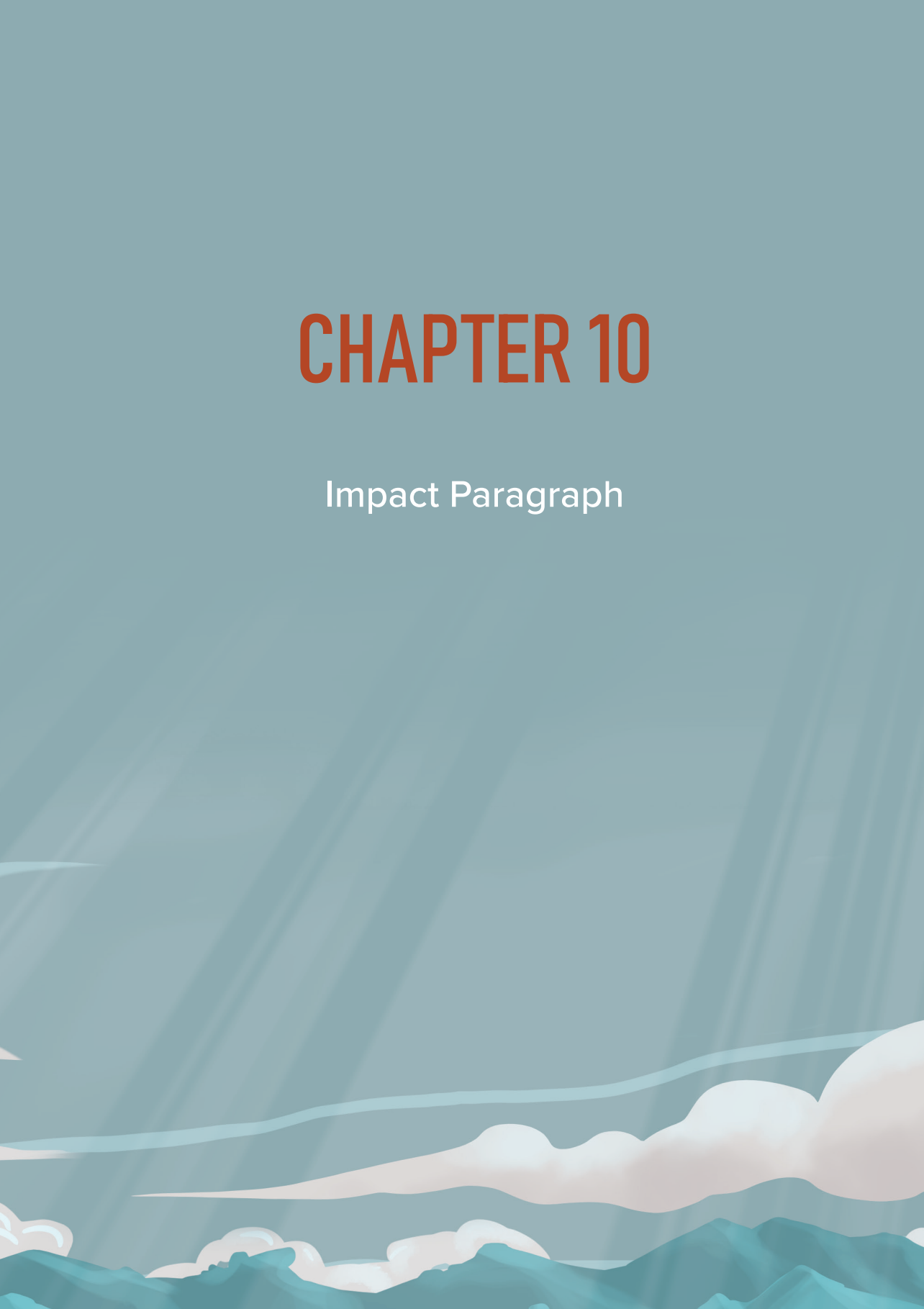
Positron emission tomography of inflammation in atherosclerosis

CHAPTER 10

Impact Paragraph



IMPACT PARAGRAPH

Inflammation plays an important role in the origin and progression of atherosclerosis. Systemic inflammation and inflammation localized in a single plaque are both associated with an increased risk of rupture of an atherosclerotic plaque. Subsequent blood clot formation at the rupture site can result in a myocardial infarction or an ischemic stroke. As such, arterial inflammation is a major contributor to cardiovascular disease, which still remains the main cause of death worldwide. Dedicated imaging of inflammation may facilitate detection of patients before the onset of clinical symptoms, which might give opportunity for preventive intervention. In addition, imaging could serve as non-invasive follow-up as well and can provide deeper insight into the pathophysiology which might open doors for the development of new treatment options.

The aim of this thesis was twofold. In **the first part**, we used the current method, ^{18}F-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography (PET), to image inflammation to study the effects of three different interventions (**chapter 2-4**). In **the second part**, we shifted our focus towards improving the current imaging techniques by exploring new molecular imaging targets and their tracers (**chapter 5-7**).

The findings of this thesis are of interest to each and every one since all of us will develop atherosclerosis at some point in our lives. However, not everyone will suffer from clinical symptoms of cardiovascular disease. Trying to reduce a risk in subjects that have not developed any symptoms yet, is called primary prevention. In addition to general lifestyle changes, such as dietary interventions and exercise, additional risk reduction can be accomplished with medication or invasive treatment. However, such medical and surgical treatments may not be ideal since subjects have no complaints (yet) and might only experience side-effects or complications of the treatment itself. A food supplement like ‘resveratrol’ may therefore be a more appealing approach. Although we were not able to demonstrate a reduction in vascular inflammation in male subjects at risk of diabetes in our explorative trial, it is still possible that another patient group, dosage or timing will have a positive effect.

In addition, our findings also apply to specific patient groups. For instance, hyperthyroidism, the presence of high thyroid hormone levels, increases arterial inflammation. This finding is relevant for the numerous patients with thyroid disease and their doctors. Treating physicians should take the negative effects of thyroid hormone on cardiovascular disease into account when treating these patients and aim to restore the thyroid hormone balance when possible. Furthermore, our findings endorse the current trend towards a more lenient thyroid stimulating hormone (TSH) suppression strategy in thyroid carcinoma patients.

Another specific subgroup possibly affected by our findings consists of patients treated with vagal nerve stimulation (VNS). Although we were unable to find an effect of VNS on vascular inflammation, we did find insulin levels to be affected. This is a previously unknown (side-) effect of this treatment and hence, deserves further attention. Moreover, this effect might be relevant in the treatment of other diseases, like diabetes, and more extensive research is therefore indicated.

The findings from the second part of this thesis are relevant to researchers interested in the mechanisms that drive atherosclerosis. The studies offer insights into the specific role of (beta-)amyloid (Aβ) and the function of the alpha 7 nicotinic acetylcholine receptor (α7 nAChR) in atherosclerosis. The overview of our current understanding of this role might inspire others to investigate the exact function of this peptide and this receptor outside the brain. Previous studies have identified multiple specific ligands for these receptors, which provide both possible imaging and treatment options. Our research did not result in a clear-cut imaging technique ready for clinical routine in cardiovascular disease management. Nevertheless, our experience with *in vivo* multimodality imaging with a new tracer might serve as a stepping stone for others to bring imaging of inflammation in atherosclerosis to the next level. In order to reach as many interested colleagues as possible, all research chapters in this thesis have been submitted as scientific articles to peer-reviewed medical journals. In addition, the major findings have been presented at local and international conferences.