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Editorial

T2 magnetic resonance mapping: The key to find the '*Brahmastra*' against atherosclerosis?

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The ancient Indian Vedic scriptures (1200 BC) mention the *Brahmastra* as the ultimate weapon, which, when invoked for very specific reasons, never misses its target and causes complete annihilation of the enemy. The *Brahmastra* was created to uphold *Dharma* (i.e., *cosmic law and order*) and *Satya* (i.e., *the truth*). It is obtained by praying to *The Lord Brahma (the creator of the Universe)* and requires strict austerity and penance.

Our recent advances in diagnosing and management of patients with significant atherosclerotic diseases have led to a projected 30% reduction in deaths due to coronary heart diseases by 2020 [1]. Yet, by 2030 almost 44% of the US population will suffer from some type of atherosclerotic cardiovascular disease (ASCVD) [1]. However, the concept of '*vulnerable plaque transformation*' is central to the development of acute coronary syndromes (ACS) and cerebrovascular accidents (CVA), which are the most devastating end products of ASCVD. Plaque morphological features, such as increased necrotic core volume, decreased fibrous content, or thin cap fibroatheroma are believed to be the precursors of the rupture-prone vulnerable plaques that cause adverse cardiac events. Hence, early identification of such vulnerable plaque features could help identity high-risk patients for initiating intensive anti-atherosclerotic therapies (e.g., high-intensity statins), thereby stabilizing the vulnerable plaque and improving outcomes.

Among patients with atherosclerotic disease, the development of new effective lipid lowering medications such as proprotein convertase subtilisin kexin 9 (PCSK9) inhibitors has again brought back the focus of the cardiology community on targeting lower serum low-density lipoproteins (LDL-c) levels to prevent cardiovascular events even in patients already on statins [2]. Direct tissue characterization of atherosclerotic plaques might provide further insights into the mechanisms behind the lipid-lowering properties of these novel agents. In addition, identification of plaque lipid content might help identify patients at risk of cardiovascular events requiring additional lipid-lowering agents on top of statins. Indeed, invasive catheter-based modalities, such as intravascular ultrasound and near infra-red spectroscopy, have been used to demonstrate the effectiveness of statins in reducing plaque lipid core volume, increasing fibrous percentage and causing plaque regression [3,4]. However, the invasive nature of these intravascular imaging modalities precludes their adoption as effective screening tools to prevent ASCVD.

Cardiovascular magnetic resonance imaging (CMR) is fast emerging as an imaging modality of choice to diagnose and monitor various cardiovascular pathologies, as it combines the ability to identify excellent anatomic details with accurate tissue characterization. Also, it has the additional benefit of being a non-invasive modality leading to faster clinical utilization and better patient acceptance. Indeed, previous studies investigating the utility of CMR to characterize atherosclerotic plaques in carotid artery and aorta have demonstrated regression of lipid rich necrotic core in response to statin therapy [5]. Furthermore, multi-contrast CMR is able to differentiate the different signal intensities of the various plaque components on T1, T2 and proton density-weighted images [6]. Therefore, CMR is able to acertain lipid-rich necrotic core, calcification, intraplaque hemorrhage and fibrous tissue and was recently validated for accuracy against histopathology in patients receiving carotid endarterectomies [6]. In addition, T2 mapping was recently utilized to demonstrate that carotid plaques from symptomatic patients have higher lipid content when compared to asymptomatic patients despite similar degrees of lumen stenosis [6]. This important result reveals that CMR-derived plaque characterization is probably more important to risk stratify and inform effective treatment strategies to prevent CVA in patients with carotid vessel atherosclerosis rather than the established norm of degree of carotid lumen stenosis derived by duplex ultrasound [6]. However, a major limitation of this technique was the observed high sensitivity of the DANTE- MESE [Delay Alternating with Nutation for Tailored Excitation (DANTE) pulse trains with chemical-shift-selective fat saturated Multiecho Spin-Echo (MESE)] sequences to motion artefact (35%) that were used to generate the multi-slice carotid T2 maps [6].

In this issue of *Atherosclerosis,* Alkhalil et al. [7] investigated the utility of carotid plaque characterization using T2-mapping to monitor the response to high intensity statins among patients with ACS. While carotid lipid percentage decreased from 10.3% to 7.4% ($p = 0.002$), fibrous plaque percentage increased from 83.3% to 85.5% ($p = 0.039$) after 3 months of high-intensity statin therapy among 23 patients with ACS. The authors also reported an improvement in the T2 mapping

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technique by reducing the rejection rate of the DANTE- MESE sequence to 13% by developing better motion correction strategies. Hence, the authors report that T2 mapping is a more sensitive modality to detect plaque stability in response to high-intensity statin therapy. Moreover, T2 mapping might be used as an effective tool for secondary prevention of cardiovascular events by identifying patients who will require additional lipid lowering drugs. Additionally, in the current study, improvement in serum biomarkers did not follow a decrease in lipid content of the plaques, suggesting that direct quantification of plaque lipid might be able to identify patients at the greatest risk for future ASCVD. This strategy might even be more cost effective and identify patients who continue to have a truly vulnerable plaque and might benefit from the addition of a new - but very costly - lipid-lowering medications e.g., PCSK9 inhibitors. Indeed, since plaque characterization by CMR is still only limited to peripheral vessels, the authors need to be congratulated for trying to extend the use of the novel T2-mapping sequence, developed by the same authors as a tool for secondary prevention in patients with history of cardiac events.

It is important to acknowledge that the current study has several limitations. Although novel, it is strictly hypothesis-generating and exploratory in nature. A small number of patients, lack of a comparison group, and low number of patients with common cardiovascular risk factors (such as only one patient with diabetes) prevent the readers from drawing robust conclusions. Large clinical outcome studies will be required to examine the impact of intensive lipid-lowering therapy among patients with persistently high carotid plaque lipid percentage and low fibrous percentage despite statin therapy. Finally, while the current results were generated using 3T scanners, most clinical grade CMR machines in the United States are 1.5T scanners and hence it would be interesting to examine the clinical adoption and validation of this novel technique by other cardiac centers in the future.

Nonetheless, a recent report found that high lipid content and thin fibrous cap in carotid plaques demonstrated by CMR strongly predict systemic cardiovascular outcomes, including myocardial infarction, ischemic stroke and cerebrovascular revascularization regardless of clinical risk factors, plaque burden or treatment strategies, further accentuating our interest in this technology [8]. In conclusion, quantitative carotid plaque characterization using T2 mapping might help us identify the vulnerable plaque, but also might be a key to find the *Brahmastra: the ultimate therapy* against atherosclerosis and vulnerable plaque transformation.

Conflict of interest

The authors declared they do not have anything to disclose regarding conflict of interest with respect to this manuscript.

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