Effective T2 histograms derived from fast spin-echo data as an integrative marker of the atherosclerotic plaque tissue composition

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Introduction: Development of non-invasive tools for measurement of integrative tissue characteristics reflecting tissue composition and response to treatment represents an emerging area of atherosclerosis research. In the context of lipid-lowering therapy, MRI-derived measures of the relative lipid content in the atherosclerotic plaque are of special importance. T2 measurements provide a well-known approach for quantitative tissue characterization in MRI. Dual-echo approach with fast spin-echo (FSE) acquisition represents attractive opportunity for quantitative characterization of T2 in atherosclerotic lesions because it provides inherently registered data, allow fast acquisition, and facilitate elimination of spatial signal non-uniformities caused by the coil sensitivity profile. Due to inherent physical differences between FSE and regular SE measurement techniques we refer below to the effective T2 as a term describing T2 data extracted from FSE imaging experiments. The purpose of this study was to develop the technique for histogram analysis of effective T2 data obtained with the FSE sequence and evaluate the feasibility of the use of effective T2 histogram parameters for characterization of lesion tissue composition.

Methods: ***Clinical MRI protocol:*** 26 patients with 15-70% stenosis of the carotid artery (by Doppler ultrasound) were scanned on a 1.5T MR scanner (GE Signa) with a specialized phased-array carotid coil (Pathway Medical). Patients were scanned with the standard carotid imaging protocol (1) including blood-suppressed multi-contrast (T1-, PD-, and T2-weighted) scans and 3D TOF angiography. PD- and T2-weighted images were acquired using a dual-echo method with a cardiac-gated shared-echo FSE sequence at following parameters: TR=3RR, TE1/TE2=20/40 ms, FOV=16x12 cm, matrix size 256x256 zero-interpolated to 512x512, NEX=2, echo train = 6, scan time 5-6 min depending on the heart rate. Blood suppression was achieved using parallel saturation bands, and spectrally-selective fat suppression was applied to improve visualization of the outer wall boundary. 18 slices centered at the carotid bifurcation were acquired for each patient.

Table 1. T2 (ms) measured with SE and FSE sequences

Method	Oil	Beef	$MnCl_2$,0.3 mM	Gd, 1 mM	Water
SE	38.6	42.8	47.5	176.0	1086.0
FSE	68.7	43.3	49.7	159.0	919.7

Phantom experiments: To evaluate the feasibility and accuracy of T2 measurements with a dual-echo FSE technique, it was compared with a traditional method based on a spin-echo (SE) sequence with variable echo time. The phantom contained oil and bovine muscle as models of lipid and fibrous tissues and a series of solutions with different relaxation properties (Table 1). SE measurements were conducted in a single slice with TR=3000 ms, and TE=15,30,60,120, and 240 ms. The multislice FSE technique was identical to that used in the clinical protocol with TR=3000 ms.

Image analysis: Multi-contrast images were reviewed by one reader in order to determine lesion type according to the modified AHA classification (2). The lesions were grouped into three categories:

- **Early lesion (Group I):** AHA type 1-3 lesions showing diffuse wall thickening and uniform signal in the wall;
- **Advanced lesion with lipid core (Group II):** AHA type 4-6 lesions showing asymmetric wall thickening with hyperintense (possibly non-uniform) signal on T1-weighted images.
- **Advanced fibrocalcified lesion (Group III):** AHA type 7 lesions showing visible amount of calcificates without formation of lipid core.

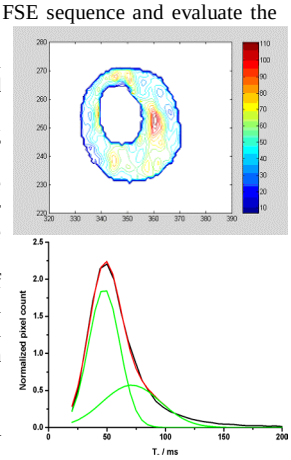

Fig. 1 Effective T2 map of an atherosclerotic plaque and scheme of histogram fit.

Histogram processing: Lumen and outer wall contours of the common and internal carotid arteries were manually outlined on PD-weighted images using custom-designed software. The dual-echo data for the vessel wall were processed to generate voxel-based effective T2 maps (Fig. 1): $T_{2eff} = (TE_{T2} - TE_{PD}) / \ln(I_{PD} / I_{T2})$.

Effective T2 histograms for each patient were obtained from these maps with bin size of 6 ms and normalized to the total number of voxels corresponding to the outlined vessel wall. Individual histograms were fitted with a two-peak Gaussian model heuristically chosen to describe fibrous and lipid components:

$$H = \sum_{i=1}^{N} A_i / (w_i \sqrt{\pi / 2}) \exp[-2(T_2 - T_{2i})^2 / w_i^2]$$

where N=2, T_{2i} are peak positions, A_i are peak areas, and w_i are peak widths. Typical fitted and experimental histograms are shown in Fig 1. Fitted histogram parameters were compared between lesion type groups using unpaired Student's *t*-test.

Table 2. Effective T2 histogram parameters and comparisons between lesion type groups

Parameter	Group I	Group II	Group III	*P*: II vs. III
A_1	**59.6±14.6**	**53.8±15.1**	**68.0±9.0**	**0.03**
w_1	26.4±5.7	23.4±5.0	24.3±1.7	NS
T_{21}	45.3±7.7	46.0±5.4	48.4±2.1	NS
A_2	**38.6±12.5**	**43.6±14.8**	**29.9±8.1**	**0.02**
w_2	46.0±10.9	45.1±19.8	40.3±3.5	NS
T_{22}	71.9±13.7	71.5±12.8	69.8±5.1	NS

Results: ***Phantom validation*****:** Both methods provided consistent measurements for all media with physiologically reasonable T2, except oil (Table 1). Effective T2 of oil measured with FSE was considerably large than the actual value. Theoretically, this can be explained as a result of decoupling of aliphatic multiplets by a train of refocusing pulses (similar to an increase of the fat signal on FSE images). From practical point of view, improved separation of water and fat peaks in the effective T2 spectrum validates the use of histograms for estimation of lipid content in fibrous matrix.

In vivo lesion characterization: The patient population represented 9 early lesions, 9 advanced lesions with lipid core, and 8 fibrocalcified lesions. Average group histograms demonstrate visible differences in their shapes (Fig. 2). Mean histogram parameters for each group are listed in Table 2. No significant differences were found in peak positions and widths between groups. Average peak positions represent excellent agreement with phantom measurements for muscle tissue and oil that facilitates interpretation of peak areas in terms of relative content of fibrous and lipid components. Peak areas were significantly different between fibrocalcified lesions and lesions with lipid core. In accordance with the hypothesis about peak origins, fibrocalcified lesions demonstrate higher fibrous tissue content and lower lipid content as opposed to lipid-rich lesions. Peak areas for early lesions did not reach statistically significant differences relative to other groups. Both peaks in the early lesion group demonstrated intermediate position between two advanced lesion groups. This indicates the possibility of two ways for evolution of early lesions: further accumulation of lipids and formation of lipid core or proliferation of fibrous tissue and calcification.

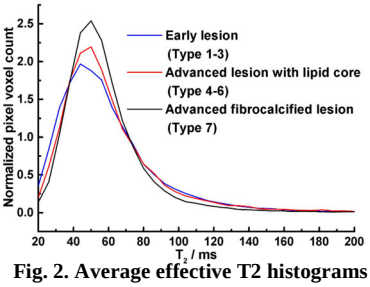

Fig. 2. Average effective T2 histograms for three lesion type groups.

Conclusions: Our results support the assumption that the balance between lipid and fibrous components in the atherosclerotic plaque is reflected by the shape of the effective T2 histogram. Effective T2 histogram analysis represents a new approach for quantitative characterization of human atherosclerotic lesions with primary focus on their integral tissue composition.

References: 1) Yuan C, et al. Radiology 2001;221:285-99; 2) Cai JM, et al. Circulation. 2002;106:1368-73.