Title:	**Brain age measured by Artificial Intelligence techniques as a personalized marker of brain health in stroke**

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Presentation of the project:

In France, each year, there are 140,000 new cases of **stroke**, i.e. one new case every 4 minutes, bringing the number of stroke survivors in France to 750,000. The **Hauts-de-France** region has the highest prevalence in France with 15,000 new cases per year. Stroke is the leading cause of acquired functional disability and the second leading cause of dementia after Alzheimer's disease. It is a considerable public health issue with an estimated annual cost of 8.5 billion in 2007. Current treatments are effective but applied to poorly selected patients, they can have no effect or even be deleterious. The challenge is to better identify patients who will respond favorably and thus present a favorable evolution.

The favorable or unfavorable evolution of a stroke patient depends on several parameters: the state of his or her brain before the stroke, the characteristics of the ischemic lesion, and the therapies implemented. Although the last two categories are known, the assessment of **brain health** remains poorly evaluated at the individual level by current methods, particularly in the acute phase. Of the prognostic factors for brain health, age is the most widely used. However, although time passes at the same rate for everyone, brains age at different rates. A person's age is an imprecise marker of brain health, relevant at the cohort level but imperfect at the individual level. It is therefore necessary to develop individualized biomarkers of brain health, especially in diseases whose risk and prognosis are largely influenced by age, such as stroke.

One candidate biomarker for assessing brain health is **brain age**. It is the result of a **supervised learning** algorithm to predict the chronological age of a subject from MRI images. Brain age allows to quantify the condition of the underlying brain and thus potentially to assess its resilience to stroke. As age is a major prognostic factor in stroke, it seems reasonable to hypothesize that brain age would be a better biomarker to more accurately assess the brain health of patients, and thus propose the best treatment and personalized follow-up.

For the past 3 years, we have been working on the development of supervised learning algorithms for the prediction of brain age in stroke and Alzheimer's disease, both by linear machine learning models and by more complex deep learning models[1,2]. Although brain age has been shown to be a useful marker of integrity and severity of these diseases, the limited size of the cohorts and the use of research data limit its clinical validation. Indeed, the main issue to the development of effective artificial intelligence (AI) models is the quality of imaging data available for model training, typically in the research setting, and the limited amount of curated data that must encompass the variability of

real-world clinical cases necessary for robust model validation. The potential difference in distribution between the population used in training and the population that will benefit from the biomarker is a problem known as "**dataset shift**"[3]. The causes can be multiple (demographics, severity, multiple pathologies, socio-demographics, MRI constructors, etc.) and they are not necessarily resolved by increasing the training database.

The objective of the PhD thesis will be to propose a methodological environment for the deployment of an AI algorithm measuring, in MRI, the brain age of a stroke patient in the Hauts-de-France region.

The project will be based on two cohorts. A **retrospective cohort**, already constituted, of 3000 patients who had an ischemic stroke in the Hauts-de-France region between 2014 and 2020 and for whom we have MRIs in the acute phase as well as their outcome at 3 months. A **prospective cohort** will be built on the scale of the Hauts-de-France region thanks to the MRI network in hospitals (ARIANES project – arianes.fr). **ARIANES** is the networking of different MRI technologies in the Hauts-de-France region, with the aim of improving the screening, early diagnosis and follow-up of patients with neurological and psychiatric diseases. A health data host will be deployed from January 1, 2022 to collect MRI scans of stroke patients in the region.

References

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3. Dockès J, Varoquaux G, Poline J-B. Preventing dataset shift from breaking machine-learning biomarkers. GigaScience. 2021;10:giab055.

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