Public Abstract

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Title:Frequency Domain Fluorescent Molecular Tomography and Molecular Probes for Small Animal Imaging

Fluorescent molecular tomography (FMT) is a noninvasive biomedical optical imaging that enables 3-dimensional quantitative determination of fluorochromes distributed in biological tissues. There are three methods for imaging large volume tissues based on different light sources: (a) using a light source of constant intensity, through a continuous or constant wave, (b) using a light source that is intensity modulated with a radio frequency (RF), and (c) using ultrafast pulses in the femtosecond range. In this study, we have developed a frequency domain fluorescent molecular tomographic system based on the heterodyne technique, using a single source and detector pair that can be used for small animal imaging. In our system, the intensity of the laser source is modulated with a RF frequency to produce a diffuse photon density wave in the tissue. The phase of the diffuse photon density wave is measured by comparing the reference signal with the signal from the tissue using a phasemeter. The data acquisition was performed by using a Labview program.

The results suggest that we can measure the phase change from the heterogeneous inside tissue. Combined with fiber optics and filter sets, the system can be used to sensitively image the targeted fluorescent molecular probes, allowing the detection of cancer at an early stage.

We used the system to detect the tumor-targeting molecular probe Alexa Fluor 680 and Alexa Fluor 750 bombesin peptide conjugates in phantoms as well as mouse tissues. We also developed and evaluated fluorescent Bombesin (BBN) probes to target gastrin-releasing peptide (GRP) receptors for optical molecular imaging. GRP receptors are over-expressed in several types of human cancer cells, including breast, prostate, small cell lung, and pancreatic cancers. BBN is a 14 amino acid peptide that is an analogue to human gastrin-releasing peptide that binds specifically to GRPr receptors. BBN conjugates are significant in cancer detection and therapy. The optical molecular probe AF750 BBN peptide exhibits optimal pharmacokinetic properties for targeting GRPr in mice. Fluorescent microscopic imaging of the molecular probe in PC-3 prostate and T-47D breast cancer cell lines indicated specific uptake, internalization, and receptor blocking of these probes. In vivo investigations in severely compromised immunodeficient (SCID) mice bearing xenografted PC-3 prostate and T47-D breast cancer lesions demonstrated the ability of this new molecular probe to specifically target tumor tissue with high selectively and affinity.