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Illuminating molecular function: Optical technologies for macroscopic fluorescence imaging

Tissue observation with light is probably the most common imaging practice in medicine and biomedical research ranging from the simple visual inspection of a patient to advanced in-vivo and in-vitro spectroscopic and microscopy techniques. While intrinsic tissue absorption and scattering yields significant information on functional and anatomical tissue characteristics, significant attention has been also given to fluorescence investigations of tissue since many biochemical markers can be retrieved due to fluorescence contrast and many more can be targeted using appropriate fluorescent markers. A number of different optical imaging approaches can be used for imaging fluorescence in-vivo. Traditionally, optical methods have been used to look at surface and subsurface fluorescent events using confocal imaging, multiphoton imaging. intravital microscopy or total internal reflection fluorescence microscopy. Recently however, light has been used for in-vivo interrogations deeper into tissue using photographic systems with continuous light or with intensity modulated light and tomographic systems. Potentially, phase-array detection, can be also applied. This recent focus in macroscopic observations of fluorescence in tissues has evolved due to the potential of transferring this technology to imaging animals and humans. Underpinning to these developments are advances in fluorescence probe technology, in illumination and detection technology and in mathematical models that allow for tomographic investigations using diffuse light. In this presentation following we discuss imaging techniques that use the diffuse component of light for probing molecular events deep in tissue. We show the capacity to resolve fluorescent objects embedded deep in mouse-like phantoms achieving sub-millimeter resolution. We further demonstrate how quantification and high molecular specificity can be achieved and that penetration depths of several centimetres are feasible. Examples of imaging enzyme up-regulation, induced apoptosis and gene-expression in-vivo are given. Limitations of the method and future directions are also discussed.