Transmyocardial Laser Therapy: A Strategic Approach

Louis Samuels,1 Robert Emery,2 Omar Lattouf,3 Michael Grosso,4 Masoud AlZeerah,5 Douglas Schuch,6 Kurt Wehberg,7 Derek Muehrcke,8 Robert Dowling9

1Lankenau Hospital, Wynnewood, Pennsylvania; 2Cardiac Surgical Associates, Minneapolis, Minnesota; 3Crawford Long Hospital/Emory Clinic, Atlanta, Georgia; 4St. Francis Hospital, Wilmington, Delaware; 5NW Texas Healthcare System, Amarillo, Texas; 6Sutter Memorial Hospital, Sacramento, California; 7Peninsula Regional Hospital, Salisbury, Maryland; 8Flagler Hospital, St. Augustine, Florida; 9University of Louisville, Louisville, Kentucky, USA

ABSTRACT

Background: Coronary artery bypass and percutaneous intervention have become the established methods of coronary revascularization in treating angina pectoris. Subsets of angina patients, however, are not amenable to either of these procedures. Transmyocardial laser revascularization (TMR) has been developed as a potential treatment to address such patients, and clinical research to date illustrates the success of TMR for this patient group.

Strategic Plan Summary: Although the symptoms of ischemic heart disease manifest themselves in a variety of ways, the best results with TMR are seen in patients with severe angina rather than in patients with silent ischemia or congestive heart failure. Potential TMR patients receive diagnostic tests to determine if and where the therapy should be applied. A recent cardiac catheterization is required to document the status of and the coronary-system suitability for the planned intervention. It is not appropriate to assume that a patient with nonbypassable, noninterventional coronary artery disease has to be relegated to medical therapy only. Additionally, echocardiography demonstrates the status of cardiac valves and segmental wall motion activity. This knowledge allows the surgeon to determine the sequence of surgery and if abnormalities are present. Once the decision to use TMR use has been made, there are 2 approaches—sole therapy or adjunctive therapy. TMR is not to be substituted for a feasible bypass graft, but the best time to make this decision may well be during the surgery itself, because grafts that appear surgically feasible on an angiogram may be less feasible after the chest has been opened. The decision to perform sole-therapy TMR in the absence of bypassable vessels clearly must be made before opening the chest. Whether to use cardiopulmonary bypass (CPB) and the sequence in which to perform TMR and bypass grafts are based on surgeon preference. The advantage of performing TMR on CPB is that channels can quickly be lased without pause. A potential advantage of performing TMR before bypass grafts is that “channel leak” (bleeding) can be minimized by the conclusion of the surgery. Complete revascularization has become technically more difficult because of the increasing use of percutaneous approaches and because patients are being referred for coronary artery bypass grafting much later in the course of their coronary disease progression than before. TMR may well be a viable alternative to bypassing a heavily diseased, previously intervened, small-diameter coronary artery. Thus, a model in which myocardial perfusion is considered within the context of the natural circulation can be perceived as an alternative to a model in which circulation is altered by interventional, surgical, and/or transmyocardial methods. TMR has been shown to be effective in accomplishing a complete revascularization when the restoration of circulation to ischemic territories with interventional therapy, bypass surgery, or a combination of both has been ineffective. We recommend that interested users follow this “complete revascularization strategy” algorithm for all ischemic vessels being considered for interventional or surgical treatment. Running each diseased vessel through this thought process will ensure that available treatment options are considered in the optimization of a patient’s outcome.

Conclusion: The use of TMR for angina relief has evolved into a clinically proven technology that has enabled physicians to address difficult revascularization cases with a therapy that is safe and effective.

INTRODUCTION

Over the last 4 decades, great advances have taken place in treating patients with angina pectoris. The historical Vineberg procedure led the way toward modern coronary artery bypass grafting (CABG). Local coronary endarterectomy, local coronary-to-coronary bypass, left main coronary artery endarterectomy, surgical angioplasty of the left main coronary artery, periaortic sympathectomy, and needle myocardial puncture have all been tried with limited success. Coronary artery bypass and percutaneous coronary intervention have become the established, universally accepted methods of coronary revascularization.
transmyocardial laser revascularization (TMR) through laser
channel formation [Mirhoseini 1988].

The mechanism of action (see Table 1), the clinical data from
TMR, and the use of transmyocardial laser revascularization
(TMR) through laser transmyocardial channel formation
[Mirhoseini 1988].

Perhaps the most interesting aspect of TMR therapy is
that despite the lack of a complete understanding of the
mechanism of action (see Table 1), the clinical data from
delayed research trials and studies illustrate a significant
patient benefit from TMR. Numerous reports on prospective
randomized trials have documented the efficacy of TMR for
patients with angina [Allen 1999, Burkhoff 1999, Frazier
1999, Horvath 2001]. A controlled prospective trial con-
ducted by the US Food and Drug Administration (FDA)
showed that TMR laser therapy improved function and long-
term survival with increased exercise tolerance at 3 years after
therapy [Horvath 1997, Horvath 2001]. Cooley et al confirmed
enhanced angina relief that was attributable to TMR laser therapy
[Cooley 1996]. Dr. Larry Cohn and colleagues reported improved clinical symptoms and increased exercise
tolerance for 2 postoperative years in 20 no-option patients
who had failed aggressive medical treatment [Horvath 1996].

In a multicenter study, TMR as sole therapy for patients
with end-stage coronary disease and prior intervention was
found to be valuable in decreasing angina level, improving
myocardial perfusion, and decreasing hospital readmission
incidence [Horvath 1997]. TMR was shown in a prospective
randomized trial to cause a decrease in angina by 2 levels in
61% of treated patients, compared with only 11% of patients
who received medical therapy without TMR [Burkoff 1999].

A multicenter prospective randomized trial conducted at 16
US medical centers with 221 patients in an FDA-approved
protocol demonstrated a significant reduction in the 30-day
mortality rate from 7.0% to 0.9% for patients with CAGB
and TMR, compared with CAGB alone [Allen 2000].

Clearly, most of the clinical results to date have been
impressive, and the data in support of TMR use continue to
grow. In this regard, a recent evidence-based review by the
Society of Thoracic Surgeons (STS) concluded, “TMR offers
consistent amelioration of severe angina in patients having no
conventional therapeutic alternative” [Bridger 2003]. The
STS workforce reviewed many of the important trials and
studies that we have discussed here and has made valuable
recommendations. Additionally, an observational retro-
spective review that identified 3717 patients who received
TMR at 173 US hospitals participating in the STS National
Cardiac Database was recently published by the Journal of the
American College of Cardiology (JACC) [Peterson 2003].

Some interpretations of this JACC article that stated that
the data collected by its authors illustrate the high procedural
risks with TMR seem misguided. In the JACC review, the
TMR operative mortality rate was stated as 6.4%. This TMR
operative mortality rate, however, is reduced to 3.7% when it
is adjusted for high-risk patients, which consist of those
patients with recent myocardial infarction, unstable angina,
and depressed ventricular function (ejection fraction [EF] <30%). This review also placed the operative mortality rate at 4.2% for patients with TMR plus CABG—a rate that was reduced to 2.6% when it was adjusted for the same risk factors. Cardiac surgeons currently account for high-risk patients through the process of TMR patient selection. The risk-adjusted TMR operative mortality rate in the range of 2.6% to 3.7% in the United States shown here is comparable to the operative mortality rates of CABG alone.

The observational data and the analysis from this JACC report provide insight into and support for observations made in the controlled clinical TMR trials, namely that recent major adverse cardiac events increase operative mortality risk, that patients with unstable symptoms have mortality rates nearly twice as high as those without such symptoms, and that risks are lower at centers with higher annual TMR caseloads. These results point out the potential for a reduction in TMR morbidity and mortality through the optimization and timing of the procedure. This statement represents the exact conclusions of the authors of the JACC review [Peterson 2003] and also represents a goal of the present report. Our purpose is to take these recommendations one step further and to describe a strategic, practical approach to TMR use within daily cardiac surgical practice.

**Guiding Principle**

The principles of safety and efficacy guide our TMR strategic plan. Each case must be considered within the context of these principles to achieve a satisfactory result. It must be remembered that the primary indication for TMR therapy is class IV angina refractory to medical management. Although the symptoms of ischemic heart disease manifest themselves in a variety of ways, our surgical experience indicates that the best results seen with TMR therapy have been in those patients with angina rather than in patients with silent ischemia or ischemic congestive heart failure.

A violation of these safety and efficacy rules is realized when TMR is introduced to patients with shortness of breath secondary to ischemic cardiomyopathy. Initially, the use of TMR in this scenario may seem appealing, particularly if the angiogenesis mechanism-of-action theory applies (Table 1) and there are no bypassable vessels. However, at this time the angiogenesis theory alone is not a valid reason to apply TMR in the hope of augmenting blood flow to a ventricle with myopathy of ischemic origin. The result of TMR in this setting may well be a more myopathic ventricle with multiple laser channels. Research has recently begun, however, that may ultimately lead to a change in this rule. The introduction of angiogenic growth factors and pluripotential stem cells or myoblasts within TMR laser channels in an attempt to restore the functional state of the failing myocardium [Hughes 1999], as well as linking the data of post-TMR improvement in myocardial perfusion and function to clinical benefit (angina relief), has the potential to change the way that TMR fits into the cardiac treatment regimen. Until these investigational procedures have been studied and validated, however, the safest and most effective strategy is to apply TMR in the treatment of angina patients with ventricular function that is normal or mildly to moderately depressed.

**Cardiac Catheterization**

Patients being considered for TMR therapy must have a recent cardiac catheterization to document the status of and coronary-system suitability for the planned intervention. Cardiac catheterizations no older than 1 year are usually considered adequate in the absence of new evidence of congestive heart failure and in the presence of stable echocardiographic findings. New-onset or unstable angina may be a function of advanced stenosis in native vessels or previously bypassed vessels. It is not appropriate to assume that a patient with previously “non-bypassable, non-interventional CAD” is to be relegated to medical therapy only.

According to recent STS guidelines and from the data that have been collected to date, TMR may be indicated as sole therapy or in conjunction with other procedures. These other procedures can include medical, interventional, and/or surgical approaches. Cardiac catheterization results will determine which technique will result in the most optimal form of revascularization. Because we know that angina is a function of myocardial ischemia, it is appropriate to consider relief of ischemia as our primary goal. TMR, therefore, is designed as one of the therapies in our treatment regimen by which to achieve this goal. Although TMR is not to be substituted for a bypass graft, it can certainly serve as an adjunct in those cases in which there are areas of the heart that are not amenable to bypass grafting or in which graft flows are suboptimal because of limited runoff. In summary, therefore, coronary angiography serves to delineate the best approach to define treatment strategy for angina of ischemic origin, whether TMR or other procedures are used.

**Echocardiography**

Echocardiography (some surgeons prefer the evaluation of the LV angiogram) can be an essential part of TMR evaluation for several reasons. Echocardiography, in addition to identifying overall right ventricular (RV) and LV function, also reveals the status of intracardiac valves and segmental wall motion activity. Although cardiac valvular disease is not a contraindication to TMR, it is essential that this information be obtained prior to the operative procedure so that the sequence of surgery can be planned. Knowledge of segmental wall motion abnormalities is important, as is knowledge of LV thickness and RV status.

Although TMR is not traditionally applied to the RV, TMR laser application to the LV may temporarily cause deterioration of LV function, thus creating an increased workload on the right side, which is a problem if the RV is already vulnerable. Intraoperative echocardiography is not necessarily routine unless TMR is being done with a valvular procedure or unless there is some concern about ventricular function. Some surgeons, however, believe that echocardiography should be done with every heart operation, and we are not recommending changes to a surgeon’s normal surgical practice.
Viability Study

Nuclear scintigraphic, dobutamine stress echocardiographic, and positron emission tomographic techniques have been applied in TMR cases, both in an effort to discern the physiological effects of laser therapy after treatment and in an attempt to explain the scientific reasons for the observed clinical benefit [Horvath 1997, Burkhoff 1999, Frazier 1999]. Although a common practice originally was to obtain myocardial viability results of some type prior to TMR (using one of the mentioned methods), such viability studies are used less often in the general setting. The role of the viability study is to determine the areas of myocardium that would benefit from revascularization and those areas that would not (eg, scar). Correlation of the coronary angiogram and the echocardiogram is helpful in assessing the need for a bypass graft, TMR, or both.

Although these viability studies are informative, they are not absolutely necessary. In a practical sense, the decision to apply TMR to a segment of the LV is based on the presence of viable-appearing myocardium and the absence of a bypassable vessel. A peri-infarction ischemic zone is another potential application. These features can often be determined by direct vision. Thus, a territory that has no bypassable or has poorly bypassable vessels would be a prime target for TMR. “Speckled areas,” which are observed through a viability study, are representative of a scattered infarct. These areas can still be considered viable, however, because the zones of permanent damage versus mere injury are often ill defined.

Surgical Approach

In common surgical application, there are 2 approaches to TMR—sole therapy and adjunctive therapy. Additional considerations include the presence of a prior sternotomy, the need for a concomitant valve procedure, and whether the operation is being performed on or off cardiopulmonary bypass (CPB). Several algorithms presented in the accompanying figures (Figures 1-3) take these issues as well as the alternative treatment paths into account.

When using these algorithms as they pertain to TMR in the adjunctive setting, the surgeon faces a major decision about when the determination of bypass graft feasibility is made. As we previously stated, TMR is not to be substituted for a bypass graft if that graft is technically feasible and will remain patent or if graft flows are optimal. However, when should the surgeon make the decision that a graft cannot be performed? Although the views of surgeons may differ on this matter, we suggest that when TMR is being performed as an adjunct to CABG, the most opportune time to make this decision is during the surgery itself. Grafts that may appear feasible on an angiogram may be less feasible after the chest has been opened. Clearly, however, the decision on the appropriateness of TMR must be made before making a chest incision when TMR is performed as a sole therapy.

Generally, the choice of incision (sternotomy versus left thoracotomy) for patients without prior cardiac surgery is a matter of surgeon preference. A primary reason to use the transsternal approach is excellent exposure to all cardiac segments. Additionally, if there were bypassable vessels not originally appreciated during catheterization, the sternal approach would more easily allow the construction of an unanticipated bypass graft. Lastly, conversion from off pump to on pump can be more readily accomplished with a transsternal approach. A primary reason to use a left thoracotomy in a patient without prior surgery may be a concern for future operations in a relatively young patient. Therefore, performing the sternotomy for subsequent procedures may need to be considered in this patient subgroup. In this regard, performing TMR thoracoscopically, either manually or robotically, is another avenue currently being explored. Success in this area can give the surgeon another alternative in using TMR in the least invasive manner.

For those patients who have had prior cardiac procedures, the left thoracotomy TMR approach is desirable to avoid adhesions and potential injury to the RV (and other structures) on reentry. The left thoracotomy begins in an anterolateral fashion, thus permitting access to most of the LV. If further exposure is necessary, the incision can be extended posteriorly. Therefore, all portions of the LV amenable to TMR can be accessed through this approach. Some surgeons find that a double-lumen endotracheal tube facilitates access to the left side of the heart, whereas others feel that a single-lumen endotracheal tube provides adequate exposure in most circumstances. Paying particular attention to prior grafts and the phrenic nerve is an important point of consideration. Also notable is that the adhesions encountered with this approach are on average not remarkably dense, even when the patient has undergone previous cardiac surgery.

Patients requiring valve procedures will need CPB for their surgery. The operations in most of these cases are done via median sternotomy. Thus, adjunctive TMR when performed with a valve procedure is done in this setting. Minimally invasive mitral valve procedures are classically performed from the right chest with the patient on femoral bypass. Access to the LV for TMR with this approach is severely limited. Similarly, partial sternotomies for minimally invasive aortic valve procedures will not expose enough of the LV to make TMR feasible. TMR therapy via a median sternotomy is therefore recommended when the procedure is to be performed in the same surgical setting as a valve procedure.

As with the choice of surgical approach, the decision to use CPB is based on the surgeon’s preference. Most sole-therapy TMR procedures are done off CPB. Depending on the preference of the surgeon, bypass graft adjunctive therapy (TMR in addition to CABG) can be done on or off CPB. An important consideration in an adjunctive-therapy setting with bypass grafting is the timing of TMR. Whether TMR is done on or off CPB, it is important to inspect the heart during surgery for bypassable vessels and to plan the operation accordingly. For example, totally occluded vessels that were not visualized via catheterization may present during surgery. In such circumstances, it is prudent to construct a bypass graft in this area. On the other hand, if a target vessel is found to be un bypassable, the surgeon can consequently apply TMR to this territory. We suggest that the sequence of grafting and TMR (which is done first) depends on whether CPB is used (see Figure 2). However, depending on the surgeon’s preference, TMR may be performed with CABG in any order—on or off
bypass. If a minimally invasive direct coronary artery bypass procedure is used, TMR may be applied to other areas of the heart, generally before the construction of the graft of the left internal mammary artery (LIMA) to the left anterior descending coronary artery (LAD) graft to avoid tension on the newly constructed anastomosis.

**Sequence**

Based on our overall experience with TMR, we have made certain observations that translate into a safe procedural approach with this therapy. A guiding principle is to apply 10 to 15 laser channels per targeted segment of the LV—the segments being defined as anterior, lateral, posterior, and inferior. TMR can be performed with the heart beating prior to the initiation of bypass, with the heart beating after CPB, or with the heart arrested (arrested-heart TMR can be performed only when a holmium:YAG laser is used, because current labeling with the carbon dioxide laser requires electrocardiographic synchronization). When TMR is performed off pump, we suggest the creation of 3 to 5 consecutive channels followed by a rest period of 1 minute before the introduction of subsequent laser channels. This procedure is an important consideration in avoiding ventricular arrhythmias and allowing for myocardial recovery. If surgery is performed on pump, however, all channels can be consecutively lased without pause.

When TMR is used in a sole-therapy approach, the first matter is to establish the absence of bypassable vessels.
Once this has been confirmed, there is no need for heparin therapy. As we have previously discussed, although a double-lumen endobronchial tube is not necessary to prepare for the procedure, it is recommended if a thoracotomy is to be performed. Again, a thoracotomy is especially recommended if a previous median sternotomy has been performed and adhesions from the pericardium to the lung are evident. The availability of external defibrillator pads is suggested during the thoracotomy and pericardial dissection because of the possibility of ventricular arrhythmias. Perioperative oral amiodarone, intraoperative lidocaine, or intraoperative intravenous amiodarone therapy is also recommended. A Swan-Ganz catheter is suggested because the judicious use of fluids is warranted during this procedure. No more than 1.5 L of fluid is recommended during sole-therapy TMR. Once all pericardial dissection is complete, the availability of pediatric internal defibrillator paddles is recommended. If all territories are to be addressed, a practical approach is to begin with the inferior and posterior segments, proceed to the lateral segment, and conclude with the anterior segment. In this fashion, the more difficult areas are treated first, with less cardiac manipulation occurring at the end of the operation. A potential advantage of this approach is that by the time the anterior segment is addressed, the inferoposterior channels are likely to have stopped bleeding. Furthermore, there is less chance for

![Figure 2: Transmyocardial laser revascularization (TMR) adjunctive therapy (with coronary artery bypass grafting [CABG]). CPB indicates cardiopulmonary bypass; LV, left ventricle; RV, right ventricle; IABP, intra-aortic balloon pump.](image-url)
Figure 3. A strategic plan of transmyocardial laser revascularization (TMR) via a complete revascularization strategy. CAD indicates coronary artery disease; PTCA, percutaneous transluminal coronary angioplasty; cath, catheterization; EF, ejection fraction; CHF, congestive heart failure; CABG, coronary artery bypass grafting; CPB, cardiopulmonary bypass; LV, left ventricle; RV, right ventricle; IABP, intra-aortic balloon pump.
hemodynamic instability if this sequence is followed, because there is no need for cardiac manipulation during the final stages of the procedure. Another sequential possibility recommended by some TMR surgeons is merely to begin creating channels in the territory most likely to cause angina symptoms.

For the adjunctive therapy approach (CABG plus TMR), the initial decision is to determine if CPB is necessary (see Figure 2). If CPB is to be used, then full heparinization is necessary. For those surgeons who choose to do TMR on an arrested heart, the advantage of performing TMR on CPB is that channels can be quickly lased without pausing after every 5 channels (to allow the heart recovery time). In addition, the advantage of performing TMR before performing bypass grafts for surgeons who choose to do so in cases using CPB is that “channel leak” (bleeding) is minimized by the time surgery is concluded. In this situation, we suggest heparin administration after TMR is complete, and cannulation can be used to minimize bleeding. Retarding the venous return slightly will distend the heart and allow easier manipulation. If bypass grafting is chosen to be done off pump (beating heart surgery), heparinization is done in accordance with institutional protocols. Our recommendations range from 10,000 U heparin to 1.0 to 1.5 mg heparin/kg body weight. In either case, all bypass grafts are completed, and graft flows are then assessed. Following graft placement, TMR is performed to all targeted segments (any nonbypassable ischemic areas or grafted segments in which the bypass flows are suboptimal or at risk of early graft failure). In an alternative method for performing adjunctive CABG plus TMR, some surgeons perform TMR on a partially filled LV while the patient is on CPB because of their experience of better tactile and auditory feedback when the heart is partially full (to assure full transmural, transmyocardial lasering). In this method, all distal and then proximal graft anastomoses would be performed first, with the TMR being carried out second. These methodologies are meant as a guide; each surgeon should use what works best.

On a final note, recent data have shown that outcomes may be improved to suboptimal targets by using TMR plus CABG instead of CABG alone [Wehberg 2003]. These data suggest that the strategy of using TMR in a region of suboptimal targets rather than attempting to place a graft improves intensive care unit times, the lengths of hospital stays, atrial fibrillation rates, and mortality rates. The authors of this report speculated that the outcomes with CABG plus TMR were most likely improved because a region of the LV was not compromised by opening up a less-than-desirable grafting target.

**Complete Revascularization**

The goal of any revascularization therapy is to restore circulation to ischemic areas and thereby relieve symptoms caused by the lack of oxygen. Complete revascularization has been traditionally achieved by interventional therapy, bypass surgery, or a combination of both. However, in the event that these conventional therapies are not feasible, TMR has been shown to be effective [Allen 1999, Burkhoff 1999, Frazier 1999, Horvath 2001]. In fact, with the increasing use of percutaneous approaches (percutaneous coronary intervention/stents), patients are being referred for CABG much later in the course of their CAD progression than before. Complete revascularization has thus become technically more difficult, if not impossible, with CABG surgery. TMR may well be a viable alternative to bypassing a heavily diseased, previously intervened, small-diameter (≤1.5 mm) coronary artery.

Thus, a model in which myocardial perfusion is considered in the context of the natural circulation can be conceived as an alternative to one in which circulation is altered by interventional, surgical, and/or transmyocardial laser revascularization methods. The model can be envisioned by plotting the myocardial territories on a grid and determining which method would address the circulation to that territory. For example, if an angina patient presents with catheterization findings showing a discrete proximal stenosis to the right coronary artery (RCA), a complex mid LAD stenosis with an unobstructed diagonal branch, and a completely occluded, nonvisible left circumflex artery system, then one approach might be the one illustrated in Table 2.

Again, this is one approach, and the opinions of cardiologist or surgeon readers may differ as to which approach to take in this particular hypothetical case. Nevertheless, the idea being advocated here is to address all territories with either interventional or surgical methods to ensure complete revascularization.

The surgery in this particular case can be done via sternotomy or left thoracotomy, with the latter approach being desirable if the patient has had a prior cardiac procedure or is young with the likelihood of a sternotomy in the future. The RCA can be surgically bypassed along with the LAD, or, alternatively, a stent can be placed prior to or following CABG. It is important to remember that patients with stents are often being treated with platelet inhibitors, thus increasing risk of bleeding during and/or after TMR. It is the opinion of some

---

**Table 2. Example of a Model of Complete Revascularization in which Myocardial Perfusion Is Considered in the Context of Natural Circulation by Plotting Myocardial Territories and Determining the Best Strategy for Each Territory**

<table>
<thead>
<tr>
<th>Anterior Territory</th>
<th>Lateral Territory</th>
<th>Posterior Territory</th>
<th>Inferior Territory</th>
</tr>
</thead>
<tbody>
<tr>
<td>Status</td>
<td>Approach</td>
<td>Status</td>
<td>Approach</td>
</tr>
<tr>
<td>High-grade mid stenosis</td>
<td>LIMA graft to LAD</td>
<td>Unobstructed diagonal branch</td>
<td>TMR to LCX territory</td>
</tr>
<tr>
<td>Lateral territory</td>
<td>Diagonal circulation intact</td>
<td>Nonvisible LCX and branches</td>
<td>Proximal high-grade stenosis</td>
</tr>
<tr>
<td>Inferior territory</td>
<td></td>
<td></td>
<td>Stent to RCA</td>
</tr>
</tbody>
</table>

*(LCX indicates left circumflex coronary artery; LIMA, left internal mammary artery; LAD, left anterior descending coronary artery; TMR, transmyocardial laser revascularization; RCA, right coronary artery)*
surgeons that such a risk may justify postponing TMR therapy for several days until the effects of antiplatelet therapy wear off, particularly if clopidogrel bisulfate (Plavix) has been used.

Figure 3 summarizes our complete revascularization strategy in algorithm form. The intent of this figure is to allow visualization and easy reference to the methodologies that we have discussed in the text. We suggest that interested users follow this algorithm for all ischemic vessels being considered for interventional or surgical treatment. We believe that running each diseased vessel through the thought processes exemplified in Figure 3 will ensure that available treatment options are appropriately considered in the optimization of a patient’s outcome.

Cardiac Support

If the angiogenesis theory for TMR holds true (see Table 1 for a listing of theories of TMR mechanisms of action), TMR is actually the creation of controlled damage to cardiac tissue, ie, controlled inflammation to initiate the angiogenic cascade. This concept means that TMR is injuring cardiac tissue with a purpose, that purpose being to initiate the inflammatory and angiogenic cascades for ultimate therapeutic benefit. Regardless of whether this concept is correct, experience has shown us that TMR tends to stun the myocardium. Therefore, the more channels that are introduced, the greater is the potential for myocardial stunning. In view of this fact, some surgeons suggest that TMR should not be used if the pulmonary artery diastolic pressure is greater than 25 mm Hg.

Two approaches may be considered in patients for whom post-TMR LV function is mild to moderately depressed: mechanical support with an intra-aortic balloon pump or pharmacologic support with inotropic drugs such as dobutamine or milrinone. Use of these supportive strategies may be considered prophylactically or therapeutically. Experience with both strategies has been favorable, and their use has been considered prophylactically or therapeutically. Experience with these supportive strategies may be considered prophylactically or therapeutically. Experience with both strategies has been favorable, and their use has resulted in a reduction in the frequency of postoperative low-output syndromes.

Antiarrhythmic Therapy

The creation of transmural channels creates zones of injury that may translate into electrically irritable foci. The transient ventricular ectopy often seen during the laser application usually subsides once the energy transmission is discontinued. However, intraoperative and postoperative ventricular ectopy may persist. In such instances, an antiarrhythmic approach becomes necessary.

Lidocaine has been a commonly used antiarrhythmic drug for ventricular ectopy. If this approach is used, we suggest that intravenous lidocaine administered at a rate of 2 mg/min starting 30 minutes before an incision and continuing 12 hours postoperatively is an appropriate and effective regimen. However, recent information suggests that amiodarone may be a superior drug for this purpose. An option to consider is the prophylactic intravenous administration of 150 mg amiodarone prior to TMR application. When the drug is given slowly over 15 to 20 minutes, the side effects of bradycardia and hypotension are avoided. In the event that further arrhythmia is encountered, an intravenous amiodarone infusion can be initiated and continued for 24 hours. Another suggestion includes loading patients with 4 to 5 g of magnesium sulfate in addition to amiodarone as prophylaxis against ventricular ectopy.

Case Illustrations

Case Studies 1A and 1B: TMR as Sole Therapy via a Limited Left Thoracotomy

A 62-year-old man, previously employed as a longshoreman and unable to work secondary to disabling angina, presented for evaluation. Cardiac catheterization revealed a completely occluded LAD with minimal distal filling of the LAD by right-side collaterals. The circumflex artery and the RCA were unobstructed. The overall EF was preserved at 55%, and mild anterior wall hypokinesis was present. The patient had been evaluated and turned down for CABG at 2 previous institutions because the patient’s target vessels were unsuitable for safe revascularization. This patient underwent sole-therapy TMR (18 channels in the LAD territory) via a limited left anterior thoracotomy. He was discharged angina free on the fourth postoperative day. Postoperatively, this patient was back at full-time employment after 8 weeks, and 3 and a half years later he remains angina free and actively employed.

An 80-year-old man with a history of CAD, CABG in 1982, and redo CABG in 1990 presented with class III angina. He continued to have chest pain despite treatment with nitrates, acetylsalicylic acid, and beta-blockers. Catheterization demonstrated the presence of a patent LIMA-to-LAD graft with a very small distal vessel. The native RCA was completely occluded, and the saphenous vein graft (SVG) to the RCA had stenosis of 30% to 40% with distal disease. The native circumflex artery was completely occluded, and the SVG to the circumflex artery was patent with diffuse disease in the lumen. A 2-dimensional echocardiogram showed an EF of 50%. The patient underwent TMR through a left anterior minithoracotomy with the placement of 10 channels in the anterior wall, 11 in the posterolateral wall, 14 in the posterior wall, and 5 in the apex. This patient had an uneventful recovery, was discharged on the fourth postoperative day, and remained angina free through the 4-year follow-up.

Case Study 2: Adjunctive TMR via Sternotomy in a Patient with a Borderline EF

An overweight 54-year-old woman presented with hypertension, hyperlipidemia, a history of myocardial infarction (1997), New York Heart Association (NYHA) class IV angina, and mild congestive heart failure well controlled with mild diuretics. The patient was hospitalized with unstable angina and was treated medically. She reentered the hospital 3 weeks later for unstable angina and received catheterization. The catheterization revealed severe 3-vessel disease, an EF of 35%, and only 1 vessel (the obtuse marginal artery) considered bypassable (see Figure 4 for patient angiograms). The patient underwent median sternotomy, a single CABG
to the obtuse marginal artery, and TMR to all areas of the myocardium (39 channels). The follow-up after 3 and a half years revealed NYHA class I, no further cardiac events, an EF of 52%, and normal test results with technetium Tc 99m sestamibi (Cardiolite).

**Case Study 3: Adjunctive TMR to an Area Where Bypass Grafts Were Also Performed**

A 55-year-old man presented with complaints of chest pain, which was felt to be indigestion, and was referred to his cardiologist for evaluation. The patient underwent a Cardiolite stress test, which revealed diffuse, global, and reversible ischemia. Maximum medical therapy including nitrates and beta-blockers was unsuccessful in relieving the chest pain. The patient underwent cardiac catheterization, which revealed severe 3-vessel disease with a preserved ventricular function. The patient underwent quadruple CABG using a LIMA to bypass the LAD and with separate saphenous veins to the first diagonal coronary artery, the circumflex marginal artery, and a diffusely diseased posterior descending coronary artery (PDA). Because revascularization of the inferior wall was felt not to have been completed, TMR was performed to the inferior wall with 14 channels. The patient was weaned from bypass on dopamine and lidocaine. There were no intraoperative or postoperative complications, and the patient was weaned from the dopamine and lidocaine therapy on the first postoperative day. He was discharged home angina free on the fourth postoperative day. Follow-up at 1 year showed the patient to be angina free.

**Case Study 4: TMR and Redo TMR as Sole Therapy via a Left Thoracotomy**

A 70-year-old man presented with severe coronary artery stenosis and angina refractory to medical therapy that were not suitable for interventional therapy because of a severe left main coronary artery lesion. A preoperative evaluation and a review of the angiogram confirmed the presence of a tight left main coronary artery stenosis, a preserved LV function, and suitable LAD and diagonal vessels for bypass; however, the circumflex artery (and its branches) was very small and not bypassable.

Plans were made for hybrid surgical revascularization to the LAD with the LIMA and to the diagonal artery with an SVG and for TMR laser therapy to the circumflex distribution. On the morning of surgery while he was being prepared in the preoperative holding area, the patient developed sudden severe chest pain with electrocardiographic changes and a dropped blood pressure. This situation required prompt mobilization to the operating room and placing the patient on CPB. Intraoperative assessment revealed signs of acute LV deterioration, thus precluding TMR therapy.

The bypass grafts were performed, and the patient made a satisfactory recovery following several days of intensive therapy on the ventilator and inotropic support. The patient was discharged on antiangina therapy because of the recognized incomplete revascularization. In the ensuing 6-week period, the patient was twice readmitted to the hospital with recurrence of angina refractory to oral antiangina therapy. A dipyridamole (Persantine)-thallium Tl 201 (201Tl) scan confirmed ischemia localized to the lateral LV wall that jeopardized approximately 30% of the LV muscle mass.

The patient was placed on intravenous heparin and nitroglycerin therapy, and Plavix treatment was discontinued in preparation for TMR laser therapy. During the 5-day waiting period to allow the recovery of platelet function from the effects of Plavix, the patient had several episodes of angina that required further management of pain control treatment.

Uneventful TMR therapy to the circumflex distribution was performed through an anterolateral thoracotomy and was carried out without difficulty. The patient was

---

**Case Study 5: Delaying TMR When Used as an Adjunctive Therapy**

A 52-year-old woman with a known history of CAD status post CABG and status post percutaneous transluminal coronary angioplasty and stents presented with recurrent bouts of angina. Maximal medical therapy with nitrates and beta-blockers had been unsuccessful in relieving her angina symptoms. Recatheterization showed severe native-vessel CAD with no bypassable vessels or interventional targets. The LIMA-to-LAD bypass graft was patent with limited runoff. The SVG bypass to the diagonal artery was patent with limited runoff. The SVG to the PDA was occluded. Echocardiography demonstrated that no valvular disease was present and that LV and RV function was preserved. A nuclear (Cardiolite) viability study exhibited global ischemia. The patient underwent a mini–left thoracotomy and sole-therapy TMR off pump. Forty channels, 10 channels to each of the 4 segments, were created during TMR. There were no intraoperative or postoperative complications. The patient was discharged on the fourth postoperative day angina free. The patient remained angina free for 3 years after the TMR, and then the angina pain returned. After the completion of repeat cardiac catheterization, the patient received 2 stents to the RCA, which improved the angina for approximately 3 months. In addition, the patient’s thyroid medication was adjusted. The return of severe angina led to complete disability and incapacitation. Recatheterization was done, and another stent was placed to the ostia of the RCA. The angina persisted. A redo TMR via a redo left thoracotomy was performed without any technical difficulty. The patient is now completely angina free.
discharged angina free 3 days later and remains stable and angina free with no requirements for any further in-hospital therapy.

**Case Study 6: TMR as an Adjunctive Procedure with 5 Bypasses in a Transplanted Heart**

A 58-year-old man had undergone cardiac transplantation in 1986. The patient, now 70 years old, underwent a \(^{201}\)Tl stress test, which revealed inferior and apical ischemic changes. An angiographic examination was carried out, and severe 3-vessel coronary disease was noted. Typical atherosclerotic changes were noted in the proximal vessels, including the anterior descending artery and the ramus intermedius (RD). However, a more diffuse transplant graft vasculopathy pattern was present in the area of the first and second obtuse marginal branches. The RCA was totally occluded.

A reoperative open heart surgery with a 5-vessel bypass procedure was performed. The IMA was used to bypass the anterior descending coronary artery proximally, and a separate SVG was used to bypass the LAD and the second obtuse marginal branch. A sequential vein graft was constructed between the distal circumflex artery and the PDA. Because the vessel near the first obtuse marginal branch was diffusely diseased and because there was a large area without revascularization that was related to transplant graft vasculopathy, 14 TMR laser channels were created in the lateral wall of the transplanted heart.

The postoperative course was uncomplicated, and the patient was discharged on the fifth postoperative day. This patient subsequently recovered well, and his last follow-up was for his 17th annual posttransplantation evaluation. The patient was asymptomatic from the cardiovascular standpoint and was doing well.

This case was one of the very first of adjunctive coronary bypass and TMR in the United States, and it provided potentially complete revascularization to areas of the transplant graft vasculopathy where formal bypass grafting could not be accomplished.

**Case Study 7: Robot-Assisted TMR**

A 48-year-old woman with diabetes, hypertension, and a strong family history of early mortality secondary to CAD began having progressive angina 3 years before presentation. A sextuple CABG procedure at that time relieved angina for only 6 months. A subsequent cardiac catheterization revealed patent LIMA-to-LAD, SV-to-PDA, SV-to-diagonal, and SV-to-RI grafts, although the runoff to all targets was small and slow. The obtuse marginal grafts were occluded, and the native circumflex system was circumflex system was diminutive. After 11 post-CABG catheterizations, including angioplasty, stenting, and brachytherapy of the circumflex system, as well as 6 months of maximum medical therapy, TMR consultation was obtained for the treatment of class IV angina. Stress Cardiolite imaging results revealed reversible ischemia in the anterolateral, lateral, and inferolateral walls and an estimated EF of 55%. An echocardiographic examination showed no structural abnormalities. A robotically assisted off-pump sole-therapy TMR was performed through a 2-inch anterolateral thoracotomy. The pericardium was dissected in an open manner, and the procedure was facilitated by improved visualization with voice-activated, robot-assisted thoracoscopy (AESOP; Computer Motion, Goleta, CA, USA). Forty-six TMR laser channels were created in the 4 regions of the LV. The patient tolerated the procedure well and was discharged angina free on the second postoperative day. Six months after the TMR procedure, the patient's lifestyle has dramatically improved with no angina and no cardiac readmissions, and she is taking no nitrates.

**Conclusion**

In summary, the use of TMR for angina relief has evolved into a clinically proven technology that has enabled physicians to address difficult angina and revascularization cases with a therapy that has been proven safe and effective. TMR can be used in a variety of ways and in conjunction with other therapies, both interventional and surgical.

Minimally invasive approaches, including off-pump approaches and limited thoracotomies, to enhance patient benefit and expand patient eligibility are becoming a routine part of TMR strategy. Future applications in this regard, including the use of port access (thoracoscopic approach) to minimize patient pain and recovery time and to avoid sternotomy in young patients, are being considered. The thoracoscopic technique can also be enhanced via robotic assistance (the da Vinci surgical robot; Intuitive Surgical, Sunnyvale, CA, USA). Studies have been initiated in this regard. Finally, research is probing the prospects of injecting agents such as angiogenic growth factors and stem cells into or around TMR channels with the idea that the angiogenic response to TMR may enhance these therapies. More research is required to determine the effect that TMR may have in such instances.

In conclusion, the use of TMR has added another important dimension to the overall management of angina patients, particularly those with no other treatment option.

**References**


