Conclusions—After successful Wingspan percutaneous transluminal angioplasty and stenting, some patients continued to experience ipsilateral stroke after 30 days. Although in selected patients, stroke or death within 30 days of the stenting procedure or ipsilateral stroke after 30 days were associated with the interruption of antiplatelet therapy or in-stent restenosis. Most of these ischemic events occurred within 6 months of the procedure and were associated with the interruption of antiplatelet therapy or in-stent restenosis.  

Key Words: angioplasty ■ intracranial atheromatous disease ■ stenting ■ symptomatic intracranial stenosis ■ Wingspan

Background and Purpose—The purpose of this study is to present 12-month follow-up results for a series of patients undergoing percutaneous transluminal angioplasty and stenting with the Gateway-Wingspan stenting system (Boston Scientific) for the treatment of symptomatic intracranial atherostenosis.

Methods—Clinical and angiographic follow-up results were recorded for patients from 5 participating institutions. Primary end points were stroke or death within 30 days of the stenting procedure or ipsilateral stroke after 30 days.

Results—During a 21-month study period, 158 patients with 168 intracranial atherostenotic lesions (50% to 99%) were treated with the Gateway-Wingspan system. The average follow-up duration was 14.2 months with 143 patients having at least 3 months of clinical follow-up and 110 having at least 12 months. The cumulative rate of the primary end point was 15.7% for all patients and 13.9% for patients with high-grade (70% to 99%) stenosis. Of 13 ipsilateral strokes occurring after 30 days, 3 resulted in death. Of these strokes, 76.9% (10 of 13) occurred within the first 6 months of the stenting procedure and no events were recorded after 12 months. An additional 9 patients experienced ipsilateral transient ischemic attack after 30 days. Most postprocedural events (86%) could be attributed to interruption of antiplatelet medications (n = 6), in-stent restenosis (n = 12), or both (n = 1). In 3 patients, the events were of uncertain etiology.

Conclusions—After successful Wingspan percutaneous transluminal angioplasty and stenting, some patients continued to experience ipsilateral ischemic events. Most of these ischemic events occurred within 6 months of the procedure and were associated with the interruption of antiplatelet therapy or in-stent restenosis.  

Key Words: angioplasty ■ intracranial atherostenosis ■ Wingspan

The Gateway balloon-Wingspan stent system (Boston Scientific, Fremont, CA), a stenting system specifically designed for the cerebrovasculature, became commercially available in the United States in 2005. The US Wingspan Registry is a 5-center collaboration in which data were prospectively collected from 158 consecutively treated patients with symptomatic intracranial atherostenosis.1 Procedural success was defined as completion of Gateway balloon angioplasty and Wingspan stent placement across the target lesion despite the degree of residual stenosis or any complications related to the procedure. Primary end points were stroke or death within 30 days of the stenting procedure or ipsilateral stroke after 30 days. Although in selected patients, the periprocedural safety of the treatment compared favorably to the documented natural history of the disease treated medically, angiographic follow-up revealed significant rates of in-stent restenosis (ISR) and occlusion.2 These findings raised a question regarding the durability of the procedure and the susceptibility of treated patients to experience continued ipsilateral ischemic events after successful treatment.

In the present study, we report the longer-term outcomes of patients treated with the Gateway-Wingspan system. Clinical data from patients meeting primary end points were evaluated in an attempt to determine a probable cause for treatment failure.

**Patients and Methods**

**Patient and Institutional Enrollment**

Patients with symptomatic intracranial atherostenosis undergoing attempted treatment with the Wingspan system were prospectively
enrolled into a multicenter intention-to-treat registry (US Wingspan Registry) that included the Barrow Neurological Institute, Cleveland Clinic, State University of New York at Buffalo, University of Texas Southwestern, and University of Wisconsin. The Institutional Review Board at each institution approved the use of the Wingspan system under a Humanitarian Device Exemption as well as the collection and sharing of registry data among the participating centers.

Data Collection
Clinical and angiographic data were typically collected at the time of the initial procedure and at 3 to 6 months and 12 to 15 months. Clinical data were also collected at discharge and between 2 and 6 weeks after the original procedure.

Stenting Technique
Percutaneous transluminal angioplasty and stenting (PTAS) was performed using the Wingspan system as described previously. In brief, access was typically achieved through the common femoral artery. Most cases were performed through a 6-Fr guiding catheter or long sheath system. Heparinization was instituted to a targeted activated coagulation time of 250 to 300 seconds. In most cases, after conventional catheter-based angiography, an SL-10 (Boston Scientific, Natick, MA), Prowler-10 (Cordis), or Echelon-10 (Microtherapeutics, Irvine, CA) microcatheter was manipulated across the target lesion using a 0.014-inch Synchro (Boston Scientific) or Transcend EX Soft Tip (Boston Scientific) microwire. The microcatheter was then exchanged over a 0.014-inch exchange microwire for a Gateway angioplasty balloon. The remaining lesions were primarily crossed with the Gateway angioplasty balloon and 0.014-inch exchange-length microwire. In each case, the balloon diameter was sized to 80% of the “normal” parent vessel diameter. The balloon length was selected to match the lesion length. Angioplasty was typically performed with a slow, graded inflation of the balloon to a pressure of between 6 and 12 atmospheres for approximately 120 seconds. After angioplasty, the balloon was removed and conventional angiography was repeated.

Next, the Wingspan delivery system was prepared and advanced over the exchange wire across the target lesion. The stent diameter was sized to exceed the diameter of the normal parent vessel by 0.5 to 1.0 mm. The stent length was selected to equal or exceed the length of the angioplasty balloon and to completely cover the entire diseased segment. The diameter of the stenotic lesion was measured using biplane angiography and compared with a reference diameter of the normal vessel (usually proximal to the lesion) per the technique used in the Warfarin-Aspirin Symptomatic Intracranial Disease (WASID) study. All patients were pretreated with antiplatelet agents (aspirin and clopidogrel); most were discharged on both aspirin (325 mg daily) and clopidogrel (75 mg daily). The dual antiplatelet regimen was usually maintained until follow-up angiography was performed. Provided that no ISR had developed, clopidogrel was usually discontinued after follow-up angiography. All patients remained on aspirin therapy (325 mg daily) indefinitely after treatment.

Follow-Up Imaging
Imaging follow-up was available for 138 lesions. Most of the lesions (n=109) were evaluated with conventional catheter-based angiography. In some cases, lesions were evaluated with CT angiography (n=28). If the entire stented segment as well as the proximal and distal parent vessel was well visualized and widely patent on CT angiography, these stents were designated as demonstrating “no ISR.” If a region of the stented segment or adjacent parent vessel could not be adequately visualized, catheter angiography was performed. In cases in which the findings on the cross-sectional imaging were ambiguous or suggestive of ISR, conventional angiography was performed. In 1 case, only MR angiography was available as a follow-up examination.

At angiographic follow-up, the minimum luminal diameter was identified and measured. The percentage of residual or recurrent stenosis was calculated using the WASID technique. ISR was defined as a lesion demonstrating (1) >50% stenosis (ie, within or immediately adjacent [within 5 mm] to the stent); and (2) >20% of absolute luminal loss. The measurements were made by the authors at each institution and then adjudicated by 1 investigator (D.J.F.). Lesion retreatment was performed at the discretion of the primary operator.

Clinical Event Adjudication
Scheduled clinical follow-up occurred at the time of discharge and at 2 to 6 weeks, 3 to 6 months, and 12 to 15 months after the Wingspan procedure. Any stroke or death occurring during or within 30 days of the procedure or any stroke within the ipsilateral vascular distribution after 30 days was counted as a primary neurological end point. Per the purpose of the present analysis, any hemorrhagic or ischemic event resulting in a new neurological deficit lasting >24 hours was considered a stroke. Any ischemic event resulting in a transient neurological deficit that resolved within 24 hours was considered a transient ischemic attack (TIA) regardless of the neuroimaging findings. The distribution of the stroke (ipsilateral or other) was adjudicated on the basis of the neurological findings evaluated within the context of any available neuroimaging study. End point adjudication was determined by investigators at the individual sites.

Results
Registry Patients
During a 21-month study period, 158 patients with 168 intracranial atherostenotic lesions (50% to 99% severity) were treated with the Gateway-Wingspan system. Patients (95 men, 63 women) ranged in age from 33 to 86 years (average age, 62.7 years). Ninety patients presented with a qualifying event of stroke (57%). The average stenosis treated measured 75.2%, and 115 of the treated lesions (69%) were in the 70% to 99% stenosis range at presentation. Periprocedural stroke was encountered in 9 patients (5.7%). In 4 patients (2.5%), these strokes ultimately resulted in death.

Clinical Follow-Up
Of the initial group of 158 patients, 147 were eligible for 3-month follow-up evaluation allowing for loss to periprocedural primary end points (n=9) or nonneurological death occurring after 30 days (n=2). A total of 143 of these patients (97.3%) had at least 3 months of clinical follow-up. One hundred ten of 127 eligible patients (86.6%) had at least 12 months of follow-up. The average length of clinical follow-up for the registry patients was 14.2 months. The cumulative rate of the primary end point was 15.7% for all patients and 13.9% for patients with high-grade (70% to 99%) stenosis. Of 13 ipsilateral strokes occurring after 30 days, 3 resulted in death. Ten of 13 (76.9%) of the ipsilateral strokes that occurred after the 30-day periprocedural period occurred within 6 months of the procedure, and no events were recorded after 12 months. An additional 9 patients experienced an ipsilateral TIA after 30 days. The composite rate of either stroke or TIA between 30 days and 12 months was 20% (22 total events in 110 patients with 12-month clinical follow-up).

Most periprocedural events (86%) were associated with interruption of antiplatelet medications (n=6), ISR (n=12),...
or both (1). In 3 patients, the events were of uncertain etiology. Specifically, for the 13 patients meeting the primary end point with ipsilateral ischemic stroke after 30 days, 5 were believed to be due to ISR and 5 to the interruption of antiplatelet medication; and in 3, a specific cause was not determined. Patients experiencing stroke from interruption of antiplatelet medications presented between 2 and 9.5 months (average, 4.4 months) postprocedure (Figure 1 through 3). Patients experiencing stroke as a result of ISR presented between 3.5 and 11.5 months (average, 6.9 months) postprocedure (Figure 4). Two patients who experienced stroke at 10.5 and 11.5 months, respectively, skewed the average time of presentation for stroke associated with ISR. These patients had been transiently symptomatic with ISR at earlier time points and had undergone ≥1 repeat angioplasties before ultimately presenting with stroke from recurrent ISR. The average time of presentation for patients with an unknown cause of stroke was 3.2 months (range, 1.5 to 5 months). In the 9 patients experiencing an ipsilateral TIA after 30 days, 7 events were associated with ISR, 1 to the interruption of antiplatelet medication; and in 1 patient, both factors were present.

Discussion
The most important findings derived from the present analysis of the US Wingspan Registry are (1) some patients continue to experience ipsilateral ischemic events after initially successful PTAS; (2) most of these delayed events can be attributed to defined factors, either early interruption of antiplatelet medication or ISR; and (3) these delayed ischemic events most frequently occurred within the first 6 months after treatment. The Gateway-Wingspan system was introduced in 2005 as a novel strategy for the treatment of symptomatic intracranial atherosclerosis. The initial experience with the system indicated that the angioplasty and stenting procedure could be achieved with rates of periprocedural stroke (approximately 5%) that compared very favorably with event rates in selected high-risk patients treated medically.1,3–5 However, midterm angiographic follow-up results from 2 independently conducted single-arm registries revealed rates of ISR or complete stent occlusion that ranged between 25 and 35%.2,6–8 These rates of late luminal loss were considerably higher than those reported in the initial Eurasian Humanitarian Device Exemption study.7 Although the majority of patients with ISR were asymptomatic, approximately one third presented with ipsilateral ischemic symptoms.2,6,8 These findings provoked questions about the durability of the treatment modality and the potential for ongoing ischemic events after initially successful treatment. The goal of the present analysis was to address this issue.

Event Rates After the Periprocedural Period
In the present study, some patients continued to accrue ipsilateral ischemic events after initially successful PTAS. These delayed events accounted for almost two thirds of the total number of cumulative events, exceeding those incurred during the actual PTAS procedure. The National Institutes of Health Wingspan Registry reported a 5% to 6% rate of delayed ipsilateral stroke after the periprocedural period in patients with high-grade (70% to 99%) symptomatic stenosis.5 However, although this study provides an excellent assessment of the periprocedural risk of the procedure in >100 patients, 12-month follow-up results were available for very few patients (n=15). As such, these data are probably not sufficient to allow an accurate estimation of postprocedural event rates.5 In the present study, there was no difference observed in either the periprocedural or postprocedural
event rates between the overall group (50% to 99% stenosis) and those patients presenting with high-grade (70% to 99%) stenosis.

Thus, although the periprocedural stroke risk associated with the PTAS procedure itself (approximately 5%) appears far lower than the risk associated with high-grade (70% to 99%) symptomatic stenosis treated medically (20% to 25% over the first year), the ischemic events occurring beyond the periprocedural period in patients undergoing stenting make the risk profile of the 2 treatment strategies appear far more comparable. As such, a direct comparison between the stenting procedure and medical therapy, as is currently underway in the Stenting and Aggressive Medical Management for Preventing Recurrent stroke in Intracranial Stenosis (SAMMPRIS) trial, will be necessary to definitively determine whether stenting can provide a meaningful additional benefit to medical therapy in high-risk patients.

Etiology of Delayed Events

In addition to better defining the overall risks related to Wingspan PTAS, it is critical to make an attempt to ascertain the circumstances under which the Wingspan stenting procedure might fail beyond the periprocedural period. In the present study, 2 predictable factors seemed to be associated with the majority (86%) of delayed ischemic events, the interruption of antiplatelet therapy and the development of ISR.

Approximately 40% of delayed strokes were associated with the interruption of antiplatelet medications. Early discontinuation of antiplatelet medications typically results from patient nonadherence, discontinuation in response to hemorrhage or a perceived risk of hemorrhage, in preparation for an upcoming invasive/surgical procedure, or at the discretion of the patient’s primary physician. Conceivably, these events could be largely overcome by more aggressive and proactive education of patients, their families, and all their managing physicians. Dual antiplatelet therapy was typically continued during the present study for 3 to 6 months with discontinuation of clopidogrel contingent on angiographic follow-up confirming the absence of ISR. Thus, intensive clinical follow-up and assurance of adherence to the recommended antiplatelet regimen is most critical during this initial 90- to 180-day period. In the present series, only 1 delayed ipsilateral stroke could be attributed to the interruption of antiplatelet medications after 6 months and this patient had stopped taking all antiplatelet medications.

ISR represents a potential limitation of any stenting procedure. In the present series, ISR was associated with almost 40% of postprocedural stroke events. In addition, the majority of patients within the registry underwent scheduled imaging surveillance of their stents as part of routine clinical follow-up. When identified at follow-up, ISR was typically managed with the continuation of dual antiplatelet therapy. When patients experienced new neurological symptoms or late luminal loss to the extent that the recurrent stenosis was of a severity greater than or equivalent to the presenting lesion before treatment, repeat angioplasty was typically performed. As such, the reported recurrent stroke risk attributable to ISR was observed in the setting of a fairly proactive program of imaging surveillance, medical management, and interventional retreatment. Thus, it seems that measures to reduce the delayed morbidity associated with ISR may be limited to...
strategies designed to improve the existing devices such as the development of drug-eluting balloons, a drug-eluting version of the current self-expanding stent platform, or an optimization of the degree of chronic outward force exerted by the device on the vessel wall.12,13

Timing of Delayed Events
The vast majority (80%) of delayed ischemic symptoms (both TIAs and strokes) occurred within 6 months of treatment. The timing of these events correlates well with the “risk period” of the 2 major factors responsible for recurrent ischemia. The discontinuation of antiplatelet medications is likely to become less of a risk with time as the implanted stent becomes fully “endothelialized” and incorporated into the parent artery. Similarly, the risk associated with ISR is almost exclusively incurred during the first 3 to 6 months after the stenting procedure. Those patients who experienced stroke attributable to ISR at later time points had been symptomatic earlier with TIAs and then represented with stroke after developing recurrent ISR months after angioplasty. The available literature suggests that after this initial 3- to 6-month postprocedural period, the tissue ingrowth along the stented segment stabilizes and, in some cases, actually undergoes a process of reorganization to become somewhat more compact, resulting in partial regression of the angiographic stenosis. This process of stabilization and/or spontaneous regression of ISR has been documented for both coronary and intracranial stents.14,15 The present data suggest that if patients with ISR do not become symptomatic during this initial 3- to 6-month period after the procedure and an appropriate medication regimen is maintained, it is unlikely that they will ultimately become symptomatic in follow-up.

Limitations
Although the present report represents the longest follow-up of a large series of patients with intracranial atherosclerosis treated with the Wingspan-Gateway system, it is important to acknowledge that the present data set has some significant limitations. Most importantly, not all eligible patients were available for follow-up at the 12-month time period (13% were lost to follow-up by 1 year). Because there is no guarantee that the patients who were lost to follow-up had event rates that were similar to those who were followed to (and beyond) 12 months, it is important to acknowledge that this represents a potential source of bias with respect to the reported 1-year event rates.

Conclusions
After successful PTAS, some patients may continue to experience ipsilateral ischemic events. Most of these events occur within 6 months of the procedure. These ischemic events can largely be attributed to premature interruption of antiplatelet medications or ISR.

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US Wingspan Registry: 12-Month Follow-Up Results

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미국 Wingspan 등록
12개월 추적 관찰 결과

US Wingspan Registry
12-Month Follow-Up Results

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Key Words: angioplasty  ■ intracranial atheromatous disease  ■ stenting  ■ symptomatic intracranial stenosis  ■ Wingspan

배경 목적: 본 연구의 목적은 증상성 두개내 축상경화증(intracranial atherostenosis)의 치료를 위하여 펌부경혈관관절관협 관성형혈(percuteaneous transluminal angioplasty) 및 Gateway–Wingspan 스텀트슬(Boston Scientific)을 받은 환자들 을 12개월간 추적 관찰한 결과를 보고하는 것이다.

방법: 참여 병원 5개소에서 환자들의 임상 및 혈관조영(cmangiography) 결과를 기록하였다. 임상 결과 변수는 스텀트슬 30일 이내의 뇌출혈 혹은 사망 발생 및 30일 이후 동측의 뇌출혈 발생이었다.

결과: 12개월의 연구 기간 동안, 158명의 환자에서 168개의 두개내 축상경화증 병변(50~99%)에 대하여 Gateway–Wingspan 스텀트슬이 시행되었다. 최소 3개월 이상의 임상적 추적 관찰이 완료된 환자 143명에서 평균 14.2개월간 추적 관찰하였으며, 110명에서 12개월 이상의 추적 관찰이 이루어졌다. 임상 결과 변수의 누적 발생률은 모든 환자에서 15.7%였으며, 현저한 혈착 (stenosis)(70~99%)가 있었던 환자에서 13.9%였다. 스텀트슬 30일 이후에 발생한 동측 뇌출혈 13례 중 3례의 환자가 사망하였다. 이 동측 뇌출혈 가운데 76.9% (13례 중 10례)가 스텀트슬 후 6개월 이내에 발생하였으며, 12개월 이후에는 뇌출혈이 발생하지 않았다. 시술 이후에 발생한 사망의 대부분(86%)은 헬혈관관협 투약 중단(n=6), 스텀트내 재혈착(in–stent restenosis)(n=12), 혹은 두 가지 모두(n=1)에 기인하였다. 3례에서는 그 원인이 불명확하였다.

결론: 펌부경혈관관절관협관성형혈 및 스텀트슬이 성공한 이후에도 일부 환자에서는 동측의 혈착성 사망이 발생할 수 있다. 이러 한 혈착성 사망의 대부분은 시술 후 6개월 이내에 발생하며, 헬혈관관협의 투약 중단 혹은 스텀트내 재혈착과 연관되어 있다.

혈관관협(cerebrovasculature) 치료를 위하여 개발된
Gateway 웅선–Wingspan 스텀트시스템(Boston Scie-
ntific, Fremont, CA)은 미국에서 2005년도에 상업적 판매
가 허가되었다. US Wingspan Registry는 5개 병원의 혈력
을 통하여 증상성 두개내 축상경화증(intracranial athero-
stenosis)에서 이 스텀트슬을 시행한 환자 158명을 전향적으

From the Cerebrovascular Center (D.J.F., H.H.W.), Department of Neurosurgery, State University of New York at Stony Brook, Stony Brook, NY; the Departments of Neuroradiology and Neurosurgery (A.S.T.), Medical University of South Carolina, Charleston, SC; the Departments of Neurosurgery and Radiology (E.I.L., L.N.H.), University at Buffalo, State University of New York, Buffalo, NY; the Departments of Neurosurgery and Neuroradiology (G.L.P., B.G.W.), University of Texas Southwestern, Dallas, TX; the Department of Neurosurgery (F.C.A., C.G.M.), Barrow Neurological Institute, Phoenix, AZ; the Departments of Neuroradiology and Neurosurgery (D.B.N., B.A.-K.), University of Wisconsin, Madison, WI; and the Cerebrovascular Center (P.A.R., T.J.M.), Neurologic Institute, Cleveland Clinic, Cleveland, OH.

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로 수록하고 있다. 1) Gateway 풍성형술(balloon angioplasty)을 시행하고 Wingspan 스테트를 목표한 범위에 걸쳐 설치한 경우, 부분적으로 협착(stenosis)이 남아 있거나 시술 과 관련된 합병증이 있었다고 하더라도 시술 성공으로 간주하였다. 임차 결과 변수는 스테트술 시행 30일 이내에 발생한 뇌졸중 혹은 사망, 그리고 스테트술 30일 이후에 발생한 동측의 뇌졸중으로 정의하였다. 일부 환자에서 시행된 이론 연구 결과, 본 치료 방법의 시술 전후 안정성은 약물 투여만으로 치료 한 사례의 자신 경과에 비하여 양호한 것으로 확인되었으나, 상당한 숫자에서 스테트를 재협착(in-stent restenosis, ISR) 및 패색 발생이 혈관조영술(angiography) 추적 검사에서 발견되었다. 2) 이러한 결과는 본 시술의 내구성(durability) 및 성공적으로 시술받은 환자에서 동측의 헤혈성 사건 발생 위험도에 대한 의의심을 촉발하였다.

본 연구에서, 저작자는 Gateway–Wingspan 스테트로 치료받은 환자들의 장기 예후를 보고하고자 한다. 임차 결과 변수가 발생한 환자의 임상 자료를 분석하여, 치료 실패의 잠재적인 원인을 밝혀보고자 하였다.

환자와 방법
환자 및 참여 기관 동록
중앙성 두개뇌 속장정중으로 Wingspan 스테트술을 받을 예정인 환자는 다기관 동록부에 전향적으로 동록되었다(US Wingspan Registry). 본 동록부는 최초 치료 방법 결정에 의거하여 환자를 동록하였으며(intention-to-treat), Cleveland Clinic, State University of New York at Buffalo, University of Texas Southwestern 및 University of Wisconsin에 참여하였다. 각 참여 병원에서는 Wingspan 스테트에 대한 의료 기기 사용의 인도적인 허가 면제(Humanitarian Device Exemption) 및 참여 기관의 동료부 구성과 자료 공유를 조건으로 윤리 위원회 승인을 취득하였다.

자료 수집
임상 및 혈관조영술 자료는 일반적으로 최초 시술 시점, 3~6개월 및 12~15개월 시점에서 수집되었다. 임상 자료는 퇴원 시점 및 최초 시술 2~6주 후에 추가로 수집하였다.

스滕트술
Wingspan 스테트를 이용한 피부경유혈관경유혈관조영술 및 스테트술(percutaneous transluminal angioplasty and stenting, PTAS)은 이전에 기술된 바와 같이 시행되었다. 1) 간략하게, 주로 총대퇴동맥(common femoral artery)을 통하여 혈관 내로 접근하였다. 대부분의 사례에서 6–Fr 유도 카테터(guiding catheter) 혹은 long sheath system을 이용하였고, 혈관 조영술은 250~300초로 유지하였다. 대부분의 사례에서 카테터를 이용한 혈관조영술을 시행한 후, 0.014인지 Synchro (Boston Scientific) 혹은 Transcend EX Soft Tip (Boston Scientific) 미세와이어(microwire)를 거쳐 SL–10 (Boston Scientific, Natick, MA), Prowler–10 (Cordis) 혹은 Echelon–10 (Microtherapeutics, Irvine, CA) 미세카테터(microcatheter)를 삽입하여 혈관 협착 부위로 접근하였다. 이후 미세와이어를 거치시간 상태에서 미세카테터를 Gateway 혈관 조영 형성술(angioplasty balloon)으로 교체하였다. 잔여 빈명은 주로 Gateway 혈관조영 형성술 및 0.014인지 미세와이어를 통해 통과하였다. 개별 사례에서 풍성의 지름은 정상적인 모혈관 직경의 80%가 되는 것을 선택하였다. 풍선의 길이와 변형의 길이를 고려하여 적절한 것을 선택하였다. 혈관조영술은 풍선을 서서히 제단식으로 부풀리, 보통 120초 동안 6~12기압 정도의 압력을 유지하도록 하였다. 혈관조영술 이후, 풍선을 제거하고 혈관조영술을 다시 시행하였다.

이후에 Wingspan 시스템을 준비하고 교체 외어(exchange wire)를 통하여 혈적이 부위까지 진전시켰다. 스테트의 직경은 해당 혈관의 정상적인 지름보다 0.5~1.0 mm 정도 큰 것을 선택하였다. 선택한 스테트는 혈관조영 형성술과 같거나 조금 더 긴 것으로 선택하여 혈적이 부위 전체에 걸쳐질 수 있도록 하였다. 혈적이 부위의 직경은 이중 평면 혈관조영술(biplane angiography)을 통해 측정하였고, Warfarin–Aspirin Symptomatic Intracranial Disease (WASID) 연구의 방법론을 적용하여 정상적인 혈관의 표준 직경과 비교하였다. 2) 모든 환자는 치료 이전에 혈액소관계(아스피린과 클로피도그레)를 복용하였다. 대부분의 환자는 퇴원 시 아스피린(하루 325 mg)과 클로피도그레(하루 75 mg)를 처방 받았다. 항혈소관계 복합 투여는 이중 혈관조영술 수술 관련이 이루어지는 시점까지 유지하였다. 혈관조영술 수술을 진행한 환자들에서 ISR이 발생하지 않은 환자는 대개 클로피도그레 투여를 중단하였다. 모든 환자들은 치료 이후 계속 아스피린(하루 325 mg)을 복용하였다.

추적 영상 검사
추적 영상 검사는 138개의 혈적이 부위에서 시행되었다. 대부분의 환자(n=109)는 카테터를 이용한 고정적인 혈관조영술로 평가하였다. 일부 사례(n=28)는 CT 혈관조영술으로 평가하였다. 스테트를 삽입한 전체 부위 및 상하부 혈관이 CT 혈관조영술에서 모두 측정하지 않고 잘 관찰되는 경우, 'ISR 없음'으로 평가하였다. 스테트를 삽입한 부위 혹은 인접한 혈관을 CT 혈관조영술에서 충분히 확인할 수 없는 경우, 카테터를 이용한 혈관조영술을 시행하였다. 단변 영상이 평가하기에 모호하거나 ISR이 의심되는 경우에도 혈관조영술을 시행하였다. 한 건
의 사례에서는 MR 혈관조영술만 시행되었다. 
혈관 영상의 추적 검사 시, 내강(luminal)의 최소 직경을 확 
인하고 측정하였다. 외관(residual) 혈착 혹은 재발한 혈착은 
WASID 기법을 이용하여 그 비율을 계산하였다.¹ ISR은 (1) 
50% 초과 혈착(스텐트 내부 혹은 5 mm 이내로 인지한 부위), 
(2) 20% 초과의 내강 소실로 인한 농증이 있는 지경하였다. 내강 단면 
의 측정은 각 기관에 속한 저자들에 의하여 이루어졌고, 1의 연 
구자(D,J,F)가 재확인하였다. 혈착 병변의 재시술 여부는 각 
사준자의 판단에 따라야 한다. 

임상적 사진의 관찰

Wingspan 스텐트술 후, 정기적인 임상적 추적 관찰은 퇴원 
시점, 2~6주, 3~6개월 및 12~15개월 시점에서 이루어졌다. 
사진은 이내에 발생한 농증은 혹은 사망, 그리고 30일 이후 
에 발생한 동측 관류 영역의 농증이 임차 신경학적 결과 변 
수를 정의하였다. 본 논문을 위하여, 24시간 이상 지속된 혈 
혈 혹은 혈혈성 사건을 농증으로 간주하였다. 신경영상학적 
소견과 관계 없이 24시간 이내에 호전된 일시적 신경학적 결 
손은 일시적혈혈발작(transient ischemic attack, TIA)으로 
분류하였다. 농증의 분류(동측 혹은 반대측)는 가능한 신경 
영상 검사 소견을 근거하여 결정하였다. 결과 변수는 각 
참여 기관의 연구자가 수행하였다.

결과

등록된 환자

21개월의 연구 기간 동안, 168개의 두개내 축방형골 병변 
(50~99% 혈착을 가진 158명의 환자가 Gateway-Wingspan 
스텐트술을 받았다. 환자들(남성 95명, 여성 63명)의 나이는 
33~86세(평균 62.7세)에 분포하였다. 90명(57%)의 환자는 농 
증으로 방문하였다. 평균 혈착 정도는 75.2%였으며, 115개 
의 병변(69%)은 70~99% 혈착을 보였다. 스텐트술 전후에 농 
증은 9명(5.7%)의 환자에서 발생하였다. 4명(2.5%)의 환자 
는 사춘 전후에 발생한 농증으로 인하여 사망하였다. 

임상적 추적관찰

본 등록부에 기록된 158명의 환자 중 147명에서 3개월 시점 
의 추적 관찰이 가능하였다. 재외된 환자는 일차 결과 변수가 
발생하였거나(n=9), 30일 이후에 신경학적 결과의 원인 
으로 사망한 환자(n=2)였다. 이들 중 중 143명의 환자(97.3%) 
에서 최소 3개월 이상의 추적 관찰이 이루어졌다. 127명 중 
110명(86.5%)이 12개월 이상 추적 관찰을 받았으며, 등록된 환 
자의 평균 임상적 추적 관찰 기간은 14.2개월이었다.

일차 결과 변수의 누적 발생률은 전체 환자에서 15.7%였고, 
현저한 혈착(70~99%)을 보이는 환자들에서 13.9%였다. 30일 
이후에 동측의 농증이 발생한 13명 가운데 3명이 사망하였다. 
30일 이후에 동측의 농증이 발생한 13명 중 10명(76.9%)이 
사춘 6개월 이내에 발생하였으며, 12개월 이후에 농증이 발 
생한 환자는 없었다. 30일 이후 9명의 환자에서 동측의 TIA 
가 발생하였다. 30일에서 12개월 사이에 농증 혹은 TIA의 
증상적 발생률은 20%(12개월 추적 관찰이 완료된 110명의 환 
자 중 22건의 사례)였다.

대부분의 설치술 이후 사망(86%)은 항혈소관계의 중단 
(n=6), ISR (n=12), 혹은 두 원인의 중복(n=1)에 기인하였다. 
3명의 환자는 외국에서 발생하지 않았다. 30일 이후 동측 
의 농증이 발생하여 일차 결과 변수가 발생한 것으로 판정된 
13명의 환자에서, 5명은 ISR, 5명은 항혈소관계의 중단에 기 
인한 것으로 생각되며, 3명에서는 원인을 밝혀지지 않았다. 항 
혈소관계 중단 이후에 농증이 발생한 환자에서, 농증은 사 
출 후 2~9.5개월(평균 4.4개월) 시점에서 발생하였다(Figure 
1~3). ISR에 기인한 농증이 발생한 환자에서, 농증은 
3.5~11.5개월(평균 6.9개월) 시점에서 발생하였다(Figure 4). 
사출 후 10.5개월 및 11.5개월 시점에 농증이 발생한 두 명 
의 환자에 의하여 ISR과 연관된 농증의 평균 발생 시점이 비 
동하였다. 이 환자들은 ISR과 관련된 일시적 증상중을 경험한 바 
있으며, ISR 재발로 인한 농증이 발생하기 전에 1회 이상의 
혈관내형성술을 받은 병력이 있었다. 원인을 알 수 없는 농증이 
발생한 환자들은 평균 3.2개월 이후(범위, 1.5~5개월)에 농증 
을 경험하였다. 30일 이후 동측의 TIA가 발생한 9명의 환 
자들 중 7명은 ISR과 연관되어 있었고, 1명은 항혈소관계의 중 
단에 기인한 것으로 생각된다. 1명의 환자는 두 가지 요소를 모 
두 가지고 있었다.

Figure 1. Adult patient originally presenting with minor stroke at the time of being on aspirin therapy. Subtracted angiogram (A) in the working angle for treatment demonstrates a high-grade (>90%) focal stenosis (dotted circle) of the distal M1 segment of the middle cerebral artery. Subtracted (B) and native (C) images from the control angiogram in the working angle immediately after angioplasty and stenting with the Gateway-Wingspan system (Boston Scientific) demonstrates no significant residual stenosis.
고찰

US Wingspan Registry를 분석한 본 연구에서 가장 중요한 결과는, (1) 일부 환자들은 Gateway-Wingspan 스탠트를 사용하여 성공적으로 PTAS를 한 후에도 동측의 혈혈성 사전을 경험한다는 점, (2) 이러한 지연성 사건은 항혈소판제의 종 단 혹은 ISR 등 일정한 요소에 기인한다는 점, (3) 이는 대개 치료 후 6개월 이내에 발생한다는 점을 들 수 있었다.

Gateway-Wingspan 스탠트 시스템은 중상성 두개내 축상 경화증에 대한 새로운 치료법으로 2005년에 소개되었다. 이 시스템의 도입 초기에는, 약물로만 치료한 고위험군 환자들에 비하여 양호한 시술 후 뇌출혈 위험(약 5%)을 보이는 것으로 알려졌다. 그러나 스탠트 이후 혈관조영술을 통해 혈착 여부를 평가한 두 연구의 중간 분석 결과, ISR 혹은 완전 패색의 발생률은 25~35%에 이르는 것으로 알려졌다. 이러한 결과는 초기의 Eurasian Humanitarian Device Exemption 연구 결과에 비해 매우 높은 혈착이라고 할 수 있다. ISR이 발생한 환자의 대부분은 무증상이나, 약 1/3에서 동측의 혈혈성 증상이 발생하였다. 이 때문에 스탠트 후의 치료 효과 지속성 여부에 대한 의문은 제기되었으며, 성공적으로 스탠트를 설치하였다 하더라도 이후 혈혈성 사전이 계속될 가능성이 있다는 의혹이 따랐다. 본 분석의 목적은 바로 이 문제를 규명하기 위한 것이었다.

스탠트술 이후의 혈혈성 사전 발생률

본 연구에서, 일부 환자들은 PTAS가 성공적으로 시행된 후에도 계속 동측의 혈혈성 사전을 경험하였다. 이러한 지연성 중상 발생은 전체 혈혈성 사전 수의 약 2/3에 달하며, PTAS 시술 전에 발생한 증상 수를 늘리고, 미국 보건복지(Wingspan 등록부(National Institutes of Health Wingspan Registry) 분석에 의하면, 현저한 중상성 혈착(70~99%) 후 동측의 지연성 뇌출혈이 발생할 위험이 약 5~6%라고 한다. 그러나 이 연구는 100명 이상의 환자를 분석하여 시술 후의 중상 발생 위험이 낮다는 것을 밝혔으며, 12개월 이상 장기간 추적 관찰 을 한 환자의 숫자는 매우 적은 편이었다(n=15). 따라서 이 연구 결과는 시술 시행 이후 장기적인 혈혈성 중상 발생률을 정확하게 추정하기에는 부족하다고 할 수 있었다. 3,8,9 정제된 분 연구에서 모두 환자군(50~99% 혈착)과 현저한 혈착(70~99% 혈착)을 보이는 환자군 사이에, 시술 직후 및 장기적인 혈혈성 중상 발생률에는 차이가 없었다.

따라서 PTAS 시술 직후의 뇌출혈 발생률 자체(약 5%)는 중상성의 현저한 혈착(70~99%) 환자를 약물 투여로 치료한 것(첫 1년간 20~25%)에 비하여 낮으나, 장기적으로 보아 스탠트 슬 후에도 뇌출혈이 발생하기 때문에 두 치료 전략 사이의 차이는 더욱 줄어들 것이라고 할 수 있었다. 8,9 따라서 현재 진행 중인 SAMMPRIS (Stenting and Aggressive Medical Management for Preventing Recurrent stroke in Intracranial Stenosis) 연구처럼 스탠트술과 약물 치료를 직접적으로 비교하는 연구가 필요 이상, 고위험 환자가 스탠트술을 통하여 추가적인 이득을 얻을 수 있는지 확실히 알 수 있을 것으로 보인다. 11

지연성 혈혈성 사전의 원인

저자들은 Wingspan PTAS에 의한 전반적 위험도를 가능하다고 있으며, 또한 시술이 완료된 이후 Wingspan 스탠트술에 의하 여 혈혈성 증상이 발생하는 상황을 파악하고자 하였다. 본 연구에서 두 가지의 예측 가능한 요소가 지연성 혈혈성 사전의

Figure 2. The patient (same patient as in Figure 1) stopped taking antiplatelet medications 6 weeks after the procedure and represented at 8 weeks with new right upper extremity weakness. Axial diffusion sequences (A-C) demonstrate multiple small infarcts within the posterior left frontal lobe (arrows) involving the motor cortex.

Figure 3. Subtracted image from an angiogram performed at 8 weeks demonstrates no significant in-stent restenosis (same patient as in Figure 1).
Figure 4. Adult patient with symptomatic right hemisphere transient ischemic attacks on aspirin therapy. Subtracted image (A) in the lateral projection demonstrates moderate stenosis (arrow) of the suprarenal segment of the internal carotid artery. Subtracted image (B) in the lateral projection after angioplasty and stenting with the Wingspan demonstrates no significant residual stenosis. Subtracted image (C) in the frontal projection after angioplasty and stenting demonstrates a normal luminal diameter of the suprarenal internal carotid artery and the M1 segment of the middle cerebral artery. The patient presented with a minor right hemisphere stroke more than 3 months after the procedure while on antiplatelet medications. Angiography demonstrates a high-grade restenosis (D, arrow) at the distal aspect of the Wingspan stent.

대부분(86%)을 차지하였다. 이는 헬로스판의 중단 및 ISR의 발병이었다. 

약 40%의 자연성 뇌졸중은 헬로스판의 중단과 연관되어 있었다. 헬로스판을 조기에 중단하게 된 환자, 주로 환자의 난은 복약 순응도, 출혈, 혹은 출혈 위험 증가로 따른 중단, 침습적 심수 혹은 수술이 예정되어 있어 중단한 경우, 환자의 일차 의료 주치의가 내린 판단 등이었다. 이러한 사례는 대개 환자, 보호자 및 의사 의료 주치의에 대하여 보다 적극적으로 교육하고 홍보하여 극복할 수 있을 것으로 생각된다. 헬로스판의 

의 복합 투여는 주로 3~6개월 정도 지속하였고, 추적 혈관조영술 검사를 시행하여 ISR이 발생하지 않았다는 것을 확인한 후 클로피드로글렌을 중단하였다. 따라서 보다 엄격한 임상적 추 

적 관찰 및 복약 순응도에 대한 강조를 통하여, 가장 중요한 사 

가인 90~180일간 헬로스판은 충분히 복용하도록 할 수 있을 것이다. 본 연구에서 헬로스판이 6개월 이후에는 헬로스판 복용 

을 중단하여 동측의 자연성 뇌졸중을 완화한 환자는 단 한 명 

이었으며, 이 환자는 모든 헬로스판을 중단하였다고 한다. 

ISR은 모든 스텔트스캔이 가지고 있는 임상적인 현상이다. 본 

연구에서 ISR은 약 40%의 사례 후 뇌졸중 발생과 관련되어 있 

았다. 또한 동록에 포함된 대부분의 환자는 정규 임의적 추 

적 관찰의 일환으로 스캔에 대한 영상의학적 검사를 받았다. 

추적 관찰 기간 동안 ISR이 발견된 경우, 보통 헬로스판 복 

합 투여를 지속하였다. 환자에서 새로운 신경학적 증상이 발생 

하거나 심시 이전보다 더 현저한 혈착으로 진행하는 경우, 혈 

관경험술을 재차 시행하였다. 반면에, ISR에 의하여 발생한 

뇌졸중 재발은 정규 영상의학적 검사, 약물 치료 및 중재적 시 

술을 통하여 진단되고 치료할 수 있다. 따라서 ISR에 

의한 자연성 혈제출 증상을 예방하는 전략은 주로 현재 사용 

가능한 치료 도구를 보완하는 것으로 가능할 것으로 생각된다. 

이로 인해 병용발생 흔영, 현재의 장기 

확장성 스텔트에 약물발생 가능성을 부과하는 것은, 혹은 혈관벽을 

양하여 장기간에 걸쳐 완전히 가하는 스텔트를 개발하는 것 

등이 포함된다.11,13

지연성 혈체출 시기의 발생 시점 

대부분(80%)의 자연성 혈체출 증상(TIA 및 뇌졸중)은 시술 한 달 후 6개월 이내에 발생하였다. 이러한 자연성 증상의 발생 시점은 두 가지 주요 위험인자의 ‘위험 기간’과 잘 상응하고 있다. 

혈관스캔의 복용 중단에 따른 위험 증기는 시간이 지남수록 

저하되기 때문에, 이는 혈관에 설치된 스텔트에 ‘내피세포화 

(endothelialized)’가 진행되기 때문이다. 이와 마찬가지로, 

ISR에 의한 뇌졸중 위험은 스텔트스캔 후 3~6개월 시점에 주로 

발생한다. 6개월 이후에 ISR에 의한 뇌졸중이 발생한 환자는 

이전에 이미 TIA 증상이 발생하였고 혈관생성성형으로도 별 

시 ISR이 일어나 뇌졸중이 발생한 사례였다. 시술 3~6개월 시 

점에서 혈관 조영이 스텔트를 설치한 부위로 자라 들어가며, 

일부 사례는 재조직화(reorganization)을 거쳐 매우 양적되어 

혈관조영술 영상에서 오히려 혈작이 완화된 것처럼 보일 수 있 

음이 이미 알려져 있다. 이러한 안정화(stabilization) 및 자연 

적인 ISR의 완화는 관상동맥 및 두개동맥의 형식에서 모두 

관찰되었다.11,13 본 연구는 ISR이 발생한 환자가 초기 3~6개월 

시점에서 혈제출 증상을 보이지 않으며 충분한 약물을 복용하 

는 경우, 장기적인 추적 관찰에서도 뇌졸중이 발생할 위험은 

높지 않음을 시사한다.

한계 

본 연구가 Wingspan-Gateway 스텔트를 설치하여 가장 오랜 기간 동안 추적 관찰을 시행한 대규모의 연구임은 분명하나, 본 연구 역시 중요한 한계를 가지고 있음을 언급하고자 한다. 가장 중요한 한계로 모든 환자들이 12개월까지 추적 관찰을 받지 못하였다는 점을 들 수 있다(13가 THAT의 1년 시점에서 추적 

관찰을 받지 못하였다). 추적 관찰을 받지 못한 환자들의 뇌졸중 

발생률이 12개월, 혹은 그 이후까지 추적 관찰을 받은 사람들 

과 동일하다고 할 수 없기 때문에, 이 점이 1년 뇌졸중 발생률을
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