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The Missing Element

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sitivity of TCD to small, clinically benign, embolic particles and the potential for real-time monitoring has been exploited in studies of right-to-left cardiac shunts, such as patent foramen ovale. Microbubbles injected in an arm vein can be identified with similar sensitivity in the middle cerebral artery among patients with patent foramen by use of TCD as with cardiac echocardiography. The real-time monitoring capability of TCD could be used to determine which steps during a procedure are associated with the greatest number of embolic events. Some evidence suggests that a large number of cerebral emboli during coronary bypass surgery occur with cross-clamping of the aorta. In carotid angioplasty and stenting, this could be during predilation or stent deployment or post stent angioplasty. Information regarding the relative embologenic potential of each step could guide the development or use of devices to prevent this occurrence. The primary drawback to TCD, with current technology, is its inability to distinguish either the nature or size of the embolic material as well as the effect of the emboli on the brain itself. Dual-frequency TCD techniques to distinguish air bubbles from solid material are under development.

DWI, as reported in this issue and prior studies, offers important complementary information: a quantitative assessment of ischemic injury (5, 6). DWI lesions can be quantified by size and number. The frequency of these lesions is in great excess to frequency of ischemic stroke. In these regards, DWI may serve as a useful surrogate endpoint for clinical stroke. Jaeger and colleagues report new DWI lesions in eight of 25 vascular territories after angioplasty of atherosclerotic lesions of the carotid, vertebral, or innominate arteries. They performed DWI before and 24 hours after the procedure. No clinical neurologic deficits were observed. Similar results were reported by Rordorf et al (5) after endovascular treatment of 14 intracranial aneurysms by means of Guglielmi detachable coils. DWI lesions were found at 48 hours in eight patients. One of the eight patients had clinical evidence of a stroke. Bendszus et al (6) reported new DWI lesions in 17 of 66 patients undergoing diagnostic cerebral arteriography.

One could argue that clinically silent lesions may not matter or that clinical stroke is a different entity than these small, silent lesions. However, it is much more likely that clinically evident stroke represents the tip of the iceberg of embolic ischemic events. The literature concerning significant neuropsychological changes in the absence of clinical stroke occurring with cardiopulmonary bypass procedures and strongly associated with probable microembolic events support this hypothesis (2, 7).

In summary, DWI may serve as a useful surrogate endpoint for ischemic stroke in the investigation of new devices, drugs, and techniques for cerebrovascular intervention. The frequency of new lesions by discovered by DWI appears to be quite high for angioplasty and aneurysm treatment. The DWI lesions are measurable in both size and number. These factors will provide good statistical power for the detection of differences in event rates between control and experimental groups. The evidence linking DWI lesions with ischemic injury is strong. TCD also plays a useful and complementary role in these investigations with its capability for real-time monitoring of embolic events.

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Progress in the development of effective stroke therapies has been generally disappointing. The results of initially promising neuroprotective drugs applied in large clinical trials have been unimpressive (1), and the results of large thrombolysis therapy trials have been inconclusive. A missing element in the development of effective stroke therapies has been the lack of available diagnostic tools capable of assessing the viability of brain tissue during the acute stages of evolving stroke. The

question that all stroke investigators want and need to know is what brain tissue is salvageable. Indeed in the absence of salvageable tissue, the utility of any therapeutic intervention is moot, but as improved therapeutic interventions are developed, the need to monitor and evaluate tissue status is critical, particularly if we are to identify a therapeutic window.

Diffusion MR imaging is now being widely used clinically for early stroke detection. The underlying mechanisms for changes in diffusion following stroke are still not completely understood; however, the prevailing opinion of many investigators is that cell swelling, along with changes in water tortuosity, are the main factors responsible for diffusion decline with ischemia. In this issue of the *AJNR* (page 1260), Desmond et al have applied diffusion MR imaging to help qualify the ischemic penumbra, which is thought to be the primary source of salvageable brain tissue. They have shown that diffusion MR imaging can be used to identify salvageable tissue within the ischemic penumbra on the basis of magnitude of decline in the apparent diffusion coefficient (ADC). Regions of the penumbra that maintained a normalized ADC value of at least 0.90 were shown to be unlikely to proceed to infarction, whereas those regions with normalized ADC values between 0.90 and 0.75 were at risk for infarction. This region may be identified as encompassing the salvageable tissue.

By providing a fast, quantitative, and early assessment of brain tissue status and viability, this approach goes a long way toward developing the missing element in our pursuit of efficacious therapeutic interventions. Further studies of this type, combined with perfusion measurements, relaxation time parametric mapping, and measurements of metabolic status should significantly improve our progress in the development of therapies to help better manage the stroke patient.

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Vein of Galen Management in Neonatal Period

In this issue of the *AJNR,* Mitchell et al (page 1403) describe endovascular management of vein of Galen malformations presenting in the neonatal period. The authors have documented in a relatively small number of patients their experience with management of these neonates, demonstrating the feasibility of endovascular treatment and the outcome they could achieve.

Criteria for treatment included uncontrollable congestive heart failure in neonates diagnosed with vein of Galen malformations, and they used a variety of approaches (retrograde transvenous, transtorcular, transarterial) and various embolic materials (coils, glue).

Endovascular treatment of vein of Galen malformations continues to be among the most challenging aspects in all of interventional neuroradiology. Although there have been significant improvements in the tools that are now available, the number of patients referred with this diagnosis to any given center is usually small and the experience, therefore, limited. While it intuitively would make sense to refer these patients to a regional or national center with expertise in the management of this rare disorder, this is often not a viable option in view of the medical instability of these neonates precluding transfer. Antenatal diagnosis by sonography and MR imaging (1) would allow for consultation to be obtained and transfer of the mother to be arranged to facilitate delivery at a center that has significant experience in the overall management of vein of Galen patients.

A significant number of neonates with vein of Galen malformation presenting in congestive heart failure can be managed successfully with aggressive medical therapy under the supervision of an experienced team of pediatric cardiologists and intensivists (2–4).

If, despite these best efforts, the high output failure continues to worsen, then a decision to treat the vein of Galen malformation itself needs to be made.

It is in our opinion critical at that point in time to take into consideration the status of the brain, heart, kidneys, and liver to determine whether endovascular treatment should be offered or withheld (4).

With respect to the choice of the arterial versus the venous or transtorcular approach, the following observations should be kept in mind. While the venous approach may be appealing because of its lesser technical challenge it is problematic from a conceptional point of view and is clearly wrong when the vein of Galen enlargement was not recognized to be caused by an adjacent pial arteriovenous malformation draining into it. In the considerable experience of Lasjaunias in Paris, Berenstein in New York, and we in Toronto during the past 15 years, we extremely rarely have had to resort to the venous approach in these neonates (4). As the published data would indicate and as was shown by the authors in the current issue of the *AJNR,* the arterial approach is more efficient in accomplishing a lasting reversal