In Search of the Optimized Excimer Laser Angioplasty System

Frank Litvack, MD; Neal L. Eiger, MD; and James S. Forrester, MD

Excimer laser coronary angioplasty has emerged as a useful therapy for selected patients with complex coronary artery disease. More than 5,000 patients worldwide have undergone excimer laser procedures with systems from three manufacturers. The laser operating characteristics and delivery catheter design vary significantly, and clinical study protocols were not equivalent. Data obtained on any one system, therefore, is not necessarily applicable to the others. This notwithstanding, the cumulative clinical experience has significantly augmented our understanding of the appropriate applications and current limitations of the technique. The observational study by van Leeuwen et al in this issue of Circulation provides further insight into an important limitation of excimer angioplasty—angiographic dissection and acute occlusion.

Excimer laser energy probably ablates material via photochemical mechanisms that involve the breaking of molecular bonds and direct desorption of material on a layer-by-layer basis with little generation of heat. In vitro excimer laser ablation of atherosclerotic tissue typically produces incision margins that exhibit little disruption and are free of thermal effects. The 308-nm excimer is the only laser capable of ablating calcified tissue. These properties have distinguished the excimer from other lasers and are responsible in part for the efficacy demonstrated in large prospective trials of excimer laser coronary angioplasty.

Data from the largest single clinical registry, which include more than 2,000 patients and 3,000 lesions, indicate the procedure success rate is 90%. Neither success nor major complication rate vary significantly between simple and complex coronary lesions. Thus, excimer angioplasty is usually limited to the treatment of selected complex disease including long lesions, diffuse disease, aorto-ostial stenoses, total occlusions, calcified and undilatable lesions, and older saphenous vein grafts. Significant complications in the registry report include in-hospital death, 0.6%; Q wave myocardial infarction, 2.1%; and urgent or emergent bypass surgery, 3.6%. The incidence of coronary perforation is 1.2% but has been significantly reduced to 0.4% in the last 1,000 patients treated, after predisposing factors were identified. The most important of the "minor" complications are coronary dissection in 16% of patients and acute occlusion in 7%, of which approximately one half are corrected by adjunctive balloon dilatation.

These two events—angiographic dissection and acute occlusion—are often unpredictable and have thus far defied identification of predisposing circumstances and preventive measures. Whereas the incidence of coronary perforation has been significantly reduced by avoiding certain anatomic morphologies and by careful catheter sizing, dissection and occlusion have not yielded to simple anatomic-correlate analysis.

The study by van Leeuwen et al in this issue may represent a step toward identifying the mechanisms of coronary dissection. By histology, they demonstrate that the use of multifiber excimer laser catheters in nondiseased rabbit iliac and femoral vessels is associated with the development of endothelial denudation, disruption of the internal elastic laminae, and small dissection planes filled with red blood cells. Further, in vitro delivery of energy into a hemoglobin solution and time-resolved photography in one rabbit demonstrated the development of rapidly expanding and imploding bubbles larger than the catheter diameter. van Leeuwen et al also observed rapid stretching and recoiling of the artery, which had the same time course of in vivo bubble formation. It is tempting to infer causality between the bubble formation and histological injury.

Can the present study be linked to the angiographic complications occasionally seen during clinical procedures in atherosclerotic human coronaries? The observation that pulsed laser energy produces cavitation or bubbles in a fluid medium is not a new one. More than 25 years ago, Carone et al demonstrated that a pulsed 694-nm ruby laser produced acoustic transients probably as the result of the development of dielectric fields. This observation was repeated by others with different pulsed lasers. It appears that the high peak powers (peak power=energy density/pulse duration) generated by the very short laser pulses can induce plasma formation in liquids by a process known as "avalanche ionization." The molecules and atoms of the fluid are ionized as a result of the enormous peak instantaneous powers focused in a small volume. In an elegant series of experiments using myocardial tissue in a blood medium, first demonstrated what may be the cardiovascular-
cullar correlate of this phenomenon. They showed a sequence of cavity formation, growth, collapse, and rebound similar to that originally described by the physical chemists.\textsuperscript{13} It appears that this same phenomenon was observed in the intact artery in a flowing blood stream by van Leeuwen et al. Whether the bubbles are created by gaseous expansion of vaporized fluid or by photoplasma is not proved by these experiments. Although the present study adds evidence of histological injury, a limitation is that all the anatomic injury described in this study was microscopic. There was no angiographic correlation of vascular dissection or occlusion.

The only in vivo human assessment of vascular pathology after excimer laser angioplasty contradicts the van Leeuwen hypothesis. Isner et al.\textsuperscript{14} studied plaque irradiated with the excimer laser by retrieving it with the directional atherectomy device. The excimer-treated plaque showed no significant disruption or thermal injury, and the authors concluded that pathological changes after laser angioplasty are similar to that predicted by in vitro study.

If acoustic phenomena are in part responsible for dissection during excimer angioplasty, it may well explain the frequent clinical observation that dissection often occurs in the apparently “normal” vascular segment adjacent to the lesion. Perhaps the rigid, diseased segment is less prone to pulsatile expansion and recoil after impact of the bubbles and acoustic transients than is the pliable normal segment. This may also explain why, in contrast to balloon angioplasty, excimer angioplasty appears to be more effective in more diffusely diseased and rigid lesions and why excimer angioplasty may be more predictable in complex than in simple lesions.

What countermeasures can we take to minimize the generation of acoustic transients and microbubbles? A randomized clinical study comparing excimer angioplasty in a blood versus a saline medium is in progress, based on the hypothesis that diminished absorption of 308-nm energy by saline will reduce the development of bubbles and other acoustic phenomenon. It is possible, however, that energy absorption by impurities within the liquid and the high power density of the laser pulse may induce both plasma formation and its secondary effects independent of the type of fluid. An alternate solution could be configuring the excimer catheter such that each fiber or small groups of fibers transmit energy in sequence over a very brief period of time rather than in unison.\textsuperscript{15} This “smooth excimer laser angioplasty” may well reduce mechanical effects, since the bubbles and transients generated will be much smaller. Finally, recent and so far unreported clinical experience suggested that advancing the laser catheter more rapidly than previously recommended (3–mm/sec) may significantly reduce dissection rates (M. Leon, K. Kent, G. Prichard, L. Sattler; personal communication). This “first-pass” technique may diminish the local rate of bubble accumulation and allow for enhanced run-off of bubbles away from the artery wall.

It is unlikely, however, that the generation of bubbles and transients is the sole cause of dissection. Dissection has been observed when laser catheters have been inadvertently advanced without emitting laser energy. Catheter “dead space” (nonemitting surface of the catheter tip) could be responsible for mechanical trauma to the artery. The nonactive area includes the space between the individual fibers and the inner and outer circumference of the catheter. The most recent catheter designs have minimized dead space, and early clinical experience is favorable.

Excimer laser angioplasty has reached its adolescence. We have demonstrated “acceptable” safety (no complication is really acceptable), gone through several generations of catheter design, and identified potential indications and contraindications. Now we begin the era of comparative clinical trials. Future protocols must be conducted within the constraints of ongoing modification of device and technical parameters. Studies such as that of van Leeuwen et al, along with careful clinical documentation, should allow for continued improvement of both our understanding and our application of excimer laser angioplasty.

References


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