Outcomes of Stereotactic Body Radiation Therapy (SBRT) for Hepatocellular Carcinoma (HCC)

J. Waller, W. Naugler, G .Vaccaro, A. Zaman, S. Orloff, K. Billingsley, K. Kolbeck, J. Kaufman, J. Tanyi, M. Fuss

Multidisciplinary Liver Tumor Group, Oregon Health & Science University, Portland, Oregon, USA

Background

Hepatocellular carcinoma (HCC) is the 6th most common cancer in the world with ~750,000 new cases diagnosed annually and is the 3rd leading cause of cancer death worldwide. Incidence in the United States rose by over 4% in the past decade and is likely to continue to rise with increasing incidence of non-alcoholic steatohepatitis (NASH).

Treatment for HCC has traditionally included resection for a minority of candidates with the only curative option being liver transplantation with 5 yr OS of ~70%. Transarterial embolization (TAE) and transarterial chemoembolization (TACE) are level 1 evidence-based treatments for HCC but have LF rates of ~50% at 6 mos. The low rates of durable control led to adjuvant treatment with radiofrequency ablation (RFA) or focal radiotherapy. Use of radiotherapy has been limited in the past given most pts history of underlying cirrhosis and unacceptably high rates of radiation-induced liver disease (RILD). Recent studies however have shown stereotactic body radiotherapy (SBRT) to be safe and effective in the treatment of HCC. The majority of the studies to date however have had a limited number of patients and did not include more advanced cirrhosis (CTP C/BCLC D).

Purpose

The specific aims were to: 1) evaluate the safety and effectiveness of SBRT for primary liver HCC as adjuvant therapy following resection and/or catheter based therapy in pts with Child-Pugh A-C (BCLC A-D) and 2) to evaluate the outcomes of patients who underwent liver transplantation following SBRT.

Materials & Methods

This is a single institution retrospective analysis of 85 patients with 96 HCC lesions treated by SBRT between August 2007 and July 2012 @ a NCI-designated cancer center. All patients were treated to 50 Gy in 5 fractions delivered every other day. 78 patients were treated under a multi-modality treatment algorithm and had undergone transarterial embolization (TAE), transarterial chemoembolization (TACE), or radiofrequency ablation (RFA) prior to SBRT. Treatment was delivered using a linear accelerator (Brainlab/Varian NovalisTx) with daily cone-beam CT image guidance. Retrospective data review included baseline Child-Turcotte-Pugh scores (CTP), as well as baseline and follow-up MELD scores (Model of End-stage Liver Disease). We assessed overall survival using Kaplan-Meyer survival curves and changes in MELD score after SBRT.

Results

- Mean follow-up was 16.4 months (range 0.8-61.6 months).
- At the time of analysis, 43 patients (50%) have died, with a median time to death of 11.4 months.
- 90-day mortality was 5.5%; n=5; CTP A(0), B(3), and C(2)
- Mean initial MELD score was 11.4
- A statistically significant increase in MELD score was observed at 3 months (mean 12.9; p=0.011) but no significant changes, compared to baseline, were observed at 6, and 12 months following SBRT.
- 14 patients (14.6%) went on to orthotopic liver transplantation between 23 days and 30 months (mean 18.6 months) following SBRT, 13 (93%) of which are alive at the time of this analysis with mean follow-up of 32.1 months (range 1.6-61.6 months).

	CTP A (n=42)	CTP B (n=41)	CTP C (n=13)	
Median survival (months)	40.5	14.5	13.1	p=0.006
1 yr OS (%)	90	61	54	
2 yr OS (%)	67	32	43	

Table 1: Survival data for all pts

	CTP A (n=42)	CTP B (n=41)	CTP C (n=13)	
Mean initial MELD score	9.2	12.5	15.3	

Table 2: Safety data for all pts

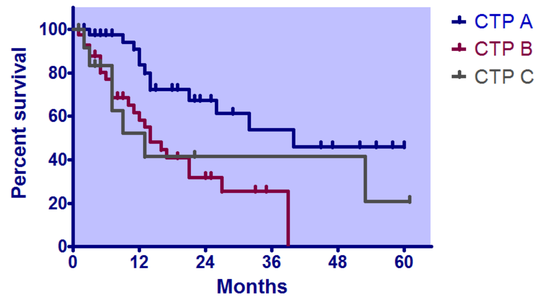

Fig. 1: Kaplan-Meier estimates of overall survival among all patients with HCC status post SBRT stratified by Child-Turcotte-Pugh class

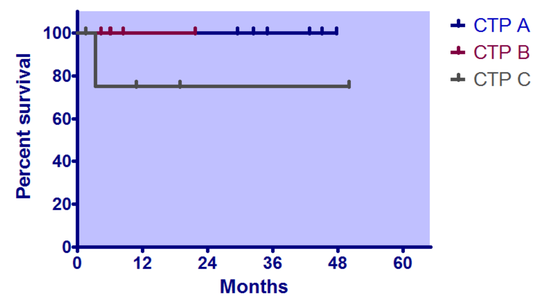

Fig. 3: Kaplan-Meier estimates of overall survival among patients with HCC status post SBRT who underwent liver transplantation stratified by CTP class

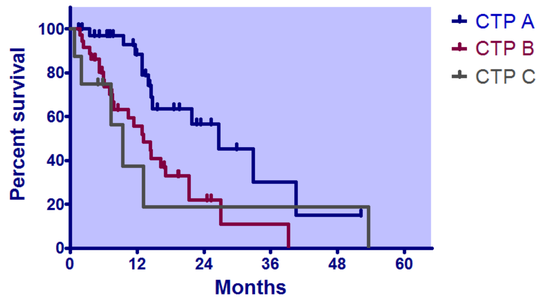

Fig. 2: Kaplan-Meier estimates of overall survival among patients with HCC status post SBRT who did not undergo liver transplantation stratified by CTP class

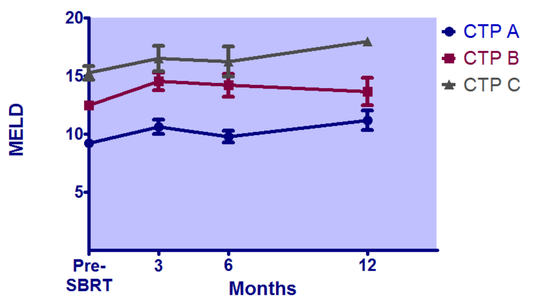

Fig. 4: Average MELD score pre-SBRT, and at 3, 6, and 12 months post-SBRT for all patients stratified by CTP class

Conclusion

- SBRT, either in combination with arterially directed therapy or as a single modality treatment for HCC resulted in encouraging survival, even in patients with more advanced baseline liver disease (CTP C/BCLC D) and patients who had multiple prior liver directed therapies (TACE, RFA, resection).
- With a low 90 day mortality rate (5.5%), and no clinically relevant impact on liver function, SBRT offers a safe adjuvant treatment option for this patient population.
- SBRT maintained transplant eligibility for a significant proportion of patients and successfully down staged one patient, originally out of Milan criteria, who ultimately went for transplant.
- An analysis of pathologic response in liver explants is currently ongoing, this data will be reported.

References

1. Dawson LA, Normolle D, Balter JM, et al. Analysis of radiationinduced liver disease using the Lyman NTCP model. Int J RadiatOncol Biol Phys 2002;53:810-821.
2. Dawson LA, Eccles C, Craig T. Individualized image guided iso-NTCP based liver cancer SBRT. Acta Oncol. 2006; 45:856–864.
3. Cardenes HR, Price TR, Perkins SM, et al. Phase I feasibility trial of stereotactic body radiation therapy for primary hepatocellular carcinoma. Clin Transl Oncol 2010;12:218-225.
4. Tse RV, Hawkins M, Lockwood G, et al. Phase I study of individualized stereotactic body radiotherapy for hepatocellular carcinoma and intrahepatic cholangiocarcinoma. J Clin Oncol 2008;26:657-664.
5. Zeng ZC, Tang ZY, Fan J, et al. A comparison of chemoembolization combination with and without radiotherapy for unresectable hepatocellular carcinoma. Cancer J 2004;10:307-316.

Acknowledgements

The authors would like to thank Dr. Charles Thomas Jr., Dr. Kristina Young, Basma Saadoun, Dorothy Hargrove, Linette Chapman, Erica Ryu, and Joanne Reasoner