Ex vivo study of carotid endarterectomy specimens: quantitative relaxation times of atherosclerotic plaque tissues

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Introduction

Previous studies reporting relaxation times within atherosclerotic plaque have typically used dedicated small-bore high-field systems and small sample sizes.[1-3] This study reports quantitative T_1, T_2 and T_2* relaxation times within plaque tissue at 1.5T using spatially co-matched histology to determine tissue constituents.

Methods

Ten carotid endarterectomy specimens were removed from patients with advanced atherosclerosis. Imaging was performed on a 1.5T whole-body scanner (Signa HDx, GE Healthcare, Waukesha, WI) using a custom built 10mm diameter receive-only solenoid coil (FES, Winterswijk, The Netherlands). A protocol was defined to allow subsequent computation of T_1, T_2, and T_2* relaxation times using multi-flip angle spoiled gradient echo, multi-echo fast spin echo and multi-echo gradient echo sequences respectively (Table 1). The specimens were subsequently processed for histology and individually sectioned into 2mm blocks to allow subsequent co-registration. The following stains were performed: hematoxylin and eosin, elastic-Van Gieson and CD68. Specimens were digitized using an electronic microscope at 5× magnification (Leica DM LB2, Leica Microsystems, Wetzlar, Germany). Each imaging sequence was imported into in-house software developed using Matlab version 7.5.0 (The Mathworks, Inc, Natick, MA) and displayed alongside the digitized histology sections. Regions of interest were defined to demarcate fibrous cap, connective tissue and lipid/necrotic core at matched slice-locations. Relaxation times were calculated using Levenberg-Marquardt's least squares curve fitting algorithm. A linear-mixed effect model was applied to account for multiple measurements from the same patient and establish if there was a statistically significant difference between the plaque tissue constituents. Variability within each patient was modeled as a random effect to account for multiple measurements acquired from the same patient.

Results

T_2 and T_2* relaxation times were statistically different between all plaque tissues (p=0.026 and p=0.002 respectively) [T_2: lipid/necrotic core 47±13.7ms was lower than connective tissue (67±22.5ms) and fibrous cap (60±13.2ms); T_2*: fibrous cap (48±15.5ms) was higher than connective tissue (19±10.6ms) and lipid/necrotic core (24±8.2ms)] (summarized in Table 2 and Figure 1). T_1 relaxation times were not significantly different (p=0.287) [T_1: Fibrous cap: 933±271.9ms; connective tissue (1002±272.9ms) and lipid/necrotic core (1044±304.0ms)]. We were unable to demarcate hemorrhage and calcium following histological processing.

Discussion

Existing limitations have confined carotid MRI to the research domain. These include the necessity to have a dedicated in vivo coil, total scan time and the expertise and time required to subjectively delineate plaque tissues by way of interpreting signal intensity differences using multi-contrast weighted sequences. Quantitative techniques have a potential to elevate this final issue and there appears to be a building body of evidence to suggest that T_2 and T_2* relaxation times are predictive of the plaque tissue constituents and may therefore be indirectly associated with risk. The identification of a shortened T_2 of lipid and necrotic core components in our study adds to the validity of using MRI to distinguish lipid from other components such as fibrous cap. T_2-weighted imaging has long been applied as a means of ascertaining lipid and fibrous cap status with an evidence bases supported by early ex vivo studies on carotid endarterectomy specimens.[1,4] Elevated T_2* may also connote risk reduction. A previous study reports a corollary finding of lower T_2* in symptomatic patients; reporting global plaque T_2* values of 20.0 ms for symptomatic patients compared with 34.4 ms for asymptomatic patients.[5] We report fibrous cap T_2* values of ~50 ms, suggesting that the elevated global T_2* wall measurements may be due to a larger spatial extent of stable fibrosis tissue. This study demonstrates that there is a significant difference between qT_2 and qT_2* in core plaque tissues types. Derivation of quantitative relaxation times shows promise for determining plaque tissue constituents or may indirectly be predictive of risk.

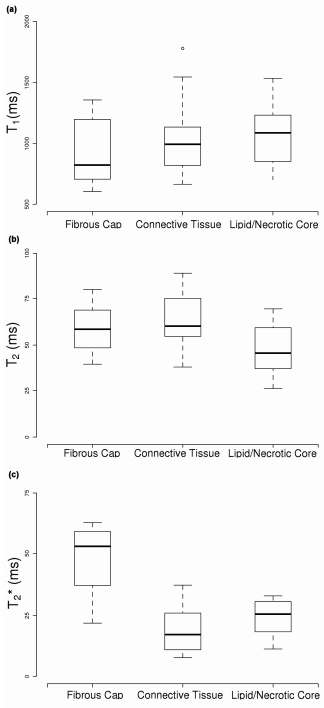

Fig 1. qT1, T2 and T2* disbributions (a, b & c respectively) are plotted for fibrous cap, connective tissue and lipid/necrotic core.

	qT_1	qT_2	qT_2*
Sequence	3D-SPGR	2D-MEFSE	2D-MEGRE
TE(ms)	10	18.1-144.5	4.0-35.3
TR(ms)	35	800	75
No. of Echos	1	8	8
Flip Angle(s)	10-90°	90°	30°
Matrix Size	256x256	256x256	256x256
NEX	1	4	4
FOV(cm)	4	3	8
Slice Thick.	1	2	2

Table 1 Pulse sequence parameters

	Fibrous Cap	Connective Tissue	Lipid/Necrotic Core	p-value
qT_1 (ms)	933 ±271.9	1002 ±272.9	1044 ±304.0	0.287†
qT_2 (ms)	60 ±13.2	67 ±22.5	47 ±13.7	0.026†
qT_2* (ms)	48 ±15.5	19 ±10.6	24 ±8.2	0.004†

Table 2 Distributions of relaxation times within plaque tissues

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