Purpose: Setup, range and anatomical uncertainties influence the dose delivered with proton pencil-beams, but a quantification of these errors for intensity-modulated proton therapy (IMPT) for oropharyngeal cancer is lacking. The purpose of this work is to quantify these effects. We also investigate whether treatment plans are more robust against errors when more beam directions are applied.

Methods: We used an in-house developed inverse treatment planning system for proton pencil-beam scanning, which performs multi-criteria optimization. First, treatment plans for 3, 5, and 7 beam directions were created for 5 oropharyngeal cancer patients. A simultaneous-integrated boost technique was used, prescribing 66Gy and 54Gy to high and low dose regions, respectively, delivered in 30 fractions. Second, 300 treatment simulations were performed, recalculating the dose while including uncertainties. Anatomical uncertainties were taken into account by using two CT scans per patient. For setup errors an online setup-protocol was simulated. DVH parameters were used for dose evaluation.

Results: The treatment plans were of high quality, with good target coverage and excellent OAR sparing. However, setup, range and anatomical uncertainties can lead to large differences between the planned and delivered dose. For the 3-beam plans, the expected V95% of the high-dose CTV reduced from 100% (planned) to on average 92% (range: 82-98%), and the expected V107% increased from 1.3% (planned) to on average 4.2% (range: 0.1%-6.7%). The expected V95% of the low-dose CTV reduced from 100% (planned) to on average 94% (range: 86-99%). The dose to the OARs generally increased. The plans with more beam directions were not more robust against errors (p>0.05).

Conclusions: Setup, range and anatomical uncertainties in IMPT for oropharyngeal cancer patients can lead to considerable underdosage of the target volume, which should be accounted for by replanning and/or robust optimization techniques. Robustness is not achieved by increasing the number of beam directions included in the treatment plan.