The principal feature and physical advantage of proton radiation therapy is the finite range of protons in the patient. In a pristine proton pencil beam (ignoring effects of finite energy spectrum and finite source size), the distal dose gradient is, for all relevant energies, approximately twice as steep as the lateral gradient. What is not so good is that the localization of the distal dose gradient in the patient can be quite uncertain. The advantage of the distal dose gradient is therefore not currently used in clinical practice for tight conformation. Rather, conformation through lateral dose shaping is preferred. Uncertainties arise from several sources: dose calculation approximations, biological considerations, setup and anatomical variations, and internal movements of low and high density organs into the beam path. Organ motion also has a major impact on the range, which is managed by adding a distal safety margin. These margins reduce the benefit of proton therapy in treatment sites where the physical properties of protons could make a significant difference, such as lung cancer. Altogether, the physical advantage of proton therapy is not fully translated into a maximized dosimetric benefit in the patient. Furthermore, tangential avoidance of critical structures and use of patch fields, as currently practiced, increases the complexity of treatment and the number of beams.

To fully utilize the finite proton range for clinical treatments, developments in three areas are necessary:

1. Management and reduction of organ motion. Organ motion can have a more severe effect on proton dose distributions than on photon dose distributions. This is because, to first order, photon therapy produces a static "dose cloud", and organs move within this fixed dose cloud. This assumption is not valid in proton therapy.

2. Improved dose calculation. Proton dose distributions and the end of proton range are strongly affected by, for example, metal implants and their resulting CT artifacts. Hence, a careful CT to stopping power conversion and correction of artifacts are required. Monte Carlo calculations can improve the dose calculation accuracy near the end of range, and model the range degradation effect more accurately. Some kind of in vivo dosimetry is also highly useful in proton therapy. One option is to do PET imaging of the positron emitters that are produced through nuclear interactions of the proton beam in the patient.
3. Reduction of the impact of residual uncertainties through robust treatment planning and intensity modulated proton therapy. Through a careful design of intensity modulated

proton therapy plans the dosimetric effect of range uncertainties can be reduced.

Educational objectives:

- 1. Estimate the magnitude of range uncertainties in various sites such as lung and prostate.
- 2. Be able to explain the "static dose cloud" assumption and why it breaks down in proton therapy
- 3. Name at least three methods to reduce range uncertainties.
- 4. Explain concept of robust proton treatment planning and tangential avoidance