THE AUTHORS REPLY: Traditionally, we have not routinely used the technique of subcortical language mapping during the course of glioma resection guided by language mapping while the patient was awake. This approach has been advocated by Bello and colleagues,[1] and as a commentator on their report, one of us (Dr. Berger) stated that it would be important to use these subcortical-stimulation-mapping techniques in the course of language mapping. This is particularly true if the surgeon attempts to resect tumor under positive or negative cortical sites when the tumor resection is within deep white-matter fasciculi, such as the superior longitudinal fasciculus connecting posterior to anterior language sites. However, for routine resections underneath the cortex, but not traversing these deep fasciculi, subcortical stimulation mapping would not be routinely advocated if the overlying cortical site is negative for language. The assumption to date is that subcortical language pathways descend perpendicularly to their cortical site of origin; thus, if a site is negative, it can be undercut with impunity, which is not the case for a positive site. The use of subcortical stimulation mapping is controversial, although recently there has been more evidence of its utility, especially in working deep within subcortical fasciculi that connect language regions.

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1. Bello L, Gallucci M, Fava M, et al. Intraoperative subcortical language tract mapping guides surgical removal of gliomas involving speech areas. Neurosurgery 2007;60:67-82.

Primary PCI in ST-Segment Elevation Myocardial Infarction

TO THE EDITOR: Le May et al. (Jan. 17 issue)[1] achieved guideline-recommended door-to-balloon times of less than 90 minutes for 79.7% of patients with ST-segment elevation myocardial infarction when paramedics interpreted the electrocardiograms (ECGs) and directly referred the patients to a percutaneous coronary intervention (PCI) center, as compared with 11.9% of patients referred from emergency departments of the area's hospitals (including the PCI center). Since about 50% of patients with ST-segment elevation myocardial infarction transport themselves to the hospital,[2] they would not benefit from this approach and would be at risk for undergoing treatment after the recommended door-to-balloon time. Exceeding the 90-minute limit may negate any survival benefit of PCI, since the 1% reduction in mortality with PCI as compared with fibrin-specific thrombolysis was observed in randomized trials involving only a median 40-minute additional delay.[3] What, then, justifies the approach proposed, given its limited applicability, its at best modest advantage, the loss of expertise in treating ST-segment elevation myocardial infarction in non-PCI centers, and the complexity inherent in imposing an upfront high-tech tertiary approach for the treatment of all patients with ST-segment elevation myocardial infarction? Since the interval between the onset of symptoms and the performance of the ECG by a paramedic was 52 minutes, well within the "golden hour" of reperfusion,[4] in-the-field thrombolysis might be a better approach.[5]

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1. Le May MR, So DY, Dionne R, et al. A citywide protocol for primary PCI in ST-segment elevation myocardial infarction. N Engl J Med 2008;358:231-40.
2. Canto JG, Zalenski RJ, Ornato JP, et al. Use of emergency medical services in acute myocardial infarction and subsequent quality of care: observations from the National Registry of Myocardial Infarction 2. Circulation 2002;106:3018-23.
3. Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. Lancet 2003;361:13-20.
4. Boersma E, Maas AC, Deckers JW, Simoons ML. Early thrombolytic treatment in acute myocardial infarction: reappraisal of the golden hour. Lancet 1996;348:771-5.
5. Bonnefoy E, Lapostolle F, Leizorovicz A, et al. Primary angioplasty versus prehospital fibrinolysis in acute myocardial infarction: a randomised study. Lancet 2002;360:825-9.

TO THE EDITOR: Le May et al. report that in their study, no patients living in Ottawa received fibrinolysis alone as primary reperfusion for ST-segment elevation myocardial infarction. Despite the time advantages of direct transfer from the field for PCI, the reality is that many patients do not

have timely access to hospitals that perform PCI; this includes both patients living in rural areas distant from PCI hospitals and those living in more populated areas with limited availability of or higher demand for emergency medical services or with high demand for health care resources.[1] Indeed, only 1200 of 5000 acute care hospitals in the United States are capable of performing PCI.[2] Furthermore, only 4% of patients with ST-segment elevation myocardial infarction who are transferred for PCI have door-to-balloon times of less than 90 minutes, a rate that improves modestly to 13% with statewide regionalization efforts.[3,4] Thus, achieving timely PCI will be challenging for many patients with ST-segment elevation myocardial infarction for a variety of reasons, including the availability of emergency medical services, geography, transfer logistics, and PCI capability. For such patients, the method of choice for primary reperfusion may be fibrinolysis.[5]

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1. Patterson PD, Probst JC, Moore CG. Expected annual emergency miles per ambulance: an indicator for measuring availability of emergency medical services resources. J Rural Health 2006;22:102-11.
2. Jacobs AK, Antman EM, Faxon DP, Gregory T, Solis P. Development of systems of care for ST-elevation myocardial infarction patients: executive summary. Circulation 2007;116:217-30. [Erratum, Circulation 2007;116(2):e77.]
3. Nallamothu BK, Bates ER, Herrin J, Wang Y, Bradley EH, Krumholz HM. Times to treatment in transfer patients undergoing primary percutaneous coronary intervention in the United States: National Registry of Myocardial Infarction (NRMI)-3/4 analysis. Circulation 2005;111:761-7.
4. Jollis JG, Roettig ML, Aluko AO, et al. Implementation of a statewide system for coronary reperfusion for ST-segment elevation myocardial infarction. JAMA 2007;298:2371-80.
5. Antman EM, Hand M, Armstrong PW, et al. 2007 Focused update of the ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2008;51:210-47. [Erratum, J Am Coll Cardiol 2008;51:977.]

TO THE EDITOR: Le May and colleagues developed a systematic mechanism to improve the time to treatment of ST-segment elevation myocardial infarction, and they report a resultant 50% reduction in mortality. The current guideline[1] regarding the time from first medical contact to first balloon inflation of less than 90 minutes seems not to have been achieved in the majority of patients in this study. The median time from ECG to first balloon inflation was 91 minutes in the field-transfer group, and the time from first medical contact to balloon inflation was not reported. We wonder whether the inherent delay was related to the requirement for direct assessment of the patient by the receiving cardiology team before a decision to transfer the patient to the catheterization facility. After an internal audit of our local program revealed unsatisfactory delays at multiple levels,[2] we embarked on a system of wireless transmission of ECG data from the field to handheld devices and direct telephone discussion between paramedics and on-call cardiologists.[3] Patients with confirmed ST-segment elevation myocardial infarction are sent immediately from the field to the catheterization laboratory, with a target interval of less than 60 minutes between first medical contact and first balloon inflation.

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1. Antman EM, Hand M, Armstrong PW, et al. 2007 Focused update of the ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2008;51:210-47. [Erratum, J Am Coll Cardiol 2008;51:977.]
2. Kaila KS, Bhagirath KM, Kass M, et al. Reperfusion times for ST-elevation myocardial infarction: a prospective audit. McGill J Med 2007;10(2):75-80.
3. Armstrong PW, WEST Steering Committee. A comparison of pharmacologic therapy with/without timely coronary intervention vs. primary percutaneous intervention early after ST-elevation myocardial infarction: the WEST (Which Early ST-elevation myocardial infarction Therapy) study. Eur Heart J 2006;27:1530-8.

THE AUTHORS REPLY: We reported the results of our citywide protocol for primary PCI. In this model, all patients with ST-segment elevation myocardial infarction presenting within the city boundaries were transferred for primary PCI to a specialized cardiac care center prepared and committed to deal with all aspects of acute myocardial infarction. By implementing strategies that

parallel the trauma model, we have substantially improved the care of patients with ST-segment elevation myocardial infarction for an entire metropolitan area, and this has been associated with a noticeable reduction in mortality.

The model was developed on the basis of evidence that primary PCI is clearly superior to fibrinolytic therapy and that shorter door-to-balloon times are needed to further improve survival with primary PCI. In a pooled analysis with data available for all 6763 individual patients from 22 randomized clinical trials that compared primary PCI with in-hospital fibrinolysis, Boersma found that primary PCI was associated with significantly lower 30-day mortality, regardless of the time from symptom onset to randomization and regardless of the PCI-related delay.[1] Furthermore, in these randomized trials, the survival benefit associated with primary PCI was significantly underestimated because the trial designs excluded patients presenting with cardiogenic shock or contraindications to fibrinolytic therapy; in these patients, mechanical reperfusion also improves survival.[2,3]

In our model, trained paramedics interpret the ECG and independently decide whether to transfer the patient. This approach is simple, is not subject to poor transmission of the ECG results, and does not depend on the immediate availability of a cardiologist to discuss the case.

We agree that fibrinolysis may be the method of choice for primary reperfusion when expertise in performing PCI is not available or timely transfer to a PCI center is not possible. However, the logistics involved when paramedics give fibrinolysis in the field are complex. In the only randomized trial that compared primary PCI with prehospital fibrinolysis, all patients were transported to a PCI center, and rescue was needed in 26% of the patients treated with fibrinolysis.[4]

A critical appraisal of door-to-balloon time needs to account for factors that delay diagnosis and treatment in patients in a real-world setting as compared with patients in randomized trials. Our median door-to-balloon time of 101 minutes for all patients compares favorably with the 180 minutes previously reported for patients needing interhospital transfer in the National Registry of Myocardial Infarction.[5] Our results are therefore quite encouraging for communities that plan to develop regional PCI programs for patients with ST-segment elevation myocardial infarction.

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1. Boersma E. Does time matter? A pooled analysis of randomized clinical trials comparing primary percutaneous coronary intervention and in-hospital fibrinolysis in acute myocardial infarction patients. Eur Heart J 2006;27:779-88.
2. Hochman JS, Sleeper LA, Webb JG, et al. Early revascularization in acute myocardial infarction complicated by cardiogenic shock. N Engl J Med 1999;341:625-34.
3. Grzybowski M, Clements EA, Parsons L, et al. Mortality benefit of immediate revascularization of acute ST-segment elevation myocardial infarction in patients with contraindications to thrombolytic therapy: a propensity analysis. JAMA 2003;290:1891-8.
4. Bonnefoy E, Lapostolle F, Leizorovicz A, et al. Primary angioplasty versus prehospital fibrinolysis in acute myocardial infarction: a randomised study. Lancet 2002;360:825-9.
5. Nallamothu BK, Bates ER, Herrin J, Wang Y, Bradley EH, Krumholz HM. Times to treatment in transfer patients undergoing primary percutaneous coronary intervention in the United States: National Registry of Myocardial Infarction (NRMI)-3/4 analysis. Circulation 2005;111:761-7.

Lung Transplantation and Survival in Children with Cystic Fibrosis

TO THE EDITOR: The analysis by Liou et al. (Nov. 22 issue)[1] is a step toward a better understanding of the risk–benefit ratio of lung transplantation in cystic fibrosis. The study, however, has several limitations.

First, the authors have neither validated their model in an independent data set nor provided an indication of its discriminative ability. Unless the concordance statistic[2] for the model was consistent with good discrimination of patients who survived from those who died, the study conclusions might not be applicable to a significant proportion of patients. Second, the model does not include any donor factors or surrogates for center experience, both of which were previously shown to be associated with a poor outcome.[3,4]

Third, the authors have handled missing covariate values by excluding patients with missing