Local Control following Stereotactic Body Radiotherapy for Liver Tumors: A Preliminary Report of the AAPM Working Group for SBRT

N. Ohri[1], A. Jackson[2], A. Mendez Romero[3], M. Miften[4], R. K. Ten Haken[5], L. A. Dawson[6], J. Grimm[7], E. D. Yorke[2], W. A. Tome[1]

1 – Montefiore Medical Center, Albert Einstein College of Medicine, Bronx NY
2 – Memorial Sloan-Kettering Cancer Center, New York, NY
3 – Erasmus MC Cancer Institute, Rotterdam, Netherlands
4 – University of Colorado Denver, Aurora, CO
5 – University of Michigan, Ann Arbor, MI
6 – Princess Margaret Hospital, Toronto, ON, Canada
7 – Holy Redeemer Hospital, Meadowbrook, PA

Conflicts of Interest

- I have no conflicts of interest to disclose.

Background

- Stereotactic Body Radiotherapy (SBRT) has emerged as a promising tool for the treatment of primary and metastatic liver tumors
- Numerous dosing and fractionation schedules have been used to treat hepatic tumors with SBRT
- The impact of dose and fractionation on local tumor control remains unclear

Purpose

- To quantitatively analyze published experiences with liver SBRT to determine if there is a relationship between dosing and fractionation and local tumor control.

Methods – Study Selection

- Sources
  - MEDLINE
- Terms – "SBRT", "SABR", "liver"
- Criteria
  - Reports describing local tumor control following liver SBRT
  - Cohorts treated with relatively uniform SBRT schedules

Methods – Data Extraction

- First author, publication year, tumor type, SBRT schedule, and median follow-up were tabulated
- Individual patient local control data were extracted from Kaplan-Meier curves as described by Guyot et al (BMC Med Res Methodol 2012).

Methods – Data Analysis

- Individual patient data extracted from each manuscript were aggregated to form a single dataset.
- Kaplan-Meier curves for local control were generated for primary liver tumors (hepatocellular carcinoma [HCC], cholangiocarcinoma [CCA]) and liver metastases.
- Kaplan-Meier curves were also generated for subsets of patients treated with biologically effective doses (BEDs) below and above 100 Gy_{10}.
- Logrank testing was used to compare local control results.

Methods – Data Analysis

- In cases where a relationship between BED and local control was detected, tumor control probability (TCP) modeling for local control (LC) at 2-years was performed.
- Bootstrap resampling (n=5,000) was used to characterize the distributions of model parameters and formulate 95% confidence bounds for the TCP curve.

$$TCP(BED) = \left[1 + \exp\left(\frac{TCD_{50} - BED}{k}\right)\right]^{-1}$$

Results – Study Selection

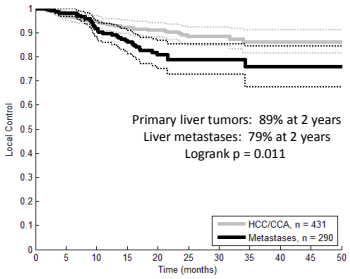
- Pubmed search → 201 hits
- 48 papers reported local control data following SBRT
  - 21 excluded for using wide BED ranges
  - 11 excluded for using overlapping patient populations
  - 2 excluded for not reporting outcomes separately for primary and metastatic liver tumors
  - 1 excluded due to use of SBRT as a bridge to liver transplant
- 13 papers met all inclusion criteria and formed the dataset for this analysis.

First author (Country)s	Disease	Sample size	SBRT schedule	Prescription point/volume	Median follow-up (range)
Dewas (France)	HCC	42 patients, 48 lesions	Median 45 Gy, 3 fx	PTV (80% IDL)	15 months
Honda (Japan)	HCC	30 patients	Median 48 Gy, 4 fx	Isocenter	12 months (6-38)
Jang (Korea)	HCC	82 patients, 95 lesions	<45 Gy, 3 fx (n=11) 45-54 Gy, 3 fx (n=47) >54 Gy, 3 fx (n=57)	PTV (70-80% IDL)	30 months (4-81)
Kwon (Korea)	HCC	42 patients	Median 33 Gy, 3 fx	PTV (70-85% IDL)	29 months (8-49)
Sanuki (Japan)	HCC	185 patients	35 Gy, 5 fx (n=48) 40 Gy, 5 fx (n=137)	PTV (70-80% IDL)	25 months (3-80)
Barney (USA)	CCA	9 patients, 10 lesions	45-60 Gy, 3-5 fx	NR	14 months (2-26)
Kopek (Denmark)	CCA	27 patients	45 Gy, 3 fx	Isocenter	5.4 years (2.3-8.6)
Mendez Romero (Netherlands)	Mets	17 patients, 34 lesions	Median 37.5 Gy, 3 fx	PTV (65% IDL)	13 months (1-31)
Rusthoven (USA)	Mets	36 patients, 49 lesions	60 Gy, 3 fx	PTV (80-90% IDL)	16 months (6-54)
Scorsetti (Italy)	Mets	61 patients, 76 lesions	75 Gy, 3 fx	PTV	12 months (2-26)
Stintzing (Germany)	Mets	30 patients, 35 lesions	24-26 Gy, 1 fx	70% IDL	35 months (6-96)
Vautravers-Dewas (France)	Mets	45 patients	40 Gy, 4 fx (n=29) 45 Gy, 3 fx (n=16)	80% IDL	14 months (2-23)
Wulf (Germany)	Mets	39 patients, 51 lesions	Median 30 Gy, 3 fx (n=25) Median 37.5 Gy, 3 fx (n=26)	PTV (65% IDL)	15 months (2-85)

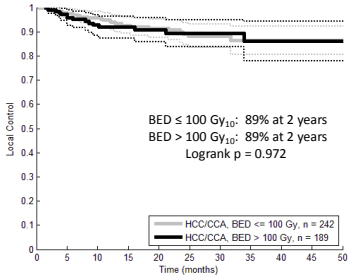
Results

- 721 lesions treated with SBRT
  - 394 HCC, 37 CCA, 290 metastases
- 24 to 60 Gy, 1 to 5 fractions
- Median BED 88 Gy_{10}, IQR 72 to 125 Gy_{10}
- 79 local failures
- 17 months median follow-up for lesions without local failure

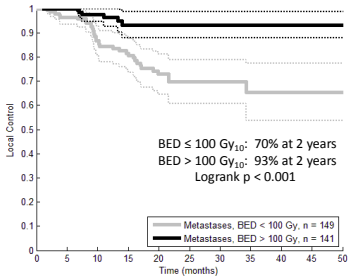
Local Control by Tumor Type



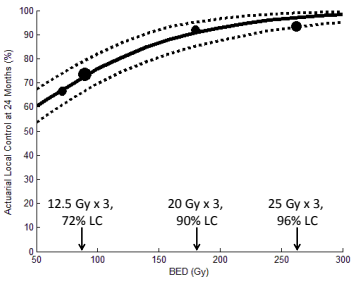
Primary Liver Tumors: LC and BED



Liver Metastases: LC and BED



Liver Metastases: TCP Model



Conclusions

- SBRT for primary liver tumors provides high rates of durable local control, with no evidence for a dose-response relationship within the range of commonly-used fractionation schedules.
- Excellent local control rates are seen following SBRT for liver metastases when biologically effective doses above 100 Gy_{10} are utilized.