Baishideng Publishing Group

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Oncology*

Manuscript NO: 76552

Title: Stereotactic radiotherapy for intrahepatic cholangiocarcinoma

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06100005
Position: Peer Reviewer
Academic degree: MD
Professional title: Doctor
Reviewer's Country/Territory: United States
Author's Country/Territory: United Kingdom

Manuscript submission date: 2022-03-21
Reviewer chosen by: AI Technique
Reviewer accepted review: 2022-03-22 13:25
Reviewer performed review: 2022-04-01 19:05
Review time: 10 Days and 5 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer	Peer-Review: [Y] Anonymous [ ] Onymous

Baishideng Publishing Group

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

statements	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Overall, very well written manuscript on a lesser-known subject. I have a few suggestions below. -Consider replacing SBRT with SABR (stereotactic ablative radiotherapy). -Accuracy is between 2-3 mm. 5-10 mm is a bit generous. Generally speaking, a distance of 5 mm to luminal gastrointestinal organs is desired for "safe" dose escalation. Perhaps consider "ablative doses may be most easily achieved if located at least 5 mm from luminal organs". Reference: Koay PRO 2020 (PMID 32061993). -A few suggestions for the side effect profile section: The side effect profile of SBRT in relation to the liver most commonly consists of [nausea and fever, which can be seen within a few hours of treatment. Give prophylactic antiemetics [Blomgren Acta Oncologica '95]. Late side effects of radiation includes radiation induced liver disease (RILD)..., which includes clinical symptoms of fatigue, elevated alkaline phosphatase (not transaminitis), tender anicteric hepatomegaly and ascites. Non-classical RILD (usually in patients with underlying liver disease) is associated with elevated transaminase or jaundice, typically within 3 months of radiotherapy, consisting of liver enzymes more than five times the upper limit of normal or a decline in liver function as measured by worsening Child-Pugh score of 2 or more in the absence of classic RILD.] This occurs [less than 5%] of patients and is associated with cumulative [conventionally fractionated] doses higher than 30[-32 Gy in patients with normal liver function and 28 Gy for patients with underlying liver disease [QUANTEC]. There is no treatment for RILD, and it may occur as soon as 2 weeks or as late as 8 months after completion of treatment. Importantly, the liver regenerates after insult at a median time of 6-9 months.] (delete "in patients with known pre-existing liver disease"). Other specific toxicities are related to off-target effects on the gastrointestinal tract, with nausea, vomiting and diarrhea being common.

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

Other effects are common to all radiation therapies, and these include skin necrosis and systemic effects such as fatigue and fever. [Skin toxicity is much less common in the era of volumetric modulated arc therapy (VMAT), which allows beams from 360 degrees and spreads out dose along the surface of the skin and has largely obviated any erythema resulting from treatment.] It should be reiterated that these side effects, when they do occur, are typically milder and less frequent than with equivalent conventional radiotherapy.[43] Please clarify: -Predictors of successful response were doses of radiation > 100 Gy. What does this mean? Is this a conversion in BED10 (alpha beta of 10)? If so, Please clarify e.g., write out doses "> 100 Gy-10 (BED10)". -"The reason is likely the lower radiation dose used at 45 Gy and the authors reported significantly higher survival with doses at >75 Gy" What does this mean? Is this a conversion in BED10 (alpha beta of 10)? Please clarify. -"...with a dose greater than 80.5 Gy" What does this mean? Is this a conversion in BED10 (alpha beta of 10)? Please clarify. An additional study to consider for Table 1: Kozak ARO 2020. https://www.sciencedirect.com/science/article/pii/S2452109419301149 Out of field failures in 23% of patients. Consider adding a discussion on the utility of elective nodal irradiation to the portal hilar area. Speaking of elective nodal irradiation, it may be worth commenting on the difficulty of irradiation around the central biliary tree due to dose constraints: Osmundson IJROBP '15 (PMID 25659885). Some common schemas for concerning portal hilar lymph nodes due to the tolerances of the central biliary tree may include 42 Gy in 15 fractions or, 35 Gy in 5 fractions, or 32 Gy in 3 fractions. For example, V66 Gy (BED10) corresponds to V40 and V37.7 for 5 fractions while V33.8 and V32 for 3 fractions. 5 fractions: V40 < 21cc, V37.7 < 24cc. 3 fractions: V33.8 < 21cc, V32 < 24cc. Please consider a few of the additions above. Overall, this was an excellent report and I enjoyed the read. Congratulations on all your hard work!

Baishideng Publishing Group

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Oncology*

Manuscript NO: 76552

Title: Stereotactic radiotherapy for intrahepatic cholangiocarcinoma

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06150368
Position: Peer Reviewer
Academic degree: Doctor, MD, PhD

Professional title: Doctor, Professor, Surgeon, Surgical Oncologist

Reviewer's Country/Territory: China

Author's Country/Territory: United Kingdom

Manuscript submission date: 2022-03-21

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-04-05 07:20

Reviewer performed review: 2022-04-05 08:56

Review time: 1 Hour

Scientific quality	[Y] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No
Peer-reviewer	Peer-Review: [Y] Anonymous [ ] Onymous

Baishideng Publishing Group

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

statements	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Thank you for the opportunity to review this excellent manuscript. SBRT is a new treatment for cholangiocarcinoma. The paper is a review of the application of SBRT in ICC. The author introduces the application and related clinical research progress of SBRT in ICC from the following aspects: (1) primary therapy in patients with technically resectable disease but precluded from resection due to medical comorbidities; (2) primary therapy in technically unresectable disease; this may be due to diffuse or metastatic disease; (3) recurrent disease after surgical resection; (4) following surgical resection to prevent local recurrence (adjuvant therapy), and (5) as a downstaging modality before surgery (neoadjuvant). The paper is rich in content, fluent in language and has high application value.