# IN VITRO STUDY OF DOSE RATE EFFECT ON LEKSELL GAMMA KNIFE PERFEXION

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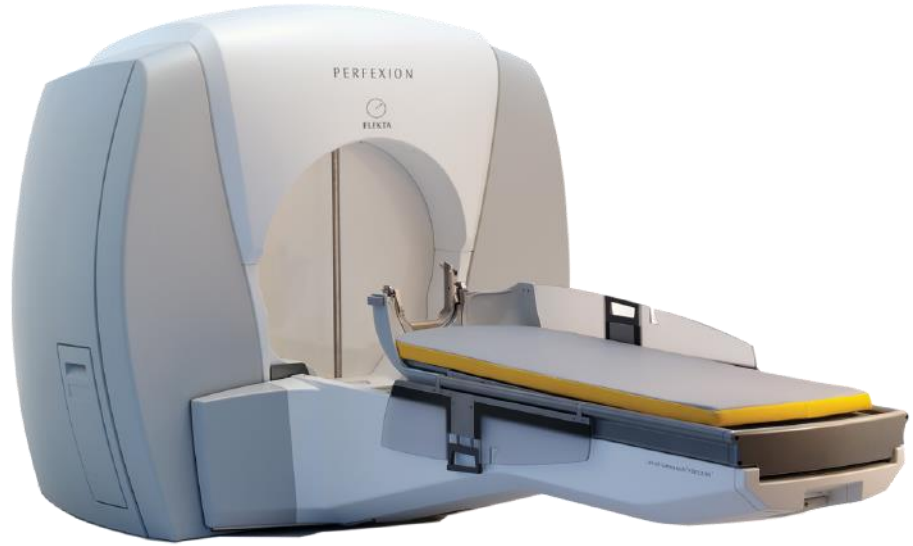
# OBJECTIVES OF THIS STUDY

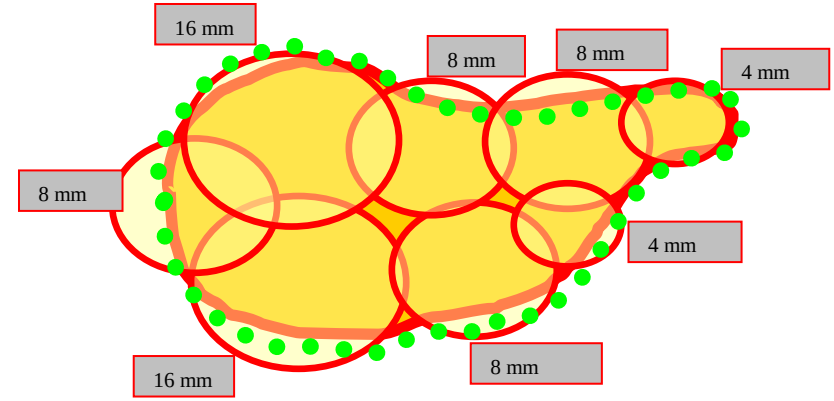
- To study and evaluate effect of dose rate in Leksell Gamma Knife clinical conditions
- This in vitro study is a pilot experimental work performed with meduloblastoma DAOY cells



# DOSE RATE CHANGES

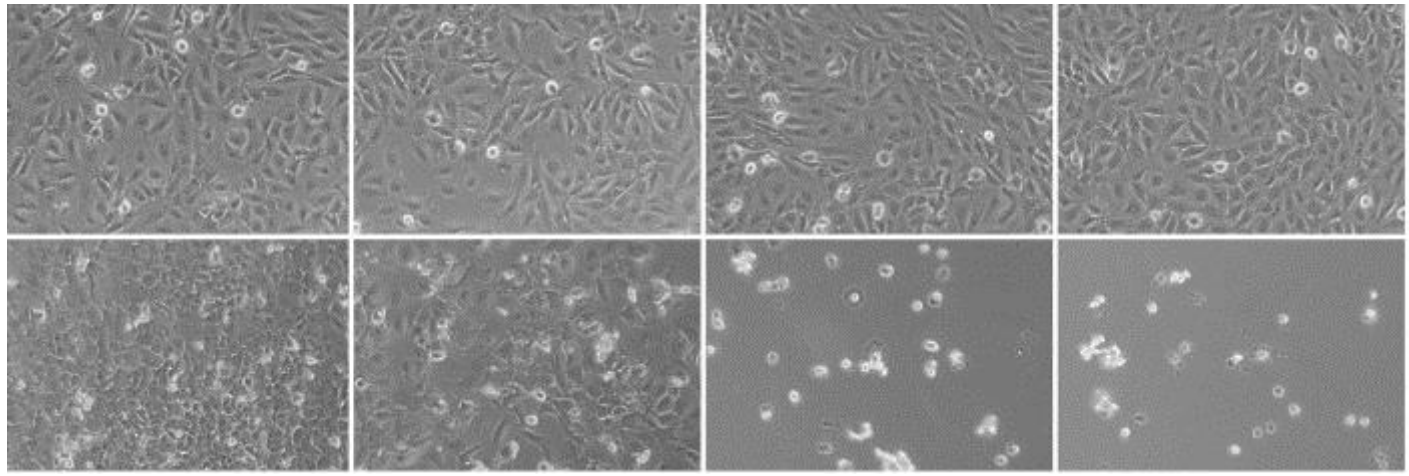
In principle there are two reasons why dose rate on Leksell Gamma Knife (LGK) is being reduced during patient irradiation:

- Co-60 sources decay with half-life of 5.26 years - less important
- Overall irradiation time is being extended by using multiple isocenters and conformal treatment plans with many small isocenters or blocked beams - more important



# DAOY CELLS

- Meduloblastoma cell line (human brain tumor cells)
  - Radiosensitive, sessile cells, forming colonies
- Clonogenic assays – evaluation of surviving fraction and $\alpha/\beta$ parameter for different doe rates of LGK Perfexion



# In vitro study of dose rate effect on Leksell Gamma Knife Perfexion

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## Motivation

The main purpose of the study is to evaluate the radiobiological effect of the dose rate changes in Leksell Gamma Knife (LGK) clinical conditions.
In principle there are two reasons why dose rate on LGK is reduced during patient irradiation: 1) Co-60 sources decay with a half-life of 5.26 years and 2) using multiple isocenters and conformal treatment plans (e.g. with blocked beams). This pilot study is an experimental work performed in vitro with medulloblastoma DAOY cells. Are there effects caused by low dose rate which could negatively influence the clinical outcome of the radiosurgery?

## Introduction

There is often discussed, that the radiobiological effect of the ionizing radiation depends not only on the total dose or the dose in one fraction but also on the dose rate. For the higher dose rate used for the irradiation, there is a higher probability of the double-strand break.

In the stereotactic LKG treatment plan, there are significant changes in the dose rate due to the use of multiple isocenters and also due to the Co-60 sources decay. One target volume can be thus treated by the whole scale of the dose rates.

LGK Perfexion in Na Homolce Hospital in Prague is used for the treatment of more than 400 patients with malignant tumors every year.
Medulloblastoma DAOY cells were chosen as representative malignant tumor cells suitable for clonogenic assays.

## Methods and Materials

A number of repeated experiments were performed with medulloblastoma DAOY cells irradiated on LGK Perfexion by several various dose rates in ranges 0.35 – 3.31 Gy/min. The irradiation was performed in a spherical Elekta ABS plastic phantom with the special insert for the Eppendorf tube containing cells.

Leksell GammaPlan treatment planning software was used to plan cell irradiation. The control of the different dose rates of LGK was achieved by two ways: 1) reloading of the Co-60 sources in our hospital after performing the first experimental campaigns and 2) sector blocking of the LGK collimator (0, 4 or 6 of 8 sectors of LGK were blocked to achieve full, half or quarter dose rate). To ensure homogeneous irradiation of the cells 16 mm collimator was used. Plating efficiency and surviving fraction were determined for each experimental cell sample. Nine different doses in the range 0 – 6 Gy were used to have enough experimental points to obtain a surviving curve. The Linear quadratic model was used to fit experimental data. Surviving curves for different dose rates were plotted and compared, as well as the α/β parameters.

All the experiments were designed to correspond with the conditions of the stereotactic radiosurgery performed by LGK.

## Results

The results obtained from the clonogenic assays on the medulloblastoma DAOY cells show partially predicted dependence.

It is possible to compare three surviving fraction curves obtained from the experiments performed with the dose rates 0.372 – 0.382 Gy/min, 0.743 -0.764 Gy/min and 1.485 - 1.600 Gy/min. Each dose rate was used for various independent experiments (at least six for each dose rate) and the surviving fraction curves shown in Figure 1 were obtained as the mean value of all performed experiments.

The negligible changes of the dose rate used for one surviving fraction curve come from the Co-60 decay. From all the surviving fraction were calculated the values of α/β and their uncertainties. Those results are shown in Figure 2.

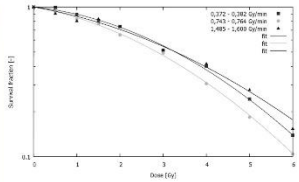


**Figure 1:** Surviving fraction for three different dose rates

## Discussion

This is an initial pilot study with very preliminary data. However, based on so far obtained data, higher cell survival could be observed for dose rates lower than 0.40 Gy/min compared to higher dose rates over 0.75 Gy/min. Currently, experiments continue with dose rates 1.60 – 3.31 Gy/min taking into account more biological endpoints of the irradiation.

From the first data, the dependence of α/β on the dose rate can be evaluated. It shows the linear dependence where the parameter α/β increases with the increasing dose rate. However, it is necessary to perform following experiments including more different dose rates of LGK.

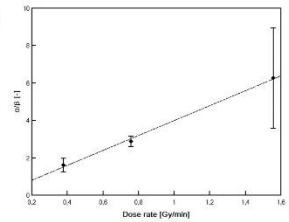


**Figure 2:** Dependance of the α/β parameter on the dose rate of the cobalt sources

## Conclusions

Preliminary data from this study do show different cell survival for studied medulloblastoma DAOY cells based on a dose rate that was used for an irradiation. Higher survival is observed for a lower dose rate. However, more experimental work, including determination of the wider range of cell response parameters such as apoptosis, senescence induction in normal and cancer cell lines, is needed to provide data beneficial for clinical practices of gamma knife.

**Figure 3:** The insert for the eppendorf tube irradiation

**Figure 4:** Setup of the PMMA phantom with the eppendorf tube for the LKG irradiation

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