*Optica Applicata, Vol. XXXI, No. 4, 2001*

# Method of intravascular low power laser illumination

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The paper presents the method of intravascular endothelial cell irradiation with low power laser radiation. A special instrument was prepared and thoroughly described. It included a laser and a fiber with specially designed fiber diffuser. The technical parameters of the set-up are provided.

## 1. Introduction

Atherosclerosis is a disease which with time leads to cholesterol plaque formation. The plaques narrow disease-changed vessel with its final occlusion (Fig.1). This process refers to the whole arterial system but is extremely dangerous in the case of coronary or brain arteries.

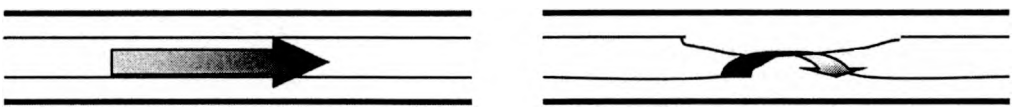

Fig. 1. Atherosclerosis of coronary artery.

Because of the importance of this phenomenon many therapeutic procedures which may lead to a decrease of the menace of already formed atherosclerotic plaques, especially in coronary arteries, are used. Such procedures are commonly called revascularization. They include surgical operations with the purpose of implantation of vain or arterial graft passing round the vessel obstruction-coronary artery by-pass graft (CABG). Recently, the leading procedure of revascularization is percutaneous transluminal coronary angioplasty (PTCA). The most important limitation of this intervention is hyperplastic response of treated artery called restenosis, which occurs in 20–40% after coronary intervention. The mechanism of this event is not well explained. Pathologic studies suggest that accumulation of smooth muscle cells and

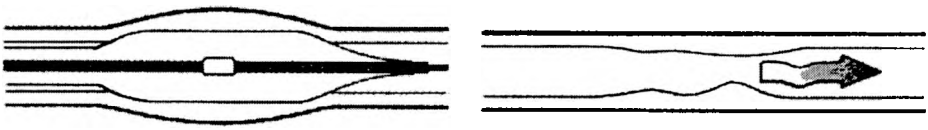

Fig. 2. Scheme of balloon angioplasty.

excessive accumulation of extracellular matrix materials contribute to restenosis following coronary intervention [1]. In the physiological conditions the endothelial -produced agents prevent this process. Unfortunately, the atherosclerosis leads to endothelium disfunction. Angioplasty procedure produces additional cell impairment in the treated part of the vessel. These are the reasons for much slower endothelial cell regeneration after PTCA. The final effect of the above is a strong predominance of restenotic agents.

At present, very diverse activity which may prevent restenosis is undertaken. There are trials with chemical agents suspected to have capacity to eliminate the natural mitogenic factors, provoke miofibroblast denudation or stimulate endothelial cell regeneration. Trials of physical effects (ionising radiation or thermal effect) and its application to prevent restenosis are also undertaken. Till now, despite application of many methods only implantation of stents into a vessel during coronary angioplasty was acknowledged as a therapeutic method, which leads to 10% limitation of restenosis. Figure 2 shows a scheme of balloon angioplasty procedure, while the procedure with stent implantation is presented in Fig. 3.

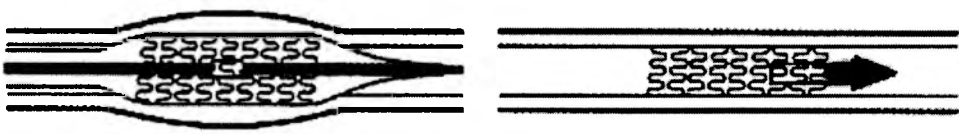

Fig. 3. Scheme of stent implantation.

One of the new procedures currently in the experimental phase is biostimulation of endothelial cells with laser light. Previously it was confirmed that energy delivered with laser light (monochromatic, coherent and polarised) to endothelial cells leads to their activation and proliferation. The influence of the absorbed dose of energy on cell proliferation is described by Arndt–Schultz curve [2]. For the values of 4–8 J/cm$^2$ an increase of proliferation is observed, in the range of 12–18 J/cm$^2$, plateau appears and at the higher doses cell impairment occurs. It seems that the optimal illumination for biostimulation processes lies in the range of 100–200 W/cm$^2$ for near infrared spectral range [2], [3]. It is known that for the radiation from the spectral range 800–1000 nm the penetration is deep enough. Our previous *in vitro* investigation on the influence of low power laser irradiation on endothelium cells confirms those findings [4], [5]. The results appeared very promising and were good warrant to perform intravascular

illumination. The first animal model experiment of laser endothelial cell biostimulation was carried out by DE SCHREEDER *et al.* [6], [7]. The same group was the first to perform recently promising clinical trials [8].

The present investigation describes our own method of biostimulating treatment, based on the activation of intravascular endothelial cell proliferation with low power laser infrared illumination *in vivo*. We can assume that biostimulation will be the most effective for endothelial cells and much weaker for the tissues located deeper because of weak penetration of laser radiation.

## 2. Description of the method

A complete set-up prepared for the intravascular illumination during PTCA procedure is shown in Fig. 4. It employs the over-the-wire balloon catheter used during the process of PTCA. The optical waveguide (optical fiber) terminated with special fiber diffuser is led via the internal duct of the catheter. The diffuser supplies the laser

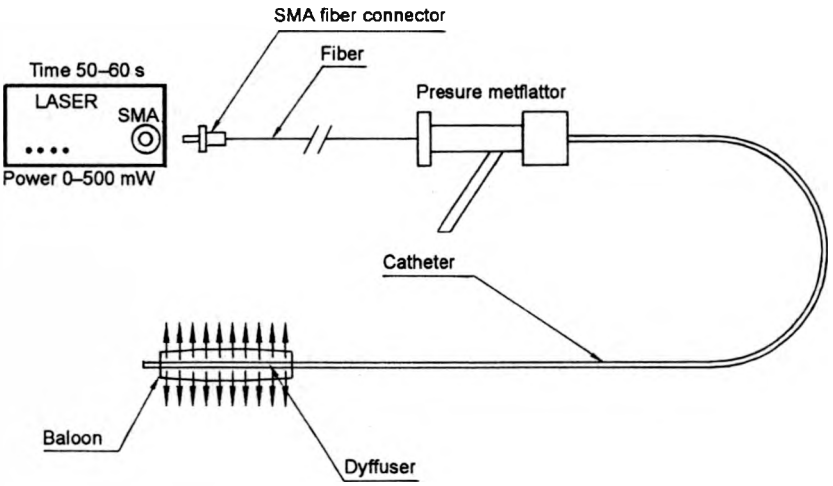


Fig. 4. Scheme of the laser/catheter system.

radiation into the disease-changed vessel and should guarantee its uniform distribution. The fact that both processes use the same catheter shaft is a great advantage of the method. The laser radiation is "injected" after PTCA treatment. The inflated balloon in the axis of the vessel positions the diffuser.

## 3. Instrumentation

The laser diode operates at the wavelength 808 nm with the maximal continuous wave output power of 2 W. When pigtailed to the multimode step-index silica fiber (200 μm core diameter and 250 μm cladding diameter) the maximal power of the laser in the

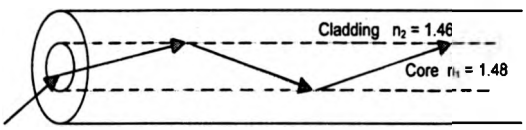


Fig. 5. Illustration of light propagation in the multimode step-index fiber.

fiber output terminated with a standard SMA connector is 1.7 W. The laser diode is thermocooled. The supply current of the laser is stabilised. Due to the above controlling system the fluctuations of the output laser power are less than 1%. The output power and time of illumination can be settled and controlled by specially designed electronics.

The laser with pigtailed multimode fibers is the stationary part of instrumentation. Generally, the set-up consists of a stationary laser part and a movable illumination part dosing laser radiation. The fiber introduced into the catheter is terminated by a diffuser. It is the same type of fiber as the stationary one in the laser source.

The symbolic way of ray propagation in the step-index fiber is shown in Fig. 5. The radiation is kept inside the core because of the simple optical rule which states that when the refractive index of the core is higher than the refractive index of the cladding the inside full reflection of light occurs.

The external diameter of the fiber used is determined by the internal diameter of the catheter (350 μm). The laser radiation is homogeneously mixed in the fiber core due to its multimode nature.

The main task of the fiber is to deliver the laser radiation with low losses into its last part. The last part of the fiber is a diffuser. The role of the diffuser is to scatter the radiation leaking from the last part of the fiber along its total length of about 20 mm. The length of the diffuser should be the same as the length of the balloon. However, it is required to have high homogeneity of radiation in the diffusive part of the fiber.

The leaking can be obtained by changing the physics of propagation. This can be done by changing the value of refractive index of the cladding as shown in Fig. 6. In order to get diffuser, the core should be covered by material with higher refractive index.

The fiber with 200 μm core diameter has cladding of 250 μm in diameter made of hard and optical quality polymer. After taking this polymer layer off, the core was

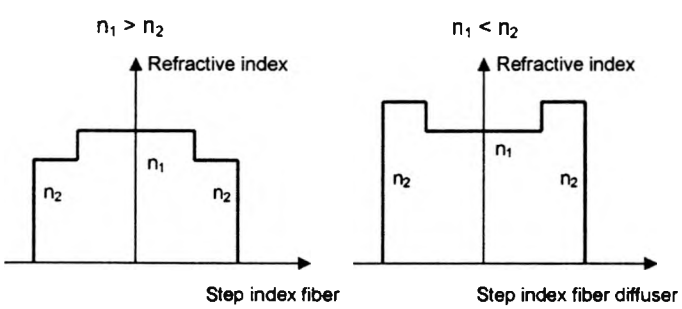


Fig. 6. Refractive index distribution in the fiber and diffuser.

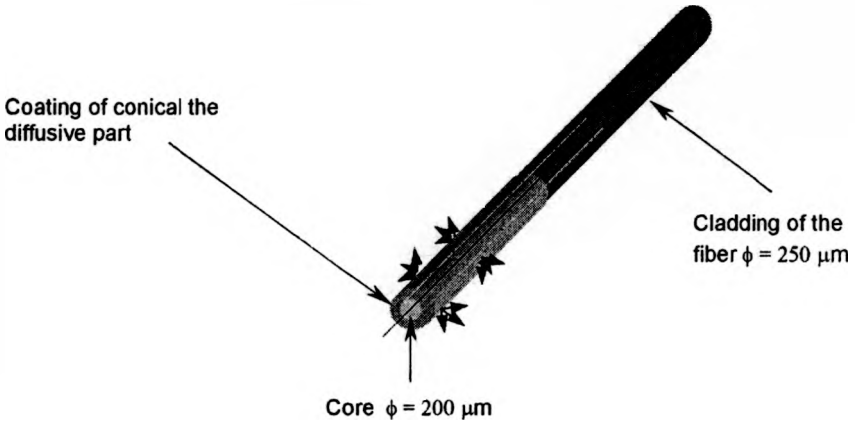


Fig. 7. Schematic view of diffuser.

coated with special material with refractive index $n = 1.54$ (Fig. 7). In order to obtain a uniform layer of coating this special material had to have appropriate viscosity.

In order to obtain homogeneous leaking of the laser radiation this extra coating has special conical shape, shown in Fig. 8 [9]. The conical angle was settled experimentally. The obtained diffuser gives quite homogeneous distribution of illumination in the front of the radial direction, along its whole length which is 20 mm. From the front of the diffuser about 10% of the laser radiation leaks.

Figure 9 demonstrates the distribution of radial laser radiation leaking from the diffuser. It was taken by the CCD camera, calibrated and specially settled for this experiment.

Diffusers are resistive to the sterilisation process, which means that they are not damaged by the NO atmosphere. These are also resistive to bending at the radius as small as 3 cm. The transmissions of seven different balloons of different producers containing the physiological liquid with the iodine contrast were measured in order to find the one with the maximal transmission. Generally, the transmission was spread between 80% and 95%. The balloon with 95% transmission was chosen as a standard.

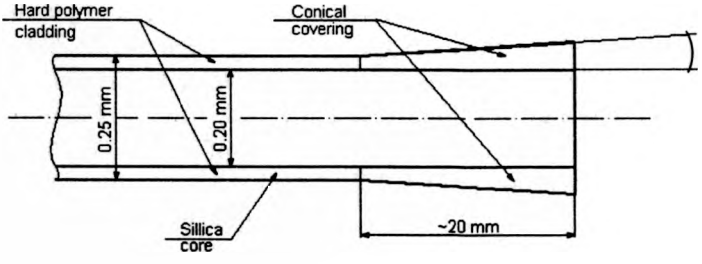


Fig. 8. Schematic of diffuser.

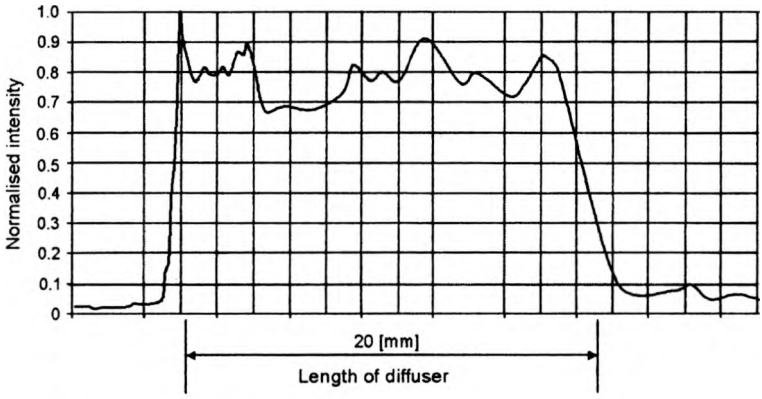


Fig. 9. Intensity distribution of laser radiation along diffuser.

Elementary calculation shows that in order to get the required illumination (energy per area) of $E = 9$ J/cm$^2$ (settled from another research [4], [5]) for biostimulating radiation with practical time of illumination of 30 seconds the required power leaking from the diffuser is:

$$E = \frac{Pt}{s}, \quad \left[\frac{\mathrm{J}}{\mathrm{cm}^2}\right] = \frac{[\mathrm{W}][\mathrm{s}]}{[\mathrm{cm}^2]}, \tag{1}$$

$$P = \frac{Es}{t}, \quad [\mathrm{W}] = \frac{[\mathrm{J/cm}^2][\mathrm{cm}^2]}{[\mathrm{s}]}. \tag{2}$$

For the typical area of the side wall of the balloon $s = 2$ cm$^2$ and illumination time $t = 30$ s, the required power delivered via side-wall of the diffuser is $P = 0.6$ W.

Taking into account 95% transmission from the diffuser into the vessel and 10% losses caused by front radiation, the necessary power delivered from the laser can be estimated at 0.7 W. However, we noticed that the connection between the fiber of the diffuser and the fiber delivering power from the laser can be a source of serious losses. This connection is made by SMA connector. The main source of losses is due to misalignment of core axes. Simple calculation shows that, for example, for 200 μm multimode fiber, 50 μm shift of core axes causes about 30% losses of propagating power. Assuming that the connection losses cannot be higher than 10%, the acceptable eccentricity should be less than 7 μm. Such requirement has been fulfilled by multimode fiber 200/250 μm with higher symmetry made by Jan Wójcik (Laboratory of Optical Fibers Technology, Maria Curie–Skłodowska University, Lublin, Poland). Low loss connections allow using diode laser with a small reserve of power. Our laser cardiodiffuser system delivers maximal power of 1.7 W, which assures quite a high margin of necessary power. All measurements of the total output power from the diffuser were performed by integrating sphere (Melles–Griot) allowing measurements of radially propagating laser radiation.

## 4. Conclusions

The diffuser presented fulfils the requirement of homogenous distribution of leakage laser radiation along the required length of 20 mm of the fiber diffuser. This system will be applied to the medical treatment of intravascular endothelial cell irradiation with low laser power.

*Acknowledgments* – This work was financed by the State Committee for Scientific Research (KBN), within the research project 4 P05C 04318.

### References

[1] BAUTER CH., ISNER J.M., *The biology of restenosis* [In] *Textbook of Cardiovascular Medicine*, [Ed] E.J. Topol, Lippincott-Raven Publishers, Philadelphia 1998, pp. 2465–2489.
[2] ADAMEK M., SIEROŃ A., *Fotostymulacja tkanek na skutek działania promieniowania laserowego*, [In] *Zarys klinicznych zastosowań laserów*, Dom Wydawniczy Ankar, Warszawa 1995.
[3] KRUK A.S., MOSTOVNIKOV W.A., CHOCHOLOV I.W., SERDUCZENKO N.S., Acta Bio-Opt. Inf. Med. **2** (1996), 95.
[4] BIAŁY D., DERKACZ A., NOWOSAD H., *et al.* Acta Bio-Opt. Inf. Med. **4** (1998), 7.
[5] DERKACZ A., BIAŁY D., DUŚ D., *et al.* Acta Bio-Opt. Inf. Med. **6** (2000), 131.
[6] DE SCHEERDER I.K., WANG K., ZHOU X.R., *et al.*, J. Invas. Cardiol. **10** (1998), 263.
[7] KIPSHIDZE N., SAHOTA H., KOMOROWSKI R., *et al.*, J. Am. Coll. Cardiol. **31** (1998), 1152.
[8] KAUL U., SINGH B., SUDAN D., *et al.*, J. Invas. Cardiol. **10** (1998), 534.
[9] Polish Patent Application No. P-347 516, 2001.05.10.

*Received June 8, 2001*
*in revised form November 29, 2001*