Radiomics to Identify High-Risk Atherosclerotic Plaque From Computed Tomography

The Power of Quantification

Damini Dey, PhD; Frederic Commandeur, PhD

Measure what is measurable, and make measurable what is not so.

—Galileo Galilei (1564–1642)

Coronary computed tomographic angiography (CTA) allows noninvasive assessment of the coronary anatomy and is increasingly used for the assessment of luminal stenosis. The time period during which CTA matured (starting in the early 1990s and continuing to this day) also coincides with dramatic increases in computational power by standard off-the-shelf computer workstations and novel methodological developments, which enable many applications in the field of medical imaging. Radiomics, which includes the extraction and mining of a large number of quantitative features from imaging, and is usually applied to quantify tumor phenotype characteristics,[1] is one of these applications.

See Article by Kolossváry et al

Beyond stenosis, CTA also allows noninvasive assessment of atherosclerotic plaque, including plaque composition, distribution, and burden, as well as coronary artery remodeling. Several qualitative high-risk plaque characteristics, including positive or outward coronary artery remodeling and low-attenuation plaque, have been shown to independently predict future major adverse cardiovascular events. In a study of 1059 patients undergoing CTA with mean follow-up of 27 months, Motoyama et al[2] have shown that patients with coronary plaques with positively remodeling or low-attenuation content were at a higher risk of developing future acute coronary syndrome. In a more recent study of 3158 patients undergoing CTA with mean follow-up of 3.9 years, plaques with positive remodeling, low attenuation, and visually assessed plaque progression were predictive of future acute coronary syndrome.[3] The napkin-ring sign is an adverse plaque feature, defined as a plaque cross section with a central area of low CT attenuation in contact with the lumen, which is surrounded by a ring-shaped higher attenuation plaque tissue. In a study of 895 patients undergoing CTA with mean follow-up of 1 year, Otsuka et al[4] have shown that the napkin-ring sign demonstrated on coronary CTA is strongly associated with future acute coronary syndrome, independent of other high-risk coronary CTA plaque features.

In this issue of *Circulation: Cardiovascular Imaging*, Kolossváry et al[5] use radiomics for the identification of the coronary plaques with napkin-ring sign. In this carefully performed feasibility study, the authors compared 30 patients with plaques with napkin-ring sign to 30 matched patients with plaques with no such sign but with similar degrees of calcification, luminal obstruction, localization, and acquisition parameters. All plaques were segmented manually using commercial software (QAngio CT), and 8 conventional quantitative plaque metrics (lesion length, area stenosis, mean plaque burden, lesion volume, remodeling index, mean plaque attenuation, minimal plaque attenuation, and maximal plaque attenuation) were computed. The segmented plaques were analyzed using a Radiomics Image Analysis package developed by the authors to quantify 4440 radiomic parameters. Performance of the radiomic parameters and conventional parameters for the identification of plaques with napkin-ring sign was compared, using Receiver Operator Curve analysis and 5-fold cross-validation. The authors showed that several radiomic features (including 3 parameters—short and long run low gray-level emphasis and surface ratio of high-attenuation voxels/total surface—which highlight low-attenuation and heterogeneous morphology in napkin-ring sign plaques) showed significantly higher discrimination of high-risk plaques than lesion volume and other conventional quantitative parameters.

The authors should be commended for this novel application of radiomics to identify plaques with napkin-ring sign. Radiomics uses voxel values and their relationship to each other to quantify image characteristics, and this work demonstrates that the small number of voxels in coronary plaques are sufficient for radiomics analysis.

Despite the novel analysis in this study; however, several limitations must be acknowledged. Notably, only plaques with napkin-ring sign but no other adverse plaque characteristics—low-attenuation, positive remodeling—were considered. Radiomics quantification required segmented plaques to be saved, an option not readily available from plaque analysis tools. Quantitative low-attenuation noncalcified plaque volume, which is relevant to plaques with napkin-ring sign, has been shown to predict future adverse cardiovascular outcomes in several studies.[6,7] Recent studies have also shown that this quantitative adverse plaque measure is significantly related to lesion-specific ischemia measured by invasive fractional flow reserve.[8,9] Radiomics parameters quantified in this study were

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compared with total plaque volume, rather than the more relevant low-attenuation noncalcified plaque volume.

From radiomics quantification, a large number of quantitative features (4400 in the current study) are extracted from the same voxels; these features are typically significantly correlated with each other. In this study, individual comparisons of each quantitative radiomics feature with lesion volume were performed because the study was limited by case–control study design and the small number of patients examined. However, to leverage the full potential of radiomics, in future studies, machine learning could potentially be used to automatically select features and combine predictive features together to enhance identification of high-risk plaques, as already demonstrated for tumor phenotyping in lung cancer.[1]

Despite the limitations, this work is a step toward measuring what has to date not been measurable and to find quantitative biomarkers for identifying high-risk atherosclerotic plaques imaged by coronary CTA.

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Dr Dey may receive royalties from Cedars-Sinai Medical Center and has a patent. The other author reports no conflicts.

References

1. Parmar C, Grossmann P, Bussink J, Lambin P, Aerts HJ. Machine learning methods for Quantitative Radiomic Biomarkers. *Sci Rep*. 2015;5:13087. doi: 10.1038/srep13087.
2. Motoyama S, Sarai M, Harigaya H, Anno H, Inoue K, Hara T, Naruse H, Ishii J, Hishida H, Wong ND, Virmani R, Kondo T, Ozaki Y, Narula J. Computed tomographic angiography characteristics of atherosclerotic plaques subsequently resulting in acute coronary syndrome. *J Am Coll Cardiol*. 2009;54:49–57. doi: 10.1016/j.jacc.2009.02.068.
3. Motoyama S, Ito H, Sarai M, Kondo T, Kawai H, Nagahara Y, Harigaya H, Kan S, Anno H, Takahashi H, Naruse H, Ishii J, Hecht H, Shaw LJ, Ozaki Y, Narula J. Plaque characterization by coronary computed tomography angiography and the likelihood of acute coronary events in mid-term follow-up. *J Am Coll Cardiol*. 2015;66:337–346. doi: 10.1016/j.jacc.2015.05.069.
4. Otsuka K, Fukuda S, Tanaka A, Nakanishi K, Taguchi H, Yoshikawa J, Shimada K, Yoshiyama M. Napkin-ring sign on coronary CT angiography for the prediction of acute coronary syndrome. *JACC Cardiovasc Imaging*. 2013;6:448–457. doi: 10.1016/j.jcmg.2012.09.016.
5. Kolossváry M, Karády J, Szilveszter B, Kitslaar P, Hoffmann U, Merkely B, Maurovich-Horvat P. Radiomic features are superior to conventional quantitative computed tomographic metrics to identify coronary plaques with napkin-ring sign. *Circ Cardiovasc Imaging*. 2017;10:e006843. doi: 10.1161/CIRCIMAGING.117.006843.
6. Hell MM, Motwani M, Otaki Y, Cadet S, Gransar H, Miranda-Peats R, Valk J, Slomka PJ, Cheng V, Rozanski R, Tamarappoo BK, Hayes S, Achenbach S, Berman DS, Dey D. Quantitative global plaque characteristics from coronary CT Angiography for the prediction of future cardiac death during 5 years of follow-up. *Eur Heart J Cardiovasc Imaging*. 2016;18:1331–1339.
7. Nadjiri J, Hausleiter J, Jähnichen C, Will A, Hendrich E, Martinoff S, Hadamitzky M. Incremental prognostic value of quantitative plaque assessment in coronary CT angiography during 5 years of follow up. *J Cardiovasc Comput Tomogr*. 2016;10:97–104. doi: 10.1016/j.jcct.2016.01.007.
8. Diaz-Zamudio M, Dey D, Schuhbaeck A, Nakazato R, Gransar H, Slomka PJ, Narula J, Berman DS, Achenbach S, Min JK, Doh JH, Koo BK. Automated quantitative plaque burden from coronary CT angiography noninvasively predicts hemodynamic significance by using fractional flow reserve in intermediate coronary lesions. *Radiology*. 2015;276:408–415. doi: 10.1148/radiol.2015141648.
9. Gaur S, Øvrehus KA, Dey D, Leipsic J, Bøtker HE, Jensen JM, Narula J, Ahmadi A, Achenbach S, Ko BS, Christiansen EH, Kaltoft AK, Berman DS, Bezerra H, Lassen JF, Nørgaard BL. Coronary plaque quantification and fractional flow reserve by coronary computed tomography angiography identify ischaemia-causing lesions. *Eur Heart J*. 2016;37:1220–1227. doi: 10.1093/eurheartj/ehv690.

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