Biologically Effective Dose (BED) for Gamma Knife treatment planning

Thomas Klinge
Supervisors: Marc Modat, Jamie McClelland
Collaborators: Ian Paddick, John W. Hopewell

UCL Department of Medical Physics and Biomedical Engineering

Context and Motivation

Background: Leksell Gamma Knife® (GK) treatments are currently described in terms of physical dose.
Cell-survival is dose-rate dependent and the effectiveness of a treatment should be more accurately described by an appropriate BED model.

Goal: Determine if and how it would be feasible to take all variables of the treatment into account to allow for **BED-optimised treatments using inverse planning**

BED-model with intra-fractional repair

- The **biologically effective dose (BED) model** describes the tissue response to fractionated irradiation (d_n) under consideration of the repair of sublethal radiation damage during treatment delivery ($\Xi, \boldsymbol{\mu}$) (**Millar et al. [1] & Pop et al. [2]):**

$$\mathrm{BED} = D_T + \frac{1}{\alpha/\beta}\left[\frac{\Phi(\Xi,\mu_1) + c\cdot\Phi(\Xi,\mu_2)}{1+c}\right]\sum_n d_n^2$$

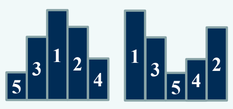
GitHub repo

- For central **nervous system (CNS) tissue** the response is best described with a **bi-exponential** model:
  - Two independent repair processes: **11.4 and 129.6 min half-time**
  - **Requires**: dose-rate maps per iso-centre (use of a custom version of Leksell GammaPlan (LGP))

Iso-centre sequencing

Brute force: infeasible for most treatments
$N_{seq} = N_{iso}!$, $N_{iso} = 17 \rightarrow N_{seq} = 3.6 \cdot 10^{14}$

Heuristic approach: sequence adjusted according to the identified dose-rate pattern from test cases (**Figure 1**):



- Increased mean BED (up to 6%)
- Window of achievable BED values scales with the number of iso-centres (up to 14%)

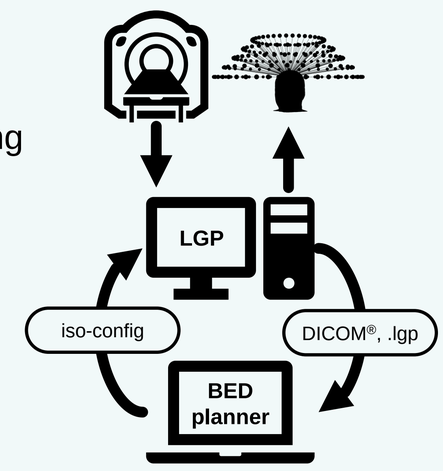
→ ***Order of delivery should be considered during treatment planning***

Custom Optimisation Framework

- BED treatment planning studies require access to: iso-centre number, location, configuration, weighting factor, and order of delivery

→ **Development of a BED planning tool** in python to be used as a testing environment for different methodological approaches

- Inverse planning is enabled by updating dose-rate maps during an iterative process
  - Tissue maximum ratio 10 (**TMR10**) algorithm relates a calibration dose-rate measurement to the dose-rate at arbitrary query point by scaling according to the patient geometry [3]
  - Source geometry is estimated (**Figure 2**)



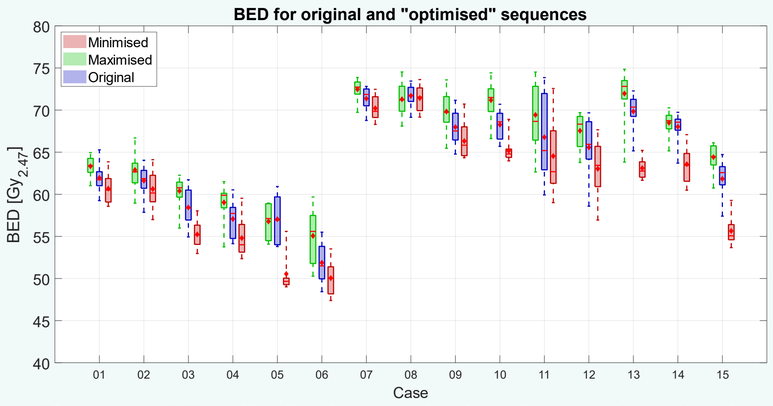
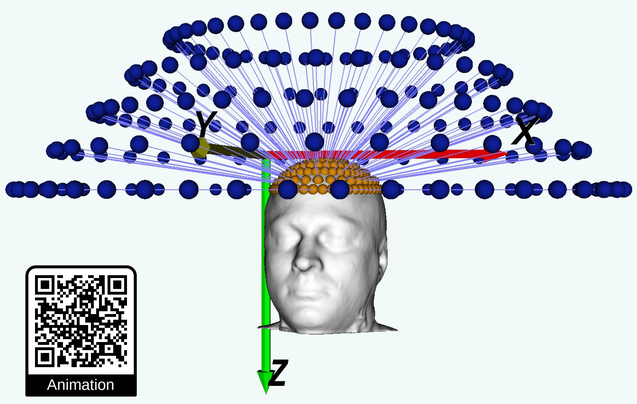
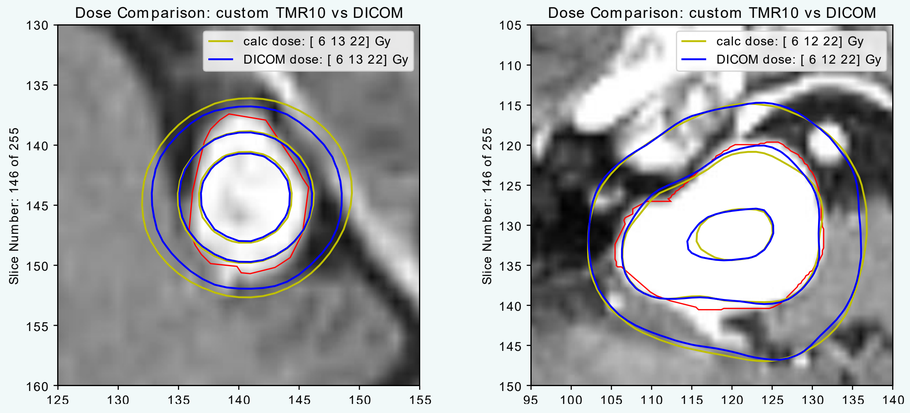


Figure 1: BED distribution on the iso-dose surface for the minimised, maximised, and original shot sequences. The boxplot shows the 25-75% quantile, the maximum, and the minimum BED. The median and mean BED are marked by a red line and diamond, respectively.



(a)



(b)

Figure 2: (a): Approximated source positions (blue) and resulting skull entry points (brown) for a single iso-centre. **(b):** Axial slice of a single iso-centre (left) and 13 iso-centre treatment plan (right) for a vestibular schwannoma (red). Iso-dose lines show the export from LGP (blue) and our TMR10 implementation (yellow).

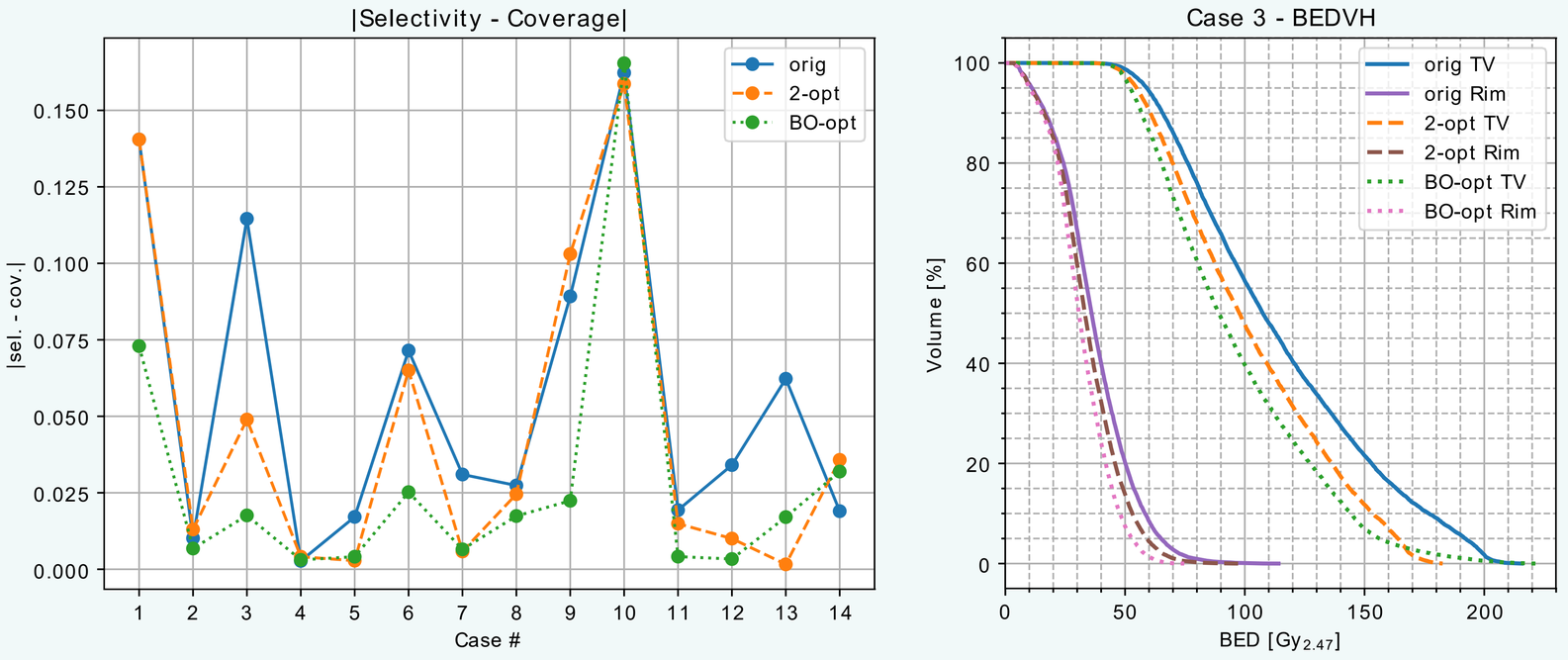


Figure 3: Difference in quality parameters for selectivity and coverage (**left**) and an example of a BEDVH (**right**) after optimisation using an evenly weighted objective function (preliminary results).

Progress & Outlook

Available now: Data import/visualisation, dose/BED calculation, customisable objective function and optimisers for iso-centre sequencing (2-opt) and beam-on time using L-BFGS-B. (Preliminary results: **Figure 3)**

Next steps: Implementation of optimisation techniques for remaining treatment variables and methods to combine these into an inverse planning workflow.

Outlook: The complexity of the problem will result in long computation times that are impractical for the current clinical workflow. We will explore machine learning techniques for the prediction of the optimised treatment plan parameters based on the given input.

References

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3. Elekta Instrument. Inverse Planning in Leksell GammaPlan 10 *[White Paper]*. Technical Report Article No. 018880.02, Elekta Instrument AB Stockholm, Sweden, 2011.

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