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Utilization of Excimer Laser Debulking for Critical Lesions Unsuitable for Standard Renal Angioplasty

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Background: The energy emitted by ultraviolet laser is avidly absorbed in atherosclerotic plaques. Conceptually, it could be applied for debulking of selected atherosclerotic renal artery stenoses. We describe early experience with revascularization of critical renal artery lesions deemed unsuitable for standard renal angioplasty. Institutional Review Board permission to conduct the data analysis was obtained.

Methods: Among 130 percutaneous renal artery interventions with balloon angioplasty and adjunct stenting, there were 12 (9%) patients who underwent laser debulking prior to stenting. These patients presented with critical (95 ± 3.5% stenoses) lesions (11 de novo, 1 stent restenosis) deemed unsuitable for standard renal angioplasty because of marked eccentricity and presence of thrombus. Indications for intervention included preservation of kidney function, treatment of uncontrolled hypertension, management of congestive heart failure, and treatment of unstable angina. Blood pressure and estimated glomerular filtration rate (eGFR) were measured pre- and 3 weeks post-intervention.

Results: A baseline angiographic stenosis of 95 ± 3.5% was reduced to 50 ± 13% with laser debulking. There were no laser-induced complications. Post-stenting the angiographic residual stenosis was 0%. The mean gradient across the lesions was reduced from baseline 85 ± 40 to 0 mmHg. A normal post-intervention antegrade renal flow was observed in all patients. Baseline mean systolic BP of 178 ± 20 mmHg decreased to 132 ± 12 mmHg ($P<0.0001$) and mean diastolic pressure of 85 ± 16 mmHg reduced to 71 ± 9 mmHg ($P = 0.01$). A pre-intervention mean eGFR of 47.7 ± 19 ml/min/1.73 m^2 increased to 56 ± 20.4 ml/min/1.73 m^2 ($P = 0.05$) post-procedure. The interventions were not associated with major renal or cardiac adverse events. During follow-up one patient developed transient contrast-induced nephropathy.

Conclusions: Debulking of select renal artery stenoses with laser angioplasty followed by adjunct stenting is feasible. Further prospective, randomized studies will be required to explore the role of debulking and laser angioplasty in renal artery revascularization. Lasers Surg. Med. 41:622–627, 2009. © 2009 Wiley-Liss, Inc.

Key words: renal artery stenosis; renal angioplasty; excimer laser; debulking; atherosclerotic plaque; thrombus; hypertension; stent; intravascular ultrasound

INTRODUCTION

Atherosclerosis accounts for approximately 90% of all renovascular flow limiting lesions. Medical therapy for renal artery stenosis is an acceptable therapeutic approach; however, it is insufficient in a considerable number of patients. Frequently, the renovascular lesions require percutaneous interventions [1]. Renal artery revascularization, either by surgical bypass or by the percutaneous approach, results in improved blood pressure control, stabilization, or improvement of renal function and congestive heart failure (CHF), as well as relief of angina pectoris [2–5]. Contemporary percutaneous renal interventions incorporate balloon dilation and adjunct stent implantation [6]. A distal protection system is also frequently used [7]. A complex morphology of the target plaque can impose considerable technical challenge. This scenario presents when a markedly eccentric ostial or proximal stenosis contains a high volume plaque with resultant critical luminal narrowing. Hence, debulking prior to balloon dilation and stent deployment could potentially reduce plaque burden and enhance equipment maneuverability. Since ultraviolet laser's energy is avidly absorbed in coronary and peripheral atherosclerotic plaques [8], conceptually, it could be applied for debulking of selected renal artery stenoses. We present experience with 12 selected patients who underwent excimer laser renal angioplasty (ELRA) for critical lesions deemed unsuitable for standard balloon dilation and stent implantation. The clinical profile, revascularization technique, procedural outcome, and follow-up results are reported. To the best of our knowledge, this represents the first publication concerning the application of excimer laser in the treatment of renal artery stenosis.

BACKGROUND

The registry of the cardiac catheterization and interventions laboratories at the McGuire Veterans Affairs

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None of the authors has a conflict of interest to disclose.

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TABLE 1. Baseline Clinical Profile

Patients	$N = 12$
Age (years)	67.7 ± 7
Male gender	12 (100%)
Indication for treatment	
Hypertension	11 (91%)
CHF	6 (50%)
Renal dysfunction	9 (75%)
Angina	3 (25%)
Systolic BP (mean ± 2 SD)	178 ± 20 mmHg
Diastolic BP (mean ± 2 SD)	85 ± 16 mmHg
Chronic renal insufficiency	12 (100%)
Pre-intervention eGFR (ml/min/1.73 m^2)	47.7 ± 19
CKD stage	
Stage II	4 (33%)
Stage III	5 (41%)
Stage IV	3 (25%)
Medications	
ACE inhibitors	8 (66%)
ARB	2 (16%)
Diuretics	9 (75%)
Anti-hypertensives	11 (91%)

CHF, congestive heart failure; eGFR, estimated glomerular filtration rate; ACE, angiotensin converting enzyme; ARB, angiotensin receptor blocker; CKD, chronic kidney disease.

Medical Center, Virginia Commonwealth University, Richmond, Virginia, contains data on 130 patients who underwent renal angioplasty from March 2003 to March 2009. This report describes 12 (9%) pilot cases treated with laser debulking in order to facilitate delivery of balloon angioplasty and deployment of stents. The Department of Veterans Affairs Computerized Patient Record System (CPRS) was used to obtain clinical parameters, ELRA interventions, and subsequent follow-up data. All patients signed informed consent for renal intervention prior to the index intervention.

PATIENT CHARACTERISTICS

The baseline clinical profile of the treated patients is presented in Table 1. There were 12 male patients (10 Caucasians, 2 African American), whose ages ranged from 57 to 82 years (mean 67.7 ± 7 years). Hypertension presented in 11 (91%) patients, diabetes mellitus in 7 (58%), hyperlipidemia and smoking in 10 (83%), CHF in 6 (50%), peripheral artery disease (PAD) in 5 (41%). All patients had chronic kidney disease with eight (66%) having estimated glomerular filtration rate (eGFR) <60 ml/min/1.73 m^2. All patients had associated coronary artery disease (CAD), two patients had a history of stroke, and one had diabetic retinopathy. In one patient, the etiology of renal artery stenosis was attributed to thromboangiitis obliterans. Mean left ventricular ejection fraction (LVEF) was 53.2 ± 10.2%. Patient characteristics and co-morbid conditions are presented in Table 2.

METHODS

This report represents a pilot feasibility approach for the use of laser in revascularization of renal artery stenosis. Prior to planned intervention in each case, the pertinent clinical data were reviewed by interventional cardiologist and a nephrologist who reached a consensus regarding the need for intervention. The indications for intervention included preservation of renal function in all patients, treatment of uncontrolled hypertension in patients who received more than three medications for blood pressure control in 91%, recurrent CHF in 50%, and management of related angina pectoris in 25%. The medications included anti-hypertensives in 91%, diuretics in 75%, angiotensin converting enzyme (ACE) inhibitors in 66%, and angiotensin receptor blockers (ARB's) in 16%.

TABLE 2. Patient Characteristics

Patient	Age	HTN	DM	Hyperlipidemia	Smoking	CAD	LVEF (%)	CHF	PAD	CKD stage
1	57	Yes	No	Yes	Yes	Yes	55	Yes	Yes	III
2	61	Yes	No	Yes	Yes	Yes	60	No	Yes	II
3	71	No	Yes	No	Yes	Yes	45	Yes	Yes	IV
4	68	Yes	Yes	Yes	Yes	Yes	62	No	Yes	IV
5	62	Yes	No	Yes	Yes	Yes	50	No	No	II
6	67	Yes	Yes	Yes	Yes	Yes	70	Yes	Yes	III
7	82	Yes	Yes	Yes	Yes	Yes	35	Yes	No	III
8	62	No	Yes	Yes	No	Yes	55	No	No	II
9	76	Yes	Yes	Yes	Yes	Yes	60	No	No	III
10	62	Yes	Yes	Yes	Yes	Yes	50	Yes	No	III
11	68	Yes	No	No	No	Yes	55	No	No	II
12	76	Yes	No	Yes	Yes	Yes	40	Yes	No	IV

HTN, hypertension; DM, diabetes; CAD, coronary artery disease; LVEF, left ventricular ejection fraction; CHF, congestive heart failure; PAD, peripheral artery disease.

TABLE 3. Angiographic Characteristics

Patients	$N = 12$
Lesion characteristics	
Ostium	5 (41%)
Ostial–Proximal	7 (58%)
Mid portion	0
Calcium	3 (25%)
Thrombus	9 (75%)
Baseline gradient[a]	85 ± 40 mmHg

[a] Gradient was not measured in two patients.

The angiographic characteristics of the target lesions are delineated in Table 3. The target lesions were considered unsuitable for standard balloon dilation and stenting due to the following: critical stenosis ($>90\%$) with a complex morphology consisting of marked eccentricity, significant gradient, and presence of thrombus. The baseline gradient across the lesions (pull back method) was measured in 10 patients. The interventions as described in Table 4 were performed with a target activated clotting time of 250 seconds which was achieved with IV heparin. Aspirin, plavix, and *N*-acetyl cysteine were used in each patient. Protection devices were not used in this series of patients. The laser catheters used (Spectranetics, Colorado Springs, CO) varied from 0.9 to 2.0 mm. Similar to utilization of excimer laser in coronary lesions, the catheter size was chosen in order to create a "pilot channel" across the targeted plaque. Thus, the laser catheter was matched to the lesion severity whereby the more severe the stenosis, the smaller the size of the catheter [9]. Laser catheters containing concentric fiber configuration were used in 50% of the patients and catheters with eccentric optic fibers were applied in the rest. In each case, after laser debulking, balloon dilatation of the target lesion was performed followed by implantation of a Genesis (Cordis, Rotterdam, The Netherlands) stent. The goal of stenting was to achieve 1:1 sizing of the vessel segment at the target lesion as compared with a normal-appearing distal segment. For ostial stenoses, the reference segment was a normal-appearing distal segment unaffected by post-stenotic dilatation. Intraluminal renal ultrasound (In-Vision Gold, Volcano, Rancho Cordova, CA) was used in three patients. The eGFR was measured using the MDRD equation [10] prior to the procedure and 3 weeks post-procedure. Following the index procedure, all patients were followed in the Cardiology and Nephrology clinics. Statistical analysis was done using a statistical package OriginPRO version 8 (Originlab, Northampton, MA).

TABLE 4. Intervention Data

Baseline stenosis (%)	95 ± 3.5
Post-laser stenosis (%)	50 ± 13
Final residual stenosis (%)	0
Final gradient	0 mmHg
Excimer laser catheter size (mm)	
0.9	1
1.4	1
1.7	1
2.0	9
Laser pulses delivered (mean ± 2 SD)	574 ± 130
Laser-induced complications	
Distal embolization	0 (0%)
Dissection	0 (0%)
Perforation	0 (0%)
Total no. of stents	11
Stent length (mm)	16.1 ± 1.5
Stent diameter (mm)	5.9 ± 0.7
Post-procedure renal flow	Normal (100%)
Post-PEI follow-up eGFR	56 ± 20.4 ml/min/1.73 m^2

PEI, percutaneous endovascular intervention.

RESULTS

The baseline angiographic stenosis was 95 ± 3.5% (mean ± SD). The baseline gradient across the lesion ranged from 35 to 165 mmHg (mean 85 ± 40 mmHg). Overall, 574 ± 130 (mean ± SD) laser pulses were applied using energy fluence of 45 mJ/mm^2/25 Hz. The target stenoses were initially reduced to 50 ± 13% with laser debulking. There were no laser-induced complications. Following balloon dilations and stent deployment, the final angiographic residual stenosis was 0%. Post-intervention antegrade flow in the targeted renal artery was normal in each case. There were no peri-procedure or post-procedure bleeding events. Figures 1 and 2 depict laser angioplasty and adjunct stenting in two patients.

A baseline mean systolic BP of 178 ± 20 mmHg improved to final 132 ± 12 mmHg ($P<0.0001$; Fig. 4). A mean pre-intervention diastolic BP of 85 ± 16 mmHg decreased to 71 ± 9 mmHg ($P = 0.01$; Fig. 5). Pre-intervention mean eGFR of 47.7 ± 19 ml/min/1.73 m^2 increased to 56 ± 20.4 ml/min/1.73 m^2 ($P = 0.05$) post-procedure (Fig. 3). Overall, there was an increase of eGFR in 10 (83%) patients. In one patient there was minimal decrease in eGFR (40–38 ml/min/1.73 m^2) and transient contrast-induced nephropathy was observed in another. No adverse cardiovascular or renal events occurred in 11 (92%) patients. One patient underwent PCI of the right coronary artery 1 month following the index procedure. The PCI was complicated by localized coronary rupture necessitating emergency cardiac operation.

DISCUSSION

The application of renal angioplasty for treatment of renal artery stenosis is currently a controversial topic [11]. However, it is clear that in selected patients with uncontrolled hypertension, CHF and/or renal insufficiency this intervention can be beneficial [12–14]. While balloon angioplasty and stent implantation for renal interventions are readily available, several technical challenges remain. The bulk of obstructive atherosclerotic plaque can impose a considerable barrier to safe delivery of protection systems, balloons and stents into the renal artery. Tight ostial or proximal stenoses, with marked eccentricity of the plaque and/or presence of accompanying thrombus, render a target lesion prone to the risk of distal embolization of atheromatous debris from equipment manipulations [15]. This raises the potential for a modified revascularization approach beginning with plaque debulking for facilitation of delivery of the standard equipment. Notably, the concept of debulking for management of atherosclerotic renal artery stenosis is not new. During the era of vascular bypass for renal artery stenosis, plaque debulking was frequently incorporated during operations. Hansen et al. [16] reported their experience with vascular bypass for ischemic nephropathy in 232 patients. In 103 (44%) cases the operation included direct thromboendarterectomy. Thus, the option of reducing plaque burden before balloon and stent delivery should at least be considered in preparation for revascularization of complex renal artery lesions.

In percutaneous treatment of selected coronary and peripheral interventions, debulking can be achieved by rotational atherectomy, directional atherectomy, and laser. Rotational atherectomy has been applied for the treatment of renal ostial restenosis [17], and laser has been utilized only for stent restenosis, but not for de novo lesions [18]. Directional atherectomy has been reported for management of eccentric stenosis [19]. The excimer laser operates within the ultraviolet 308 μm wavelength of the optic spectrum. This wavelength is well absorbed within atherosclerotic material with a shallow penetration depth of only 35–50 μm [20] which enables precise control of energy and ensures debulking without plaque disintegration. In 151 patients with atherosclerotic/thrombotic coronary lesions, excimer laser debulking caused distal embolization in only 1 (0.6%) patient [21]. Importantly, the excimer laser facilitates removal of the thrombus which frequently accompanies atherosclerotic plaques. This has been validated in patients with acute myocardial infarction or unstable angina pectoris whereby quantitative analysis by an independent core laboratory demonstrated 96% reduction of thrombus burden with the laser emission in the acute myocardial infarction group and 97% reduction in the unstable angina group [22]. Furthermore, it appears that the larger the thrombus content, the higher the yield of the laser as a thrombectomy device [21]. It also suppresses platelet aggregation ("stunned platelet phenomenon" [23]) thereby reducing their adverse effect on the revascularization process. A careful lasing technique that incorporates very slow antegrade and retrograde catheter movement enhances debulking of the target plaque [24] and reduces complications [25]. In each of our patients, laser debulking created a "pilot channel" corresponding to desired recanalization.

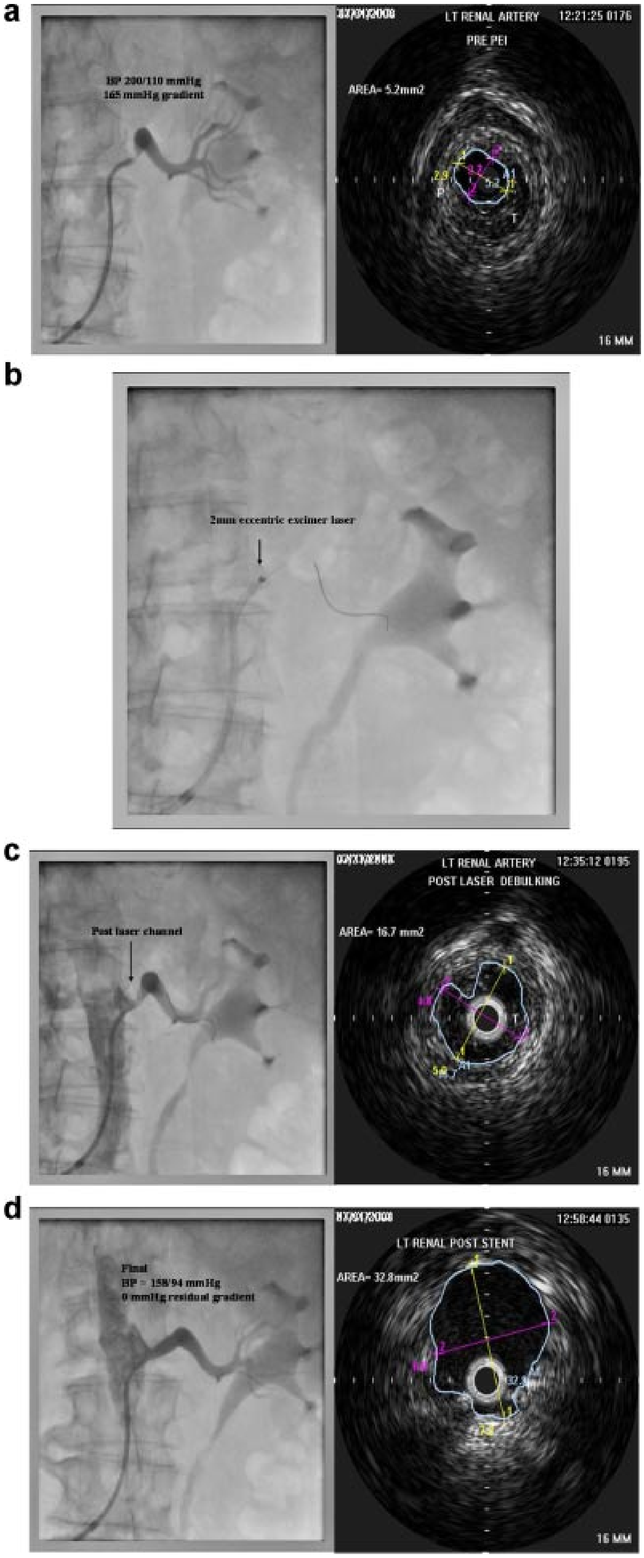
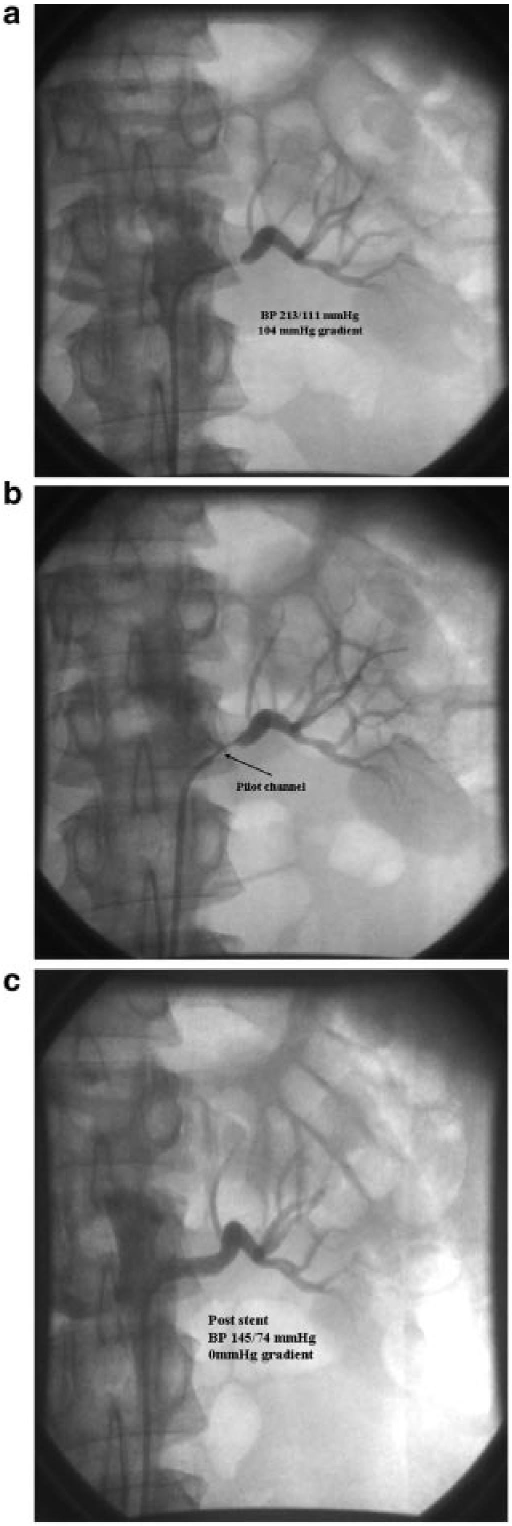


Fig. 1. Excimer laser angioplasty in a patient with uncontrolled HTN and angina. Left renal artery eccentric, 95% ostial–proximal stenosis is present. **a**: Pre-intervention angiogram and corresponding renal ultrasound (P denotes plaque, T denotes plaque/possible thrombus). **b**: Debulking of the ostial stenosis with a 2-mm eccentric laser catheter. **c**: Post-laser recanalization with corresponding ultrasound (T denotes residual thrombus). **d**: Final angiographic result with corresponding ultrasound.

In the present series, we used coronary laser catheters with a maximum size of 2.0 mm. It is possible that larger plaque content could have been successfully removed from the target lesions if peripheral laser catheters (sizes 2.3 or 2.5 mm) had been used. We used eccentric laser catheters, which offer arrangement of the optic fibers enabling the operator to debulk 3–4 quadrants within the target plaque. Intraluminal renal ultrasound was used to assess the effect of the laser energy on the plaque and for verification of adequate stent deployment. Based on angiography, ultrasound images, and clinical data, no adverse effects of the excimer laser on the plaque and surrounding vessel wall were noted. Specifically, endovascular complications including spasm, dissection, thrombosis, or perforation were not encountered.



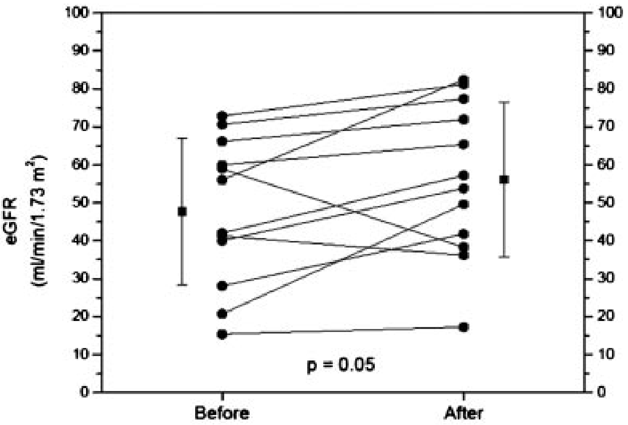


Fig. 3. eGFR measurements pre-intervention and at follow-up.

The clinical follow-up demonstrated improvement of renal function in 10 (83%) patients. Significantly, all patients had improved systolic and diastolic BP control. While these early results are encouraging, this experience should be carefully corroborated before further acceptance of laser technology for the treatment of selected percutaneous renal artery revascularizations can take place.

STUDY LIMITATIONS

This report represents early experience with debulking of lesions deemed unfavorable for standard renal artery revascularization. This approach was used in a selected, small group of patients. While demonstrating acceptable safety, acute gain, and follow-up results, this experience is limited and cannot serve either as a recommendation nor confirmation of an exclusive role for excimer laser in treatment of RAS.

SUMMARY

In early experience with utilization of ultraviolet excimer laser for percutaneous treatment of renal artery stenosis,

Fig. 2. A patient with uncontrolled HTN, CHF, and angina. A 99% thrombotic ostial stenosis of the left renal artery. **a**: Pre-intervention angiogram of the left renal artery. **b**: Debulking with a X-80 0.9 mm excimer laser catheter containing concentric optic fibers. This is the smallest debulking device available in interventional cardiology. The application resulted in creation of a pilot channel. **c**: Final angiogram post-intervention.

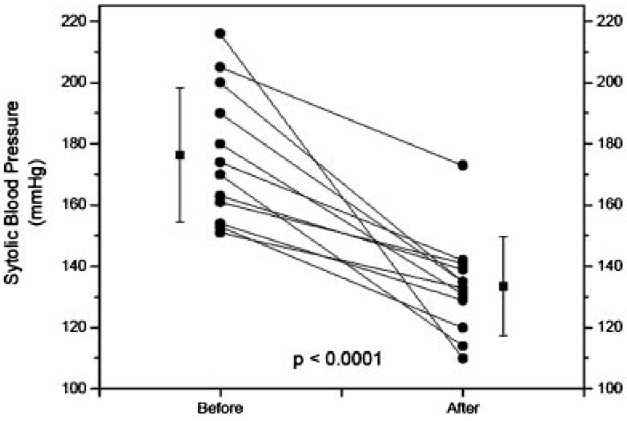


Fig. 4. Systolic BP measurements pre-intervention and at follow-up.

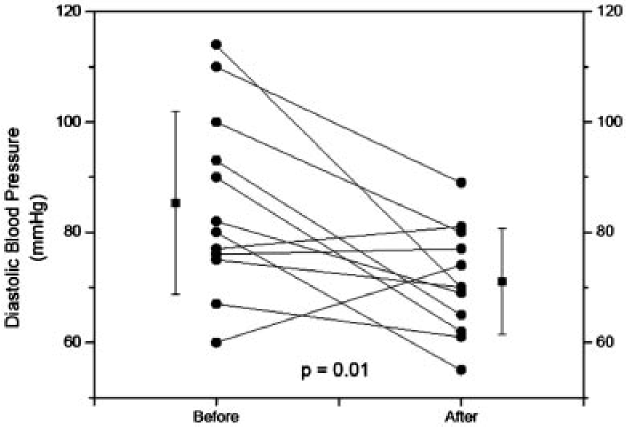


Fig. 5. Diastolic BP measurements pre-intervention and at follow-up.

this technology provided safe and efficacious debulking in selected patients. The unique absorption of excimer laser energy in atherosclerotic and thrombotic material results in adequate debulking, facilitating balloon and stent delivery. The future role of this technology for selected renal artery interventions requires further study.

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