Possibility of deep photodynamic action on tumor tissues using Aluminium Phtalocyanine.

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1. ABSTRACT.

We have determined the efficacy of PDT and depth of necrosis for advanced tumors. Clinical results of PDT have shown that it's possible to get the depth of tumors necrosis till 20 mm using lasers providing high power density of laser irradiation. One of the possible models can be enlightenment of sensitizer during laser irradiation.

2.BACKGROUND.

One of the main problems of modern photodynamic therapy (PDT) is the depth of photodynamic action on tissues. It was considered that it correlated only with the wavelength of laser irradiation, used for PDT [1]. Normally this parameter is 4 - 8 mm in spectral range 670-680 nm[2,3]. We have determined the efficacy of PDT and depth of necrosis for advanced tumors using second-generation photosensitizer $Pc^{S}Al$ - sulfonated aluminium phthalocyanine and different lasers.

3.MATERIALS AND METHODS.

Clinical part of work has been done in frames of 1 stage clinical trials of sulfonated aluminium phthalocyanine. PDT have been applied to 12 patients with advanced tumors of different hystological type. Phthalocyanine in a dose 0,5-2,0 mg per body weight was injected intravenously. As a source of light we used different lasers with irradiation in the spectral range 670-675 nm: pulse type - quantoscope (scanning electron beam pumped semiconductor laser, λ=672+2 nm, P up to 10W), solid state laser with doubled frequency (λ=669+1 nm, P=1W), tunable dye laser excited by Cu-laser (λ=640-690 nm, P=0,6 W), and continuous type - krypton laser (λ =647, 675, P= 1,2 W). The desired average light power density on the skin was 50-400 mW/cm^2, mean pulse power density while using quantoscope and pulse lasers was up to $5 \cdot 10^4$ W/cm^2.

PDT using quantoscope and $Pc^{S}Al$ as photosensitizer have been provided in nine patients (27 tumor sites) with spread skin malignancies at the department of head and neck tumors of Cancer Research Center of AMS of Russia. Four patients (8 tumor sites) had spread basal cell cancer (tumor size from 1,5 till 6 cm in diameter), three - squamous cell (cancer of the cheek T3N0M0, cancer of low lip T2N0M0 and T1N0M0), one patient - breast cancer T4N3M0 (adenocarcinoma), and one patient - melanoma. In 7 patients treated lesions were located on the face and in 2 (basal skin cancer and subcutaneous metastases of breast cancer) on the chest wall.

$Pc^{S}Al$ dissolved in 0,9 % NaCl in a dose 1,5- 2,0 mg of body weight was injected intravenously. Immediately after infusion and 24 hours later on fluorescent diagnostics of tumor, accumulation of photosensitizer in tumor, adjacent tissue, skin and mucous of oral cavity was fulfilled with the help of spectroanalizer "LESA-5". PDT was provided 24 hours after $Pc^{S}Al$ infusion. All surface treatments were done to cover an area extending at least 1 cm beyond the borders of the gross tumor. The rest of the patients exposed areas were covered with few layers of drapes.

The quantoscope laser system consists of a cathode-ray tube (CRT) with a semiconductor flat-parallel screen covered by a refractive layers. A powerful focused electron beam from an electron gun excites the semiconductor screen-plate and generates laser emission from excited point. Electromagnetic deflection coil makes the cathode ray scan the screen, thus exciting laser beam scan function. Beam current modulation causes laser emission power modulation. Electron beam scan and modulation functions are provided by traditional CRT methods. In this way one can form a certain power

 0-8194-2326-2/96/$6.00

distribution of a laser beam emission made by laser CRT providing the scan velocity not lower than TV scan velocity. To get the high efficiency and average generating power the laser CRT screen is cooled down to cryogenic temperature. To provide cooling we use simple and inexpensive nitrogen devices like Dewar vessel with hydropump. Laser CRT emission wavelength is defined by a band gap of a semiconductor laser screen plate. By choosing proper semiconductor materials from the elements of A_2B_6 and A_3B_5 groups one can provide laser generation practically at any point of a spectral range from 360 to 1000 nm. The developed and functioning now laser CRT generates light power up to 10 W in λ=672+2 nm. On the basis of the developed laser CRT there was made an experimental prototype version of a treatment-diagnostic complex system . The prototype device includes laser CRT therapy unit , optical system for transmission and overlaying laser CRT emission, supply unit, photoluminescence registration unit, including high sensitive CCD-camera , and control unit of therapy emission intensity. The size of irradiated field is chosen by physician with the help of remote control from minimal to 10 x 10 cm. Surface power densities were measured with Ratiometer S370 (Digital Instruments Inc., USA) placed on the surface at the beginning and the end of PDT. For pulse measurements we used coaxial photoelement PC20 (Russia) with the oscilloscope. From the power density and the time of exposure, the number of joules/ cm^2 for surface irradiation was calculated. In 7 cases the desired power density was approximately 400 mW/cm^2 and in 2 cases 200-300 mW/cm^2. Time of treatment was in interval 9-19 minutes, light dose - 200-444 J/cm^2 during PDT session. The spotside of laser beam on the skin was about 50 - 100 μm.

4. RESULTS AND DISCUSSION.

Clinical results of PDT of locally advanced tumors of different hystological type have shown that it's possible to get the depth of tumor necrosis till 20 mm using lasers providing high pulse power density of laser irradiation. In this variant PDT alone can be efficient treatment for such patients. We have got mostly superficial necrosis using Kr-laser for PDT. One of possible models, explaining our results, can be enlightenment of Pc^SAl during laser irradiation of high power density, at least in superficial layers and tissues.

According to [4], the dependence of absorption's coefficient for phthalocyanine derivatives would be estimated as:

$$\alpha(p)=\frac{\alpha(0)}{1+\dfrac{p\tau\sigma\gamma}{h\nu}} \qquad (1)$$

for continuous wave lasers, and

$$\alpha(w)=\frac{\alpha(0)}{1+\dfrac{w\sigma\gamma}{h\nu}} \qquad (2)$$

for pulse lasers, where:

p[W/cm^2] is the power density of laser radiation;

w[W/cm^2] - the density of energy in laser pulse;

$h\nu$[J]-the energy of photon (in investigated spectral range this value is about $3\cdot10^{-19}$J):

α -the effective section of absorption (this value is about $7\cdot10^{-16}$ cm^2);

γ -the quantum yield (this value is about 0,5);

τ -the lifetime of triplet state.

Such dependence for pulse lasers is shown in the Fig.1,

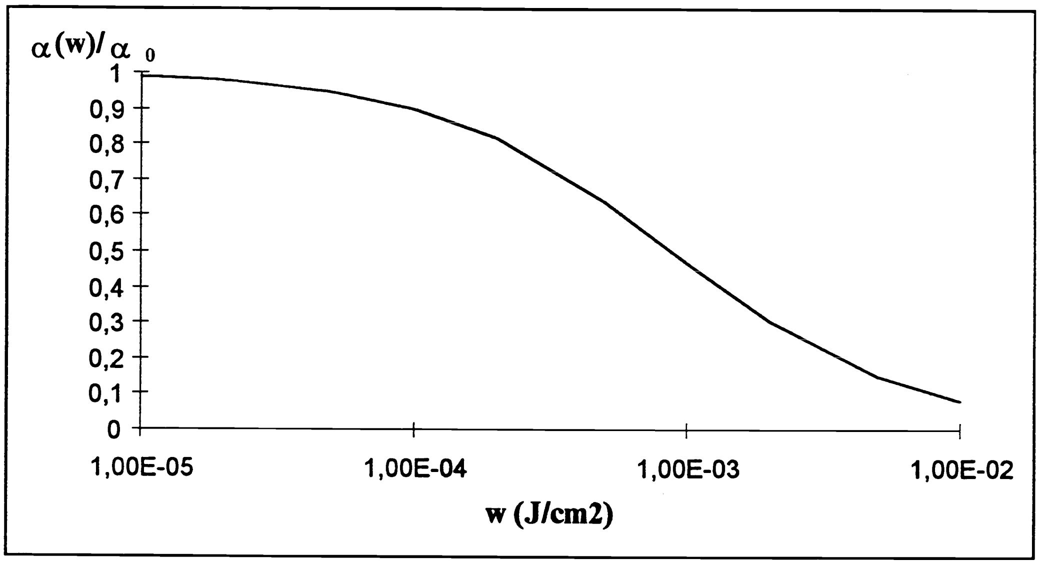

Fig.1. The dependence of decreasing of Pc^SAl absorption on the pulse light energy density.

The pulse density of light energy in our investigations was up to 10^{-2} J/cm^2 when quantoscope was used (power density up to $2 \cdot 10^5$ W/cm^2, t_{point}=50...80 ns) and up to 10^{-3}J/cm^2 when tunable dye or solid state lasers were used (power density up to 10^5 W/cm^2, t_{point}=10...20 ns). According to results of our estimations (see Fig. 1) it leads to the redistribution of energy of excitement in tissues, to deeper penetration of laser irradiation and as a result to more efficient PDT and tumor necrosis.

5.REFERENCES.

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