Purpose: To develop an inverse optimization algorithm that is capable of generating non-uniform dose distribution with sub-regional dose escalation based on spatially inhomogeneous radiosensitivity in the target, while keeping the critical structure doses as low as possible.

Method and Materials: A matlab package with GUI was developed. The software system reads in structure contours, reference 3D-dose distribution (e.g., conventional uniform dose), dose to each voxel from all beamlets, as well as the voxel radiosensitivity from biological images. This system is able to optimize beamlet weights based on sequential quadratic programming (SQP) method to achieve maximum equivalent uniform dose (EUD) for target and minimum EUD for critical structures. The beamlets were generated using a commercial planning system (XiO, CMS). The EUD was calculated based on 3D-dose distribution and spatial radiosensitivity distribution which is extracted from biological images. Constraints that limit the doses to critical structures not to exceed the corresponding maximum for the reference plan are applied. Sample spatial radiosensitivity distributions based on physiological MRI of brain tumor were used to test the developed system. DVHs and EUDs for the uniform and non-uniform dose distributions are compared.

Results: Using the newly develop system, we have generated non-uniform 3D-dose distributions for selected patient cases. Sub-regional dose escalation can be as high as 30% of the uniform dose as planned conventionally. The target EUDs are found to be higher than those for the uniform dose planned ignoring the spatial inhomogeneous radiosensitivity. The EUDs for organs at risk are found to be equal or lower than those for the uniform dose plans.

Conclusion: We have developed a package that is capable of generating non-uniform dose distributions optimized for spatially inhomogeneous radiosensitivity. Sub-regional dose escalation may lead to increased treatment effectiveness as indicated by higher EUDs. The current development will impact biological image guided radiotherapy.