Development of a Novel Spatial Frequency Domain Method for Fluorescence Imaging in Tumor Detection

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Optical imaging plays an integral role in pre-operative tumor detection. In molecular imaging with fluorescent contrast agents, non-flat surfaces scatter excitation light across the region of interest, creating superficial signals from tissue absorption and surface reflectance. A recently developed method known as spatial frequency domain imaging (SFDI) projects sinusoidal patterns to isolate and remove surface defects, allowing for image reconstruction into three-dimensional models. By combining SFDI with near-infrared (NIR) fluorescence, this project optimized and validated a novel process named spatial frequency domain fluorescence molecular imaging (SFD-FMI), which improved contrast and detection sensitivity for tumor imaging in vitro and in vivo. Using a projector-camera system, NIR fluorescent phantom tests were conducted to compare patterns at multiple frequencies for analyzing frequency-dependent depth sensitivity. Analysis of uniform illumination and demodulation images revealed 70% contrast improvement and a lateral resolution increase of 20%. Based on these promising results, the image processing technique was applied to an in vivo tumor model. Skov3 ovarian cancer cells were transfected with an infrared fluorescent protein and subcutaneously injected into NCr nude mice. Imaging of the resulting tumors and their three-dimensional reconstructed meshes were compared to in vitro fluorescent phantom test results, verifying that the method was similarly effective in vivo. Application of SFDI to NIR fluorescent molecular probes in SFD-FMI significantly improved the quantification of detection sensitivity and signal depth dependence. The enhancement of fluorescent signal in subsurface imaging, especially in vivo, will enable more effective diagnosis of human tumors.

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