Letter by Stone and Mintz Regarding Article, “Unreliable Assessment of Necrotic Core by Virtual Histology Intravascular Ultrasound in Porcine Coronary Artery Disease”

To the Editor:

We read with interest the article by Thim et al in which no correlation was found between the size of necrotic core determined by virtual histology intravascular ultrasound (VH IVUS) and actual histology in adult atherosclerosis-prone minipigs. The authors’ implication that caution is therefore warranted “in the interpretation of [human] studies relying on VH IVUS for monitoring of treatment effects, event prediction, and validation of other imaging modalities” would appear to exceed what may reliably be concluded from this study on several grounds.

First, although the authors acknowledge that coregistration of VH IVUS frames and histological sections may be problematic, IVUS images are sampled every 0.5 mm on average, compared to every 4 mm for pathological sections in the study by Thim et al, introducing even greater error in matching (which cannot be overcome by use of fiducial branch points or use of balloon angioplasty footprints). Moreover, tissue sections usually are 4 to 5 μm in thickness compared to VH images, which are produced from IVUS beams typically 200 to 300 μm in thickness. Therefore, given the marked longitudinal pathological variability that can be present every few micrometers, it is inappropriate to align a given histological section to an IVUS frame and expect high correlation in quantification of individual tissue components.

Second, despite this limitation, the lack of correlation between VH IVUS and histology, necrotic core area in the present report was driven primarily by 1 point in the upper left quadrant of Figure 1A. Using the data in this graph, if this outlier is removed, one can calculate that r = 0.79 (P = 0.0003), indicating very good correlation.

Third (and not commonly appreciated), there often is major disagreement between pathologists when assessing histology. Pertinent to the present report, from a study in which 4 highly experienced cardiac pathologists assessed 30 Movat pentachrome coronary histology slides, in only 7 (23%) cases was there agreement about histological classification among all, with the greatest source of variability being in the location and quantity of necrotic core (G.M. Sangiorgi, oral communication, May 18, 2010).

Fourth, the authors state that “for grayscale IVUS, it is generally agreed that echolucent plaque areas represent collagen-poor areas with high lipid content within a preserved (lipid pool) or degraded (necrotic core) extracellular matrix. Thereby grayscale IVUS offers tissue characterization to some extent.” This statement is incorrect. Echolucency is a sign of tissue homogeneity, whereas necrotic core tissue is heterogeneous with multiple tissue interfaces and therefore is often hyperechoic.

Fifth, the VH IVUS algorithm was “trained” from human histology, with which it has been shown to highly correlate. Indeed, high correlation also has been observed in vivo between human histology and VH IVUS plaque composition from both coronary atherosclerosis-prone minipigs and carotid endarterectomy specimens. To the extent that the chemical composition of the necrotic core from miniswine and human beings differ may explain the lack of correlation observed in the present experimental study.

Sixth, the IVUS contours of the lumen and external elastic membrane seen in the examples in the article are very different from histological borders because of fixation artifact, which can significantly distort absolute necrotic core measures. To overcome this limitation, geometric transformation was used in the validation studies to correct for fixation artifacts.

Lastly, and of greatest relevance to the human condition, the prognostic utility of VH IVUS recently has been demonstrated in the Providing Regional Observations to Study Predictors of Events in the Coronary Tree (PROSPECT) study where >2800 coronary lesions in 697 patients were assessed by VH IVUS and prospectively followed for >3 years. By multivariable analysis, lesions determined to be thin-cap fibroatheromas by VH IVUS had a >3-fold increased hazard of resulting in future major adverse cardiovascular events, independent of clinical characteristics, biomarkers, and other gray-scale IVUS characteristics.

Disclosures

Dr Stone is a consultant to Volcano Corp and Infraredx and is a member of the scientific advisory board for and has received honoraria from Boston Scientific. Dr Mintz has received honoraria and grant support from Volcano Corp and Boston Scientific and is consultant to Volcano Corp.

Gregg W. Stone, MD
Gary S. Mintz, MD
Columbia University Medical Center and the Cardiovascular Research Foundation
New York, NY

References

Letter by Stone and Mintz Regarding Article, "Unreliable Assessment of Necrotic Core by Virtual Histology Intravascular Ultrasound in Porcine Coronary Artery Disease"

Gregg W. Stone and Gary S. Mintz

Circ Cardiovasc Imaging. 2010;3:e4
doi: 10.1161/CIRCIMAGING.110.958553

Circulation: Cardiovascular Imaging is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2010 American Heart Association, Inc. All rights reserved.
Print ISSN: 1941-9651. Online ISSN: 1942-0080

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circimaging.ahajournals.org/content/3/5/e4

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation: Cardiovascular Imaging can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation: Cardiovascular Imaging is online at:
http://circimaging.ahajournals.org//subscriptions/