Postprocessing and Cross Validation

New Imaging Tools: Cerenkov Luminescence Imaging

Cerenkov Specific Contrast Agents

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Learning Objectives:

- Contrast agents can be synthesized to exploit the unique properties of Cerenkov imaging
- These radiolabeled contrast agents selectively absorb a band Cerenkov radiation dependent upon a specific biological function
- Cerenkov specific contrast agents provide complementary molecular information to anatomical and functional data provided by PET

A number of recent publications have demonstrated the feasibility of detecting Cerenkov radiation using optical imaging techniques. Cerenkov radiation occurs when a travelling charged particle, such as an electron or positron, exceeds the speed of light in the medium, emitting the excess energy in the form of a photon. While the sensitivity of Cerenkov imaging is limited by a number of factors including absorption and scattering of visible photons by tissue, limited depth penetration and low signal to noise associated with the low photon release rate of most radioisotopes, there are also a number of distinct advantages to this method. First, Cerenkov radiation is emitted by both positrons and electrons, enabling the imaging of a number of nuclei that have not previously been accessible. Secondly, optical scanners can typically image 3-5 mice simultaneously, thus allowing the imaging of radioisotopes with higher throughput in animal models. Third, because Cerenkov imaging measures photon release, optical imaging techniques such as photon quenching and resonant transfer to longer wavelength fluorophores can be utilized. Finally, Cerenkov radiation is multispectral, emitting continuously across the bandwidth of 300-800 nm with intensity proportional to $1\lambda^2$.

In this presentation we will discuss contrast agents that we have designed specifically for Cerenkov imaging. These contrast agents exploit the optical and multispectral properties of Cerenkov light to add functional imaging capabilities, thus enhancing the information available from radiolabeled tracers. The functional contrast is based on selective bandwidth quenching of the Cerenkov emission spectrum. Both intermolecular (tracer on a different molecule) and intramolecular (tracer on the same molecule) selective bandwidth quenching are possible. As proof of principle, we present the synthesis and characterization of ^{18}F labeled pH indicators. A change from acidic to basic environment causes a color change in the indicator, resulting in increased photon absorption and a bandwidth selective reduction in the Cerenkov emission. The PET signal remains invariant. Using ratiometric imaging, or a scaling of the emitted intensity from different bandwidths, we can directly estimate the pH *in vitro* and *in vivo.*