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Magnetic Resonance Imaging Compatible Biomaterials For Realization of Interventional Operations

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ABSTRACT

Realization of interventional therapeutic procedures with guidance of Magnetic Resonance Imaging (MRI) is a promising novelty in area of interventional surgery because of eliminating x-ray exposure to patient body. Together with radiation free nature, advances in MRI techniques present superior soft tissue contrast and real time physiologic parameters from related tissue. However, the strong static magnetic field, magnetic radiofrequency (RF) pulses, and time-varying gradient fields applied during MRI, may result in exceeded heating risk over interventional instruments and adjacent tissue inside patient body. Additionally, since real time tracking and determination of device position inside patient body is critical for operators, sufficient visibility under MRI is another challenging issue to overcome. Therefore, proper biomaterials must be utilized for designing and development of MRI compatible interventional instruments by considering many factors including biocompatibility, MRI safety, MRI visibility, and other mechanical needing.

Keywords: Magnetic Resonance Imaging (MRI); MRI Compatible Biomaterials; Biocompatibility; MRI Safety; Nanoparticles.

1. INTRODUCTION

Interventional therapeutic procedures of varied diseases generally benefits of x-ray based imaging modalities including fluoroscopy, computed tomography (CT), angiography and etc. Together with well-known deleterious effects of ionizing radiation on human body, infants are theoretically more vulnerable to the carcinogenic effects of ionizing radiation than adults, and new borns have a greater cancer risk as the long term chromosomal damage [1]. On the other hand x-ray based imaging modalities do not provide sufficient image contrast especially for the soft tissues that are generally necessary for tracking of implanted device inside the related tissue or vessel. Interventional therapeutic procedures under x ray-based modalities do not only suffer from poor soft tissue contrast, but also are not feasible due to the nephrotoxic effects of radio-contrast materials injected to the patient during imaging [2]. X-ray exposures during surgery also increases the risk of cataract [3] and protective lead clothes increase the risk of orthopedic injuries [4] for the personnel occupied in surgery room.

Magnetic Resonance Imaging (MRI) guidance was intended to be a new platform by operators to realize imaging of implanted devices or materials for therapeutic procedures without usage of x-ray. Additionally, operators favor MRI to perform complex interventional operations because of many advantages of MRI including superior intrinsic soft tissue contrast and multi slice imaging technique [5]. Accordingly, it is possible to collect reliable and real time physiologic parameters from related tissue via MRI such as flow, volume, pressure, diffusion, perfusion, temperature, motion, etc. [6].

Biomaterials are natural or synthetic materials utilized for treating or replacing of all kind of damaged tissues, vessels, or organs to increase functionality in patient body. A biomaterial not only have to be non-toxic and compatible with the tissue, but also must keep mechanical properties without causing injuring or perforating the tissue structures. Biomaterials can be generally classified as metallic biomaterials, bioceramics, polymer biomaterials and biocomposites [7].

Since MRI physical nature has a high magnetic field inside operation room, there is a constraint to application of metallic based biomaterials for instruments and devices under MRI. Beside of MRI safety concerns with magnetic field effect and RF induced heating problems, medical devices implanted into patient body must be visible and possible for tracking while operator locating a specific material through a tissue or an organ.

2. VISUALIZATION OF DEVICES UNDER MRI

For the realization of invasive operations under MRI scanner, MRI safety is the most challenging issue to overcome. Presence of any kind of metal is not safe in the strong magnetic field environment of a

MRI scanner. Metallic biomaterial-based instruments have the potential to interact with the activated RF transmitter that result in amplified RF heating at vicinity tissue of the instrument [8].

RF induced heating problem under MRI is characterized by the specific absorption rate (SAR), which is expressed as the power dissipated in specific volume [9]:

$$SAR = \frac{\sigma E^2}{2\rho} \quad (1)$$

where σ is the electric conductivity, ρ is the tissue density and E is the magnitude of the electric field. For all metallic components and conductive lines that interact with body under MRI, SAR must be examined because the electric field is maximum at the adjacent tissue.

Limited energy dissipation at adjacent tissue of biomaterials is possible under MRI by considering many factors including strength of the static magnetic field, the strength of the spatial gradient, the mass of the object, the shape of the object, and the magnetic susceptibility of the object [10]. For the detection of these conditions, electrical and magnetic computational analysis of biomaterials can be performed by using a computer environment based finite element method analysis [11].

Visualization of instruments and devices inside human body with the guidance of MRI is a place of interest by researchers for many years. While the interventionist locates an implant properly through a tissue or navigates vascular structures by using guidewires or catheters, a conspicuous distal tip and a detectable shaft under MRI is necessary during operation.

Because metallic materials result in artifacts on image or cause heating risk under MRI, studies focus on plastic and polymer based materials, surfaces and coatings to develop invasive instruments, guidewires and catheters, that is difficult to visualize in MR imaging [10-13].

Considering both safety and visualization issues, 3 main approaches have been presented for tracking of instruments under MRI so far.

A. Passive Imaging Techniques Using Biomaterials

Passive device imaging corresponds to interventional instrument is directly visualized in the acquired image by its own effect on the spins in the specific area of the implant, catheter, or guidewire. Passive imaging techniques are based on markers with specific contrast agents or biomaterials mounted on instrument distal tip and/or shaft without any external connections to the MRI scanner. Since passive devices comprise paramagnetic, ferromagnetic and ferrimagnetic materials that result in distortion effect on T1 and T2 relaxation times of MRI signal, it is possible to obtain a positive or negative contrast between implanted instruments and background anatomy. Accordingly, passive devices do not incorporate metal components and conductive parts, threfore MRI safety concerns and many mechanical problems can be eliminated inherently [14].

The presence of biomaterials and markers with a magnetic susceptibility that are different from the magnetic susceptibility of background tissue distorts the uniform main magnetic field, B_0. As a result of the difference in magnetic susceptibility with respect to the surrounding anatomy, the paramagnetic markers produce a local magnetic field inhomogeneity. This inhomogeneity results in magnetic field variations within voxels that cause spins to precess at different frequencies with respect to Larmor frequency of MRI scanner [14, 15].

Simplest way for implantation of passive tracking is contrast-enhanced MRI tools applied by utilizing implants, catheters or guidewires filled with some contrast agents such as 19F [16] and hyperpolarized 13C [17].

Positive contrast tracking technique may also consists of ring shaped paramagnetic markers such as dysprosium oxide (Dy2O3) [18], iron oxide particles [19], gadolinium diethylenetriamine pentaacetic acid (Gd-DTPA) [20-23] placed within the lumen or on the surface of an instrument that cause T1 shortening and bright signal spots (positive contrast) relative to adjacent tissue. The plastic multi chamber cylinders can be used for positioning of both titanium (paramagnetic) and graphite (diamagnetic) pieces over invasive implant within different layers to develop a positive contrast tracking device [24].

Similarly, negative contrast tracking usually benefits high magnetic susceptibility property of some ferromagnetic materials such as stainless steel, nickel, and copper zinc ferrite. These materials are utilized to impair magnetic homogeneity of main magnetic field under MRI and that result with local signal loss (void) due to intra-voxel dephasing [25-26].

Despite many advantages of passive approaches such as cost effectiveness, resistance to health hazards, and practical to manufacture compared to other methods, generating sufficient contrast between the implanted instruments and adjacent tissue is still a problematic issue. For better depiction of markers and suppression of background signals, additional subtraction sequences or post processing reconstruction methods can be needed that result with additional time consumption. Besides, susceptibility artifact of markers that is necessary for imaging also result in obstruction at surrounding anatomy that hampered to in vivo diagnostic or therapeutic procedures [17, 18, 27].

B. Active Imaging Techniques

The active visualization methods rely on hardware components connected to the MRI scanner via a coaxial cable or a fiber optic cable. Active tracking techniques comprise small receiver coils or antennas placed into the interventional instruments for receiving and/or transmitting the signal via separate channels to the MRI scanner. The implantation can be performed independently from the imaging and so more detailed imaging can be achieved together with accurate coordinates of interventional devices through tissue or vessels. Contrary to passive techniques, long conductive lines used in active approaches for transporting electrical signals between the catheter and MRI scanner, result in significant heating that is induced during RF transmission [28]. Active catheterization may also suffer from limited ability to steer and flexibility in tortuous blood vessels and cardiac chambers due to the rigid and nonflexible mechanical properties of incorporated RF receiver coils and antennas [29].

C. Semi-Active (Hybrid) Imaging Techniques

Semi-active imaging techniques can also be named as hybrid imaging technique since it embodies some of the specific properties of both passive and active imaging techniques. Semi-active methods benefit wireless resonant circuits (RC) as a fiducial RF marker that inductively couples the standard transmitter/receiver coil of MRI scanner without any connection hardware in between. Excitation of RF signal by transmit coil results in locally induced B_1 field over the RF coil and thus substantially enhancing the excitation angle in the directly adjacent surroundings of the RF marker [30]. For semi-active designs since the RF coil is completely activated by RF coupling, heating hazards caused by long conductive lines will be avoided inherently.

Two of the most recent and promising studies presented ultra-thin, flexible and MRI compatible RF markers that provide a robust localization under MRI [31, 32]. As a result of evaluations in phantom and in vitro experiments, the proposed structures may be accepted as feasible for anatomic marking, miniaturization of device and safety. However, the coupling between RF resonator and transmitter and so the visualization of the RF marker is still directly depending on resonator's orientation with respect to the standard transmitter of the MRI scanner [32].

D. Nanoparticles For MRI

Many studies were presented for biomedical applications that benefit nanoparticles with specific electronical (semiconductor etc), optical and magnetic (metal, etc.) properties [33]. Nanoparticles are generally utilized with varied medical imaging modalities as contrast agents and signaling molecules that increase diagnostic capability, drug delivery carriers and therapeutic elements [7]. Radiocontrast agents comprise iron oxide nanoparticles are novel agents for MRI to advance imaging contrast. Semiconducting quantum dots act as optical labels for imaging cells under MRI [33].

3. DISCUSSION

In this review, approaches to develop MRI safe and compatible interventional devices composed of biomaterials has been discussed that will provide sufficient image contrast without impairing effect of mechanical properties and visibility under MRI. Fabrication of interventional instruments that will be used under MRI guidance should be realized by considering many factors involving B_0 magnetic strength, B_1 field orientation, minimization of RF heating, re-manufacturability, biocompatibility, and mechanical properties. These parameters are directly effective on performance of MRI safe and compatible devices including induced current, tuning, Signal to Noise Ratio (SNR), and Quality factor (Q).

Although all mentioned approaches are promising for construction of safe and visible MRI compatible devices, studies should devote more time to present optimized and robust designs to overcome challenges for realization of interventional procedures under MRI.

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