

Hepatocellular Carcinoma in the COVID-19 Era: Primetime for Stereotactic Body Radiotherapy and a Lesson for the Future?

As the COVID-19 pandemic spreads across the globe, major transformations are rapidly being implemented because of the unprecedented pressure on health care systems. Management of patients with cancer has been particularly affected by the reduced access to cancer treatments related to prolonged wait times for diagnostic and interventional procedures, treatment delays or interruptions, fragmentation of multidisciplinary management with a shrinking oncology workforce, and self-isolation for fear of nosocomial infection. Consequently, there is a risk of detrimental consequences for this highly vulnerable patient population. This dire scenario represents an opportunity to evaluate current practices and provide a lesson for the future in the post-COVID-19 era. The case of stereotactic body radiotherapy (SBRT) in hepatocellular carcinoma (HCC) is emblematic.

SBRT has emerged as a noninvasive, painless, and effective therapeutic modality delivered in a few daily fractions over less than 1 week for patients with HCC, from early to advanced stage.

In early stage HCC, local therapy can be offered as a definitive or bridging treatment [1]. Because of current restrictions in access to operating rooms and the redeployment of anesthesiologists to intensive care units, SBRT represents an appealing option compared with invasive local therapies such as surgery, radiofrequency or microwave ablation, and regional therapies such as transarterial or radioembolization, which may require general anesthesia and recovery. Although randomized trials are lacking, indirect comparisons suggest comparable efficacy of SBRT with these treatment modalities for similar stage patients [2–4]. The use of SBRT may reduce the need for systemic therapy in advanced patients with symptomatic involvement or poor responders to standard treatment, e.g., macroscopic vascular invasion [5].

Despite the numerous studies demonstrating efficacy, long-term survival, and low toxicity rates [6–8], many current HCC treatment algorithms do not incorporate SBRT in the management of HCC. Most limit its use to patients who are ineligible for or refractory to other invasive local

and/or regional therapies. The significant time and effort required, coupled with the limited funding and lack of pharmaceutical and vendor support, have been an impediment to conducting large-scale, potentially practice-changing clinical trials of SBRT for HCC: thus, SBRT may be indefinitely relegated to an ancillary role.

It is expected that, during the COVID-19 pandemic and its aftermath, SBRT will increasingly represent a preferred treatment that may relieve the burden of interrupted and deferred cancer treatments, the overload of chemotherapy facilities, and patient exposure and risk of COVID-19 infection because of repeated visits and prolonged stays in the hospital [9]. With more widespread clinical use of SBRT, there may be an increase in support for trials of this effective HCC treatment. It is crucial that outcome and toxicity data be recorded during this time when nonstandard therapies are offered. These data will hopefully provide further evidence to reconsider SBRT as a first-line treatment option for HCC (proposed algorithm is shown in Fig. 1).

It is our hope that the cumulative global experience gained during the COVID-19 pandemic may allow for a full recognition of SBRT as a useful therapy in the management of HCC based on real-life evidence.

MARTA SCORSETTI

Humanitas Clinical and Research Center - IRCCS, Department of Radiotherapy and Radiosurgery, Milan, Italy; Department of Biomedical Sciences, Humanitas University, Milan, Italy

KARYN A. GOODMAN

Department of Radiation Oncology, The Mount Sinai Hospital, New York, New York, USA

JINSIL SEONG

Department of Radiation Oncology, Yonsei Cancer Center, Yonsei University College of Medicine, Republic of Korea

MAURO LOI

Humanitas Clinical and Research Center – IRCCS, Department of Radiotherapy and Radiosurgery, Milan, Italy

FLORENCE HUGUET

Department of Radiation Oncology, Hôpital Tenon, AP-HP Sorbonne Université, Paris, France

LAURA A. DAWSON

Department of Radiation Oncology, University of Toronto, Toronto, Canada; Radiation Medicine Program, Princess Margaret Cancer Center, Toronto, Canada

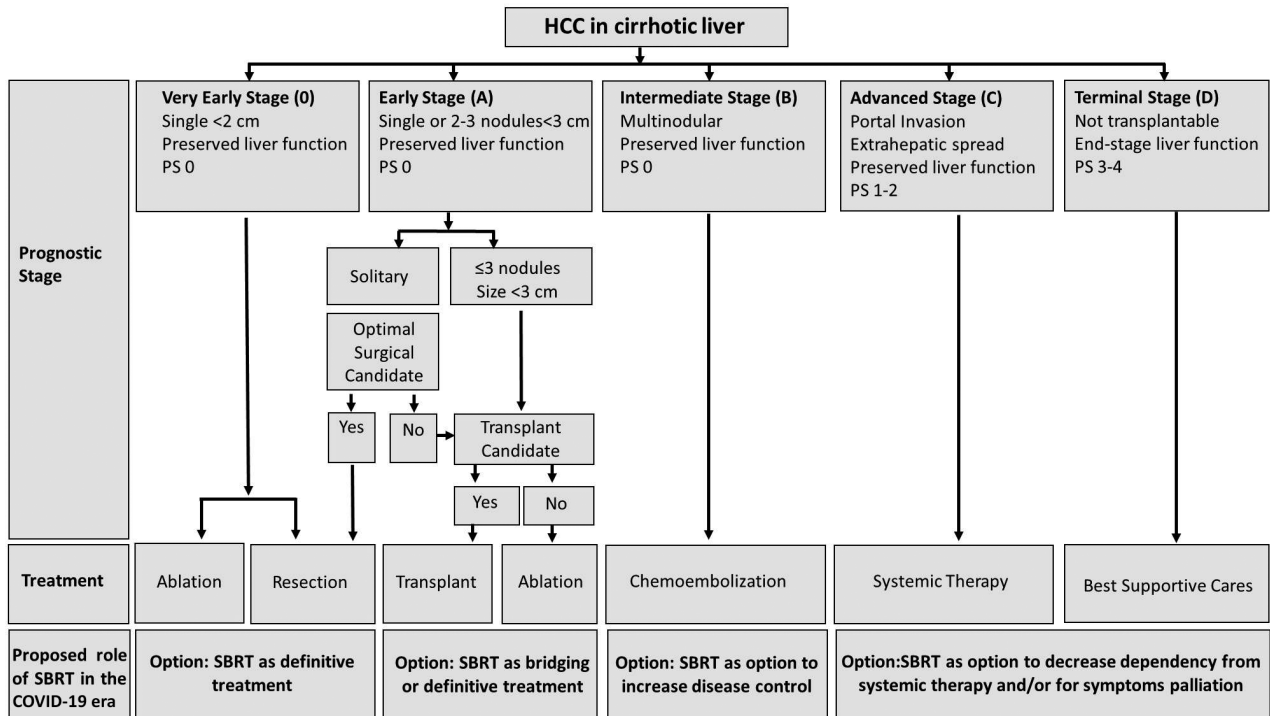


Figure 1. Proposal for a modified Barcelona Clinic Liver Cancer staging system (BCLC)-based treatment algorithm during the COVID-19 pandemic. Abbreviations: HCC, hepatocellular carcinoma; PS, performance status; SBRT, stereotactic body radiotherapy.

DISCLOSURES

Jinsil Seong: Accuray (RF); **Laura A. Dawson:** Raysearch Oncology (OI). The other authors indicated no financial relationships.

(C/A) Consulting/advisory relationship; (RF) Research funding; (E) Employment; (ET) Expert testimony; (H) Honoraria received; (OI) Ownership interests; (IP) Intellectual property rights/inventor/patent holder; (SAB) Scientific advisory board

REFERENCES

- Durand-Labrunie J, Baumann AS, Ayav A et al. Curative irradiation treatment of hepatocellular carcinoma: A multicenter phase 2 trial. *Int J Radiat Oncol Biol Phys* 2020 [Epub ahead of print].
- Lee J, Shin IS, Yoon WS et al. Comparisons between radiofrequency ablation and stereotactic body radiotherapy for liver malignancies: Meta-analyses and a systematic review. *Radiother Oncol* 2020;145:63–70.
- Shen PC, Chang WC, Lo CH et al. Comparison of stereotactic body radiation therapy and transarterial chemoembolization for unresectable medium-sized hepatocellular carcinoma. *Int J Radiat Oncol Biol Phys* 2019;105:307–318.

- Sapir E, Tao Y, Schipper MJ et al. Stereotactic body radiation therapy as an alternative to transarterial chemoembolization for hepatocellular carcinoma. *Int J Radiat Oncol Biol Phys* 2018;100:122–130.
- Shui Y, Yu W, Ren X et al. Stereotactic body radiotherapy based treatment for hepatocellular carcinoma with extensive portal vein tumor thrombosis. *Radiat Oncol* 2018;13:188.
- Jang WI, Kim MS, Bae SH et al. High-dose stereotactic body radiotherapy correlates increased local control and overall survival in patients with inoperable hepatocellular carcinoma. *Radiat Oncol* 2013;8:250.
- Takeda A, Sanuki N, Tsurugai Y et al. Phase 2 study of stereotactic body radiotherapy and optional transarterial chemoembolization for solitary hepatocellular carcinoma not amenable to resection and radiofrequency ablation. *Cancer* 2016;122:2041–2049.
- Kim N, Cheng J, Jung I et al. Stereotactic body radiation therapy vs. radiofrequency ablation in Asian patients with hepatocellular carcinoma. *J Hepatol* 2020 [Epub ahead of print].
- Tchelebi LT, Haustermans K, Scorsetti M et al. Recommendations on the use of radiation therapy in managing patients with gastrointestinal malignancies in the era of COVID-19. *Radiother Oncol* 2020 [Epub ahead of print].

<http://dx.doi.org/10.1634/theoncologist.2020-0416>