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Stereotactic Radiosurgery for Spinal Metastases: Tumor Control Probability Analyses and Recommended Reporting Standards for Future Publications

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Acknowledgements: TCP SPINE

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Overview of Spine TCP Literature

- In accordance with the guidelines established by the Hytec project, spinal TCP from SBRT and hypofractionated protocols have been evaluated from the reports in the literature.
- The Spinal HyTec TCP presentation will review the relevant issues in defining the dose to tumor control effect for spinal SBRT, including goal of treatment (tumor control, pain relief, and reduction in neurological symptoms), challenges in tumor volumes, margins, dose, fractionation, and imaging strategies for follow-up evaluation.
- Much of the data extracted from 15 manuscripts and 329 tumors demonstrate a clinically acceptable range of 16 – 24 Gy in a single fraction or a similar biologically effective dose in multiple fractions (with common dosing schemes of 24Gy in 2 fractions and 27-30Gy in 3 fractions).

CLINICAL SIGNIFICANCE

- Metastatic disease to the spine represents one of the most significant causes of morbidity in patients with cancer, occurring in approximately 40% of patients
- Ref; Klimo P, Jr., Schmidt MH. Surgical management of spinal metastases. The oncologist 2004;9:188-96

Treatment Endpoints

- It is challenging to assess local tumor control in spinal metastases treated with SRS.
- Post-SRS imaging and clinical changes reflect the combined effects of tumor response, tumor progression (perhaps in a sub-region), and treatment-related side effects such as pain flare and vertebral body compression fracture

Treatment Endpoints

- The traditional tumor measurement-based response criteria (e.g. RECIST) might not be appropriate for bone metastasis since controlled osseous tumor does not decrease in size.
- Thus, tumor control is typically defined as lack of progression on imaging.

Treatment Endpoints

- For the present TCP analysis, we recorded tumor control rates as defined by each manuscript, acknowledging that each report may have slightly different criteria for tumor control

Treatment Options

- Treatment options have traditionally consisted of open surgical resection for relief of spinal cord and nerve compression or for mechanical stabilization, and fractionated external beam irradiation.
- Goals of therapy include tumor control as well as relief of pain and neurologic symptoms.
- Multiple prospective studies have demonstrated equivalent short-term pain control with short course hypofractionated approaches (eg. 8Gy in 1 fraction, 20 Gy in 5 fractions) compared to longer conventional fractionation schemes (eg. 30 Gy in 10 fractions, 40 Gy in 20 fractions)

*Ref Wu JS, et al JROBP 2003;55:594-605

Treatment Options.... SRS

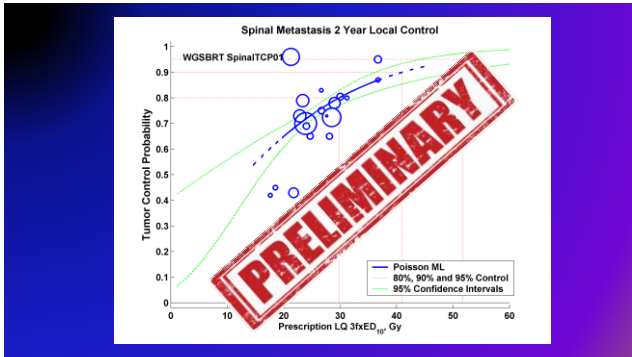
- However, the rate of retreatment after the low-single-dose option is higher than after the higher dose fractionated option, thus suggesting that the former does not provide optimal longer-term tumor control.
- This early finding that higher radiotherapy doses may lead to better tumor control led to interest in stereotactic, hypofractionated treatment as a means for biologically effective dose escalation

The analysis was performed as follows:

- (1) prescription dose was taken as the physical dose;
- (2) as reporting of tumor coverage is largely absent, TCP was directly related to the named prescription dose rather than to the minimum dose or other measures of tumor under-coverage, as previously reported
- (3) conformity indices was mostly absent, the dose to the tumor was taken to be the same as the prescription dose
- (4) data from metastases that had not been previously treated and those that were recurrent following prior RT were pooled

MATHEMATICAL/BIOLOGICAL MODELS

- *Jimin Grimm the man, the legend...*
- Challenges of interpreting data
- TCP scoring
- Analysis type



Recent data to be added:

- Guckenberger M, Mantel F, Gerszten PC, Flickinger JC, Sahgal A, Létourneau D, Grills IS, Jawad M, Fahim DK, Shin JH, Winey B, Sheehan J, Kersh R. Safety and efficacy of stereotactic body radiotherapy as primary treatment for vertebral metastases: a multi-institutional analysis. *Radiat Oncol.* 2014 Oct 16;9:226.
- Ho JC, Tang C, Deegan BJ, Allen PK, Jonasch E, Amini B, Wang XA, Li J, Tatsui CE, Rhines LD, Brown PD, Ghia AJ. The use of spine stereotactic radiosurgery for oligometastatic disease. *J Neurosurg Spine.* 2016 Aug;25(2):239-47.
- Bernard V, Bishop AJ, Allen PK, Amini B, Wang XA, Li J, Tatsui CE, Rhines LD, Brown PD, Ghia AJ. Heterogeneity in Treatment Response of Spine Metastases to Spine Stereotactic Radiosurgery Within "Radiosensitive" Subtypes. *Int J Radiat Oncol Biol Phys.* 2017 Dec 1;99(5):1207-1215.

• Potentially one more dataset if it is published in time before HyTEC deadline

FACTORS AFFECTING OUTCOMES

- Minimum target dose:**—Correlating reported dose with clinical outcomes is hindered by the reality that the portion of the target immediately adjacent to the spinal cord is often not receiving the prescription dose (due to normal tissue constraints), and the degree of "under-dosage" of this portion is not always evident in the published reports."

RTOG 0631 / Spine clinical trial

- We await the results of RTOG 0631, the only prospective randomized trial in spinal SRS, to determine pain response to 16-18Gy of spinal SRS compared to a 8 Gy in a single fraction of 3D conformal irradiation.

Future Spine clinical trial

- Future research on spinal cord NTCP would directly translate into improved tumor TCP. In light of that, if dosimetric data from future studies corroborate optimal tumor control with a minimum tumor dose of 15 Gy, then improved outcomes may be expected from the larger therapeutic window if the spinal cord tolerance is determined to be higher than the current limit of 12-14 Gy

Thank You -
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