a region of interest. The existence of lung fibrosis was confirmed by a histopathological examination of the lungs after sacrificing the mice at the end of the experiment. Additionally, the histopathological examination also revealed local inflammation of the lung, which will be analysed in a follow-up study.

Conclusion

Dark-field imaging is a useful method for early detection of radiation induced lung fibrosis in mice, as it provides a clearer image of the changes in the murine lung than the corresponding absorption images. Local lung irradiation in mice is a useful model to study normal tissue response and volume effects for the optimization of radiation therapy.

Poster: Radiobiology track: Normal tissue biology of central nervous system

PO-1036 Brain modifications after stereotactic radiotherapy recorded by Functional MRI

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Purpose or Objective

Brain irradiation is commonly used in malignant diseases (i.e. metastases or Glioblastoma) and in benign diseases (i.e. meningioma, epilepsy, vestibular schwannoma or Parkinson disease). The use of stereotactic radiosurgery (SRS) allows the administration of very high doses in a single fraction (e.g. 120Gy), in a small brain volume. After irradiation, morphological and functional cerebral changes occur depending on the total dose, dose per fraction and the irradiated brain volume. The aim of this work is to use f-MRI to record adult normal brain tissue modification after irradiation with different radiotherapy doses and schedules and to identify new parameters of brain radio-damages.

Material and Methods

With a dedicated small animal radiotherapy device allowing IGRT (PXI, X-Rad SmART), we specifically irradiated with a 2mm-collimator, mimicking SRS, a small part of adult brain mice (n=72), known to have no impact on vital function, with dose schedules: 1X20Gy, 3X10Gy, 4X5Gy and no RT as control. We imaged brain mice longitudinally with a dedicated 9.4-T MRI (Agilent). Imaging was realized once before as reference level and after irradiation every month for the first 6 months and every 3 months during one year. For each mouse we acquired 14 slices of 1 mm thickness and 0.5 mm gap with an "in plane voxel resolution" of 0.5 mm. We performed T1-weighted, T2-weighted, T1-mapping, T2-mapping and DW-MRI. For DW-MRI, we performed Fast Spin Echo MultiSlice sequences, with 9 different B-value and B0 (from 20 to 1000). We performed IntraVoxel Incoherent Motion (IVIM) analysis to obtain information on intravascular diffusion, related to perfusion (*F*: perfusion factor).

Results

Only mice irradiated with 120Gy showed brain modifications in T1 and T2 anatomic images and in T1 mapping, ADC, D and F but no changes were recorded in D* or T2 mapping. All these changes started 5 weeks after SRS and then stabilized after 7 weeks. The mean values for the control group were stable during the 5 months (ADC 0,73µm²/ms; D 0,66µm²/ms; F 4,67%, T1 1,25 sec). For the 120Gy group, values were significantly higher after 5 weeks (Δ = compared to the control group) with ADC 1,66µm²/ms (Δ=151%); D 1,37µm²/ms (Δ=107%); F 18,84% (Δ=303%); T1 1,99 sec (Δ=59%). No specific behaviour changes were observed during all the experiment.

Conclusion

In this work, we studied normal brain modifications after SRS therapy with anatomical and functional MRI. SRS doses and schedules in this work reflected those used in clinic for tumor treatment or functional SRS. We showed an increase of ADC value 5 weeks after one single dose of 120Gy, compared to normal brain tissue. These results are consistent with radio-necrosis. In addition, we highlighted an increase of IVIM parameters D and F and an increase of T1 mapping in radio-necrosis area. These results increase the numbers of MRI parameters that could be used for following brain damage after radiation.

Poster: Radiobiology track: Radiobiology of the intestinal track

PO-1037 Intestinal radiation plays a pivotal role in CTLA-4 Ab induced an autoimmune enteritis mouse model

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Purpose or Objective

Checkpoint inhibitors have been approved in specific types of cancers. While the results are promising, severe immunotherapy-related adverse events (irAEs) have been reported. The one of the most common grade 3/4 adverse events was enterocolitis (17%). However, there are currently no mouse models that develop robust autoimmune enterocolitis following checkpoint inhibitors. The aim of the study was to set up a robust CTLA-4 Ab induced autoimmune enteritis mouse model.

Material and Methods

C57BL/6J mice were injected intraperitoneally (i.p) with 200µg of anti-CTLA-4 mAb every 3 days. In order to deplete CD4+ and CD8+ T cells, CD4 and CD8 antibodies were injected at 200µg/mice 4 days before anti-CTLA4 treatment. Two different tumor models were used: (1) for subcutaneous injection 2.5 $\times 10^5$ melanoma B16 F10 cells in 100 µl PBS were injected into the right flank, (2) for intravenous injection 5×10^4 melanoma B16 F10 cells in 100 µl PBS were injected into the tail vein of the animals. Mice received 1100 cGy intestinal irradiation as a split dose with 3 hours interval. The whole small intestine was stained with terminal deoxy transferase-mediated deoxyuridine triphosphate nick end labeling (TUNEL), CD3 and hematoxylin and eosin.

Results

Intestinal epithelial villous apoptosis was induced after injection of CTLA-4 Ab. But, there was no enteritis even after 11 doses of CTLA-4 Ab. 11Gy intestinal radiation alone induced intestinal epithelial crypt apoptosis, not villous apoptosis. However, radiation can increase CTLA-4