Response to Letter Regarding Article, “Current Status of Endovascular Stroke Treatment”

We thank Drs Körhmann and Schellinger for their interest in our article.1 They expressed concern about the subset of the National Institute of Neurological Disorders and Stroke (NINDS) rtPA (recombinant tissue-type plasminogen activator) Stroke Study2 data summarized in this article, as presented in Table 1.

The NINDS rtPA Stroke Study2 led to Food and Drug Administration approval of ActiVase for the treatment of acute stroke in 1996, yet the intravenous stroke literature has its own controversies. The NINDS rtPA Stroke Study was divided into 2 groups: patients treated in 0 to 90 minutes and those treated in 91 to 180 minutes. There was no statistical difference in outcomes between rtPA- and placebo-treated patients in the 0 to 90–minute cohort at 24 hours. In part 1, the trial effectively showed no benefit to earlier treatment of stroke with intravenous rtPA, thus suggesting that time to treatment is not relevant. The findings in part 1 of the NINDS rtPA Stroke Study contradict the basis of ongoing medical practice.

Skewed randomization (false-negative type II error) is probably responsible for population variance between the rtPA and placebo cohorts in NINDS. The rtPA cohort had 50% more small-vessel strokes than the placebo group. Small-vessel occlusions are more likely to respond to intravenous rtPA. Meanwhile, there was an asymmetrical preponderance of large-vessel strokes, causing higher National Institutes of Health Stroke Scale scores and poor outcomes in the placebo cohort. Marler et al3 acknowledged this problem in their analysis: “[T]he effect of rtPA may have appeared to be greater than it actually was.”

The limited effect of intravenous rtPA on occlusion of large cerebral arteries may have been discounted. As early as 1992, there was evidence that intravenous fibrinolytic was less effective recanalizing large-vessel strokes.4 Imaging of the acute stroke victim with nonenhanced computed tomography scans alone often does not define the location or extent of the thromboembolus. Tomski et al5 were among the first to recognize the significance of the dense middle cerebral artery sign and middle cerebral artery stroke in terms of response to intravenous fibrinolysis and a possible role for intra-arterial drug therapy instead.

Because the NINDS rtPA Stroke Study is complicated, we tried to select the component of the data most applicable to the purposes of the review article: endovascular treatment. The manner in which the data were handled for Interventional Management of Stroke II (IMS-2)6 seemed most appropriate. It remains data from the NINDS rtPA Stroke Study and was referenced accordingly. In terms of the other issues raised, labeling of trial and control groups in the NINDS rtPA Stroke Study was inadvertently interchanged in Table 1, thus affecting Figure 5. We thank Drs Körhmann and Schellinger for pointing out these errors, and we have submitted a correction to our article. The taxonomy of intracranial hemorrhage is variable. The Safe Implementation of Thrombolysis in Stroke-Monitoring Study (SITS-MOST) definitions of hemorrhage are more stringent. The Stenting and Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis (SAMMPRIS) trial was halted on April 6, 2011. When the results of SAMMPRIS became available to trial investigators, the manuscript for this article had been typeset for publication. SAMMPRIS has important implications for the treatment of subacute stroke.

Disclosures
None.

Philip M. Meyers, MD
Departments of Radiology and Neurological Surgery
Columbia University
College of Physicians & Surgeons
New York, NY

H. Christian Schumacher, MD
Departments of Neurology and Internal Medicine
LeHigh Valley Hospital and Health Network
Allentown, PA

E. Sander Connolly, Jr, MD
Department of Neurological Surgery
Columbia University
College of Physicians & Surgeons
New York, NY

Eric J. Heyer, MD, PhD
Departments of Anesthesiology and Neurology
Columbia University
College of Physicians & Surgeons
New York, NY

William A. Gray, MD
Department of Cardiology
Columbia University
College of Physicians & Surgeons
New York, NY

Randall T. Higashida, MD
Departments of Radiology, Neurology, Neurosurgical Surgery, Anesthesiology, and Critical Care Medicine
University of California at San Francisco
San Francisco, California

References
Response to Letter Regarding Article, "Current Status of Endovascular Stroke Treatment"

_Circulation_. 2012;125:e238
doi: 10.1161/CIRCULATIONAHA.111.076463
_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2012 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/125/1/e238

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation_ 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_ is online at:
http://circ.ahajournals.org//subscriptions/