Arterial Response During Cutting Balloon Angioplasty: A Volumetric Intravascular Ultrasound Study

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Background and Purpose: Previous studies have demonstrated that the mechanism of acute lumen enlargement after balloon angioplasty is a combination of vessel expansion and plaque redistribution, but not plaque compression. The purpose of this study was to clarify, from a three-dimensional aspect, the vascular response to cutting balloon angioplasty.

Methods: Serial intravascular ultrasound (IVUS) studies, including pre- and post-intervention, were performed in 36 native coronary lesions treated with the cutting balloon device. External elastic membrane (EEM), lumen, and plaque + media cross-sectional area were measured at 16-frame intervals (30 frames = 1 mm) over a lesion length of 16 mm with the center on the smallest pre-intervention lumen area. Volumetric calculations were based on Simpson's rule.

Results: EEM volume (261.16 ± 89.59 *vs.* 279.59 ± 85.92 mm^3; $p < 0.01$) and lumen volume (106.48 ± 37.83 *vs.* 133.72 ± 36.57 mm^3; $p < 0.01$) significantly increased after cutting balloon angioplasty. Furthermore, the plaque + media volume throughout the lesion changed significantly after cutting balloon angioplasty (154.68 ± 63.36 *vs.* 145.87 ± 59.20 mm^3; $p < 0.01$). The change in lumen volume correlated strongly with the change in EEM volume ($r = 0.75$; $p < 0.01$), but poorly with the change in plaque + media volume ($r = 0.08$; $p = 0.64$). Less longitudinal plaque redistribution was also observed throughout the vessel after angioplasty.

Conclusion: The results of this study indicate that the predominant mechanism of lumen enlargement from cutting balloon angioplasty is vessel expansion, although total plaque mass reduction and longitudinal plaque redistribution do occur.

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Key words:
cutting balloon angioplasty
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The cutting balloon (Boston Scientific/IVT Corp., San Diego, CA, USA) is a novel device with three or four longitudinal atherotome blades mounted on the outer surface of the balloon. It was designed to produce sharp, clean, longitudinal incisions [1]. This controlled incision supposedly produces less traumatic injury to the vessel wall during balloon dilation. Although many studies have demonstrated the safety and efficacy of cutting balloon angioplasty (CBA) [2–7], the mechanism of vessel response following this procedure is still unclear. Intravascular ultrasound (IVUS) can accurately depict vascular anatomy, plaque size and plaque distribution. In addition, recent studies have demonstrated the clinical feasibility and usefulness of three-dimensional IVUS analysis [8, 9]. Plaque compression, as a mechanism of balloon angioplasty, was originally documented by Dotter and Judkins [10] and Gruntzig [11]. However, IVUS studies have suggested that improvements in luminal dimensions from balloon angioplasty result from a combination of arterial expansion, plaque dissection and plaque redistribution [8, 12, 13]. Recently, the issue of debulking before stenting has been raised, and an early pilot study has shown promise in terms of reduced restenosis [14]. Therefore, it is important to understand plaque behavior, especially in response to interventional

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modalities such as CBA. The aim of this study was to clarify the three-dimensional behavior of vessel response during CBA.

Patients and Methods

Patients and lesions

A total of 36 lesions in 36 patients who underwent CBA between June 1, 1997, and May 30, 1998, at the Stanford University Medical Center Cardiovascular Core Analysis Laboratory were included in this study. All lesions were *de novo* or first restenotic lesions of native coronary arteries. There were 26 men and 10 women, with a mean age of 64.03 ± 8.86 years. The lesion was in the left anterior descending artery in 15 patients (41.7%), left circumflex artery in 11 (30.5%), and right coronary artery in 10 (27.8%). IVUS images using an automated pullback system were acquired pre- and post-intervention.

Quantitative intravascular ultrasound analysis

All IVUS studies were performed using a commercially available system (CVIS / Boston Scientific Corp., San Jose, CA, USA). The ultrasound system consisted of a single-element, 30-MHz transducer mounted on the tip of a flexible shaft, rotating at 1800 rpm within a 2.9 Fr rapid exchange / common distal lumen imaging sheath, or within a 3.2 Fr short monorail imaging sheath. All IVUS images were acquired following intracoronary administration of 200 μg nitroglycerin or 2 mg isosorbide dinitrate. Images were acquired using motorized pullback at a speed of 0.5 mm / second. Images with excessive nonuniform rotational distortion, significant sheath and catheter artifact, and > 30° of circumferential or 1.0 mm of axial target lesion calcium were excluded from the analysis. Ostial and bifurcation lesions were excluded because of the difficulty in identifying the media-adventitia border and the possibility of plaque shifting out of range of the ultrasound image. All images were recorded on super-VHS videotape for offline quantitative analysis by a core analysis laboratory. Digitized images were analyzed using commercially available planimetry software (TapeMeasure, Indec Systems, Inc., Mountain View, CA, USA). Quantitative parameters consisted of lesion lumen cross-sectional area (CSA) as well as external elastic membrane (EEM) CSA. The EEM CSA was defined as the area within the medial / adventitial border. Plaque + media CSA was calculated as EEM CSA minus lumen CSA. The lesion site selected for analysis was the image slice with the smallest lumen CSA prior to intervention; if there were several image slices with an equally small lumen, the image slices with the largest EEM CSA and plaque + media CSA were analyzed [15]. The same cross-sectional IVUS image was analyzed before and after CBA. To further investigate the vessel response in the entire lesion segment, serial volumetric analysis was performed before and after the intervention. All three-dimensional IVUS reconstruction and quantitative volumetric IVUS analyses were performed using commercially available software (Echoplaque, Indec Systems, Inc., Mountain View, CA, USA). After digitization of IVUS recordings, lumen and EEM areas were manually traced at 16-frame intervals (30 frames = 1 mm) and the interpolated measurements of the remaining frames were automatically generated. Each target lesion was measured for vessel and lumen areas over a 16-mm lesion length, centered on the smallest pre-intervention lumen CSA. EEM volume, lumen volume, and plaque + media volume were calculated using Simpson's rule [16, 17]. To ensure that the same segment and slices were analyzed in both pre- and post-intervention studies, reproducible axial landmarks (usually the aorto-ostial junction, a large proximal side branch, and / or reference segment calcific deposits) were used as axial reference points.

Statistical analysis

Statistical analyses were performed using Statview version 5 (SAS Institute Inc., Berkeley, CA, USA). Quantitative data are presented as means ± standard deviation (SD) and qualitative data are presented as frequencies. Paired numerical data obtained by serial study were compared using the paired *t*-test and other continuous variables were compared using unpaired *t*-tests. Linear regression analysis was used to assess the correlation among the change in EEM volume, lumen volume and plaque + media volume. A p value of 0.05 or less was considered significant.

Results

Thirty-six lesions treated using CBA were included in this study. Clinical characteristics of patients and lesions are summarized in Table 1. Angiographic results and balloon angioplasty results are shown in Table 2. The average reference segment was 2.97 ± 0.43 mm and the average balloon size was 3.43 ± 0.42 mm, with a balloon-to-artery ratio of 1.16 ± 0.12. Following CBA, the minimal lumen diameter and percent diameter stenosis were significantly improved ($p < 0.01$).

Intravascular ultrasound

Planar and three-dimensional (volumetric) quantitative IVUS results are given in Table 3. In planar IVUS analyses, plaque + media CSA decreased significantly

Table 1. Clinical characteristics of the patients and lesions

Characteristics	*n*	%
Age (yr)	64.03 ± 8.86	
Male sex	26	72.2
Hypertension	12	33.3
Diabetes mellitus	9	25
Dyslipidemia	16	44.4
Smoking	10	27.7
Prior myocardial infarction	16	44.4
Prior CABG	1	2.7
Prior PTCA	13	36.1
Lesion location		
LAD	15	41.7
LCX	11	30.6
RCA	10	27.7
ACC/AHA type		
A	7	19.4
B1	14	38.9
B2	11	30.6
C	4	11.1

CABG = coronary artery bypass graft; PTCA = percutaneous transluminal coronary angioplasty; LAD = left anterior descending coronary artery; LCX = left circumflex artery; RCA = right coronary artery; ACC/AHA = American College of Cardiology/American Heart Association.

after CBA ($p < 0.01$). EEM CSA and lumen CSA increased significantly (both $p < 0.01$).

In three-dimensional IVUS analyses, the EEM volume ($p < 0.01$) and lumen volume ($p < 0.01$) increased significantly following CBA. The overall plaque + media volume was significantly decreased from 154.68 ± 63.36 to 145.87 ± 59.20 mm^3 ($p < 0.01$). The change in lumen volume correlated strongly with the change in EEM volume ($r = 0.75$, $p < 0.01$), but poorly with the change in plaque + media volume ($r = 0.08$, $p = 0.64$) (Fig. 1). Figure 2 shows the average change in plaque-media volume at each 1-mm segment. The sum of the average change in plaque volume in the center zone, distal, and proximal part of the lesions were –8.07 mm^3, 1.23 mm^3, and 0.13 mm^3, respectively. Thus, in the center zone of the lesion, there was a greater decrease in plaque + media volume, with a corresponding slight increase in plaque + media volume at both proximal and distal segments. There was no obvious longitudinal redistribution of the atherosclerotic plaque away from the center of the lesion to the proximal and distal ends of the lesion. Therefore, acute lumen gain was achieved mainly by vessel expansion, not plaque reduction.

Table 2. Angiographic and cutting balloon angioplasty procedure results

Procedure characteristics	
Balloon size (mm)	3.43 ± 0.42
Balloon-to-artery ratio	1.16 ± 0.12
Balloon length (mm)	14.17 ± 1.90
Inflation pressure (atm)	7.86 ± 1.79
Angiographic results	
Reference vessel diameter (mm)	2.97 ± 0.43
Lesion length (mm)	12.86 ± 5.91
Minimal lumen diameter (mm)	
Pre-intervention	1.23 ± 0.37
Post-intervention	2.28 ± 0.40*
Diameter stenosis (%)	
Pre-intervention	58.7 ± 10.4
Post-intervention	23.7 ± 9.10*

*$p < 0.01$ post-intervention *vs.* pre-intervention

Discussion

The results of this study show that the mechanisms of CBA include vessel stretch, some plaque reduction, and less plaque redistribution. Although total plaque mass was decreased after CBA, this reduction was not primarily responsible for lumen enlargement at the target site. Acute lumen gain was achieved mainly by arterial expansion. A previous *in vivo* peripheral artery study found that lumen enlargement by balloon dilation was achieved primarily by overstretching the arterial wall [18]. In contrast, a similar *in vivo* study of iliac stenoses demonstrated that plaque fractures and compression of atherosclerotic plaque were the principal factors responsible for increased luminal patency after balloon angioplasty [19]. Although the relative contribution of each mechanism varied among previous IVUS studies, a recent study using volumetric IVUS analysis reported that plaque compression does not appear to be a mechanism of balloon angioplasty, and that lumen enlargement is the result of combined plaque dissection, arterial expansion and plaque axial redistribution [8]. Thus, unlike volumetric analysis of conventional balloon angioplasty, lumen enlargement after CBA results largely from arterial expansion, partly from plaque reduction, and to a small extent from plaque redistribution. These discrepancies between conventional balloon and cutting balloon dilation may be due, in part, to the design aspects (i.e., microtomes) of the cutting balloon. One possible explanation for our results may be that plaque incisions made by the cutting balloon microtome blades may induce less squeeze but more compression effect, with less subsequent plaque redistribution.

CBA is a strategy proposed to minimize vascular injury and reduce further vascular biologic response

Table 3. Planar and volumetric intravascular ultrasound results

	Pre-intervention	Post-intervention	*p* value
Planar results (mm^2)			
Lumen area	2.19 ± 0.64	5.87 ± 1.44	< 0.01
EEM CSA	13.22 ± 4.05	15.03 ± 3.97	< 0.01
Plaque + media CSA	11.03 ± 3.79	9.16 ± 3.21	< 0.01
Volumetric results (mm^3)			
Lumen volume	106.48 ± 37.83	133.72 ± 36.57	< 0.01
EEM volume	261.16 ± 84.59	279.59 ± 85.92	< 0.01
Plaque + media volume	154.68 ± 63.36	145.87 ± 59.20	< 0.01

EEM = external elastic membrane; CSA = cross-sectional area.

contributing to restenosis [1, 20]. Although the clinical safety and efficacy of the cutting balloon, as an alternative to conventional coronary angioplasty in noncomplex lesions, has been shown in previous studies [2, 3], the clinical utility of CBA remains controversial. Fortunately, with more experience, better acute and late outcomes have been obtained, with several clinical studies demonstrating the effectiveness of CBA in special subsets such as small vessels and ostial lesions, where CBA results are superior to conventional balloon angioplasty [4, 5, 7]. Currently, with the expanded application of coronary stenting, stent restenosis has emerged as a new disease entity. Therefore, the cutting balloon device may gain wider acceptance for the treatment of in-stent restenosis as well as being a strategy for use prior to stent deployment [21–23]. Compared to conventional balloon angioplasty, which is associated with the watermelon seeding effect, CBA does not "squeeze" out of a stenotic arterial segment.

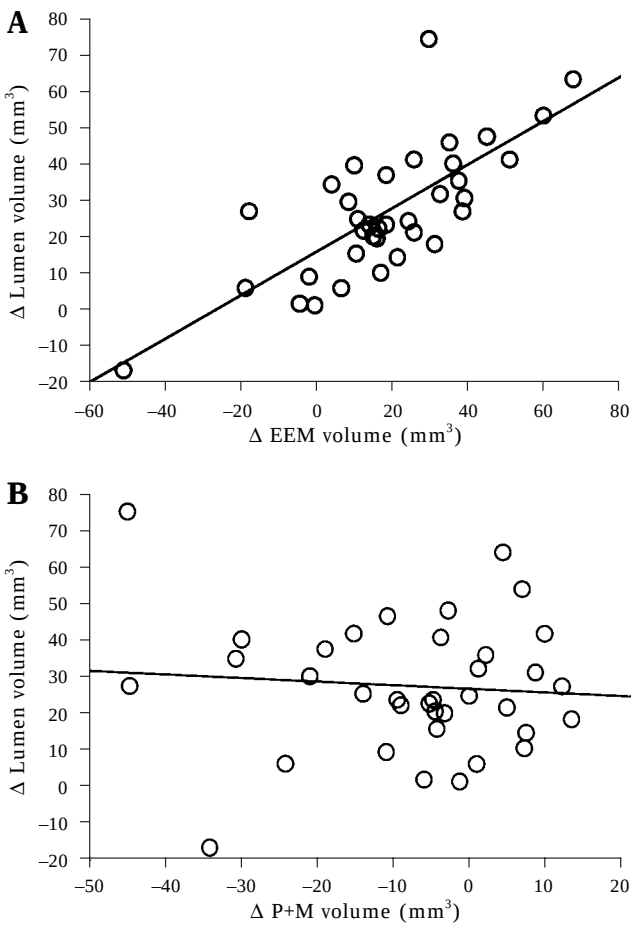

Fig. 1. *Change in lumen volume correlates strongly with change in (A) external elastic membrane (EEM) volume (*r = *0.75,* p < *0.01), but poorly with the change in (B) plaque +media (P+M) volume (*r = *0.08,* p = *0.64).*

Additionally, lower inflation pressures with controlled vascular injury may be another potential advantage of CBA for treating stent-related stenoses and pre-stenting dilation.

There were several limitations in the present study. The lesions were highly selected to exclude potential measurement error (highly calcified, ostial lesions) and the possibility of plaque shifting to branch segments. Thus, it is uncertain whether these results reflect those of more complex lesions and particular geometries. Previous reports have suggested that successful angioplasty causes a continuum of arterial responses that vary with plaque composition and patterns of pre-intervention arterial remodeling, shown to affect the mechanism of lumen gain after balloon angioplasty in coronary artery disease [24–26]. Therefore, the mechanisms of cutting balloon dilation affected by plaque composition and vessel remodeling need to be clarified. Additionally, we did not quantify tears and dissections in this study, so the relation of coronary dissections to acute gain is not clear. Accurate identification of the same anatomic cross section on serial studies remains a challenge. The three-dimensional IVUS analysis system used in this study assumed that the vessel was relatively straight over the extent of the structure and did not account for deviations

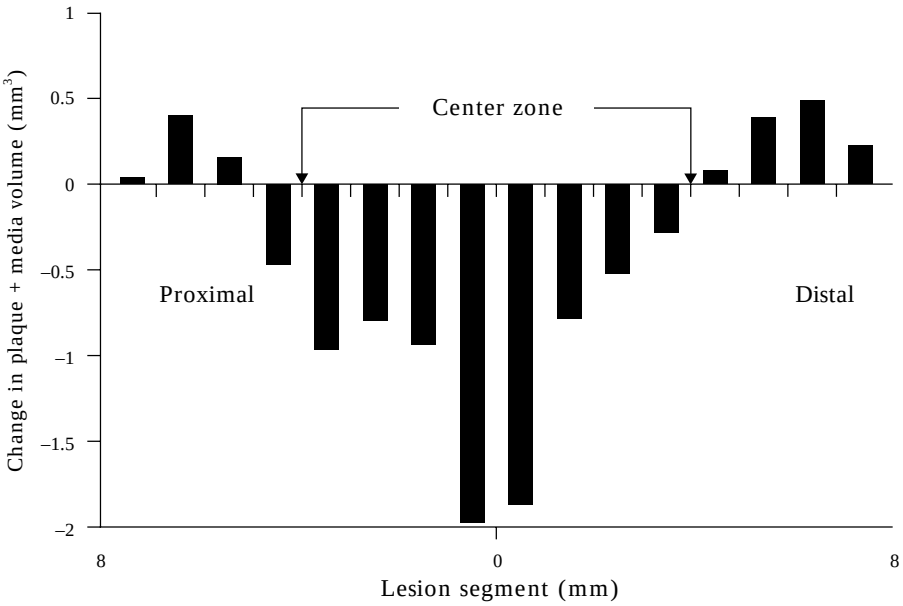

Fig. 2. *Average change in plaque + media volume at each 1-mm segment of all lesions. A much greater decrease in plaque mass was evident in the central zone of the lesion and was associated with an increase in both proximal and distal end plaque mass.*

in spatial geometry. Thus, we may have over- or underestimated the volumes, particularly in curved vascular segments. Another concern is that movement of the IVUS catheter during the cardiac cycle might have induced some artifacts. Because the total sample size was relatively small, these issues need further evaluation. Finally, because this was a retrospective study of patients selected from the IVUS database, prospective study is needed to confirm the results.

In conclusion, serial automated three-dimensional IVUS analysis demonstrated that the predominant mechanism of lumen enlargement from CBA was vessel expansion or stretching, although total plaque mass reduction and longitudinal plaque redistribution also occurred. This enhanced understanding of the mechanisms of lumen enlargement after CBA may influence its clinical application and improve strategic approaches to treatment in coronary intervention.

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