Appendix EA1: The Format of Actuarial Atlases of the Dose-Volume Incidence of Grade ≥2 Chest Wall Pain

To make our chest wall toxicity data set available for meta-analysis (1, 2), we organized the dosimetric data using the dose-volume atlas concept described by Jackson et al. (3).

The atlas data is provided in Excel files in Appendix EA3. These files are compressed by WinRAR, software that can be downloaded from the website http://www.win-rar.com/download.html. The format of these files, similar to those provided in Mutter et al. (4). We emphasize that the endpoint used for all these atlases was CTCAE V.4 Grade ≥2 chest wall pain. To allow subsequent investigators to account for effects of the number and size of the fractions delivered as well as the patient BMI, we have also separated the patient data by fraction number (either 3, 4, 5, or 6) and by whether the patient was clinically obese (BMI ≥ 30) at time of treatment. Therefore, we provide seven Excel files, each labeled by fraction number and BMI classification. For example, the file "cwp_aoc_bmi_gt30_4fr" contains the actuarial dose volume atlas of complication (aoc) of chest wall pain (cwp) for patients with BMI greater than 30 (bmi_gt30) treated with three fractions (4fr).

Within each Excel file, the first sheet (definitions) provides endpoint and chest wall definitions. Each sheet providing atlas data is labeled by follow-up time, in intervals of 3 months up to 20 months, then a follow-up time of 50 months and up to 67 months (see Fig. EA1). For example "t=6m" contains data from patients who either had a complication or were censored before 6 months. Note that at time zero there can be no events to record, so this sheet is omitted. Given a maximum follow-up time of 67 months, there are a maximum of 9 data sheets in a file.

We define $np(D_i,V_j,t_k)$ as the number of patients whose DVHs pass through or above (D_i,V_j) who either developed the complication or were censored at or before the time t_k, and $nc(D_i,V_j,t_k)$ as the number of those patients who developed the complication. The main body of

each of the sheets of the Excel files consists of repeating sets of two consecutive columns. The numbers in the first column are $nc(D_i,V_j,t_k)$, and those in the second column are $np(D_i,V_j,t_k)$ (see Fig. EA1).

Around the main body of the sheet are dose and volume labels. Across the top row in each sheet, each set of two columns is labeled by one dose value, increasing from zero in steps of 1 Gy. In the first two columns of the sheet are the volume labels for each row. In the first column, this label is given in cc; in the second, it is given as the log to base 10 of the volume in cc. Volume values increase in steps on 0.05 in $\log_{10}(V_{cc})$ (see Fig. EA1). Note that the first volume value is zero, and the $\log_{10}$ entry is consequently omitted.

To illustrate the use of the atlas for statistical analysis, we explain how to construct the information required to perform a log-rank test for each candidate cutpoint (D_i, V_j). We divide patients into two groups; one contains patients whose DVHs pass through or above (D_i, V_j) and the other patients whose DVHs pass below (D_i, V_j). The log-rank test determines if the KM curves of these two groups are significantly different. To calculate a KM curve, at each time interval $t_k \rightarrow t_{k+1}$, we calculate the number of patients at risk, and the number of patients who developed the complication. For patients whose DVHs pass over or under the point (D_i,V_j), the numbers at risk (n_r^+ or n_r^-, respectively) during $t_k \rightarrow t_{k+1}$ are

$$n_r^+(t_k) = [np(D_i,V_j,t_{kmax}) - np(D_i,V_j,t_k)] \quad \text{(A1)}$$

and

$$n_r^-(t_k) = [np(0,0,t_{kmax}) - np(0,0,t_k) - n_r^+(t_k)] \quad \text{(A2)}$$

respectively. Here, t_{kmax} is the maximum time, at which point all patients have either been censored or developed complications; hence $np(D_i,V_j,t_{kmax})$ is the total number of patients whose

DVHs pass through or above (D_i,V_j). Note that $np(0,0,t_k)$ is the total number of patients who had been censored or developed complications at or before time t_k, (regardless of dose/volume considerations) and $np(0,0,t_{kmax})$ is the total number of patients.

The number of patients whose DVHs pass over or under the point (D_i,V_j) who develop complications during $t_k \rightarrow t_{k+1}$ ($\Delta n_c^+(t_k)$ or $\Delta n_c^-(t_k)$, respectively) are

$$\Delta n_c^+(t_k) = [nc(D_i,V_j,t_{k+1}) - nc(D_i,V_j,t_k)] \quad \text{(A3)}$$

and

$$\Delta n_c^-(t_k) = [nc(0,0,t_{k+1}) - nc(0,0,t_k) - \Delta n_c^+(t_k)] \quad \text{(A4)}$$

respectively. Note that $nc(0,0,t_k)$ is the total number of patients who developed complications at or before time t_k.

References

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3. Jackson A, Yorke ED, Rosenzweig KE. The atlas of complication incidence: a proposal for a new standard for reporting the results of radiotherapy protocols. *Semin Radiat Oncol* 2006;16:260-268.

4. Mutter RW, Liu F, Abreu A, *et al.* Dose-volume parameters predict for the development of chest wall pain after stereotactic body radiation for lung cancer. *Int J Radiat Oncol Biol Phys* 2012;82:1783-1790

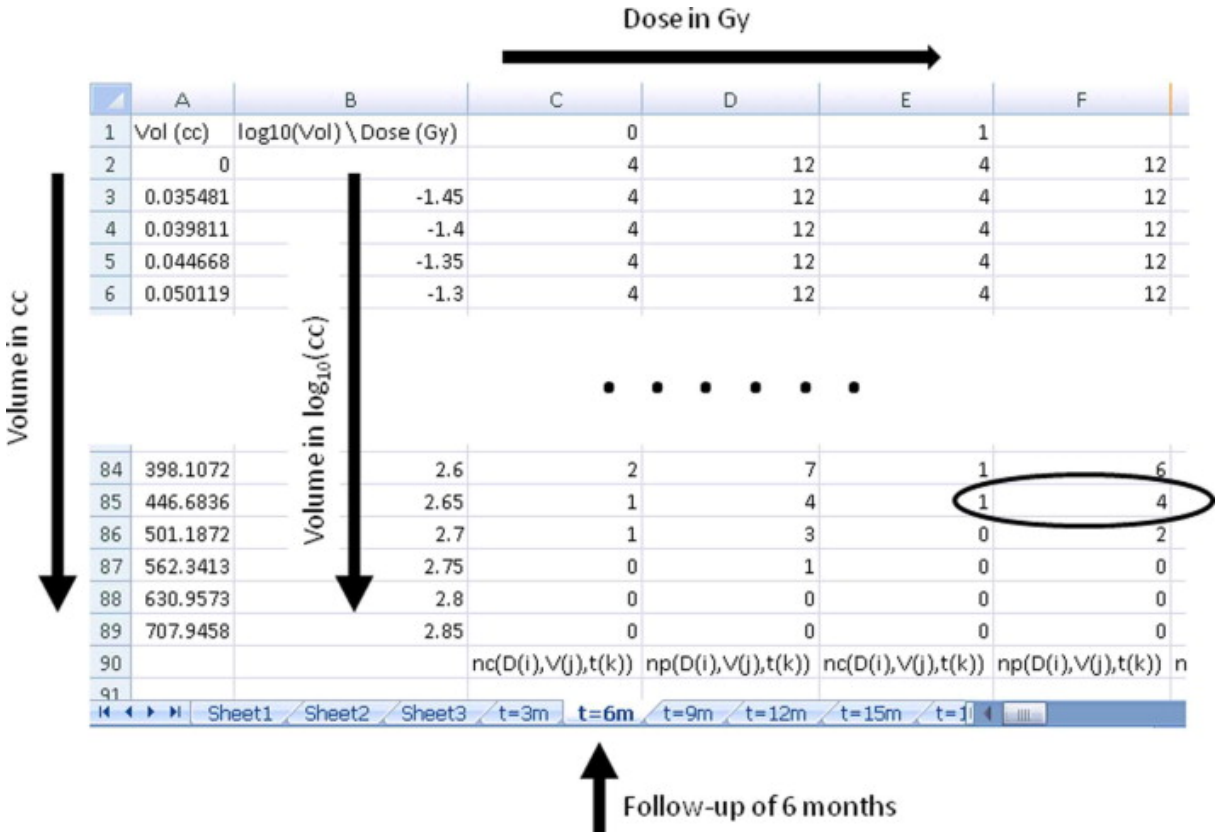

Fig. EA1. Showing the structure of an atlas with the same format as those in the Excel files.The entries at 6 months at dose 1 Gy, $\log_{10}$(Vcc) 2.65 (V~447 cc) volume show that, of the patients whose DVHs passed above the position (1 Gy, 447 cc) at 6 months there were four ($np(D_i,V_j,t_k)=4$) who had either developed a complication ($nc(D_i,V_j,t_k)=1$ pt) or had been lost to follow up (4-1=3pts).