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

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

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

![Brain MRI of a patient with brain lesions](image1)
![Segmentation of a brain lesion visible on the MRI on figure 2](image2)

**EpiBrainRad cohort**

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

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, 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

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**:
  - for each patient: brain MRIs, computed tomography (CT) images used in brain RT treatment planning, clinical features, cognitive scores following neuropsychological exams
  - perform dose-response analyses
  - predict individual cognitive impairments following brain RT

Authors (RADIO-AIDE consortium)

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