Background for April Literature Review: Molecular Imaging

What do we need imaging?

PET scan and probe

Positron emission tomography (PET) is a technique that measures physiological function by looking at blood flow, metabolism (glucose uptake), neurotransmitters, and radiolabelled drugs. PET offers quantitative analyses, allowing relative changes over time to be monitored as a disease process evolves or in response to a specific stimulus. The technique is based on the detection of radioactivity emitted after a small amount of a radioactive tracer is injected into a peripheral vein. The tracer is administered as an intravenous injection usually labelled with oxygen-15, fluorine-18, carbon-11, or nitrogen-13. The total radioactive dose is similar to the dose used in computed tomography.

In general, PET scans may be used **to evaluate organs and/or tissues for the presence of disease or other conditions**. PET scans **detect early signs of cancer, heart disease and brain conditions** as well as the evolution of treatments. It involves an injection of a safe radioactive tracer that helps detect diseased cells. A common use for PET is to measure the rate of consumption of glucose in different parts of the body. Accumulation of the radiolabelled glucose analogue 18-fluorodeoxyglucose (FDG) allows measurement of the rate of consumption of glucose. It is well established that malignant tumors metabolise glucose at a faster rate than benign tumors. Thus, whole body scans are often performed to stage a cancer.

Other applications of PET include looking at the blood flow and oxygen consumption in different parts of the brain—for example, in understanding strokes and dementia. Tracking chemical neurotransmitters (such as dopamine, in Parkinson's disease) can also be performed with this technique.

Because this method of detection is safe, researchers are developing probes to be used for other diseases for which diagnosis or follow up of treatment is difficult to achieve such as in pulmonary fibrosis.

In the selected publication, the authors are using an imaging probe **a gallium-68 labeled collagen binding PET imaging probe**, named 68Ga-CBP8 that is injected into the bloodstream and sticks to type I collagen, a key biomarker of fibrosis. The probe lights up collagen using positron emission tomography. This may allow doctors to track disease activity and response to treatment, better predict prognosis and accelerate the development of new therapies one day. The tool also may be useful in other types of fibrosis and in other parts of the body.
Part of the validation of the probe consisted of evaluating its stability after injection.

Reference: doi: 10.1136/bmj.326.7404.1449

Pulmonary fibrosis (https://www.nhlbi.nih.gov/health/idiopathic-pulmonary-fibrosis)

Idiopathic pulmonary fibrosis (IPF) is a serious chronic (long term) disease that affects the tissue surrounding the air sacs, or alveoli, in your lungs. This condition develops when that lung tissue becomes thick and stiff for unknown reasons. Over time, these changes can cause permanent scarring in the lungs, called fibrosis, that makes it progressively more difficult to breathe.

It's not clear what causes it, but it usually affects people who are around 70 to 75 years old and is rare in people under 50. The risk for IPF is higher if you smoke or have a family history of IPF, and the risk increases with age. The most common symptoms of IPF are shortness of breath and cough. Some people may not have symptoms at first, but symptoms can develop and get worse as the disease progresses.

The way that IPF progresses varies from person to person, and scarring may happen slowly or quickly. In some people, the disease stays the same for years. In other people, the condition quickly gets worse. Many people with IPF also experience what are known as acute exacerbations, where symptoms suddenly become much more serious. Other complications of IPF include pulmonary hypertension and respiratory failure, which happen when the lungs cannot deliver enough oxygen into the bloodstream without support. This prevents the brain and other organs from getting the oxygen they need.

There is currently no cure for IPF. However, certain treatments may slow the progression of IPF and help your lungs work better. This may extend the lifespan and improve the quality of life of people who have the disease.

IPF was originally thought to be an inflammatory-driven fibrosis, that is, a fibrotic process caused by unresolved inflammatory processes. However, a growing body of evidence reveals that the pathological process of IPF may be driven by aberrantly activated AECs [1]. Aberrantly activated AECs express most of the growth factors and chemokines responsible for the proliferation, migration, and activation of fibroblasts. In regard to ARDS, disruption of the integrity and reconstitution of AECs barrier is an important determinant of the clinical outcome [8, 9]. Collectively, fragility of AEC barrier to lung injury, abnormal activation of alveolar epithelial cells, and aberrant repair of AEC integrity plays a critical role in the pathogenesis of IPF.

One of the major difficulties in caring for patients with lung fibrosis is that no clinical tests can be made to determine how active someone's disease is at any one time or how someone is responding to treatment. There is a need to be able to assess disease activity to improve prognostication and determine treatment response for an individual both in terms of clinical care and clinical trials. Therefore development of new tools such as PET probe is highly relevant for the field of pulmonary fibrosis from the research and clinical point of view.