Purpose:
Intensity-modulated proton therapy (IMPT) has a great potential to further advance proton therapy. However, it is widely accepted that IMPT is very sensitive to uncertainties. The worst-case analysis (WA) originally proposed by Lomax has been adopted in our institute to evaluate IMPT plan sensitivity to range and setup uncertainties. Here, we propose an evaluation method by exhaustively sampling uncertainties and apply it to validate WA.

Methods:
A series of perturbations to modify proton beam ranges and to shift the iso-center in x-, y- and z-directions were sampled for 500 times to generate the probability distribution of plan qualities. The magnitude of a perturbation was assigned randomly following a normal distribution with specified standard deviations in each perturbation dimension. Perturbed dose was calculated for each sampling and compared to the WA dose. Dose-volume-histograms (DVH) were obtained for all perturbed doses. The distribution of DVHs and dose-volume indices were examined. Prostate and head/neck cases were selected for demonstration.

Results:
In both cases, the DVHs of 500 perturbed doses spread over bands with various widths, and the DVH curves of WA lie within these bands and near the “worst” edges. For CTV, 97.6% in the prostate case and 97% in the head/neck case of the perturbed doses show a D95 value higher than the value given by WA. For normal tissues, at least 96.4% of the perturbed doses show lower dose-volume indices (e.g. V70 of rectum and bladder) than the ones by WA.

Conclusions:
After exhaustively sampling the possible uncertainties, we verified that the worst-case analysis may reasonably evaluate the IMPT plan sensitivity to setup and range uncertainties without considerably over- or under-estimating it. The exhaustively sampling approach proposed here could offer a great outset toward comprehensively evaluating the IMPT plan sensitivity to a broader spectrum of planning and delivery uncertainties.