Myocardial Perfusion: New Techniques

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Coronary artery disease is the leading cause of death in the Western world. It is estimated that nearly 7 million people are living with coronary artery disease (CAD) in the United States and about half a million people die from it each year. The most common form of CAD leads to narrowing of the coronary arteries (stenosis) resulting in reduced blood flow and oxygen supplied to the heart muscle. Accurate early detection of flow deficits may permit interventional revascularization procedures (pharmacological intervention, percutaneous transluminal angioplasty, and/or bypass surgery) to re-establish flow to the hypo-perfused regions. The absence of revascularization increases the risk of sudden cardiac death.

Accurate non-invasive methods for detecting coronary artery disease are necessary to determine which patients should undergo revascularization therapy. The gold standard for detecting coronary artery stenosis is x-ray angiography with iodinated contrast agent which is expensive, invasive, and does not provide information regarding the functional status of the myocardium, which is perhaps more important than morphological information in treating the disease.

In order to identify CAD on the basis of functional status of the myocardium, significant research efforts have been devoted to the development of noninvasive methods, but the establishment of such methods remains challenging. Current approaches include computed positron emission tomography (PET), single photon emission computed tomography (SPECT), and myocardial contrast echocardiography (MCE). PET is a promising method for detecting regional myocardial blood flow differences. However, PET studies are limited by low spatial resolution, limited availability, and administration of ionizing radiation. SPECT imaging is the technique most widely used for detecting both metabolic activity and perfusion. However, like PET, SPECT techniques are also limited by low spatial resolution and/or potentially harmful ionizing radiation.

First-pass MRI with gadolinium conjugates has been used for assessing perfusion changes due to coronary artery disease. First-pass methods rely on the detection of changes in myocardial perfusion reserve due to coronary artery disease and thus typically require the use of pharmacological stress agents, such as adenosine or dipyridamole. Unfortunately, since these agents impart physical discomfort in patients, the infusion time of the agent is limited to only six minutes. This method is evaluated most commonly using rapid imaging techniques with multi-slice capabilities. While this approach can identify regions of perfusion deficits, the method is limited by inadequate myocardial coverage and sub-optimal temporal and spatial resolution because of the need to capture the first passage of the contrast media at relatively high temporal resolution (1 frame/heartbeat). These limitations can decrease the diagnostic sensitivity and specificity.

An alternate method for identifying perfusion deficits relies on endogenous contrast mechanism mediated by red blood cells. It is known that magnetic susceptibility of red blood cells is determined by the oxygen saturation ($\%O_2$) of the hemoglobin. Differential $\%O_2$ of hemoglobin molecules affects the local magnetic field variations in the intra- and the extra-vascular spaces. The changes in field inhomogeneities, due to changes in $\%O_2$, are realized as MR signal changes. This is known as blood-oxygen-level-dependent (BOLD) MRI and has enabled the detection of regional activation patterns in the brain.

The potential benefits of BOLD MRI for detecting global or regional myocardial ischemia due to coronary artery disease were demonstrated at least a decade ago. A number of studies have demonstrated the feasibility of using the MR BOLD effects to assess myocardial blood oxygenation secondary to flow changes in both animals and humans. Current BOLD methods rely on deriving oxygen-sensitive contrast with pharmacological stress agents by inducing coronary artery vasodilation, with minimal change in myocardial oxygen demand. Under normal conditions, these stress agents increase baseline coronary venous $\%O_2$ from 20-30% to 70-80%. However, the presence of stenosis limits the coronary venous $\%O_2$ from changing markedly during pharmacologic stress, leading to differential venous $\%O_2$ between ischemic and non-ischemic (healthy) myocardium. The first method used for myocardial BOLD imaging relied on detecting changes in transverse relaxation constant T_2^* due to changes in $\%O_2$ using vasodilatory agents. Although T_2^* studies have shown promising results, large magnetic susceptibility artifacts from the lungs have significantly limited the image quality. More robust T_2-prepared methods have provided improved image quality overcoming susceptibility artifacts from the lungs. However, long data acquisition times, cardiac and respiratory motion, and signal modulation during acquisition have been significant obstacles. More recently, SSFP imaging methods have been used to overcome many of the limitations and have demonstrated the capability of SSFP imaging to detect cardiac phase-resolved regional myocardial BOLD signal changes under pharmacological stress in canines and in patients with suspected coronary artery disease.

While recent advances in myocardial BOLD imaging are promising, the newer techniques need to be validated and extended through prospective clinical studies in patients. Next, all myocardial BOLD imaging methods currently require multiple breath-holds for full myocardial coverage. Since typical myocardial oxygenation changes are assessed in the presence of pharmacological vasodilation, there are pragmatic limitations with 2D approaches that reduce the achievable myocardial coverage within the typical 4-6 min adenosine infusion protocol. Moreover, multiple breath-holds require multiple recovery periods for patients during adenosine infusion, further reducing the time available for imaging. It is expected that free-breathing methods combined with parallel imaging strategies can significantly enhance the myocardial coverage and reduce patient discomfort associated with breath-holding during the adenosine protocol. Finally Successful adoption of recent advances through clinical studies and additional technical improvements can propel myocardial BOLD MRI to becoming a powerful noninvasive diagnostic method in the early detection and post-treatment monitoring of ischemic heart disease.