

Express LD Vascular Stent for the Treatment of Iliac Artery Lesions

The 24-month results from the MELODIE trial.

BY JILL S. BLEUIT, PhD

Peripheral artery disease of the lower extremities affects up to 8 million people in the United States and is especially common in people older than 50 years of age.¹ The major symptoms of lower extremity peripheral artery disease range from intermittent claudication to ischemic rest pain to critical ischemia with major tissue loss.^{2,3} These symptoms can have a great impact on patient quality of life and may eventually lead to amputation of the affected limb.

Although bypass surgery was the former standard of care for iliac artery disease, endovascular treatments, particularly percutaneous transluminal angioplasty (PTA), are now much more commonly performed.⁴ PTA is well-suited for treating highly localized lesions in the iliac arteries.⁵ However, due to elastic recoil of the vessel, residual post-treatment stenosis, and vessel wall dissection, the results of PTA often lack long-term durability. Direct stent placement in the iliac artery has proven to be effective in overcoming the limitations of PTA and improving long-term patency^{6,7} and thus has become an increasingly more frequent treatment option. However, few randomized studies have shown clinical benefit of stenting over PTA.

Two types of stents may be used for treating iliac artery disease: balloon-expandable and self-expanding. The advantages of balloon-expandable stents include high radial force, precise placement, less foreshortening, and the possibility of further expansion. In contrast, self-expanding stents offer greater flexibility and deliverability than their balloon-expandable counterparts. The Express LD Vascular Stent (Boston Scientific Corporation, Natick, MA), developed to treat iliac artery atherosclerosis, is a balloon-expandable stent that is designed to be flexible and conformable to the iliac vessel wall. The MELODIE trial was conducted to demonstrate the safety and efficacy of this stent, particularly with regard to long-term patency in iliac arteries.

TRIAL DESIGN

MELODIE was a prospective, single-arm, multicenter study that was designed to obtain safety and efficacy data for the Express LD Vascular Stent in the treatment of

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stenosed or occlusive atherosclerotic disease (*de novo* or restenosis) in iliac arteries.

Patient Selection

Between January 2004 and February 2005, 151 patients were enrolled at 10 study centers (nine were in Europe and one was in Canada). For inclusion in the trial, patients were required to have Fontaine class IIa, IIb, or III symptoms and a *de novo* or restenotic iliac artery lesion no longer than 10 cm in length with a visually estimated stenosis of $\geq 50\%$. The lesion had to be treatable with a maximum of two stents and have at least one patent ipsilateral runoff vessel. Patients with acute leg ischemia or Fontaine class I or IV symptoms were excluded from the trial, as were patients who had lesions with heavy calcification, excessive tortuosity, or lesions that were located within or near an aneurysm or in an area of persistent thrombus. Additional inclusion and exclusion criteria have been previously presented.⁸

Procedure

Before stent placement, diagnostic angiography was performed on each patient to assess the magnitude of the lesion and the availability of collateral vessels. Angiography was also performed after treatment to ensure that the stent was properly deployed and correctly positioned. During the course of the procedure, anticoagulant and/or antiplatelet therapy were administered based on the routine practice of the study center.

Patient Follow-Up

Patients in the MELODIE trial were required to have follow-up assessments at hospital discharge and at 30 days, 6 months, and 1 and 2 years after the procedure. Throughout

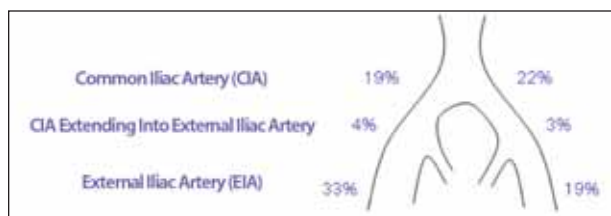


Figure 1. Target lesion distribution. The proportion of MELODIE patients with lesions in the right or left common iliac artery, external iliac artery, and common iliac artery extending into the external iliac artery.

the follow-up period, patients were required to take a daily dose of aspirin; clopidogrel or ticlopidine were substituted if aspirin was contraindicated. Ankle-brachial index measurements and symptom assessment based on the Fontaine classification were performed at all follow-up visits. In addition, arteriography was performed on each patient at the 6-month follow-up visit. Arteriograms were subjected to independent quantitative analysis at a core laboratory. Computed tomographic angiography was performed at the 1- and 2-year visits and was also analyzed by the core laboratory.

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Study Objectives

The primary goal of the MELODIE study was to compare the angiographic mean percentage of lumen diameter loss with the Express LD Vascular Stent against a prespecified performance goal representative of outcomes with the Palmaz first-generation iliac stent (Cordis Corporation, Bridgewater, NJ). The Palmaz stent was chosen as the comparator because at the time the MELODIE trial was initiated, it was the only balloon-expandable stent approved by the US Food and Drug Administration for use in the percutaneous treatment of atherosclerotic disease in the iliac arteries. However, the Palmaz stent was not commercially available in Europe at the time of the study; therefore, a randomized study was not feasible. Other effectiveness parameters assessed across the study included lesion patency, technical and procedural success, and percent diameter stenosis.

Important clinical objectives included an analysis of MAEs (device- or procedure-related death, target lesion revascularization [TLR], and device-related distal embolization), as well as improvement in ankle-brachial index and patient symptoms, which were evaluated based on the Fontaine classification.

TABLE 1. KEY BASELINE, LESION, AND PROCEDURAL CHARACTERISTICS (N = 151 PATIENTS WITH 163 LESIONS)

Baseline and Lesion Characteristics	
Age in years (mean ± SD)	60.1 ± 8.4
Male gender	74.8%
Diabetes	12.6%
Current or previous smoker	87.4%
Hypertension	60.3%
Previous myocardial infarction	22%
Previous vascular surgery in legs	13.9%
Claudication ^a	
> 1,000 meters	1.3%
200–1,000 meters	15.3%
< 200 meters	83.3%
Target lesion length (mm, mean ± SD)	32 ± 21.7
Procedural Results	
Technical success ^b	98%
Procedural success ^c	97.1%

^aClaudication indicates the distance patients were able to walk without pain at baseline.
^bTechnical success is defined as the successful delivery and deployment of the Express LD Vascular Stent to the target lesion with 30% stenosis. Technical success was assessed per lesion.
^cProcedural success is defined as technical success in the absence of in-hospital major adverse events (MAEs). Procedural success was assessed per patient.
 Abbreviation: SD, standard deviation.

STUDY OUTCOMES

Patients and Lesions

The MELODIE trial enrolled and treated 151 patients with 163 lesions in 159 limbs. As shown in Table 1, the average age of enrolled patients was 60.1 years. Most were men who smoked currently or in the past and suffered from a level of claudication that left them unable to walk > 200 meters. A total of 13.9% had previous vascular surgery in the legs, and 12.6% had medically treated diabetes. The distribution of treatment in the iliac arteries is shown in Figure 1. Approximately 60% of the patients in the MELODIE trial required stenting of the external iliac artery.

Lesion-Based Results

Technical success and procedural success, as defined in Table 1, were achieved in 98% and 97.1% of treated lesions, respectively. In addition, the angiographically

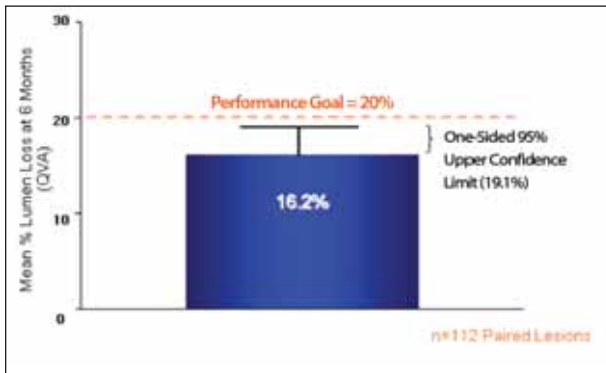


Figure 2. Angiographic success at the primary endpoint. Six-month mean percent lumen loss by quantitative vascular angiography in MELODIE patients compared to a performance goal based on outcomes with the Palmaz iliac stent (literature-reported rate plus upper confidence interval = 20%).

assessed 6-month mean percentage of luminal diameter loss plus upper confidence interval of 19.1% with the Express LD Vascular Stent was shown to be noninferior to a performance goal based on outcomes with the Palmaz iliac stent plus upper confidence interval (20%) (Figure 2).⁹ Thus, the primary endpoint in the MELODIE trial was achieved.

Furthermore, at 2 years after treatment, primary patency and assisted primary patency were maintained in 87.8% and 98.2% of patients, respectively (Figure 3).¹⁰ The durability of the results is also illustrated by the stability of the percent diameter stenosis through 2 years (Table 2).

MAEs

As illustrated in Figure 4A, the composite rate of MAEs in the MELODIE trial at 1 year was 11.1% plus an upper

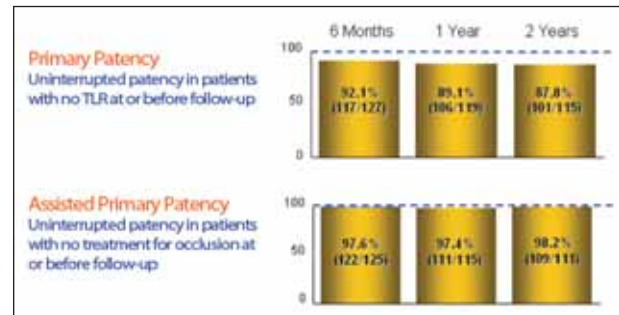


Figure 3. Target lesion patency sustained through 2 years. Primary and primary-assisted patency rates at 6 months and 1 and 2 years. Target lesion patency was assessed by quantitative vascular angiography at 6 months and by computed tomographic angiography at 1 and 2 years.

TABLE 2. PERCENT DIAMETER STENOSIS AT BASELINE THROUGH 2 YEARS	
163 Lesions	% Diameter Stenosis
Baseline	62.9 ± 19.3 (116)
Postprocedure	10.2 ± 9 (150)
6 months	24.3 ± 16 (124)
1 year ^a	34.7 ± 6.4 (106)
2 years ^a	34.5 ± 8.3 (101)

^aMeasurements at 1 and 2 years were assessed by computed tomographic angiography; measurements at all other timepoints were assessed by quantitative vascular angiography. Numbers are mean ± standard deviation. Note: several patients could not complete quantitative vascular angiographic assessment at baseline due to occlusion.

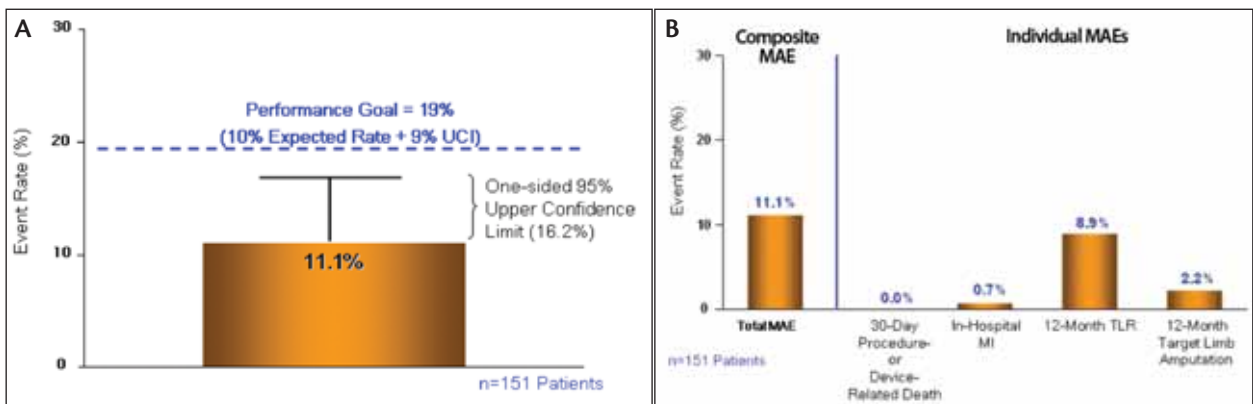


Figure 4. MAE versus a literature-based performance goal. The composite rate of MAEs (30-day procedure- or device-related death, in-hospital myocardial infarction, 1-year TLR, and 1-year major amputation) compared to a performance goal of 19% (10% expected rate plus 9% upper confidence interval [UCI]) derived from literature-reported iliac stenting results (A). Composite MAE rate and its components. The binary rates of composite MAE and its individual components are shown (B).

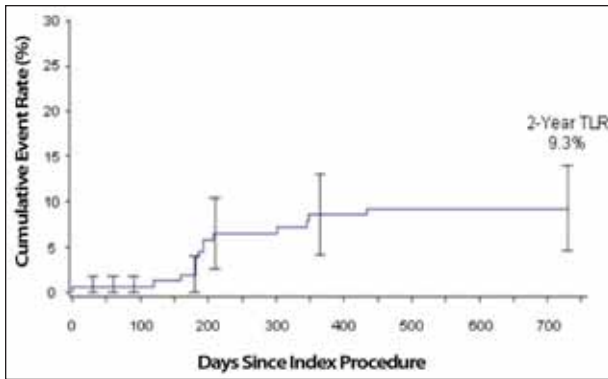


Figure 5. TLR through 2 years. Kaplan-Meier estimates of TLR through 2 years.

confidence boundary of 5.6%. This rate compared favorably to the literature-based performance goal for current-generation iliac stents of 19% (expected MAE rate + upper confidence interval). The components of the composite MAE rate include 30-day procedure- or device-related death, in-hospital myocardial infarction, 12-month TLR, and 12-month target limb amputation. No device- or procedure-related deaths occurred within 30 days postprocedure or over the entire 2-year course of the MELODIE trial. The individual rates of other adverse clinical events, as shown in Figure 4B, are low and acceptable. Through the 2-year follow-up period, the rate of TLR remained stable (Figure 5), and no patients had a distal embolization.

“There were no reports of distal embolization or iliac rupture in the MELODIE trial.”

TLR in Clinically Relevant Subgroups

Patients with diabetes. Diabetic patients treated in the MELODIE trial had consistently higher TLR rates through 2 years compared with patients who did not have diabetes. Of the diabetic patients who had a TLR during the MELODIE trial, more than one-third occurred before hospital discharge. By comparison, none of the nondiabetic patients were reported to have had a TLR until later than 30 days postprocedure.

Patients treated in the external iliac artery. As shown in Figure 6, patients who were treated in the external iliac artery had a slightly greater rate of TLR events throughout the trial compared to patients who received treatment only in the common iliac artery.

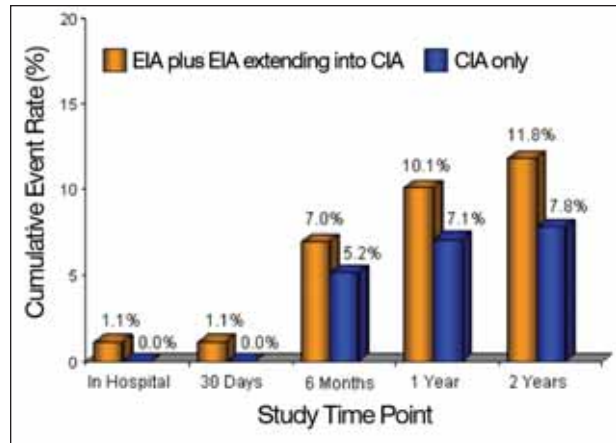


Figure 6. TLR in patients treated in the external iliac artery (EIA) versus patients treated in the common iliac artery (CIA) only. Cumulative binary rates of TLR in patients treated in the EIA plus EIA extending into the CIA and patients treated in the CIA only during hospitalization and at 30 days, 6 months, and 1 and 2 years.

TABLE 3. ANKLE-BRACHIAL INDEX THROUGH 2 YEARS	
N = 159 Limbs	Ankle-Brachial Index (Mean ± SD)
Baseline (157)	0.63 ± 0.22
Discharge (156)	0.85 ± 0.22
6 months (136)	0.87 ± 0.24
1 year (121)	0.86 ± 0.23
2 years (116)	0.85 ± 0.26

Abbreviation: SD, standard deviation.

Clinical Improvement

The vast majority of patients in MELODIE experienced significant improvement in clinical symptoms after iliac stenting. As shown in Figure 7, a total of 84.1% of patients had Fontaine class IIb symptoms or worse at baseline. At 2 years after the procedure, only 16.8% of patients had symptoms considered Fontaine class IIb or worse. Also, the mean ankle-brachial index pretreatment improved from a measurement of 0.63 ± 0.22 to 0.85 ± 0.22 at discharge (Table 3). This mean ankle-brachial index measurement was sustained through the end of the study at 2 years.

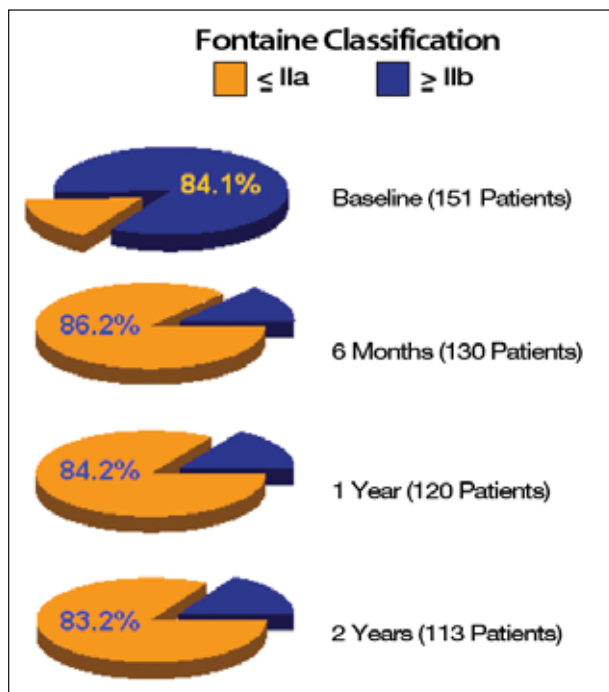


Figure 7. Clinical improvement in MELODIE patients. Binary rates of patients with Fontaine class I/IIa symptoms (\leq IIa) or Fontaine class IIb/III/IV symptoms (\geq IIb) at baseline, 6 months, and 1 and 2 years.

CONCLUSIONS

In summary, patients in the MELODIE trial who were treated with the Express LD Vascular Stent experienced substantial and sustained improvements in Fontaine class clinical symptoms and ankle-brachial index through the entire 2 years of the trial. The percentage of patients with Fontaine class IIb symptoms or worse improved from 84.1% before the procedure to 16.8% at 2 years after the procedure ($P < .0001$). The 2-year ankle-brachial index remained significantly improved compared to preprocedure measurements (0.85 vs 0.63; $P < .0001$). The primary endpoint of 6-month mean percentage of luminal diameter loss was 16.2% and was noninferior to the performance goal (upper 95% confidence boundary of 19.1% vs performance goal of 20%; $P = .0061$). Primary patency rates were 92.1% at 6 months and were maintained at 2

years with a rate of 87.2%. The safety of the Express LD Vascular Stent was demonstrated by the complete absence of device- or procedure-related deaths or distal embolization in the MELODIE population throughout the entire trial. Furthermore, rates of major amputation, TLR, and in-hospital myocardial infarction were low and acceptable throughout the trial.

As expected, patients with diabetes had a somewhat higher rate of TLR throughout the trial and required revascularization procedures earlier compared to their nondiabetic counterparts. However, neither diabetic nor nondiabetic patients experienced distal embolization or device- or procedure-related death during the trial.

Patients treated in the external iliac artery had a higher rate of TLR through 2 years compared to patients who were only treated in the common iliac artery.

In conclusion, the 2-year results of the MELODIE trial show that the Express LD Vascular Stent is safe, effective, and durable in the treatment of stenosed or occlusive atherosclerotic common or external iliac arteries. ■

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- Hirsch AT, Criqui MH, Treat-Jacobson D, et al. Peripheral arterial disease detection, awareness, and treatment in primary care. *JAMA*. 2001;286:1317-1324.
- Norgren L, Hiatt WR, Dormandy JA, et al. Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). *Eur J Vasc Endovasc Surg*. 2007;33(suppl 1):S1-75.
- LaPerna L. Diagnosis and medical management of patients with intermittent claudication. *J Am Osteopath Assoc*. 2000;100(10 Su Pt 2):S10-14.
- Goodney PP, Beck AW, Nagle J, et al. National trends in lower extremity bypass surgery, endovascular interventions, and major amputations. *J Vasc Surg*. 2009;50:54-60.
- White C. Clinical practice. Intermittent claudication. *N Engl J Med*. 2007;356:1241-1250.
- Leung DA, Spinosa DJ, Hagspiel KD, et al. Selection of stents for treating iliac arterial occlusive disease. *J Vasc Interv Radiol*. 2003;14(2 Pt 1):137-152.
- Reekers JA, Vorwerk D, Rousseau H, et al. Results of a European multicenter iliac stent trial with a flexible balloon expandable stent. *Eur J Vasc Endovasc Surg*. 2002;24:511-515.
- Stockx L, Poncyjusz W, Krzanowski M, et al. Express LD vascular stent in the treatment of iliac artery lesions: 24-month results from the MELODIE trial. *J Endovasc Ther*. 2010;17:633-641.
- Palmaz JC, Laborde JC, Rivera FJ, et al. Stenting of the iliac arteries with the Palmaz stent: experience from a multicenter trial. *Cardiovasc Intervent Radiol*. 1992;15:291-297.
- Sacks D, Marinelli DL, Martin LG, Spies JB; Society of Interventional Radiology Technology Assessment Committee. Reporting standards for clinical evaluation of new peripheral arterial revascularization devices. *J Vasc Interv Radiol*. 2003;14(9 Pt 2):S395-404.

Express LD Iliac Stent System

The Express® LD Iliac Stent System is a premounted balloon-expandable stent made of 316L stainless steel, has a unique patented stent design known as Tandem Architecture, and is the only commercially available balloon-expandable stent in the United States with an iliac indication.*

The Tandem Architecture stent design is comprised of two key elements:

- Micro™ Elements, which are designed to provide flexibility during placement and conformability on deployment
- Macro™ Elements, which are designed to provide consistent radial strength and enhanced radiopacity

The Express LD Stent System is available in the following matrix in both 75- and 135-cm catheter lengths with a recommended guidewire size of 0.035 inches. The Express LD Iliac Stent System is compatible with 6-F introducer sheaths up to 8 X 37 mm and then 7 F throughout the remainder of the matrix.

Several additional benefits that the Express LD Iliac Tandem Architecture may provide are:

- Balanced deployment accuracy, especially at the aortoiliac region
- Customized balloon lengths to minimize foreshortening

Express® LD Iliac Premounted Stent System
Size Matrix



		Diameters (mm)				
		6	7	8	9	10
Lengths (mm)	17	Available	Available	Available	Available	Available
	25	Available	Available	Available	Available	Available
	27	Available	Available	Available	Available	Available
	37	Available	Available	Available	Available	Available
	57	Available	Available	Available	Available	Available

■ Available Sizes

For more information, please visit www.bostonscientific.com/expressld or contact your Boston Scientific Sales Representative.

*INTENDED USE/INDICATIONS FOR USE: The Express LD Iliac Premounted Stent System is indicated for the treatment of atherosclerotic lesions found in iliac arteries up to 100 mm in length, with a reference diameter of 6 to 10 mm.