(PSC) for treatment at a comprehensive stroke center (CSC).

The rationale for the SAST system involved the knowledge that, while the chance of complete recovery from severe stroke improves with treatment like injection of tissue plasminogen activator (t-PA) that can be done at many PSCs, overall treatment success is low [Adams HP Jr. et al. *Stroke* 2007].

The SAST bypass system legislated in Florida requires emergency medical services (EMS) providers to transport suspected stroke patients to a CSC capable of administering t-PA, rather than to the nearest PSC.

Dr. Allen reported the results of a 7-year (2006–2012) retrospective analysis of therapeutic bypass yield (percentage of patients receiving treatments not available at the bypassed PSC), diagnostic accuracy of EMS providers, and outcome effect of bypassing a PSC located closer to the site of stroke. The analysis involved suspected acute strokes that occurred in the Orlando region and were ultimately treated at Florida Hospital Orlando CSCs in Orange County (Table 1).

Table 1. Summary of 526 Suspected Acute Strokes in Two Florida Counties

EMS Location	Stroke Assessment	Scale Score	Severe Strokes	Mild Strokes
Seminole County	3-item Simple Stroke Scale	≥4	310	0
Lake County	Los Angeles Motor Scale	≥4	190	26

EMS=emergency medical services.

Of the 526 patients, 77 (15%, ~1 in 7 patients) received CSC-specific interventions that included acute endovascular intervention for ischemic stroke (7.5%), neurosurgery for intracranial bleeding (5%), neurosurgery for intracranial tumor (2%), and other procedures including aneurysm coiling and extra-intra cranial arterial bypass (0.5%). Comparison of therapeutic bypass yields for patients who suffered stroke and trauma revealed 15% (77/526) of stroke patients received CSC-specific care and 18% (35/193) of trauma patients received surgery within 48 hours at a Level 1 trauma center. The difference was not statistically significant (OR, 0.77; 95% CI, 0.5 to 1.2).

Comparative analyses of data for 643 patients who were transported directly to a single PSC for treatment and 209 SAST bypass patients treated at the CSC revealed the potential benefit in the bypass triage strategy. CSC patients experienced significantly higher rates of major complications and fatal/debilitating intracerebral hemorrhage (Table 2), which were immediately treatable at the CSC as opposed to transferring a patient from the PSC to a CSC for treatment.

Table 2. Comparative Analyses of PSC and CSC Care

	Direct to PSC	SAST Bypass to CSC	OR; 95%CI	p Value
Average age (years)	70.6	72.7	—	—
Average length of stay (days)	5.5	6.0	—	—
Major complications	13%	34%	2.54; 1.78 to 3.62	<0.0001
Fatal or debilitating intracerebral hemorrhage	0.6%	9.6%	15.38; 5.2 to 45.5	<0.0001

CSC=comprehensive stroke center; PSC=primary stroke center; SAST=severe stroke adjusted triage.

The results indicate the potential benefit of the SAST bypass system. In-field identification of patients with severe stroke-like symptoms enables these patients to receive prompt treatment available at a CSC.

Molecular Imaging of Thrombosis and Thrombolysis

Written by **Brian Hoyle**

Francesco Blasi, PharmD, PhD, Martinos Center for Biomedical Imaging, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts, USA, described the use of a novel probe in the positron emission tomography (PET) molecular imaging of thrombosis and thrombolysis *in vivo*.

Diseases including stroke, coronary artery disease, pulmonary embolism, and deep vein thrombosis are often triggered by the formation of a thrombus. Noninvasive assessment of thrombosis is crucial in diagnoses and to monitor disease progression. In seeking to develop a thrombus-specific imaging tool, Dr. Blasi and colleagues exploited fibrin as a target (Table 1).

Table 1. Fibrin Targeting for Thrombus Imaging

Attributes of Fibrin
- High sensitivity: present in all thrombi
- High specificity: high levels in clots, but not in circulating blood
- Small fibrin-specific peptides available; they have low affinity for fibrinogen and plasma proteins (low blood background)
- PET and magnetic resonance probes based on fibrin-binding peptides can be made

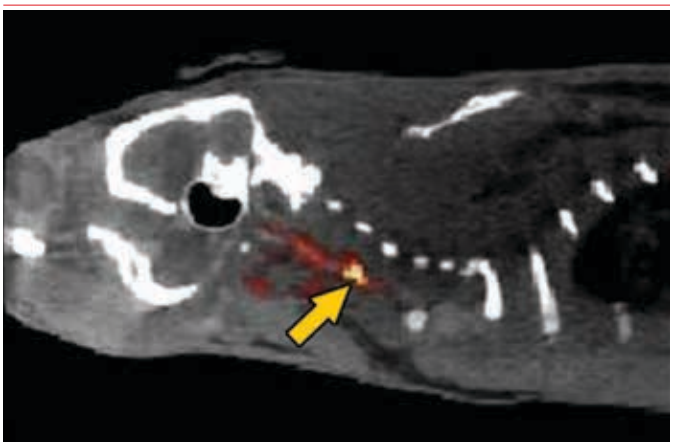
PET=positron emission tomography.

In this study, a fibrin-specific probe labeled with 64Cu was used. Fibrin-binding probe 7 (FBP7) has high affinity for fibrin, is metabolically stable, has a short half-life of 18 minutes (rapid clearance from blood) and a favorable biodistribution. The *in vivo* prowess of FBP7 was evaluated using rat models of crush-induced mural thrombosis and occlusive embolic stroke. PET and computed tomography (CT) imaging were performed following intravenous administration of FBP7. The stroke model also included

observations following treatment with recombinant tissue plasminogen activator (rt-PA) to quantitatively assess clot bursting. Following sacrifice, *ex-vivo* assessments of thrombolysis, and probe biodistribution were also performed.

Imaging revealed the specificity of FBP7 for the thrombus (Figure 1). Binding to the thrombus exceeded binding in the left carotid, brain, and heart by ~4-, 12-, and 2.5-fold, respectively, soon after the injection of FBP7. The binding specificity to the thrombus was maintained with time (90 minutes), while binding to the other regions diminished. Examination at 4 hours post injection revealed the same uptake of FBP7 to the thrombus, but reduced binding in the other regions, resulting in lower background; thrombus binding of the probe exceeded binding to the left carotid, brain, and heart by ~15-, 65-, and 10-fold, respectively.

Figure 1. FBP7 Detects Mural Thrombosis at the Level of the Common Carotid Artery (arrow). Fused PET-CT image.



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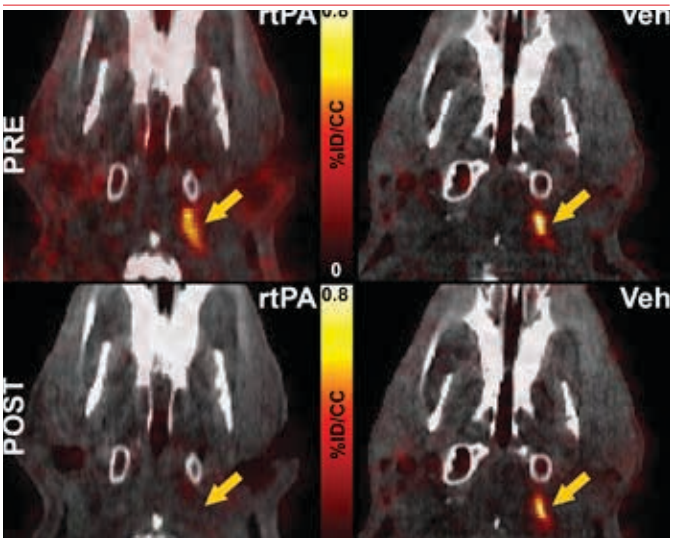
PET-CT imaging in the embolic stroke model revealed the specificity of FBP7 for the detection of the embolus at the level of the internal carotid artery and the middle cerebral artery, common sites of occlusion in human strokes. Furthermore, the dissolution of the embolus following administration of rt-PA was evident, while probe binding remained constant in rats who received vehicle instead of rt-PA (Figure 2).

Figure 2. FBP7 Detects Thrombolysis in the Internal Carotid Artery After Treatment With rt-PA, but Not Vehicle. Fused PET-CT images.



rt-PA=recombinant tissue plasminogen activator; Veh=vehicle.

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Table 2 summarizes the study conclusions.

Table 2. Study Conclusions

- PET imaging of thrombosis and thrombolysis is feasible using FBP7
- FBP7 imaging enables detection of nonocclusive (mural) and occlusive thrombi
- FBP7 can be used to visualize and quantify thrombolysis after rtPA administration

FBP7=fibrin-binding probe 7; PET=positron emission tomography; rt-PA=recombinant tissue plasminogen activator.

FBP7 is a very promising candidate for clinical testing. Dr. Blasi added that this proof-of-concept study is now being followed by assessments of the capability of the probe to quantify the level of fibrin in thrombi and to detect different stages of the thrombus evolution.

Dr. Blasi received the Mordecai Y. T. Globus New Investigator Award in Stroke at the International Stroke Conference 2014 for his work on molecular imaging of thrombosis.

Stroke Neuroprotection of Prehospital Magnesium Sulfate Explored

Written by **Brian Hoyle**

Magnesium sulfate administered to patients <2 hours after stroke fails to provide neuroprotection. The primary findings of the Field Administration of Stroke Therapy–Magnesium trial [FAST-MAG] were presented by Jeffrey L. Saver, MD, Stroke Center, University of California at Los Angeles, Los Angeles, California, USA.