

Effects and Complications of Laser in Transmyocardial Laser Revascularization (TMLR)

Thesis

***Submitted for the fulfillment of Ph.D Degree in Medical
and Biological Application of Laser Science in
Cardiothoracic Surgery***

By

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Abbreviations

ACC: American College of Cardiology.
AHA: American Heart Association.
AV: Atrioventricular.
BP: Blood Pressure.
CAD: Coronary Artery Disease.
CCs: Canadian Cardiovascular Society.
CHD: Coronary Heart Disease.
CI: Confidence Interval.
Cx: Circumflex artery.
ECG: Electrocardiography.
ETT: Exercise Tolerance Test.
HR: Heart Rate.
HRR: Heart Rate Reserve.
LAD: Left Anterior Descending branch.
LBBB: Left Bundle Branch Block.
LM: Left Main.
LV: Left Ventricle.
METs: Metabolic Equivalent.
MR: Metabolic Reserve.
RBBB: Right Bundle Branch Block.
RCA: Right Coronary Artery.
RCTs: Randomized Clinical Trials.
RR: Relative Risk.
TMLR: Transmyocardial Laser Revascularization.
TMR: Transmyocardial Revascularization.
VF: Ventricular Fibrillation.
Rx: Treatment.
PVCs: Premature Ventricular Contractions.
VT: Ventricular tachycardia.

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INTRODUCTION

Transmyocardial laser revascularization (TMLR) is an emerging surgical therapy for the treatment of ischemic heart disease not amenable to conventional percutaneous or surgical revascularization techniques (*Schoebel et al, 1997, Sundt and Rogers, 1997, Frazier and Kadipasaoglu, 1996*). Although an analogous network of myocardial sinusoids exists in humans, its role in perfusion remains poorly defined. Myocardial needle acupuncture was an earlier attempt to model the reptilian circulation; however, the success of this technique was limited by premature channel closure due to fibrous ingrowth. In order to minimize fibrosis, thereby improving channel patency, Mirhoseini et al proposed the use of a CO₂ laser to create transmyocardial channels (*Mirhoseini et al, 1994*). The majority of human and animal studies, however, have failed to demonstrate channel patency following TMR. Alternative mechanisms such as denervation and angiogenesis have more recently been promoted as the explanations underlying the clinical benefits following TMR (*Kohmoto et al, 1998*). Transmyocardial revascularization using laser technology has been demonstrated to improve functional class of angina pectoris, reduce ischemia during noninvasive stress testing, and increase relative endocardial perfusion in patients with ischemic heart disease. This study was conducted to evaluate the intermediate clinical outcomes among patients at National Heart Institute, Cairo, Egypt treated with TMLR.

Despite the success of current medical and surgical management of ischemic heart disease, a growing number of patients have diffuse obstructive coronary artery disease that is not amenable to coronary-artery bypass grafting or catheter-based interventions. The failure to revascularize even a single ischemic coronary artery due to poor graftability is associated with a decrease in both survival and freedom from angina in these patients, regardless of the

presence of a patent left internal thoracic artery bypass to the left anterior descending artery (*Scott et al, 2000*).

This problem has stimulated interest in developing alternative therapeutic approaches. Early attempts at indirect myocardial revascularization had limited success. Beck's use of omentopexy, reported in 1935, (*Beck, 1935*) and Vinberg's use of thoracic-artery implantation, reported in 1954, (*Vinberg, 1954*) were attempts to provide direct myocardial perfusion and were based on the description by Wearn et al., in 1933, (*Wearn et al, 1933*) of a sinusoidal network in the human heart. This concept was based on the model of the reptilian heart, in which the left ventricle is directly perfused from endothelium-lined channels that radiate out from the left ventricular cavity.

In 1965, Sen et al studied the benefits of transmyocardial channels produced with needle punctures. Using a canine model, they placed numerous needle punctures in an ischemic area subtended by an occluded left anterior descending artery. They showed that the acupuncture-created channels resulted in decreased mortality, increased long-term survival, and decreased infarct size. Although patent channels were identified at 8 weeks, no evidence suggested that the channels had developed an endothelial cell lining, thus confirming successful rearterialization.

During the next 2 decades, numerous studies were undertaken to evaluate the effects of needle-created transmyocardial channels in revascularizing ischemic myocardium. However, much of this research received little attention because it was not considered nearly as promising as the emerging techniques involving direct myocardial revascularization, such as CABG and angioplasty.

The development of laser energy sources in the 1980s stimulated investigators to restudy myocardial acupuncture. In *1981, Mirhoseini and Cayton* demonstrated that the carbon dioxide laser could generate small

transmyocardial channels in the ischemic myocardium of a dog. In 1983, *Mirhoseini et al* used TMLR on a patient with coronary artery disease. They used a carbon dioxide laser in conjunction with CABG to treat a hypokinetic area of the left ventricle. The patient did well, with normal ventricular function demonstrated during a postoperative nuclear scan. These initial clinical studies provided further impetus for the use of TMLR. Since the early 1990s, carbon dioxide laser systems have been used to perform TMLR in humans, with excellent results.

AIM OF THE WORK

- To study the intermediate-term (2 years) effectiveness and complications of Transmyocardial Laser Revascularization (TMLR) in patients with end stage coronary artery disease not candidate to other methods of revascularization using CO₂ laser as a sole maneuver.

Development of the Coronary Vessel System

Formation of the coronary vessels is a fundamental event in heart development. Congenital abnormalities in the coronary system can have major deleterious effects on heart function. It is also possible that subtle variation in the patterning of coronary vessels has significant but uncharacterized effects on myocardial structure and function. In addition, generation of the coronary vascular system represents a complex system for analysis of regulation of cell fate determination, cell and epithelial migration, epithelial/mesenchymal transition, and patterning of a complex three-dimensional structure (*David et al, 2002*).

Problems of the coronary vascular system lead to major problems with the heart. Nearly all, cardiac myocytes in mammalian hearts are in contact with a capillary and that the mammalian heart is one of the most vascularized organs of the body. The cells that make up the coronary system come from outside the heart are brought to the heart and differentiate into blood vessels only when they are in the heart. Indeed, all of this happens without ever tapping into the blood that courses through the heart lumen (*David et al, 2002*).

Not Everyone Has Coronary Vessels:

Not all organisms with a heart have coronary vessels. No invertebrates with hearts have coronary vessels. Among the vertebrates, mammals, reptiles, and avians have coronary systems complete with arterial output and venous return. What these three classes of vertebrates have in common is their dependence on pulmonic respiration and the lack of cutaneous respiration. (*Kul'chitskii and Romenskii, 1986, Liem et al, 2001*).

One of the remaining vertebrate classes, the amphibians, has cutaneous respiration. Most amphibians, such as newts, salamanders, and bullfrogs have

no coronary vessels. In fish, the last vertebrate class, the presence of coronary vessels is variable (*Robleto et al 1988, Moore et al, 1976, Hu et al, 2001*).

Structure of the Coronary Vascular System:

The blood supply to the heart of higher vertebrates actually originates outside the heart from the ascending aorta. The origins or ostia of the right and left coronary arteries are located in the sinuses of the aortic valves and thus are superior to the heart. These arteries travel well-defined routes along the surface of the heart in the epicardium and give rise to branches that penetrate the substance of the myocardium. Small muscular arteries are found throughout the myocardium that further branch into an extensive capillary bed that embraces all, or nearly all, cardiac myocytes. The venous return to the coronary sinus courses over the surface of the heart with accompanying arteries. The coronary sinus returns blood to the right atrium just inferior to the opening of the vena cava. (*David et al, 2002*).

Histologically, the arteries of the coronary system are similar to arteries seen throughout the body. The tunica intima consists of a continuous endothelium and associated subendothelial connective tissue space bounded externally by an internal elastic membrane. Smooth muscle cells and elastic laminae occupy the tunica media, and the adventitia comprises connective tissue cells and fibers. Coronary arteries that run in the epicardium have been characterized as "elastic" arteries, although the number of smooth muscle cells is greater and the amount of elastic fibers is less than in other elastic arteries. Branches of the major epicardial arteries that penetrate the myocardial wall are classified as "muscular" arteries that in turn give rise to arterioles and eventually to the capillary bed (*Baroldi and Scomazzoni, 1967*).

Normally, two coronary arteries arise from the aorta. These major arteries course over the surface of the heart in the subepicardial connective

tissue. Right and left coronary arteries contribute to an arterial ring that encircles the atrioventricular sulcus. Major epicardial arteries "descend" from this atrioventricular circle formed from branches of the right and left main coronary arteries.

In the slight majority of human hearts (54%), three vessels arise from the left coronary and one from the right. The other 46% of cases have variation in contributions from left and right coronary arteries. Similar variation is seen in the arteries that supply the anterior and lateral surfaces of the ventricles.

The smaller muscular arteries that penetrate the myocardium, known as the intramural arteries, comprise the next level of branching. These arteries are highly variable when visualized by plastic casting or ink injection. One is struck by the total lack of pattern in the arteries that penetrate the myocardium, that is, except for two important things: There appears to be a fairly consistent spacing between these penetrating muscular arteries. The branching of these arteries leaves no space untouched (*Baroldi and Scomazzoni, 1967*). Thus, it seems that the overriding issue in coronary artery patterning is unimpeded delivery of blood to the capillaries rather than the particular route that the blood takes. Variation in the origin, number, and patterning of the major coronary arteries is far greater than variation seen in valves, myocardium, and/or great vessels. This may reflect the catastrophic nature of valve, muscle, and great vessel anomalies but also may reflect the "latitude" or "play" in the system of generating coronary arteries. In addition, the complex or even dynamic nature of coronary vessel development may lead to wide variation in the adult structure. Thus, the representations seen in texts of cardiology may be the most frequently observed arterial pathways, but it is helpful to understand that the pattern of coronary arterial structure can vary greatly (*Fishman and Chien, 1997*).