

Improved calcification detection accuracy on human atherosclerotic plaque using Ultra-short TE (UTE) imaging

J. Wang¹, M. S. Ferguson², N. Balu², C. Yuan², and P. Boernert³

¹Clinical Sites Research Program, Philips Research North America, Seattle, WA, United States, ²University of Washington, ³Philips Research Europe

Introduction

Ultra-short TE (UTE) images can provide positive contrast for short T₂ species to facilitate their visualization and identification when combined with imaging techniques such as dual-echo subtraction or magnetization preparation (1,2). In human atherosclerotic plaques, calcium deposits in the thin fibrous cap could result in increased risk of plaque rupture (3). The identification of calcification at such locations, however, has been challenging based on traditional MR images because the dark signal of calcification can not be easily differentiated from the dark lumen. UTE images can potentially identify such juxtalumenal calcification because of their ability to visualize very short T₂ species with positive contrast. UTE MR is a better imaging approach than CT imaging because of the lack of radiation and blooming effects. Although the calcified regions identified on UTE images were demonstrated to agree with CT images (4), its accuracy has not been validated against histology. This study is aimed at comparing the accuracy of UTE calcification detection in human carotid plaques against regular turbo spin echo MR images, as well as validating it against histology.

Methods

MR scans

Five human carotid endarterectomy specimens were imaged on a 3T clinical scanner (Philips Achieva 3T, R2.6.1, Best, the Netherlands) using a 4-channel solenoid small animal coil. The 3D UTE imaging parameters were: TR/TE1/TE2 31/0.09/4.6ms, FA 10°, FOV 28×28×28mm³, isotropic imaging voxel size 0.25×0.25×0.25mm³, 1 NSA, 60% filled 3D radial sampling matrix (~33,900 radial profiles), acquisition time 17min31sec. The PDw imaging parameters were: TSE sequence, TR/TE 4000/9ms, FOV 24×24mm, pixel size 0.12×0.12mm, slice thickness 1mm, 32 slices, ETL 8, 1NSA, acquisition time 3min20sec.

Image processing

Both UTE and PDw images were reconstructed in the axial direction with resolution 0.25×0.25×1mm to facilitate the following comparison. Subtraction between images from the first and second echo of UTE was used to generate the positive calcium contrast on UTE images. The presence or absence of calcification was reviewed on a slice basis. The contours of the calcification regions were only delineated on UTE images by an experienced MR image reviewer. After blinded review, images were compared directly with histology to identify reasons for discrepancy.

Histology processing

After fixation and decalcification the plaque specimen was processed and embedded *en bloc* in paraffin. Sections of 4μm were collected at 1mm intervals throughout the plaque. Calcification regions were outlined by an experienced histologist on a slice basis.

Statistical comparison

MR and histology images were matched based on the location of the carotid bifurcation and the shape of the lumen on each slice. Identification of calcium on UTE and PDw images was evaluated by Cohen's Kappa compared to histology. For UTE calcification measurements, Pearson's correlation was used to evaluate size measurement accuracy when compared with histology. Bland-Altman plot was used to evaluate the measurement agreement.

Results

78 MR slices were matched with corresponding histology slices. The rest of the slices were excluded for further analysis. A visual inspection found good correspondences between UTE, PDw and calcification regions identified on histology (Fig. 1a-c), except on six locations where calcification can be identified on UTE but missed on the corresponding PDw images (Fig. 1d-f). Quantitatively, UTE provides a higher Kappa value (UTE 0.84, PDw 0.66), higher sensitivity (UTE 0.96, PDw 0.83) and better specificity (UTE 0.88, PDw 0.84) compared to PDw, when using histology as a reference for calcification detection. In all 43 slices with calcification on histology, size measurements on UTE images was highly associated with histology ($r = 0.88$, $p < 0.01$). Further, no obvious trend was found between UTE and histology measurements on Bland-Altman plot (Fig. 2). The area measurement on histology was 10% smaller than that from UTE, likely caused by the sample shrinkage during the histology processing.

Discussion and Conclusion

To our best knowledge, this is the first histology validated atherosclerotic plaque calcification imaging using UTE technique. Calcification missed on PDw was identified on UTE showing that UTE images are more sensitive to calcification because of the positive calcification contrast it provides. The partial volume effect may prevent the dark signal on regular MR images to be detected, especially for smaller or speckled calcification pieces. In general there was good agreement for identification and measurement of calcium on UTE images, the minor disagreement with histology are attributed to: 1) Small air bubbles introduced during specimen preparation usually carries bright contrast; 2) The shrinkage of histology specimens can frequently cause slice mismatches with MR slices; 3) the slice thickness difference between histology and MR images (4μm vs. 1mm).

In conclusion, when compared with regular MR images, UTE was found to be more sensitive for calcification detection and can provide very good size measurement when comparing against matched histology. The improved sensitivity and accuracy offered by UTE can help in understanding the role of calcification in atherosclerosis through future serial *in vivo* imaging.

References

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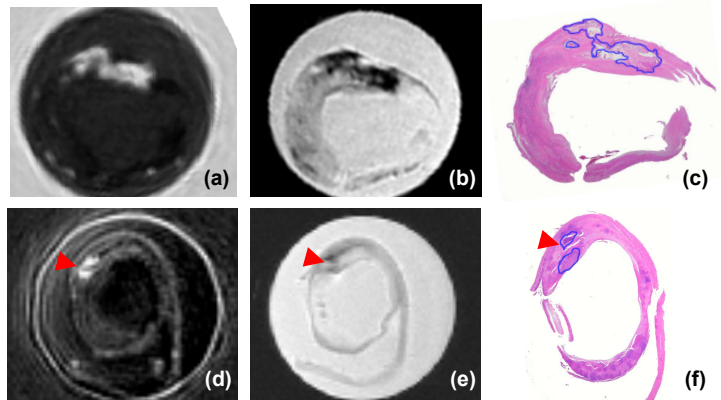


Fig. 1 Calcification identification comparison between UTE (a, d), regular PDw (b, e) and corresponding histology (c, f) slices. Both UTE and PDw images corresponded well with histology on most locations (a-c), except on a few locations where calcification can be detected on UTE images but missed on the corresponding PDw images (Arrowheads on d-f).

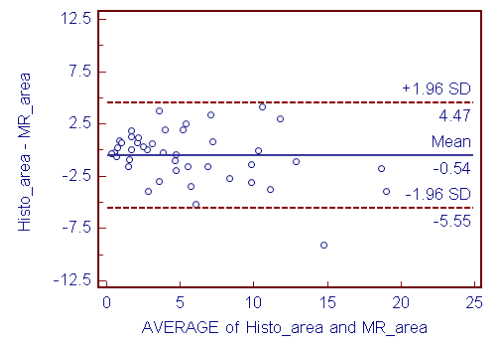


Fig. 2 The Bland-Altman plot comparing the calcification measurements obtained on UTE images and matched histology slices. No obvious trend can be observed on the plot.