Hiding beyond plain sight: Textural analysis of positron emission tomography to identify high-risk plaques in carotid atherosclerosis

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Over the last few decades, technological advances in hardware and acquisition techniques have produced ever more complex and sophisticated data-rich medical images. By comparison, the interpretation of these images has remained largely dependent on manual processing by expert humans with more recently variable levels of operator-driven software assistance. The latter has proven to be a dependable and successful model. Arguably, nothing need change, but on the other hand, if we accept that there may be additional clues beneath the surface and beyond our human perception in increasingly data-rich images, it would be against our pioneering spirit as medical investigators to sit complacently and not explore methods of extracting that hidden data.

Currently, most medical imaging is assessed visually, with substantial amounts of imperceptible but feature-rich information unwittingly discarded. Medical images from most modalities using modern scanner hardware typically contain between 12 and 16 bits/pixel, which corresponds to 4,096–65,536 shades of gray.¹ However, even on medical-grade displays, we have a much lower number of gray shades available to review (typically up to 1,024); and it is estimated that the human eye can perceive no more than around 900

shades of gray anyway.¹ So, for as long as image analysis remains a human enterprise, it is subject to the limitations of human ability and the extraction of additional features to finesse interpretation requires a more technologically advanced approach. One potential way of accessing this hidden information is by using radiomics, which is the mathematical extraction of large amounts of quantitative features from clinical imaging using data characterization algorithms.²

Texture analysis is one form of radiomic assessment that specifically assesses the variation in grayscale image intensities within an image, i.e., radiologic texture.³ The underlying assumption in texture analysis is that grayscale values and their spatial and temporal interrelationships within an image reflect phenotypic variations in the imaged tissue and may indicate molecular variations.^{3,4} Recently, there has been a substantial interest in texture analysis in the oncology setting. Several studies have utilized texture analysis of Fluorine-18 fluorodeoxyglucose positron emission tomography (18F-FDG PET) to assess intra-tumoral heterogeneity which is associated with tumor aggressiveness^{5,6}; and have shown promising results in predicting treatment response and patient survival.^{7–12}

By comparison, there has been only limited study of texture analysis techniques in vascular PET imaging and atherosclerosis. However, in this issue of the Journal of Nuclear Cardiology, Kafouris et al assess the feasibility of texture analysis in carotid arteries using 18F-FDG PET-CT images to predict histological and immunohistochemical features of event-prone plaque.¹³ Sixty-seven different 18F-FDG PET-based textural features were extracted from carotid images of 21 patients with high-grade carotid stenosis undergoing endarterectomy. Accepting the acknowledged limitations including a small sample size and a considerable spectrum bias, the authors found several textural-based metrics showing

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significant promise in independently identifying confirmed histopathological features of plaque vulnerability and in some cases with incremental accuracy over standard target-to-background ratio (TBR) assessments.

Regarding the concept of identifying carotid artery event-prone plaque more broadly, some cautions are worth noting from parallel studies of coronary artery disease (CAD). In the latter, the search for the vulnerable plaque has been extensive and resource-intensive, and so far, has also failed to change clinical care.¹⁴ Although retrospective studies have successfully linked culprit plaque to different adverse imaging characteristics, prospective studies have suggested that these supposedly high-risk plaques rarely go on to cause clinical events themselves.¹⁵ The likely explanation for this apparent discrepancy is that the majority of ‘high-risk’ plaques actually heal without rupturing. Intuitively, these same limitations may also apply to carotid artery atherosclerosis.¹⁶ However, combining multiple adverse plaque characteristics does seem to improve the positive predictive value of events in CAD, and possibly this supports attempts at more sophisticated analysis such as texture analysis.^{14,15} Whether such approaches in coronary or carotid atherosclerosis will ever be sufficient to prompt plaque-specific revascularization or aggressive systemic therapies is, however, the subject of considerable debate.^{14,17}

Leaving aside the occasional hysteria of artificial intelligence replacing all radiologists, the principle of radiomics tackles a more fundamental recognition that there is a biological limitation to human capability.¹⁸ Until perhaps human evolution catches up—and incidentally there are already a small number of women called tetrachromats possessing a mutation allowing them to perceive 100 million rather than just 1 million colors—radiomics provides us with more information than comprehensible by visual inspection with each lesion being characterized by hundreds of different parameters.¹⁹

Finally, although visual inspection is sufficient for clinical diagnosis, there is a growing need for quantitative image analysis techniques that can further increase our understanding of disease processes and the precision of image-based risk prediction. Radiologic examinations are vast spatial data sets, where every voxel is a potential data mine itself, and radiomics tries to utilize this information by quantifying properties beyond plain human sight. However, clinical translation is still a challenge as we currently lack adequate large-scale evidence to support the scientific claims—but with ongoing development the potential for this emerging field is bewildering.

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