Novel Use of a High-Energy Excimer Laser Catheter for Calcified and Complex Coronary Artery Lesions

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This study was designed to evaluate safety and effectiveness of the 0.9 mm excimer laser coronary catheter with increased laser parameters. We report a prospective trial of 100 calcified and/or balloon-resistant lesions where a new 0.9 mm excimer laser catheter was used at standard or higher energy level to facilitate angioplasty. Standard in-hospital clinical and angiographic parameters were collected and measured. Laser technical success was obtained in 87 lesions (92%), procedural success was reached in 88 lesions (93%), and clinical success in 82 lesions (86%). Increased laser parameters were used for 29 resistant lesions. This new 0.9 mm excimer laser coronary catheter using higher energy parameters seems to be safe and effective for management of calcified and nondilatable lesions. Catheter Cardiovasc Interv 2004;62:155–161. © 2004 Wiley-Liss, Inc.

Key words: xenon-chlorine laser; coronary angioplasty; artery disease

INTRODUCTION

Today, facing an aging patient population, cardiac interventionalists performing angioplasty are forced to revascularize a progressively more complex coronary artery disease. Among some of these difficult lesions, calcified stenosis, chronic total occlusions, and noncompliant plaques remain major technical challenges. Despite advances in equipment and technique, these lesions may be resistant to or unapproachable by percutaneous technique restricting the therapeutic options. Description of recent nonselective cohorts of patients requiring coronary angioplasty included 12% of severely calcified lesions [1], 10% of chronically occluded arteries [2], and 1.5% of nonresilient plaques to balloon angioplasty (non-dilatable or uncrossable) [3].

A new xenon-chlorine (excimer) pulsed laser catheter (X80; Spectranetics, Colorado Springs, CO) capable of delivering higher energy density with lower heat production (smaller area of ablation) has been suggested for treatment of these complex lesions [4]. This 0.9 mm diameter, 6 Fr-compatible catheter incorporates 65 concentric 50 μm fibers with the potential of delivering excimer energy (wavelength 308 nm, pulse length 185 nanoseconds) from 30 to 80 mJ/mm² (fluences) at pulse repetition rates (frequency) from 25 to 80 hertz, using a 10-sec on and 5-sec off lasing cycle (Fig. 1). This compares with existing excimer catheter technology (1.4, 1.7, and 2.0 mm catheters) delivering 30–60 mJ/mm² at 25–40 hertz using a 5-sec on and 10-sec off lasing cycle. In addition to reducing catheter’s size, these modifications in laser energy delivery were proposed to maximize tissue penetration while keeping photomechanical and photothermal damages within acceptable limits. The catheter features high optical fibers packing density to maximize the cutting area at the distal tip. It has been well documented since the early days of coronary laser use that highly fibrocalcific plaques were laser-resistant and that higher energy could overcome these limitations [5,6].

We therefore performed a self-controlled prospective trial to examine the acute outcome of laser-facilitated coronary angioplasty on a cohort of patients presenting with calcified and/or balloon-resistant lesions.
MATERIALS AND METHODS

Patients were enrolled in this prospective multicenter, self-controlled comparative study by four centers experienced in excimer laser angioplasty. Safety and effectiveness data were compared from two groups, namely, patients treated with standard laser therapy (SLT) defined by laser energy at 60 fluence and 40 hertz and patients treated with increased laser therapy defined by laser energy at 60 fluence and 80 hertz or 80 fluence and 80 hertz. The treatment scheme mandated use of the X80 catheter at standard laser parameters on all patients and increase of these parameters to higher levels in stepwise increments if deemed necessary to cross the target lesion. In proceeding as described, all patients treated with increased laser parameters had to present lesions refractory to treatment with standard laser parameters.

The primary endpoint was the ability of the X80 catheter to cross the lesion. The secondary endpoints included procedural success defined as reduction of the target lesion to < 50% residual diameter stenosis after adjunctive therapy as measured by quantitative coronary analysis with absence of major adverse cardiac events at hospital discharge.

All eligible patients for coronary revascularization ≥ 18 years old presenting a single primary or restenotic lesion in a native coronary artery or a saphenous vein bypass graft were screened. To be included in the study, the target lesion had to be severely stenotic (≥ 80% diameter stenosis as assessed by visual estimation) with angiographic evidence of calcification or a chronic total occlusion (TIMI) 0 flow with absence of acute events, unstable angina, or creatinine kinase rise 3 months prior to index procedure) traversable by a guidewire or, a lesion crossed by a guidewire but uncrossable by a 1.5 mm diameter (smallest available) balloon. Patients with acute ischemic events, shock (cardiogenic or noncardiogenic), left ventricular ejection fraction ≤ 25%, previous coronary angioplasty within 6 months, and contraindication to aspirin or heparin were excluded from the study. Only one lesion was allowed to be treated during index hospitalization. Vessels with reference diameter smaller than 2.0 mm and lesions uncrossable with a guidewire were excluded. Angulated lesions and extreme tortuosity

Fig. 1. Lasing cycle: 10 sec on and 5 sec off. Top: 0.9 mm rapid-exchange excimer laser catheter. Bottom left: Distal tip marker. Bottom right: Cross-section of catheter showing the 65 concentric 50 μm laser fibers.
were allowed to be included. This protocol was approved by Canada’s Therapeutic Products Program in March 2000. A pilot study of 36 patients was concluded in September 2000 and was expanded to 100 patients with Canada’s Therapeutic Products Program approval in January 2001. Written informed consent form was obtained from all patients before enrollment after local investigator received board review approval.

**Study Protocol**

Patients were pretreated with ≥ 80 mg of aspirin daily for ≥ 24 hr and intravenous heparin was administered during the index procedure to maintain an activated clotting time > 250 sec. All anti IIb/IIIa agents use was left to the operator’s discretion with proper heparin dosage adjustments. Intracoronary nitroglycerine (≥ 100 μg) was given before intervention and at the end of index procedure prior to final angiogram. Patients falling within inclusion criteria were treated with the X80 laser catheter starting at 60 fluence, 40 hertz laser parameters (SLT). After successful laser passage, adjunctive balloon angioplasty and stenting were performed to complete treatment according to standard procedure. If the laser catheter failed to cross target lesion completely, laser parameters were increased to 60 fluence, 80 hertz and then to 80 fluence, 80 hertz increased laser therapy in an attempt to traverse the lesion. If still unsuccessful, the laser catheter was withdrawn, recalibrated, reinserted, and three more laser sequences were attempted. Three successive laser sequences without catheter tip progression had to be experienced before increasing laser parameters. At least 12 laser trains were attempted before failure was declared (3 × 60 fluence/40 hertz, 3 × 60/80, 3 × 80/80, and 3 × 80/80 postrecalibration). After the procedure, sheaths were removed immediately (radial approach) or 6 hr later. Creatinine kinase measurements and electrocardiogram were obtained on all patients prior to and 24 hr after index procedure. No clinical follow-up was recorded after hospital discharge.

**Laser Procedure**

The excimer laser is a pulsed xenon-chlorine-based mid ultraviolet wave length (308 nm) laser relying on absorption in the nonaqueous components of the atherosclerotic plaque, such as proteins and nucleic acids, for debulking [7]. This laser technology has been approved for coronary use since 1992 by the U.S. Food and Drug Administration. So far, 1.4, 1.7, and 2.0 mm catheters built with concentric or eccentric fiber distribution were available. Maximal energy delivered by this equipment produces 60 mJ/mm² at 40 hertz. The penetration depth in noncalcified tissue is approximately 100 μm with an ablation threshold of 15–20 mJ/mm² (Spectranetics, data on file). The lasing cycle classically used includes 5 sec of active firing followed by 10 sec of silence, allowing for assessment of catheter position or catheter pullback to reestablish blood flow and refill of saline infusion syringe. The new X80 catheter measures 0.9 mm in diameter with concentric fibers. It was built to deliver energy up to 80 mJ/mm² at 80 hertz with a lasing cycle characterized by 10 sec of active firing and 5 sec of silence. As a consequence, it potentially doubles the device penetration rate and offers the possibility of targeting harder tissue. Regardless of catheter specifications, the preparation and technique for operation remain the same. The laser system requires a 5-min warm-up period to turn on. The catheter is prepared by flushing the central guidewire lumen and connecting the proximal end to the laser console. Calibration of the catheter is then performed and the desired energy level is set up. The catheter is then passed over the guidewire just proximal to the lesion. The flush-and-bathe technique [8] for blood and dye clearance from the entire system by saline infusion is mandatory prior to each lasing train. Lasing is performed by applying gentle forward pressure to the catheter in order to cross the lesion under fluoroscopy while energy is emitted from the catheter distal tip during foot pedal activation. The procedure is then finalized by laser catheter removal and additional balloon and stent use according to standard practice. Repeat arteriography after intracoronary nitroglycerine was recorded after laser but prior to adjunctive therapy and at the end of the procedure.

**Definitions**

Laser technical success was defined as the laser catheter crossing the entire length of the stenotic lesion determined by angiographic evidence of the catheter tip in the artery distal to the stenosis. Procedural success was defined as < 50% residual stenosis after laser and adjunctive therapy. Clinical success requested procedural success with absence of major adverse cardiac events at hospital discharge. Major adverse cardiac events included death of all causes, non-Q-wave and Q-wave myocardial infarction, need for target lesion revascularization, and tamponade. Q-wave myocardial infarction myocardial infarction was defined as elevation of creatinine kinase levels > 3 times above laboratory normal values with any abnormal MB fraction and the development of new pathology Q-waves on the electrocardiogram. A non-Q-wave myocardial infarction was defined as the development of similar creatinine kinase elevation without Q-waves.

Antegrade flow was assessed by the thrombolysis in myocardial infarction scale [9]. Lesion morphology was characterized by the modified American College of Cardiology/American Heart Association (ACC/AHA) score [10]. Laser complications included dissection type C or worse according to the National Heart, Lung and Blood
Institute classification [11], coronary spasm, thrombus formation, no reflow, embolization, perforation, loss of major side branch (> 2 mm in diameter), and acute closure. Spasm was defined as transient reduction in blood flow with vessel caliber narrowing relieved either spontaneously or by nitroglycerine. Thrombus formation was defined as the new appearance of an intraluminal filling defect, lucency, or haziness refractory to intracoronary nitroglycerine. No reflow was determined by reduction of ≥ 1 thrombolysis in myocardial infarction flow grade without angiographic demonstration of embolization, whereas embolization was characterized by new appearance of a distal intraluminal filling defect or loss of a distal branch. Perforation requested demonstration of a persistent extravascular collection of contrast medium beyond the vessel wall. Finally, acute closure was defined as sustained thrombolysis in myocardial infarction 0 to 1 flow grade caused by obstruction of the target lesion.

Data Collection and Analysis

Detailed in-hospital case report forms were prospectively completed for each patient. A study monitor traveled to each site for independent verification of case report form accuracy. Angiograms were evaluated by individual operators using local online quantitative coronary analysis software and visual assessment. However, 65 angiograms were evaluated at the Montreal Heart Institute QCA Core Laboratory. No significant discrepancies between the online and offline analyses were seen. Final outcomes were similar in these 65 patients when compared to the remaining 30. Data were entered into an SAS database (software version 7.2, SAS Institute). Statistical calculations used Wilcoxon scores (rank sums) and McNemar analysis for frequency tables. A P value < 0.05 was required for statistical significance.

RESULTS

A total of 95 patients with 100 treated lesions were enrolled in the study at four centers, namely, Montreal Heart Institute (Montreal, Quebec; 43 lesions), Royal Jubilee Hospital (Victoria, British Columbia; 35 lesions), Gent University Hospital (Gent, Belgium; 16 lesions), and Catharina Hospital (Eindhoven, The Netherlands; 6 lesions). Fifty-five patients (57.9%) were enrolled under the calcification primary indication, 35 patients (36.8%) were enrolled under the balloon failure primary indication, and 5 patients (5.2%) under the chronic total occlusion primary indication (Table I). Enrollment inclusion criteria violation occurred in 20 lesions. The primary violation was multiple lesions treated during the interventional procedure and totaled 12. Discovery of a second lesion distal to the treated lesion and treatment of this lesion for patient and/or economic considerations was the reason for this violation in most cases. Treatment of calcified lesions with less than 80% stenosis occurred in three cases, treatment of noncalcified 99% stenosis occurred in two cases, and enrollment of three total occlusions before guidewire crossing occurred in three cases.

Mean patient age was 67 ± 11 years old, with 53% presenting unstable angina. Seventy-two percent of patients were male. The left anterior descending artery was the target vessel in 46% of cases, the right coronary artery in 35%, the circumflex in 14%, and the left main artery in 2%. Three saphenous vein grafts were enrolled.

Procedural Outcome

In five lesions, failure to deliver treatment per protocol was recorded (Fig. 2). In three cases, the guidewire did not cross, the procedure was aborted, and patients were treated medically. In two cases, there were laser software problems preventing increased laser therapy use. One case was training-related (laser energy detector was covered with contrast) and the other case was a laser system failure. Overall, laser success was obtained in 87 lesions (92%), procedural success was reached in 88 lesions (93%), and clinical success in 82 lesions (86%). A total of eight lesions could not be crossed by the X80 catheter even with increased laser energy use. Of these, four were treated successfully with adjunctive balloon angioplasty, one had a successful rotational atherectomy, two were treated medically (including one failed rotational atherectomy), and one required coronary artery bypass surgery. Major adverse cardiac events were recorded in seven patients, including two deaths, two Q-wave myocardial infarctions, two non-Q-wave myocardial infarctions, and one reintervention. One patient died from pneumonia 9 days postindex procedure and one patient

<table>
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<tr>
<th>Lesion Characteristics (n = 100)</th>
<th>n</th>
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<tr>
<td>Calcification</td>
<td>80</td>
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<tr>
<td>Percutaneous transluminal coronary angioplasty failure</td>
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<td>Chronic total occlusion</td>
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<td>Target vessel distribution</td>
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<td>46</td>
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<tr>
<td>Right coronary artery</td>
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<td>35</td>
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<td>Left circumflex coronary artery</td>
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<td>Left main artery</td>
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<td>Saphenous vein graft</td>
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died from an adult respiratory distress syndrome 1 month after laser. The two non-Q-wave myocardial infarctions were observed after uneventful procedures. One patient experienced a Q-wave MI 3 days after a successful procedure and a repeat angiogram revealed a normal laser-treated vessel but an occluded nontarget vessel. Another patient suffered a Q-wave MI after type C dissection with unsuccessful attempt at stenting. He was finally discharged on medical treatment. Finally, one patient needed a reintervention for a third distal target artery lesion.

The results of the quantitative coronary analysis are shown in Table II. A total of five laser complications (5.3%) were observed, namely, five grade C or worse dissections, all properly treated by stents but one. Ventricular fibrillation during laser was experienced in one patient requiring cardiopulmonary resuscitation. This resulted in a non-Q-wave myocardial infarction despite absence of flow disturbances. No perforation, major side branch occlusion, spasm, no-reflow phenomenon, or acute vessel closure was seen with laser treatment even with increased energy use in 29 lesions (30.5%).

Increased Laser Parameters

Of the 95 laser-treated lesions, 66 (69.5%) were successfully crossed with standard laser parameters, namely, 60 mJ/mm² at 40 hertz. Increased laser parameters were used for 29 resistant lesions. Among these, 21 were successfully crossed by the X80 catheter and 4 were finally adequately treated by balloons and stents despite the fact that the laser catheter tip had not entirely crossed the target lesion. Energy of 60 mJ/mm² at 80 hertz was required in 12 lesions (12.6%) and levels up to 80 mJ/mm² at 80 hertz were needed in 17 lesions (17.9%). This possibility of increasing laser energy delivery resulted in an increase from 69% to 92% (P < 0.0001) in laser success rate and, as a consequence, also theoretically improved from 69% to 93% (P < 0.0001) and from 65% to 86% (P < 0.0001) the technique procedural and clinical success rates, respectively (Table III). Thirteen of the 29 increased parameter uses were on lesions, which failed prior balloon angioplasty. Laser-induced complications did not seem to be related to increased laser parameters (Table IV). However, small sample size precluded statistical significance.

DISCUSSION

The excimer laser coronary angioplasty was approved by the U.S. Food and Drug Administration in 1992. Original indications included angioplasty of some very specific lesions such as saphenous vein graft, total occlusions, calcified lesions, ostial lesions, lesions greater than 20 mm in length, and balloon dilatation failures.
These indications have been substantiated by numerous registries. Unfortunately, prospective randomized studies failed to demonstrate the superiority of this technique over balloon angioplasty in some of these predefined complex lesions. The Amsterdam-Rotterdam (AMRO) trial investigated the comparison of excimer laser coronary angioplasty and conventional balloon angioplasty in lesions greater than 10 mm on 308 patients. Procedural success and 6-month cumulative rates of major complications were identical in both groups [13]. Despite these deceiving results, at least partially attributed to first-generation devices used on relatively non-complex disease, excimer laser technology kept some niche applications and enthusiastic promoters [14]. The Excimer Laser Rotational Atherectomy Balloon Angioplasty Comparison (ERBAC) trial randomly assigned 620 patients presenting type B and C lesions to excimer laser angioplasty, conventional balloon angioplasty, or rotational atherectomy. Procedural success rate was 84% for balloon angioplasty, 88% for excimer laser angioplasty, and 93% for rotational atherectomy with 6-month clinical events rate of 45%, 49%, and 53%, respectively [15]. In 1995, the need for intracoronary saline infusion during excimer laser angioplasty to prevent vapor bubble formation and its corresponding acoustomechanical trauma to the vessel wall was well demonstrated. This modification in laser technique led operators to minimize their procedural complications, most commonly dissections [8]. Despite the improvements seen with saline infusion, coronary laser uses have been restricted to niches applications such as treatment of in-stent restenosis [16] and debulking of undilatable or uncrossable lesions [17].

Some earlier reports suggested an 89% success rate at safely debulking lesions where balloons could not properly expand and dilate or could not simply cross after successful wire placement [14]. However, a clear distinction was made between calcified and noncalcified lesions with respective procedural success rates of 79% and 96% (P < 0.05). In addition, the presence of calcifications has been clearly identified, since the early years of coronary laser use, as an independent predictive factor for failure of the technique and complications [18–20]. It has also been suggested that increased laser energy could improve laser success in calcified lesions. In an attempt at creating a smaller excimer laser coronary angioplasty catheter with lower total energy and lower heat production but higher energy intensity, the laser industry proposed a 0.9 mm coronary catheter with 65 concentric 50 μm fibers capable of delivering energy level up to 80 mJ/mm² at 80 hertz for treatment of complex calcified plaques. This technology proved its efficacy in vitro on bovine tendon with maximum generated power of 832 mW and penetration capacity of 0.59 mm/sec compared with existing technology generating 1,704 mW and 0.26 mm/sec penetration rate [21]. The first human report by Fretz et al. [4] described the efficacy of this new catheter technology on seven patients presenting with complex calcified lesions. The use of this high laser energy proved to be safe and efficient on this small series of patients.

We reported the prospective safety and effectiveness data on 100 complex coronary lesions debulked with this new high-energy excimer laser catheter. A procedural success rate of 93% and a clinical success rate of 86% characterized the use of this 0.9 mm X80 excimer laser catheter on this subgroup of patients with extremely complex lesions. Thirteen of the 29 increased parameter uses were on lesions that failed prior balloon angioplasty and in 11 cases (85%) the catheter successfully crossed the lesion, suggesting this therapy would be beneficial in this subgroup presenting with limited interventional options. Among the eight lesions on which the laser failed to cross, balloons and stents were successfully used in four, raising the possibility that even though the laser did not completely cross, it had changed the plaque compliance allowing final lesion management. While obtaining very favorable results on hard-to-treat lesions, including calcified plaques, procedures were performed with a low rate of procedural complications. No perforations, spasm, or no-reflow phenomenon were observed. The most common complication was the presence of dissections after laser despite the use of the flush-and-bathe technique with normal saline infusion. Overall potentially laser-related complications were similar or lower than those observed in comparable studies [17,22,23].

In addition, this X80 system was extremely simple to use, the catheter being 0.014" wire-compatible and requiring 6 Fr guiding catheter. It comes in over-the-wire or rapid-exchange versions. Being efficient for treatment of calcified lesions and much more user-friendly, this X80 excimer laser catheter could potentially replace most rotational atherectomy procedures. A direct comparison of these two techniques for treatment of calcified and undilatable lesions would be extremely valuable.

In conclusion, this new X80 excimer catheter using higher laser coronary parameters seems to be safe and effective for management of calcified and nondilatable lesions. Higher laser energy levels delivered by this catheter seem to improve device performance without increasing complications. Its applicability widens the spectrum of coronary excimer laser use, which includes debulking in ostial stenoses, total occlusions, saphenous vein graft occlusions, stent restenoses, nonresilient plaques to balloon angioplasty, and thrombolysis in complex lesions.
REFERENCES


