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 needs to be considered if dose constraints from photon therapy are to be adopted. 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, beam energy or the tissue. Quantitative dependencies of the RBE on various physical and biological properties are disregarded. The variability of RBE in clinical situations is believed to be within 10%. Elevated RBE values might be expected particularly near the edges of the high-dose volume because doses may be deposited by high-LET particles. Furthermore, the increase in RBE as a function of depth in the patient results in an extension of the bioeffective range of the beam, which is being considered in treatment planning. The magnitude of RBE values and their variations is significantly larger in Carbon ion therapy than in proton therapy. 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, there are considerable variations in RBE within the irradiated volume that have to be considered in treatment planning and delivery. At present there are still considerable uncertainties in RBE values and their dependencies on dose, LET, and alpha/beta ratio. This presentation will illustrate the magnitude of RBE variations in proton and Carbon beams. Furthermore, it will demonstrate the clinical significance for proton therapy treatments involving tissues with low alpha/beta ratio and show a method for biologically optimized treatment planning in proton therapy.