

Non-small cell lung cancer

Lee VH, Chan WW, Lee EY, Choy TS, Ho PP, Leung DK, Lam KO, Kwong DL, Leung TW, Khong PL. Prognostic Significance of Standardized Uptake Value of Lymph Nodes on Survival for Stage III Non-small Cell Lung Cancer Treated With Definitive Concurrent Chemoradiotherapy. *Am J Clin Oncol*. 2016 Aug;39(4):355-62. doi: 10.1097/COC.000000000000070. PMID: 24710123.

Lee et al. report the distant metastasis-free survival (DMFS) of 43 patients with unresectable non-small cell lung cancer (NSCLC). In the publication, survival curves are stratified by total tumor volume planned to be irradiated (< or $\geq 500 \text{ cm}^3$). Assuming a sphericity, this implied an irradiation diameter of 9.85 cm. As the authors noted radiation margins of 1 to 1.5 cm around the tumor, we assumed the tumor diameter would be 2.5 cm ($1 * 1.25$) lower than the irradiated volume diameter, or 7.35 cm.

From the DMFS curves, we could estimate an incremental number of events per time period and convert this to events per patient per day for tumors above or below the diameter threshold.

Two additional assumptions were made:

- Tumors above 7.35 cm would have similar event rates as tumors 7.35 cm in diameter, given the size indicates highly advanced disease
- Tumors below 7.35 cm were set to 50% of the largest spherical tumor associated with a 500 cm^3 irradiation volume, allowing for 2.5 mm measurement error (i.e., 0.75 cm margins). This value was 4.175 cm.

A Hill function was then fit using three data points:

- 0 mm and 0 events/pt/day
- 41.75 mm and 2.972×10^{-3} events/pt/day
- 73.5 mm and 3.917×10^{-3} events/pt/day

Yielding $V_{\max} = 4.44 \times 10^{-3}$, $K_m = 30.73$, and $h = 2.29$ for the following Hill equation, where T represents tumor burden:

$$\text{Events/patient/day} = \frac{V_{\max} T^h}{K_m^h + T^h}$$

Melanoma

Kumar R, Thiagarajan K, Jagannathan L, Liu L, Mayawala K, de Alwis D, Topp B. Beyond the single average tumor: Understanding IO combinations using a clinical QSP model that incorporates heterogeneity in patient response. *CPT Pharmacometrics Syst Pharmacol.* 2021 Jul;10(7):684-695. doi: 10.1002/psp4.12637. Epub 2021 Jun 5. PMID: 33938166; PMCID: PMC8302246.

Kumar et al. report in the supplement parameters for their model of melanoma metastasis as a function of tumor burden: $V_{\max} = 4.2 \times 10^{-3}$, $K_m = 80$, and $h = 3.5$. In addition, event rates below 1×10^{-4} were set equal to 1×10^{-4} .

Comparing these two models, we have (same data, different X axes):

