The relative biological effectiveness (RBE) is defined as the ratio of the doses required by two radiations to cause the same level of effect. Thus, the RBE depends on the dose and the biological endpoint.

Proton therapy has been based on the use of a generic RBE of 1.1, which is applied to all treatments independent of dose/fraction, position in the irradiated volume, initial beam energy or the particular tissue. The variability of RBE in clinical situations is believed to be within 10% but quantitative dependencies of the RBE on various physical and biological properties are disregarded. The magnitude of RBE values and their variations is significantly larger for Carbon ion therapy. Studies have demonstrated significant RBE values of more than 3 in clinically relevant scenarios for Carbon ions. Further, there might be considerable variations in RBE within the irradiated volume that are being considered in treatment planning and delivery Heavy ions have a potential advantage compared to protons when it comes to their therapeu-

Heavy ions have a potential advantage compared to protons when it comes to their therapeutic ratio due to an elevated RBE in the tumor (based on the oxygen enhancement ratio and higher average LET values) compared to the surrounding tissue. However, on the other hand, at present there are still considerable uncertainties in heavy ion RBE values.

Elevated RBE values (even for protons) might be expected particularly near the edges of the high-dose volume because doses may be deposited by high-LET particles. The increase in RBE as a function of depth in the patient results in an extension of the bio-effective range of the beam. Further, because RBE values may increase with deceasing dose causing elevated RBE values for organs at risk compared to the target area.

In order to incorporate detailed RBE modeling in treatment planning as a function of LET, dose and endpoint, two aspects have to be considered. Firstly, the available information from experimental studies and secondly, our ability to calculate RBE values for a given treatment plan based on parameters extracted from such experiments. RBE values are often based on cell survival data because this is the main endpoint of interest in radiation therapy. However, one migt expect differences in RBE for cell survival compared to cell mutation, the latter being an important endpoint for late effects.

This educational session will focus on summarizing the mechanisms behind RBE variations among treatment modalities. Further, RBE variations as a function of LET, tissue and dose will be presented based on experimental and simulated data for proton and Carbon ion beams. Finally, different approaches for theoretical modeling of RBE values for treatment planning purposes will be discussed briefly.

## **Educational Objectives:**

- 1. Understand the mechanisms behind heavy charged particle RBE values
- 2. Understand the variations of RBE as a function of physical and biological parameters
- 3. Understand the clinical implication of RBE values in proton and Carbon ion therapy