# Summary

Regenerative medicine has made great strides in recent years, promising to treat a wide range of pathologies, including stroke and osteoarthritis. Among these, stem cell therapies are the subject of a large number of studies aimed at democratizing their use. What's more, the use of stem cells can be accompanied by a hydrogel acting as a scaffold, enabling them to be much better integrated by the receiving body. These two elements form a "repair kit" whose optimal design can be achieved by accompanying in vitro studies with in vivo studies in animals. For this reason, it is necessary to develop an imaging method that can monitor each component of this "repair kit" individually, i.e. the stem cells and the hydrogel. Among the most widely available imaging methods, X-ray CT is the most widespread and one of the most accessible. In recent years, this technology has seen a real breakthrough with the development of spectral imaging, with the development of spectral photon counting scanners (SPCCT). Until now, spectral imaging could only be performed with X-rays from synchrotron radiation sources providing a very high photon flux over a wide energy range (20-150 keV), enabling monochromatic X-ray beams (energy bandwidth of around 50 eV) and high spatial resolution.

The aim of this thesis is to develop and optimize numerical tools for quantifying two contrast agents using X-ray-based imaging for cell therapy monitoring. We mainly focused on synchrotron imaging data processing and compared the results with the SPCCT available on the Cermep platform for two application cases: osteoarthritis and ischemic stroke.

In addition, the wide freedom of synchrotron acquisition parameters makes it essential to develop dedicated post-processing tools prior to analysis. As tomographic reconstructions of sequential acquisitions of the same sample are not superimposed, material decomposition is impossible. I have developed a gradient descent-based registration approach that makes the superposition of acquired samples fast and automatic, making the data ready for quantification. In addition, these registration tools have been extended to multimodal registration, enabling comparison of SPCCT and synchrotron material decomposition performance. SPCCT quantification is in agreement with the synchrotron, despite lower resolution and contrast for gold. In the case of iodine, SPCCT performance was not satisfactory at the low concentration we used.

With regard to applications on small animals, we first compared the results of *in vivo* evaluation of the distribution of the two contrast agents using SPCCT and synchrotron. The results showed that SPCCT achieves synchrotron performance for tracking gold-labeled cells in the brain, but is limited for detecting hydrogels at low concentrations.

Secondly, we evaluated the improved version of the repair kit composed of human adipose stem cells and an iodinated hydrogel newly developed by our collaborators. We first evaluated it in a proof-of-concept experiment on healthy rat brains and mouse knees imaged *ex vivo* at the synchrotron. We showed that iodinated hydrogel could be detected in both brain and knee despite a lower iodine concentration. It could also be detected in mouse knees, *ex vivo*, in phase-contrast images acquired at 3-micron resolution. We then evaluated this "repair kit" in vivo in mouse models of osteoarthritis using synchrotron spectral imaging. We showed that the hydrogel could be detected between one and three days after administration.

Finally, we conducted a longitudinal study with osteoarthritis mouse models and the designed therapeutic kit. The relatively low spatial resolution of the SPCCT device is not suitable for mouse knees, and we imaged using synchrotron images only.