Radiation-induced neurotoxicity assessed by spatio-temporal modelling combined with artificial Intelligence after brain radiotherapy: the RADIO-AIDE project

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Context

- **High-grade glioma:** the most frequent high-grade brain tumor in adults
- **Radiotherapy (RT):** one of the most important treatments, generally combined with surgery and/or chemotherapy
  - ➢ increased patient survival;
  - ➢ but increase of side effects like cognitive impairments (ex: attentional, executive and memory disorders) => Altered quality of life for patients.
- **Potential toxicity of RT on the central nervous system?**
  - ➢ Which neurotoxic mechanisms are potentially associated with the initiation and progression of post-RT brain lesions ? Are there spatio-temporal (ST) signatures of these post-RT brain lesions ?
  - ➢ Could these post-RT brain lesions be associated with the initiation and temporal progression of cognitive impairments?
  - ➢ What about the radio sensitivity of the brain structures implied in cognitive processes?

Objectives

The RADIO-AIDE project is a multidisciplinary project of 4 years, that started in April 2022.

- **Clinical objective:** To generate new knowledge about the neurotoxic mechanisms implied in the initiation and temporal progression of cognitive impairments following brain RT
- **Methodological objectives:**
  - ➢ To provide to clinicians a usable academic software to perform an automated longitudinal extraction of clinically relevant image-based biomarkers from brain magnetic resonance images (MRI) acquired in clinical routine;
  - ➢ To develop artificial intelligence (AI) tools to predict individual cognitive impairments at early stage after brain RT

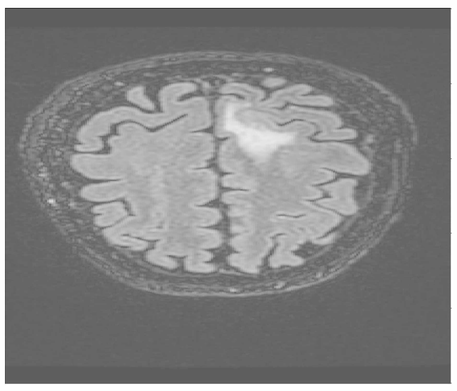

Figure 2. Brain MRI of a patient with brain lesions

Figure 3. Segmentation of a brain lesion visible on the MRI on *figure 2*

RADIO-AIDE

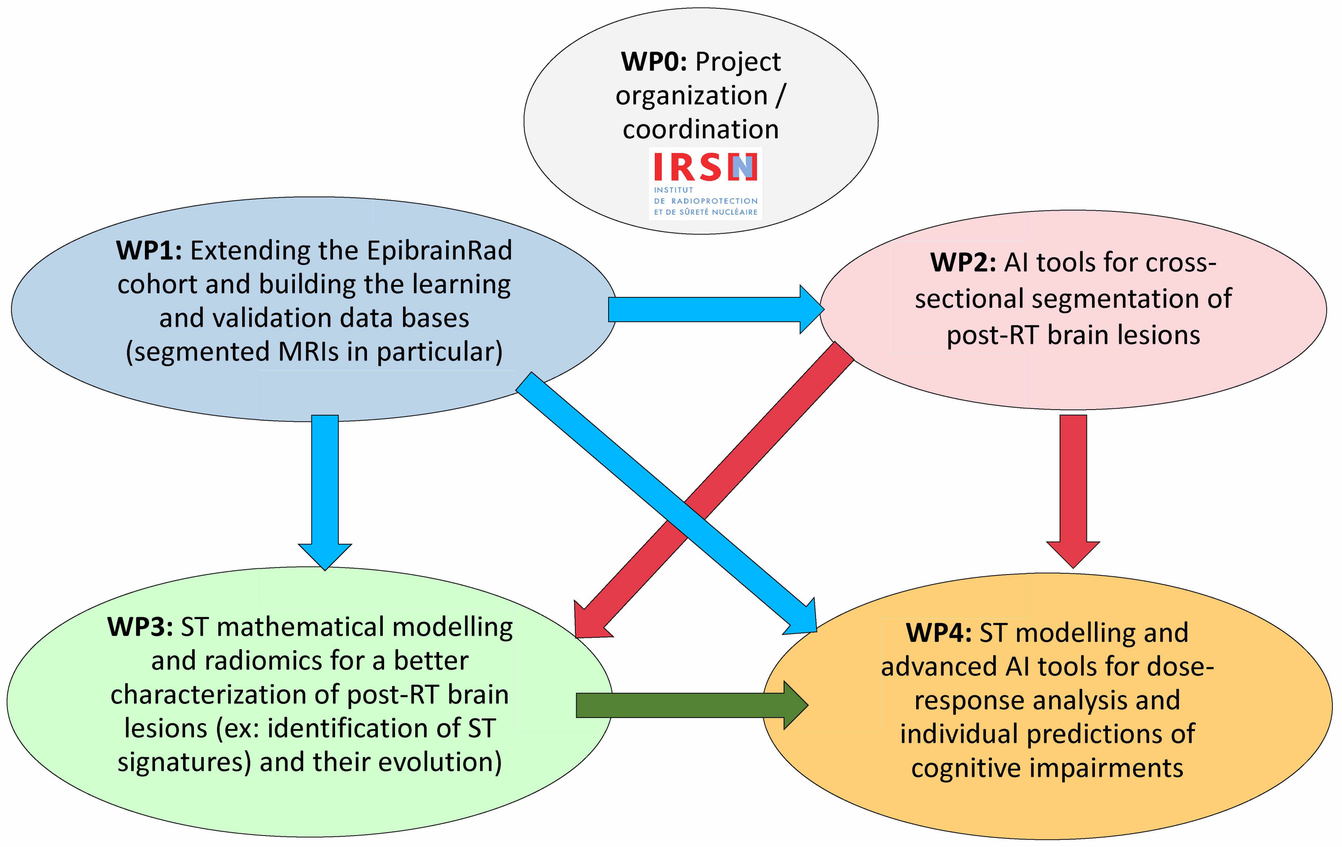

Figure 1. RADIO-AIDE Project Structure Flowchart

Methods

- **Data:** The prospective EpiBrainRad cohort including patients treated by RT for a high-grade glioma
  - ➢ For each patient : brain MRIs, computed tomography (CT) images used in brain RT treatment planning, clinical features, cognitive scores following neuropsychological exams
- **Development of fully automated algorithms based on deep learning (DL) architectures** to extract clinically relevant image-based biomarkers like white-matter hyperintensities (WMH), vascular lesions, brain tissues volume quantification, tumoral lesions.
- **Development of ST mathematical models, radiomics and AI tools based on DL and Bayesian learning algorithms to:**
  - ➢ extract, if it exists, a set of features which characterize brain lesions of different nature that may be associated either to post-RT side-effects (leukoencephalopathy, radio-necrosis, post-RT oedema) or to treatment responses (brain tumor progression, peritumoral oedema)
  - ➢ perform dose-response analyses
  - ➢ predict individual cognitive impairments following brain RT

EpiBrainRad cohort	AP-HP Pitié Salpêtrière	ICANS	Total	
Number of patients included	172	71	243	100%
Deceased patients	154	44	198	81%
Lost (%)	0	3	3	1%
Total number of MRIs (Average per individual; Max)	1779 (10; 29)	310 (5; 13)	2089	(7.5; 29)
Number of patients with at least 3 MRIs	160	43	203	83%
Number of MRIs per patient with at least 3 MRIs scan (Average per individual; Max)	1761 (11; 29)	277 (6; 13)	2038	(8.5; 29)
Number of patients with neuropsychological exams at baseline (BL) and at 12 months	64	30	94	39%
---------- at BL, 12 and 24 months	22	15	37	15%
---------- at BL, 12, 24 and 36 months	10	8	18	7%

Results and perspectives

- An extension of the EpiBrainRad cohort is in progress. New patients will be included from 2023.
- An annotated dataset including ground truth labels for post-RT WMH, vascular lesions and tumoral lesions as well as many brain regions of interest implied in cognitive functions is being produced from the brain MRIs of the EpiBrainRad cohort. This large and well curated learning data set will feed the ST models and AI tools subsequently developed.

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