recently observed no reductions of late fecal incontinence rates in a prostate cancer population treated with image-guided intensity modulated radiotherapy (IGIMRT), with a large anal canal dose reduction compared to a 3D conformal RT (3DCRT) population, although significant reductions of 'increased stool frequency' and 'mucous discharge' were observed. It is currently unknown which local dose distributions are associated with fecal incontinence using IGIMRT and whether this differs from 3DCRT. Such knowledge is essential for treatment optimization strategies. We explored dose-effect relationships by constructing dose surface maps of the anorectum for both 3DCRT and IGIMRT patients.

Material and Methods

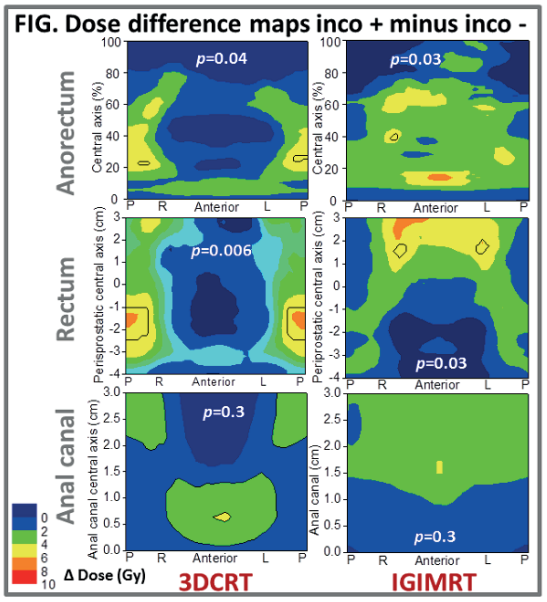
Selected study patients were treated to 78Gy (39x2Gy) with either 3DCRT (n=189) or IGIMRT (n=242), in two different prospective studies with identical toxicity questionnaires. Bladder and anorectum were delineated as Organ at Risk. Three types of maps were calculated: (1) total anorectum using regular intervals along a central axis with perpendicular slices, (2) the rectum next to the prostate, and (3) the anal canal (horizontal slicing). Dose maps were constructed and averaged over patients with and without incontinence, and dose difference maps were generated. Significance testing was based on a permutation method. Contours were drawn around regions with p<0.05.

Results

Patient-reported rates of fecal incontinence (y1-y3) were 37% (3DCRT) and 34% (IGIMRT) versus <5% at baseline. Local anorectal dose levels and dose variations were different between both techniques because of different margins, steeper dose gradients, and differen t beam angles. Dose difference maps (Figure) for the anal canal showed no dose-effect for either technique (p=0.3). The anorectal and rectal mapping showed significant local effects for both techniques, with observed dose differences mainly in the lower part of the rectum for 3DCRT, and mainly in the upper part for IGIMRT.

Conclusion

Rectal dose is associated with fecal incontinence risks and therefore treatment optimization to reduce fecal incontinence risks seems feasible for both 3DCRT and IGIMRT. However, we currently do not fully understand the underlying mechanisms causing fecal incontinence after radiotherapy with either 3DCRT or IGMRT. Further investigations are urgently needed. For the purpose of optimal planning strategies, delineation of additional structures at risk might be indicated, such as the muscles and nerves associated with the complex process of defecation.



PO-0930 Influence of inhomogeneous radiosensitivity and intrafractional movement on TCP in prostate cancer

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Purpose or Objective

The study investigates the influence of inhomogeneous radiosensitivity distributions and intrafractional organ movement in primary prostate cancer (PCa) patients on the tumour control probability (TCP) for IMRT treatment plans including simultaneous integrated boosts (SIBs).

Material and Methods

The simulation study includes 13 contoured cases of patients with PSMA PET/CT prior to prostatectomy. There are two different GTVs for each simulation case: GTV-PET and, based on co-registered histology slices of the resected prostatic gland, GTV-histo, which is considered being the true PCa volume. IMRT plans are created to administer 77 Gy in 35 fractions to the whole prostate and up to 95 Gy to PTV-PET in a SIB (FLAME trial dosimetry protocol). TCP is calculated for the actual tumour volume GTV-histo, using the Poisson distribution and the linear quadratic model. The impact of reduced tumour radiosensitivity on the TCP is simulated by increasing cell survival probability at a 2 Gy fraction by 0% to 30% in 1%-steps. This is achieved by adjusting the values of the α and α/β LQ-parameters of randomly chosen proportions of voxels (ranging from 0% to 50% in 1%-steps) within the PCa volume. Intrafractional prostate movements are simulated by applying asymmetrical Gaussian filtering on the 3D dose matrix (grid size 1 mm^3). For every case, TCP is calculated for every combination of radiosensitivity levels and affected

populations in the true tumour volume with and without intrafractional movement (averaged over a minimum of 10^4 simulations to account for the randomized distributions).

Results

TCP results are presented in figure 1 for all radiosensitivity patterns, averaged over the normalized TCP results of all cases. Decreasing tumour radiosensitivity by 10-20% compared to the baseline scenario already leads to TCP reductions of up to 2-24% and 10-68% for 1% and 5% affected tumour voxels, respectively. More importantly, changes in radiosensitivity and TCP do not correlate linearly. Instead, there is a sudden breakdown of the TCP values within a small range of radiosensitivity reduction levels. Intrafractional movement increases the TCP by up to 10.2% in individual cases and by up to 1.2% averaged over all cases if no or only small decreases (<7%) in radiosensitivity are applied (figure 2). This can be explained by the observed mismatch between imaging based SIB volume and actual tumour volume. For lower radiosensitivity levels however, intrafractional movement results in a decrease of the TCP.

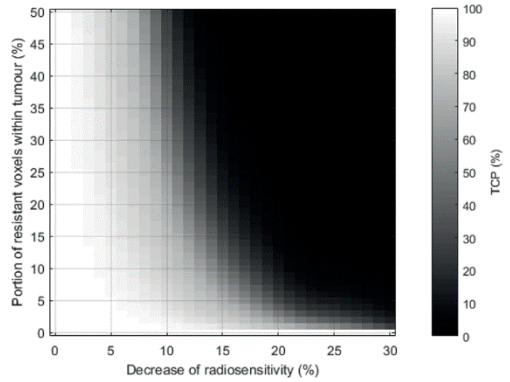

Figure 1 Mean values of the normalized TCP results from all 13 simulated cases. TCP is shown in dependence on the portion of resistant voxels within the cancer tissue and their respective decrease of radiosensitivity. No intrafractional movement is assumed.

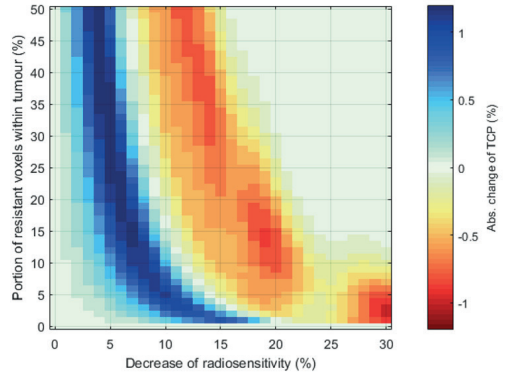

Figure 2 Influence of intrafractional movement on the TCP, given as absolute changes of TCP as a function of the level of decrease of radiosensitivity and size of affected tumour volume.

Conclusion

Even low decreases of the assumed radiosensitivity in very few PCa voxels result in a significant reduction of TCP values. For tumours with medium levels of radioresistance, moderate intrafractional movements can actually increase the TCP for IMRT plans including a SIB, if the prescription dose outside of the SIB volume is sufficiently high.

PO-0931 Dependency of patient risk stratification on PET target volume definition in Oesophageal cancer

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Purpose or Objective

A personalised approach to therapy is hoped to improve oesophageal cancer survival rates. Recently, the inclusion of radiomic features extracted from PET images into prognostic models has gained substantial interest. However, radiomic features are dependent on the target volume definition (TVD) [1]. Many automatic PET segmentation methods exist and are regularly used for feature extraction. The aim of this study is to investigate the dependency of patient risk stratification on TVD, defined by different PET segmentation methods, when prognostic models are developed with radiomic features.

Material and Methods

Consecutive patients (n=427) with biopsy-proven oesophageal cancer staged with PET/CT were included. Patients received 4MBq/kg of ^{18}F-FDG before image acquisition at 90 minutes. In each case, the Metabolic Tumour Volume was defined using Clustering Means (KM2), General Clustering Means (GCM3), Adaptive Thresholding (AT) and Watershed Thresholding (WT) PET segmentation methods. All tumour segmentations were reviewed by a radiologist to ensure accuracy. Prognostic models using identical clinical data but different radiomic features defined by each segmentation method were developed. Changes in patient classification between risk groups were analysed. A p-value of <0.05 was considered statistically significant. Primary outcome was overall survival (OS).

Results

Age, treatment and radiological stage were significant variables in all prognostic models. Skewness was a significant variable in GCM3 and WT based models. Table 1 shows the number (percentage) of patients that changed risk stratification between developed prognostic models. Figure 1 shows the overall survival for the KM2, GCM3, AT and WT developed models. There was no significant difference in median OS between KM2, GCM3, AT and WT low risk groups (P > 0.5), intermediate-risk (P > 0.5) and high-risk groups OS (P > 0.5).