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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.

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

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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 10<sup>th</sup> day following

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.

**POSTER** 

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

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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|AnB|/(|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

and DVH2, defined on 0,DHax

RDA = (int<sub>[0,Dmax]</sub> (DVH1 − DVH2) dx)/

max{int<sub>[0,Dmax]</sub> DVH1 dx, int<sub>[0,Dmax]</sub> 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) =  $(int_{An}B D(x) dx)/(int_{AvB} D(x) dx)$ .

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

## **POSTER**

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

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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