

# A Brief Survey of Photodynamic Therapy (PDT) and Its Clinical Applications for Early Stage of Cancer

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**ABSTRACT:** For the treatment of the most dangerous diseases like cancer number of medicinal therapies were tried by doctors around the world photodynamic therapy (PDT) is one among them which is used to destroy the cells in the early stage of cancer in different parts of human body effectively. In this paper we have briefly discussed about the device used for the administration of medicines, dosage required and time required for the complete treatment and precautions taken for the treatment so as to give good results for the therapy.

**KEYWORDS:** PDT, photosensitizer, AMD, in VIVO, pharmacodynamics, photochemical reactions, photofrin, ALA, mTHPC, endobrothies, esophageal, cholangio carcinoma Dosimetry & biopsy.

## I. INTRODUCTION

PDT refers to photodynamic action in vivo to destroy or modify tissues. Originally this therapy is used for the treatment of various solid cancers but now it has been extended for the treatment of precancerous conditions. E.g.: Eye diseases and age related macular degeneration (AMD), PDT is a worldwide approved treatment for various cancers (lungs esophagus) and for cholangio carcinoma (late diagnosis)

## II. DISCUSSION ON PDT

Basic requirements for PDT:

PDT requires

1. a drug (Photosensitizer)
2. Light (may be laser) corresponds to the absorption band of photosensitizer and
3. Endogenous oxygen, absence of any of these agents will eliminate the

### Photodynamic effect:

Here the important cytotoxic agent is singlet oxygen, (an electronically excited state of ground state triplet oxygen) formed according to the following photochemical reactions (process)

$P + h\nu \rightarrow P^*(S)$  (absorption of light ( $h\nu$ ) by photo sensitizer)

$P^*(S) \rightarrow P^*(T)$  (intersystem crossing) S-singlet

$P^*(T) + O_2 \rightarrow O_2^* + P$  (energy transfer) T- triplet

### Drug photosensitizer:

Drug usually a photosensitizer which only undergoes efficient inter system crossing from  $P^*(S)$  &  $P^*(T)$  (triplet excited state) and this triplet state is relatively long lived which allow more time for collision of  $P^*(T)$  with oxygen and after many path ways to give high yield of singlet oxygen. Most of the sensitizers used in clinical purpose have triplet quantum yields in the range from 40%-60%. There is a loss of energy takes place by deactivation to ground state of fluorescence or internal conversion (loss of energy to environment)

### Characteristics of photosensitizer:

1. Pharmacokinetics, pharmacodynamics, stability in vivo and acceptable toxicity are important factors of consideration for the selection of photosensitizer (drug).
2. Also it is desirable than drug and must have a selective absorption in human tissue relative to normal tissue which exposed to excitation light. Certain organells are sensitive to PDT damage than others (mitochondria). For complete response to treatment high doses of photosensitizer is necessary in which it becomes a main issue. Due to toxicity break down of product takes place which should be removed in various stages of trials for U.S food and administration (FDA)
3. Light (for excitation of drugs)

A limitation factor in PDT is the penetration of light (activating) into the tissue visible light in the red region of spectrum is the most penetrating one. It has penetrating depth ( $\frac{1}{e}$ ) in the range of 2-6 mm. but depth of biological effect in DDP is generally found to occur twice this depth (4-12mm). Here only 10% of incident light is present at this depth. Though intensity drops off quickly at twice the depth of tissue, it is sufficient for P.D effect. For e.g. liver is the most opaque of tissue and whereas muscles are transparent. Most of the solid cancers originate from epithelial muscles and have optical penetration depth of 3-6mm which lies in the practical range at 600nm wavelength of light and 6-10mm range for 800nm light.

### III. LIGHT SOURCES

Sources of light used are

1. Gas vapor laser
2. Wavelength tunable dye laser (dye laser)
3. Solid state laser such as frequency doubled Nd:YAG laser
4. Diode lasers (most frequently used because of low power and compactness are used in PDT for the treatment of actinic keratoses (abnormal growth of keratin on the skin)

### IV. OPTICAL FIBERS

Light from laser is generally coupled with quartz optical fiber which guides the light into tissues accurately.

**For e.g.:**

1. For lesion involving the skin and certain other cases a lens fiber is used to produce a homogeneous spots.
2. For treatment of esophageal and lung tumours a fiber with a diffuser on its end is used to allow the scattering light laterally from fiber for a distance of 1-5 cm.
3. For bladder treatment a bulb type tip fiber is used to produce a uniform distribution of radiation over entire bladder wall.

Methodology of clinical PDT:

When photosensitizer photoprin is used in PDT we get most of the information's.

#### a. **Photosensitizer injection:**

For PDT usually patients are given an intravenous bolus injection of photofrin in doses ranging from 1-2mg/Kg body weight. But certain photosensitizer including photofrin after taken by the skin, patients are susceptible to severe burns when exposed to light a condition lasts from 4-6 weeks. Hence patients are given appropriate precautions by wearing clothing to cover the body completely and a covering hat. But in darkness low level light become ineffective to drug. Hence patients are advised to expose a small area on the back of their hand to light sunlight for minimum 4 weeks of injection

If reaction occur patients are advised to wait for one week more before testing sun's activity.

**Time interval between injection and exposure of light varies from one photo sensitizer to other photo sensitizer.**

**Light dosimetry (dosage)**

Quantum of light used in PDT is important since optimum light dose is one organ may be ineffective in other /toxic in another.

For single photosensitizer like photofrin light dose ranges starts from 200J/cm<sup>2</sup> for skin lesion.

**Photodynamic therapy with photofrin:**

Photofrin (poly hematoporphyrin ether) is the first and only photo sensitizer approved by health agencies worldwide for the treatment of cancer of all types.

**Approved indication for photofrin PDT:**

Here the indication is given for the treatment of obstructing tumours in the esophagus. For this treatment, photofrin obtained as lyophilized powder is dissolved in 5% dextrose for injection shortly before a single bolus injection of 2mg/Kg body weight . since the photo sensitizer is accumulated and retained in the skin, precautions should be taken for exposure of light. Since it is light sensitive but to make the drug active the patients should expose small patch of skin in bright sunlight for 10 min (30 days) for post injection and if reaction occurs patients has to wait for more times before exposure to light.

After 48 hours of post injection photo sensitizer localized in tumour is activated by light at 630nm that is directed by single quartz fiber and delivered to the tumour through biopsy channel of endoscopes. The distal end of the fiber is fitted with a diffusing surface with 2 to 2.5cm length which allows the light laterally into the tumour on the wall of the esophagus. The light dose is 300J/cm<sup>2</sup>, with power density of 400mW/cm requiring 30 min to deliver the required dosage usually Nd: YAG laser is used.

**For Non small cell lung cancer:**

The treatment is similar for obstructing esophageal tumour but with a slight difference 2mg/Kg body weight photofrin and 630nm light treatment are required for 48 hrs light dose is 200J/cm<sup>2</sup> diffuses (8.3nm) with diffuser fiber of 1.00 to 2.5 cm. after 2 days again patients are re-endoscoped and all necrotic tumours debris must be removed. Since they obstruct the air way Nd:YAG laser is used for treatment of other cancers, we can tabulate the procedures followed in a different types of laser tabular column.

tumour/cancer	treatment
early stage of endobronchial tumour	Dosage of 2mg/Kg should be injected. 2 days later endoscope with diffuser fiber(1-2.5 cm) delivering energy of 200J/cm <sup>2</sup> by 630nm laser and fiber is held closed to lesions since they are very small
early stage of esophageal cancer	Photofrin dosage of 2mg/Kg is injected, 2 days before light dosage 130J/cm by diffuser fiber -follow up action is necessary for 6 months
cholagio carcinoma	since they are diagnosed very late, surgery is not curative photofrin dosage of 2mg/Kg is injected, 2 days before endoscopic Fiber test. Light dosage of 180J/cm <sup>2</sup> is given by the 630nm laser to diffuser fiber of length 2.5-4 cm.
head neck cancer	For this radiation therapy is ineffective. for early cancers (Head & Neck), patients received 2mg/Kg of photofrin followed,2 days later, excitation by laser of 630nm at energy dose of 80J/m <sup>2</sup> . Patient remains free from disease after follow up action of 27 months
brain tumour	Photofrin dosage of 2mg/Kg is injected, 12-16 hours before light dosage mean survival 12-16 hours of light treatment of 630nm at energy dosage of 110J/cm

**Disadvantages or side effects:**

Number of preclinical studies shows that PDT has triggered an inflammatory reaction in tissue if photofrin is used as photo sensitizer but HPPH-PDT induces a mixed inflammatory reaction in tissues compared to photofrin. Hence HPPT is preferred in some therapies.

**Advantages:**

Even though PDT induces some mild inflammatory reaction in tissues it enhances the host antitumour immunity by not killing much of natural killer (NK) cells. This argumentation of NK activity will enhance the

chance of PD tumour control effectively by natural immunity. Also PDT will not affect the metastases outside treatment area.

#### V.CONCLUSION

Though PDT therapy has been used mainly in cancer therapy its applications are extended to many non-cancerous conditions and also the other areas in which PDT is currently is employed are rheumatoid activities, prevention of restenosis after balloon angioplasty for cardiac artery diseases and early detection of certain cancer like diseases.

Thus PDT has found many application of medicinal therapy and it kills the cancer cells at early stages effectively and efficiently. Even though the treatment takes some days to months depending upon the location and stages of cancer in the human body.

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