Study of the Efficacy of Low level laser in Myocardial Perfusion of Patients with Chronic Stable Angina

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Abstract

Background: In the vast majority of patients with angina pectoris caused by underlying coronary artery disease, effective treatment is available. Most patients respond to antianginal medication, and for the remainder either percutaneous coronary Revascularization or coronary artery bypass grafting can be performed. (1)
Low-energy laser radiation through its direct influence on tissue repair processes without heating effect may have vital importance in the therapy of patients with advanced coronary artery disease (CAD).(2)
The purpose of the study was to assess the safety and efficacy of low energy laser therapeutic procedures in patients with advanced multi-vessel CAD not suitable for myocardial revascularization. Many clinical parameters as well as results of laboratory tests were evaluated to find any indices of potential impact of the laser therapy in the examined population.

Method: 22 patients with advanced CAD were assigned (mean age 61, male gender 68.1%, 100% with history of myocardial infarction), to undergo two sessions of irradiation of low energy laser. Each session was 10 time and each time of radiation was 20 min. Pre laser evaluation was included, blood pressure, heart rate, basic biochemical test , ECG, 6 minute walk test, TTE, gated MPI. Before the first and the second period of laser therapy with 3 months break pre and post laser parameters, were measured.

Results: No side effects associated with the laser biostimulation or performed clinical tests were noted. Improvement in SBP, Higher functional class, longer distance of 6-min walk test in both group were noted. There was significant change in myocardial perfusion of most anterior segments of heart by single photon emission computed tomography (SPECT) (visually and by computer soft ware)($P<0.05$). There was no significant change in DBP, HR, and in LVEF by TTE and gated MPI.

Conclusion: An improvement of functional capacity and myocardial perfusion and less frequent angina symptoms during 6-min walk test, without significant change in left ventricular function by TTE and gate MPI, were observed. Low level laser in short term was a very safe method. These encouraging results should be confirmed in a larger, placebo-controlled study.

Key word: low level laser, chronic stable angina, myocardial perfusion imaging.

*I would like to thank Dr M. Weber for his guidance and valuable supervision

Background:

The importance of Chronic coronary artery disease (CAD) in contemporary society is attested to by the almost epidemic number of persons afflicted (see Chap. 1) . In 2003, CAD accounted for 53 percent of all deaths caused by cardiovascular disease and was the single most frequent cause of death in American men and women, resulting in more than one in five deaths in the United States.[1] Approximately every 26 seconds, someone in the United States will suffer a coronary event, and approximately every 60 seconds a coronary event will result in a fatal outcome.[1]

Ischemic heart disease is now the leading cause of death worldwide, and it is expected that the rate of CAD will only accelerate in the next decade; contributory factors include aging of the population, alarming increases in the worldwide prevalence of obesity, type 2 diabetes, and the metabolic syndrome, as well as a rise in cardiovascular risk factors in younger generations.[2] The World Health Organization has estimated that by 2020, the global number of deaths from CAD will have risen from 7.2 million in 2002 to 11.1 million.[3]

In the vast majority of patients with angina pectoris caused by underlying coronary artery disease, effective treatment is available. Most patients respond to antianginal medication, and for the remainder either percutaneous coronary revascularization or coronary artery bypass grafting can be performed. There are, however, an increasing number of patients who have angina which is not controlled by medical treatment and have disease which is not suitable for conventional revascularization techniques. Typically, such patients have atherosclerotic disease throughout their coronary arterial tree, with no “target” lesions for angioplasty and no “target” vessels for surgery.[4]

Low-energy laser radiation through its direct influence on tissue repair processes without heating effect may have vital importance in the therapy of patients with advanced coronary arery disease (CAD).[5]

Laser biostimulation (low level laser therapy, LLLT) has been applied in medicine for more than 30 years. Its action consists of direct impact on the intracellular mechanisms and activation of heat-independent tissue repair processes without tissue damage. The LLLT effects may be either local or systemic, thus involving not only sites of direct influence of laser radiation.

Since the first application of LLLT more than 2000 scientific reports with respect to this still controversial issue have been published. Although most of these controversies regarding the impact of laser radiation have been solved, nowadays the main interest of scientific research is its impact on intracellular processes, their excitation pathways and the possibility of interactions between activated cells at the tissue level [6-8].

Studies performed mostly on animal models and in vitro provided evidence of LLLT effects: anti-inflammatory, improved microcirculation and cardio protective effects. Reduced infarct area after artificially induced myocardial infarction (MI) as well as favorable influence on post infarction myocardial remodeling were noted [9, 10]. The aforementioned action may have an important impact on quality of life and prognosis in patients with multi-vessel coronary artery disease (CAD) who are not suitable for the conventional techniques of myocardial revascularization. The early studies on LLLT performed in humans involved patients suffering from MI treated with intravascular irradiation. Reduction of ischemic area, decreased levels of myocardial necrosis markers and reduced incidence of cardiac arrhythmia were observed [11, 12]. Also, exposure to external irradiation of patients with ischemic heart disease was beneficial as it reduced angina complaints, inhibited lipid peroxidation processes [13] and improved rheology of blood, showing a protective effect on the erythrocyte membranes [14] and a drop in the arterial blood pressure and pulse pressure.

We did not find any studies investigating the influence of low energy laser irradiation applied externally to the chest in patients with advanced multi-vessel CAD by myocardial perfusion imaging .

Our concept is to apply external low energy laser irradiation to the chest. A potential biostimulation impact, through a local and systemic effect on inflammatory reaction alleviation, stimulation of

microcirculation development and tissue regenerative processes, may be potentially beneficial in advanced CAD.
The purpose of the study was to assess the safety and efficacy of low energy laser therapeutic procedures in patients with advanced multi-vessel CAD not suitable for myocardial revascularisation. Many clinical parameters as well as results of laboratory tests were evaluated to find any indices of potential impact of the laser therapy in the examined population.

Methods:
The research protocol was approved as prospective and experimental study. Inform consent was obtained from 22 subject who were referred to Rajeae cardiology center due to CAD since April 2007-September 2008.
Inclusion criteria were as follows:

1) multi-vessel CAD documented with coronary angiography and not suitable for revascularisation, either percutaneous or surgical.
2) Advanced angina: class II or III according to the Canadian Cardiovascular Society (CCS) functional classification [15].
3) Optimized medical therapy according to the current standards of patient management in cardiology and ACC/AHA guidelines [16].
4) Informed written consent to participate in the study.

Exclusion criteria:

1) Significant structural valvular disease or congenital malformation.
2) Acute coronary syndrome.
3) Serious systemic disease that might have a significant impact on patient prognosis.

Diabetes mellitus was not considered a contraindication.
After initiation of optimized medical therapy all patients were discharged with successful control of clinical symptoms achieved.
Patients were treated according to the ACC/AHA guidelines [16] with aspirin, statins, angiotensin-converting enzyme inhibitors and beta-blockers, and this therapy was not changed significantly throughout the study period.
Baseline clinical assessment consisted of complete clinical examination, basic biochemical studies including, Hb, BUN, Cr, Na, K, TG, Chol, LDL, HDL,FBS, resting ECG, 6-minute walk test and gated myocardial perfusion imaging as well as complete echocardiographic examination with Doppler measurements.
The same parameters as at baseline were evaluated after three months of laser therapy procedures.
The degree of clinical significance of CAD was classified according to the Canadian Cardiovascular Society classification [15]. History of MI, typical
atherosclerosis risk factors (arterial hypertension, diabetes mellitus, smoking, familiar history of atherosclerosis, total cholesterol level, LDL, HDL and triglyceride concentrations) were also taken into account. All data of patients were gathered in one check list for final analysis. (Appendix1)

Six-minute walk test
All patients underwent walk test with calculation of walking distance covered by each individual within 6 minutes. Patients were instructed to walk without stopping at a pace as fast as possible not to provoke either angina or heart failure symptoms. This test was carried out at the laser clinic of Shaheed Rajaeae Cardiology center with the facilities of an immediate qualified response team.

Echocardiography

In the echocardiographic study (M and 2D mode), global as well as regional left ventricular (LV) myocardial contractility were assessed according to the 16-segment model of the American Echocardiographic Society recommendations [18]. A four-stage system of contractility assessment was employed, where 1 meant normokinesia, 2 – hypokinesia, 3 – akinesia, and 4 – dyskinesia. A LV contractility index was calculated in the typical manner as the sum of the score of individual segments and divided by the number of analysed segments. Ejection fraction (EF) was evaluated using the Simpson equation (four-chamber apical and LV long-axis projection).

Flow through the cardiac valves and cardiac chambers were examined employing methods of pulse wave Doppler, continuous wave Doppler and color blood flow visualization techniques. Severity of mitral valve regurgitation and diastolic dysfunction grading were evaluated.

Gated MPI

All patients underwent gated myocardial perfusion imaging, before the first and second period of low level laser therapy by General Electric – Dual Head Gamma Camera Equiped with High Resolution Colliwaters 99MTC – Sestamibi 140 - KCV . After reconstruction of imaging by Vision 6.00 software, percent of myocardial perfusion were assessed by Myoflex software quantitatively. Gated ejection fraction, end systolic volume, end diastolic volume and stroke volume were assessed by Multidim software.

Laser therapy procedures

The patients were exposed to laser irradiation of low energy produced by Weber Medical GmbH, Sohnreystr.6, D – 37687 Lauenforde both intravenous and local low level laser via protocol (Appendix2).

1-Intravenous laser produce by Weber Needle Blood 12/2006, that generates garish red light of a wavelength of 680 nm and green light 534nm. This laser emits continuous energy of 5 mW at the tissue level.

2-Local low level laser produce by Weber needle Basic 10/2005, that generate garish red light of a wavelength of 658nm with 40mW at the tissue level and infrared light of a wave length of 810nm with 90mW at the tissue level.

The irradiation time was 20 minutes and procedures were repeated every other days till 10 time. The procedures were supervised by a trained study nurse responsible for the assessment of possible local complications. Throughout the whole study, physician team of Rajaei Cardiovascular center was available, being responsible for proper functioning and safety of the laser equipment employed in this study.

Statistical analysis

Data are expressed as means and standard deviations. Differences between the individual parameters in the patient groups were analysed by paired T test, Wilcoxon test and McNemar test. A p value <0.05 was considered significant. SPSS 15 for Windows (SPSS Corp., Chicago, Illinois) was used for statistical analysis.

Results:

The baseline clinical parameters and risk factors are outlined in Table I. The study involved 22 patients at the mean age of 61 years (68.1% male, 31.8% female). The majority of them had a history of MI (72.2%). The examined population had a significant burden of such risk factors as arterial

hypertension (50%), diabetes mellitus (61%), dyslipidemia (66.7%), smoking history (33.3%), opium (11.1%), overweight (11.1%).

All of the patients presented angina of CCS class III, and had multi-vessel CAD documented in coronary angiography. There were no adverse events associated with laser biostimulation, either systemic or local. In three patients procedures were temporarily discontinued because of respiratory tract infections.

The characteristics of patients are presented in Table I.

Table I. Characteristics of patients.

Parameter	**Value**
Number of patients	22
Men	15 (68.1%)
Age [years]	61.0±9.4
Clinical status	
NYHA FC class III	22 (100%)
History of MI	15 (72.2%)
Previous CABG	8 (38.9%)
Risk factors	
Arterial hypertension	11 (50%)
Diabetes mellitus	13 (61.1%)
Hyper cholesterolaemia	15 (66.7%)
Smoking history	7 (33.3%)
Opium	2 (11.1%)
Overweight (BMI 25-30)	2 (11.1%)
Selected parameters	
Cholesterol [mg/dL]	183.1±43.1
HDL-cholesterol [mg/dL]	45.4±10.6
LDL-cholesterol [mg/dL]	97.88±41.173
Triglycerides [mg/dL]	159±60.8
Haemoglobin [mg/dL]	13.09±1.5
Permanent ST depression	17(77.2%)
Six minute walk test	229.72±82m
LVEFTTE [%]	30±11.3
LV diastole [mm]	75±11.8
LV systole [mm]	58±0.81
LVEF Gated [%]	37±14.4
LVEDV ml	217.13±105.40
LVESV ml	144.67±94.21
SV ml	72.47±21.88

LVEF – left ventricular ejection fraction, LV – left ventricle, LVEDV-left ventricle end diastolic volume, LVESV-left ventricle systolic volume, SV-stroke volume

After the first irradiation statistically significant improvement in systolic blood pressure, functional class and longer distance of 6-minute walk were observed. ($P<0.05$).(Table II)

No favorable changes with respect to LVEF, diastolic blood lpressure, mitral regurgitation and diastolic dysfunction were observed. In laboratory data there was no significant difference pre and post low level laser therapy. ($p>0.05$)

According to statistical analysis quantitative measurement of perfusion in 18 segment of myocardium significant improvement has seen in most anterior part of apex, apicoanterolateral, anteroapical, apicoanteroseptal, apicoinferoseptal, midanterolateral, mid anterior, mid inferior.($P<0.05$)(Table III)(Fig.1)

Although mean LV EF by TTE and gate MPI was increased, there was no significant change statistically. (Fig.2)

Table II. Selected clinical parameters pre and post laser			
	Pre laser (n=22) Mean (Std. Deviation)	Post laser (n=22) Mean (Std. Deviation)	P value Sig. (2-tailed)
SBP	117.94 (16.683)	110.00 (12.119)	.007
DBP	71.76 (10.889)	66.47 (6.793)	.058
HR	75.35 (9.360)	70.59 (10.032)	.088
EFTTE	30.00 (11.376)	30.00 (11.220)	.058
LVEDd	7.511 (.8143)	5.878 (.8247)	.186
LVESd	5.739 (11.8976)	4.506 (1.0707)	.317
SIXMINUTE	229.72 (82.006)	336.67 (83.596)	.001
gatedEF	37.40 (14.406)	41.33 (14.960)	.055
LVEDV	217.13 (105.406)	203.80 (89.837)	.282
LVESV	144.67 (94.218)	128.53 (82.010)	.082
SV	72.47 (21.889)	75.27 (24.726)	.654
Hb	12.880 (1.3187)	12.493 (1.5045)	.178
BUN	27.09 (9.844)	24.44 (11.437)	.509
Cr	1.300 (.2556)	1.350 (.2875)	.584
FBS	135.44 (69.100)	111.94 (25.909)	.209
TG	155.69 (60.272)	146.25 (65.246)	.507
CHOL	171.38 (57.715)	165.88 (47.272)	.641
LDL	97.06 (42.380)	94.88 (33.314)	.799
HDL	37.31 (14.211)	41.31 (13.195)	.055

Table III. Quantitative measurement of perfusion in 18 segment of myocardium pre laser and 3 months post laser.			
	Pre laser (n=22) Mean (Std. Deviation)	Post laser (n=22) Mean (Std. Deviation)	P value Sig. (2-tailed)
Ant. Part of apex	45.00(27.859)	52.61(25.018)	.014
Inferior part of apex	46.22(29.186)	51.89(25.335)	.108
Apico anterolateral	68.72(23.889)	76.56(21.178)	.025
Anteroapical	53.33(27.592)	60.00(26.995)	.036
Apico anteroseptal	55.78(28.200)	63.00(27.069)	.006
Apico inferoseptal	66.33(26.221)	72.50(25.093)	.045
Apico inferior	54.39(24.782)	59.61(23.672)	.097
Apico inferolateral	76.11(16.073)	78.28(13.813)	.0572
Mid anterolateral	83.78(18.935)	90.94(9.065)	.026
Mid anterior	69.11(23.534)	73.17(21.194)	.051
Mid anteroseptal	74.06(23.849)	76.33(23.086)	.440
Mid inferoseptal	75.28(20.035)	80.11(17.623)	.071
Mid inferior	62.17(13.094)	70.28(10.436)	.013
Mid inferolateral	81.17(20.010)	83.28(13.940)	.437
Basal anterolateral	75.89(15.507)	80.67(8.331)	.096
Anterobasal	74.67(16.029)	78.17(11.967)	.086
Inferobasal	59.50(15.186)	65.94(12.762)	.186
Basal inferolateral	68.11(17.766)	73.56(9.630)	.087

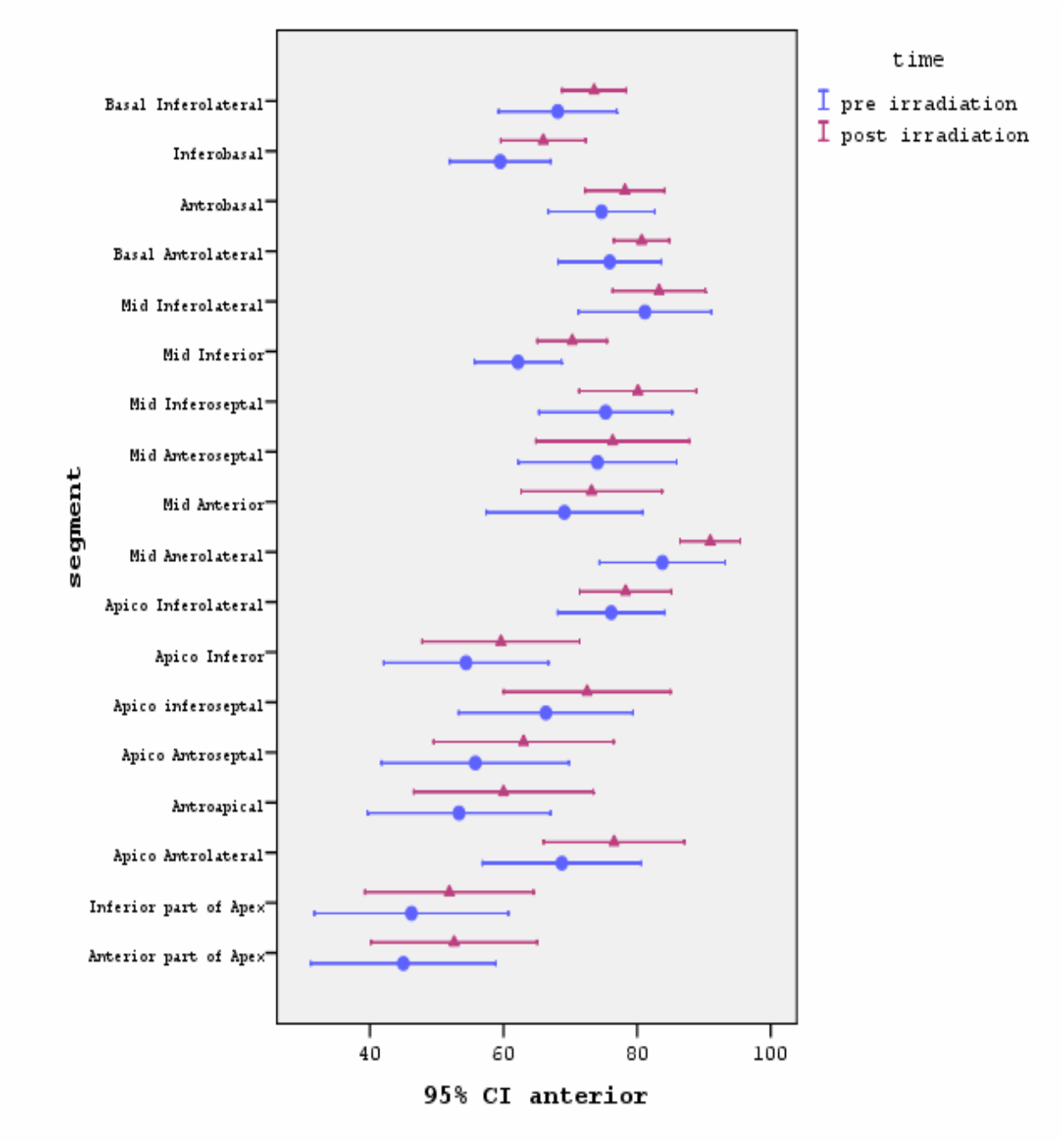
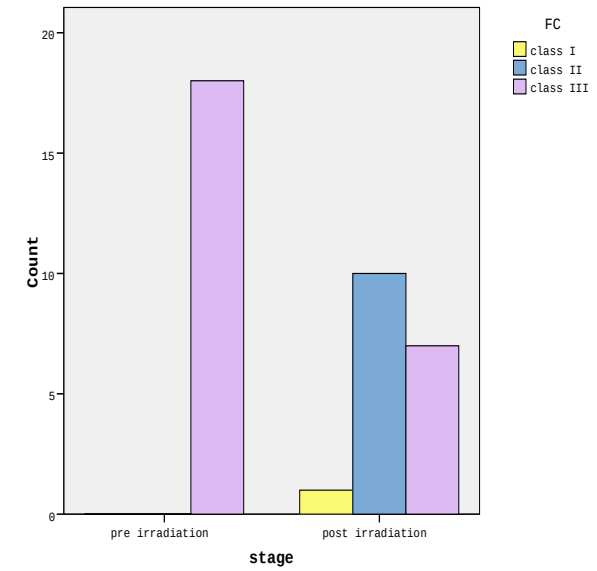
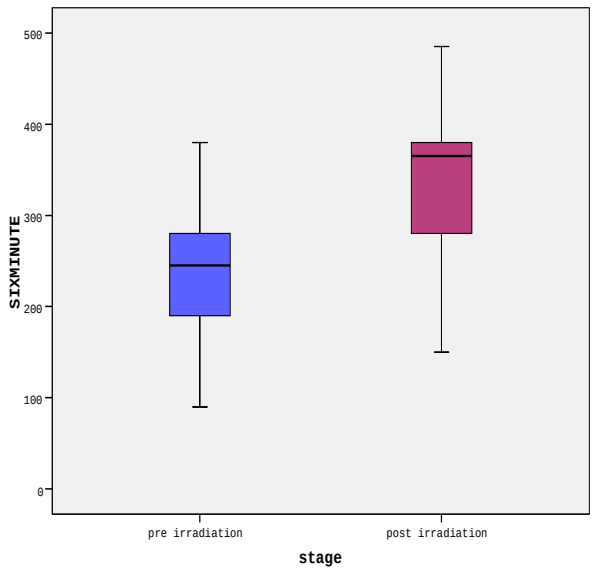


Figure1.percent of myocardial perfusion of 18 segment of myocardium by single photon emission computed tomography(SPECT)



A



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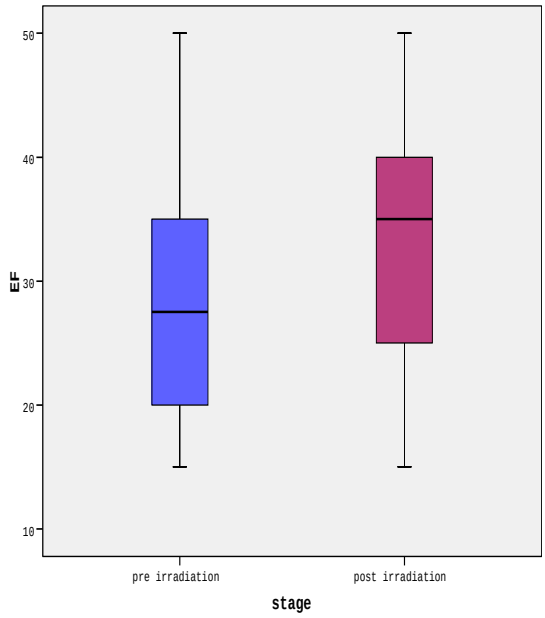

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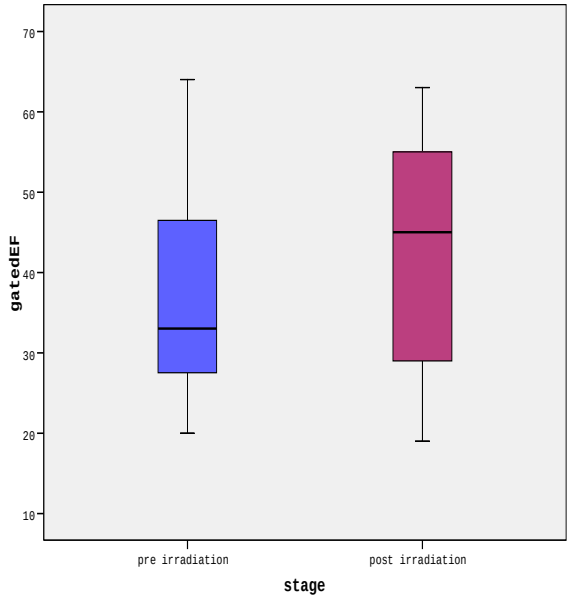


D

Figure 2. Graph presenting change of selected parameter. A.FC –functional class

B. six minute walk test C. EF-ejection fraction by transthoracic echocardiography D. Gated EF

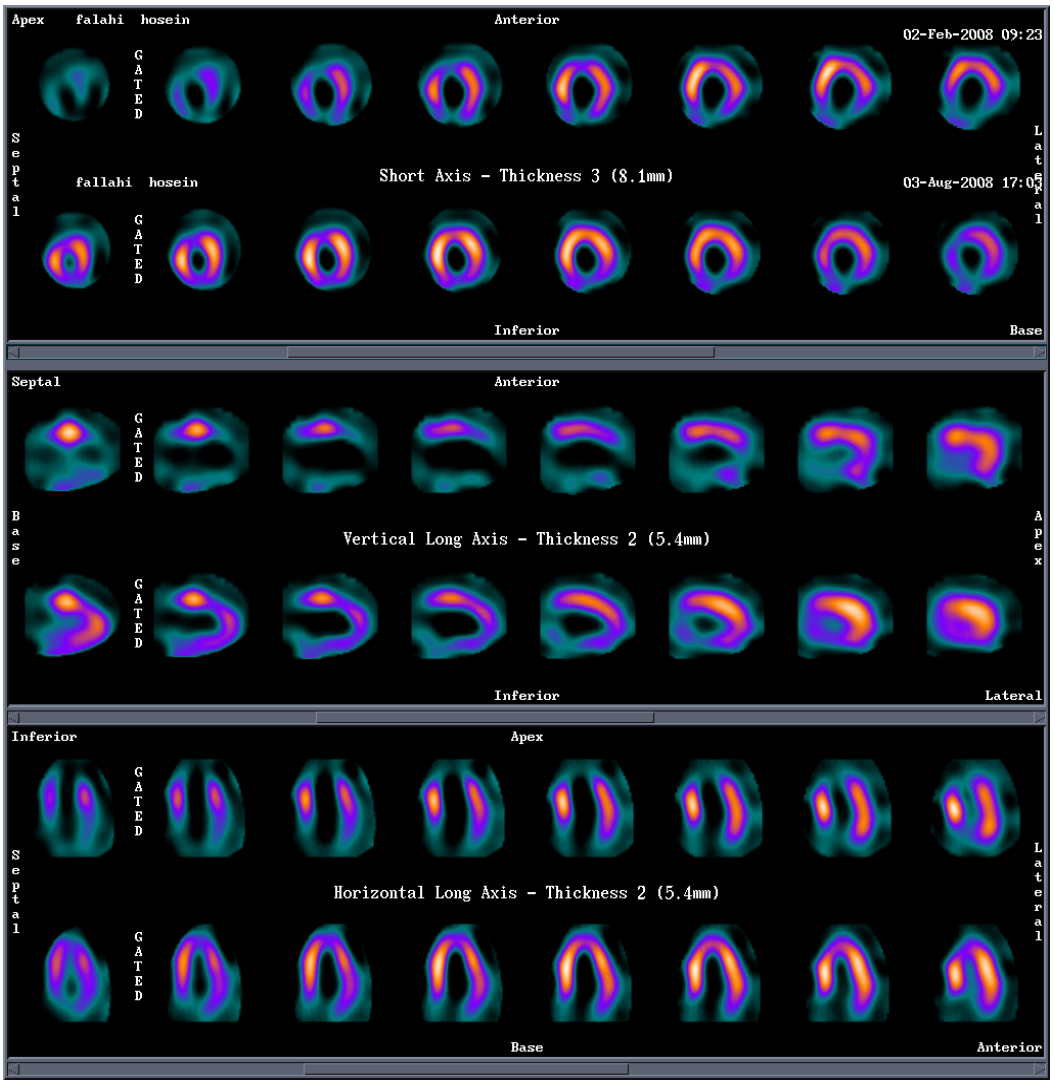
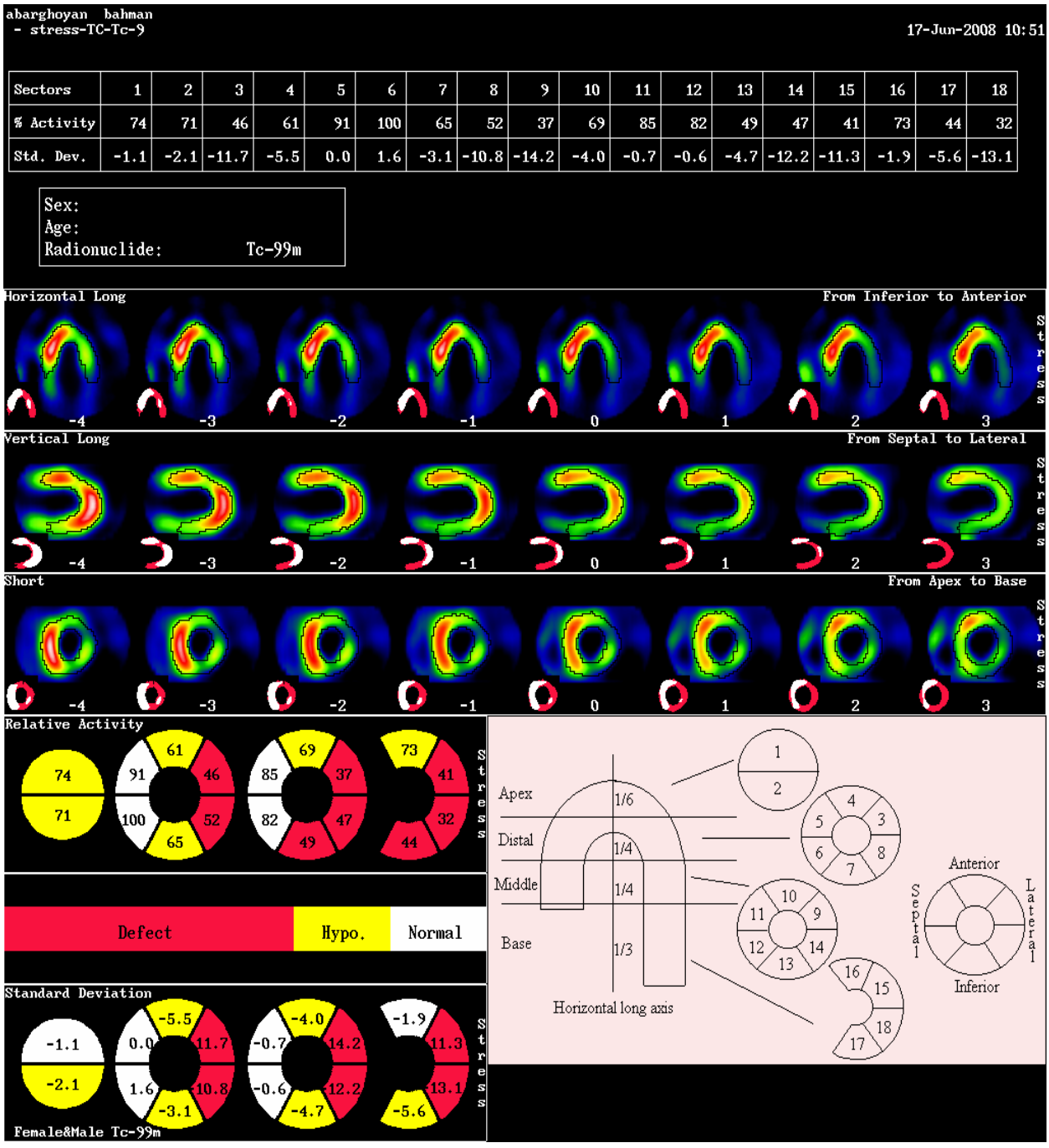


Figure III: One sample of single photon emission computed tomogeraphy (SPECT) of patient pre & post laser



Sectors	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
% Activity	74	71	46	61	91	100	65	52	37	69	85	82	49	47	41	73	44	32
Std. Dev.	-1.1	-2.1	-11.7	-5.5	0.0	1.6	-3.1	-10.8	-14.2	-4.0	-0.7	-0.6	-4.7	-12.2	-11.3	-1.9	-5.6	-13.1

FigureIV: Percent of myocardial perfusion via quantitative measurement

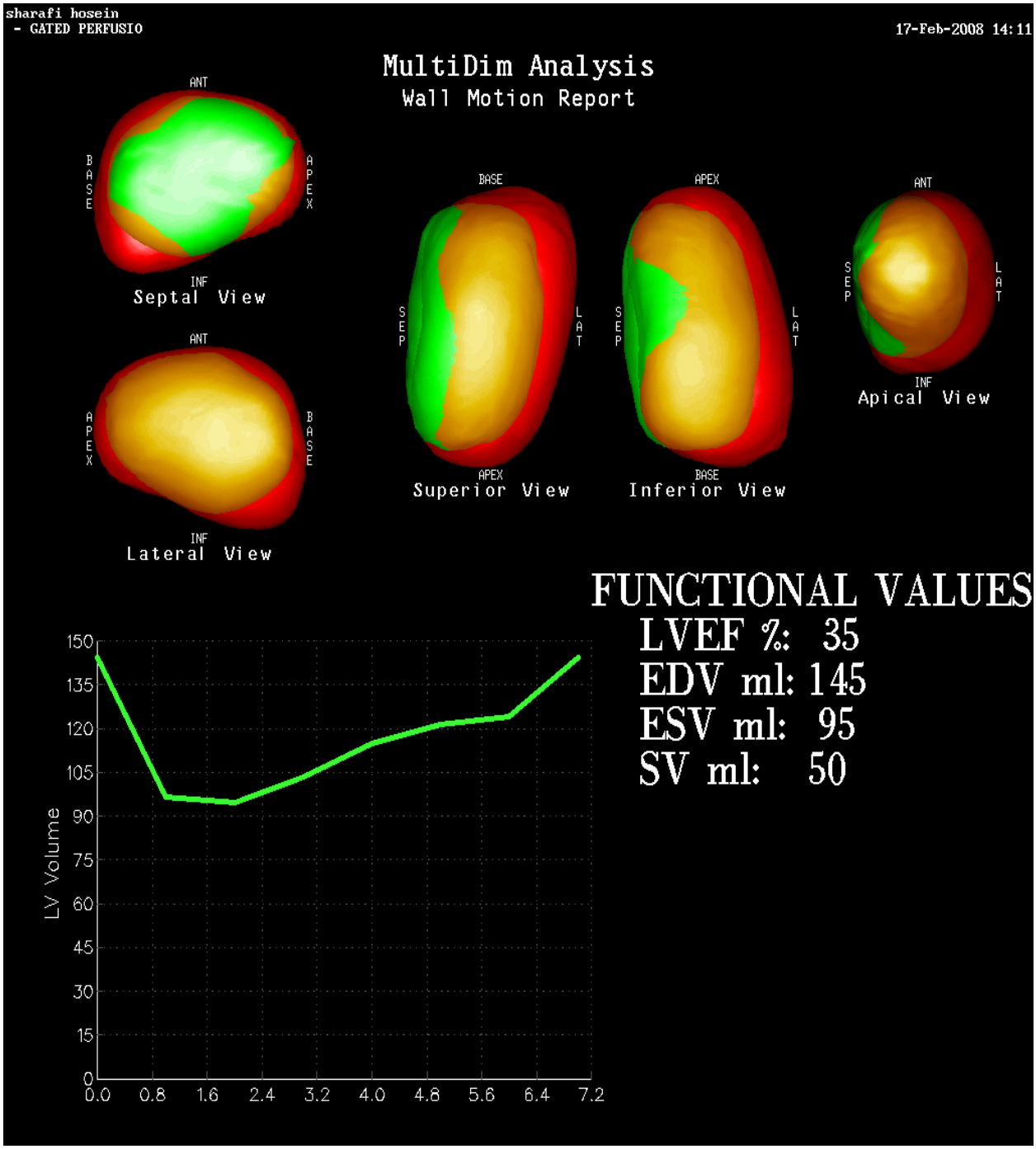


Figure V: Measurement of left ventricular ejection fraction via gated MPI

Discussion

The low energy laser radiation also called laser biostimulation may be considered a phototherapy method and even a form of physiotherapy. The aforementioned designations apply to radiation of energy ranging between a few to a dozen or so J/cm2 and power not exceeding several hundred MW, most often in the range from 1 to 30 mW, penetrating tissue to the depth of 20-50 mm. This level of power is not sufficient to produce a thermal effect and the increase of temperature does not exceed 0.1-0.5°C. The features of such radiation involve a reduction of inflammation, increased rate of cellular regeneration and higher activity of repair processes, including wound healing. Simultaneously, such radiation prevents negative, uncontrolled cellular hypertrophy activated by an inflammatory response. It should be emphasised that biological effects are observed much deeper than the level of direct radiation penetration.

Owing to these features, LLLT has been applied widely in many medical disciplines, including cardiology, where it has been tried on coronary artery segments during angioplasty and stenting procedures to prevent restenosis as a result of physiological activation of endothelial hyperplasia with simultaneous inhibition of neointima proliferation [17, 18].

The observed improvement in the FC class and decrease of angina symptoms in the examined patient group was supported by the results six minute walk test.

This improvement may be a result of the analgetic effect of LLLT, well documented in the medical literature. Such an effect may be associated with cellular membrane hyper polarization, changes of cellular redox status, increased endorphin and prostaglandin release and improvement of the intracellular metabolic processes, and also with an impact on the functional status of arterial and capillary vessels or with enhanced lymphatic drainage from inflammation-involved sites.

Low energy laser radiation causes vascular dilatation via nitric oxide (NO) (decreased intracellular Ca2+ concentration in vascular smooth muscle cells controlled by NO). It is supposed that alongside cytokines, lymphokines and free oxygen radicals produced by phagocytes, NO as a second transmitter is also responsible for the systemic effect of low energy laser therapy [19]. Also the impact of LLLT on rheological blood parameters seems interesting. Favorable changes of blood rheological features were observed after in vitro exposure to a radiation. They included decreased blood viscosity, increased compliance of erythrocytes and decrease sedimentation index [20].

It seems that the mechanisms described above may be responsible for the reduction of arterial blood pressure, improvement in functional circulatory status and lower incidence of ischemic events observed in our study.

The results presented herein seem to justify considering LLLT a safe procedure because no complications related to irradiation, either systemic or local, were observed in the short-term follow-up. However, an evaluation of the late effects of the irradiation is mandatory because one must be aware of the possible mutagenic impact of free radicals produced in the irradiated cells and the likelihood of inheritance of the intracellular changes, although no evidence of cyto- and genotoxic effects of such radiation have been found so far.

There is strong evidence of cardio protective effects of LLLT and the mechanisms of its influence on tissue are becoming better recognized. It is seems that in the near future an important issue will be to establish the optimum site of irradiation, radiation dose, time and wavelength of light.

To conclude, an observed improvement in the functional circulatory status and alleviation of angina symptoms may improve quality of life in patients with severe CAD. It is impossible at this time to answer the question as to whether the biostimulation procedures do improve patient prognosis and further follow-up study involving more patients and a control group will be mandatory.

Although no changes in LVEF were observed, a statistically significant decrease of arterial blood pressure, improvement in FC and myocardial perfusion in most anterior segments of myocardium was noted that may have a favorable impact on subjects in this particular patient population. Weather that

significant change were occurred in most in anterior segment of myocardium, it may be due to near anatomical distance of these segment to LL Laser irradiation. This hypothesis is needed further investigation. Although this functional improvement might be secondary to an improved blood supply to hibernating cardiomyocytes, it is also conceivable that hibernating myocardium may provide a more favorable microenvironment for the cardiomycyte when compared to scar tissue.
Several open questions are likely to be answered in the future: (1) what is the optimal dose, wave length, power of LL Laser? (2) Is there a dose response relationship? (3)What is the optimal break between two protocol of laser?One of the most urgent questions in basic science, to elucidate the mechanism by which LL laser achieve a functional improvement, is difficult to test in the clinical scenario. Although clinicians can measure flow reserve and heart function, the underlying detailed mechanism cannot be determined with an ethically applicable technology in the near future. In chronic ischemic HF, a superimposed question is whether identifying hibernating myocardium to LL laser is essential to an effective outcome. For established scar tissue late in the disease, specific strategies might be needed. The treatment of non ischemic heart disease is not yet addressed.

Study limitations

This study involved a relatively small number of 22 patients, and lacked a sham procedure group, precluding objective analysis of clinical parameter changes. Although the examinations were performed by the same physician team, our study methods are of limited accuracy and reproducibility. In the study presented here in we focused on a presentation of the examined patient group and aimed to show no complications associated with therapy based on a novel LLLT method. Additionally, a favorable impact of the therapeutic environment and reproducibility of follow-up examinations may have resulted in a placebo effect possibly affecting the results of the exercise stress tests. It should be mentioned that some of the patients that were diagnosed before initiation of irradiation had received optimum medical therapy according to the Polish Cardiac Society and ACC/AHA guidelines. Taking into account the prolonged period of time needed to reach full action of some drugs, the observed hypotensive effect might be a result of the aforementioned circumstances, although the final clinical assessment was performed 3 months after initiation of irradiation, medical therapy did not change significantly throughout the study.

Conclusions

In our clinical study, no adverse events of laser biostimulation were seen. Analysis of results suggests a slight, though statistically significant, improvement of exercise capacity and myocardial perfusion and decrease of arterial pressure in patients with advanced ischemic heart disease not suitable for any revascularization. However, no improvement of LV performance was noted as a result of biostimulation. These promising results should be confirmed in another study with a placebo control group.

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Appendix1

Check list for low level laser Therapy in Chronic Stable Angina

Unite number	First name:	Age:
Cell number:	Last name:	Sex: ☐male ☐Female

Charactristic finding:

History of MI: ☐Yes ☐No
History of CABG: ☐Yes ☐No
History of PCI: ☐Yes ☐No
→If yes which vessel: ☐LAD ☐LCX ☐RCA

CAD risk factor:
☐HTN ☐C/S
☐DM ☐Opium addict
☐HLP ☐Overweight (BMI 25-30)
☐Obesity (BMI>30)

The last angiography Report:

Number of vessel Diagnosis:
☐S.V.D
☐2.V.D
☐3.V.D

Which vessel was occluded:
☐LAD ☐Lima to LAD
☐LCX ☐SVG
☐RCA

Prelazer evaluation:

P/E :
BP ……..
HR ……..
ECG: ☐NSR
☐AF
☐Q wave ☐Inf. lead ☐Ant. lead
☐LBBB
☐RBBB
☐ST dep: ☐inf. lead ☐Ant. lead ☐High lat (I, avl) ☐Low lat (V5-V6)

TTE:
EF:
LVEDd:
LVESd:
Diastolic dysfunction: ☐Grade I ☐Grade II ☐Grade III ☐Grade IV
MR severity: ☐Mild ☐Mild to mod. ☐Mod. ☐Mod to severe ☐Severe

Gate MPI:
-Myocardial perfusion …….%
-EF:
-LVEDV:
-LVESV:

Six minute walk test:
☐FC I>450 met.
☐FC II>350 met.
☐FC III<350 met
☐FC IV→ no activation.

Lab data:
Hb: …… TG: ……
BUN: …… Chol: ……
Cr: …… LDL: ……
FBS: …… HDL: ……

Post lazer evaluation : (3 months later)

P/E :
BP ……..
HR ……..
ECG: ☐NSR
☐AF
☐Q wave ☐Inf. lead ☐Ant. lead
☐LBBB
☐RBBB
☐ST dep: ☐inf. lead ☐Ant. lead ☐High lat (I, avl) ☐Low lat (V5-V6)

TTE:
EF:
LVEDd:
LVESd:
Diastolic dysfunction: ☐Grade I ☐Grade II ☐Grade III ☐Grade IV
MR severity: ☐Mild ☐Mild to mod. ☐Mod. ☐Mod to severe ☐Severe

Gate MPI:
-Myocardial perfusion …….%
-EF:
-LVEDV:
-LVESV:

Six minute walk test:
☐FC I>450 met.
☐FC II>350 met.
☐FC III<350 met
☐FC IV→ no activation.

Lab data:
Hb: …… TG: ……
BUN: …… Chol: ……
Cr: …… LDL: ……
FBS: …… HDL: ……

Appendix2

Protocol of low level laser therapy
Rajaei Cardiovascular Medical & Research Center

No of patient:	**Unite Number:**
First Name:	**Last Name:**
Date of first Referral:	**Name of Patient's cardiologist:**

☐ **1st time**	**Date: .....**	IV	Red light with 50% CW power	20min
			Concomitant with	
		local	Red light with 50% CW power on V3, V4	20min
			Infrared light with 50% CW power on V5, V6	20min
☐ **2nd time**	**Date: .....**	IV	Red light with 50% CW power	20min
			green light with 10% CW power	10min
			Concomitant with	
		local	Red light with 50% CW power on V3, V4	20min
			Infrared light with 50% CW power on V5, V6	20min
☐ **3rd time**	**Date: .....**	IV	Red light with 50% CW power	20min
			green light with 10% CW power	20min
			Concomitant with	
		local	Red light with 50% CW power on V3, V4	20min
			Infrared light with 50% CW power on V5, V6	20min

☐ **4th time**	**Date: .....**	as the same on third protocol
☐ **5th time**	**Date: .....**	as the same on third protocol
☐ **6th time**	**Date: .....**	as the same on third protocol
☐ **7th time**	**Date: .....**	as the same on third protocol
☐ **8th time**	**Date: .....**	as the same on third protocol
☐ **9th time**	**Date: .....**	as the same on third protocol
☐ **10th time**	**Date: .....**	as the same on third protocol

1: on ECG Recording V3: Midway between V2 and V4 (V2: left sternal margin, forth intercostals space)
2: on ECG Recording V4: Left mid ventricular line, fifth intercostals space
3: on ECG Recording V5: Left anterior axillary line
4: on ECG Recording V6: Left mid axillary line