Postprocessing and Cross Validation

Modeling and Quantification

Measurement of plasma input functions using optical techniques

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Learning Objectives:

- Arterial sampling
- Pulsed dye-densitometry
- Image derived input function
- Reference tracer imaging

The concentration of a molecular imaging agent in the blood plasma over time – or the "plasma input function" – can provide critical information about tracer delivery to tissues of interest, and is therefore a key component to measure in more quantitative molecular imaging approaches. In optical imaging, tracers are selected based on their absorption or fluorescent properties within the visible and near-infrared range of the electromagnetic spectrum, and a variety of systems have been developed to detect concentration of optical tracers, based on one of these two mechanisms (absorption or fluorescence). Within the field of molecular imaging, optical tracers permit unique techniques to be employed in the measure of plasma concentrations. Like in nuclear medicine, it is possible to measure plasma input functions by analysing periodically sampled arterial blood; however, since the tracers are not radioactive, their concentration is typically measured by spectrophotometry or fluorimetry, rather than with a scintillator. More specifically, the blood samples are spun down to remove light absorbing and scattering red blood cells, leaving the more-or-less optically clear plasma for analysis. Light absorption properties or fluorescence properties of the plasma are then analysed at one or more wavelengths in a spectrophotometer or fluorimeter, respectively, and the results are compared to known specific absorption or fluorescence spectra of the tracer to quantify tracer concentration. Less invasive approaches have also been developed in optical imaging. Perhaps the most established of these is called pulsed dye-densitometry (PDD). This approach was initially developed from pulse oximetry methodology, wherein the oxygen saturation level of haemoglobin in the arterial blood is quantified by measuring fluctuations in light absorption in tissue (typically through a finger in adult humans) at two or more wavelengths of light in the near-infrared range. The fluctuations occurring at the heart rate are assumed to arise only from the arterial blood and differences in the absorption spectra of oxygenated and deoxygenated haemoglobin are incorporated to quantify oxygenation. This approach can be expanded to quantify changes in concentration of an optical tracer, and thus the plasma input function of a tracer, if the tracer has different absorption properties at the wavelengths measured. Other methods that have been employed to measure the plasma concentration in optical molecular imaging include direct measure from the left ventricle, which can be applied in small animals, and a dual-tracer approach wherein a second, untargeted tracer can be injected with a targeted tracer. If the tracers have different absorption or fluorescent properties, the sophistication of spectral imaging in optics can be used to resolve uptake of the two tracers simultaneously, allowing the untargeted tracer to be used as a surrogate of the plasma input function for quantitative kinetic modelling. This educational session will cover all of the points mentioned above and expand on their implementation, applications, and future directions.

Relevant Publications:

1. Iijima T, Aoyagi T, Iwao Y, et al. Cardiac output and circulating blood volume analysis by pulse dye-densitometry. J Clin Monit 1997;13:81-9.
2. Elliott JT, Wright EA, Tichauer KM, et al. Arterial input function of an optical tracer for dynamic contrast enhanced imaging can be determined from pulse oximetry oxygen saturation measurements. Phys Med Biol 2012;57:8285-95.

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