Canadian Association of Physicists
Association canadienne des physiciens et physiciennes

Contribution ID: **4092** Type: **Oral Competition (Graduate Student) / Compétition orale (Étudiant(e) du 2e ou 3e cycle)**

(G*) Investigating the spatiotemporal neuroinflammatory response of half-brain irradiation in a murine model using 18F-FEPPA PET

Wednesday 29 May 2024 10:45 (15 minutes)

Brain metastases have been effectively treated with stereotactic radiosurgery (SRS) delivered to visible growths followed by whole brain radiotherapy (WBRT) for microscopic disease. SRS alone is the preferred treatment despite high recurrence, as conventional WBRT is associated with increased cognitive decline. With improved systemic treatments breast cancer patients are living longer challenging the decision to withhold WBRT. Cognitive decline has been linked to chronic inflammation; radiation induces inflammation via glial cell (microglia, astrocytes) activation. When glial cells are activated, translocator proteins (TSPO) on the mitochondria upregulate and promote inflammation. Glial activation has been assessed in neurological disease using 18F-FEPPA (https://pubchem.ncbi.nlm.nih.gov/compound/24875298) ligand with high affinity for TSPO with positron emission tomography(PET).The aim of this study is to investigate the neuroinflammatory response of half brain irradiation using 18F-FEPPA PET.

To evaluate radiation induced glial activation, half brain irradiation was performed on non-tumor bearing immunocompetent mice (BALB/c) using a micro-CT/RT system with sham (n=9), 4Gy (n=9) and 12Gy (n=9) in one fraction. Dynamic 18F-FEPPA PET was acquired for 90 minutes at 48 hours, 2 weeks, and 4 weeks post-irradiation to quantify level and duration of glial activation. Immunohistochemistry was completed with stains for TSPO the specific ligand of 18F-FEPPA.

Currently, 18F-FEPPA-PET dynamic scans were acquired for n=8 mice, with n=2 additional mice at each dose and timepoint for immunohistochemistry. Unirradiated and irradiated hemispheres of the brain for all mice showed similar radiotracer uptake with 18F-FEPPA-PET and histology signal for TSPO; suggesting partial brain irradiation triggers global inflammation in the brain at 48 hours, 2 weeks, and 4 weeks. However, differences were present in the TSPO stain signal corresponding to different areas of the brain.

This study will map the brains spatiotemporal dose-response when partially irradiated. Further PET and histology data collection with glial activation immunofluorescent stain and analysis is on-going. Following this, half brain irradiation will be investigated in a breast cancer brain metastasis model to provide a comprehensive understanding of radiation and subsequent glial activation.

Keyword-1

Radiation

Keyword-2

PET

Keyword-3

Neuroinflammation

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Session Classification: (DPMB/DAPI) W2-6 Medical Imaging II | Imagerie médicale II (DPMB/DPAE)

Track Classification: Symposia Day (Wed May 29) / Journée de symposiums (Mercredi 29 mai): Symposia Day (DPMB/DAPI - DPMB/DPAI) - Medical Imaging / Imagerie médicale