

Objectives

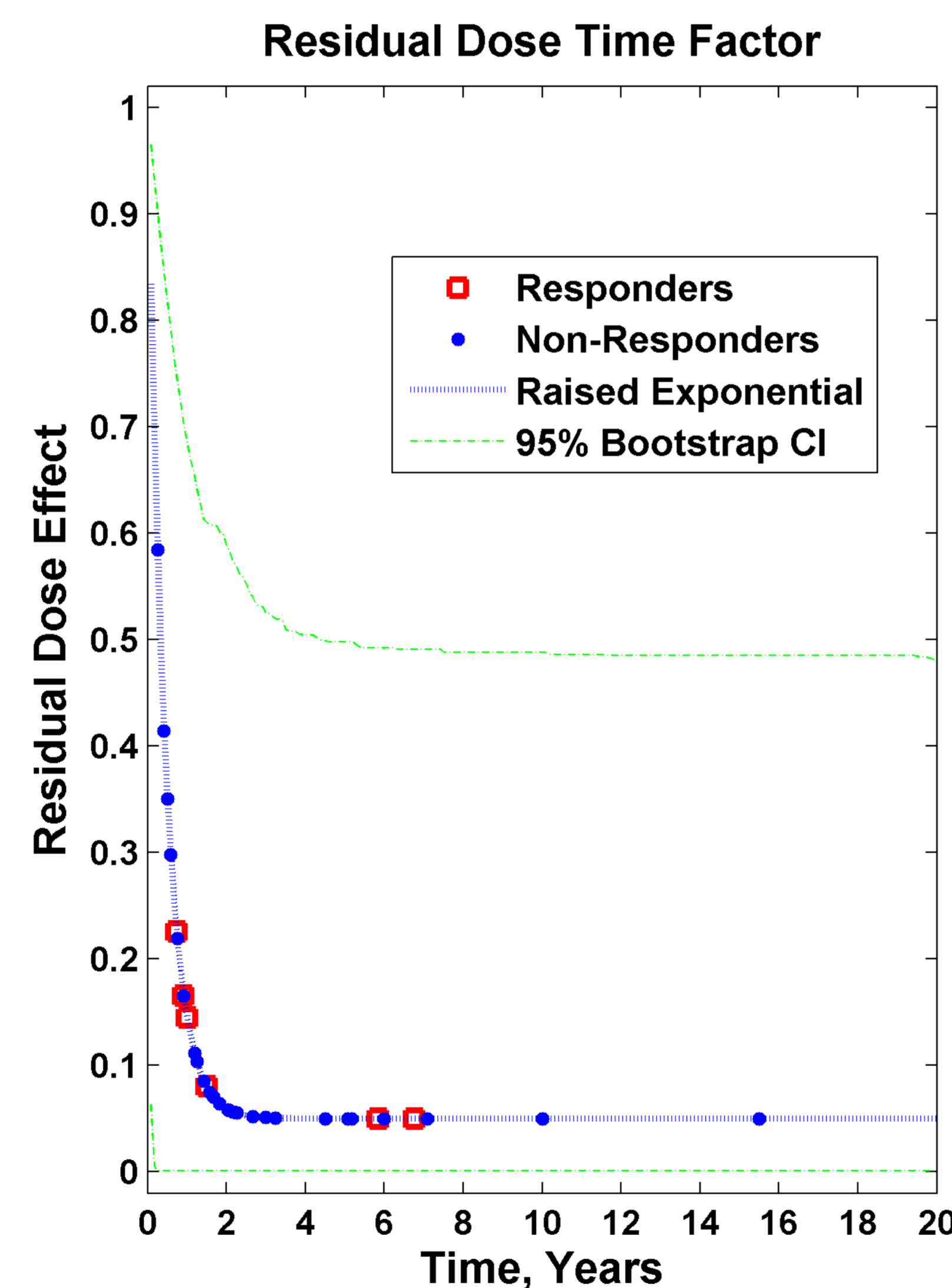
- Reirradiation of spinal metastases with radiosurgery in 1-5 fractions is being increasingly used after prior radiation.
- However, the dose-time recovery factors remain uncertain.
- To address these uncertainties, a preliminary cumulative normal tissue complication probability (NTCP) model was developed based on existing published data, incorporating the essential recovery factors.

Methods

- Initial simple models incorporating data from existing published literature would provide sufficient information for more advanced models in the near future.
- Therefore, our first recovery model is simply a raised exponential with two parameters: the saturation level, representing the residual dose effect that may not fully recover, and the recovery half-time, which describes the time required for the portion of the dose effect that does recover.
- A PubMed search using the terms (myelopathy OR neuropathy) AND (reirradiation OR re-irradiation) identified 282 cases of spine stereotactic body radiation therapy (SBRT) reirradiation from 13 studies, including 6 cases of myelopathy.
- All initial and reirradiation spinal cord maximum point doses were converted to the biological effective dose (BED) using the linear quadratic (LQ) model with an alpha/beta ratio of 2 Gy.
- The prior doses were then multiplied by the recovery time discount factor.
- Maximum likelihood parameter fitting was used to estimate the best saturation level, recovery half-time, and the logistic model's TD50 tolerance dose and slope parameter.

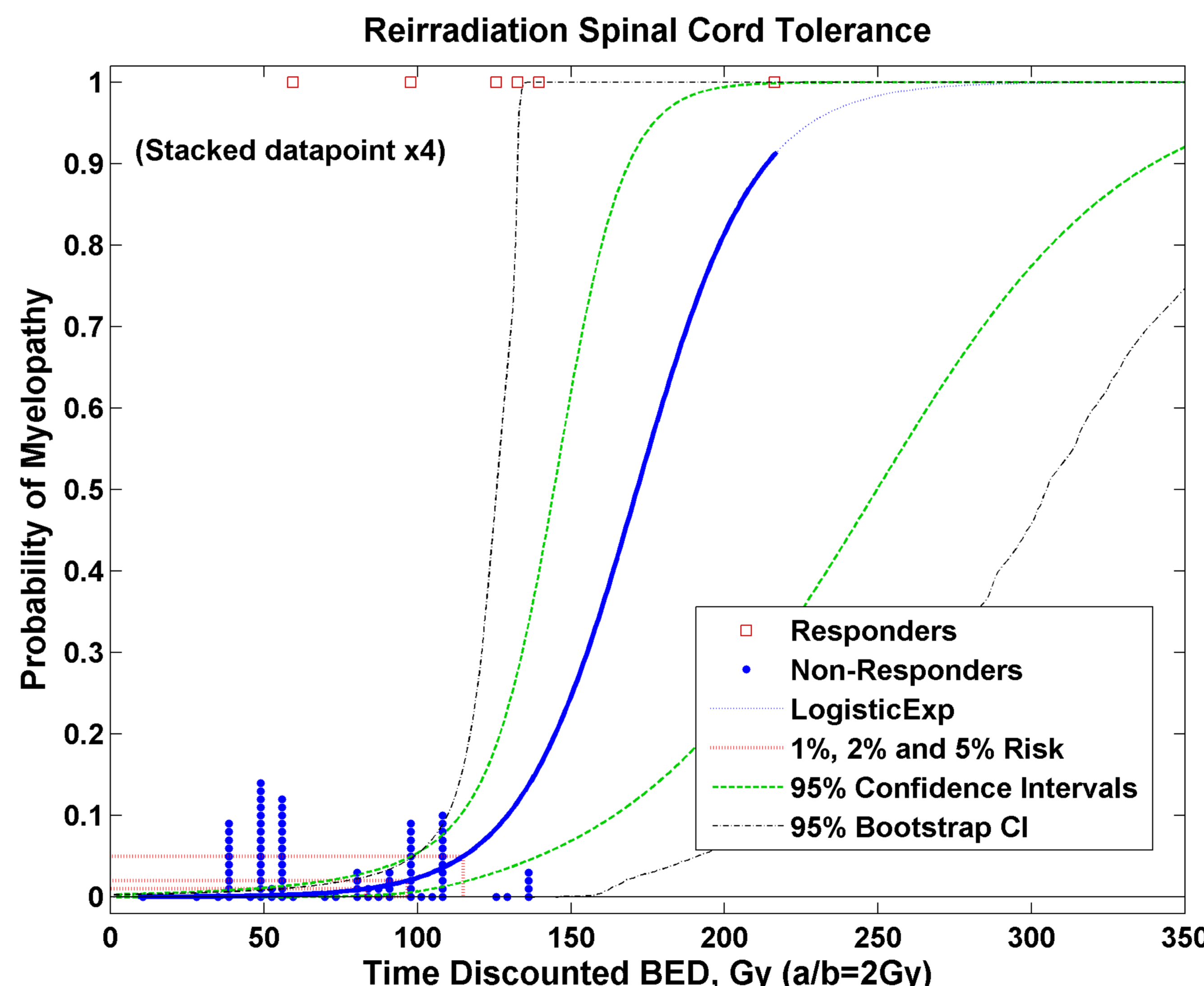
Reirradiation Treatment Effects in the Clinic (ReTEC) proof-of-concept:

Spinal Cord Recovery



- Estimated spinal cord recovery at 1 year was 85% (bootstrap 95% CI 31-99.9%).
- After applying the recovery factor and accumulating the Dmax values, a significant dose response was observed (p=0.01).

Spinal Cord Composite Dose Response



Important Caveat: Hot spots may occur at different locations in each course, so full 3D composite plans are needed, but this analysis has only Dmax, therefore this is only a proposal to conduct a large-scale data pooling project of full composite 3D data.

Results

- The maximum likely recovery half-time for this dataset was estimated to be less than 24 months, with a saturation level of less than 20%.
- However, due to the limited availability of data, these parameters were conservatively set to 24 months and 20%, respectively, for subsequent analyses.
- Therefore, the recovery half-time shorter than 24 months or an asymptotic recovery level exceeding 80% was not used until further high-quality data becomes available for validation.
- As a clinical example, including the dose-time recovery factor for a spine SBRT reirradiation two years after the initial course, the model estimates risk of myelopathy of 1-2% for cumulative spinal cord maximum point dose BED up to about 100 Gy.
- Many caveats and limitations will be discussed, along with a roadmap of future work to overcome them.

Conclusions

- Preliminary evaluation of published data provides a conservative estimate of recovery half-time and recovery saturation level of dose-time parameters of radiation tolerance for spinal cord reirradiation.
- Validation with more complete datasets is needed before this model could be widely adopted.

Conflicts of Interest

- Dr. Grimm, designed and holds intellectual property rights to the DVH Evaluator software tool which is an FDA-cleared product in commercial use, and was used to analyze this data