Contrast-Echocardiography: Confirmation of Patency of Laser Channels after Transmyocardial Laser Revascularization

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**Aims:** Apart from casuistic autopsy results there is no long-term evidence for channel perfusion after transmyocardial laser revascularization in humans.

**Methods and Results:** Fifteen consecutive patients aged 63±17 years were investigated 71±15 days after coronary artery bypass surgery and/or transmyocardial revascularization with 13–37 (20±5) channels (CO2 laser, 40 J/pulse). Echocardiography was performed after injection of 6 ml echo contrast medium into left ventricular cavity and after injection of 3 ml contrast medium into the left main coronary artery. In five patients with additional bypass surgery to the same region, we also injected 3 ml contrast medium into bypass graft. We could prove in 10 of 15 patients (67%) one or two laser channels in the apical left ventricular myocardium. Channels were perfused exclusively during systole. During following heart cycles myocardium was opacified up to a mean width of 1.4±0.4 cm, a mean depth of 0.71±0.1 cm, and a mean area of 1.0±0.6 cm². Contrast medium was washed out via coronary venous system in 9±8 systoles.

**Conclusion:** This is the first clinical evidence of long-term laser-channel patency in humans showing perfused myocardium via left ventricular cavity.


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**Key Words:** transmyocardial laser revascularization; myocardial contrast echocardiography; channel patency.

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**Introduction**

Percutaneous transluminal coronary angioplasty and coronary artery bypass graft surgery are proved methods for treating ischaemic heart disease, but a significant number of patients are not amenable to these therapies. Direct revascularization involving application of a high-energy CO2 laser to create transmural channels in the left ventricular myocardium has been suggested as an alternative therapeutic technique[1] especially in patients with diffuse coronary artery disease.

The basis for attempting direct myocardial revascularization came from Wearns and colleagues in 1933[2]. They described a unique aspect of the myocardial microanatomy involving the presence of myocardial sinusoids in reptiles. These sinusoidal communications vary in size and structure, but represent a network of direct arterial–luminal, arterial–arterial, arterial–venous, and venous–luminal connections. The further development included the Vineberg Operation[3,4] with implantation of the left internal mammary artery into the myocardium, which was, however, overshadowed by the emergence of coronary artery bypass graft surgery. Sen et al.[5], and later on Hershey and White[6], attempted to deliver oxygenated blood directly from the left ventricle into the myocardial sinusoids. They used needle acupuncture to create transmural channels. However, fibrous tissue ingrowth caused early closure of the communications[7].

Mirhoseini and Cayton[1,8–12] developed the use of a laser to create transmyocardial channels that would allow ventricular blood to directly perfuse ischaemic myocardium.

In 1991, Mirhoseini et al.[13] began clinical studies with an 800 W CO2 laser, which made it possible to create channels in the contracting myocardium.
Apart from recent first casuistic autopsy results\[14,15\], there has been no evidence of perfusion over the laser-mediated channels in the beating heart. We therefore sought to examine long-term channel patency in humans and the perfusion behaviour of the laser-mediated channels.

**Methods**

### Patients

Fifteen consecutive patients (all men, mean age 63 ± 17 years) were investigated 71 ± 15 days after transmyocardial laser revascularization. Six patients underwent transmyocardial laser revascularization surgery only, two patients underwent transmyocardial laser revascularization and coronary artery bypass graft to another coronary bed, and seven patients received laser channels and coronary artery bypass graft in the same region. Baseline patient characteristics are depicted in Table 1.

### Study Design

Diagnostic left heart catheterization and coronary arteriography were performed by a standard percutaneous femoral approach. Patients received no premedication. In nine patients with additional coronary artery bypass graft, we could demonstrate open bypass grafts. Five minutes after routine angiography, we performed myocardial contrast echocardiography by injecting 3 ml of echo contrast medium into the left main coronary artery as well as in the bypass-graft of seven patients, which perfused the region of the laser channels. To assure that the inflow of echo contrast medium was taking place under physiological conditions, an injection pump with an injection pressure of 120 mmHg and a flow rate of 3 ml/s was used\[16\]. Thereafter, we changed the Judkins catheter against a 7 F pigtail catheter and introduced it into the left chamber. After measurement of basal haemodynamics, 6 ml of echo contrast medium were injected into the left heart chamber at a flow rate of 6 ml/s.

### Echocardiography

The patients were examined in the supine or slight 10° left lateral decubitus position with a commercially available electronic sector scanner (Sonos 1000 from Hewlett Packard) with a 2·5 Mhz transducer. The apical four-chamber view was obtained during slight expiration to eliminate cardiac motion due to respiration. The images were recorded on videotape (S-VHS formate) with simultaneous recording of a lead II electrocardiogram for timing purposes. Data were assessed blindly.

### Echo Contrast Medium

The echo contrast medium used by us is a mixture of oxypolygelatine (as carrier substance, Gelifundol\[29\], Table 2. Contents of echo contrast medium.

<table>
<thead>
<tr>
<th>Contents of echo contrast medium.</th>
</tr>
</thead>
<tbody>
<tr>
<td>+5.0 ml oxypolygelatine (Gelifundol[29])</td>
</tr>
<tr>
<td>+3.0 ml oleum sojae and lecithinum (Lipovenos%[29])</td>
</tr>
<tr>
<td>+0.2 ml sodium-iron(3)-gluconat (Ferrlecit[29])</td>
</tr>
</tbody>
</table>

=8.45 ml echo contrast medium.

Apart from recent first casuistic autopsy results\[14,15\], there has been no evidence of perfusion over the laser-mediated channels in the beating heart. We therefore sought to examine long-term channel patency in humans and the perfusion behaviour of the laser-mediated channels.

### Table 1. Baseline patient characteristics.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angina</td>
<td>15</td>
</tr>
<tr>
<td>Left ventricular ejection fraction</td>
<td>2</td>
</tr>
<tr>
<td>&lt;30%</td>
<td>13</td>
</tr>
<tr>
<td>Regional contraction disturbances in the region of laser channels</td>
<td>9</td>
</tr>
<tr>
<td>normokinetic</td>
<td>3</td>
</tr>
<tr>
<td>hypokinetic</td>
<td>3</td>
</tr>
<tr>
<td>akinetic</td>
<td>5</td>
</tr>
<tr>
<td>dyskinetic</td>
<td>4</td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>9</td>
</tr>
<tr>
<td>Thinned myocardium (≤9 mm) and echocardiographic signs of fibrosis in the laser region</td>
<td>4</td>
</tr>
</tbody>
</table>

Baseline patient characteristics are depicted in Table 1.

### Table 2. Contents of echo contrast medium.

<table>
<thead>
<tr>
<th>Time between injection of contrast medium and visualization of laser channels (systoles)</th>
<th>Evidence of contrast medium (systoles)</th>
<th>Laser channels demonstrable in the apex</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=15</td>
<td>1·9 ± 0·2</td>
<td>1·5 ± 0·5</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± SD.
oleum sojae fractionate and lecithinum fractionate (building of a lipid monolayer of the microbubbles, Lipovenös®), low quantities of a sodium-iron(3-)-gluconat-complex (increasing the stability of the lipid monolayer, Ferlecit®), and small amounts of air. The solution is distributed into two 10 ml syringes, and is then agitated by rapid transfer from one syringe to another 20 times through a plastic three-way stopcock. The microbubbles obtained are smaller than 3·9 μm; 66·7% of the microbubbles are in the range of 1·0 μm, and the whole solution consists of 7·1 × 10¹¹ microbubbles. The echo contrast medium applied by us lies within relatively physiological ranges at an osmolality of 345 mosmol/kg (arterial blood 310 mosmol/kg), and a relative viscosity of 3·3 at 33°C (arterial blood 3–5), thus differing considerably from the echo contrast medium otherwise applied (Table 2).

In animal studies, we could demonstrate no changes in coronary blood flow after intracoronary injection of 1 ml echo contrast medium for 25 g myocardial tissue. Transferring these results to human myocardium with approximately 180–220 g of left ventricular myocardium being perfused by the left coronary artery, this means that 7·2–8·0 ml echo contrast medium do not produce any changes in coronary blood flow.

**Laser Procedure**

Transmyocardial laser revascularization was performed with the Heart Laser CO₂ system (Laser Engineering, Inc. Milford, Massachusetts, U.S.A.), which has a peak output of 1000 W. The laser was set to operate at a pulse energy of 40 J, which corresponds to a pulse duration of 40 ms. The delivery of each laser pulse was synchronized with the R wave on the electrocardiographic signal. A total of 13–37 (20 ± 5) pulses were delivered, approximately 1 cm apart, to the apical, anterior, and anterolateral aspects of the beating heart. Transmyocardial penetration of the pulses was confirmed by intraoperative transoesophageal echocardiography on observation of intra-cavitary bubbles that were produced by the contact of the laser beam with intra-ventricular blood. Adequate haemostasis was ensured by applying external digital pressure or by placing epicardial purse-string sutures.

**Results**

None of the 15 consecutive patients experienced any complications peri- or postoperatively. Coronary
angiography and ventriculography revealed no patent laser channels in the 15 patients with transmyocardial laser revascularization surgery.

**Myocardial Contrast Echocardiography**

Echo contrast medium was injected into left ventricle during catheterization. In 10 of 15 patients (67%) one or two laser channels were detected in the apical or supra-apical left ventricular myocardium. In almost all patients the laser channels and the subendocardial and middle part of the myocardium were opacified during the second systole after echo contrast medium injection into the left ventricle, representing the time point of maximum concentration of microbubbles and maximum contrast intensity.

In all patients perfusion through laser channels took place during systole exclusively. During the following diastoles and systoles, the myocardium was opacified up to a mean width (i.e., horizontal distance in the apex) of \(1.4 \pm 0.4\) cm, a mean depth (i.e., distance of endocardium in direction to the epicardium) of \(0.7 \pm 0.1\) cm, and a mean area of \(1.0 \pm 0.6\) cm\(^2\). The mean evidence of echo contrast medium in the myocardium was \(9 \pm 8\) systoles which is dependent on the echo contrast medium washout from the left ventricular cavity (Table 3).

Our attention was directed to the apical region with the ultrasound beam being focused at a transducer distance of 3 cm. Here, we were able to demonstrate one or two patent laser channels (1.5 ± 0.5).

Myocardial contrast echocardiography is divided into three phases. After injecting the contrast medium the whole ventricular cavity is filled (Phase I, Fig. 1). In Phase II the micro-bubbles can be detected in the intra-myocardial laser channels (Fig. 2). Thereafter, in Phase III, the bubbles have opacified the subendocardial myocardium (Fig. 3), while the ventricular cavity shows no remaining contrast medium.

In the other five patients without transmyocardial laser revascularization surgery, channels or opacified myocardium in the apex could not be seen.

**Discussion**

As far as we know, this is the first clinical study proving functional evidence of long-term laser channel patency in the beating human heart. We were able to demonstrate in real time motion that the laser channels were

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Figure 2. Phase II: Laser-channels are perfused by micro-bubbles (white arrow).
perfused from the left ventricular cavity to the subendocardial and middle part of the myocardium (Figs 4 and 5). The 16 laser channels that were found patent in 10 patients were perfused during systole only, supplying the surrounding myocardium at a width of $1.4 \pm 0.4\, \text{cm}$, a depth of $0.7 \pm 0.1\, \text{cm}$, and an area of $1.0 \pm 0.6\, \text{cm}^2$. The echo contrast medium was washed out over the native coronary venous system in $9 \pm 8$ systoles. When the echo contrast medium was injected into the bypass or the native coronary arteries, the laser channels did not drain into the cavity.

In a recent study in humans with coronary artery disease, we were able to demonstrate and describe the perfusion behaviour of Thebesian veins\cite{18}. In addition, we were able to image the perfusion bed of coronary collaterals smaller than $100\, \mu\text{m}$\cite{19}, which is the maximum X-ray resolution in coronary angiography\cite{20}. Compared with this, maximum axial resolution of two-dimensional echocardiography is $1\, \text{mm}$, but with the microbubbles reflecting 100 times more ultrasound energy than the myocardium, the resolution of myocardial contrast echocardiography is thus $10\, \mu\text{m}$.

A recent study reported the anatomic evidence of channel patency at cardiac autopsy of a patient who died of myocardial infarction on postoperative day 94, due to acute occlusion of the middle and distal right coronary arteries. Histological evidence of patent, endothelium-lined tracts within the laser-created channels supports the assumption that the lumen of the laser channels is or can become haemocompatible and that it resists occlusion caused by thromboactivation and/or fibrosis\cite{15}. The hypothesis was formulated that compression of the laser channels may lead to their occlusion when regional myocardial normokinesia reoccurs\cite{21}. However, our results showed the laser channels to be patent also in patient no. 2 with restoration of wall motion.

Investigations using positron emission tomography described an increase of the mean subendocardial/subepicardial perfusion ratio of $14\%$ 3 months after transmyocardial laser revascularization. On dobutamine echocardiography, the mean resting wall-motion score index was improved by $16\%$ in lased segments\cite{21}. There was also finding of an unexpected increase in the non-lased septal perfusion ratio during stress. The authors suggest that if a collateral network develops postoperatively between the laser-revascularized free wall and the perforating branches of the anterior and posterior descending coronary arteries, additional blood might be driven towards the septum due to the increased left ventricular pressure during stress\cite{21}.

After initial opacification of the laser channels and the surrounding myocardium in the apical region, the present study which was performed in real-time motion and frame by frame (every 33 ms) demonstrated opacification also in the distal septum shortly before complete washout. It remains to be clarified whether the echo contrast medium was washed out from the apical region
Figure 4. Myocardial contrast echocardiogram of apical four-chamber view in a 49-year-old patient with QS configuration in V1-V5 after transmyocardial laser revascularization and coronary artery surgery. The original copies and the schematic drawings are shown in the upper and lower panel, respectively. On the left side during diastole, the left ventricular cavity is opacified by the contrast medium, while the myocardium is not opacified. On the right side during the following systole, the contrast echocardiogram shows an opacification more of the subendocardial (right arrow) and intramural myocardium (left arrow) over patent laser channels (for details see text).
via the distal septum over the coronary venous system or a collateral network.

In animal experiments, the results obtained after transmyocardial laser revascularization surgery were different. Mirhoseini and Cayton[12] found no infarcts in dogs that had received laser channels before coronary occlusion, and Jeevanandam et al.[22] reported much smaller infarcts in laser-treated dogs compared to control dogs. Others observed open laser channels after up to one year in patients with endstage coronary artery disease undergoing transmyocardial laser revascularization[15,23,24]. However it is reported that fibrotic tissue fills the entire channel[24]. In a recent study of Whittaker et al.[25], laser channels failed to increase blood flow to acutely ischaemic myocardium in a canine model of coronary artery occlusion, whereas the authors were able to prove long-term protection of laser- and needle-made channels in a rat heart model[26]. These findings were in contrast to those of Horvath et al.[23] in sheep experiments that demonstrated both short-and long-term improvement in contractility as well as reduced necrosis in the area at risk.

The preliminary results obtained by us with evidence of patent laser channels and perfusion of the surrounding myocardium to a width of 1·4 ± 0·4 cm in the apical region suggest a channel-spacing distance of 1·0 cm to be sufficient, with this distance being possibly extended to 1·4 cm.

In the present study, we were able to show long-term laser channel patency and the supply of opacified blood from the cavity over the channels to the surrounding myocardium. Further studies including a greater number of patients will be necessary to decide which patients with previous infarction and fibrosis or myocardial thinning will derive benefit from transmyocardial laser revascularization surgery. The present study with first findings of functional evidence of long-term laser channel patency gives encouragement for performing further studies embracing a greater number of patients so that the questions raised above might be answered.

**References**


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**Figure 5.** Example of perfusion over the left main coronary artery and the laser channels in a 63-year-old man without previous infarction and with laser revascularization only. (A) Native apical four-chamber view without echo contrast medium. (B) After injection of 3 ml echo contrast medium into the left main coronary artery, the myocardium is opacified except for a small distal part of the septum (white arrow). This corresponds to the occlusion of the second septal branch. There is no draining of blood via the laser channels into the cavity. (C) The left ventricle is filled with contrast medium. (D) With the beginning of systole, we can see two patent laser channels at a distance of 1 cm. (E) After five systoles, only slight evidence of an opacification in the subendocardial myocardium is left.


