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The Microcirculation in Neodymion-YAG Laser Irradiated and in Electro Coagulated Urinary Bladder Tumors Evaluated with Laser Doppler Flowmetry

H. O. Beisland[1] and K. Kvernebo[2]

[1]Department of Urology and [2]Department of Vascular Surgery, Aker Hospital, Oslo, Norway

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Summary. Neodymion-YAG laser irradiation is a relatively new therapeutic modality for the treatment of urinary bladder tumors which is suggested to produce an instantaneous arrest of the blood circulation and a homogenous coagulation of the tumor tissue. Utilizing the laser Doppler flowmetry principle the microcirculatory changes in laser irradiated tumors were compared to the changes in tumors coagulated with diathermy. In laser treated tumors the blood cell flux decreased to near baseline levels throughout coagulated area. Vascular stasis was demonstrated in the erythematous zone encircling the necrosis. In tumors coagulated with diathermy a corresponding constant decrease in blood cell flux could not be demonstrated. Thus the Neodymion-YAG laser irradiation seems preferable to electro coagulation in the treatment of urinary bladder tumors as more complete and homogenous arrest of the blood circulation in the treated area is achieved.

Key words: Urinary bladder tumors, Neodymion-YAG laser irradiation, Electro coagulation, Microcirculation, Laser Doppler flowmetry.

Introduction

Neodymion-YAG laser irradiation of bladder tumors is based on transformation of light energy into heat within the tissue. The depth of penetration is determined by the applied laser power and the duration of irradiation. The instruments do not touch the tumor and there is no removal of tissue. It is suggested that the laser beam arrests the blood circulation instantaneously producing a homogenous coagulation with sharp boundaries to non irradiated structures. Accordingly, this technique is presumed to reduced the risk of hematogenous, lymphogenous and intracavitary spread of tumor cells and may therefore prove favourable to other surgical techniques such as electro resection and electro coagulation.

The development of the laser Doppler flowmetry technique has made possible clinical monitoring of the microcirculation. The procedure can be carried out endoscopically using a special probe.

The main purpose of the present study was to verify the instantaneous, complete arrest of the microcirculation in the entire area irradiated with Neodymion-YAG laser. An additional aim was to demonstrate any microcirculatory changes in the mucosa encircling the irradiated area. Finally a comparison to the microcirculatory changes in electro coagulated tumors was carried out.

Material and Methods

Twenty superficial bladder tumors of diameter < 1 cm were selected for the study. Ten tumors were laser irradiated. The treatment was performed with a Neodymion-YAG laser (Messerschmidt-Bölkow-Blohm GmbH, Munich-Ottobrunn; West Germany) according to the technique described by Hofstetter et al. [3]. A laser power of 45–50 W was used and the tumor was irradiated with repeated pulses of 4 seconds duration until the tissue was transformed into a grey-whitish mass. Ten tumors were electro coagulated with diathermy.

The microcirculation level was recorded with a laser Doppler flowmeter (Periflux, Perimed KB, Sweden). The principle of this method is based on the fact that the frequency of light changes when scattered from a moving object, e.g. an erythrocyte (Doppler shifted). The change in the reflected light spectrum depends on the product of the number of moving erythrocytes in the illuminated tissue volume and their mean velocity (the blood cell flux). The applied laser light is a low power 2 mW Helium-Neon laser operating at a wavelength of 632,8 nm. The penetration depth is 2–4 mm and the measuring volume is 2–5 mm^3. The monochromatic laser light is conducted through an optical fibre (ϕ 0,8 mm) to the area in question. Two similar optical fibres arranged in parallel with the laser conducting fibre enclosed in a plastic sheath transmit the reflected light to two photodetectors. A processing unit transforms the Doppler shifted light into an electrical output signal. The relation between this output signal and the blood cell flux has been shown to be linear [6] except for high flux values where this method underestimates the circulation level [1]. The flowmeter output signal is registered on a linear recorder (Watanabe Mark V), the flux values being expressed in arbitrary units. The zero level is obtained by placing the laser probe against a white reflecting surface.

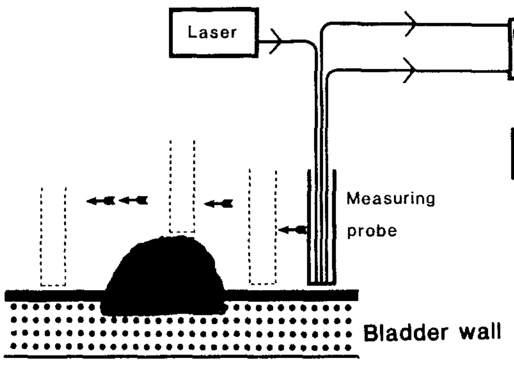

Fig. 1. The monitoring procedure starts on macroscopically normal mucosa beside the tumor and is continued in steps corresponding to the diameter of the measuring probe across the coagulated area until normal mucosa on the opposite side. The processing unit transforms the reflected light into an electrical output signal

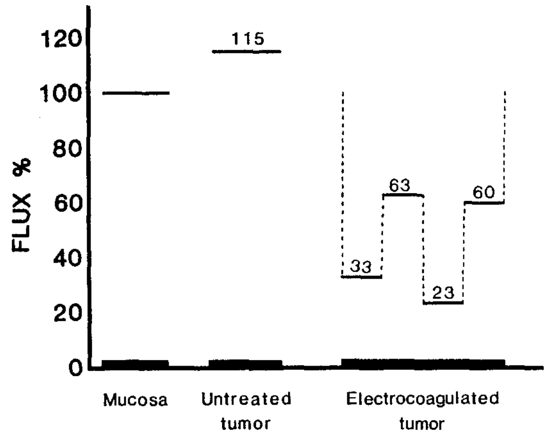

Fig. 2. Flux values in a bladder tumor before and after coagulation with diathermy. In the untreated tumor increased flux was recorded compared to the flux in macroscopically normal mucosa. After electro coagulation reduced but variable flux values were recorded within the coagulated area. Vascular stasis around the coagulated area could not be demonstrated

The monitoring procedure was carried out with a flexible probe (length 240 cm, ϕ 2,3 mm) containing the optical fibres, specially manufactured for endoscopic use. The probe was introduced through the cystoscope and moved into position by the handle of the working element. The Helium-Neon laser beam is red coloured and the probe could be exactly and preferably perpendicularly directed against the area to be examined. The filling volume of the bladder was standardized to 200 ml of water. The recording procedure was carried out during treatment. The monitoring was initiated on macroscopically normal mucosa beside the tumor and continued in consecutive intervals corresponding to the diameter of the probe across the coagulated area until normal mucosa was reached on the opposite side (Fig. 1). The probe was kept in position for at least 30 seconds at each point in order to obtain steady state.

For purpose of evaluation the recorded flux values were expressed in percentages of the flux in macroscopically normal mucosa (100%). Mean values, standard deviation (SD) and standard error of the mean (SEM) were used for comparison between the two therapeutic principles. Statistical analysis were performed according to Student's t-test for unpaired differences. Values of $p < 0,05$ were considered statistically significant.

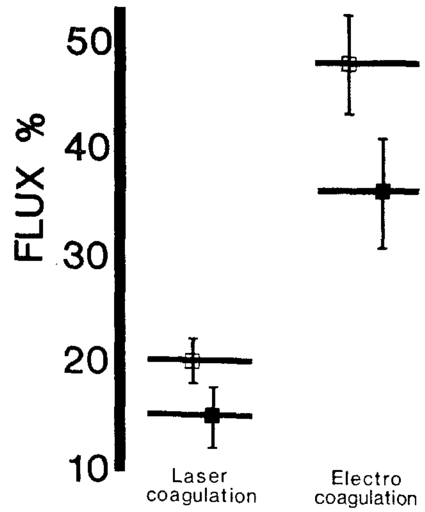

Fig. 3. Mean flux ± SEM in laser coagulated and in electro coagulated tumors expressed in percentage of the flux in macroscopically normal bladder mucosa. ■ When refering to the lowest recorded flux in each tumor (n = 10 in each group). □ When refering to all the recorded flux values within coagulated areas (n = 22 in the laser group and n = 25 in the diathermy group)

Results

The tumors which were electro coagulated were also monitored before treatment. In some of them increased flux was seen compared to normal mucosa beside the tumors (Fig. 2), but this was not consistent in all cases. In laser irradiated tumors the flux decreased to a mean value of 15.2% (SD ± 9.2) of the flux in normal mucosa when refering to the lowest value monitored in each tumor. With reference to all the monitored values within laser coagulated tissue, the mean flux was 20.3% (SD ± 9.7) (Fig. 3). Only small differences in the flux values were recorded within one and the same coagulated tumor (Fig. 4).

Just after laser irradiation a zone of erythema appeared around the coagulated areas, clinically resembling hyperemia. Increased circulation, however, could not be demonstrated in these areas. On the contrary, decreasing flux values were recorded from the periphery towards the necrosis (Fig. 4). The median flux for all tumors was 83% in the peripheral part, 64% in the central part and 32% in the inner part of these erythematous areas. Around the diathermy coagulated tumors this pronounced erythematous zone could not be observed. Considerable differences in the flux values were recorded in the electro coagulated tumors, even within a single tumor (Fig. 2). The mean flux value was 36.1% (SD ± 16.3) when determined from the lowest monitored value of each tumor and 48.7% (SD ± 22.0) when determined from all the recorded values within electro coagulated tissue (Fig. 3). Statistically significant differences were achieved between the laser irradiated and the electro coagulated tumors for the lowest recorded values ($p < 0.005$) as well as for all the values ($p < 0.001$).

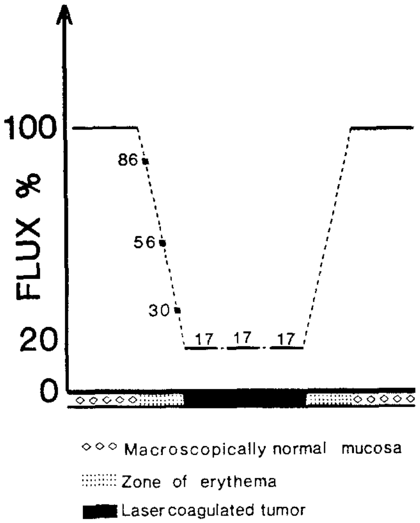

Fig. 4. Flux values in a bladder tumor after Neodymion-YAG laser irradiation. In the coagulated area a constant decrease to 17% of the flux in macroscopically normal mucosa was recorded at 3 different locations. In the erythematous zone encircling the irradiated area decreasing flux values were recorded from the periphery towards the necrosis

Discussion

The use of laser Doppler technique for blood flow measurement was first presented by Riva et al. (1972) studying the flow in retinal vessels in rabbits [8]. The laser Doppler flowmeter used in the present study was originally intended for skin blood flow determination [6, 7], but has also been used for microcirculatory studies on surgically exposed organs in anaesthesized animals [2, 9, 10, 11, 12]. The first report on endoscopic laser Doppler flowmetry in humans was presented by Kvernebo et al. (1983) studying the microcirculation in the gastric mucosa [4, 5]. Prior to the present study the applicability of the method and the equipment for urinary bladder investigations was tested on urological patients undergoing diagnostic cystoscopy.

Quantitative measurements of microcirculatory blood flow are difficult to perform in humans with available methods for blood flow evaluation. The laser Doppler flowmetry is basically a semiquantitative method and thus suited for measuring variations in the flux values, for example healthy versus pathological comparisons within an organ. There is a linear relation between the blood cell flux and the electrical output signal for low and medium flux levels [1, 6].

Theoretically it was expected that the output signal should decrease to zero level in the coagulated areas. A reproducible flux activity persisted, however. Previous studies have demonstrated that zero level is not achieved when monitoring biological tissue because of the sensitivity of the method. This activity is defined as the baseline level [10]. Measuring skin blood flow of the forearm, a steady baseline level can be observed when a proximal pressure cuff is inflated to above systolic blood pressure. In excised devascularized tissue steady baseline levels persist for hours. The origin of this baseline activity is still unknown, but it is suggested to be caused by internal tissue motion other than blood flow or by Brownian movements [10]. Even in laser lesions produced in cystectomy and gastrectomy specimens we could demonstrate baseline activity for hours after excision. In excised devascularized bladder tissue we found a constant baseline at the 5% level of the mean flux in normal mucosa. The baseline activity is probably higher in coagulated areas within a vascularized organ than in excised tissue and this may explain why the mean flux in laser irradiated areas did not fall below the 15% level. It is not likely that circulation from parts of the bladder wall deep to the coagulated areas is recorded because of the limited penetration depth of the Helium-Neon laser light (2–4 mm). The minor deviation in the flux values in the laser group and in each individual tumor indicates complete homogenous coagulation.

The laser Doppler flowmetry revealed a decreased microcirculation in the mucosa encircling the laser necrosis. Accordingly, this zone is in vascular stasis and not reactive hyperemia. Whether this prevents hematogenous metastasis is not known.

Electro coagulation with diathermy did not decrease the flux to the same degree and in the same constant manner as did the laser irradiation. This confirms that electro coagulation does not produce a homogenous coagulation. Neodymion-YAG laser irradiation therefore seems to be a more reliable technique for destruction of bladder tumors than electro coagulation.

Endoscopic laser Doppler flowmetry is simple to perform, but some experience is mandatory for correct management of the equipment. In particular, it is important to have standardized positioning of the probe in order to obtain steady state monitoring and to avoid motion artifacts. Whether this method will be suitable for routine investigation of the microcirculation in internal organs remains to be seen, but for the purposes of this study the method was satisfactory.

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Dr. Hans Olav Beisland
Department of Urology
Aker Hospital
Oslo 5
Norway