experimental rat model of radiation proctitis, and to assess the severity of microangiopathy.
Materials and Methods: A total of 57 Wistar rats were used. 45 of the rats were exposed to selective rectal irradiation with a single fraction of 25 Gy. These rats were sacrificed at the 4th, 12th, 24th, and 37th week following the irradiation. The remaining 12 rats comprised the control group without irradiation. The microangiopathy was examined pathologically regarding the rectum in 20 mm from the anus of each rat. The absolute number of vessels was counted by microscopy. In addition, the diameter stenosis of stenosed vessel was evaluated and graded the degree from 0 to 4. The specimens of the rats, which had been sacrificed at the 10th day following irradiation in the previous study, were also examined pathologically to compare the differences between acute changes and chronic changes following irradiation.
Results: The sequential changes of radiation-induced microangiopathy were examined well. The microangiopathy was observed selectively in the arteries. The vascular endothelial damage was observed mainly due to nuclear bulging in the rats on the 10th day following irradiation. Whereas, the thickening that accompanied the fibrinoid necrosis after 4th week, and the thickening of endothelial lining was significant later. The absolute number of vessels per individual was 289.7 ($\pm$63.5), 385.8 ($\pm$60.6), 256.6 ($\pm$70.0), 282.1 ($\pm$57.1), and 141.4 ($\pm$47.5) at 4th week, 12th week, 24th week, and the 37th week following irradiation, respectively. The number of vessels was significantly smaller in the rats without irradiation than the irradiated rats and was significantly greater at the 12 weeks following irradiation than the other groups ($P < 0.05$). The degree of stenosis was evaluated in the microvessels microscopically. No significant differences were found among the groups in terms of the proportions of severe vascular stenosis. The proportions of the stenosed vessels that occupied a portion of the absolute number of the vessels were 16.0%, 10.6%, 13.3%, and 14.6% at 4th week, 12th week, 24th week, and the 37th week following irradiation, respectively.
Conclusions: We examined the sequential changes of radiation-induced microangiopathy. Our assessment strategy of microangiopathy seems to be useful to evaluate the severity of late radiation proctitis.

2033 POSTER

Radiation-induced Rectal Toxicity in Rats on Low-dose Aspirin Therapy

H. Doi[1], N. Kamikonya[1], Y. Takada[1], M. Fujiwara[1], H. Miura[1], H. Inoue[1], M. Tanooka[1], T. Nakamura[2], T. Tsujimura[3], S. Hirota[1]. *[1]Hyogo College of Medicine, Department of Radiology, Nishinomiya Hyogo, Japan; [2]The Hospital of Hyogo College of Medicine, Department of Pharmacy, Nishinomiya Hyogo, Japan; [3]Hyogo College of Medicine, Department of Pathology, Nishinomiya Hyogo, Japan*

Background: The purpose of the present study was to establish an animal experimental model of radiation proctitis in rats receiving antiplatelet therapy, and to examine the correlation between the administration of aspirin and the severity of radiation proctitis.
Materials and Methods: A total of 34 female Wistar rats were used. The rats were divided into five groups: aspirin 5 mg/kg/day group (ASA5; n = 10), aspirin 10 mg/kg/day group (ASA10; n = 10), aspirin 20 mg/kg/day (ASA20; n = 7), and saline group (Saline; n = 7). The rats were administered with aspirin at dose of 5, 10, 20 mg/kg or saline orally, day by day before and after irradiation. On the fifth day following the start of administration, all rats were irradiated and the tail transection bleeding time was measured. A single fraction of 25 Gy was delivered selectively for the rectum without any surgical procedures. The administration of aspirin or saline continued daily following irradiation. All rats were sacrificed at the 10th day following irradiation.
The rectal mucosal changes of each rat were evaluated macroscopically and pathologically. In the pathological examination, the severity of proctitis was described the morphological mucosal damage and the degree of inflammation in each specimen.
Results: The bleeding time was prolonged in rats receiving aspirin.
The proportion of the severe changes in macroscopic findings was 100.0%, 50.0%, 66.7% and 66.7% in the ASA5 group, the ASA10 group, the ASA20 group, and the Saline group, respectively. In the morphological mucosal damage, the propotion of the severe changes was 70.0%, 71.4%, 50.0% and 80.0% in the ASA5 group, the ASA10 group, the ASA20 group, and the Saline group, respectively.
There were no apparent correlation between the administration of aspirin and the severity of radiation proctitis in the macroscopic findings, and the morphological mucosal damage in the pathological examination.
The proportion of the severe degrees of inflammation was 90.0%, 100.0%, 16.7% and 100.0% in the ASA5 group, the ASA10 group, the ASA20 group, and the Saline group, respectively. The ASA20 group showed significantly milder inflammation than the other groups ($P < 0.05$).
Conclusions: We established an animal experimental model of radiation proctitis in rats receiving antiplatelet therapy with the use of low-dose aspirin. There were no apparent correlations between the administration of aspirin and the severity of radiation proctitis.
The influence of low-dose aspirin on radiation proctitis is presently under investigation in more detail.

2034 POSTER

Evaluation of Two Registration Strategies for Inter-patient Dose Mapping in Prostate Radiotherapy

G. Dréan[1], O. Acosta[1], J.J. Bellanger[1], A. Simon[1], G. Cazoulat[1], J.D. Ospina[1], J.I.A.N. Zhu[1], P. Haigron[1], R. De Crevoisier[1]. *[1]LTSI, Laboratoire du Traitement du Signal et de l'Image − INSERM U 642, Rennes, France*

Purpose: Compare dose distributions from different patients is necessary to assess correlations between toxicity and organ at risk dose distribution. This comparison implies mappings in a common template. Registration methods are classically validated with spatial overlap metrics (DiceScore (DS)), which are not designed to validate dose mapping (DoM). The objective of the work was to evaluate 2 elastic registration methods by using usual and new metrics.
Methods: The study included 24 patients (pts) receiving 3D conformal radiotherapy for prostate cancer.
Registration Methods: The planning data (CT scan images, contours, dose distribution) of 23 pts were registered on the planning data of the 24th chosen as template (the most representative pt according to mutual information results). Two registration strategies initialized by CT-Scan intensity based affine registration (AR) were used:
- Iconic: a CT-Scan intensity based non-rigid FFD registration was applied to the AR results,
- Hybrid: After AR, distance maps (DiM) were computed for each delineated organ (prostate, bladder, rectum) of each pt and of the template. The CT-Scans images were then combined with the 3 organs DiMs, and an intensity based non-rigid demons registration was applied.

Eventually the elastic transformations were applied to the delineated organs and dose distribution to propagate them in the template.
3 Metrics to validate registration Methods:
- DS between two structures A and B: $DS(A,B) = 2|A \cap B|/(|A| + |B|)$.
- Relative Difference of Areas (RDA): The DVH is assumed to be conserved before (time1) and after (time2) deformation. This conservation can be evaluate by computing the distance (RDA) between normalized DVH1 and DVH2, defined on 0,Dmax
  $RDA = (\int_{[0,Dmax]}(DVH1 - DVH2)\,dx)/\max\{\int_{[0,Dmax]} DVH1\,dx, \int_{[0,Dmax]} DVH2\,dx\}$.
- Dose and Organs Overlaps (DOO): The DOO compares the propagated dose D received by the template organ A and the propagated organ B: $DOO(D,A,B) = (\int_{A \cap B} D(x)\,dx)/(\int_{A \cup B} D(x)\,dx)$.

Results: In heterogeneous dose areas, different RDA/DOO values were found for a same DS, showing the interest of the new proposed metrics. The hybrid registration method provided significantly more accurate results than the iconic one, for each organ and with each metric (t-test, $p < 0.05$).

	Median DS	Median RDA	Median DOO
Iconic	0.69	0.56	0.11
Hybrid	0.75	0.70	0.09

Conclusion: The hybrid registration method using both organs delineations and intensity provides better results than the iconic one and should be used to analyze dose distributions and toxicity from different patients.

2035 POSTER

Early Mortality After 40,670 Courses of External Beam Radiotherapy in Unselected Patients

G. Hall[1], A. Crellin[1], R. Turner[1], K. Franks[1], C. Johnson[1], D. Sebag-Montefiore[1]. *[1]St James's Institute of Oncology, Oncology, Leeds, United Kingdom*

Background: The UK Government have recently published their strategy for cancer, aimed at improving outcomes for patients. In this, they have recommended the measurement of 30 and 90 day mortality after palliative and radical/adjuvant radiotherapy respectively. We are unaware of any published data regarding these end-points in unselected patients and hence feel this outcome measure is poorly defined.
Material and Methods: St James's Institute of Oncology (SJIO) is a regional cancer centre providing radiotherapy for the 2.7 million population

of the Yorkshire Cancer Network. PPM, an in-house electronic patient record, has recorded all cancer treatment delivered since 2003 and through links to local and national demographic services is able to relate this to patient outcome. PPM was therefore used to identify patients undergoing external beam radiotherapy in which treatment intent was recorded as radical, adjuvant or palliative. Median survival and cumulative mortality at 7, 14, 30, 60 and 90 days was calculated with comparisons made by year of treatment, treatment intent and the number of fractions of radiotherapy used.

Results: Between Jan 2004 and Dec 2010 a total of 40,607 courses of radiotherapy were delivered with validated survival data on 40,593 (99.9%). Treatment intent was recorded as radical, adjuvant and palliative in 12,045 (30%), 11,757 (29%) and palliative 16,791 (41%) respectively. Median survival and cumulative mortality for each subgroup is shown in the table.

Intent	Median survival (months)	Cumulative mortality (%) at time point (days)				
		7	14	30	60	90
Radical	58 months	0.1	0.3	1.1	3.0	4.8
Adjuvant	85.3 months	0.0	0.0	0.2	0.8	1.7
Palliative	5.1 months	1.3	4.4	12.0	24.5	34.2

No significant differences were observed between each treatment year. The observed 30 day mortality for palliative patients according to fractions received was 16.1% for a single, 9.0% for 2−5, 3.7% for 6−10 and 2.4% for 11−20 fractions respectively.

Conclusions: This large dataset demonstrates reassuringly low 90 day mortality for radical and adjuvant patient groups. The 30 day mortality for palliative patients and the subset analysis of mortality by fractions given, supports appropriate selection of patients for palliative radiotherapy.

2036 POSTER

Voxel Based Analysis of Dose for Prediction of Urinary and Rectal Toxicity in Prostate Cancer Radiotherapy

O. Acosta[1], G. Dréan[1], J.D. Ospina[1], A. Simon[1], P. Haigron[1], R. De Crevoisier[2]. *[1]LTSI, Laboratoire du Traitement du Signal et de l'Image − INSERM U 642, Rennes, France; [2]LTSI − Département de Radiotherapie − Centre Eugène Marquis, Laboratoire du Traitement du Signal et de l'Image − INSERM U 642, Rennes, France*

Background: In prostate cancer radiotherapy the models for prediction of side effects on the ogans at risk (bladder, rectum) are traditionally based on the dose volume histograms (DVH), (NTCP) computed at an organ-basis during the planning step. However, since these models lack spatial accuracy, they may be inappropriate to explain toxicity events related with the local distribution of the dose.

Purpose: To investigate the relationship between toxicity events in bladder (GRAD>2 in two years) and rectum (bleeding in two years) and the dose spatial distribution in prostate cancer radiotherapy. We propose a new voxel based statistical analysis framework, including a non rigid mapping of 3D dose distributions to a common template.

Methods: We selected 121 prostate cancer patients treated with external radiotherapy. Clinical outcomes (rectal bleeding and urinary toxicity GRAD>2) within a two year follow up and 3D dose distributions were available. For each patient the dose was computed on the 512x512x256 pelvic CT scans, using the manual delineations, according to the standard clinical protocol. We first mapped the organs and the dose to a common template using a hybrid organ/intensity non rigid registration method, allowing to align barycentres and neighbouring structures across the population. Finally, two sample t-tests were performed at a voxel-basis leading to the computation of three dimensional maps for both, the dose differences and the p-values. Two comparisons were performed, namely rectal bleeding (20 individuals) vs non bleeding (44 individuals) and urinary toxicity(21 individuals) vs non toxicity (51 individuals). Anatomical regions were the differences were statistically significant were identified and correlated with the corresponding toxicty event.

Results: 3D Dose difference and p-values maps suggest that there is a strong correlation between a higher dose delivered to the organs at risk and the toxicity events. More importantly, the method allowed to highlight the specific regions where the dose was delivered and produced the organ damage. (81.99% of the voxels for the rectum and 50.24% for the bladder).

Conclusion: We proposed a new voxel wise statistical models of toxicity which allows to explain the risks associated with the dose spatial distribution in case of toxicity. The new model may help to find accurate relationships between local dose distribution and the damage to the and organs at risk.

2037 POSTER

Principal Components Analysis of Dose Distribution for Characterizing Toxicity in Prostate Cancer Radiotherapy

B. Chen[1], O. Acosta[1], A. Kachenoura[1], J.D. Ospina[1], G. Dréan[1], A. Simon[1], P. Haigron[1], R. De Crevoisier[2]. *[1]LTSI, Laboratoire du Traitement du Signal et de l'Image − INSERM U 642, Rennes, France; [2]LTSI − Département de Radiotherapie − Centre Eugène Marquis, Laboratoire du Traitement du Signal et de l'Image − INSERM U 642, Rennes, France*

Background: Although image guided radiotherapy (IGRT) is one the most indicated treatment for prostate cancer, severe complications may appear as a consequence of high delivered doses to the neighboring organs at risk, namely the bladder and the rectum. The prediction of this toxicity events are commonly based on clinical data and dose volume histograms through the models such as the NTCP. However different spatial dose distributions may produce the same toxicity prediction using NTCP models and new models for analyzing dose distributions are needed.

The purpose of this work is to study the underlying characteristics of the 3D dose distributions, using a voxel based Principal Component Analysis (PCA), across a population of 120 patients treated for prostate cancer. This method allows to build appearance models of dose and to extract meaningful features that may be used in a further classification step in order to separate individuals with dose related toxicity events.

Data and Methods: 120 patients treated for prostate cancer with external radiotherapy were selected. Their 3D CT scans and planned doses were non-rigidly registered towards a single template based on a hybrid organ/intensity demons algorithm. Thus, all the doses corresponded voxel to voxel to the same anatomical structure. We then applied the PCA method across the whole population, considering each voxel of the warped dose as a feature. The PCA generative model of dose allowed us to decompose them into a new orthogonal space representing the directions where their variation was more significant, therefore reducing the representation of the whole dose distributions to only some features. Using the main eigenvalues, each individual was projected as a point into a new basis leading to a compact representation of the doses. A further classification method may be used to cluster the population into toxicity/non toxicity individuals based on the planned dose distribution.

Results: Reducing the voxel space from 5'954 625 features to only 75 main eigenvalues allowed us to represent the 90% of the dose variation across the whole population. Using these features, for example, we predicted rectal bleeding with a specificity of 62%, and urinary toxicity with 52% of specificity with a simple classifier such as k-means.

Conclusion: PCA Analysis allows to decompose dose distributions and to identify the most meaningful features to further classify individuals with toxicity. Further validation with different models is in progress as well as the implementation of better classifiers and non rigid registration methods to improve the specificity.

2038 POSTER

Investigating the Associations Between Late Rectal Morbidity and Simulated Rectal Motion

M. Thor[1], A. Apte[2], J.O. Deasy[2], M. Væth[3], L.P. Muren[1]. *[1]Aarhus University Hospital, Departments of Medical Physics and Oncology, Aarhus, Denmark; [2]Memorial Sloan-Kettering Cancer Center, Department of Medical Physics, New York, USA; [3]Aarhus University, Department of Biostatistics, Aarhus, Denmark*

Background: Rectum is the main dose-limiting organ in radiotherapy (RT) of prostate cancer (PC). The motion of this organ is extensive which leads to uncertainties in the rectum dose-volume histogram (DVH). This is likely to also influence the associations between rectal DVHs and morbidity. The aim of this study was to investigate the associations between motion-inclusive rectum DVHs and late rectal morbidity and compare to the static DVH as obtained from the treatment planning CT.

Method and Materials: Late rectal morbidity was defined as late gastro-intestinal (GI) toxicity according to the RTOG scoring system in 232 PC patients previously treated to 70 Gy with conformal RT. Rectal motion was simulated over the 35 treatment fractions assuming normally distributed translational random and/or systematic motion of different magnitude by changing the standard deviations (SDs) in steps of 0.1 cm (σ=0.1−1.0 cm). The motion was simulated in both isotropic and anisotropic (anterior-posterior) direction. The associations with dichotomized GI toxicity investigating patients with vs. without GI grade $\geqslant 2$ and the motion-inclusive DVHs as well as the static DVH was explored using Spearman's rank correlation coefficient.

Results: Overall, increased associations with rectal morbidity were obtained for intermediate doses (40−60 Gy) with the motion-inclusive DVHs over the static DVH. These associations peaked with randomly applied motion. For combined random and systematic motion the associations were