

## **Five Years' Experience of Photodynamic Therapy with New Chlorin Photosensitizer**

Valery A. Privalov, Alexander V. Lappa\*, Elena V. Kochneva

Medical Physics Center  
at Chelyabinsk State University and Chelyabinsk State Medical Academy  
Br. Kashirinykh 129, Chelyabinsk, 454021, Russia.

### **ABSTRACT**

Clinical results of photodynamic therapy (PDT) with a novel natural second generation chlorin-type photosensitizer "Radachlorin", mainly consisting of sodium chlorine e6, are presented. This sensitizer possesses a number of advantages over sensitizers of hematoporphyrin and phthalocyanine types. In particular, Radachlorin is excreted from organism much faster (in 1-2 days), as a result the problem of patient light hypersensitivity for a few months is non-actual for Radachlorin. As light source there was used a 662 nm diode laser specially designed for PDT with Radachlorin. The 5 year clinical results of PDT application to 89 patients with different malignant tumors are summarized and analysed. It is shown in particular that PDT with Radachlorin is a radical high efficient method for treatment of basal cell carcinoma of skin. At intravenous introduction in drug dose 0.5 mg/kg with light fluence 300-350 J/cm<sup>2</sup> or in dose 1 mg/kg with fluence 200-250 J/cm<sup>2</sup> the method gives full recovery in almost 100% cases with excellent cosmetic effect. The method was successfully combined with surgical operations, laser ablations, radio- and chemotherapy. Preoperative and intraoperative PDT favors improvement of results in complex treatment of malignant tumors. The method has a potential as palliative measure; in a number of incurable cases it allowed us to achieve recanalization of obturated hollow organs, eliminate the inflammatory complications, and as a result to improve life quality.

**Keywords:** photodynamic therapy, malignant tumor, chlorines, Radachlorin, clinical trials, diode laser

### **1. INTRODUCTION.**

In 2002 at "Photonic West", San Jose, we presented a novel natural second generation chlorin-type photosensitizer for photodynamic therapy "Radachlorin" and reported the first encouraging results of its clinical application<sup>1</sup>. Now our experience of application PDT with Radachlorin in clinic has appreciably increased, it includes more than 100 patients with follow-up periods up to 4.5 years. A summation of the experience is the subject of this article.

### **2. MATERIALS AND METHODS**

#### **2.1 Photosensitizer Radachlorin**

Radachlorin is a trademark of a drug substance, registered as pharmaceutical preparation and permitted for clinical use in Russia (registration number P №001580/01-2002 of 26.07.2002). It has been developed by RADA-PHARMA International Group of Companies by way of a chemical modification of chlorophyll a, extracted from *Spirulina* microalgae on the basis of a patented technology in Russia<sup>2</sup> and some other countries<sup>3</sup>. The substance represents an aqueous solution of chlorines, mainly including sodium chlorine e6 (90-95%) and sodium chlorine p6 (5-7%). From the substance Radachlorin a few drug forms are produced: aqueous solution for injection, 0.35% (of dry Radachlorin), and gels for external applications with different concentrations (0.1%-1%). The forms are permitted for clinical trials in Russia (Russian Health Ministry permissions №120 of 04.07.02 and №221 of 18.08.03). Photophysical, toxicological, pharmacokinetic, and stability properties of Radachlorin are presented in table 1.

\* lappa@csu.ru

Table 1. Radachlorin's properties

Property type	Parameter	Value	Unit
Photophysical characteristics (in the presence of human serum albumin)	<b>Absorption maximum in the red region</b>	662 <sup>1</sup> , 661 <sup>4</sup>	nm
	Fluorescence maximum	668 <sup>1</sup> , 665 <sup>4</sup>	nm
	Fluorescence quantum yield	4 <sup>1</sup>	%
	Extinction coefficient	34200 <sup>2</sup>	M <sup>-1</sup> cm <sup>-1</sup>
	Singlet oxygen quantum yield	(0.52-0.62) <sup>4</sup>	%
Toxicity in the dark (white breedless mice)	Drug dose of 50% acute survival	147 <sup>1</sup>	mg/kg
	Drug dose of 90% acute survival	119 <sup>1</sup>	mg/kg
Pharmacokinetics and contrast (mice with inoculated embryocarcinoma T36, intravenous injection)	Accumulation maximum in tumor	(0.5-5) <sup>1</sup>	hour
	Clearance for 24 hour	98 <sup>2</sup>	%
	Full clearance period	48 <sup>1</sup>	hour
	Contrast maximum	(2-4) <sup>1</sup>	hour
	Tumor-to-skin ratio	14 <sup>1</sup>	
Chemical stability	Shelf life at 0 - +8 °C in the dark	> 1.5 <sup>1</sup>	year

These properties are good for PDT. Comparing to hematoporphyrin-type photosensitizers (Photofrin II, Photogem and others), Radachlorin in biological media has intensive absorption band at larger wavelength, this shift increases distinctly light penetration in biological tissue. Other advantage over hematoporphyrin-type photosensitizers, as well as over phthalocyanines (Photosence), is much faster excretion from organism, as result the problem of patient light hypersensitivity for a few months is non-actual for Radachlorin. High yield of singlet oxygen provides high phototoxicity, good accumulation contrast provides good PDT selectivity, and fluorescence ability allows photodynamic diagnostics.

## 2.2 Patients

Since middle of 2000 we have applied PDT with Radachlorin to more than 100 volunteer patients aged from 10 to 93 years with different malignant tumors. The treatments were performed in frame of official programs of clinical trials. All the patients were informed that the treatment method is an experimental one; each of them signed the Informed Consent. In this work we are analysing 89 cases: 39 males (44%) and 50 females (56%) with total number of 263 tumors. Average age of patients was 63. Distribution of patients in type, stage, and location of tumors is presented in Table 2.

So, 89 patients had 263 tumors. Primary-multiple tumors were observed in 11 patients with basalioma, one of them had 112 tumors. One patient had lower lip cancer, basalioma, and central lung carcinoma.

18 patients underwent PDT because of contraindications to traditional treatments. 19 patients had recurrent tumours after standard methods of treatment (surgery, radiotherapy, chemo- and cryotherapy), the capabilities to treat residual or recurrent tumors with these methods were exhausted. In these patients, photodynamic therapy was carried out not earlier than one month after radiotherapy or drug therapy. 22 patients entered the hospital with IV stage of disease, 56 patients had I-II stage tumors, mainly basaliomas.

## 2.3 PDT Procedure

Before PDT Procedure all patients underwent the meticulous examination including clinical and biochemical blood tests, ECG, arterial pressure measurement, etc. The procedure begins with introduction of Radachlorin into organism. We used 3 ways: intravenous injections of 0.35% solution in doses 0.5-1.2 mg/kg (of dry drug per body mass) for 71 patients; surface application of 0.1% gel for 10 patients; and interstitial injections of 0.35% solution into the tumor tissue for 8 patients. The last two ways were applied to basalioma only.

After an accumulation period the tumors light irradiation was performed. Fast accumulation of Radachlorin (in comparison with the hematoporphyrin and phthalocyanine photosensitizers) allowed us to start the irradiation in 0.5-3 hours. We did it in 2 hours after intravenous administrations, in 1 hour after gel applications, and in 30 min after interstitial injections.

Table 2. Patients and tumors treated by PDT

Histological type, location of tumour	Number of patients/ tumours	Recurrent tumors, pat./tum. num.	Patients number with primary- multiple tumors	Number of patients with the stage			
				I	II	III	IV
Basal cell carcinoma of skin (basalioma)	51/219	8/18	11	27	21	3	
Squamous cell carcinoma of skin	1/1			1			
Melanoma	2/2			1		1	
Synchronous primary-multiple cancer of the skin, lip and lung.	1/3		1			1	
Oesophageal carcinoma	2/2						2
Stomach carcinoma	1/1						1
Rectal carcinoma	5/5	2/2				2	3
Choledoch carcinoma	1/1						1
Central lung carcinoma	3/3						3
Tumors of CNS*:							
Astrocytoma	1/1	1/1		-	-	-	-
Ependymoma	1/1	1/1		-	-	-	-
Ganglioneuroma	1/1			-	-	-	-
Thyroid gland cancer	4/4	2/2					4
Lymphosarcoma of thyroid gland	2/2						2
Breast cancer	2/2	1/1				1	1
Cancer of urinary bladder	4/6	1/2		1	3		
Carcinoma of vulva	2/2			2			
Fibrosarcoma of forearm	1/1						1
Leiomyosarcoma uteri	1/1	1/1					1
Implantation metastasis of larynx cancer	1/3						1
Cancer of salivary parotid gland	1/1	1/1					1
Cancer of oral cavity mucosa	1/1	1/1					1
<b>Total</b>	89/263	19/30	12	32	24	8	22

\* The stage classification is not applied to these tumors.

As a light source we used a fiber coupled diode laser MILON-662, specially designed by Milon Laser Company (Russia) for PDT with Radachlorin. The laser irradiates  $662 \pm 2$  nm wavelength light of 0.1-2.5 W power with 0.11 numerical aperture in 0.25-1 mm diameter fiber under CW and pulse modes. Four techniques of tumor irradiation were used:

- distant external irradiation (by means of quartz fibers),
- intracavitary irradiation (with fibers, diffusers, standard endoscopes),
- intratissue irradiation (fiber through the needle, sometimes under ultrasonic control),
- combination of surface and intratissue irradiation.

In the external cases a fluorescence diagnostics device was used to visualize the accumulation of Radachlorin in a tumor and around. The device includes a CCD camera equipped with an optical interferential filter mainly transmitting Radachlorin fluorescence and mainly blocking 662 nm laser radiation. By displaying a sensitized tissue illuminated with laser (the same as in PDT) one can see luminous spots of regions with increased accumulation of Radachlorin.

As measure of radiation action in PDT we used the generally accepted value of *energy fluence*: light energy incident on a unit of irradiated surface. In our treatments the fluence varied from 150 to 300-600 J/cm<sup>2</sup>.

The irradiation was performed under local or intravenous anaesthesia. At external irradiations (cancers of skin, lip, and so on) no anaesthesia was required as a rule. For a day after irradiation patients stayed in black-out rooms without TV to avoid light reactions of skin and eyes because of some presence of Radachlorin. Then patients were free in respect to

light and TV.

The only PDT procedure turned out to be sufficient for most patients. Repeated procedure was conducted in 24 cases.

### 3. RESULTS

#### 3.1 Direct reaction to PDT

Introduction of Radachlorin did not cause any side effect. The state of health of patients remained stable. Arterial pressure, and pulse showed no essential deviations from initial values. Complaints and unpleasant feelings were not marked during and after introduction of the drug. There were no complications connected with increased photosensitivity of skin and mucosa. Sunburns, hyperemia and other attributes of phototoxicity were not marked.

The fluorescent diagnostics device as a rule displayed an increased accumulation of Radachlorin in the place of tumor by the time of PDT irradiation. The tumors really glow (Fig. 1). Often the luminous spot spread out visible borders of tumor, showing tumor sizes more adequately.



Fig. 1 Fluorescence of Radachlorin in a tumor (basalioma). (a) Before introduction: no fluorescence; (b) 2 hours after intravenous introduction: bright fluorescence indicates high concentration of Radachlorin.

Local photodynamic reaction (Fig. 2,3,5) began in a few minutes after the beginning of irradiation. Patients noticed local pain, feeling of burning in the zone of irradiation. By the end of irradiation, the tumour and surrounding skin became anemic, and "halo" of hyperemia appeared around. Surface of the tumor became humid with sites of dark color which increased in sizes, merged with each other, and in 2-3 hours became violet or black, apparently, because of hemorrhagic necrosis.

In 20 - 60 minutes after irradiation an edema of surrounding tissues and bright hyperemia of skin formed. The most expressive edema formed on the face and hairy part of head. To the end of the first day the local reaction was maximum. The edema reached maximum, gradually decreasing to 3-4 day. There developed dry necrosis in a tumor with a clear border between surrounding skin and necrotized tumor tissue. Tumors of oral cavity, larynx, hollow organs (esophagus, stomach) reacted to PDT in the same way: edema of surrounding tissues, change of tumor colour, appearance of fibrin patches. Patients felt pain that sometimes demanded analgesic administration; low grade fever was marked in some patients. Blood analysis, pulse, blood pressure remained stable.

By the end of the first week local changes were marked only in the tumor zone, which looked like a dense black scab. Surrounding tissues looked intact. Tumors of esophagus, stomach, larynx, oral cavity mucosa were covered with a thick layer of fibrin. In 2-4 weeks the necrosis was rejected and then gradual cicatrization and epithelization began, which was completed by 6th-12th weeks.

For external applications of Radachlorin gel the initial reaction was the same as for the injections, but less expressive in spite of increasing of light dose up to 500-800 J/cm<sup>2</sup>. Local reaction to interstitial introduction was the similar to intravenous one.

### 3.2 Grouping

For analysis of PDT results we divided all patients into 5 groups (Table 3). All patients of the first 3 groups were treated under radical program (to achieve full recovery). To patients of 4<sup>th</sup> group this program was applied where possible. All patients of 5<sup>th</sup> group were treated under non-radical program (to achieve some improvement).

Table 3. Patient groups

N	Group name (number of patients)	PDT goal	Quantities to estimate, efficiency criterion
1	Basalioma (50)	Full recovery	Optimal drug and light doses
2	1-2 stage non-basalioma (5)	Full recovery	Recurrence rate
3	Intraoperative (7)	Reduction of recurrence risk	Recurrence rate
4	Preoperative (6)	Tumor reduction to make an operation possible	Operable state rate
5	Palliative (21)	Life-saving, improvement of life quality	Life time

1<sup>st</sup> group was the largest in radical program; it included 50 patients with basaliomas only. 2<sup>nd</sup> group included 5 patients with I-II stage tumors of non-basalioma histological type, for which it was possible to expect for complete resorption of tumor after PDT. 3<sup>rd</sup> group included 7 patients, for whom PDT was performed intra-operatively: tumor bed was irradiated after surgical removal of the tumor. Patients of 4<sup>th</sup> group had extensive tumours of 3-4 stages and underwent PDT to reduce the tumor sizes before surgical operation. 5<sup>th</sup> group included incurable patients who underwent PDT with palliative purpose only.

### 3.3 Treatment results in groups

#### 3.3.1 Basalioma group

The research was performed in 50 patients aged 66±12 years with total number of 216 tumors. Results were estimated depending on Radachlorin dose, light fluence, and way of drug introduction. For that all basalioma group patients were divided into 6 comparable subgroups (Table 4).

Table 4. PDT of Basaliomas (group 1)

N Subg.	Drug introduction way	Drug dose and light fluence	Pat./tum. number	Full resorption* (tumors/percent)	Recurrence (tumors/percents)
1	Intravenous	0.8-1 mg/kg-body 200-250 J/cm <sup>2</sup>	9/112	112/100	no
2	Intravenous	0.8-1 mg/kg-body 300-350 J/cm <sup>2</sup>	11/41	41/100	3/7.3
3	Intravenous	0.8-1 mg/kg-body <200 J/cm <sup>2</sup>	5/5	4/80	2/40
4	Intravenous	0.5 mg/kg-body 300-350 J/cm <sup>2</sup>	7/36	36/100	no
5	Interstitial	0.5 mg/g-tumor	8/10	10/100	no
6	Gel applications	0.1% gel	10/12	4/33.3	no
	Total		50/216	201/93	5/2.3

\*Number of partial tumor resorptions is equal to difference between total number of tumors and number of full resorptions, there were no cases with resorption absence.

32 patients of 1<sup>st</sup> - 4<sup>th</sup> subgroups received Radachlorin intravenously. At this introduction the full resorption of all tumours was achieved in 31 patients (97%) and only in 1 it was partial. In 2 patients of third subgroup and 3 of the second the recurrences developed in 8-12 months. These 3 patients received comparably high drug dose and fluence. Since in all these cases the recurrences of tumor growth were marked on periphery of the primary tumors, we suppose that the recurrences were not connected with fluence and drug dose, but with an insufficient area of laser irradiation. Repeated PDT procedures were applied to these 5 patients as well as to a patient of 3<sup>rd</sup> subgroup with partial resorption. That resulted in complete regress of tumors in all these cases, with the remission period from 2 to 3.5 years.

Table 4 show that PDT in intravenous subgroups 1,2,4 was quite successful, and there was no significant difference in PDT results over these subgroups. That means that for light fluence 300-350 J/cm<sup>2</sup> the increasing of drug doses from 0.5mg/kg to 1 mg/kg does not result in adequate increasing in PDT efficiency (it is already high at 0.5mg/kg). Similarly, at drug dose 0.8-1.2 mg/kg no significant efficiency increase is caused from increasing light fluence higher 200 J/cm<sup>2</sup>. But reductions of fluence lower 200 J/cm<sup>2</sup>, applied in 3<sup>rd</sup> subgroup, decreased distinctly the PDT efficiency in spite of large drug dose.

PDT with interstitial (0.5 mg/g of tumor tissue) introduction of Radachlorin was also quite successful, the full tumor resorption without recurrence was achieved in all 8 patients at fluence 200-300 J/cm<sup>2</sup> (subgroup 5). Unfortunately, this economic introduction is applicable only to small tumors, less than 1-1.5 cm in diameter.

When the drug was used in the form of 0.1 % gel application, the complete tumor resorption was achieved only in 1/3 patients, despite of initial phototoxic reaction. Repeated PDT procedures (2-7 times) failed to provide complete tumour resorption in 5 patients, despite of increase in fluence up to 500-600 J/cm<sup>2</sup>. All 5 patients underwent the repeated PDT procedures with intravenous introduction of Radachlorine in dose 1 mg/kg and with light fluence 300-350 J/cm<sup>2</sup>. After that the stable positive results were achieved in all cases.

Finally, the complete regress of basaliomas with excellent cosmetic effect was achieved in 100 % cases, and this status lasts for 1-4.5 years. The remission period is 1-2 years in 17 patients, 2.5-3.5 years in 17 patients, 4 and more years in 16 patients. Four not simple cases of basalioma treatment with PDT are presented on Fig. 2-4 and 6.

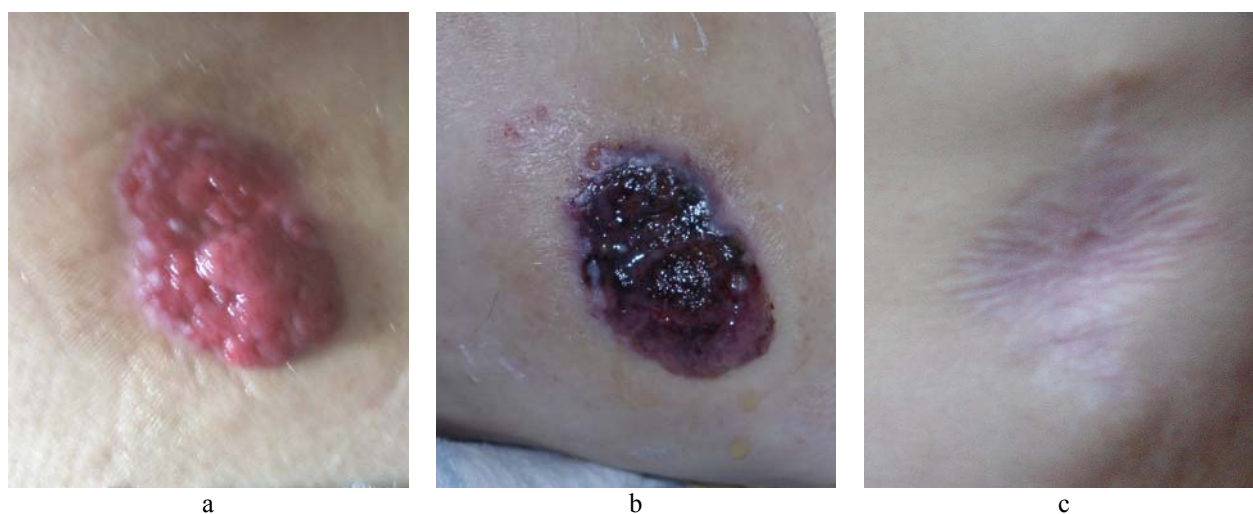
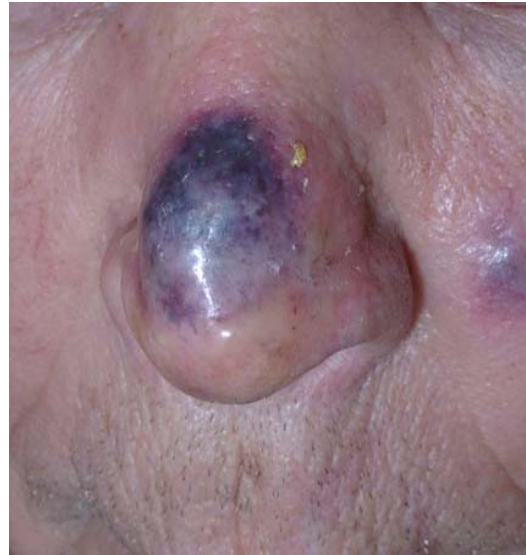


Fig. 2 Basal cell carcinoma of thigh skin Tumor size 4.5x2 cm, (a) before PDT, (b) 1 day after PDT. Dry necrosis, (c) 4 years after PDT. No recurrences.



a



b



c



d

Fig. 3. Basal cell carcinoma of nose skin. Recurrence after beam and combined treatment (a) before PDT (b) 1 day after PDT: edema, cyanosis of tumor (hemorrhagic necrosis formation) (c) 2.5 weeks after PDT – dry necrosis, beginning of rejection, (d) 2 months after PDT – full resorption of tumor with epithelisation and formation of barely visible scar.



Fig. 4 Repeated recurrence of basal cell carcinoma of parietotemporal region after surgical and combined treatments (a) Before PDT. Vast defect of soft tissues of parietotemporal region and auricle with baring of skull and spreading of the process to the external acoustic meatus. (b) 7 days after PDF. Zone of dry necrosis along the borders of soft tissues. (c) 4 months after PDT. Complete rejection of necrotized tissues with formation of clean granulating wound (d) 5 months after PDT, 1 month after defect plasty

### 3.3.2 1-2 stage non-basalioma group

5 patients of this group (Table 4) were treated with PDT to achieve complete recovery.

Table 4. PDT of I-II stage tumors (group 2)

Histological type, localization, stage	PDT features	Resorption	Follow-up period, results
Squamous cell carcinoma of skin, I	Distant irradiation	Full	3 years, remission
Maxillary sinus melanoma, II	Intracavitary irradiation	Full	2 years, recurrence in 1.5 years
Vulva cancer, I	Distant irradiation	Full	3 year, remission
Vulva cancer, I	Distant irradiation	Full	3 years, recurrence in 1 year, surgical operation, remission
Transitional cell cancer of urinary bladder, II	Intracavitary irradiation, laser ablation	Full	8 month, remission



The initial reaction to PDT was full tumor resorption in all 5 cases, and in 3 of them this status lasts to this day. In 2 cases (squamous cell skin cancer and vulva cancer) the remission period is three years. In 2 patients with vulva leukoplakia and maxillary sinus melanoma the recurrences occurred in 11 and 18 months respectively. Of course, statistics of this group is too little to make well-definite conclusions. But achieved full resorptions and fairly long remissions speak for efficiency PDT for such type tumors.

### 3.3.3 Intraoperative group

7 patients of this group (Table.5) underwent intraoperative PDT in view of uncertainty that only surgical removing of tumor would be radical.

Table 5. Intraoperative PDT (group 3)

Histologic type, localization, stage (number of patients)	PDT features	Follow-up period, results
Transitional cell cancer of urinary bladder, II (3)	PDT before and after laser ablation	2-3 years, remission
Thyroid gland cancer, IV (3)	PDT of tumor bed after surgical removal	2-3.5 years, remission
Melanoma of soft palate, metastases in neck lymph nodes, III (1)	Neck lymphadenectomy, PDT and laser ablation of tumor	3 years, recurrence after 2.5 years

All patients received Radachlorine intravenously in dose 1 mg/kg before operation. Time of introduction was determined as 2 hours before completion of tumor removing. There used 2 technologies of removing: conventional surgical one - 3 patients - and laser ablation with power infrared diode laser (970 nm, 30 W) - 4 patients with urinary bladder cancers and with melanoma. After tumor removing, a tumor bed was irradiated in fluence 200-300 J/cm<sup>2</sup>.

All patients with transitional cell cancer of bladder are alive during 2-3 years without recurrence. PDT of one of these cases is shown on Fig. 5. Irradiation of the tumour bed of thyroid gland resulted in clinical remission for 2-3.5 years in all three cases. There was no recurrence of melanoma for 2.5 years. We consider that intraoperative PDT increases radicality of operations.

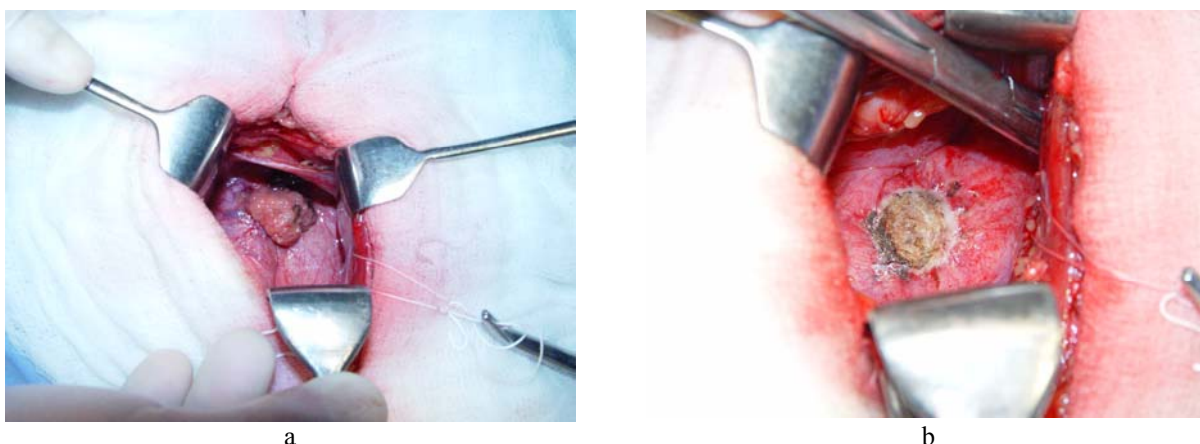


Fig. 5 Transitional cell carcinoma of urinary bladder (a) Before treatment. Exophytic tumor rising over intact mucosa of urinary bladder (b) After PDT and laser ablation. Cup tissue defect replacing the tumor with surface dry necrosis 3 year remission.

### 3.3.4 Preoperative PDT group

Preoperative PDT was performed in 6 patients with locally advanced tumors of III-IV stages (Table. 6) to reduce tumor volume, to prevent tumor recurrence, to eliminate local infectious complications, and as a result to make a surgical treatment possible.

Table 6. Preoperative PDT (group 4)

Histologic type, localization, stage	PDT features	PDT effect	Treatment after PDT	Follow-up period, results
Breast adenocarcinoma, III	Interstitial PDT	Partial tumor regress (PTR)	Polychemo-therapy before and after surgery	4 years, remission 3 years, progression of disease, death from metastases
Mucoepidermoid cancer of salivary parotid gland, IV	External PDT before and during operation, PDT of tumor bed	PTR, dry necrosis, infection elimination	Surgical	3.5 years, remission 3 years, recurrence
Fibrosarcoma of forearm, III	Interstitial PDT with laser thermotherapy	PTR	Surgical, arm amputation	1 year, progression of the process in lungs
Recurrence of rectal cancer at anastomosis, III	Intracavitary PDT, 3 procedures	PTR, cicatrization of anastomosis	Surgical	2.5 years, remission
Recurrence of rectal cancer at cicatrix, III	External PDT	PTR or full tumor resorption, wound healing	Surgical cicatrix excision	2.5 years, remission, full tumor resorption
Recurrent basalioma of anterior abdominal wall, III	External PDT	PTR, dry necrosis	Necrosis and residual tumor excision, plastic of skin defect	3 years, remission, full tumor resorption

In all patients the partial tumor regress was achieved. In 5 cases PDT made it possible to fulfill the adequate surgical actions. One of such cases is demonstrated on Fig. 6. PDT had not a desirable effect in the case of extensive soft tissue fibrosarcoma. (amputation of the upper limb). In 2.5-4 years of follow-up 4 patients are alive without recurrence. One patient with breast adenocarcinoma died four years after the combined therapy. So, preoperative application of PDT is expedient.

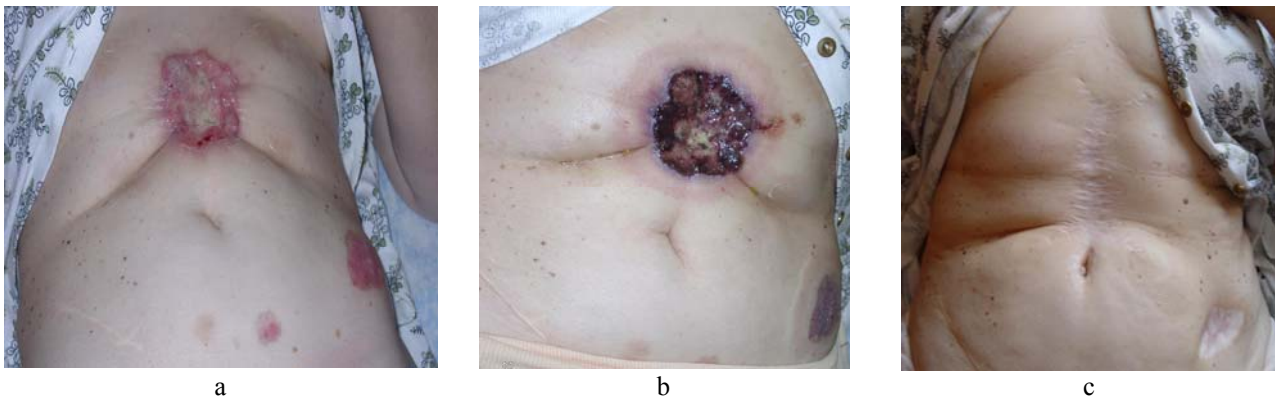


Fig.6 Vast primary-multiple basal cell cancer of abdominal wall. Recurrence after surgical, cryo and radiotherapy (a) Before PDT Exophytic infiltrating tumor with secondary inflammation, 10x8 cm, and two surface tumors, 1x1 и 4x2 cm, (b) 1 day after PDT. Dry necrosis of all tumors. First-degree photo-chemical burn of surrounding skin. PDT caused partial necrosis of exophytic tumor and eliminated the inflammation. 3 weeks after PDT the tumor excision with skin plasty was fulfilled. (c) 2 years after PDT. Exophytic tumor is replaced by the vast post-operative scar, surface tumors is replaced by scars after PDT. No signs of recurrence.

### 3.3.5 Palliative group.

PDT in this group was applied to 21 incurable patients with advanced malignancies of different localizations to improve life quality. The group included patients with tumors of IV stage and CNS (Table 2). For all patients prognosis for the disease was pessima. However, we managed to improve the condition of 7 patients by recanalization of obturated hollow organs in 5 cases (esophagus, rectum, bronchial tube) and by elimination of inflammatory complications caused by tumor decay in 2 cases. A case with successful recanalisation is presented on Fig. 7.

In two patients with esophagus and central lung cancers, tumor necrosis after PDT promoted the formation of internal fistulas (esophagotracheal and tracheoesophageal), that worsened patient's conditions. In one patient, an external purulent-mucous fistula formed on cheek after rejection of necrosis of oral mucosa tumor that also worsened patient's conditions. In all other cases PDT did not affected significantly the disease course.

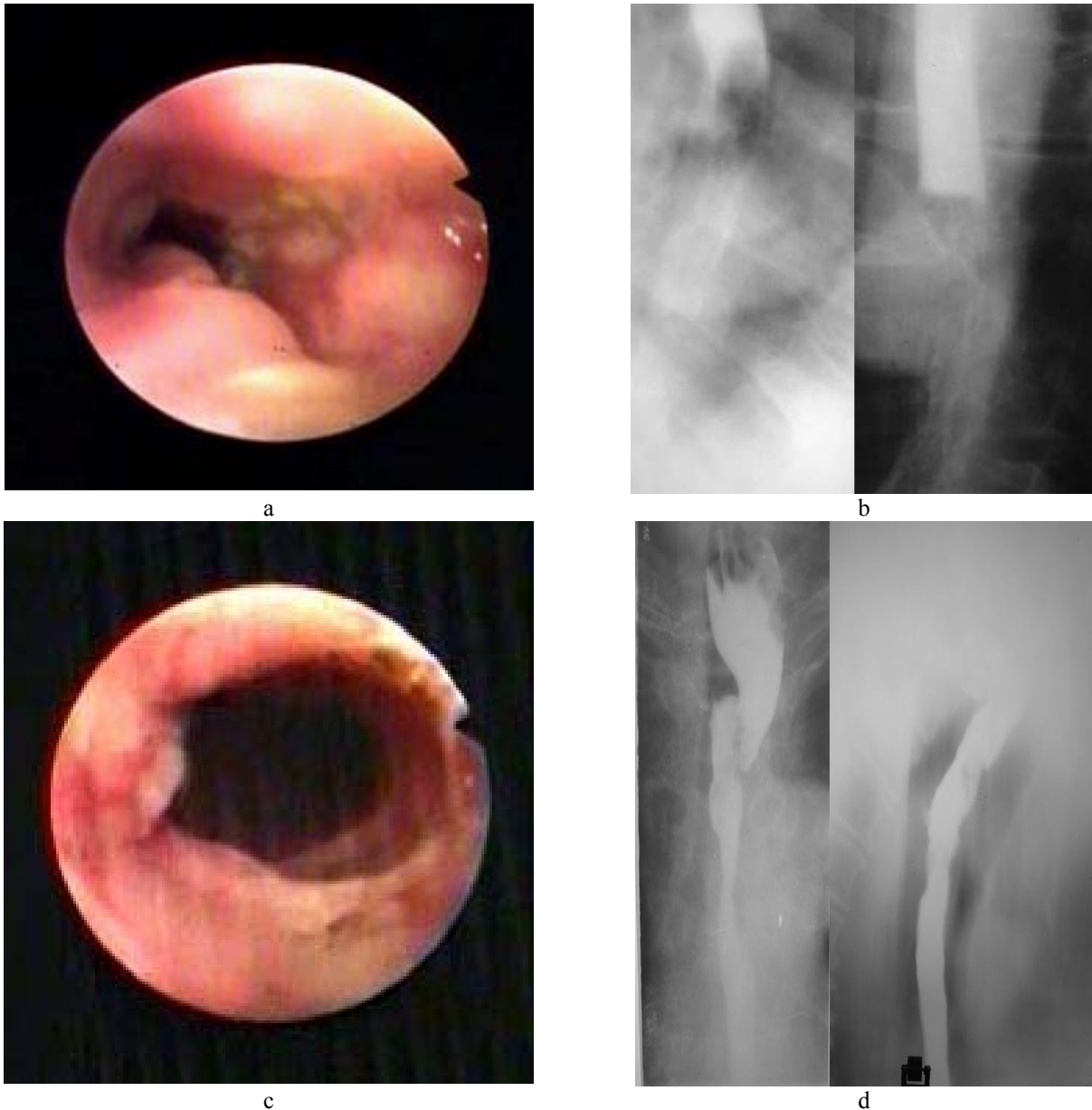


Fig. 7 Esophageal cancer. Endoscopic and rontgenologic picture (a,b) After beam therapy. Before PDT. The tumor obturates 2/3 of esophageal lumen (c,d) 2 months after PDT – recanalization of esophagus.

#### 4. CONCLUSION

PDT with Radachlorin is

- a radical highly efficient method of treatment of skin basal cell carcinoma. For intravenous introduction of Radachlorin with the combination of drug doses and light fluence (0.5 mg/kg and 300-350 J/cm<sup>2</sup>) or (1 mg/kg and 200-250 J/cm<sup>2</sup>), the method gives full recovery in almost 100% cases with excellent cosmetic effect. The only PDT procedure is usually enough. In the case of small tumors the method is also effective with interstitial introduction of drug (0.5 mg/g of tumor mass), light fluence 200-300 J/cm<sup>2</sup>.
- capable to treat radically the tumors of I-II stage of non-basalioma histological type.
- successfully combined with surgical operations, laser ablations, radio- and chemotherapy. Preoperative and intraoperative PDT favor improvement of results in complex treatment of malignant tumors. The method has a potential as palliative measure; in a number of incurable cases it allowed us to achieve recanalization of obturated hollow organs and eliminate the inflammatory complications.

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