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Mini Review

Recent Advances in Diagnostic Imaging Biotechnologies and Nanomedicine Applications

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Abstract

Diagnostic imaging biotechnologies represent essential approaches that are recently used for rapid diagnosis and evaluation of a wide range of pathologies in the healthcare field. These technologies have now replaced a multitude of conventional medical diagnostics that have been established throughout decades of years, both in human medicine and veterinary practice. In order to enhance diagnostic imaging sensitivity and popularize its utility, many imaging technologies such as computed tomography (CT) and magnetic resonance imaging (MRI) need to be set up in practice with updated modalities and biomaterials. However, these still rely on the availability of adequate income source to provide such state-of-the-art equipment, as well as acquisition of competent radiological skills in understanding of the normal anatomical species and diagnostic interpretation of detectable diseases. The use of intravenously administered contrast agents has been proved to be feasible and easy-to-use method that can be suitable in complicated clinical cases and also at reasonably-equipped veterinary/medical settings. The purpose of this mini-review is to highlight the recent advances in diagnostic imaging biotechnologies with a special emphasis on novel contrast radiation agents and their nanomedicine applications. Whilst the present generation of contrast media has enabled quick diagnosis, these agents still encounter a number of undesirable disadvantages such as the lack of tissue specificity and possibility of systemic toxicity. Researchers are now working on a new generation of contrast media that aims to overcome many of these drawbacks, and to provide more sensitive imaging features and highly specific diagnostic information through modern advances in nanotechnology applications and materials science.

Keywords: *Diagnostic Imaging; Contrast Agents; Radiation; Nanomedicine; Biotechnology*

MRI

Magnetic resonance imaging (MRI) is a sophisticated imaging technique used in medical diagnosis to generate comprehensive anatomical pictures of the body and its physiological processes both in healthy and diseased conditions. Scanners of MRI utilize potent magnetic fields, gradients, as well as radio waves to form variant images of the organs. What distinguishes MRI from CT or CAT and PET scans is that MRI does not encompass x-rays or ionizing radiation. Nuclear magnetic resonance can be used for diagnostic imaging in other applications such as spectroscopy. MRI is the method of choice in preoperative procedures for staging of numerous tumors of rectal and prostate origin. It also plays a critical role in diagnosis, staging, and follow-up of brain tumors, malformations of arteriovenous circulation, and other surgically curable conditions [1,2].

CT

A computed tomography scan, formerly known as a computerized axial tomography scan or CAT scan, makes use of computer-processed combinations of multiple x-ray measurements taken from different angles to produce tomographic (cross-sectional) images (i.e. virtual "slices") of specific areas of a scanned object, allowing the clinician to see inside the object without cutting. Cross-sectional images are useful for a wide range of diagnostic and therapeutic objectives in medical disciplines. Uses of CT have risen in a speedy pace since 2000s in several countries around the globe. More recently, it has been applied in preventive medicine and disease screening. For example, CT colonography is a key diagnostic tool for patients with a high risk of colon cancer and CT cardiography can provide full-motion heart scans for those with high risk of heart disease [2].

PET

Positron-emission tomography (PET) is a functional imaging technique of nuclear medicine that is used to monitor metabolic processes within the body aiding to the diagnosis of diseases. PET is both a medical and research tool, used heavily in clinical oncology. PET is also employed in pre-clinical studies on animals, as it enables recurrent investigations into the same subject. This is effective in cancer research particularly, where it enhances the statistical quality of the obtained data and significantly minimize the numbers of animals needed for a specific study (since the animal subjects can represent as their own control) [2].

SPECT

Single photon emission computed tomography (SPECT) is a nuclear imaging scan that integrates computed tomography (CT) and a radioactive tracer. The tracer is what allows medical and veterinary doctors to see how blood flows into tissues and organs. Before the SPECT scan is made, a tracer is injected into the bloodstream. The method demands a gamma-emitting radioisotope to be transmitted into the patient, normally through an intravenous injection into the bloodstream. It is analogous to conventional planar imaging of nuclear medicine using a gamma camera and is able to give valid three-dimensional information. While this information is generally displayed as cross-sectional slices across the patient, it can be reformatted whenever required [2].

Fluoroscopy

Fluoroscopy employs x-rays to create real-time animated images of the interior depths of an object. A fluoroscope allows the radiologist to examine the internal structures and physiological functions of a patient. Thus, the cardiac pumping action, the oesophageal swallowing motion, or the gastro-entereic emptying, for instances, can be monitored. This is quite helpful for both the diagnosis and therapy of diseases, and these usually happens in diagnostic and interventional radiology, and image-guided/microsurgery. Simply, a fluoroscope is comprised of an x-ray source and a fluorescent screen, whereas a patient is placed in between. Though, most fluoroscopes have involved x-ray intensifiers and cameras to enhance image visibility and display it on a remote screen. For many years, fluoroscopy has a tendency to produce live pictures unrecorded, but now as the technology has greatly improved, animated image recording and playback have become the normal trend. Fluoroscopy is similar to radiography and CT in that it generates images using x-rays. The main difference is that radiography is fixed as still images on photosensitive films while fluoroscopy provides live-moving images that were not previously possible to be stored. Yet, radiography, CT, and fluoroscopy are all digital, supplemented with softwares for image analysis and data storage or retrieval [2].

Contrast agents

Contrast agents are of high importance in diagnostic imaging as these can markedly increase the sensitivity of an imaging method, allowing for definite diagnosis of previously undetectable pathologies. In this perspective, the development of novel and improved contrast agents that are based on nanotechnology is making a great impact into the field of diagnostic imaging. Through nano-scale manipulations and nuclear or radiation medicine, researchers are progressing to improve the sensitivity, biocompatibility, and biodistribution profile of various contrast materials. Thus, the use of nano-scale agents has opened up entirely new horizons of imaging technologies and applications, such as fluorescence imaging. The different types of contrast agents based on nanotechnology for each of the major diagnostic imaging biotechnologies are here highlighted, in addition to their clinical or pre-clinical usage and the challenges to be addressed in future research. The biological interactions and *in vivo* fate of these contrast media, as well as the major themes of application in medical nanotechnology are here described in brief. Table 1 summarizes the various types of contrast media used in clinical practice or pre-clinical research for various imaging techniques [1,2].

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Imaging Type	Contrast Agents	Current Status	Examples
MRI	Gadolinium Chelates and Salts	Clinical use	• Gadofosveset trisodium (ABLAVAR®) • Gadoxetate disodium (EOVIST®) • Gadobutrol (Gadavist®) • Gadopentetate dimeglumine (MAGNEVIST®) • Gadobenate dimeglumine (MultiHance®) • Gadodiamide (OMNISCAN®); • gadoversetamide • (OptiMARK™) • Gadoteridol (ProHance®)
	Gadolinium Nanostructures	Pre-clinical	
	Iron Oxide Nanoparticles	Clinical use and some clinical trials	
CT	Conventional Iodine	Clinical use	• Diatrizoate anion (Renografin®) • Diatrizoate anion (Hypaque®) • Iothalamate anion (Conray®)
		Clinical use	• Iohexol (Omnipaque®) • Iopamidol (Isovue®) • Ioversol (Optiray®) • Iopromide (Ultravist®)
		Clinical use	• Ioxaglate (Hexabrix®)
		Clinical use	• Iotrol and Iodixanol (Visipaque®)
	Bismuth sulfide nanoparticles	Pre-clinical	• N/A
	Iodinated nanostructure	Pre-clinical	• N/A
	Gold nanoparticles	Clinical trials	• N/A
PET and SPECT	Radio-pharmaceuticals: Labeled biomolecules or elemental emitters	Clinical use and pre-clinical	• Fludeoxyglucose F-18 • AdreView (Iobenguane I-123 Injection) • DaTscan™ • Ioflupane I-123 Injection • F-18 • I-123 • O-15 • N-13 • C-11 L-methionine
	Nanostructures with radionuclides	Pre-clinical	• F-18 FETos
Fluorescence and Optical Imaging	Fluorescent silica particles	Pre-clinical	• N/A
	Quantum dots	Pre-clinical	• N/A
	Polymer encapsulated fluorophores	Pre-clinical	• N/A

Table 1: *Summary of the various types of contrast media in clinical use or pre-clinical development for various diagnostic imaging techniques. N/A= Not applicable or not available as commercial preparations, or instead prepared ex vivo. Table reproduced in courtesy to Rosen., et al. 2011 [1].*

Challenges to be addressed

The radiation utilized in CT scans can damage body cells, including DNA, which can lead to radiation-induced cancer. The doses of radiation received from CT scans are variable. Compared to the lowest dose x-ray techniques, CT scans can have 100 to 1,000 times higher dose than the conventional X-rays. The author believes that CT scans can be implemented with different settings/modalities for minimal exposure in animals, just in a manner as routinely performed in children, whereas most manufacturers of CT scanners support this function as a built-in feature. Furthermore, certain situations may require pediatric patients to be exposed to frequent CT scans. Contrast agents can result in hypersensitivity reactions and may lead to nephropathy. In addition to the advantageous use of intravenously administered contrast agents, oral contrast media are typically used for abdominal examination. The intravenous and oral contrast agents are usually diluted into about 10% of the original concentration. However, there are oral alternatives to iodinated contrast, such as extremely diluted suspensions of (0.5 - 1%) barium sulfate. These dilute agents have the advantage that they do not ignite allergic-type reactions or renal failure, but are contraindicated in patients with suspected bowel perforation, because leakage of barium sulfate from the perforated bowel will likely result in fatal peritonitis [1].

Research prospects

Photon-counting computed tomography is a novel diagnostic imaging technique developed by physicists and radiologists that is now under investigation for clinical practice and research. However, this technique is liable to noise and additional factors that may influence the relationship for linearity of the voltage to x-ray intensity. Although photon counting detectors (PCDs) are still affected by this noise, it does not alter the total counts of photons measured. PCDs have multiple advantages; including minimizing radiation doses improving contrast to the noise ratio, improving resolution of spaces and, by the use of several modalities of energy, characterizing a great deal of contrast agents. Recently, PCDs have become available in CT scanners owing to the current advances in detector biotechnologies that are pertinent to the volume and the rate of required data. As of 2016, photon counting CT is now in use at a number of research centers. Some preliminary studies have found the prospects of dose reduction for photon counting CT in imaging control and progressive detection of mammary cancer to be very promising [1].

Conclusions

The expanding use of diagnostic imaging biotechnologies continues to remove the boundaries of our diagnostic capabilities. Using these imaging techniques, medical and veterinary doctors will be able to diagnose diseases earlier and more precisely and will obtain a variety of structural and functional information about the body systems. Contrast agents are a key part of these techniques, allowing us to retain greater detail and sensitivity in diagnostic images. Nanotechnology offers us the opportunity to overcome concerns with systemic toxicity, imaging time, tissue specificity, and signal strength. Thus, progress in the field of nano-scale contrast agents will play a key role in the persistent enhancement of our diagnostic imaging capabilities in the coming years.

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