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

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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.

- 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.

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

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.
Results

• 721 lesions treated with SBRT
  – 394 HCC, 37 CCA, 290 metastases
• 24 to 60 Gy, 1 to 5 fractions
• Median BED 88 Gy<sub>10</sub>, IQR 72 to 125 Gy<sub>10</sub>
• 79 local failures
• 17 months median follow-up for lesions without local failure
Primary Liver Tumors: LC and BED

BED ≤ 100 Gy_{eq} \quad 89\% \text{ at } 2 \text{ years}
BED > 100 Gy_{eq} \quad 89\% \text{ at } 2 \text{ years}
Logrank p = 0.972

Liver Metastases: LC and BED

BED ≤ 100 Gy_{eq} \quad 70\% \text{ at } 2 \text{ years}
BED > 100 Gy_{eq} \quad 93\% \text{ at } 2 \text{ years}
Logrank p < 0.001

Liver Metastases: TCP Model

12.5 \text{ Gy } x 3, \quad 72\% \text{ LC}
20 \text{ Gy } x 3, \quad 90\% \text{ LC}
25 \text{ Gy } x 3, \quad 96\% \text{ LC}
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.