# Spatiotemporal fractionation schemes in radiotherapy

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## Spatiotemporal fractionation: Main concept and rationale of a new treatment approach

- Radiotherapy treatments are often delivered over multiple days (or fractions), as most normal cells have a better capability to repair from sublethal radiation damage in between fractions compared to most tumor cells (Figure 1)
- The net benefit of uniformly splitting the dose over multiple fractions is however limited by the fact a higher total dose must be delivered to the tumor in order to maintain the same biological damage (mainly due to tumor cell repopulation and repair)

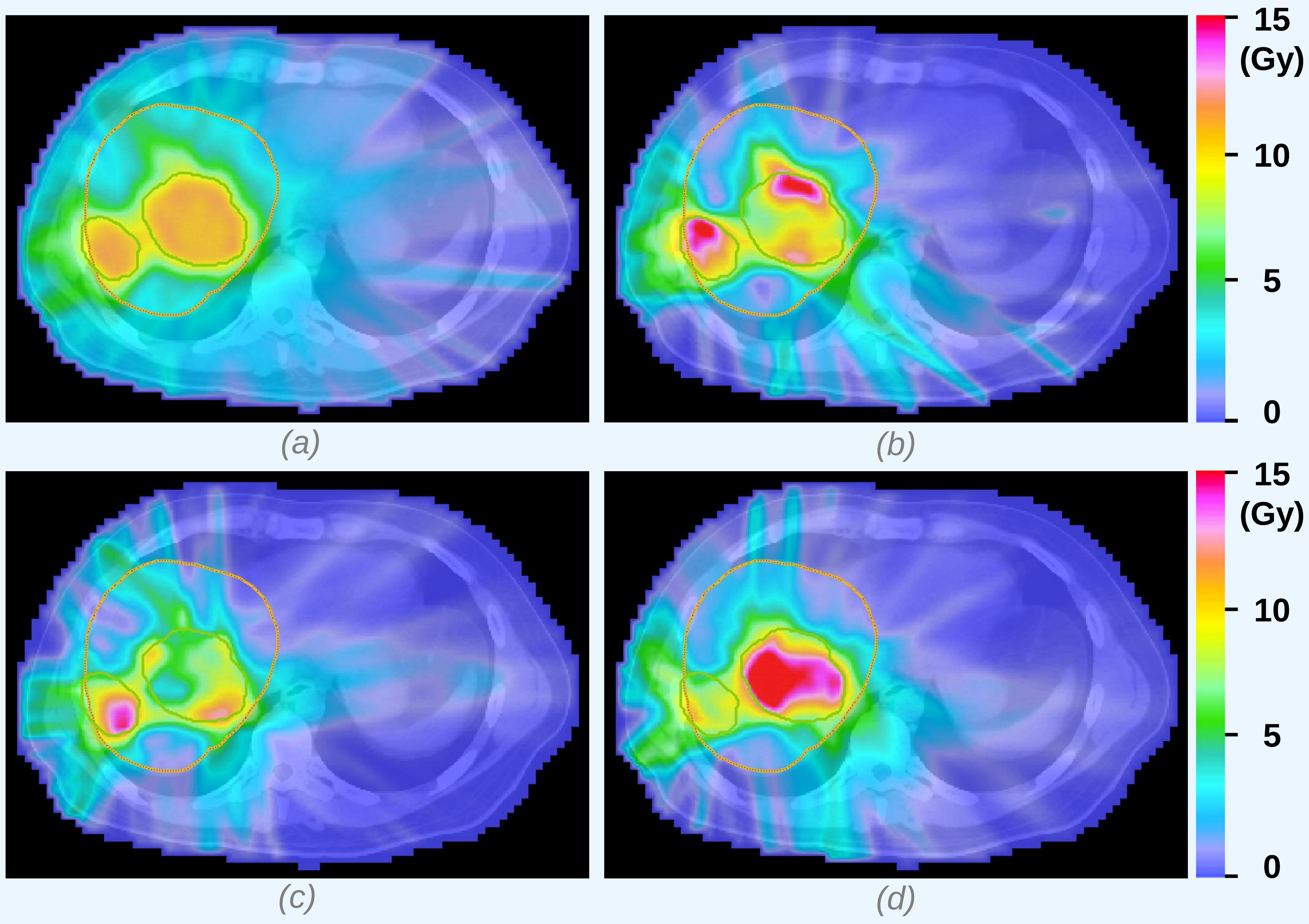


*Figure 2: Dose distributions for a patient with four liver metastases for (a) a conventional treatment delivering the same dose in every fraction and (b)-(d) a spatiotemporally fractionated treatment delivering different dose distributions in distinct fractions.*

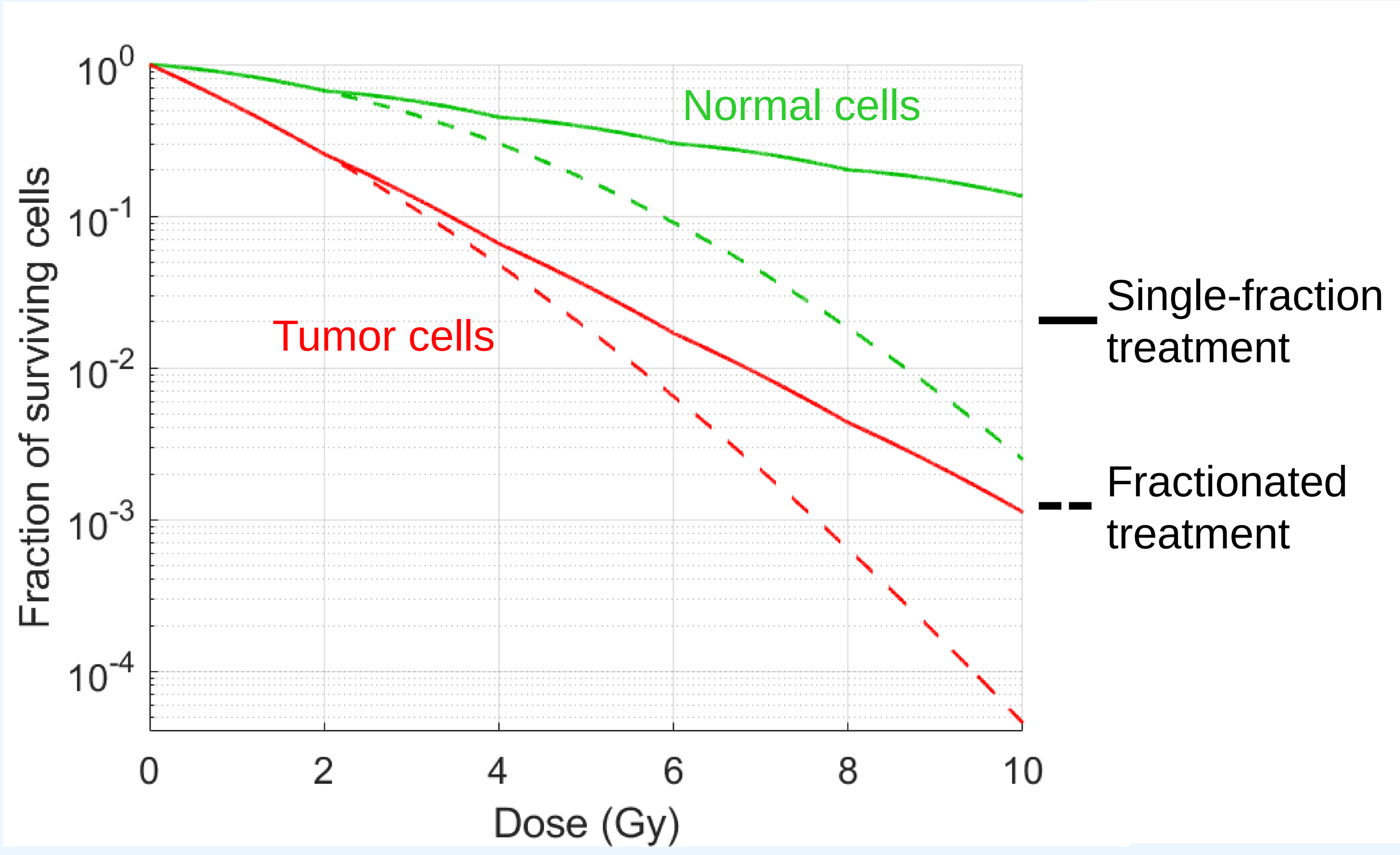


*Figure 1: Linear-quadratic cell survival model for normal and tumor cellls. Dotted lines represent the case for a treatment delivering the full radiation dose in a single fraction, whereas solid lines describe the situation where a treatment is fractionated over 2 Gy fractions.*

- In that regard, the ideal treatment would fractionate the dose in the normal tissue (in order to achieve the fractionation effect) and at the same time deliver high doses to the tumor in few fractions (in order not to increase the total dose to the tumor)
- Interestingly, this can be achieved by delivering distinct dose distributions in different fractions, where each fraction treats complementary parts of the tumor to a high dose while the normal tissue dose is distributed more uniformly throughout all fractions (Figure 2)

## Treatment plan optimization

- Spatiotemporally fractionated treatments are obtained by simultaneously optimizing $n$ different dose distributions $\boldsymbol{d}_t$ to be delivered over $n$ distinct fractions, solving the following treatment plan optimization problem:

$$\begin{aligned} \underset{x_1,\dots,x_n}{\text{minimize}} \quad & f(\boldsymbol{b}) & \\ \text{subject to} \quad & b_i = \textstyle\sum_{t=1}^{n} b_{it} & \forall i \\ & b_{it} = d_{it}\left(1 + \frac{d_{it}}{\left(\frac{\alpha}{\beta}\right)_i}\right) & \forall i, \forall t \\ & d_{it} = \textstyle\sum_j x_j D_{ij} & \forall i, \forall t \\ & x_{tj} \geq 0 & \forall j, \forall t \end{aligned}$$

where $f$ is a mathematical function that models the clinical goals (i.e. it penalizes low doses in the tumor and high doses in the normal tissues), $b$ is the biological dose delivered to each voxel $i$ within the patient (accounting for how the radiation dose $d$ is fractionated) and $x_t$ is the intensity of each beamlet (see Figure 3)

- We conduct research on mathematical optimization methods which are used to optimize intensities and incident directions of external radiation fields in order to irradiate the tumor while minimizing the radiation dose to surrounding normal tissues

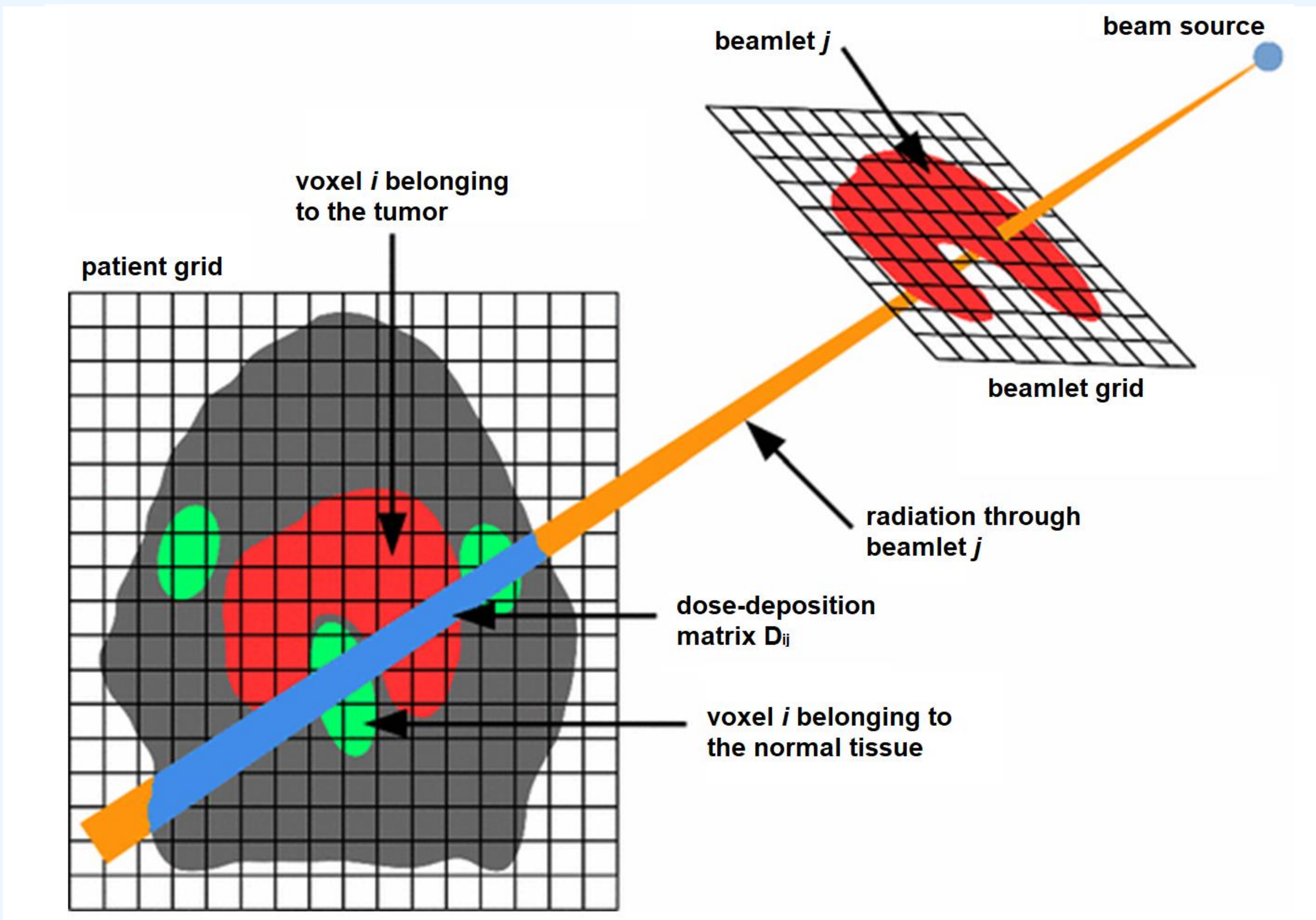


*Figure 3: In radiotherapy treatment planning, the incident radiation field is discretized into multiple beamlets and for each beamlet it is calculated how radiation deposits energy within the patient per unit intensity (by means of dedicated algorithms which model the interaction of radiation in tissue). Mathematical optimization methods are then used to optimize the intensities of radiation through each beamlet leading to high doses in the tumor and sparing normal tissues.*

## Results of treatment planning studies

- Spatiotemporal fractionation schemes have been demonstrated in-silico to reduce the biological dose to critical organs by approximately 10-20% for several treatment sites compared to state-of-the-art treatments
- This may result in lower radiation-induced toxicities for cancer patients treated with radiotherapy and longer overall survival

## Contact information

Are you interested in getting to know more about this or other projects in our group? Feel free to contact us:

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https://www.physik.uzh.ch/en/groups/unkelbach.html