OC-0067: An automated patient-specific and quantitative approachfor deformable image registration evaluation

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Conclusion: Salvage I-125-BT patients can be selected based on their disease free survival interval after primary therapy and the PSA-doubling time pre-salvage, ensuring sufficient biochemical control of >70% until three years.

OC-0065

Risk of second malignancies after seed prostate brachytherapy as monotherapy in a single institution

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Purpose or Objective: To report the incidence of second primary cancer (SPC) after Iodine-125 brachytherapy for early prostate cancer in a single institution with an intense urological surveillance and to compare it with the cancer incidence in the Australian population

Material and Methods: This retrospective, single-institution study included 889 patients treated with Iodine-125 brachytherapy alone. All the patients had a baseline cystoscopy before the implant. Data were collected on all subsequent SPC diagnoses. SPC incidences were retrieved for all type of cancers and for cancers close to the radiation field. Interval since the implant was evaluated for potential association to the treatment. Standardized incidence ratios (SIRs) were calculated for all cancers and for bladder cancers and matched with the general population. The absolute excess risk (AER) was expressed in relation to 10000 persons-years in the study. Kaplan-Meier analysis was used to determine the actuarial second malignancy and pelvic malignancy rates and the death from SPC and from any cause

Results: Patients were followed for a median of 4.16 (0-12) years with 370 (42 %) patients having 5 years or more follow up. 62 % patients were older than 60 years. 61 patients (6.8%) subsequently developed a SPC with 12 pelvic malignancies : 8 bladder and 4 rectal cancer. The 5- and 10- year cumulative incidences are 6.9% (95% Confidence Interval 5.0-9.4) and 19% (95% CI 14-26) for any second malignancy, 1.3% (95%CI 0.6-2.7) and 3.9% (95% CI 1.9-7.8) for any pelvic malignancy and 1% (95% CI 0.4-24) and 3.2% (1.4-7.1) for bladder cancer, respectively. The SIR was significantly higher for all pelvic malignancies at 2.10 (95% CI 1.09-3.67) and for all bladder cancers at 3.33 (95% CI 1.44-6.57). In the subgroup analysis bladder SPC risk was higher than expected for patients under 60 years (SIR 6.52; 95%CI 1.3-19; AER 13) and within the first 5 years of follow up (SIR 2.9 ; 95% CI 0.97-6.95; AER 10). Rectal cancer SIR were not significant or close in any of the categories. The 5- and 10-year rates of death from SPC were 1.9 % (95% CI 1.0-3.5) and 9.1% (95% CI 5.2-16) and from any cause were 3.2% (95% CI 2-5) and 14.4% (95% CI 9.5-21.6). On multivariable analysis, older age was associated with increased SPC risk (HR 1.05, p=0.021) , all cause mortality (HR 1.13, p<0.001) and mortality due to SPC (HR 1.09, p=0.014). Smoking status was associated with all cause mortality (HR 2.15, p=0.026) and with mortality from second malignancy (HR 2.59, p=0.045)

Conclusion: There may be an increased but small risk of second pelvic malignancy after prostate brachytherapy. A tendency towards a higher risk of bladder SPC after brachytherapy was found in the first 5 years of follow-up , probably resulting from screening bias . There was no significant increased rate of rectal cancer in any of the categories. Longer follow up is needed to draw strong conclusions.

OC-0066

Adaptive cone-beam CT planning improves progression-free survival for I-125 prostate brachytherapy

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Purpose or Objective: To determine the independent effect of additional intraoperative adaptive C-arm cone-beam computed tomography (CBCT) planning versus transrectal ultrasound (TRUS)-guided interactive planning alone in primary permanent I-125 brachytherapy for prostate cancer on long term biochemical disease free survival (bDFS).

Material and Methods: All patients with biopsy proven T1/T2-stage prostate cancer treated with I-125 brachytherapy were included in this cohort. Treatments were performed with TRUS-guided primary brachytherapy (+/- neoadjuvant hormonal therapy (NHT)) in a single institution in the period of November 2000 to December 2014. From October 2006 onwards, all patients received additional intraoperative adaptive CBCT planning for dosimetric evaluation and, if indicated, subsequent remedial seed placement in underdosed areas (which was performed in 15% of all patients). These procedures lasted 1-1.5 hours and were performed by a team of 2 radiation oncologists and 2 therapeutic radiographers. Pre-operative characteristics, follow-up PSA and mortality were prospectively registered. Patients were stratified into National Comprehensive Cancer Network (NCCN) risk groups. Kaplan-Meier analysis was used to estimate bDFS (primary outcome), overall survival (OS) and prostate cancer specific survival (PCSS) (secondary outcomes). Cox-proportional hazard regression was used to assess the independent predictive value of CBCT use on biochemical failure (BF) (Phoenix definition) and overall mortality (OM).

Results: 1623 patients were included. Median follow-up was 99 months (interquartile range (IQR) 70-115) for TRUS patients (n=613) and 51 months (IQR 29-70) for CBCT patients (n=1010). BF occurred 203 times and 206 patients died, of which 26 due to prostate cancer. For TRUS and CBCT patients, estimated 7-year bDFS was 87.2% vs. 93.5% (log rank: p=0.04) for low risk patients, 75.9% vs. 88.5% (p<0.001) for intermediate risk patients and 57.1 vs. 85.0% (p<0.001) for high risk patients. For TRUS and CBCT patients with low, intermediate and high risk disease, estimated 7-year OS was respectively 86.5% vs. 90.4% (p=0.11), 79.6% vs. 85.1% (p=0.30) and 66.4% vs. 84.2% (p=0.01). For TRUS and CBCT patients, 7-year PCSS was 96.0% vs. 100% (p<0.0001). After Cox regression, CBCT patients had lower rates of BF: HR 0.45 (95%-CI 0.33-0.61; p<0.0001). Corrected for age, IPSA, Gleason grade, T-stage, NHT-status and duration of NHT use, year of implantation, activity of the implant and prostate volume, CBCT showed to be an independent predictor of BF: HR 0.54 (95%-CI 0.33-0.89; p=0.02). CBCT was not an independent predictor of OM: HR 0.66 (95%-CI 0.40-1.07; p=0.09).

Conclusion: Additional intraoperative adaptive C-arm cone-beam CT planning in I-125 prostate brachytherapy leads to a significant increase in biochemical disease free survival in all NCCN risk groups.

Proffered Papers: Physics 1: Images and analyses

OC-0067

An automated patient-specific and quantitative approach for deformable image registration evaluation

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Purpose or Objective: In adaptive radiotherapy, deformable image registration (DIR) is used for contour propagation and dose warping. Contour evaluation is visual and qualitative and only accurate in high contrast regions. Dose warping requires fully spatial and quantitative DIR evaluation measures also valid in low contrast regions. While

quantitative measures such as the target registration error can be used during commissioning, such measures are not fully spatial and too user intensive in clinical practice. Therefore, we propose a fully automatic and quantitative approach to DIR quality assessment including multiple measures of numerical robustness and biological plausibility.

Material and Methods: Ten head and neck cancer patients who received weekly repeat CT (rCT) scans were included. Per patient, the first rCT was deformable registered (using B-spline DIR algorithm) to the planning CT. The ground-truth deformation error of this registration was derived using the scale invariant feature transform (SIFT), which automatically extracts and matches stable and prominent points between two images. Moreover, complementary quantitative and spatial measures of registration quality were calculated. Numerical robustness was derived from the inverse consistency error (ICE), transitivity error (TE), and distance discordance metric (DDM). For the TE calculations a third CT was used. The DDM was calculated using five CT sets per patient. Biological plausibility was based on the deformation vector field between the planning CT and rCT. Relative deformation threshold values were set based on physical tissue characteristics: 5% for bone and 50% for soft tissues. All measures were evaluated in bone and soft tissue structures and compared against the ground-truth deformation error.

Results: On average, SIFT detected 133 matching points scattered throughout the planning CT, with a mean (max) registration error of 1.6 (8.3) mm. Our combined and fully spatial DIR evaluation approach, including the ICE, TE and DDM, resulted in a mean (max) error of respectively 0.6 (2.0), 0.7 (2.7), and 0.6 (2.7) mm within the external body contour, averaged over all patients. The largest errors were detected in homogeneous regions and near air cavities. Furthermore, 87% of the bone and 2% of the soft tissue voxels were classified as unrealistic deformations. Figure 1 shows the planning CT, DDM, tissue deformation, and error volume histograms of the ICE, TE, and DDM of the body contour of one patient.

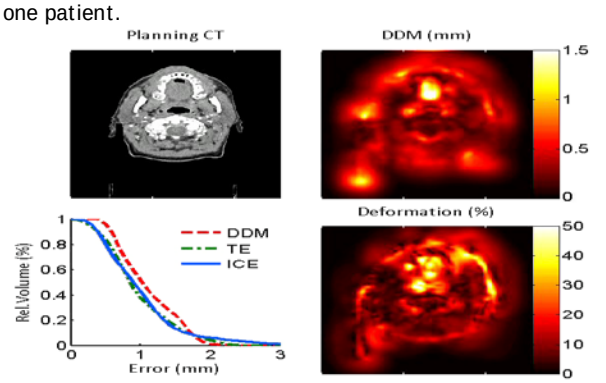

Figure 1. Axial cross section of a planning CT, distance discordance metric (DDM) and tissue deformation of a representative patient. The error volume histograms show the DDM, transitivity error (TE), and inverse consistency error (ICE) of the body contour.

Conclusion: The combination of multiple automatic DIR quality measures highlighted areas of concern within the registration. While current methods on DIR evaluation, such as visual inspection and target registration error are time-consuming, local, and qualitative, this approach provided an automated, fully spatial and quantitative tool for clinical assessment of patient-specific DIR even in image regions with limited contrast.

OC-0068

Can atlas-based auto-contouring ever be perfect?

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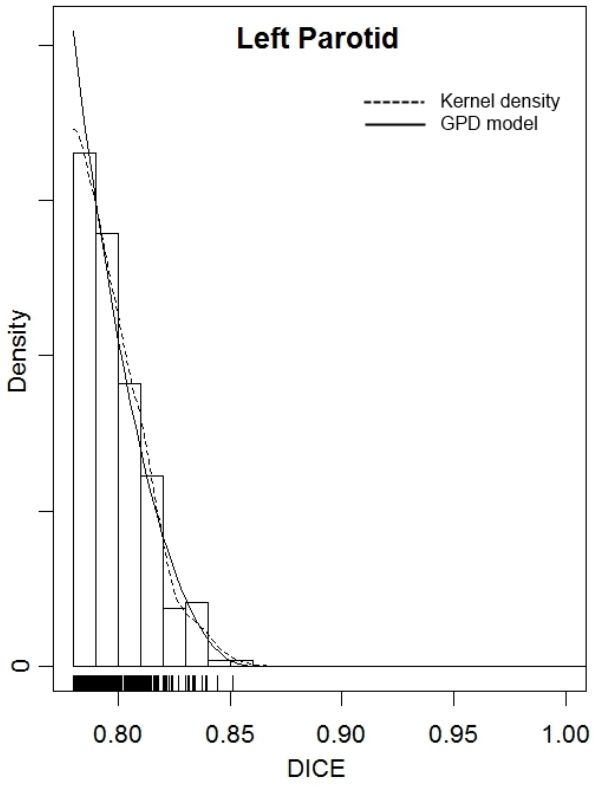
Purpose or Objective: Various approaches have been proposed to select the most similar atlases to a patient for atlas-based auto-contouring. While it is known that increasing the size of an atlas database improves the results of auto-contouring for a small number of atlases, such selection assumes the hypothesis that increasing the atlas pool size always increases the chance of finding a good match. The objective of this study is to test this hypothesis, and answer the question; "Given a large enough database of atlases, can single atlas-based auto-contouring ever be perfect?".

Material and Methods: 35 test cases were randomly selected from a dataset of 316 clinically contoured head and neck cases, and were auto-contoured treating each of the remaining cases as potential atlases to be used. Thus, results of contouring were available for approximately 11000 atlas-patient pairs. Dice Similarity Coefficient (DSC), Hausdorff distance (HD), Average Distance (AD) and Root Mean Square Distance (RMSD) were computed between the auto-contours and the clinical contours for each structure and atlas-patient pair. In order to estimate achievable performance under the assumptions of an infinite size atlas database and "perfect" atlas selection, the Extreme Value Theory statistical technique Points over Threshold, used in other domains to perform tasks such as estimating the magnitude of one-in-a-hundred-years flooding, was used to model the distribution of the best scores. Analysis was performed for the ten most commonly contoured structures within the database, with a minimum of 6800 atlas-patient pairs per structure being considered.

Results: The figure shows the distribution of observed extreme values for the left parotid DICE scores, together with the model fit.



For all measures and structures, the model fit indicated a limit on the performance in the extreme. While this is expected since all measures have a limit at perfection, the performance limit in the extreme fell short of a perfect result. Variation was observed between structures, with well-defined structures performing better than more complex ones. This may indicate that the limit on performance reflects the inter-observer variation in delineation. The table shows the best observed score for the experiments performed, together with the expected achievable result predicted by the model assuming an atlas database of 5000 atlases.