Transmyocardial Laser Revascularization: Effect of Laser Parameters on Tissue Ablation and Cardiac Perfusion

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Dr. Mahmood Mirhoseini from Milwaukee, WI, transformed transmyocardial revascularization (TMR) into transmyocardial laser revascularization (TMLR) more than 2 decades ago. The controversial nature of this laser procedure and the prospect of its successful application to refractory cases of chronic debilitating angina have created spirited interest in TMLR. As a natural component of this interest, various laser modalities have been proposed and employed during the performance of the TMLR procedure both in the experimental and the clinical setting. However, it is the nature of laser-tissue interactions that is primarily responsible for the long-term fate of the channels, the angiogenesis that occurs in the vicinity of these laser channels, and the resulting increase (if any) in myocardial perfusion. These interactions with tissue are, in turn, determined by laser variables such as photonic absorption and scattering by the target tissue, pulse energy and duration, and the peak power generated. The CO_2 laser has the advantages of producing high-energy pulses that create a transmural channel with a single pulse, low-peak power that minimizes structural tissue trauma, and high photonic absorption to minimize thermal damage. The holmium: YAG and excimer lasers, in turn, have the advantage of being coupled to a fiber optic catheter for transluminal endocardial delivery. Importantly, long-term clinical and perfusional data showing a cause and effect relationship between the use of TMLR and these end-points are available for the CO_2 laser only. Prospective randomized trials are, therefore, warranted to delineate the use of each laser modality in relation to that of the CO_2 laser in the TMLR setting.
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Key words: Laser, transmyocardial, tissue interactions, perfusion.

Transmyocardial laser revascularization (TMLR) with a CO_2 laser has recently been approved as a safe and effective new surgical intervention in the treatment of refractory chest pain secondary to coronary artery occlusive disease. Sen et al.[1] first used needle acupuncture in the 1960s as a means of carrying left ventricular blood into ischemic myocardium. Subsequently, others tried to create channels with needles, knobbed cannulae, and larger diameter cylinders. Eventually, in the early 1970s, Mirhoseini and Cayton[2] suggested the use of lasers. Several energy sources have been used since, which include high- and low-energy beam carbon dioxide lasers, holmium:YAG (Ho:YAG) and excimer lasers, argon lasers, and even radiofrequency devices. Because the tissue-interaction characteristics of the laser's beam are highly dependent on the wavelength of the emitted radiation, it is not surprising that each modality acts in a unique way to create a transmural channel. Further, each imparts a different sort of damage to the tissue adjacent to the channel itself. The eventual fate of the channel depends on these initial interactions. Therefore, the choice of light source is a major factor in determining the success of the procedure and eventually, the prognosis of the patient.

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Effect of the Laser Source on Laser-Tissue Interactions

Laser Principle

The word *laser* is an acronym for "light amplification by stimulated emission of radiation." A laser works by bombarding molecules in a laser medium with an outside energy source, thereby carrying the orbital electrons of these molecules to a higher level of excitation. As the excited electrons return to their natural-energy state, they emit a photon. The photon

is made to oscillate back and forth between two reflective mirrors placed on either end of the laser cavity, which contains the laser medium. Each newly created photon hits numerous other molecules and excites their electrons during this process. In turn, the molecules release a new photon that adds to the flurry of photonic traffic crossing the laser cavity. This process of amplification continues until the cavity is filled to capacity with photons. When the operator activates the laser by removing one of the reflective surfaces from the path of the photons, they are released from the laser cavity in the form of a beam.

Effect of Laser Wavelength

The type of molecule in the laser medium dictates the wavelength of the emitted photons. Since the initial molecules in the medium are identical (the medium is pure), the photons all have the same wavelength and frequency, which adds to the potency of the laser beam. The wavelength of the photons determines the "color" of the radiation, and the frequency of the photons determines the energy of the radiation. (The wavelength and frequency of the photons are inversely proportional and related to each other by Planck's constant.) Furthermore, when this beam of identical photons hits the target tissue, the natural vibration frequency of the molecules that make up the tissue determines the type of interaction between the incident laser photon and the resident tissue molecule. If, in its natural state, the tissue molecule vibrates at a frequency similar to the vibration frequency of the laser photon, the interaction between the molecule and the photon is maximized. Therefore, the photon's energy is absorbed by the first molecule the laser photon hits. However, if the vibration frequencies of the laser photon and the tissue molecule are not similar, only a small fraction of the incoming photon's energy can be imparted on the tissue molecule. The photon is then deflected toward another molecule with which it interacts. In this case, "scattering" is said to dominate the laser-tissue interaction. The ratio of absorption to scattering (albedo) of a light beam inside a particular tissue determines the nature of the interaction. If the albedo is high (if absorption dominates), then the effect of the laser is limited to the relatively few molecules directly hit by the incoming beam. If the albedo is low (if scattering dominates), a relatively larger volume of tissue is affected by the scattering photons of the incoming beam, thereby causing more "collateral damage." Thus, using a laser that "vibrates" closer to the target tissue will achieve a precision ablation, whereas using a laser that vibrates "out of tune" with the target tissue will achieve a volume ablation. The depth of penetration of a laser beam in tissue, therefore, is determined by the albedo of that particular laser-tissue combination. Obviously, the operative task dictates the choice of laser for any particular tissue. Delicate processes such as ophthalmologic or cardiovascular interventions require precision ablation, whereas removal of tumors in gynecologic or dermatologic procedures is more suited to volume ablation.

Effect of Optical Properties of Target Tissue

The nature of laser-tissue interactions in cardiovascular applications is dominated by the absorption peaks of water (water molecules are the major constituents of cardiovascular tissue) and of dipeptide bonds (protein molecules are the major constituents of cardiac muscle). As mentioned previously, photonic vibrations (wavelength and frequency) are associated with the "color" and energy of the individual photons. Photons with more energy (such as cosmic rays or gamma rays) vibrate faster and have a shorter wavelength, whereas less energetic photons (microwaves or radiowave radiations) have a lower vibrational frequency and longer wavelength. If the photon's wavelength falls within the 400 to 700 nm range, it interacts with the retinal molecules in the human eye; hence, the light in this range becomes "visible" (Fig 1). The color of light that vibrates at the lower range of the visible spectrum (400 nm) appears violet to the eye. Any light with a shorter wavelength is referred to as ultraviolet (UV) because it is more energetic than violet light. The excimer laser is an example of a UV laser. Its high photonic energy is capable of breaking the dipeptide bonds in the tissue just as UV light in the sun can mutate the DNA molecule in human skin following excessive exposures.

By contrast, light made of photons vibrating at the upper range of the visible spectrum is perceived as red by the human eye. Any light with a wavelength longer than the red light (any less energetic light) is called infrared (IR). The photons of the IR light vibrate at frequencies similar to the vibrational frequency of water molecules. Therefore, IR light is predominantly absorbed by water (much like the IR light in a microwave, which cooks the water-containing chicken but not the ceramic plate). The

Ho:YAG and CO_2 lasers are examples of IR lasers that interact with tissue by heating water molecules. Because cardiovascular tissue is made up both of water and protein, it is possible to conduct cardiovascular procedures such as laser angioplasty or TMLR using excimer, Ho:YAG, or CO_2 lasers.

Effect of Pulse Parameters

A laser can emit a beam of photons in a continuous or pulsating fashion. The emission of a continuous wave laser can be interrupted at regular intervals (chopped) to create a pulselike effect. A pulsed laser can deliver the photon beam in varying frequencies (number of pulses delivered per second) and varying duration (the width of the pulse in seconds). Furthermore, the total energy carried by a pulse of a certain width can vary according to the capacity of the laser and the needs of the operator. The energy of the laser photons loaded in each pulse perform the so-called tissue ablation (i.e., actual tissue removal by vaporization or tissue disruption by charring and degeneration). Laser ablation occurs both coaxial with and perpendicular to the direction of the advancing photons. The extent of vaporization and disruption of tissue in the coaxial direction with each pulse is termed *ablation depth* while that in the perpendicular direction is called collateral damage. Ablation depth and collateral damage are a direct function of pulse energy. Ablation depth is not to be confused with penetration depth; the former pertains to the laser beam and the latter to individual photons.

Characteristics of Tissue Ablation

Tissue ablation may be due to thermal effects (as is the case with low photon energy IR lasers) or to molecular dissociation (as is the case with high photon energy UV lasers). In both instances, only a percentage of photon energy is used to perform the actual work of ablation; the rest of the photon energy is washed and converted to heat. Thermal conductive processes in the tissue dissipate this excess heat into neighboring tissue molecules. The net result is increased tissue temperature in the vicinity of the laser beam.

In pulsed lasers, the arrival of two successive pulses must be separated by a sufficient time interval to allow for complete thermal dissipation; otherwise, the accumulated heat will "boil" the tissue, causing it to expand and, eventually, explode under the pressure. Such explosive ablations create acoustic waves, which travel laterally along planes of lower resistance, causing substantial structural trauma as well as thermal coagulation. A shorter laser pulse delivers more energy to the tissue per unit time. Therefore, the energy converted to heat (the energy not used for the actual tissue ablation) will be higher with shorter pulse lasers. Consequently, at certain albedos, lasers operating at high-peak powers (high energy per unit time) are more prone to induce collateral heating and damage in some tissues.[3]

Effect of Laser Parameters in TMLR

Over the last decade, TMLR has proven to be an effective new option for the treatment of refractory coronary artery occlusive disease. As a result, many other laser modalities have been proposed as an alternative to the CO_2 laser. Among these, the most notable are the Ho:YAG and the excimer lasers. The Ho:YAG laser, a near IR laser with a pulse energy of approximately 1 J and a pulse duration of microseconds, characteristically operates at a peak power range of 5 to 10 kilowatts (kW) and can be pulsed at 1 to 20 pulses/sec. In contrast, the excimer laser is a UV laser that operates at pulse energy of approximately 250 mJ and can be pulsed at approximately 50 pulses/second. Despite this low energy level, the extremely short duration of its pulse (nanoseconds) imparts very high levels of peak power to excimer laser irradiation (on the order of gigawatts). Because tissue disruption by molecular bond breakup prevails over tissue heating, however, ablation with the excimer laser never involves the explosive properties that are notoriously associated with the Ho:YAG laser. The pulse energy is a particularly important parameter in the application of the various types of lasers to TMLR. Because the pulse energy determines the depth of ablation, lasers operating at lower pulse energy levels require more than one pulse to create a single channel. Arrhythmias may result when one or more of these pulses unavoidably coincides with the T wave of the electrocardiogram (ECG) where the heart is repolarizing. Therefore, the excimer laser's high pulsing frequency may be an irritant to the electrical stability of the heart.[4] Moreover, the motion of the beating heart under the laser beam is also problematic: The formation of a straight channel, which has a better chance of remaining patent, becomes impossible if multiple pulses are required to form a single channel.

By comparison, the CO_2 laser operates at 20 to 80 J/pulse, with a pulse duration of 25 to 100 msec and a

peak power of 800 W. At this level, the IR energy of the laser photons does not cause explosive ablation, thereby limiting the extent of structural damage. Further, the high-pulse energy is capable, even at the low end of 20 J/pulse, of crossing the myocardial thickness with a single pulse. Because the firing of the CO_2 laser is synchronized to the R wave, and the duration of the pulse is less than the S-T interval, arrhythmic complications are minimized. However, the CO_2 laser has a relatively long pulse duration compared with the Ho:YAG and excimer lasers. The longer exposure of the cardiac tissue to the incident beam increases the amount of thermal injury. Excessive thermal injury may amplify the tissue response and reduce channel patency in the long term. This problem can and should be addressed by using the lowest energy setting capable of crossing the myocardium with a single pulse. In normal myocardium, this usually coincides with 20 J/pulse, but in the presence of myocardial scarring or epicardial fat, the energy level may have to be as high as 60 J/pulse.

Controversies and Clinical Considerations

Since its inception, the TMLR procedure has been controversial. Questions and opinions usually belong to one of three categories: feasibility of the procedure, mechanism(s) of action, and the suitability and efficacy of various laser modalities. An in-depth discussion of the first two categories has been described previously.[5]

Briefly, the first category deals with the following questions: (1) Does the human myocardium have a sinusoidal anatomy that may lend itself to subendocardial perfusion from an intracavitary source? (2) Is it physiologically possible to conduct blood from the ventricle into the contracting myocardium? (i.e., Is there a positive pressure gradient in that direction?) (3) Do the laser channels stay patent in the long term to convey blood from the ventricle into the myocardial sinusoids? (4) Is it possible to demonstrate an increase in the subendocardial perfusion following the TMLR procedure? (5) Most important, do patients benefit from the procedure? Unfortunately, there seems to be no clear-cut answer to these questions at the anatomic, physiological, histological, diagnostic, and clinical level, which adds to the controversy surrounding TMLR.

The second category includes the possible mechanisms of action that may be responsible for the clinical benefits. The various mechanisms that have been proposed are increased perfusion via patent channels, laser-induced angiogenesis, cardiomyocyte denervation due to laser-induced tissue removal, placebo effect, and any combination of the aforementioned. No scientifically valid answer exists to confirm or deny the role of any of these possibilities.

The third category of questions regards the suitability of various laser modalities. The CO_2 laser cannot be transmitted via fiberoptics, so TMLR using the CO_2 laser must be performed via a left thoracotomy. However, the Ho:YAG and excimer lasers can be transmitted via fiberoptics and, therefore, provide the option of percutaneous TMLR (PTMR). Although PTMR may be attractive because surgical trauma to the patient is limited and financial cost is reduced, it still is not a proven technique. The laser modalities associated with PTMR are plagued by creation of excessive tissue trauma and/or arrhythmogenicity. Multicenter, randomized clinical trials comparing the three modalities are necessary to delineate the differences, if any, in safety and efficacy.

The most relevant aspect of the controversy is whether the patient's symptoms can be improved with an accompanying improvement in perfusion and without loss of myocardial function. Demonstrating positive perfusional changes has been difficult, mainly because of the subtle nature of the changes involved (if any) and to the limitations of the specificity and accuracy of available diagnostic methods. The gold standard in nuclear perfusion imaging is still positron emission tomography (PET), but this expensive test is not available in most hospitals. At the Texas Heart Institute, we have followed up a limited series of patients and reported our findings of significantly improved subendocardial perfusion of laser treated areas of the myocardium 12 months or more after the procedure.[6,7] We believe that those data are still the strongest evidence of the utility of TMLR in the clinical setting of refractory coronary artery occlusive disease.

Improved Cardiac Function and Perfusion After TMLR

We have previously reported anatomic evidence for the patency of laser channels 3 months after the procedure. In that one isolated clinical case, the patient had died of a recent inferoposterior infarct in the area of the right coronary arterial distribution.[8] The present case report outlines the 12-month postoperative course of a patient treated with TMLR.

Clinical Protocol

The research protocol included patients with angina whose symptoms were not responsive to maximal medical treatment. Patients were preselected if review of their cineangiogram revealed distal and diffuse coronary artery disease not amenable to aortocoronary bypass grafting or percutaneous transluminal coronary angioplasty (PTCA). Patients were evaluated to identify and locate ischemic myocardial regions. Rest-stress (dipyridamole-handgrip) myocardial perfusion and resting glucose metabolism were determined by PET using ^{13}N-ammonia and ^{18}F-deoxyglucose as radioactive tracers, respectively. Left ventricular ejection fraction (LVEF) and regional wall motion indices were determined by echocardiography before and after administration of dobutamine. LVEF at rest was also measured by multiple gated acquisition (MUGA) scan. Exercise tolerance was determined by treadmill testing according to a Bruce protocol standardized for this study. To assess the effects of the treatment, the functional and perfusional status of the laser-treated regions were reevaluated at 3, 6, and 12 months.

Preoperative Evaluation

A 55-year-old white man with a history of severe coronary artery disease, hypertension, and tobacco use was seen for recurrent angina that had worsened over the last 3 months. At the time of evaluation, he was experiencing severe chest pain if he walked the distance of one block or up an incline. His pain was responsive to sublingual nitroglycerine. He had undergone an aortocoronary bypass in 1980 and repeat bypass surgery in 1988. At the time of his repeat surgery, the left internal mammary artery (LIMA), which was used for the bypass, was anastomosed to the distal diagonal branch of the left anterior descending artery (LAD). At the time of his evaluation, his hypertension was successfully controlled with calcium channel blockers and angiotensin-converting enzyme inhibitors. There was no evidence of congestive heart failure. On review of his cineangiogram, it was noted that the patient had severe coronary artery disease in multiple arteries, with 100% occlusion of the LIMA and the right coronary artery (RCA) grafts, and distal and diffuse involvement of the LAD, the circumflex, and the RCA distributions, none of which was deemed amenable to repeat revascularization by bypass surgery or balloon angioplasty. At that time, the patient was asked whether he would be willing to participate in the TMLR study. He agreed and, after signing the informed consent form, he was evaluated for the presence of reversible ischemic myocardium.

PET images of myocardial glucose metabolism (Fig 2A) and rest perfusion (Fig 3A) revealed an old, nontransmural scar located in the inferolateral aspect of the apex. There was a significant rest perfusion defect in the lateral wall (Fig 3A). After dipyridamole was administered, the defect became larger and more severe, extending to the inferior wall as well (Fig 4A). Steal in the lateral and inferior myocardium during stress was suggestive of extensive collateral flow. In addition, the ^{18}F-deoxyglucose images (Fig 2A) showed a large, severe metabolic defect in the mid-septal wall, extending anteriorly into the mid-LAD area. By contrast, the mid and basal segments of the inferolateral wall were metabolically active. On echocardiography, the LAD territory and the inferobasal wall demonstrated resting hypokinesis. With low-dose dobutamine (10 mg/kg/min), the inferobasal wall was not well seen but systolic function improved elsewhere. The overall LVEF by echocardiography was estimated to be 50% at rest and 55% at maximum stress. MUGA with intravenous (IV) injection of 20.7 pCi 99mTc-pertechnetate revealed an LVEF of 46%. On demonstration of reversible ischemia in a significant viable area of the left ventricular myocardium, the patient was taken to surgery for the TMLR procedure on January 14, 1994.

Surgical Procedure

General anesthesia was administered through a double-lumen Carlens endotracheal tube for selective right pulmonary ventilation. The left anterolateral aspect of the chest wall was draped, and the chest cavity was entered from the fifth intercostal space. The heart was placed in a pericardial cradle. A focusing probe was mounted at the working end of the 7-mirror-articulating arm of the CO_2 laser (PLC Systems, Inc, Milford, MA). The probe was brought in contact with the epicardial surface of the ischemic myocardium. Activation of the laser was synchronized with the electrocardiographic signal of the patient to coincide with the early R-T interval. The initial output energy level of the laser was set at 40 J, but depending on the amount of epicardial adipose tissue present, the energy level varied between 40 and 15 J (higher pulse energies were used in areas of more fat). A total of 31 energy bursts were delivered

to the ischemic areas (4 at 40 J, 6 at 35 J, 3 at 30 J, 7 at 25 J, 1 at 20 J, and 10 at 15 J). The transmyocardial penetration of 25 of these 31 bursts was confirmed by observing, through intraoperative transesophageal echocardiography, the instantaneous formation of intraventricular steam on contact of the laser beam with blood inside the left ventricle. Hemostasis at the site of each hole was established by gentle external digital pressure for 1 to 2 minutes and by applying Surgiseal (Johnson & Johnson, Arlington, TX) soaked in thrombin, or, in the case of 2 holes, by placing purse-string sutures. A right-angle probe was used for access to the inferoposterior aspect of the heart. On completion of the procedure, the pericardium was left open, and the chest incision was closed in the routine manner. There were no intraoperative complications, and the patient tolerated the procedure well. He had standard postoperative care. The postoperative course was unremarkable, and the patient was discharged on postoperative day 6 in good condition with moderate incisional pain.

Follow-up

After the procedure, the patient reported immediate cessation of angina. Over the next 3 months, he gradually returned to his normal level of daily activity. At no time during the 12-month observation period did the patient have a need for oral or IV nitroglycerin. At 12 months, he remained asymptomatic. He was active at work and was exercising regularly on his treadmill machine at home for 30 minutes daily. At the 3- and 6-month follow-up evaluations, the patient had achieved 8.2 and 9.1 metabolic equivalents of task (METs), respectively, on the treadmill machine. His ECG at baseline and at peak exercise revealed nonspecific changes of 1-mm, down-sloping ST depression in leads 1 and 2. Exercise time was 15 minutes at 3 months and 23 minutes 26 seconds at 6 months. At 12 months, he was able to produce 10.2 METs on the treadmill machine in 25 minutes 57 seconds. At 12 months, his ECG tracings were similar to the tracings at 3 and 6 months.

At 3 months, we were unable to conduct a metabolic PET study because of technical problems with the equipment. Perfusion imaging, however, was performed under resting conditions and showed major improvement throughout the myocardium (with the exception of a small apical defect located inferolaterally, which appeared to be a remnant of the preoperative ischemic zone) (Fig 3B). After dipyridamole infusion, the overall distribution of blood throughout the myocardium was significantly improved over that in the preoperative state (Fig 4B). The dipyridamole/rest perfusion ratio indicated the presence of myocardial steal in the basal inferolateral wall only, suggesting residual collateral insufficiency to this region. At 3 months (Fig 4B) and 12 months (Fig 4C), the inferolateral perfusion defect with dipyridamole was still present; but there was major improvement in the anterior, sepal, and inferior myocardium. The metabolic images from PET scanning with ^{18}F-deoxyglucose at 6 months (Fig 2B) and at 12 months (Fig 2C) showed increasing improvement in the entire myocardium, including the lateral wall. LVEF measured by MUGA was 44% at 6 months and 53% at 12 months. By dobutamine echocardiography, the resting LVEF remained at 50% through the 12-month period, but increased to 70% during peak exercise at 6 months and 12 months. Echocardiographic analysis of the patient's wall motion throughout the follow-up period was negative for ischemia.

Discussion

In this study, we report the case of a man who when initially seen at our institution had Class IV angina (Canadian Cardiovascular Society [CCS]) resulting from distal, diffuse coronary artery disease that was causing systolic dysfunction in essentially viable myocardium. One year after treatment with TMLR, the patient remained well on the basis of both objective and subjective criteria. Immediately after TMLR treatment, the patient's angina class improved to I-II, and his sublingual nitroglycerin was discontinued. He remained symptom-free for 12 months while engaging daily in mild-to-moderate physical activity. Presently, 60 months after TMLR, the patient's symptoms are still consistent with CCS class II.

On a more objective scale, the patient's exercise tolerance improved steadily over the 12-month postoperative period, as indicated by increased time on the treadmill and the increased number of METs produced during exercise. The resting LVEF, as measured by MUGA, increased from 46% to 53% (15% of baseline). The stress LVEF by dobutamine echocardiography increased from 55% before TMLR to 70% at 12 months (an increase of 27% over baseline), despite persistent hypokinesia in the untreated septum and anterior septum.

Before TMLR, the overall PET picture was consistent with a generally viable myocardium (with the

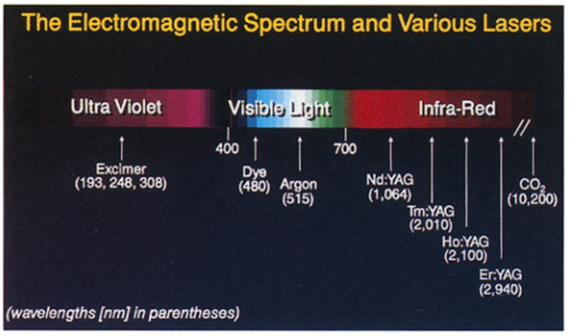


Figure 1. The electromagnetic spectrum of various lasers demonstrating the wavelength of each modality, from high-energy (left) to low-energy (right) lasers.

exception of a small apical scar located inferolaterally), which exhibited reduced resting flow apically and laterally and reduced coronary flow reserve inferiorly. At the end of 1 year, major improvements in the metabolic status of the myocardium were evident. Resting and stress blood flow was restored to the anterior, septal, inferior, and apical portions of the heart wall. The most significant improvement in cardiomyocyte metabolism was noted in the septal, anteroseptal, and mid to distal inferolateral walls (Figs 2A and 2C). Within the laser-treated myocardium, perfusion distribution during dipyridamole stress at 12 months after surgery was improved most

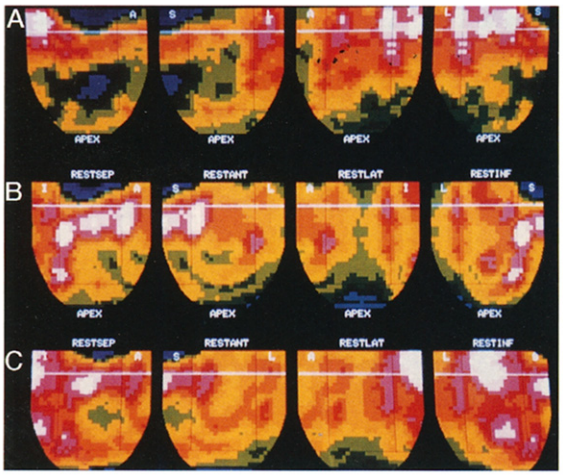


Figure 2. Metabolic imaging of the heart using ^{18}F-deoxyglucose. (A) Preoperative images showing severe metabolic defects in mid-septal and anteroseptal, as well as distal inferolateral walls. (B) Postoperative images at 6 months, showing significant improvement in septal, anterior, and distal inferior defects. (C) Images at 12 months, showing further improvement of the cardiac metabolism in all regions with the exception of the lateral apex, which possibly contains a small, old myocardial infarction. Color index of tracer uptake: red and white = high, yellow = normal; blue and black = low.

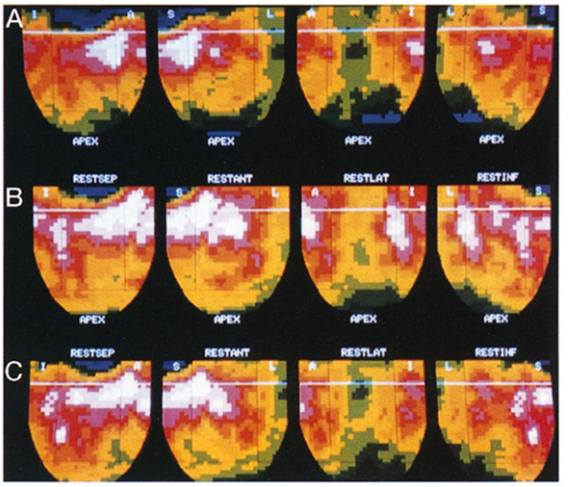


Figure 3. See Fig 2 legend for color scale. Perfusion imaging of the heart under resting conditions using $^{13}NH_3$-labeled red blood cells. (A) Preoperative images showing impaired perfusion to the entire lateral wall as well as the distal inferolateral wall and the apex. (B) Postoperative images at 3 months, suggesting marked improvement in lateral perfusion, as well as in the septal, anterior, and inferior myocardium. The lateral apex is still ischemic. (C) Images at 12 months, showing essentially the same perfusion status as at 3 months.

significantly in the anterior wall. On the dipyridamole/rest perfusion ratio image, there was evidence of myocardial steal in the inferolateral and inferior myocardium, indicating new collateral formation to

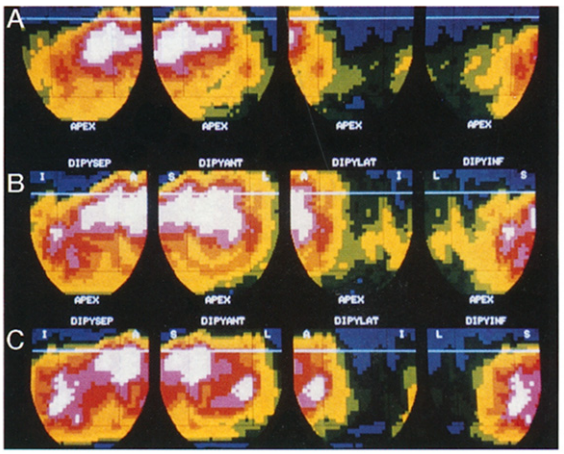


Figure 4. See Fig 2 legend for color scale. Perfusion imaging of the heart during dipyridamole-handgrip, using $^{13}NH_3$ labeled red blood cells. (A) Preoperative images showing a significant stress-induced perfusion defect along the lateral and inferolateral wall. (B) Postoperative images at 3 months, showing marked improvement in the mid-lateral wall, as well as in the septal, anterior, and the inferior walls. (C) Images at 12 months, showing significant improvement in the septal, anterior, and inferior walls.

Table 1. Regional Myocardial Perfusion Analysis by Positron Emission Tomography (SE_n/SE_p) Before and After TMLR

	Nontreated Segments			*Laser-Treated Segments*		
	*BL**	*6 mo*	*12 mo*	*BL*	*6 mo*	*12 mo*
Rest	.94	1.02	1.00	.93	1.13	1.11
Stress	.83	1.01	.99	.88	1.17	1.15

*BL, before laser.

the viable muscle in these regions of the myocardium. The patterns of blood flow distribution in the laser-treated myocardium were investigated independently by computer-aided regional analysis using the PET data at baseline and at 6 and 12 months postoperative. The rationale was based on the hypothesis that the epicardial segment of the laser channels does not connect with myocardial sinusoids due to coagulated blood inside, such that the main increase in perfusion occurs in the inner two thirds of the myocardium. In turn, this differential in the radial direction would manifest itself as a shift toward unity and beyond in the subendocardial/subepicardial perfusion ratio (SE_n/SE_p) in the period after TMLR.[6] Comparison of the SE_n/SE_p before and after laser treatment indicated a trend in the predicted direction at 6 months and 12 months after TMLR (Table 1). The calculated values of the SE_n/SE_p ratios within the laser (anterior, lateral, and mid and distal inferoposterior) regions at 6 months indicated that subendocardial perfusion exceeded subepicardial perfusion by 13% at rest and 17% during stress. This represented an increase over preoperative values of 22% at rest and 36% during stress. At 6 months, the SE_n/SE_p ratio in the nontreated regions (septal, basal inferoposterior) also had a similar, but less pronounced, shift toward and beyond unity. This shift was possibly due to the effect of the collateral circulation. At 12 months, the increase in relative subendocardial perfusion remained constant.

In conclusion, the combined clinical and PET evidence in this study indicates that TMLR effectively relieved advanced anginal symptoms of the patient over a 12-month period. His symptoms were relieved by significant improvement in the perfusion and metabolism of the essentially hibernating myocardium. These results suggest that TMLR may be useful in the treatment of symptomatic patients whose coronary artery disease is not optimally treatable by coronary artery bypass grafting (CABG) or PTCA. The efficacy of this promising technique in treating coronary artery occlusive disease as a standalone modality or as an adjunct to CABG remains to be determined by prospective clinical trials. Determining which laser modalities are suitable for TMLR, both for efficacy in reducing symptoms and for minimizing unnecessary damage to the patient's heart, is also necessary.

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