## Appendix A

According to Ballhausen et al., intra-fraction prostate motion can be modelled as a 3D random walk ${ }^{1,2}$. In 1D, the random walk can be represented as:

$$
x_{n}=x_{n-1} \pm \Delta
$$

where $x_{n}$ is the position after step $n$ for $n \geq 1, \Delta$ is the step size and the sign is picked randomly with equal probability. For this model, as the number of steps increases the expectation of the displacement is zero, since a negative or a positive step is equally likely. Thus, the random walk can be better characterized using the average of the square of the displacement or variance:
$\sigma_{x}^{2} \equiv\left\langle\left(x_{n}-x_{0}\right)^{2}\right\rangle=n \Delta^{2}$ where $x_{0}$ is the initial position. We assumed the random walk characteristics of the prostate motion were the same in all directions, so the average squared displacement in 3D was:

$$
\sigma^{2} \equiv\left\langle\left(\vec{r}_{n}-\vec{r}_{0}\right)^{2}\right\rangle=3 n \Delta^{2}
$$

where $\vec{r}_{n}=\left(x_{n}, y_{n}, z_{n}\right)$ is the position in 3D after n steps.
The number of steps in a random walk is equal to the duration T of the random walk divided by the time resolution $\delta_{t}$.

$$
n=\frac{T}{\delta_{t}}
$$

So we can write:

$$
\sigma^{2}=3 b^{2} T
$$

where $b^{2} \equiv \Delta^{2} / \delta_{t}$.


Figure 1: The maximum and the average prostate displacement (black squares) for a patient during different treatment
fractions ${ }^{2}$.

To compute $b^{2}$, we used the prostate displacements reported in Ballhausen's work (Figure 1) ${ }^{2}$. In the figure the maximum and the average displacement for the prostate in different fractions are reported for a prostate cancer patient. The ensemble average of the square of the distance travelled by the prostate at time $t\left(\left\langle\sqrt{\left\langle r^{2}\right\rangle_{t}}\right\rangle\right)$ was extracted directly from the graph shown in Figure $1^{2}$. The relation between the average displacement and the variance in time can be expressed as

$$
\left\langle\sqrt{\left\langle r^{2}\right\rangle_{t}}\right\rangle \equiv \frac{1}{T} \int_{0}^{T} \sqrt{3 b^{2} t} d t=\frac{2 \sqrt{3}}{3} b \sqrt{T}
$$

where $T$ is the treatment time duration ( 20 min ). Thus

$$
b^{2}=\frac{3}{4} \frac{\left\langle\sqrt{\left\langle r^{2}\right\rangle_{t}}\right\rangle^{2}}{T}
$$

Using the values of $b^{2}$ determined from the 22 values obtained from Figure 1, different random walks were generated in MatLab (version 2014, The MathWorks, Inc., Natick, Massachusetts, United States). The step size $\Delta$ was obtained by choosing a time resolution $\delta_{t}$ of 2 seconds. Among the 22 values used, the variance generating the largest displacement was selected:

$$
\begin{aligned}
& b^{2}=0.0090 \mathrm{~cm}^{2} / \mathrm{min} \\
& \Delta=\sqrt{b^{2} \delta_{t}}=0.017 \mathrm{~cm}
\end{aligned}
$$

The reason for selecting a variance which generated a large drift of the prostate was to have a high probability that some of the random walks in our work would have a large final displacement (about 1 cm or more). This way, some critical cases could be included in the simulations.

## References:

1. H Ballhausen, M Li, N-S Hegemann UG and CB. Intra-fraction motion of the prostate is a random walk. 2014;549. doi:10.1088/0031-9155/60/2/549.
2. Ballhausen H, Reiner M, Kantz S, Belka C, Söhn M. The random walk model of intrafraction movement. Phys Med Biol. 2013;58(7):2413-2427. doi:10.1088/0031-9155/58/7/2413.
