR can be safely delivered in carefully selected synchronous bilateral RCC with an associated acceptable decline in renal function from baseline. We recommend international collaboration and sharing of such cases to be published to further assess feasibility of this approach.

References

1. Siemer S, Uder M, Zell A, et al. Bilateral kidney tumor. Therapy management and histopathological results with long-term follow-up of 66 patients. *Urologe A*. 2001;40:114–120.
2. Blute ML, Amling CL, Bryant SC, Zincke H. Management and extended outcome of patients with synchronous bilateral solid renal neoplasms in the absence of von Hippel-Lindau disease. *Mayo Clin Proc*. 2000;75:1020–1026.
3. Pahernik S, Cudovic D, Roos F, Melchior SW, Thüroff JW. Bilateral synchronous sporadic renal cell carcinoma: Surgical management, oncological and functional outcomes. *BJU Int*. 2007;100:26–29.
4. Zhang S, Zhao X, Ji C, et al. Radiofrequency ablation of synchronous bilateral renal cell carcinoma. *Int J Urol*. 2012;19:241–247.
5. Frick MA, Chhabra AM, Lin L, Simone 2nd CB. First ever use of proton stereotactic body radiation therapy delivered with curative intent to bilateral synchronous primary renal cell carcinomas. *Cureus*. 2017;9:e1799.
6. Siva S, Pham D, Kron T, et al. Stereotactic ablative body radiotherapy for inoperable primary kidney cancer: A prospective clinical trial. *BJU Int*. 2017;120:623–630.
7. Siva S, Louie AV, Warner A, et al. Pooled analysis of stereotactic ablative radiotherapy for primary renal cell carcinoma: A report from the International Radiosurgery Oncology Consortium for Kidney (IROCK). *Cancer*. 2018;124:934–942.
8. Siva S, Devereux T, Kron T, et al. Vacuum immobilisation reduces tumour excursion and minimises intrafraction error in a cohort study of stereotactic ablative body radiotherapy for pulmonary metastases. *J Med Imaging Radiat Oncol*. 2014;58:244–252.
9. Becker F, Siemer S, Tzavaras A, Suttmann H, Stoeckle M. Long-term survival in bilateral renal cell carcinoma: A retrospective single-institutional analysis of 101 patients after surgical treatment. *Urology*. 2008;72:349–353.
10. Blute ML, Itano NB, Cheville JC, Weaver AL, Lohse CM, Zincke H. The effect of bilaterality, pathological features and surgical outcome in nonhereditary renal cell carcinoma. *J Urol*. 2003;169:1276–1281.
11. Ljungberg B, Albiges L, Abu-Ghanem Y, et al. European Association of Urology guidelines on renal cell carcinoma: The 2019 update. *Eur Urol*. 2019;75:799–810.
12. Breen DJ, Rutherford EE, Stedman B, et al. Management of renal tumors by image-guided radiofrequency ablation: Experience in 105 tumors. *Cardiovasc Intervent Radiol*. 2007;30:936–942.
13. Zagoria RJ, Traver MA, Werle DM, Perini M, Hayasaka S, Clark PE. Oncologic efficacy of CT-guided percutaneous radiofrequency ablation of renal cell carcinomas. *AJR Am J Roentgenol*. 2007;189:429–436.
14. Siva S, Correa RJM, Warner A, et al. Stereotactic ablative radiotherapy for ≥T1b primary renal cell carcinoma: A report from the International Radiosurgery Oncology Consortium for Kidney (IROCK). *Int J Radiat Oncol Biol Phys*. 2020;108:941–949.