Introducing *Radiology* Select: *Stroke*

Radiology Select

Michael H. Lev, MD
Shervin Kamalian, MD

Video
Online Education Edition and Tablet Edition of *Radiology* Select include a video with David F. Kallmes, MD (moderator), Michael H. Lev, MD, Catherine M. Phan, MD, and Rajiv Gupta, MD, PhD.

The prevention, diagnosis, and treatment of acute stroke continue to be a challenge, despite recent advances in screening, risk factor modification, imaging evaluation, and novel thrombolytic and endovascular therapies. Approximately 85% of strokes are ischemic and 15% are hemorrhagic. The majority of the morbidity and mortality of adult ischemic stroke is attributable to emboli to the circle of Willis from cardiac (left atrial appendage thrombus accompanying atrial fibrillation) or large-vessel atheromatous (internal carotid artery [ICA] bifurcation plaque) sources; in children and young adults, dissection and paradoxical embolus through a patent foramen ovale are leading causes of stroke. It has been estimated that most strokes in adults could be prevented simply by means of appropriate control of high blood pressure (1). Indeed, in the recently launched Million Hearts Initiative—aimed at preventing 1 million strokes and heart attacks nationally over the next 5 years—management of the "ABC'S" (aspirin for high-risk patients, blood-pressure control, cholesterol management, and smoking cessation) is paramount (2).

We are delighted to serve as guest editors for this collection of 30 of the most compelling representative articles on stroke that have appeared in the *Radiology* over the past 5–7 years. Selection was no easy task; a simple PubMed search of *Radiology* articles published since July 2004 using the keywords *stroke* or *carotid* identifies over 150 outstanding articles, reflecting, on average, almost two stroke-related articles per issue. Of necessity, we have excluded many noteworthy topics.

Selection criteria were similar to those applied routinely for peer review of original research considered for publication in *Radiology:* specifically, *(a)* clinical importance, *(b)* novelty, and *(c)* potential influence on setting the neuroimaging research agenda. An additional criterion, scientific rigor, was (of course) already present in all of the screened articles. With regard to study design, articles that made the first cut generally fell into one of two categories: early innovative pilot studies of historic importance, or larger, prospective, confirmatory studies with substantial clinical or research importance. When many reports addressed a single limited theme (such as magnetic resonance [MR] arterial spin labeling [ASL] perfusion imaging), preference was typically given to more current, definitive studies—as well as to recent comprehensive reviews—with noteworthy early pioneering studies cited as references for the ambitious reader.

Stroke imaging research published in *Radiology* since late 2004 has primarily centered on two major subject areas: *(a)* penumbral markers for both prediction of tissue and clinical outcomes and patient selection for advanced treatment options and *(b)* newer computed tomographic (CT), MR imaging, and ultrasonographic (US) diagnostic markers for assessment of ICA vulnerable plaque and stroke risk. The articles chosen have emphasized trends in physiologic mechanistic imaging (as distinct from anatomic structural imaging), underscoring advances in postprocessing, validation, and standardization of newer radiologic techniques. Although many of the selected reports are too recent to have established themselves as widely cited "enduring classics," they are nonetheless notable for highlighting priority areas of ongoing stroke research likely to have high clinical impact. Many of the articles serve to address contentious and as yet unsolved issues, as well as to identify gaps in knowledge and new areas of investigation that have arisen in the past 5–7 years (3).

Historical Perspective

Before the introduction of CT in 1974, brain imaging required invasive pneumoencephalography or catheter-based arteriography, with the latter typically performed by means of direct carotid puncture. Since the widespread adoption of CT as an essential imaging tool in the late 1970s, numerous frequently cited manuscripts tracking the development of a variety of other CT, US, MR imaging, and catheter-based methods for cerebrovascular evaluation have appeared in *Radiology*.

The earliest CT investigations, of necessity, focused on subacute and chronic stroke diagnosis, not only because of logistic and scanner speed limitations but also because acute interventions that could alter patient management were not yet available to motivate rapid assessment. Early clinical studies compared the accuracy for stroke detection of first-generation CT scanners with that of existing modalities (including nuclear medicine and angiography) (4–6), but it took another 10 years for the critical acute unenhanced head CT findings of obscuration of the lentiform nucleus and insular ribbon to be reported (7,8). Although as long ago as 1980, authors anticipated the value of coronal and sagittal reconstruction of cranial CT scans for improved lesion conspicuity, the thick axial sections with poor z-axis resolution made clinical implementation impractical at that time (9).

Even more farsighted were early descriptions of CT perfusion imaging (10,11). It was not until the start of the 21st century, however, that both the level of technology and the clinical need made it feasible for acute stroke CT perfusion imaging to become a routine diagnostic test (12–14).

The evolution of MR imaging has also been featured in *Radiology*. Ischemic stroke detection was reported in cats in 1982 (15) and in humans in 1983 (16,17), followed by gadolinium-enhanced stroke evaluation in 1986 (18) and three-dimensional volume MR angiography of the circle of Willis in 1989 (19). More recent technical advances of great potential value in cerebrovascular evaluation include correlative positron emission tomographic (PET) examinations performed by using dedicated dual PET/MR systems (20), MR microscopy with 7-T very high magnetic field strength units (21), susceptibility-weighted imaging (22), and resting-state functional MR imaging (23).

Discussion of Selected Manuscripts

Unenhanced CT, Dual-Energy Scanning

Food and Drug Administration approval in 1996 of intravenous thrombolytic treatment for acute stroke within 3 hours of onset brought the role of imaging for patient selection to the forefront. To this day, unenhanced head CT to exclude hemorrhage remains the standard of care for intravenous thrombolytic agent administration (24). Indeed, the 1997 *Radiology* article "Acute Stroke: Usefulness of Early CT Findings before Thrombolytic Therapy" has been widely cited (25). Other investigators expanded on this theme in attempts to improve the accuracy of acute stroke detection—for example, by optimizing display settings on picture archiving and communication system monitors (26).

Dual-energy CT, although first proposed soon after the invention of CT in the 1970s (27), has only recently become a clinical reality and, together with multidetector CT angiography and iterative reconstruction techniques, represents one of a few new truly paradigm-shifting advances in CT since Hounsfield's development of filtered back projection. With dual-energy CT, atomic number can be directly calculated (unlike conventional CT, for which the gray scale reflects only a single parameter, attenuation). Thus, dedicated iodine, calcium, or water images can be created, effectively allowing tissue characterization with CT analogous to that of MR imaging. Clinically, such images could be used for bone subtraction, optimized three-dimensional CT angiography and CT perfusion reformatting, creation of "virtual" unenhanced and monochromatic images from contrast agent–enhanced CT data sets, and reduction of beam-hardening artifacts and to distinguish hemorrhage from calcium and from contrast enhancement in diagnostically challenging cases.

In the first article selected for this collection, Gupta et al (28) report on the use of dual-energy technology to distinguish hemorrhagic conversion from routine parenchymal contrast blush after endovascular stroke therapy—an essential clinical distinction that cannot routinely be made, even by using advanced MR techniques (29).

CT Angiography

The advent of multidetector CT made possible rapid low-cost CT angiography of the neurovascular system. Head CT angiography had the additional advantage of not only accurately depicting major vascular stenoses and occlusions, but also, by using the same CT angiographic source image data set, providing perfusion-weighted contrast-enhanced whole-brain parenchymal images (12). Indeed, in the next article, Camargo et al (30) show that CT angiographic source images, compared with unenhanced CT scans, are more sensitive for detection of early irreversible ischemia and more accurate for prediction of final infarct volume.

Because much of the morbidity and mortality of acute stroke can be attributed to cardiac embolic sources, there has also been strong recent interest in using cardiac CT angiography to noninvasively detect left atrial thrombus (31) and patent foramen ovale (32, 33), rather than the reference standard, transesophageal echocardiography (TEE). Hur et al (34) reported favorable sensitivity and specificity of CT angiography relative to TEE. More recently, Boussel et al (35) have proposed a combined neurovascular/cardiac CT angiography protocol for rapid, efficient, single-session multidetector CT angiographic workup of acute stroke.

CT Perfusion and Multimodal Imaging

Although diffusion-weighted MR imaging remains the reference standard for emergency determination of infarct core (ischemic tissue likely to be irreversibly infarcted despite early, robust recanalization), CT perfusion, with its relative availability, low cost, and speed, has increasingly been recommended for aid in the diagnosis and characterization of acute stroke, transient ischemic attack, carotid occlusive disease, and vasospasm, especially when MR imaging is unavailable (36,37). CT perfusion has also been applied as a biomarker to help predict functional outcome in patients with severe head trauma (38) and to estimate the risk of hemorrhagic transformation in acute stroke (39).

A major concern for both CT perfusion and perfusion-weighted MR imaging has been the validation and standardization of technique across different acquisition and postprocessing platforms from different vendors and with the use of different algorithms. These issues are addressed by Kudo et al (40) in their important study and discussed at length in the accompanying review (41).

Not surprisingly, given the need for rapid assessment and treatment of acute stroke patients (”time is brain”), there has been strong interest in integrating CT, CT angiography, and CT perfusion into a comprehensive stroke imaging protocol that can be accomplished in a single session (“one stop shopping”). This concept is nicely introduced by Kloska et al (42) and is brought up to date by Hopyan et al (43).

MR Imaging Penumbral Markers for Outcome Prediction and Patient Selection

Mismatch between Diffusion-weighted and Perfusion-weighted Imaging

Diffusion-weighted imaging is the reference standard for emergency evaluation of infarct core (44–46). Together with perfusion-weighted MR imaging measurement of the “at-risk” penumbra (critically ischemic but potentially salvageable tissue likely to infarct in the absence of early robust reperfusion), the concept of the diffusion-weighted/perfusion-weighted imaging “mismatch” has been widely applied as a potential selection tool for identifying patients most likely to benefit from (and least likely to be harmed by) advanced stroke treatments administered outside established time windows. An early report by Edelman et al (47) described cerebral blood flow assessment by using dynamic contrast-enhanced T2*-weighted pulse sequences. A 1996 landmark article by Sorensen et al (48) introduced the mismatch concept.

More recently, in a report on a major multicenter study, the Diffusion and Perfusion Imaging Evaluation for Understanding Stroke Evolution (DEFUSE) study, Marks et al (49) suggested that the diffusion-weighted/perfusion- weighted imaging mismatch might help to predict clinical outcome in patients with recanalization treated with intravenous thrombolysis 3–6 hours after symptom onset. Despite this, the use of the mismatch for patient selection has yet to be validated in a large prospective randomized trial, and there remains much controversy not only as to the optimal parameter (and threshold) with which to measure “penumbra”, but also—as highlighted by Copen et al (50)—with regard to how long the mismatch (and, hence, penumbral tissue) persists in the setting of a proximal occlusion in the circle of Willis.

Arterial Spin Labeling

Many patients with signs and symptoms of acute stroke at the time of presentation have poor or unknown renal function. Given recent concerns regarding gadolinium-based contrast administration and the risk of nephrogenic systemic fibrosis in this cohort, a rapid reliable technique for determining cerebral perfusion would be a welcome addition to the stroke imaging armamentarium. Arterial spin labeling (ASL) is such a technique (51–53).

Recently, Zaharchuk et al (54) reported that ASL may reveal hemodynamic abnormalities not detectable on perfusion-weighted images. Bokkers et al (55) used ASL to measure cerebrovascular reserve in response to acetazolamide challenge in patients with symptomatic ICA stenosis.

Other Physiologic “Penumbral” Imaging

Many other non-ASL techniques for determining potentially salvageable ischemic tissue at risk, without the use of intravenous gadolinium-based contrast agents, have been proposed. (57–59).A substantial percentage of acute stroke patients have an unknown symptom-onset time, making them ineligible for intravenous thrombolytic therapy which must be administered within 3–4.5 hours of stroke ictus. An important goal of advanced imaging is to expand eligibility in this cohort. Petkova et al (60) suggested that this might be accomplished by using the signal intensity on fluid-attenuated inversion-recovery MR images as a surrogate marker of stroke age.

Finally, cerebral hyperfusion syndrome is a feared complication of carotid endarterectomy in patients with longstanding severe ICA stenosis. Murakami et al (61) suggest that brain temperature measured with MR spectroscopy may help identify patients at highest risk.

Novel Imaging Markers for Carotid Artery Vulnerable Plaque and Stroke Risk

US and MR Imaging of Vulnerable ICA Plaque

The degree of ICA origin stenosis is a well-established biomarker for stroke risk: A greater-than-70% stenosis is considered an indication for endarterectomy or stent implantation rather than continued maximal medical therapy. The mechanism of carotid artery strokes is embolic. The endothelial surface of a denuded or ulcerated atheromatous plaque releases tissue factors that, in an area of sluggish turbulent blood flow adjacent to a severe stenosis, serves as a nidus for platelet-fibrin–red cell clumping, causing formation of emboli that can subsequently propagate through a patent ICA to lodge in a proximal branch of the circle of Willis (typically the middle cerebral artery), causing a stroke (62).

Although the percentage of ICA stenosis remains the most important clinical determinant of embolic ICA stroke risk, there is increasing evidence that this risk can be further stratified on the basis of the histologic characteristics of the plaque, the so-called plaque vulnerability (63). Pertinent findings include inflammatory changes associated with contrast enhancement and neovascularity of the overlying vasa vasorum, intraplaque hemorrhage, and fibrous cap thinning or ulceration (64).

On US studies, hypoechoic plaque and late-phase contrast enhancement are signs of plaque vulnerability (65–69).

Analogous findings can be demonstrated with MR imaging and can be used to accurately monitor serial changes such as response to lipid lowering therapies (70,71). Astor et al (72) studied over 2000 patients to determine that ICA luminal narrowing occurs when carotid wall thickness exceeds 1.5 mm, suggesting "that the carotid arteries are able to compensate for a greater degree of thickening than are the coronary arteries."

That intraplaque hemorrhage is associated with emboli is suggested by correlation with white matter lesions (73, 74). Importantly, highly vulnerable plaque with intraplaque hemorrhage can occur in symptomatic patients with even mild ICA stenosis (<50%) (75).

Conventional Arteriography: Neurointerventional

Although CT angiography has largely replaced conventional arteriography for routine diagnostic screening of cerebrovascular disease, digital subtraction arteriography (DSA) remains the reference standard for definitive characterization of aneurysms, arteriovenous malformations, and vasculitis, as well as a prerequisite for neurointerventional procedures. The qualifications required to perform cerebral arteriography are nicely outlined by Connors et al (76).

The potential complications of DSA must always be weighed against the anticipated diagnostic and therapeutic benefits (77, 78). That microemboli sufficiently large to cause lesions seen on diffusion-weighted MR images are common—even in "routine" interventional cardiac procedures—was nicely demonstrated by Busing et al (79), who showed that "asymptomatic cerebral infarction following cardiac catheterization occurred in 15% of patients in whom duration of the procedure was significantly longer than in those without infarction".

Carotid artery stent implantation has been another frequent topic in the pages of *Radiology* (80). Early reports, such as that from Groschel et al (81), helped to establish procedural guidelines—including the potential benefits of statin administration—that could assist in the design of prospective clinical trials.

Societal and Cost-effectiveness Analyses

Given the current interest in utilization review and appropriateness criteria, *Radiology* has served as a valuable forum for cost-effectiveness and outcome studies in general (82,83), and for comparisons among various screening imaging modalities for the evaluation of carotid artery stenosis and stroke risk in particular (84–88).

Pediatric Stroke

Two important themes of the pediatric stroke studies published in *Radiology* over the past decade are sickle cell disease and perinatal ischemic and traumatic hemorrhagic injury (89–93), and these areas are highlighted in this issue of Radiology Select.

References

1. Fisher CM. A career in cerebrovascular disease: a personal account. Stroke 2001;32:2719–2724.
2. Frieden TR, Berwick DM. The "Million Hearts" initiative: preventing heart attacks and strokes. N Engl J Med 2011;365:e27. http://www.nejm.org/doi/full/10.1056/NEJMp1110421. Published September 29, 2011. Accessed April 18, 2012.
3. Grotta JC, Jacobs TP, Koroshetz WJ, Moskowitz MA. Stroke program review group: an interim report. Stroke 2008;39:1364–1370.
4. Inoue Y, Takemoto K, Miyamoto T, et al. Sequential computed tomography scans in acute cerebral infarction. Radiology 1980;135:655–662.
5. Campbell JK, Houser OW, Stevens JC, Wahner HW, Baker HL, Jr., Folger WN. Computed tomography and radionuclide imaging in the evaluation of ischemic stroke. Radiology 1978;126:695–702.
6. Hinshaw DB, Jr., Thompson JR, Hasso AN, Casselman ES. Infarctions of the brainstem and cerebellum: a correlation of computed tomography and angiography. Radiology 1980;137:105–112.
7. Tomura N, Uemura K, Inugami A, Fujita H, Higano S, Shishido F. Early CT finding in cerebral infarction: obscuration of the lentiform nucleus. Radiology 1988;168:463–467.
8. Truwit CL, Barkovich AJ, Gean-Marton A, Hibri N, Norman D. Loss of the insular ribbon: another early CT sign of acute middle cerebral artery infarction. Radiology 1990;176:801–806.
9. Baker HL, Jr. The clinical usefulness of routine coronal and sagittal reconstructions in cranial computed tomography. Radiology 1981;140:1–9.
10. Dobben GD, Valvassori GE, Mafee MF, Berninger WH. Evaluation of brain circulation by rapid rotational computed tomography. Radiology 1979;133:105–111.
11. Shih TT, Huang KM. Acute stroke: detection of changes in cerebral perfusion with dynamic CT scanning. Radiology 1988;169:469–474.
12. Hunter GJ, Silvennoinen HM, Hamberg LM, et al. Whole-brain CT perfusion measurement of perfused cerebral blood volume in acute ischemic stroke: probability curve for regional infarction. Radiology 2003;227:725–730.
13. Koenig M, Klotz E, Luka B, Venderink DJ, Spittler JF, Heuser L. Perfusion CT of the brain: diagnostic approach for early detection of ischemic stroke. Radiology 1998;209:85–93.
14. Eastwood JD, Lev MH, Azhari T, et al. CT perfusion scanning with deconvolution analysis: pilot study in patients with acute middle cerebral artery stroke. Radiology 2002;222:227–236.
15. Buonanno FS, Pykett IL, Kistler JP, et al. Cranial anatomy and detection of ischemic stroke in the cat by nuclear magnetic resonance imaging. Radiology 1982;143:187–193.
16. Crooks LE, Ortendahl DA, Kaufman L, et al. Clinical efficiency of nuclear magnetic resonance imaging. Radiology 1983;146:123–128.
17. Bryan RN, Willcott MR, Schneiders NJ, Ford JJ, Derman HS. Nuclear magnetic resonance evaluation of stroke: a preliminary report. Radiology 1983;149:189–192.
18. Virapongse C, Mancuso A, Quisling R. Human brain infarcts: Gd-DTPA–enhanced MR imaging. Radiology 1986;161:785–794.
19. Masaryk TJ, Modic MT, Ross JS, et al. Intracranial circulation: preliminary clinical results with three-dimensional (volume) MR angiography. Radiology 1989;171:793–799.
20. Uppal R, Catana C, Ay I, Benner T, Sorensen AG, Caravan P. Bimodal thrombus imaging: simultaneous PET/MR imaging with a fibrin-targeted dual PET/MR probe—feasibility study in rat model. Radiology 2011;258:812–820.
21. Marques JP, van der Zwaag W, Granziera C, Krueger G, Gruetter R. Cerebellar cortical layers: in vivo visualization with structural high-field-strength MR imaging. Radiology 2010;254:942–948.
22. Colbert CA, Holshouser BA, Aaen GS, et al. Value of cerebral microhemorrhages detected with susceptibility-weighted MR Imaging for prediction of long-term outcome in children with nonaccidental trauma. Radiology 2010;256:898–905.
23. Tang L, Ge Y, Sodickson DK, et al. Thalamic resting-state functional networks: disruption in patients with mild traumatic brain injury. Radiology 2011;260:831–840.
24. Wardlaw JM, Mielke O. Early signs of brain infarction at CT: observer reliability and outcome after thrombolytic treatment—systematic review. Radiology 2005;235:444–453.
25. von Kummer R, Allen KL, Holle R, et al. Acute stroke: usefulness of early CT findings before thrombolytic therapy. Radiology 1997;205:327–333.

26. Lev MH, Farkas J, Gemmete JJ, et al. Acute stroke: improved nonenhanced CT detection—benefits of soft-copy interpretation by using variable window width and center level settings. Radiology 1999;213:150–155.

27. Chiro GD, Brooks RA, Kessler RM, et al. Tissue signatures with dual-energy computed tomography. Radiology 1979;131:521–523.

28. Gupta R, Phan CM, Leidecker C, et al. Evaluation of dual-energy CT for differentiating intracerebral hemorrhage from iodinated contrast material staining. Radiology 2010;257:205–211.

29. Greer DM, Koroshetz WJ, Cullen S, Gonzalez RG, Lev MH. Magnetic resonance imaging improves detection of intracerebral hemorrhage over computed tomography after intra-arterial thrombolysis. Stroke 2004;35:491–495.

30. Camargo EC, Furie KL, Singhal AB, et al. Acute brain infarct: detection and delineation with CT angiographic source images versus nonenhanced CT scans. Radiology 2007;244:541–548.

31. Hur J, Kim YJ, Lee HJ, et al. Left atrial appendage thrombi in stroke patients: detection with two-phase cardiac CT angiography versus transesophageal echocardiography. Radiology 2009;251:683–690.

32. Revel MP, Faivre JB, Letourneau T, et al. Patent foramen ovale: detection with nongated multidetector CT. Radiology 2008;249:338–345.

33. Kim YJ, Hur J, Shim CY, et al. Patent foramen ovale: diagnosis with multidetector CT—comparison with transesophageal echocardiography. Radiology 2009;250:61–67.

34. Hur J, Kim YJ, Nam JE, et al. Thrombus in the left atrial appendage in stroke patients: detection with cardiac CT angiography—a preliminary report. Radiology 2008;249:81–87.

35. Boussel L, Cakmak S, Wintermark M, et al. Ischemic stroke: etiologic work-up with multidetector CT of heart and extra- and intracranial arteries. Radiology 2011;258:206–212.

36. Waaijer A, van Leeuwen MS, van Osch MJ, et al. Changes in cerebral perfusion after revascularization of symptomatic carotid artery stenosis: CT measurement. Radiology 2007;245:541–548.

37. Hoeffner EG, Case I, Jain R, et al. Cerebral perfusion CT: technique and clinical applications. Radiology 2004;231:632–644.

38. Wintermark M, van Melle G, Schnyder P, et al. Admission perfusion CT: prognostic value in patients with severe head trauma. Radiology 2004;232:211–220.

39. Aviv RI, d'Esterre CD, Murphy BD, et al. Hemorrhagic transformation of ischemic stroke: prediction with CT perfusion. Radiology 2009;250:867–877.

40. Kudo K, Sasaki M, Yamada K, et al. Differences in CT perfusion maps generated by different commercial software: quantitative analysis by using identical source data of acute stroke patients. Radiology 2010;254:200–209.

41. Konstas AA, Lev MH. CT perfusion imaging of acute stroke: the need for arrival time, delay insensitive, and standardized postprocessing algorithms? Radiology 2010;254:22–25.

42. Kloska SP, Nabavi DG, Gaus C, et al. Acute stroke assessment with CT: do we need multimodal evaluation? Radiology 2004;233:79–86.

43. Hopyan J, Ciarallo A, Dowlatshahi D, et al. Certainty of stroke diagnosis: incremental benefit with CT perfusion over noncontrast CT and CT angiography. Radiology 2010;255:142–153.

44. Pierpaoli C, Jezzard P, Basser PJ, Barnett A, Di Chiro G. Diffusion tensor MR imaging of the human brain. Radiology 1996;201:637–648.

45. Gonzalez RG, Schaefer PW, Buonanno FS, et al. Diffusion-weighted MR imaging: diagnostic accuracy in patients imaged within 6 hours of stroke symptom onset. Radiology 1999;210:155–162.

46. Schaefer PW, Grant PE, Gonzalez RG. Diffusion-weighted MR imaging of the brain. Radiology 2000;217:331–345.

47. Edelman RR, Mattle HP, Atkinson DJ, et al. Cerebral blood flow: assessment with dynamic contrast-enhanced T2*-weighted MR imaging at 1.5 T. Radiology 1990;176:211–220.

48. Sorensen AG, Buonanno FS, Gonzalez RG, et al. Hyperacute stroke: evaluation with combined multisection diffusion-weighted and hemodynamically weighted echo-planar MR imaging. Radiology 1996;199:391–401.

49. Marks MP, Olivot JM, Kemp S, et al. Patients with acute stroke treated with intravenous tPA 3–6 hours after stroke onset: correlations between MR angiography findings and perfusion- and diffusion-weighted imaging in the DEFUSE study. Radiology 2008;249:614–623.

50. Copen WA, Rezai Gharai L, Barak ER, et al. Existence of the diffusion-perfusion mismatch within 24 hours after onset of acute stroke: dependence on proximal arterial occlusion. Radiology 2009;250:878–886.

51. Hendrikse J, van Osch MJ, Rutgers DR, et al. Internal carotid artery occlusion assessed at pulsed arterial spin-labeling perfusion MR imaging at multiple delay times. Radiology 2004;233:899–904.

52. van Laar PJ, Hendrikse J, Klijn CJ, Kappelle LJ, van Osch MJ, van der Grond J. Symptomatic carotid artery occlusion: flow territories of major brain-feeding arteries. Radiology 2007;242:526–534.

53. Hendrikse J, Petersen ET, Chng SM, Venketasubramanian N, Golay X. Distribution of cerebral blood flow in the nucleus caudatus, nucleus lentiformis, and thalamus: a study of territorial arterial spin-labeling MR imaging. Radiology 2010;254:867–875.

54. Zaharchuk G, Bammer R, Straka M, et al. Arterial spin-label imaging in patients with normal bolus perfusion-weighted MR imaging findings: pilot identification of the borderzone sign. Radiology 2009;252:797–807.

55. Bokkers RP, van Osch MJ, van der Worp HB, de Borst GJ, Mali WP, Hendrikse J. Symptomatic carotid artery stenosis: impairment of cerebral autoregulation measured at the brain tissue level with arterial spin-labeling MR imaging. Radiology 2010;256:201–208.

56. van Laar PJ, van der Grond J, Hendrikse J. Brain perfusion territory imaging: methods and clinical applications of selective arterial spin-labeling MR imaging. Radiology 2008;246:354–364.

57. Rosso C, Hevia-Montiel N, Deltour S, et al. Prediction of infarct growth based on apparent diffusion coefficients: penumbral assessment without intravenous contrast material. Radiology 2009;250:184–192.

58. Haller S, Bonati LH, Rick J, et al. Reduced cerebrovascular reserve at CO2 BOLD MR imaging is associated with increased risk of periinterventional ischemic lesions during carotid endarterectomy or stent placement: preliminary results. Radiology 2008;249:251–258.

59. Siemonsen S, Fitting T, Thomalla G, et al. T2′ imaging predicts infarct growth beyond the acute diffusion-weighted imaging lesion in acute stroke. Radiology 2008;248:979–986.

60. Petkova M, Rodrigo S, Lamy C, et al. MR imaging helps predict time from symptom onset in patients with acute stroke: implications for patients with unknown onset time. Radiology 2010;257:782–792.

61. Murakami T, Ogasawara K, Yoshioka Y, et al. Brain temperature measured by using proton MR spectroscopy predicts cerebral hyperperfusion after carotid endarterectomy. Radiology 2010;256:924–931.

62. Edwards JH, Kricheff, II, Riles T, Imparato A. Angiographically undetected ulceration of the carotid bifurcation as a cause of embolic stroke. Radiology 1979;132:369–373.

63. Yuan C, Mitsumori LM, Beach KW, Maravilla KR. Carotid atherosclerotic plaque: noninvasive MR characterization and identification of vulnerable lesions. Radiology 2001;221:285–299.

64. Saam T, Hatsukami TS, Takaya N, et al. The vulnerable, or high-risk, atherosclerotic plaque: noninvasive MR imaging for characterization and assessment. Radiology 2007;244:64–77.

65. Reiter M, Effenberger I, Sabeti S, et al. Increasing carotid plaque echolucency is predictive of cardiovascular events in high-risk patients. Radiology 2008;248:1050–1055.

66. Staub D, Partovi S, Schinkel AF, et al. Correlation of carotid artery atherosclerotic lesion echogenicity and severity at standard US with intraplaque neovascularization detected at contrast-enhanced US. Radiology 2011;258:618–626.

67. Polak JF, Shemanski L, O'Leary DH, et al. Hypoechoic plaque at US of the carotid artery: an independent risk factor for incident stroke in adults aged 65 years or older. Cardiovascular Health Study. Radiology 1998;208:649–654.

68. Owen DR, Shalhoub J, Miller S, et al. Inflammation within carotid atherosclerotic plaque: assessment with late-phase contrast-enhanced US. Radiology 2010;255:638–644.

69. Xiong L, Deng YB, Zhu Y, Liu YN, Bi XJ. Correlation of carotid plaque neovascularization detected by using contrast-enhanced US with clinical symptoms. Radiology 2009;251:583–589.

70. Boussel L, Arora S, Rapp J, et al. Atherosclerotic plaque progression in carotid arteries: monitoring with high-spatial-resolution MR imaging—multicenter trial. Radiology 2009;252:789–796.

71. Dong L, Kerwin WS, Chen H, et al. Carotid artery atherosclerosis: effect of intensive lipid therapy on the vasa vasorum—evaluation by using dynamic contrast-enhanced MR imaging. Radiology 2011;260:224–231.

72. Astor BC, Sharrett AR, Coresh J, Chambless LE, Wasserman BA. Remodeling of carotid arteries detected with MR imaging: atherosclerosis risk in communities carotid MRI study. Radiology 2010;256:879–886.

73. Altaf N, Morgan PS, Moody A, MacSweeney ST, Gladman JR, Auer DP. Brain white matter hyperintensities are associated with carotid intraplaque hemorrhage. Radiology 2008;248:202–209.

74. Altaf N, Goode SD, Beech A, et al. Plaque hemorrhage is a marker of thromboembolic activity in patients with symptomatic carotid disease. Radiology 2011;258:538–545.

75. Cheung HM, Moody AR, Singh N, Bitar R, Zhan J, Leung G. Late stage complicated atheroma in low-grade stenotic carotid disease: MR imaging depiction—prevalence and risk factors. Radiology 2011;260:841–847.

76. Connors JJ, 3rd, Sacks D, Furlan AJ, et al. Training, competency, and credentialing standards for diagnostic cervicocerebral angiography, carotid stenting, and cerebrovascular intervention: a joint statement from the American Academy of Neurology, the American Association of Neurological Surgeons, the American Society of Interventional and Therapeutic Neuroradiology, the American Society of Neuroradiology, the Congress of Neurological Surgeons, the AANS/CNS Cerebrovascular Section, and the Society of Interventional Radiology. Radiology. 2005 Jan;234(1):26–34.

77. Willinsky RA, Taylor SM, TerBrugge K, Farb RI, Tomlinson G, Montanera W. Neurologic complications of cerebral angiography: prospective analysis of 2,899 procedures and review of the literature. Radiology 2003;227:522–528.

78. Kaufmann TJ, Huston J, 3rd, Mandrekar JN, Schleck CD, Thielen KR, Kallmes DF. Complications of diagnostic cerebral angiography: evaluation of 19 826 consecutive patients. Radiology 2007;243:812–819.

79. Busing KA, Schulte-Sasse C, Fluchter S, et al. Cerebral infarction: incidence and risk factors after diagnostic and interventional cardiac catheterization—prospective evaluation at diffusion-weighted MR imaging. Radiology 2005;235:177–183.

80. Nedeltchev K, Brekenfeld C, Remonda L, et al. Internal carotid artery stent implantation in 25 patients with acute stroke: preliminary results. Radiology 2005;237:1029–1037.

81. Groschel K, Ernemann U, Schulz JB, Nagele T, Terborg C, Kastrup A. Statin therapy at carotid angioplasty and stent placement: effect on procedure-related stroke, myocardial infarction, and death. Radiology 2006;240:145–151.

82. Beinfeld MT, Gazelle GS. Diagnostic imaging costs: are they driving up the costs of hospital care? Radiology 2005;235:934–939.

83. Gazelle GS, Halpern EF, Ryan HS, Tramontano AC. Utilization of diagnostic medical imaging: comparison of radiologist referral versus same-specialty referral. Radiology 2007;245:517–522.

84. Heijenbrok-Kal MH, Buskens E, Nederkoorn PJ, van der Graaf Y, Hunink MG. Optimal peak systolic velocity threshold at duplex us for determining the need for carotid endarterectomy: a decision analytic approach. Radiology 2006;238:480–488.

85. Chappell FM, Wardlaw JM, Young GR, et al. Carotid artery stenosis: accuracy of noninvasive tests—individual patient data meta-analysis. Radiology 2009;251:493–502.

86. Derdeyn CP, Powers WJ, Moran CJ, Cross DT, 3rd, Allen BT. Role of Doppler US in screening for carotid atherosclerotic disease. Radiology 1995;197:635–643.

87. Tholen AT, de Monye C, Genders TS, et al. Suspected carotid artery stenosis: cost-effectiveness of CT angiography in work-up of patients with recent TIA or minor ischemic stroke. Radiology 2010;256:585–597.

88. Buskens E, Nederkoorn PJ, Buijs–Van Der Woude T, et al. Imaging of carotid arteries in symptomatic patients: cost-effectiveness of diagnostic strategies. Radiology 2004;233:101–112.

89. McArdle CB, Richardson CJ, Hayden CK, Nicholas DA, Amparo EG. Abnormalities of the neonatal brain: MR imaging. Part II. Hypoxic-ischemic brain injury. Radiology 1987;163:395–403.

90. Steggerda SJ, Leijser LM, Wiggers–de Bruine FT, van der Grond J, Walther FJ, van Wezel–Meijler G. Cerebellar injury in preterm infants: incidence and findings on US and MR images. Radiology 2009;252:190–199.

91. Steen RG, Emudianughe T, Hankins GM, et al. Brain imaging findings in pediatric patients with sickle cell disease. Radiology 2003;228:216–225.

92. Pawlak MA, Krejza J, Rudzinski W, et al. Sickle cell disease: ratio of blood flow velocity of intracranial to extracranial cerebral arteries—initial experience. Radiology 2009;251:525–534.

93. Looney CB, Smith JK, Merck LH, et al. Intracranial hemorrhage in asymptomatic neonates: prevalence on MR images and relationship to obstetric and neonatal risk factors. Radiology 2007;242:535–541.

Michael H. Lev, MD

Michael H. Lev, MD, has been an attending neuroradiologist at Massachusetts General Hospital in Boston, Mass, since 1995. He is currently Director of Emergency Neuroradiology and the Radiology Neurovascular Laboratory and associate professor of radiology at Harvard Medical School in Boston.

He is board certified in both internal medicine and radiology, with a Certificate of Added Qualification in neuroradiology. He served as deputy editor for neuroimaging of *Radiology* from August 2007 through March 2009 and continues his service on the *Radiology* editorial board as consultant to the editor.

He has been on the editorial board of the *American Journal of Neuroradiology* since 2000 and is a principal investigator for both the CT perfusion stroke imaging project of Partners Healthcare's National Institutes of Health–funded Specialized Program of Translational Research in Acute Stroke (SPOTRIAS) program project grant and for the Department of Defense/National Institute of Biomedical Imaging and Bioengineering–funded point-of-care center study of the clinical feasibility of electrical impedance spectroscopy.

Shervin Kamalian, MD

Shervin Kamalian, MD, is a research fellow and neuroimaging research laboratory director for CT dose reduction. He receives support in the form of two federally funded grants to study the feasibility of electrical impedance spectroscopy at the Neuroradiology Section of the Massachusetts General Hospital (Boston, Mass).

He was selected to participate in the Scholars in Clinical Science Program at Harvard Medical School in Boston, where he is scheduled to receive an MSc degree in clinical investigation in 2013.

He received his MD degree from Tehran Azad University of Medical Sciences (Tehran, Iran), where he completed a clinical internship.

His current research interests also include advanced ischemic and hemorrhagic stroke imaging, and his efforts to date have been published (or are pending publication) in journals such as *Stroke,* the *American Journal of Neuroradiology, Cerebrovascular Disorders, Neurology,* and *Radiology.*

Dr Kamalian is a member of the Radiological Society of North America, the American Roentgen Ray Society, and the American Heart Association/American Stroke Association.

Radiology Select is a continuing series of *Radiology* articles chosen by a guest editor for their importance in radiologic science. It is published biannually with each volume focusing on a specific subspecialty topic. The series will be available to members and nonmembers for a fee and will be offered in three formats--online, tablet, and print. Both *Radiology* and *Radiology* Select are owned and published by the Radiological Society of North America, Inc.

For more information on the *Radiology* Select series, please contact RSNA Publications, 630-590-7771.