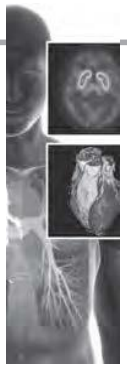

An overview of Internal Medicine-Ultrasound

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Review Article

There are two broad categories for medical imaging by X-rays: structural imaging, which reveals anatomical structure, and functional imaging measuring changes in biological function including metabolism, blood flow, and regional chemical composition and biochemical processes [1]. X-rays are widely used in structural imaging of bone, teeth, microcalcinations, lungs, and orthopedic devices. However, endogenous soft tissue types are difficult to distinguish using conventional X-ray projection imaging. Distinguishing tissue types for functional imaging requires either exogenous contrast agents (e.g. radiopaque agents to view vasculature and flow in angiography), or technique that are more sensitive to tissue differences (or both). This review describes the opportunities for functional imaging based upon X-ray attenuation, X-ray fluorescence (XRF), and X-ray excited optical luminescence (XEOL) for non-invasive biochemical imaging. In addition, different types of contrast agents and their contrast mechanisms are discussed in order to increase the contrast to noise ratio and reduce the X-ray dose. These functional imaging techniques promise to dramatically improve our ability to study *in situ* biochemistry and disease pathology [2]. These various X-ray methodologies utilize several different types of interactions between X-rays and matter that may be employed for imaging and analysis [1]. First, X-rays can be absorbed or scattered by the tissue thereby attenuating the transmitted X-ray intensity. This is the most widely used technique for structural, vasculature, and gastrointestinal tract imaging, First, X-rays can be absorbed or scattered by the tissue thereby attenuating the transmitted X-ray intensity. This is the most widely used technique for structural, vasculature, and gastrointestinal tract imaging; however, it is not very sensitive to small amounts of X-ray absorption because noise on the transmitted X-ray signal can obscure small decreases due to attenuation. Second, when atoms in a tissue sample absorb X-rays, some of the energy is released via secondary X-ray emission (i.e. X-ray fluorescence, XRF). Each element has a unique XRF spectrum providing a robust fingerprint for elemental analysis. Third, the absorbed X-ray energy can also generate optical luminescence in scintillators such as rare-earth doped phosphors. Optical luminescence has been used to detect X-rays since Röntgen's original discovery in 1895. In these studies, the scintillators are placed outside the tissue and used to detect X-ray attenuation and fluorescence. Recently, these nanophosphors have been injected into tissues as a contrast agent [3]. The optical luminescence can be combined with colorimetric indicator dyes for high resolution chemical imaging in tissue. Each technique has advantages and limitations for various applications, and they can also be used together to provide complimentary structural and functional information. X-ray excited luminescent nanoparticles are also very promising as contrast agents [4]. Typically a few thousand visible photons are generated per absorbed X-ray photon (depending upon the incident X-ray energy) compared to at most one fluorescent X-ray for XRF. Some light is lost during propagation through the tissue, but a reasonable flux of near-infrared light penetrates through several centimeters of tissue.

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