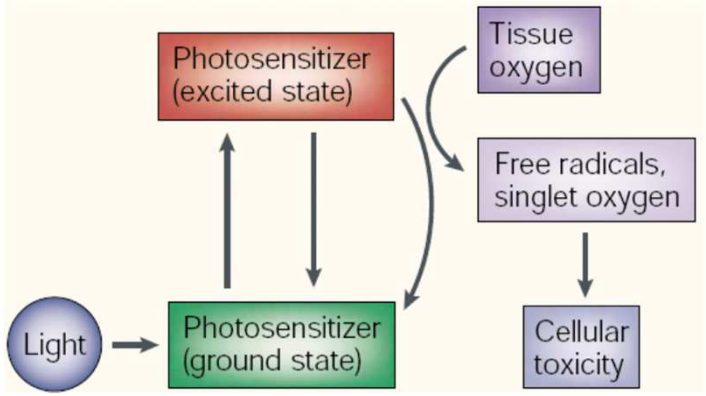
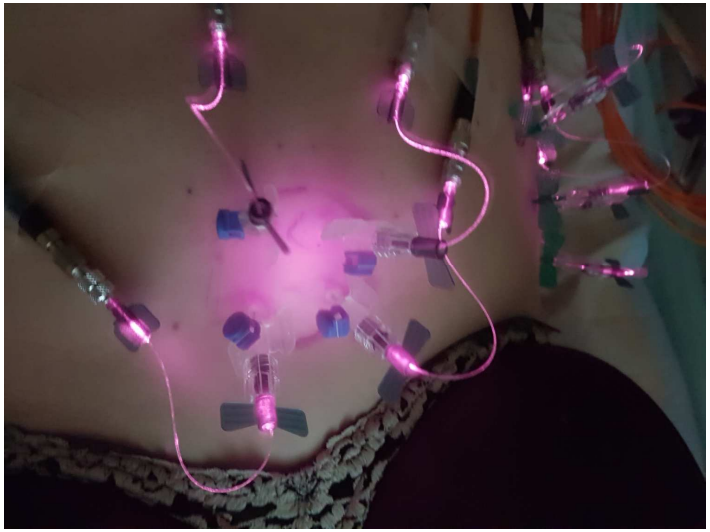
Intravenous and Interstitial Photodynamic Laser Therapy Producing Groundbreaking Results in the Treatment of Cancer

Dr. med. Dipl. Chem. Michael Weber
Weber Medical GmbH
Sohnreystr. 4
37697 Lauenfoerde
Germany
info@webermedical.com /
www.webermedical.com
+ 49 5273 367780

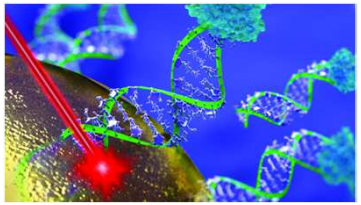




Content:

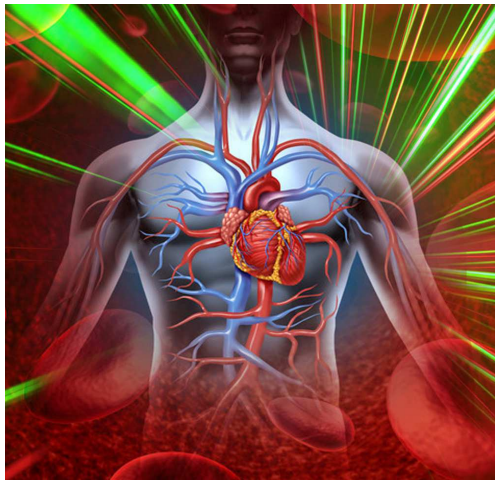
1. Basic Principles and Applications of Laser Therapy
2. Mechanisms of Photodynamic Therapy
3. Traditional Photosensitizers and their limitations
4. The new Nano ICG Photosensitizer
5. Applications and Protocol
6. First clinical results

Basic Principles of Laser Therapy

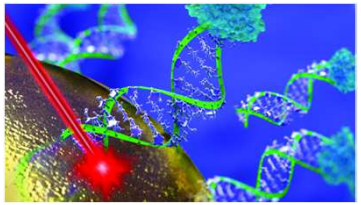


What is Medical Laser Therapy?

- The therapy concept of LLLT has been developed in Germany and is based on the usage of **soft lasers**
- Unlike surgical lasers that destroy tissue and cells, soft lasers supply our body with energy to trigger numerous **regenerative processes**
- Medical laser therapy applies blue, green, yellow, ultraviolet, red and infrared lasers. Each color develops different effects which are evoked by the **stimulation of specific cellular components**, such as growth factors or cells of our immune system
- These effects have been proven by a large number of **clinical studies**



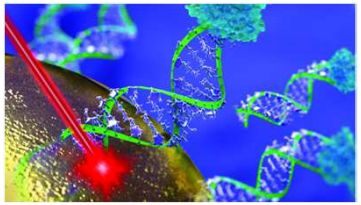
Basic Principles of Laser Therapy



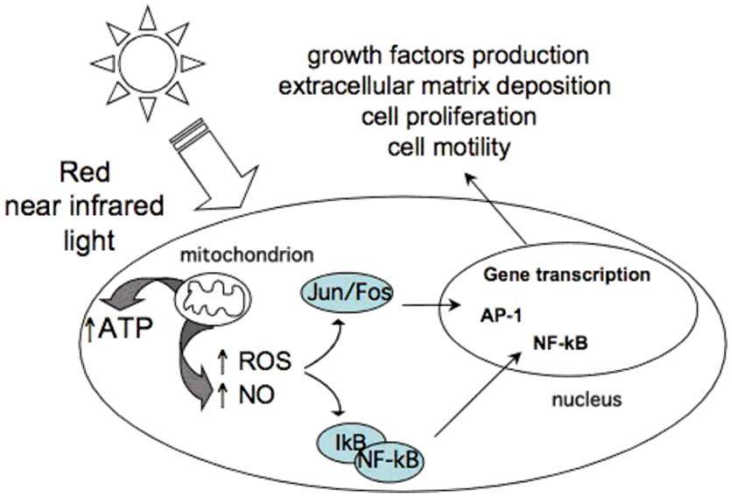
Main applications of Laser Therapy:

- Local Laser Therapy / Laserneedle Acupuncture for Pain Management and Tissue Regeneration
- Transcranial Laser Therapy
- Dermatological Therapy / Cosmetic Laser Therapy
- Interstitial / Intra-articular Laser Therapy
- Intravenous Laser Therapy
- **Photodynamic Tumor Therapy**

Basic Principles of Laser Therapy

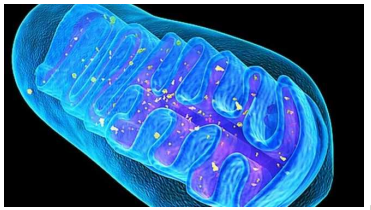


- In general, there are specific cellular structures that are able to absorb specific wavelengths (colors) of light (known as photoreceptors)
- The light stimulus gives a cellular signal affecting the chemical behavior, metabolism, movement and gene expression
- All associated enzymes and/or proteins are now affected
- This cascade event can ripple across an entire cell

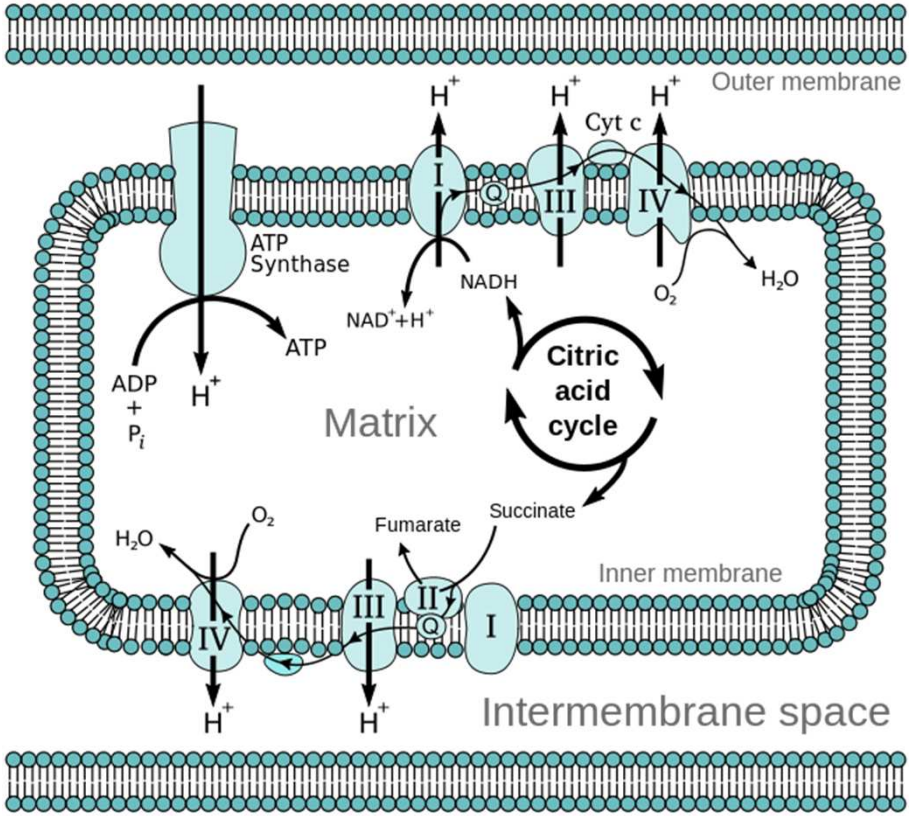


Hamblin:
http://photobiology.info/Hamblin.html

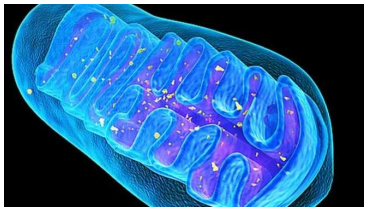
Absorption of Difference Light Wavelengths (Colors) in Mitochondria



- One example for the absorption of different colors within cells is the process in the mitochondrial respiratory chain [21]
- Complex 1 (NADH dehydrogenase) absorbs blue and ultraviolet light
- Complex 3 (cytochrome c reductase) absorbs green and yellow light
- Complex 4 (cytochrome c oxidase) absorbs red and infrared light

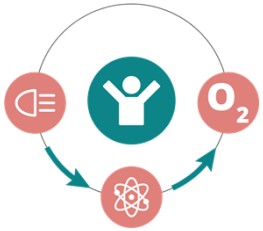


Basic Principles of Laser Therapy

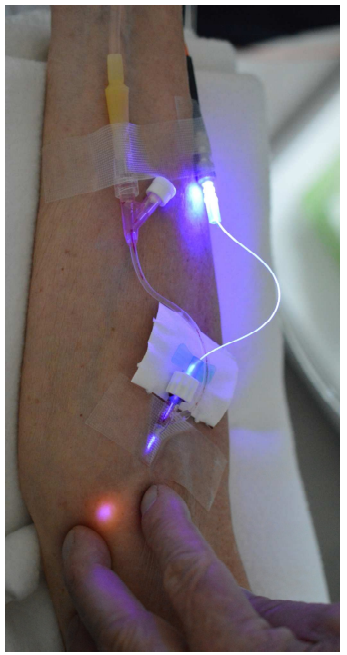


- Laser Light may help restore cellular homeostasis by inducing physiologically reparative activity for disease reversal in cancer and other degenerative diseases with minimal adverse side effects, and with potentially marked improvements in quality of life even in patients with advanced neoplasms
- Of major importance to achieve this is the activation and modulation of mitochondrial oxidative energy pathways
- Lasers have the potential to activate and modulate the production of ATP, GTP, AMPK and inositol pirophosphates P7-P8, not only through the respiratory chain but also through absorption and transportation of light by water
- A major goal for laser therapy in cancer is to control apoptosis (programmed cellular death) and differentiation, thus providing another cancer therapy tool

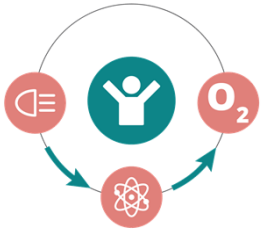
What is Photodynamic Therapy ?



- Photodynamic therapy is one of the most interesting and promising approaches in the treatment of various cancers
- The principle is the stimulation of a light sensitive drug which is injected into the blood (or given orally) and accumulates in cancer cells
- Tumor tissue is subsequently destroyed by irradiation with light of appropriate wavelength according to the absorption spectra of the various photosensitizers (by development of ROS)



What is Photodynamic Therapy ?

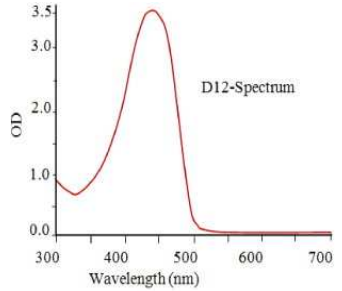


- Intravenous laser therapy in combination with photosensitive substances kills circulating tumor cells and stimulates the immune system

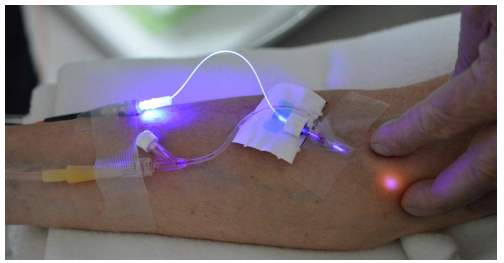
- Cancer tissue is targeted by local photodynamic therapy (i.e. interstitial or topical laser application)

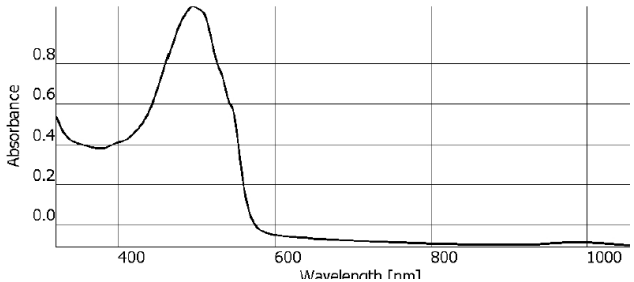
- Common photosensitizers:
  - **Liposomal Indocyanine Green (ICG)**
  - Chlorin/Chlorophyllin
  - Curcumin (Turmeric)
  - Hypericin (St. John's Wort)
  - Riboflavin
  - Phycocyanin
  - Poly MVA

- Several chemo drugs are light-sensitive as well and can be enhanced by intravenous laser significantly (with lower dosage), i.e. Doxorubicin, Mitoxantron, Paclitaxel, Cisplatin or 5-FU



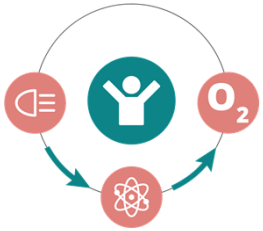
Light Absorption of Curcumin





Light Absorption of Doxorubicin

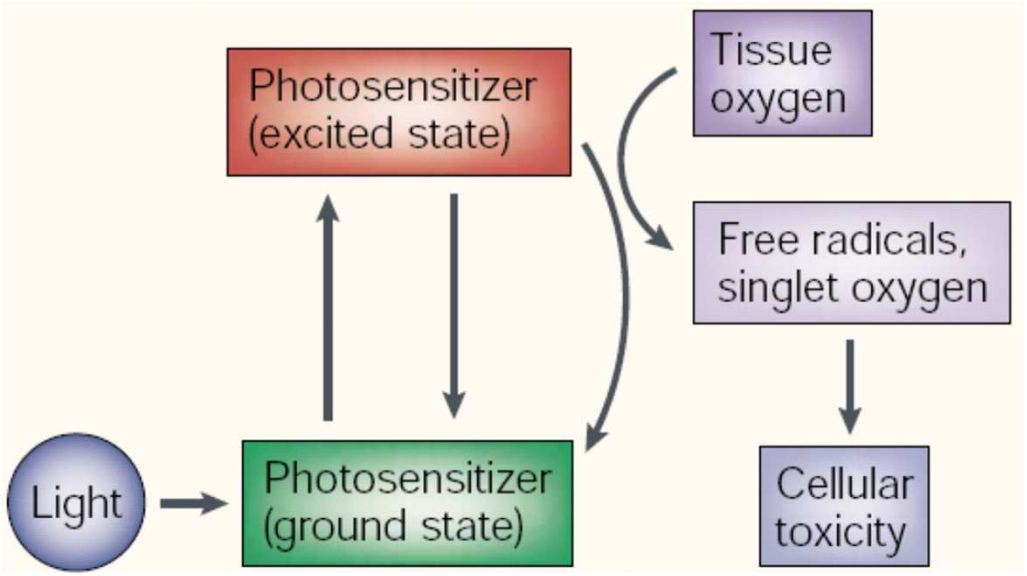
Mechanisms of Photodynamic Therapy



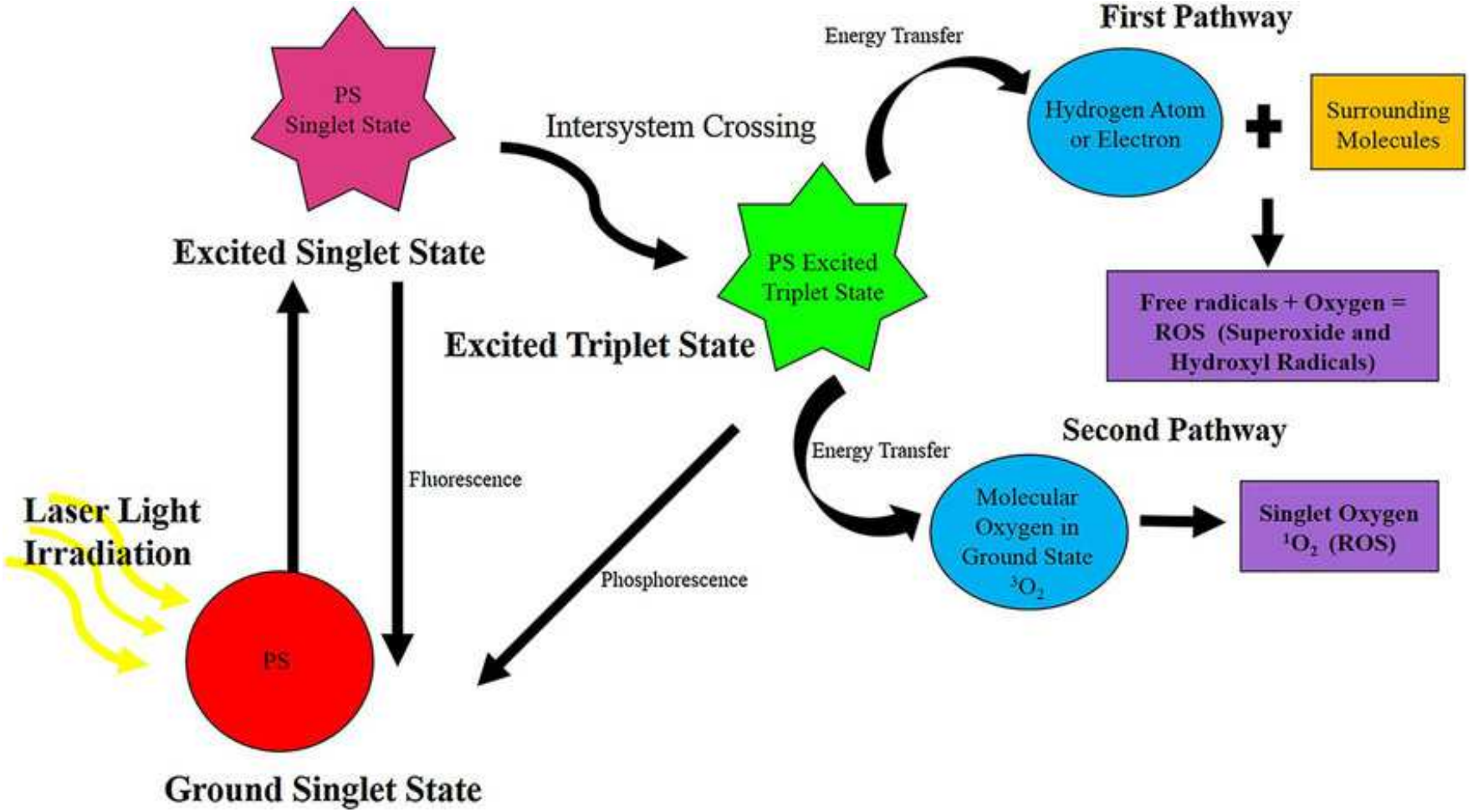
Two individually non-toxic components brought together to cause harmful effects on cells and tissues:

1. Photosensitizing agent

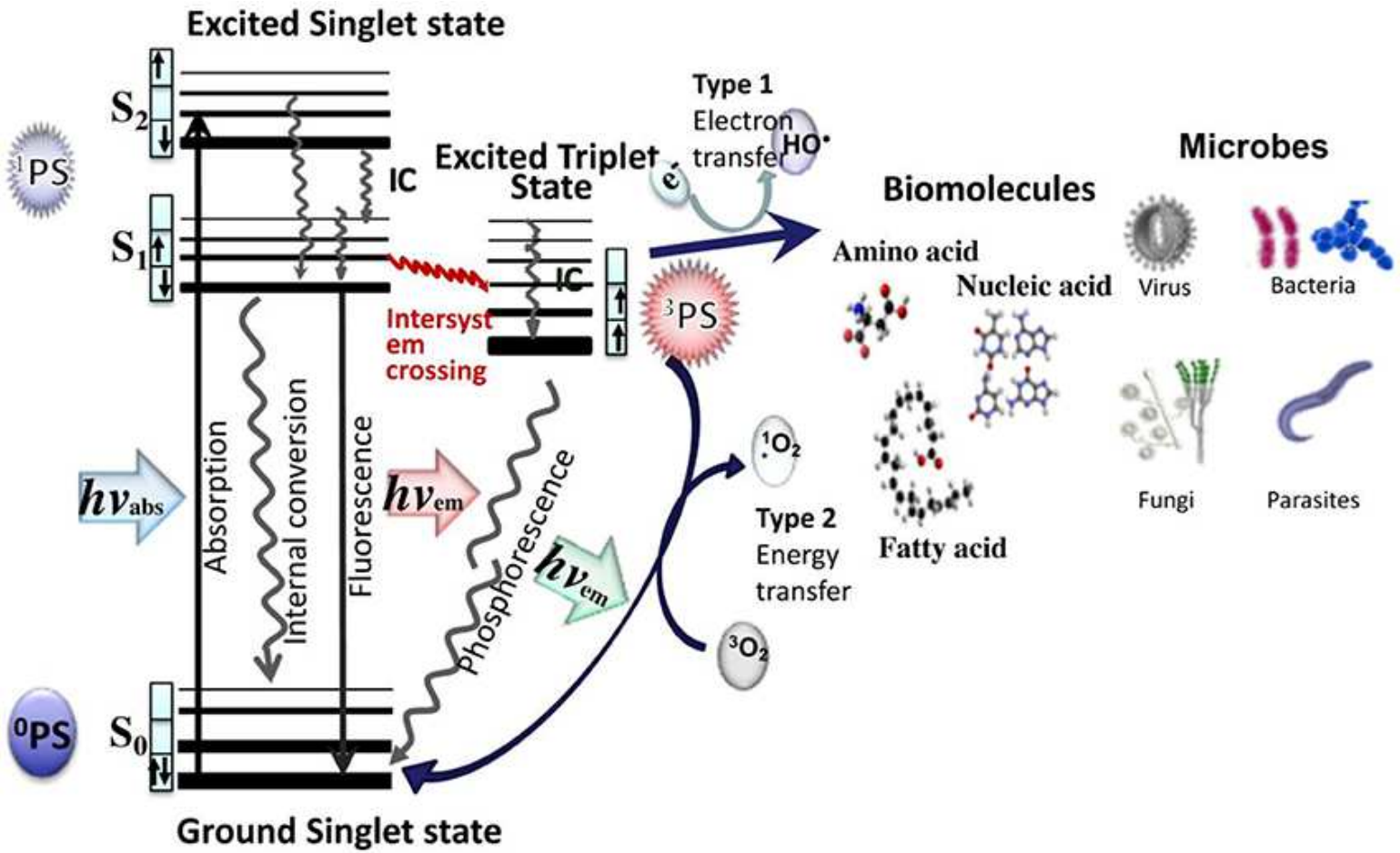
2. Light of specific wavelength



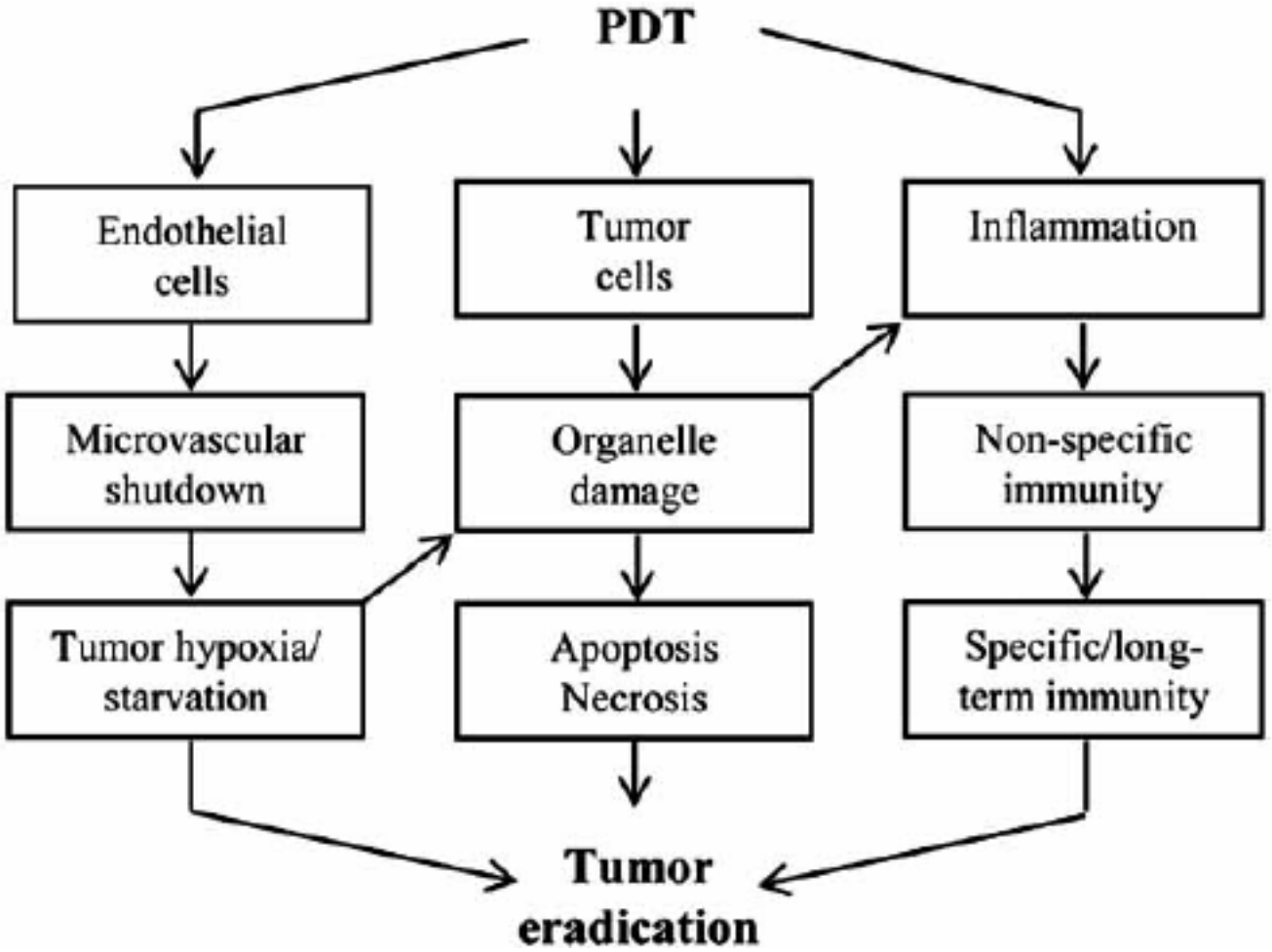
Mechanisms of Photodynamic Therapy



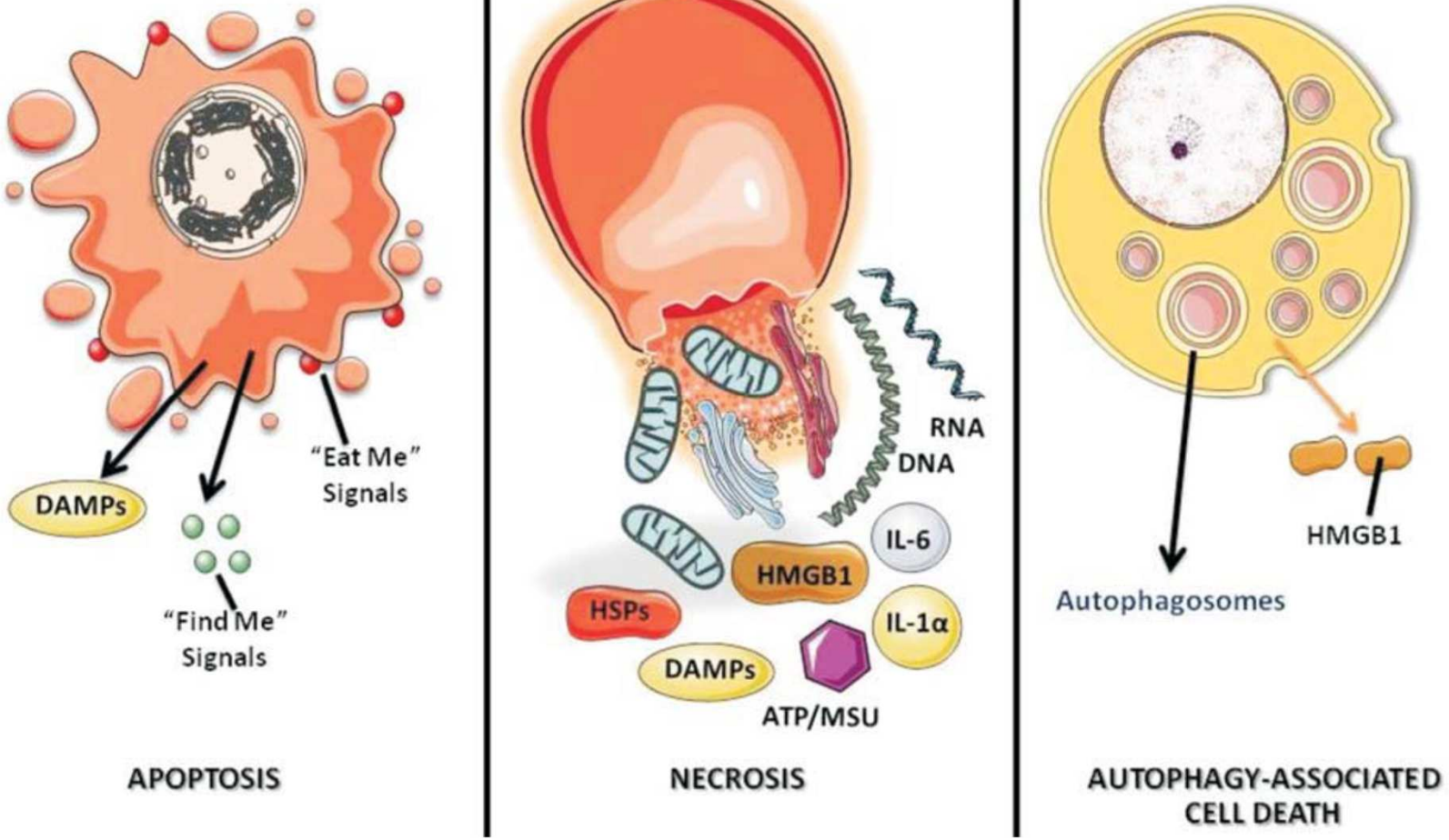
Mechanisms of Photodynamic Therapy



Mechanisms of Photodynamic Therapy



Mechanisms of Photodynamic Therapy



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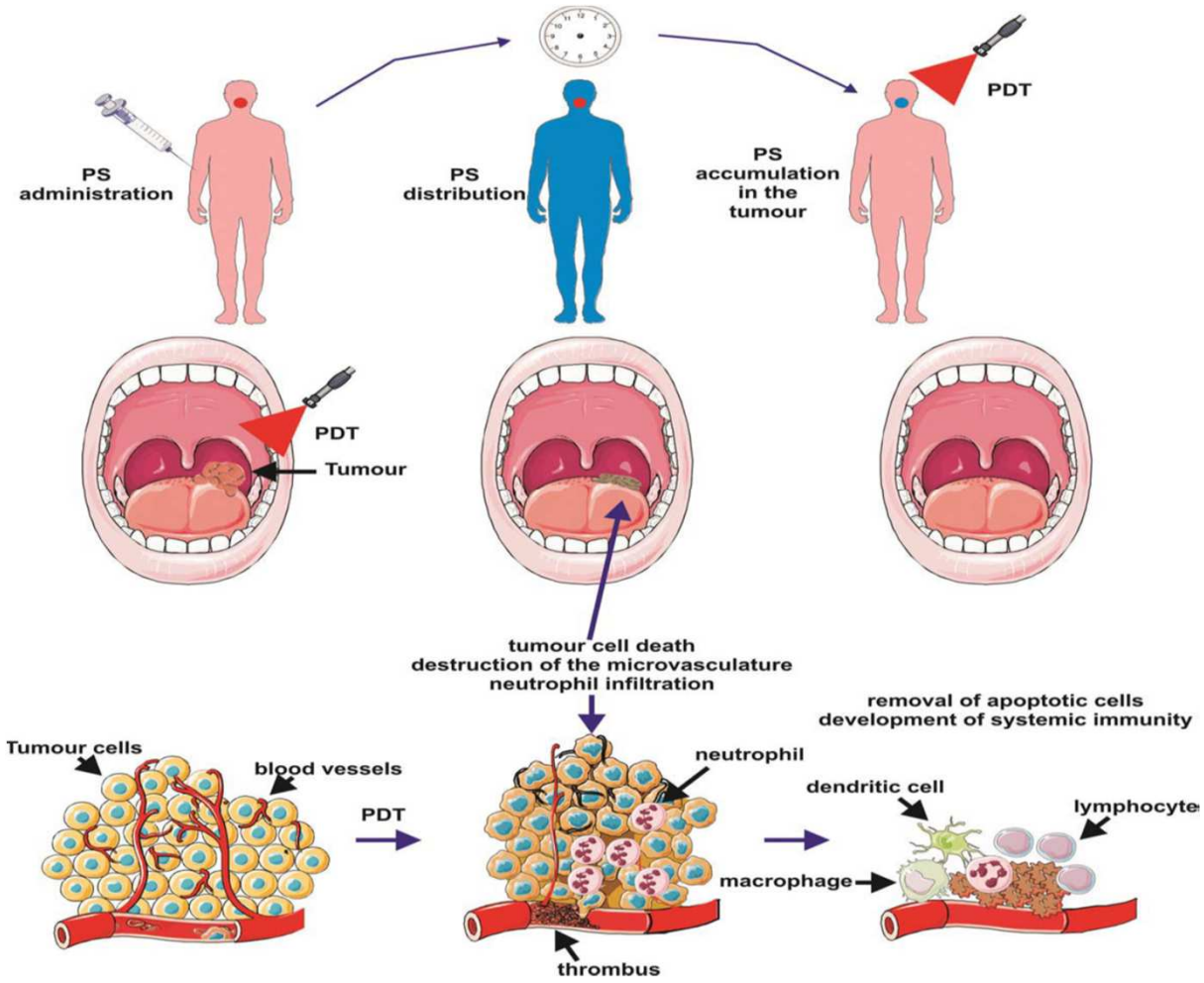

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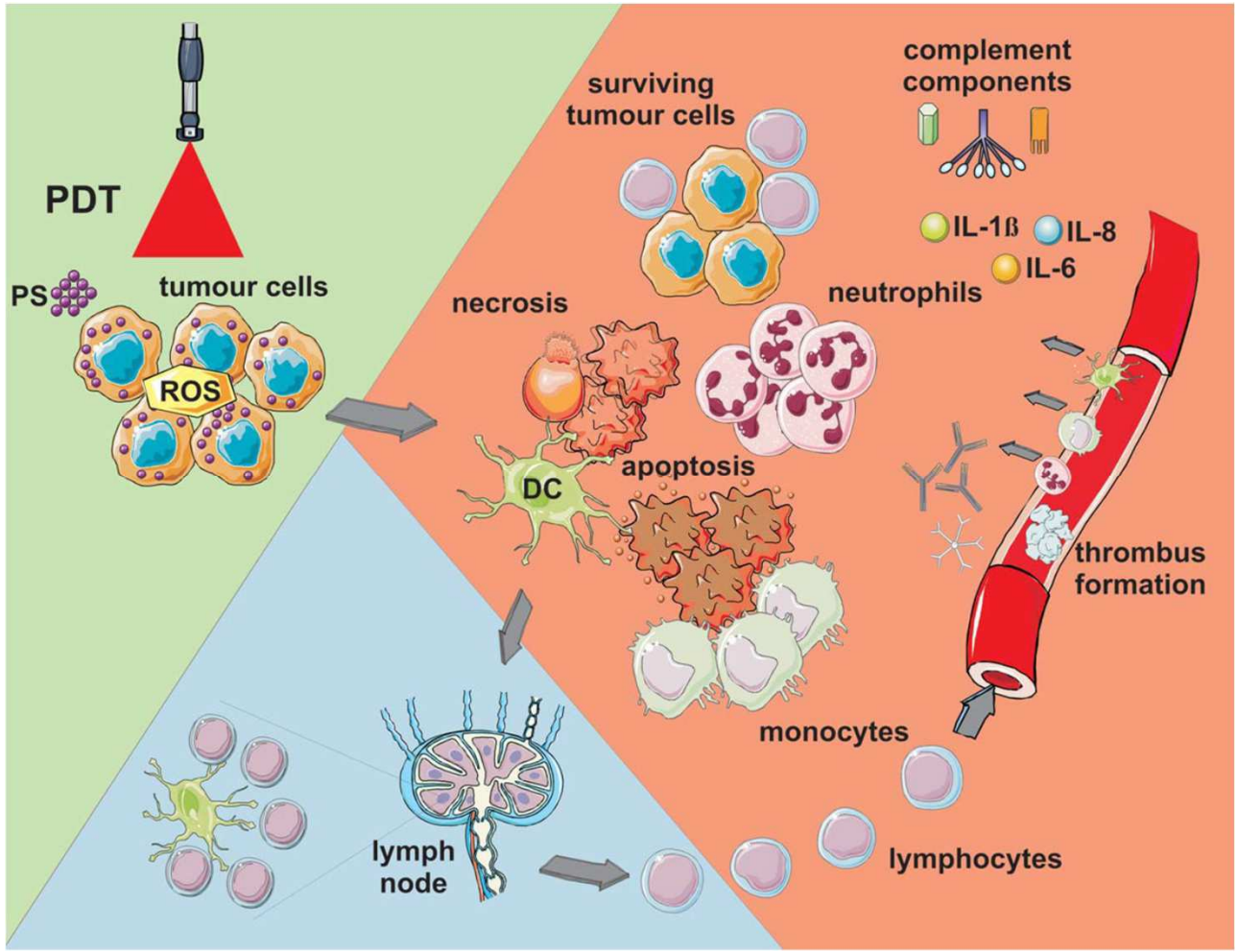

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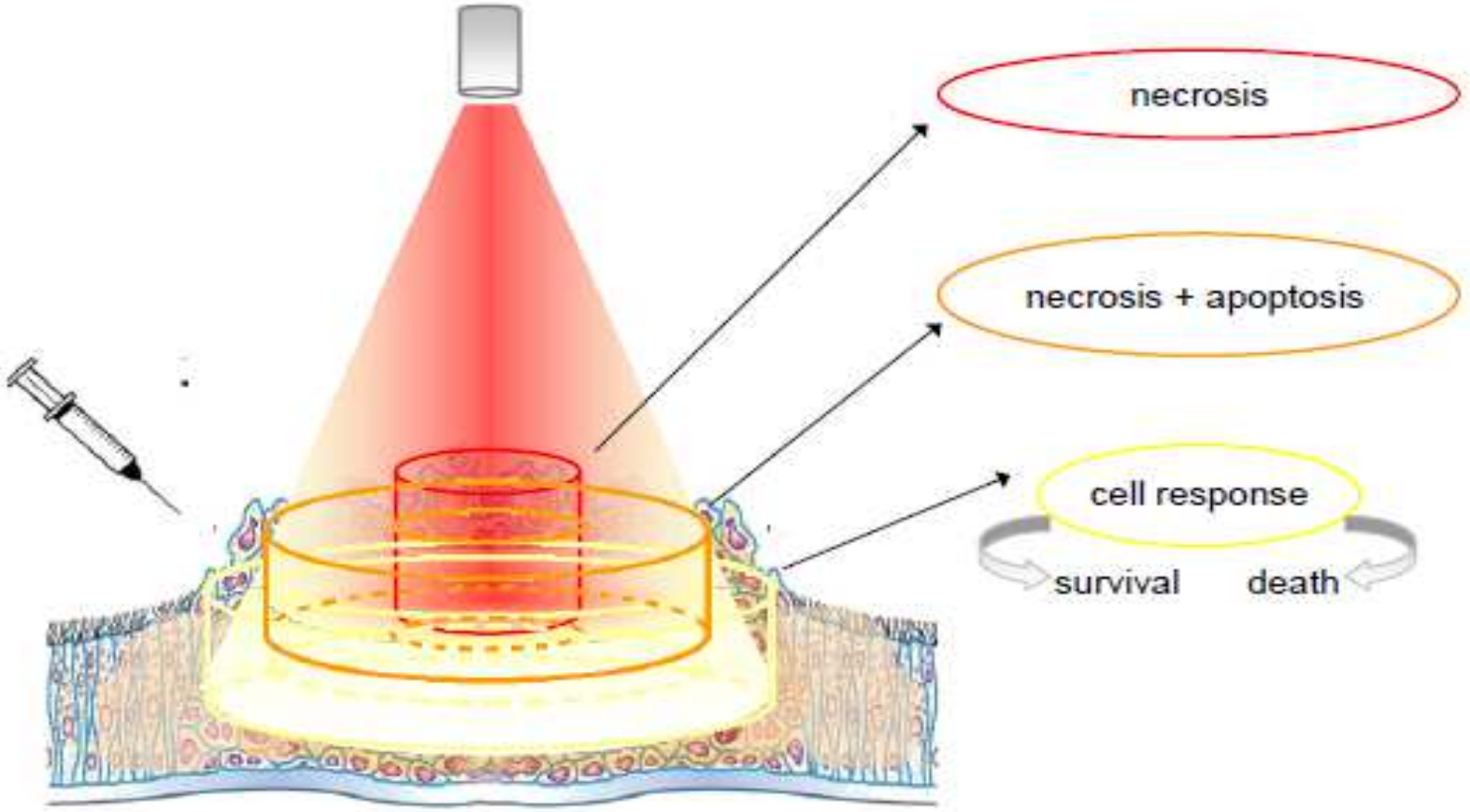
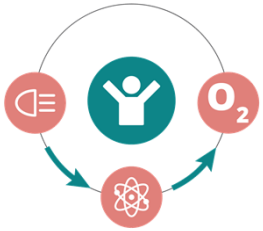
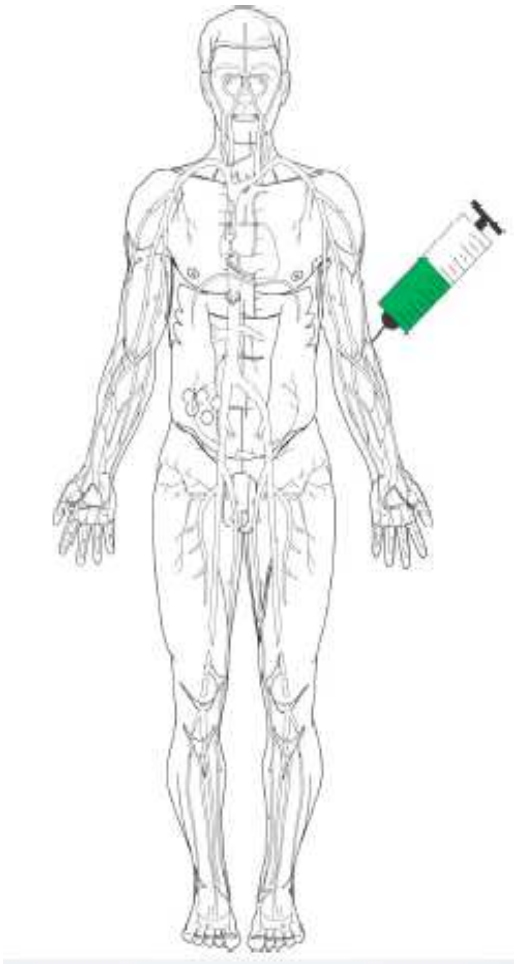


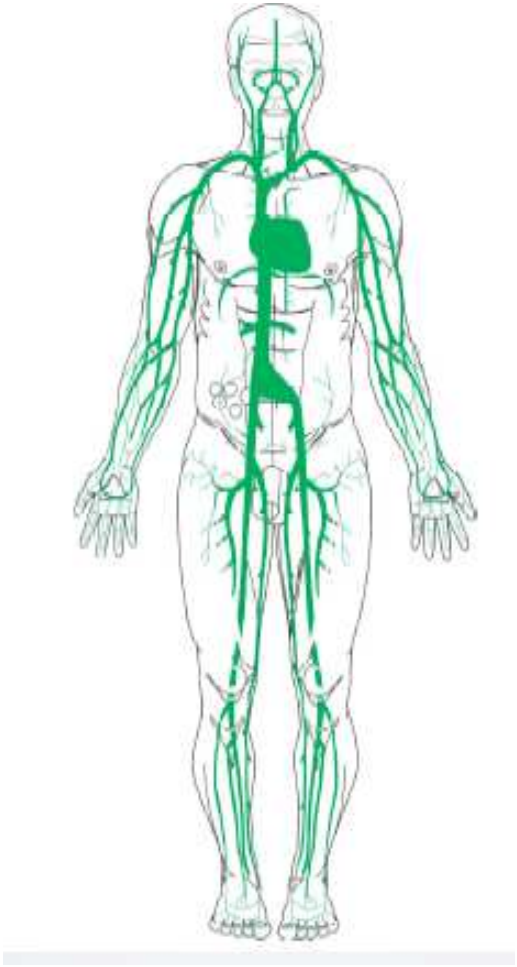
Light Distribution and Cellular Response during PDT

Mechanisms of Photodynamic Therapy

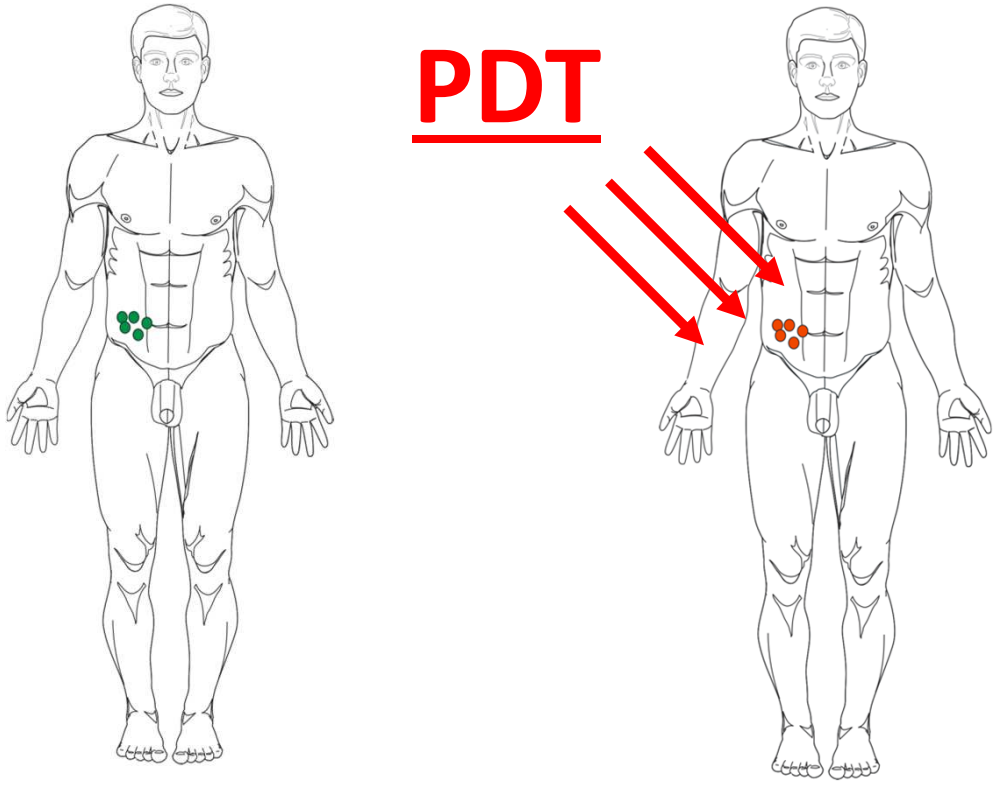




3 – 5 min



Mechanisms of Photodynamic Therapy



Accumulation of PS in tumor

Result:

- Generation of reactive Oxygen Species (ROS)
- Apoptosis / Necrosis
- Elimination of PS from blood

Traditional (approved) Photosensitizers

APPROVED

- Hematoporphyrins, HpD
  - Derivatives of Hem (Photofrine and others)
- Chlorines
  - Derivatives of Chlorophyll
- Porphyrins
  - Synthetic Porphyrins

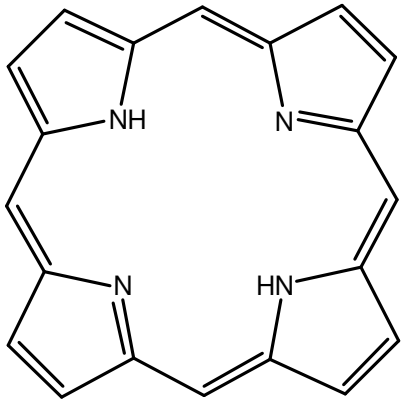


Table 1 Currently available photosensitizers.

Platform	Drug	Substance	Manufacturer	Web site
Porphyrin	Photofrin®	HpD	Axcan Pharma, Inc.	www.axcan.com
Porphyrin	Levulan®	ALA	DUSA Pharmaceuticals, Inc.	www.dusapharma.com
Porphyrin	Metvix®	M-ALA	PhotoCure ASA	www.photocure.com
Porphyrin	Visudyne®	Vertiporfin	Novartis Pharmaceuticals	www.visudyne.com
Texaphyrin	Antrin®	Lutexaphyrin	Pharmacylics	www.pharmacyclics.com
Chlorin	Foscan®	Temoporfin	Biolitec Pharma Ltd.	www.bioletcpharma.com
Chlorin	LS11	Talaporfin	Light Science	www.lightsciences.com
Chlorin	Photochlor	HPPH	RPCI	www.roswellpark.org
Dye	Photosens®	Phthalocyanine	General Physics Institute	www.gpi.ru

Traditional (approved) Photosensitizers

TABLE 2. Clinically Applied Photosensitizers

PHOTOSENSITIZER	STRUCTURE	WAVELENGTH, nm	APPROVED	TRIALS	CANCER TYPES
Porfimer sodium (Photofrin) (HPD)	Porphyrin	630	Worldwide		Lung, esophagus, bile duct, bladder, brain, ovarian
ALA	Porphyrin precursor	635	Worldwide		Skin, bladder, brain, esophagus
ALA esters	Porphyrin precursor	635	Europe		Skin, bladder
Temoporfin (Foscan) (mTHPC)	Chlorine	652	Europe	United States	Head and neck, lung, brain, skin, bile duct
Verteporfin	Chlorine	690	Worldwide (AMD)	United Kingdom	Ophthalmic, pancreatic, skin
HPPH	Chlorin	665		United States	Head and neck, esophagus, lung
SnEt2 (Purlytin)	Chlorin	660		United States	Skin, breast
Talaporfin (LS11, MACE, NPe6)	Chlorin	660		United States	Liver, colon, brain
Ce6-PVP (Fotolon), Ce6 derivatives (Radachlorin, Photodithazine)	Chlorin	660		Belarus, Russia	Nasopharyngeal, sarcoma, brain
Silicon phthalocyanine (Pc4)	Phthalocyanine	675		United States	Cutaneous T-cell lymphoma
Padoporfin (TOOKAD)	Bacteriochlorin	762		United States	Prostate
Motexafin lutetium (Lutex)	Texaphyrin	732		United States	Breast

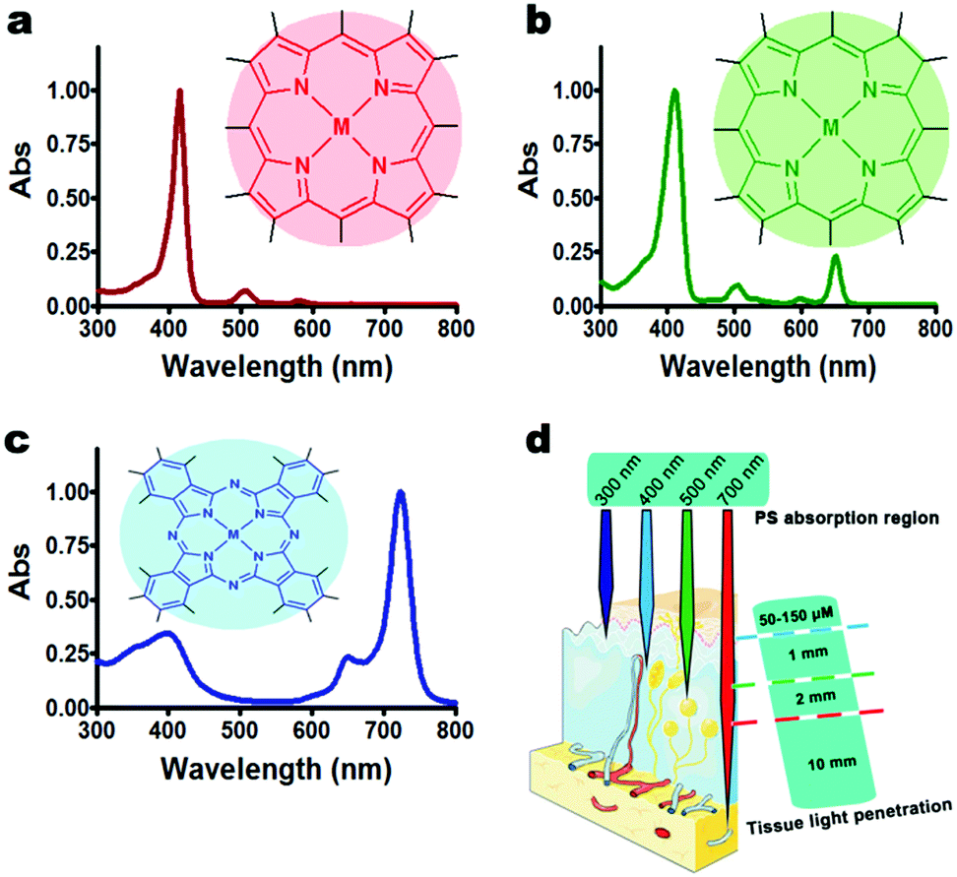
Traditional (approved) Photosensitizers

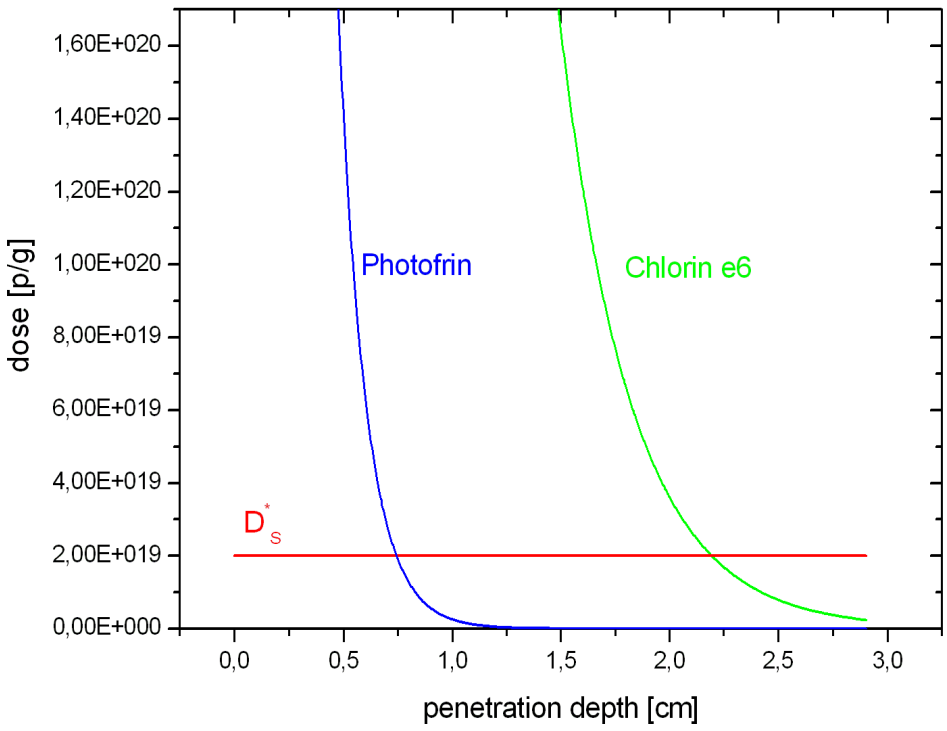
APPROVED

Photosensitizer	Type of diseases	Country
(*5-ALA*) 5-aminolevulinate	Actinic keratosis, Basal cell carcinoma	U.S., EU
Photofrin	Barrett's displasia	U.S., Canada, EU, UK
Photofrin	Cervical cancer	Japan
Photofrin	Endobronchial cancer	Canada, Most EU Countries, Japan, U.S.
Photofrin	Esophageal cancer	Canada, Most EU Countries, Japan, U.S.
Photofrin	Gastric cancer	Japan
Photofrin	Papillary bladder cancer	Canada
Foscan	Head and neck cancer	EU, Norway, Iceland
Verteporfin	Age-related Macular Degeneration	Canada, Most EU Countries, Japan, U.S.

Limitations of traditional Photosensitizers

KEY ISSUES





Limitations of traditional Photosensitizers

- Limited success by using red, blue and yellow lasers due to limited penetration depth (max 2 cm for red laser)
- Limited tumor size: max 2 cm
- Risk of burning and ulceration due to overdosage
- Light sensitivity
- Low success rate for liver and bone metastases
- No success in treatment of brain tumors

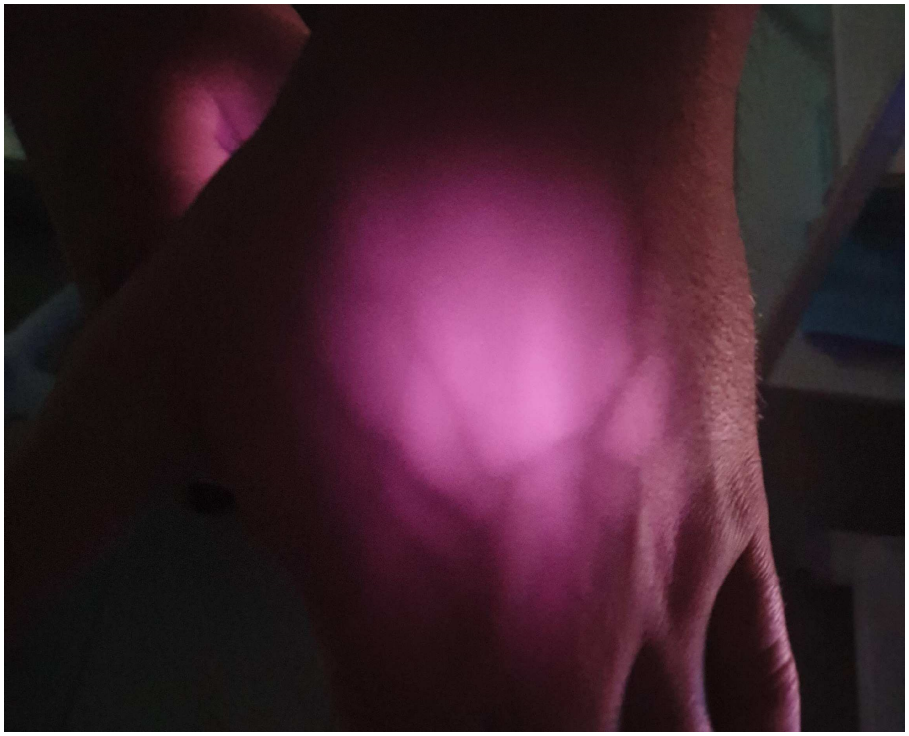
The new Nano ICG Photosensitizer

Key Features:

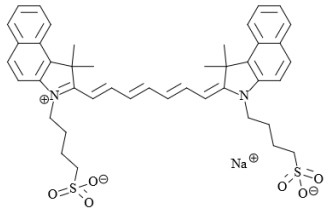
- First Photosensitizer in infrared range (infrared lasers have the best penetration depth into the body; even into bone tissue)
- Improved tumor targeting and accumulation with new nanotechnology
- Strong accumulation and tissue lifetime in tumors for several days: A series of laser treatments can be done after just one infusion/injection
- Large quantum yield of about 36 %
- Very safe substance with almost no side effects and negligible light sensitivity
- Highest quality standards guaranteed by a certified German sterile laboratory

The new Nano ICG Photosensitizer

Penetration of infrared laser through bones



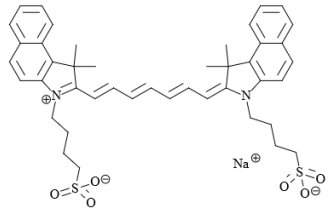
The new Nano ICG Photosensitizer



What is Indocyanine Green (ICG)?

- Indocyanine Green (ICG) is a cyanine fluorescent dye used in medical diagnostics (for determining cardiac output, hepatic function, liver blood flow and for ophthalmic angiography)
- The hydrophilic, anionic tricarbocyanine photosensitizer has been developed by Kodak Research Labs and got FDA approval in 1956
- It has a peak spectral absorption at about 800 nm. These infrared frequencies penetrate retinal layers, allowing ICG angiography to image deeper patterns of circulation than fluorescein angiography
- ICG binds tightly to plasma proteins like albumin and is confined to the vascular system
- When ICG is administrated intravenously half-life is approx. 3 - 4 min
- Around 3,000 scientific papers on ICG have now been published worldwide

The new Nano ICG Photosensitizer



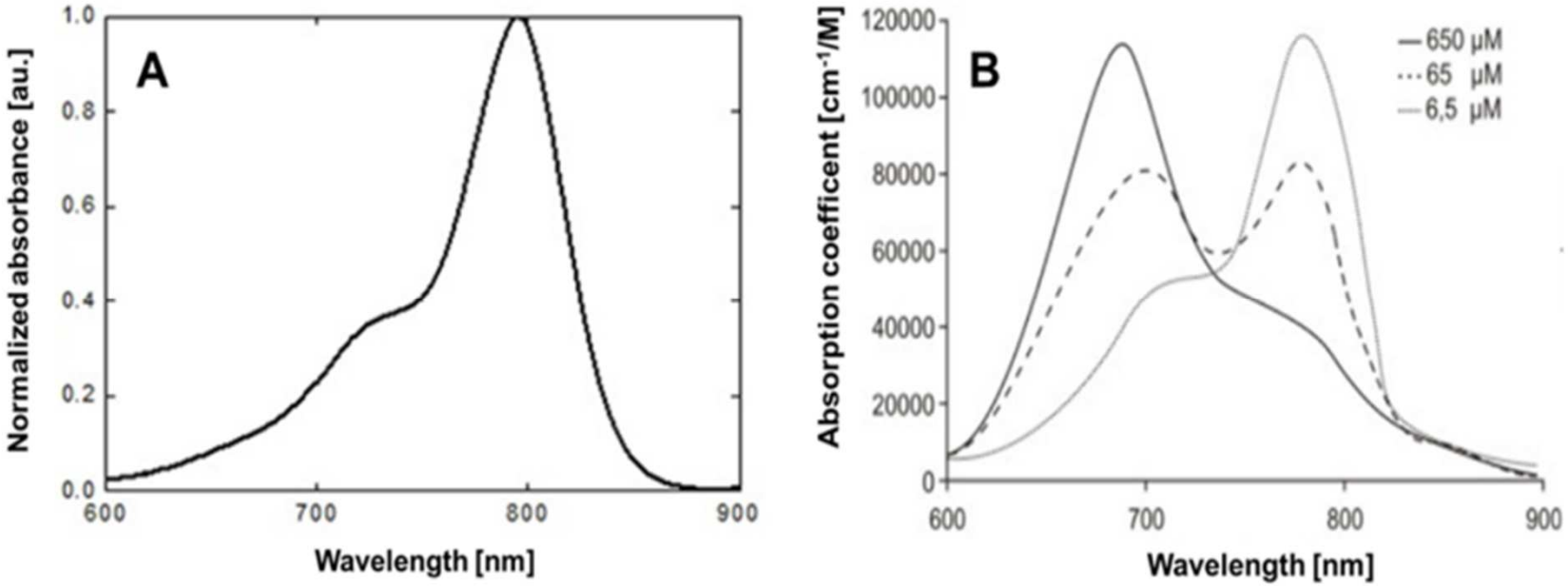


Fig 1: Absorption spectra of Indocyanine Green (ICG, 1,7-Bis[1,1-dimethyl-3-(4-sulfobutyl)-1H-benz[e]indol-2-yl]heptamethinium-betain sodium salt. A) Normalized spectra of a 10 mg/ml solution in water. B) Concentration dependence of the ICG spectra. Higher concentrations lead to a molecular assembly of the ICG molecules and a strong shift in the wavelength maximum could be observed. The effectivity of ICG decreased with the molecular assembly.

The new Nano ICG Photosensitizer

Limitations of regular ICG for Photodynamic Therapy:

- After intravenous injection, regular ICG binds to serum proteins almost completely (98 %) within 1-2 s; therefore, an accumulation in peripheral tissue, organs or even tumors is practically impossible (Cherrick et al., 1960)

- The tissue lifetime/stability of regular ICG in normal tissue and tumor tissue is about 10 min (Licha et al., 2002)

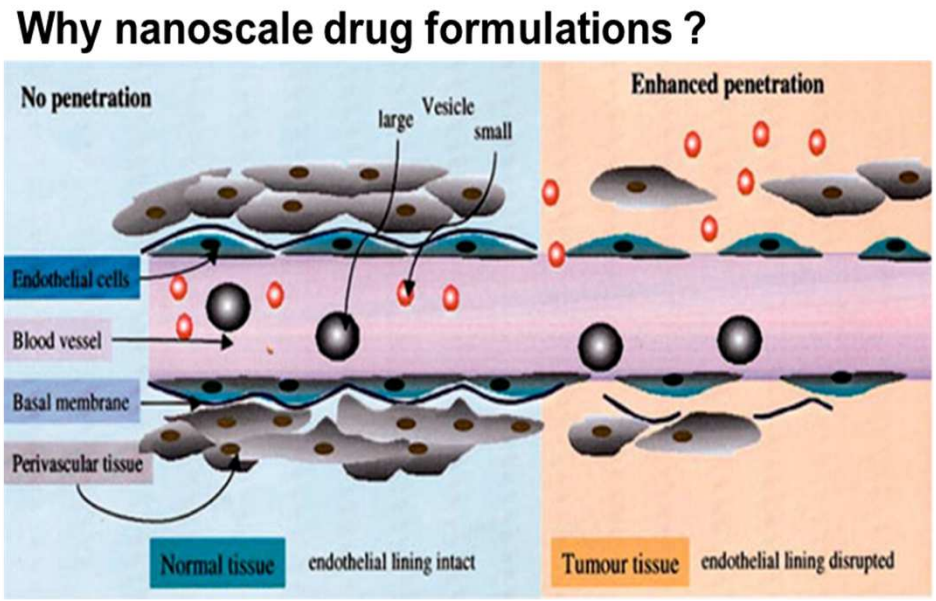
- The quantum yield of regular ICG in physiological NaCl and in plasma is about 3-5 % (Sutterer et al., 1996)

➔ **These properties do not allow any application in Photodynamic Therapy (PDT)**

The new Nano ICG Photosensitizer

Solution: Nanoscale drug formulation

- One of the most useful advantages of nanoscale drug formulations is the utilization of the so-called enhanced permeability and retention effect (EPR)
- The concept of EPR describes all the mechanisms of passive transport of drug carriers of a defined size of about 200 nm or smaller, typically liposomes, micelles or nanoparticles to accumulate in tumor tissue much more than they do in healthy tissues

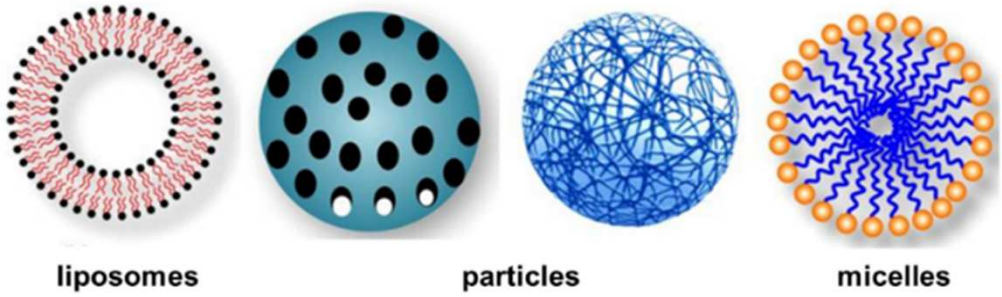


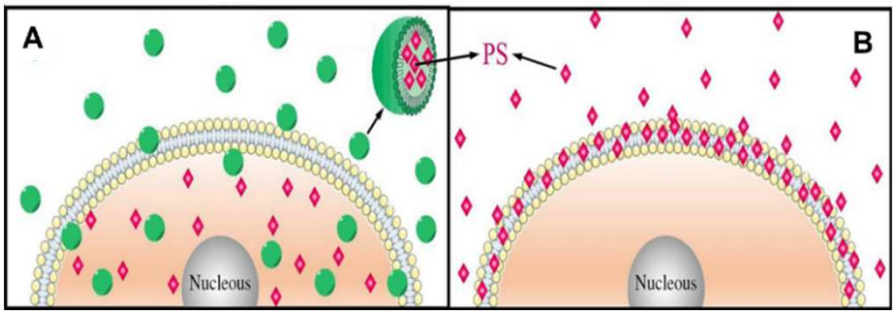
- Explanation: In order for tumor cells to grow quickly, they must stimulate the production of blood vessels by VEGF; additionally, the area surrounded by the fast-grown tumor is permanently inflamed; these newly formed tumor vessels are usually abnormal in form and architecture; they are poorly aligned defective endothelial cells with wide fenestrations; furthermore, tumor tissues usually lack effective lymphatic drainage

The new Nano ICG Photosensitizer

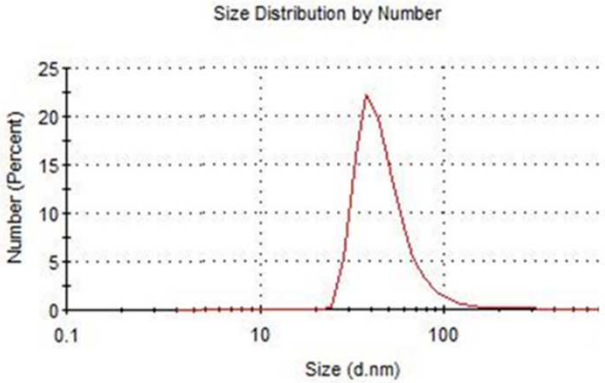
Development of Nano-ICG:

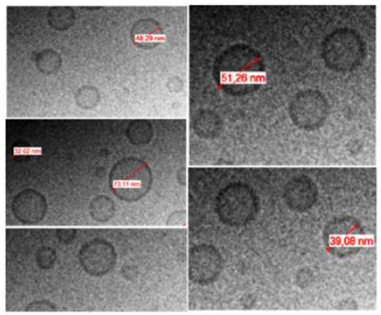
Liposomes and micelles were the first investigated nano systems for improved and better targeted introduction of photosensitizers into tumor cells. They have similar structures characterized by a core/shell model and thus can incorporate hydrophilic, hydrophobic and amphiphilic substances for delivery into cancer cells (Fig 3 and 4). The result is a considerable improved and selective uptake into tumor cells with an extended retention time of the photosensitizer.



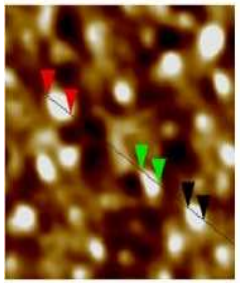


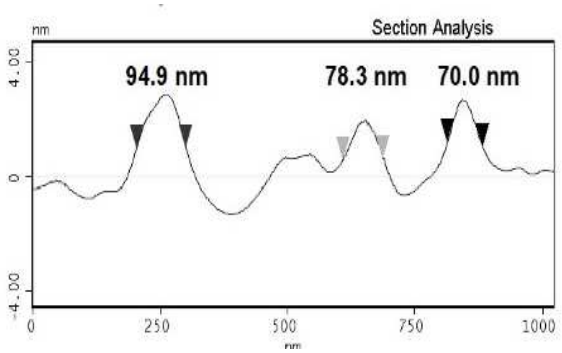
The new Nano ICG Photosensitizer

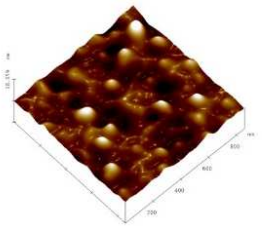




The Transmission Electron Microscopy images visualizing the formulation confirm the PCS results of a monomodal and homogenous size distribution with an average hydrodynamic diameter below 100 nm.

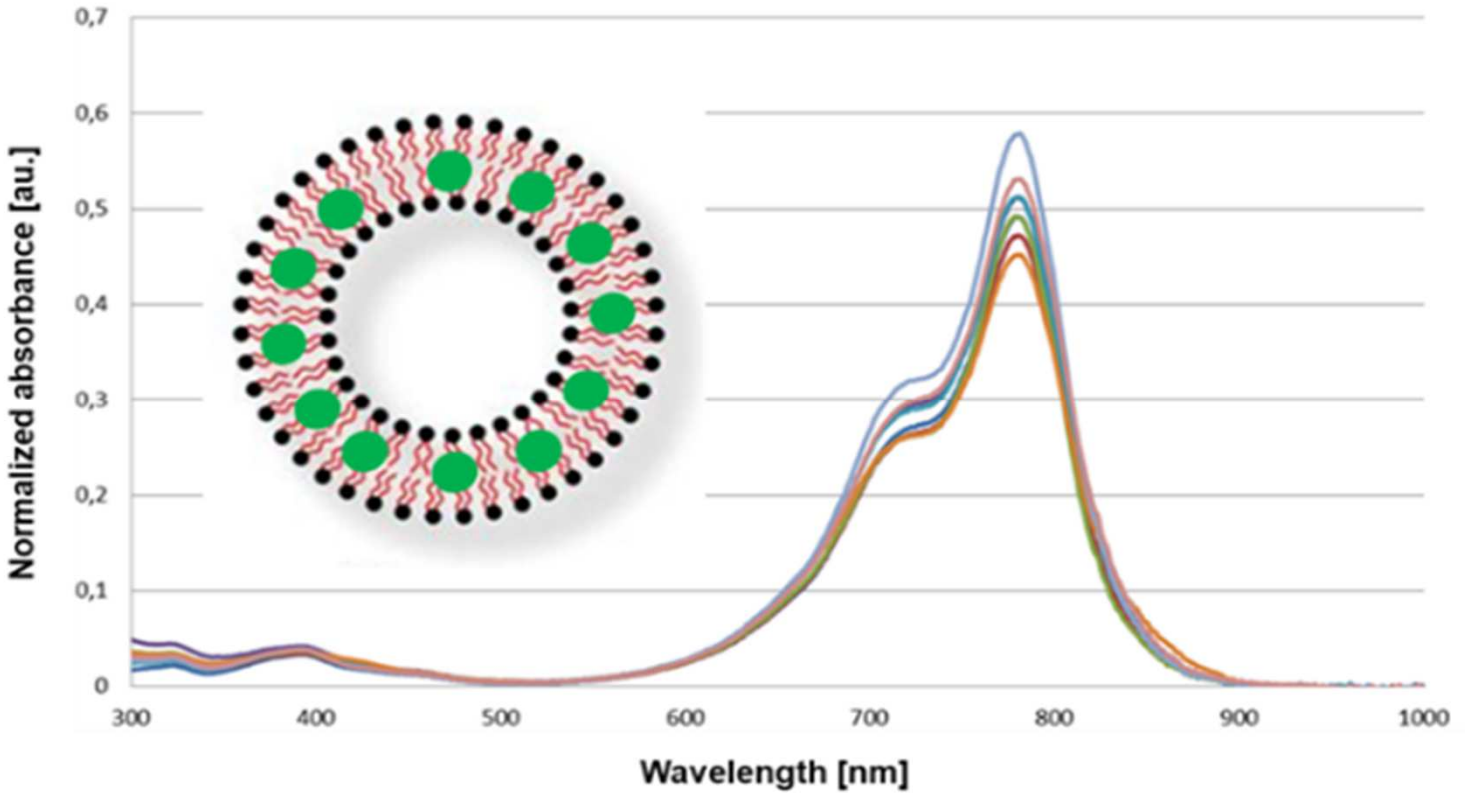




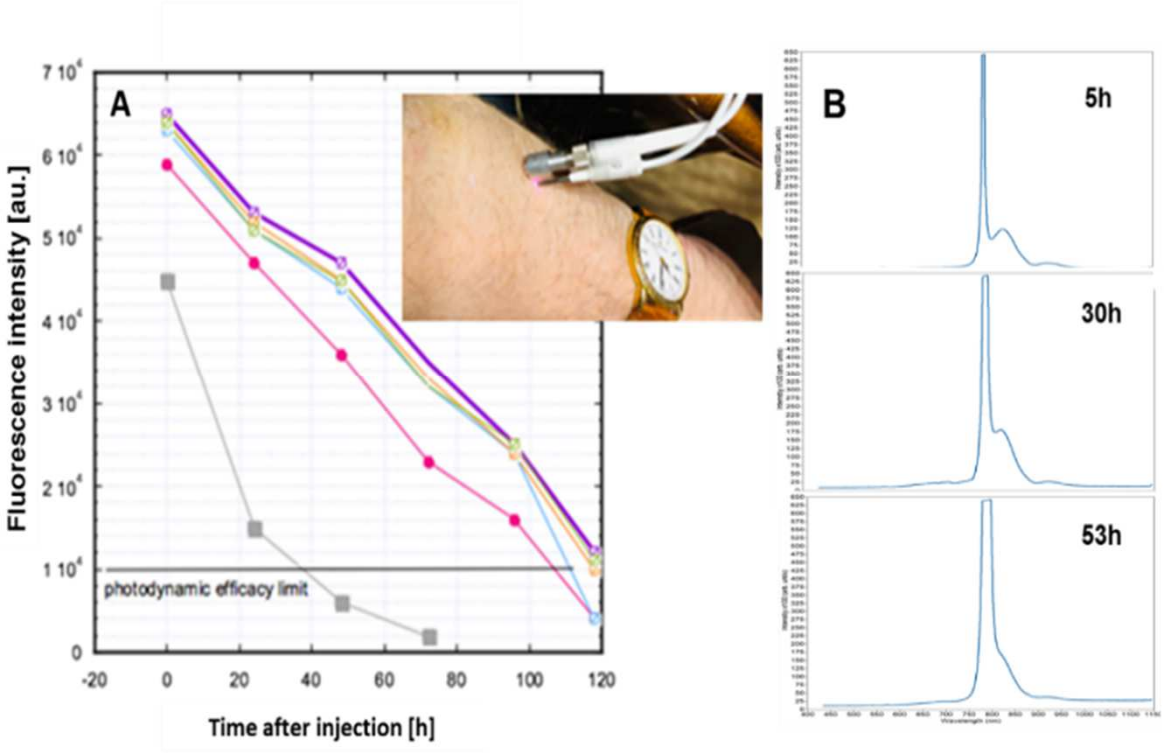


Measurement with atomic force microscopy.

The new Nano ICG Photosensitizer

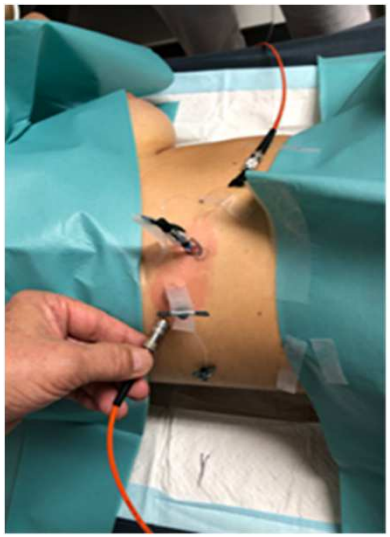


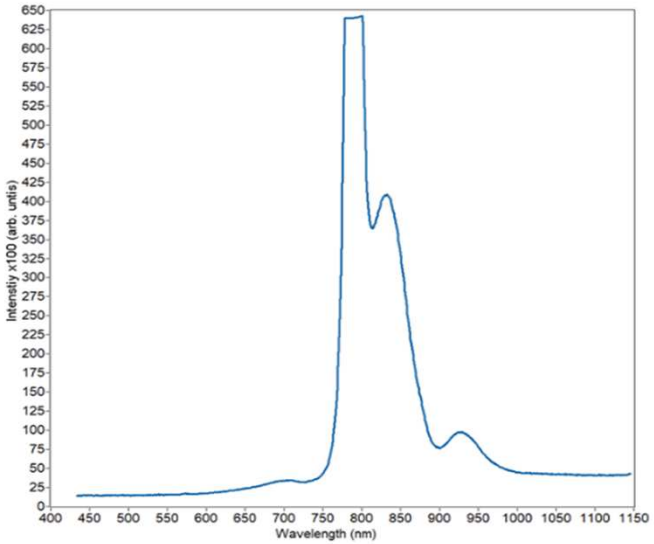
The new Nano ICG Photosensitizer



The baseline stability of Nano-ICG in normal muscle tissue is about 5 days. This is much longer than any other known formulation. The stability of Nano-ICG in tumorous tissue depends on the tumor type and tumor size; however latest measurements indicate it will be at least 3-4 days.

The new Nano ICG Photosensitizer





Accumulation in tumors: First measurements

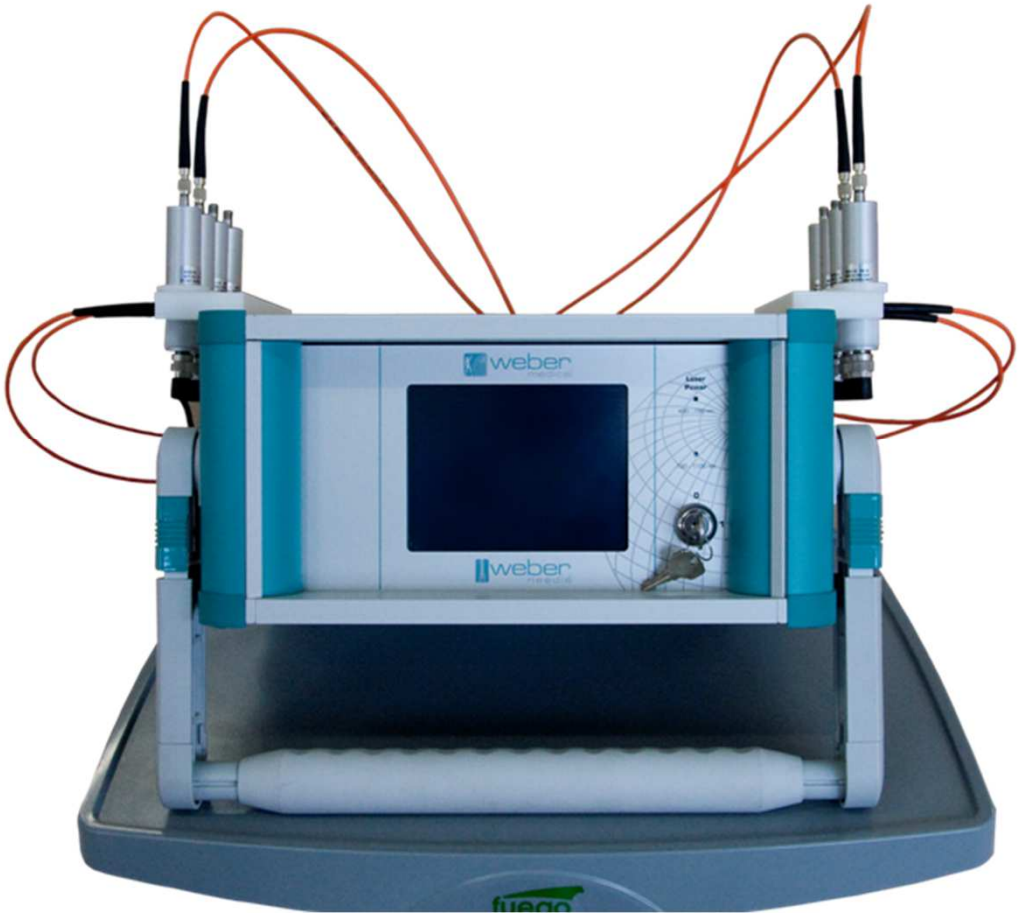
Recent measurements now even confirm significant endogenous accumulation of Nano-ICG in liver carcinoma 3 days after infusion (interstitial measurement by infrared spectroscopy directly inside the liver). Thus, liver carcinoma and liver metastasis may effectively be treated (after infusion of 150 mg Nano-ICG) by local PDT using interstitial and external infrared irradiation.

Applications of PDT with new Nano ICG

- Besides local injection of Nano-ICG into the tumor it is now finally possible **to achieve accumulation in the tumor by intravenous infusion of Nano-ICG**
- After infusion and/or local injection the tumor is then irradiated by infrared laser light
- Irradiation of superficial tumors on or below the skin can be performed externally without penetration of the skin by using infrared laser sources with high power density
- Deeper tumors or metastases should be treated by interstitial laser technology
- Treatment of bladder, prostate or rectal cancers is done with special fiber optic catheters
- As infrared lasers are known to achieve good bone penetration this could also be a new treatment option for brain tumors and bone metastases

The Technology: Weberneedle® Endolaser with high power infrared lasers for interstitial PDT

HIGH QUALITY
MADE IN GERMANY



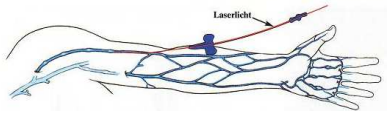
International Medical Approvals:

- CE Approval (Europe)
- Health Canada
- US-FDA for External Laser Therapy (PDT = off-label use)
- TGA Australia for External Laser Therapy
- Taiwan-FDA

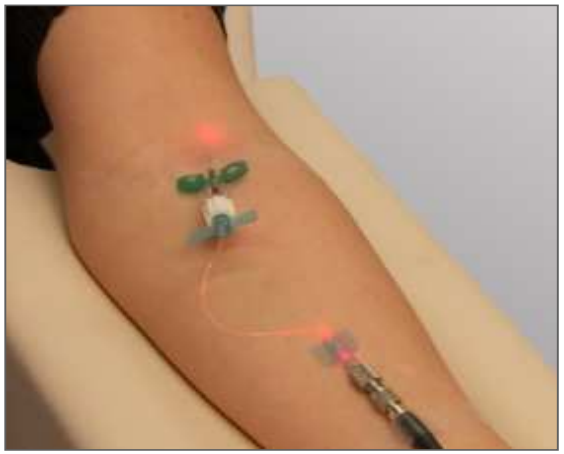
Development with Support of German Government and European Union

Health Canada Santé Canada FDA TGA Health Safety Regulation FDA 食品藥物管理署 Food and Drug Administration

Application of Intravenous Photodynamic Therapy:

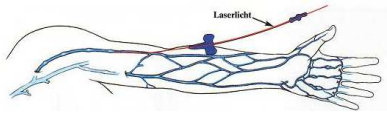


Demonstration video: https://www.youtube.com/watch?v=Ika1GkefjSU&feature=youtu.be

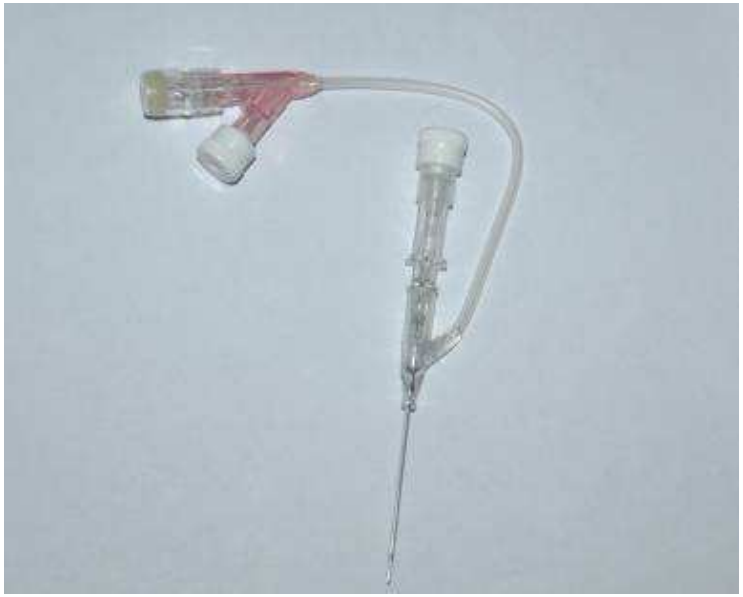


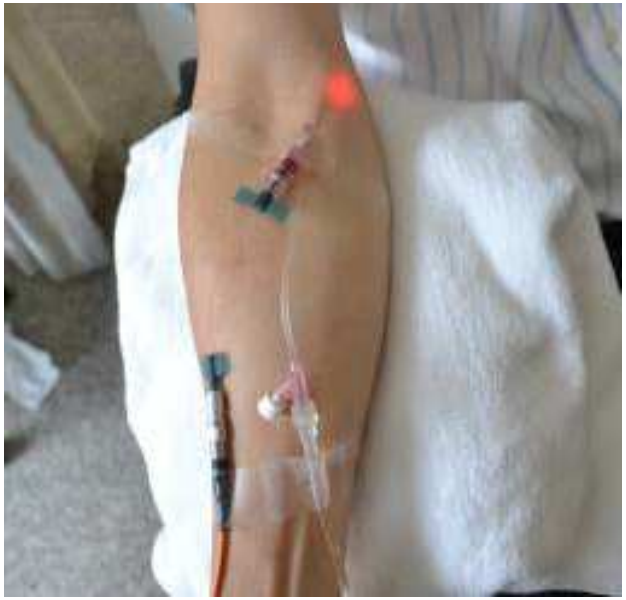
For application of intravenous lasers the physician can chose between a standardized 22G canula (blue) or our specific weberneedle® butterfly.
After placing the canula (or butterfly) into the vein the so-called laser catheter (sterile weberneedle® lasercath) is inserted into the canula.
The laser is then connected to the lasercath guiding the light directly into the flowing blood.
No saline or other fluid is needed.

Application of Intravenous Photodynamic Therapy:



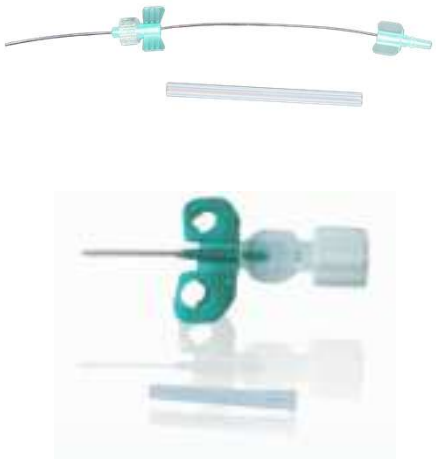
New Development: Y-Canula (3-way canula) for infusion and intravenous laser application

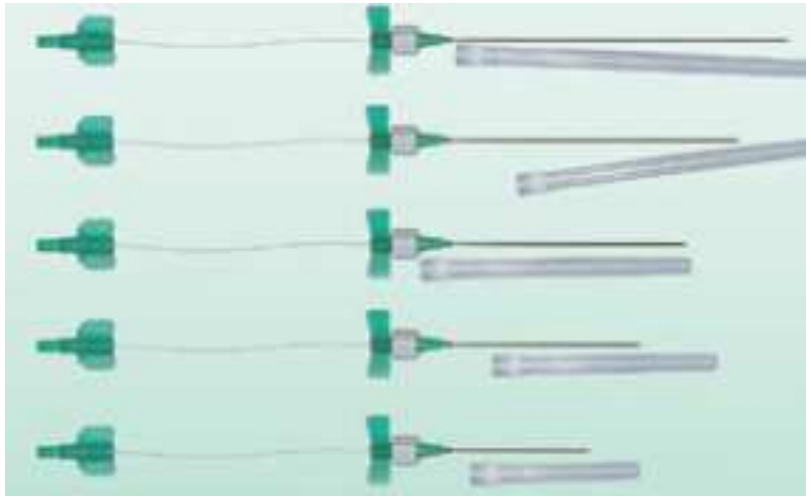




Application of interstitial Photodynamic Therapy:

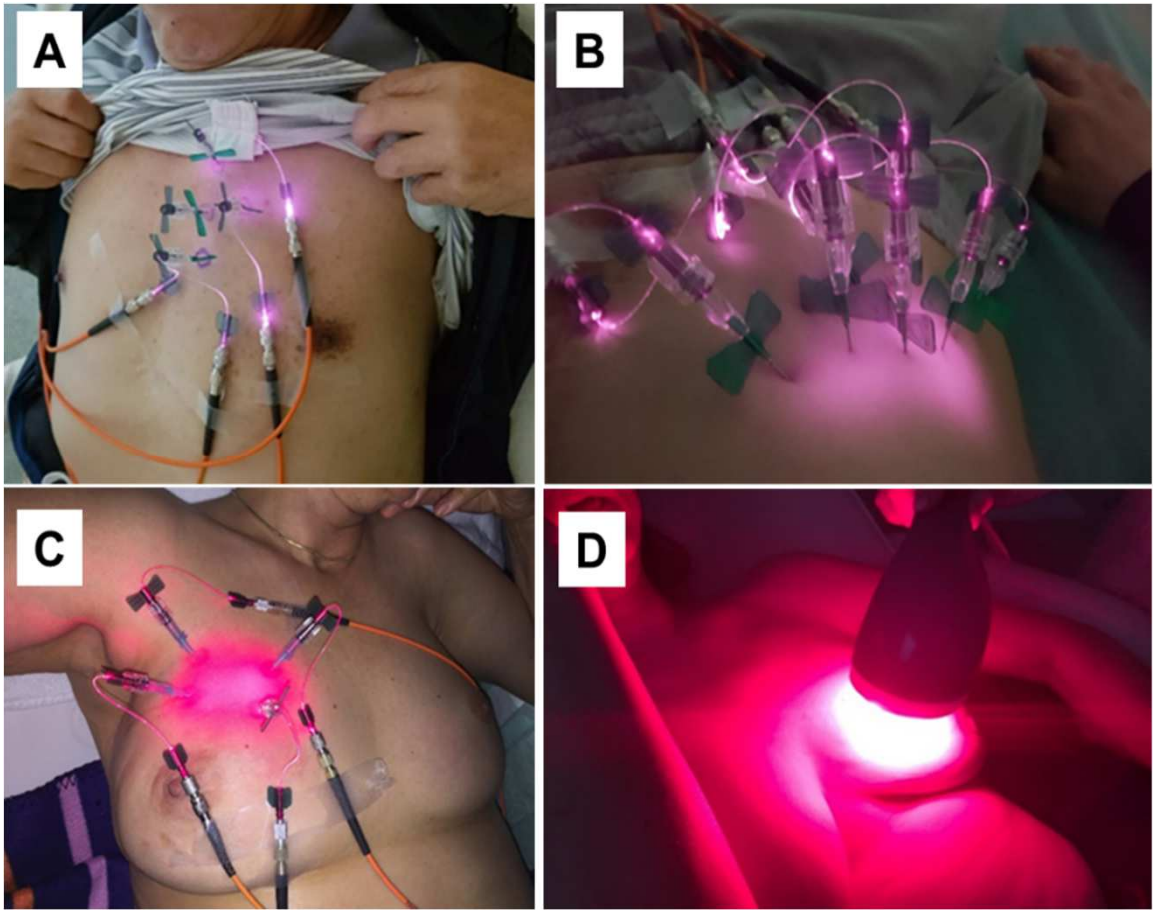
Demonstration Video:
https://www.youtube.com/watch?v=dIBoH-EoRGE&list=PLwmaC9-LsMKDP89IjVZghqcmjpkIEfwau&index=11





After placing the the needle in or close to the tumor the fiberoptic light guide is inserted into the needle.
The laser is then connected to the light guide. It directly targets the tumor without losing any energy in the skin barrier.

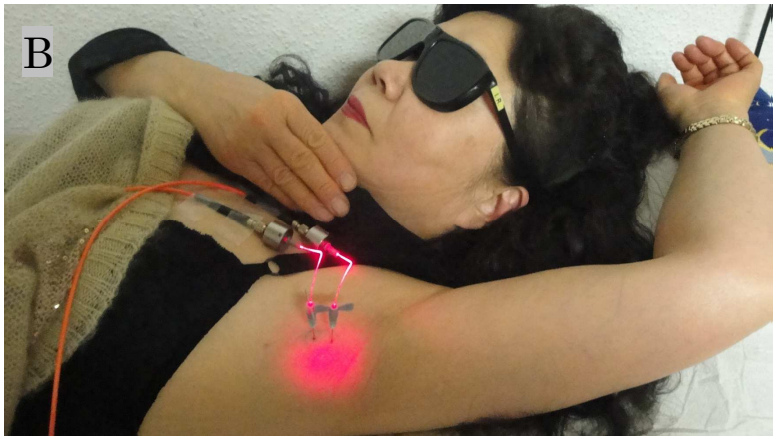
Applications of PDT with new Nano ICG

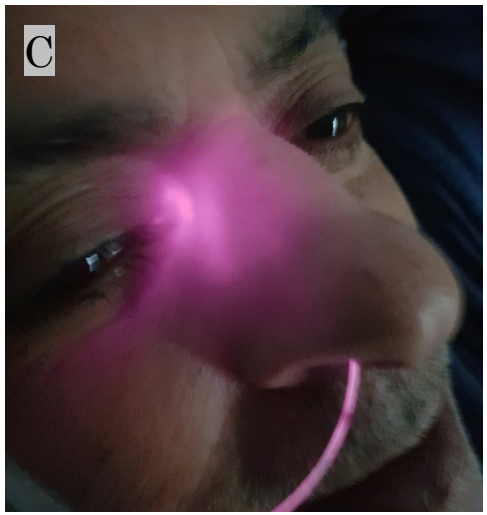


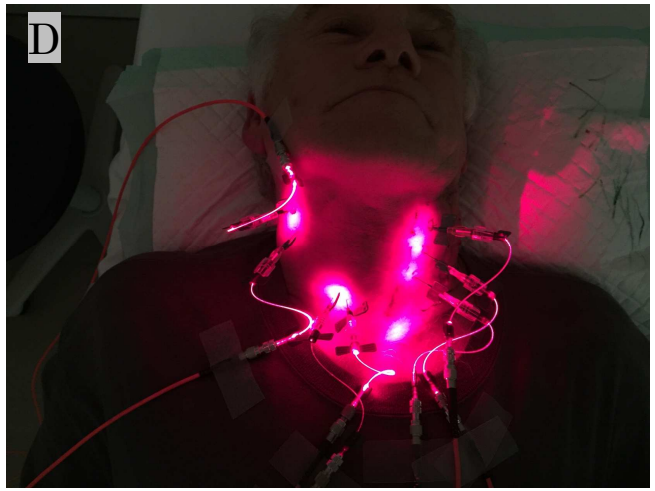
Interstitial PDT treatment with several infrared lasers (A, B)

PDT of breast cancer patient with interstitial and external laser irradiation (C, D)

Applications of PDT with new Nano ICG







Application of PDT in

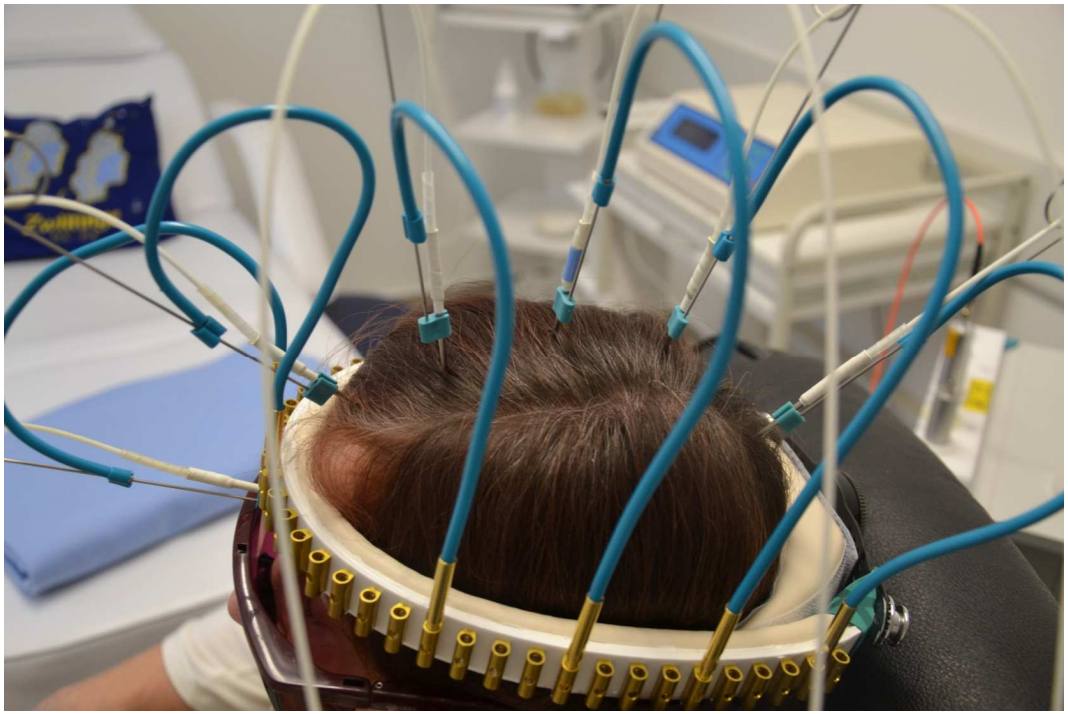
A) Tongue cancer

B) Lymph metastases

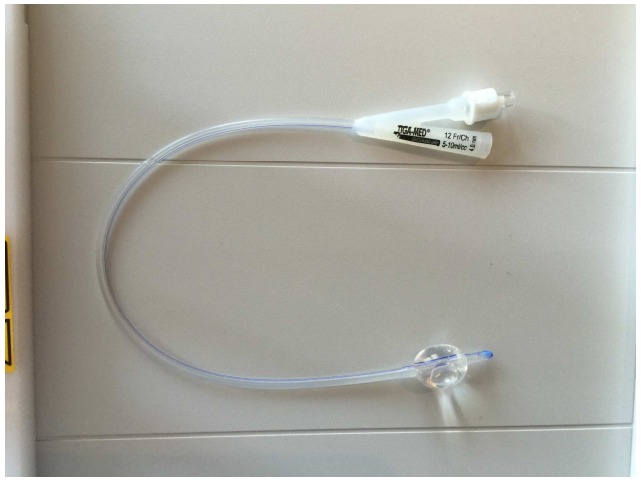
C) Nasopharyngeal Cancer

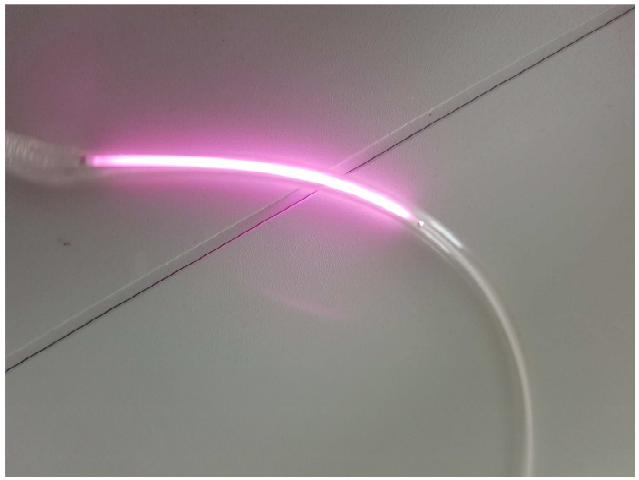
D) Thyroid Cancer

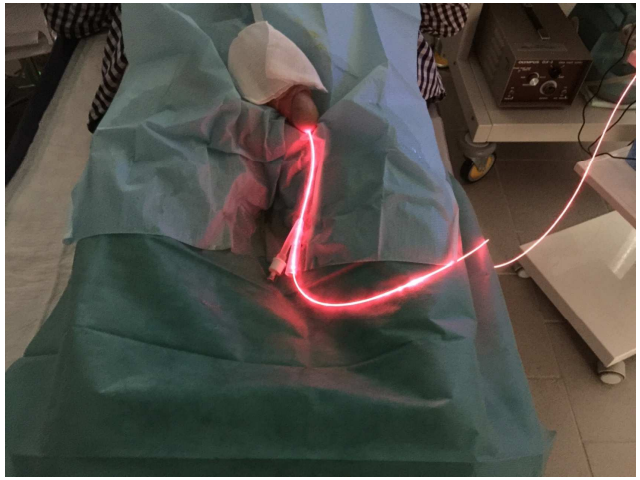
Applications of PDT in Brain Tumors



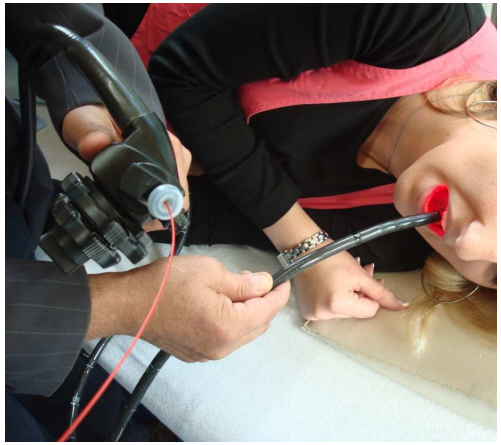
Applications of PDT in Urology

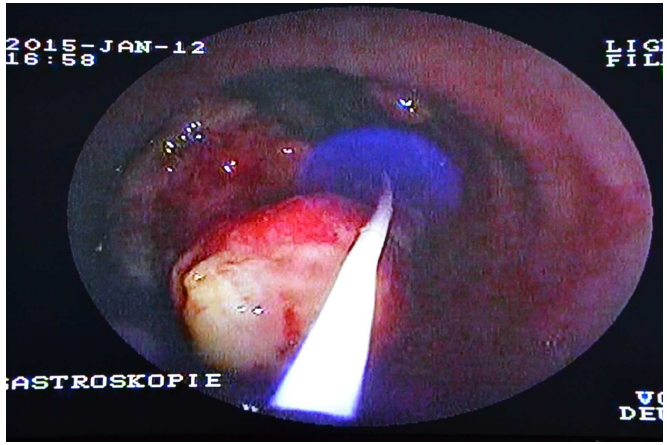






Applications of PDT in Gastroenterology





Protocol for PDT with Nano ICG:

Dosage Information and Protocols:

Dosage/vial: 150mg/10ml

Application and 7-day treatment protocol:

Day 1: Dissolve 50 % of the vial (75 mg) in 500 ml glucose 5 % and infuse within 60 min.

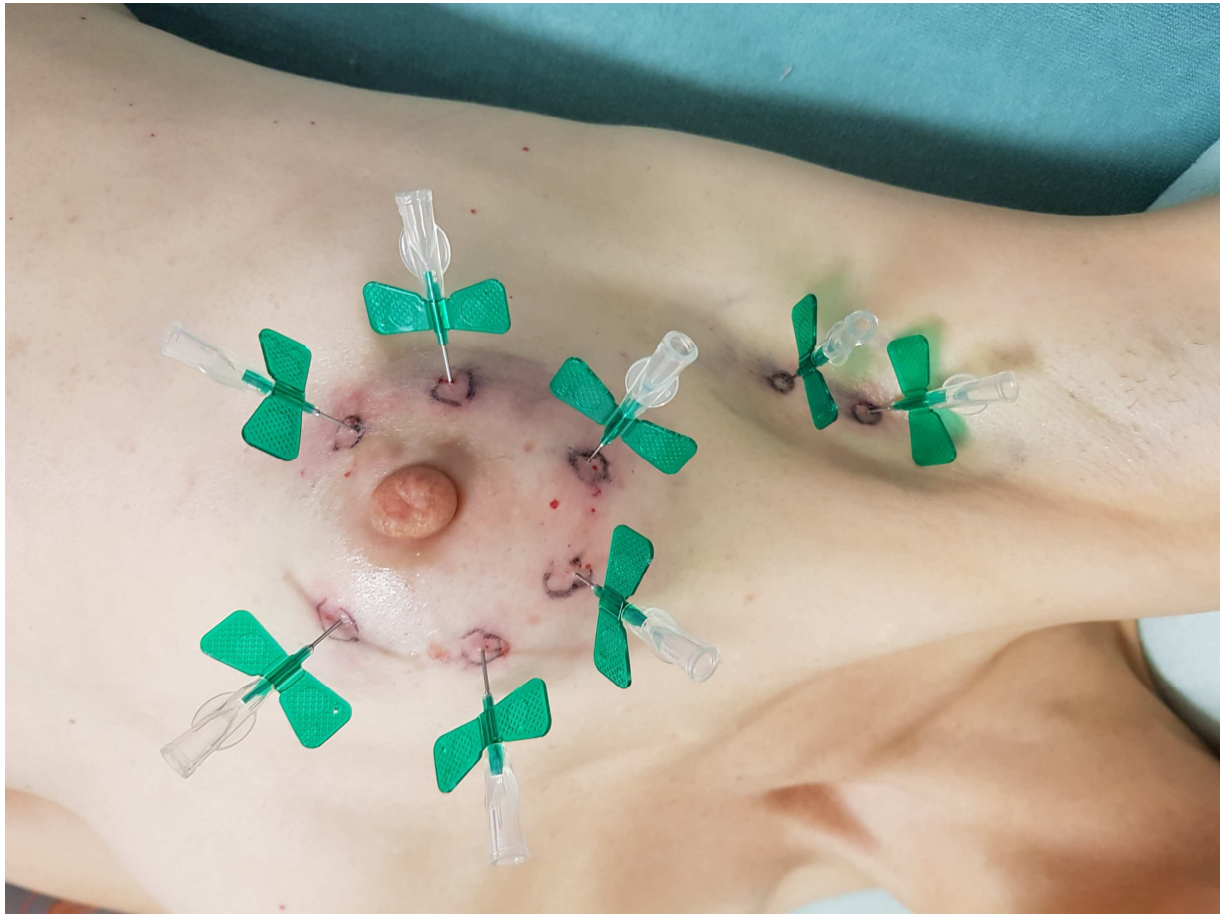
Day 2: Repeat. If possible, do local injections into tumor*.

Day 2-7: Daily intravenous laser therapy** with red (50 mW), green (25 mW), blue (75 mW) and yellow (50 mW) laser as well as local irradiation of the tumor by interstitial and/or external infrared laser.

*If local injections of Nano-ICG into tumors are possible (i.e. breast cancer), injection of up to 30 mg (dissolved in 100 ml glucose 5 %) directly into the tumor followed by interstitial laser treatment is recommended. The remaining 120 mg (60 mg on day 1 and 60 mg on day 2) should still be given intravenously to generate high plasma concentration and long-lasting tumor accumulation.

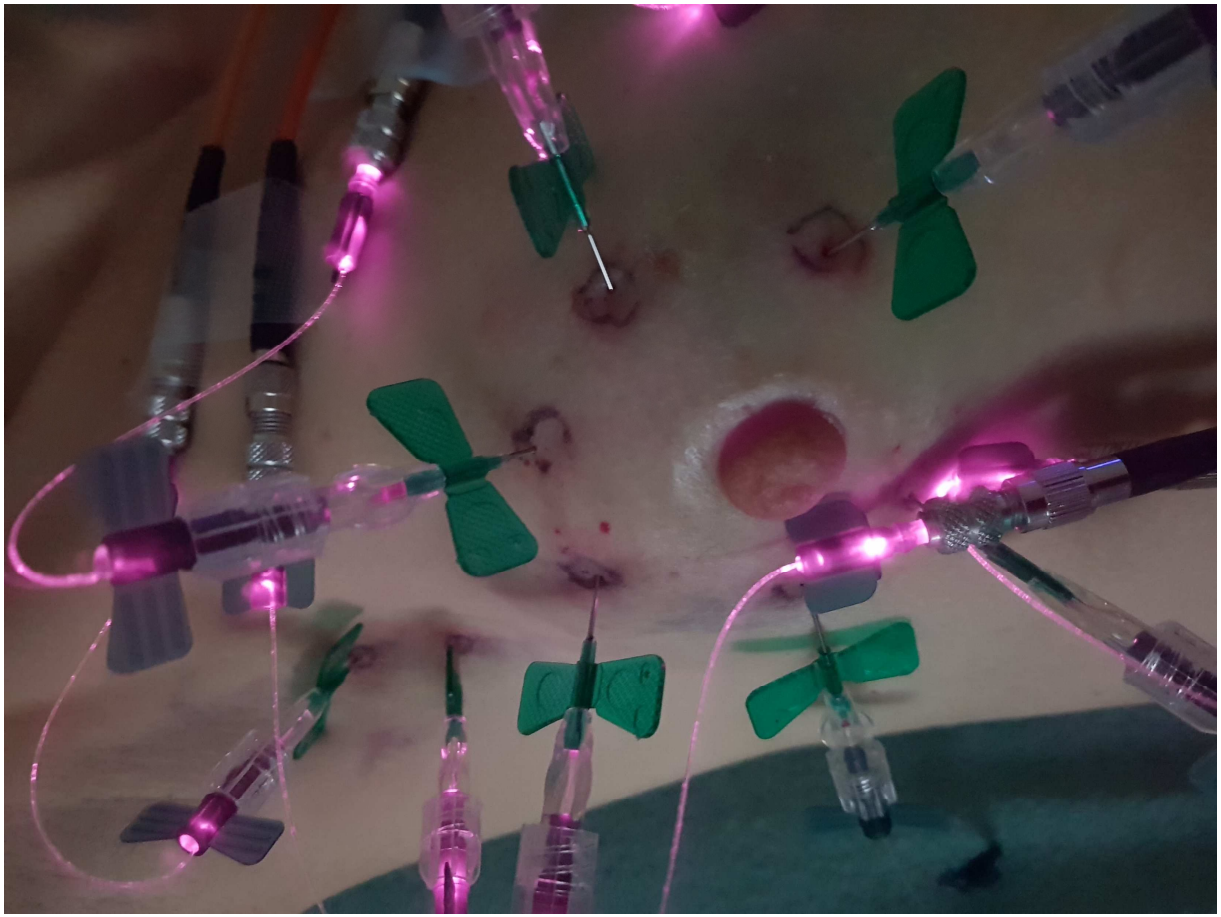
** Add infrared to intravenous laser protocol on day 3.

First clinical results: Breast Cancer



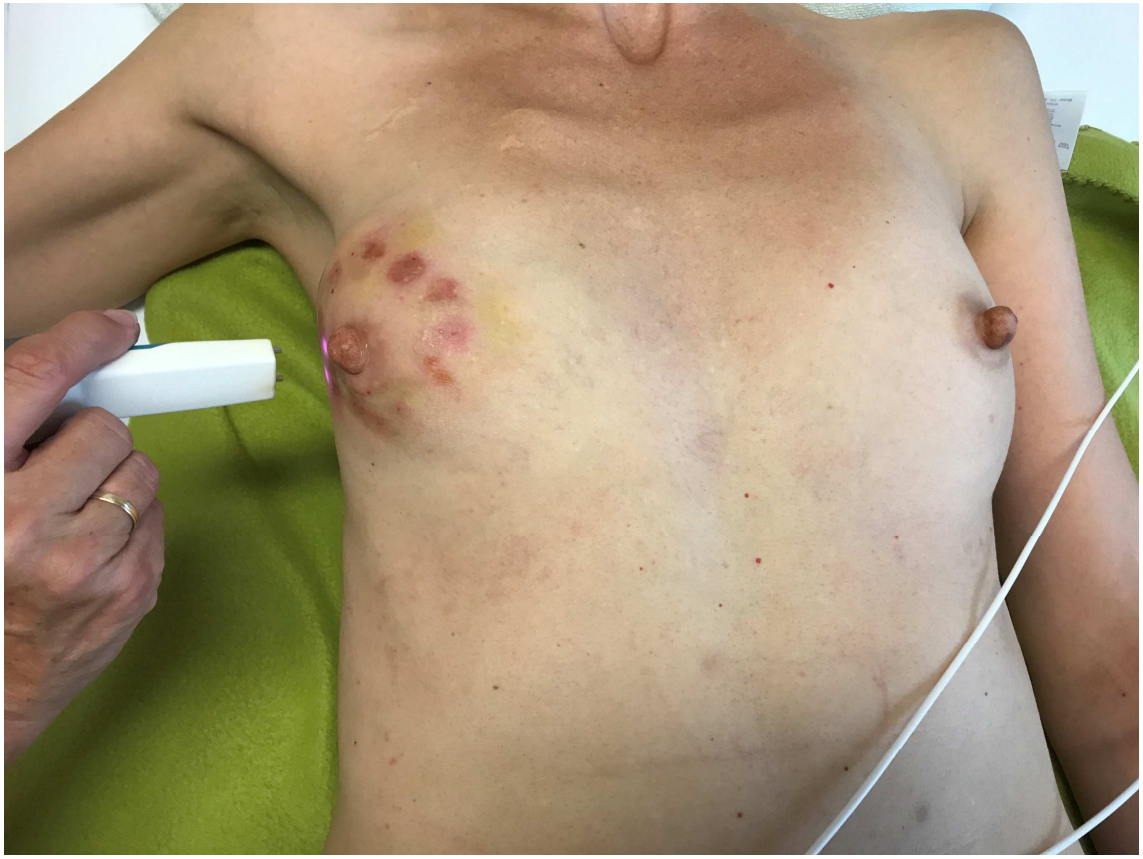
6 cm right breast with lymph metastasis

First clinical results: Breast Cancer



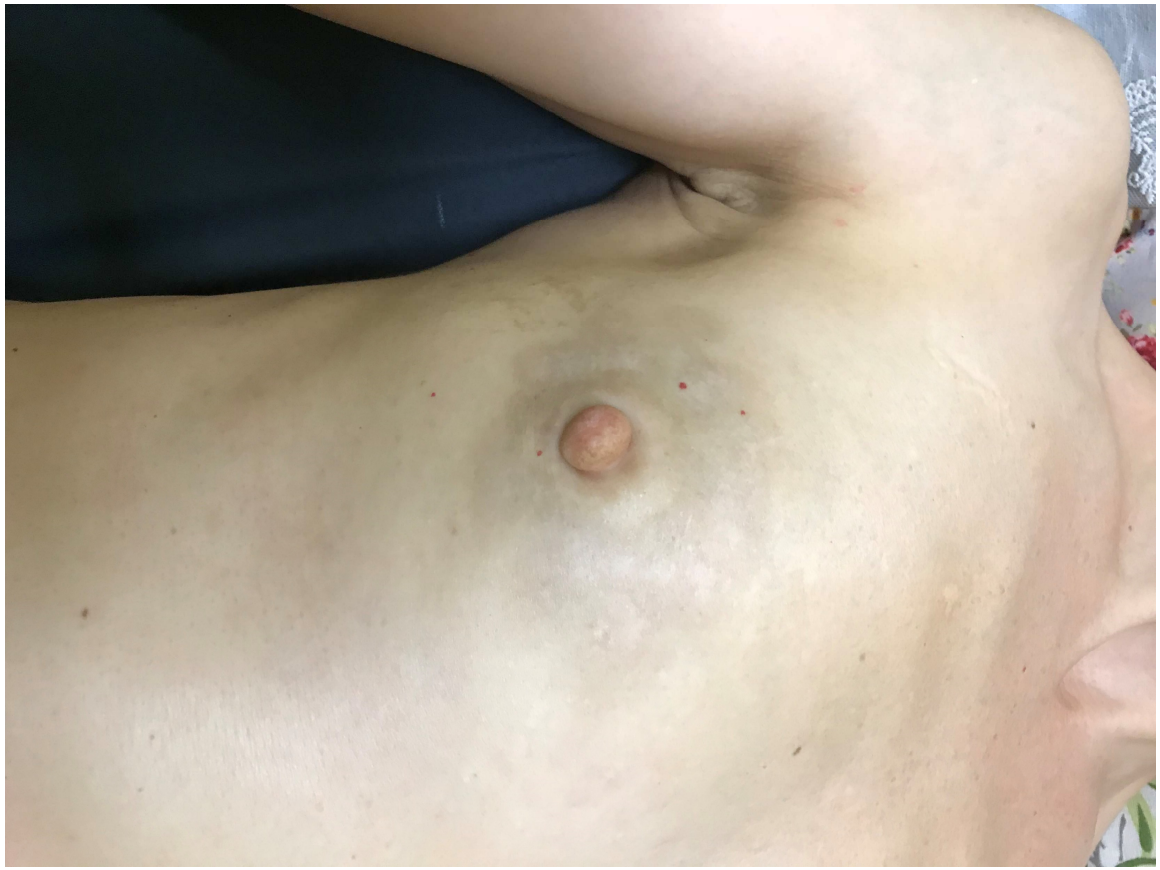
Interstitial laser therapy after injection of diluted Nano ICG, 3 ml each needle)

First clinical results: Breast Cancer



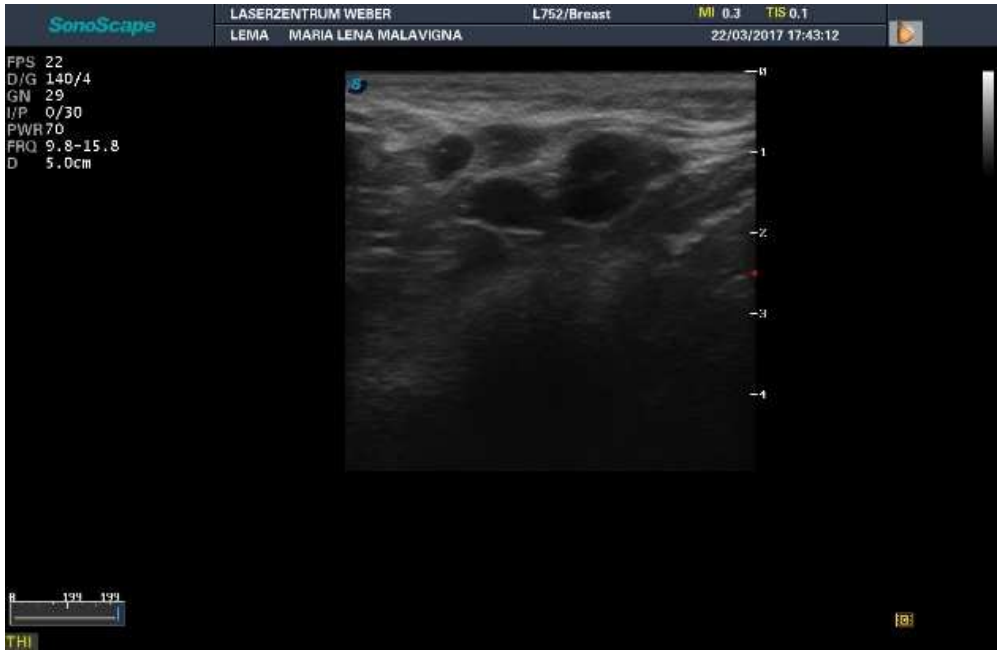
Additional topical infrared irradiation and sonodynamic therapy

First clinical results: Breast Cancer



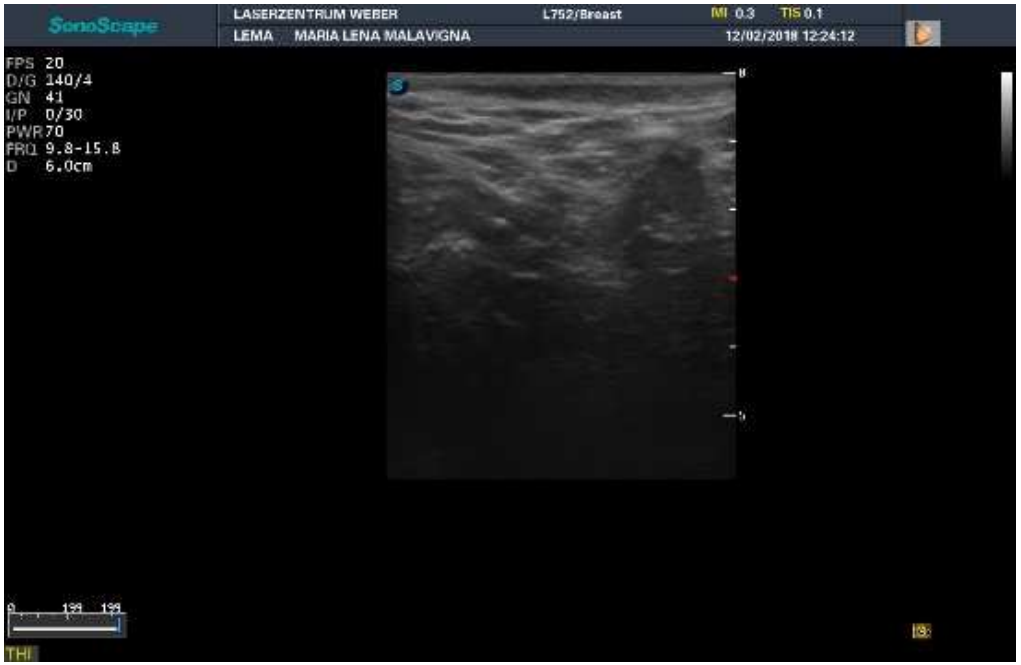
Result: Complete healing after 4 courses (every 3 months)

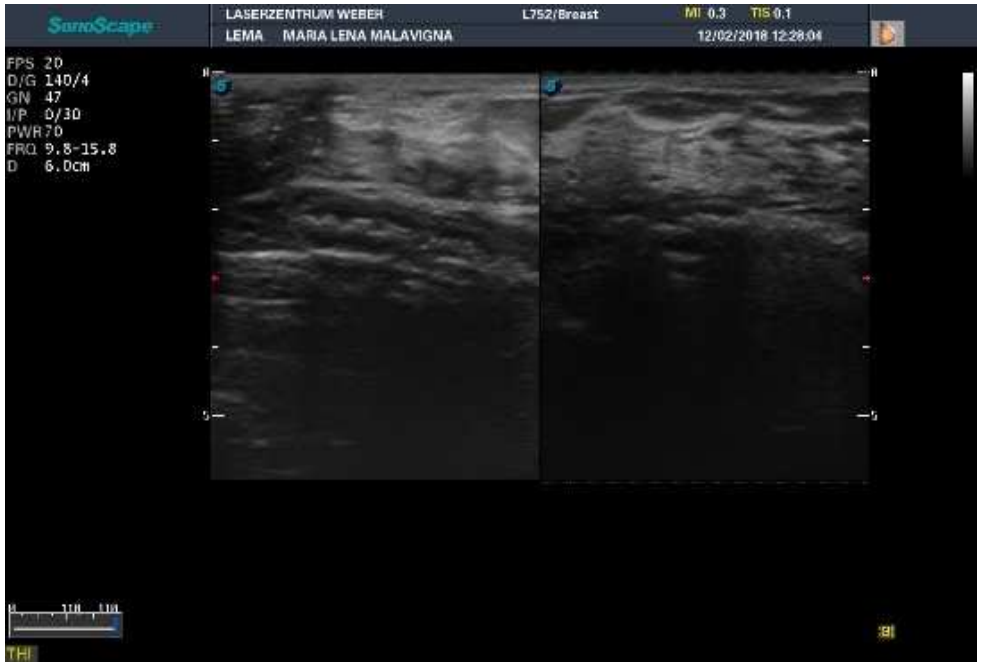
First clinical results: Breast Cancer



Ultrasound before therapy

First clinical results: Breast Cancer

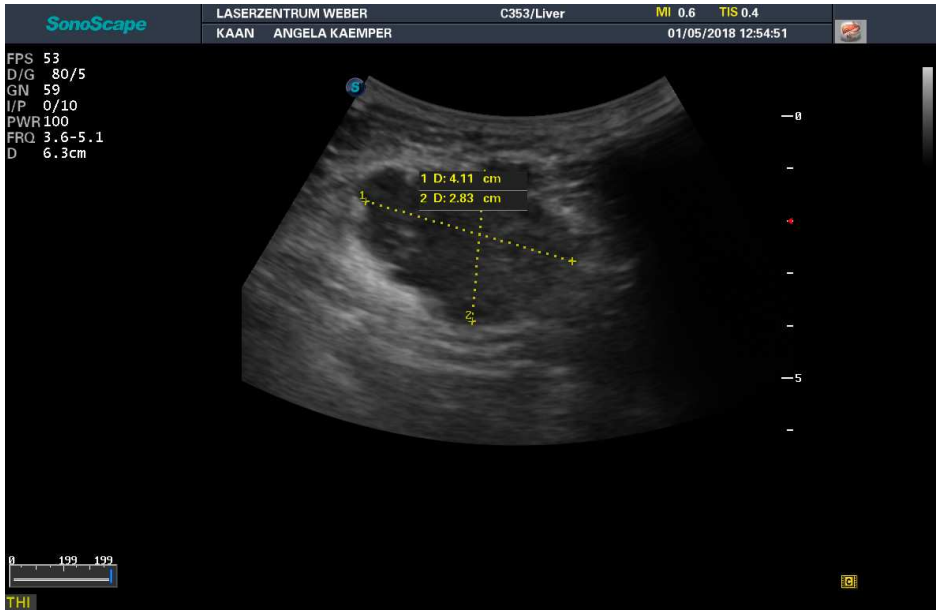




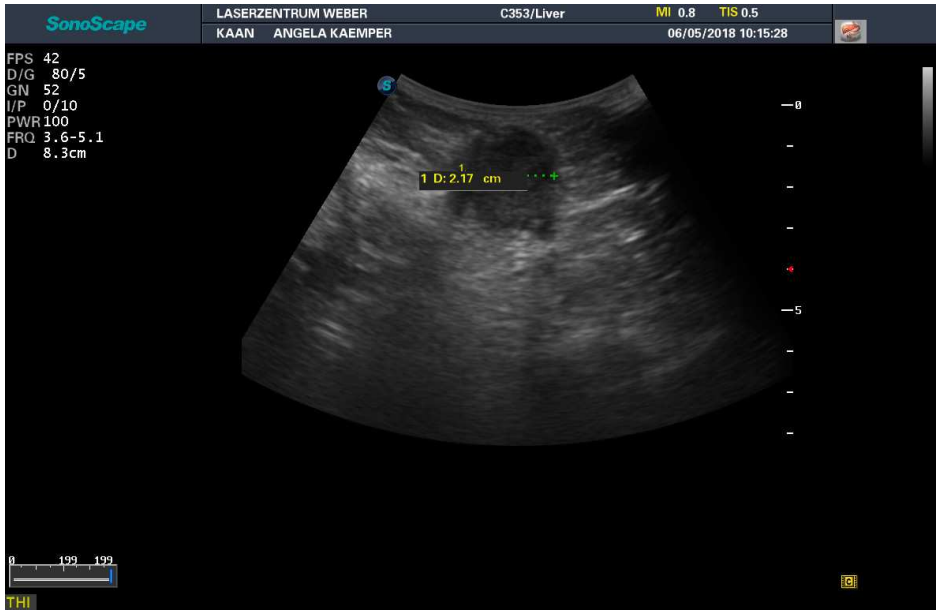
Ultrasound after 4 treatment cycles

First clinical results: Breast Cancer

Case report: Breast cancer left side, diagnosis 11/2017
Photodynamic Therapy in May 2018



30.4.2018



6.5.2018

First clinical results: Breast Cancer

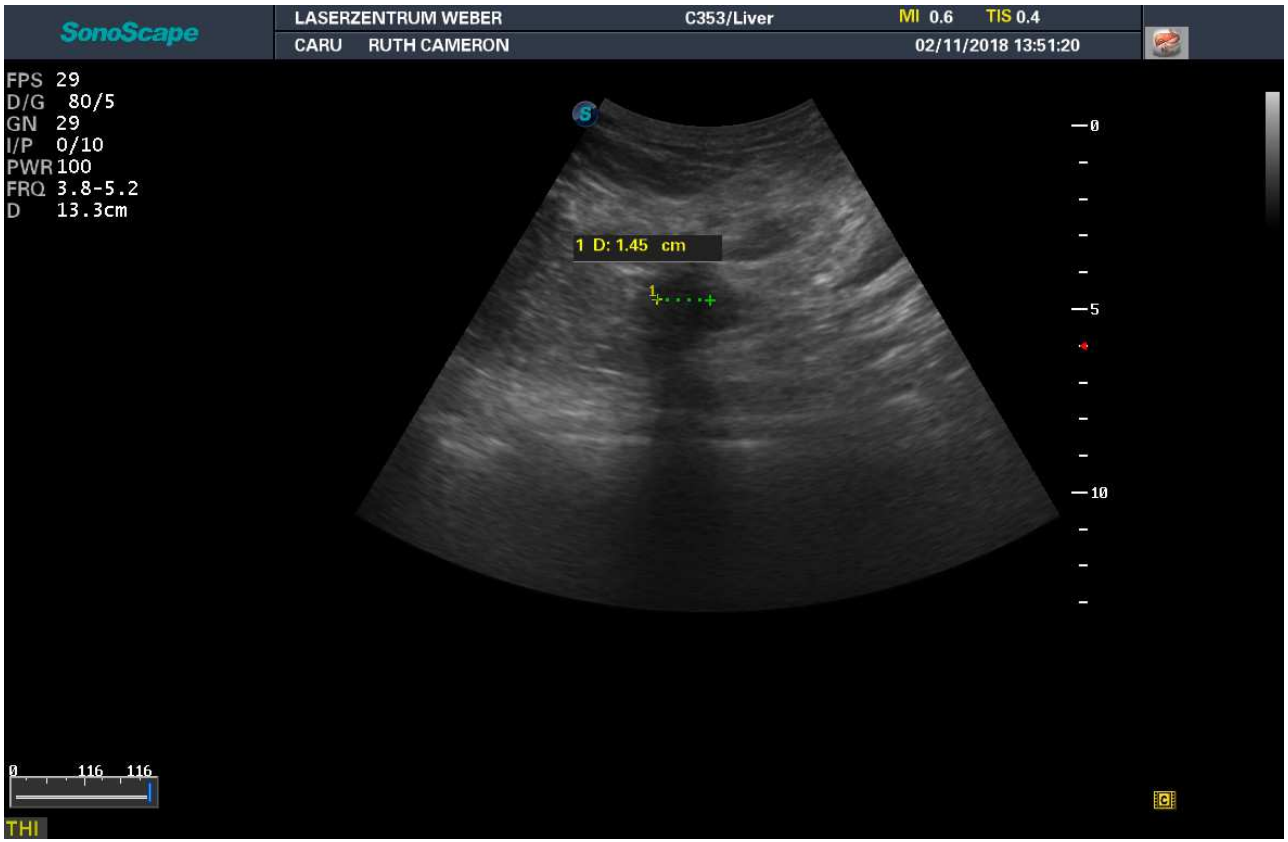
Patient: 71 years, USA

FINDINGS:
There are scattered fibroglandular elements in both breasts that could obscure a lesion on mammography.
Images were obtained using Hologic Selenia Dimensions full field digital mammography with tomosynthesis (3D).
Current study was also evaluated with a Computer Aided Detection (CAD) system.
The patient reports a history of right breast outer hemisphere pain, both upper outer and lower outer quadrantst.
Mammography demonstrates evidence of a spiculate mass/focal architectural distortion in the right upper outer quadrant. The margins are indistinct but the area appears to measure 3.5 cm in long axis. No associated suspicious appearing calcifications are identified.
There are separate bilateral benign appearing calcifications.
No additional masses are identified.

First clinical results: Breast Cancer

First ultrasound 29.10.2018

First clinical results: Breast Cancer



Third ultrasound 06.11.2018
(after first treatment week)

First clinical results: Breast Cancer

2nd treatment course: 2.2.2019

Result of PET scan from 3.4.2019:

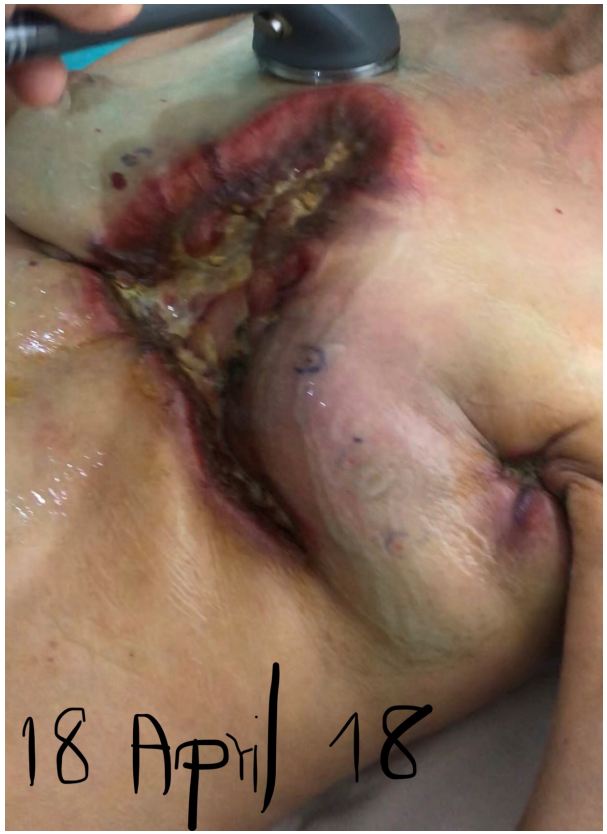
IMPRESSION:

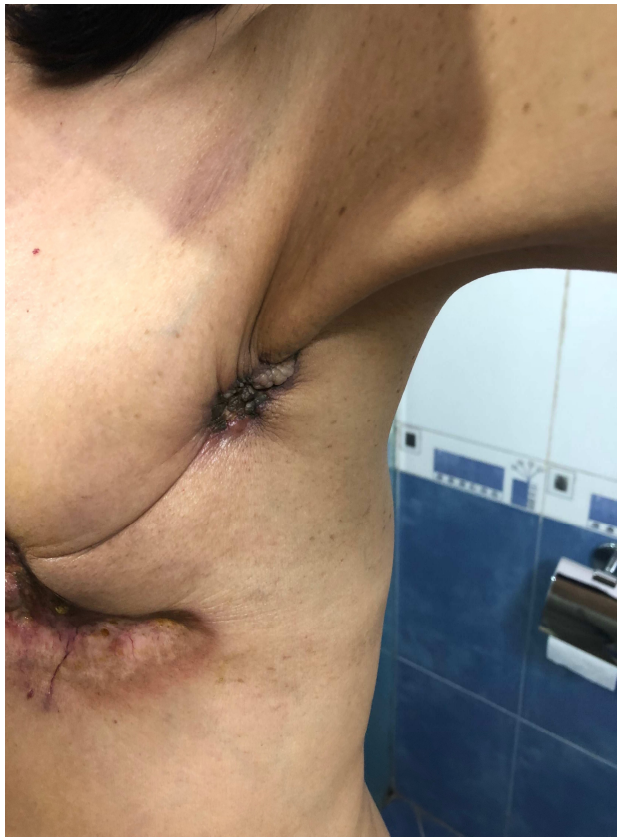
1. Discrete focus of hypermetabolic activity in the region of the sigmoid colon without a discrete underlying CT abnormality. Although this finding may represent physiologic activity, this finding is concerning for an underlying colonic malignancy. Correlation with endoscopic evaluation is recommended.
2. With regards to patient's known right breast cancer, no evidence of hypermetabolic right breast mass or hypermetabolic metastatic disease.

Reviewed and Interpreted by: Navid Moradshahi 3/4/2019 2:40 PM

First clinical results: Breast Cancer

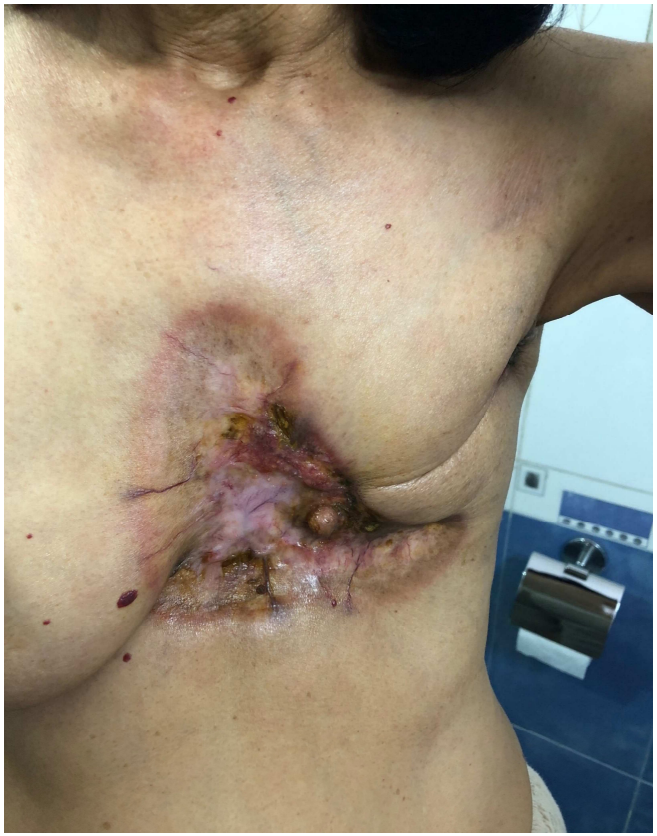
Breast cancer patient with ulceration and 4 treatment cycles (last one with Nano-ICG):

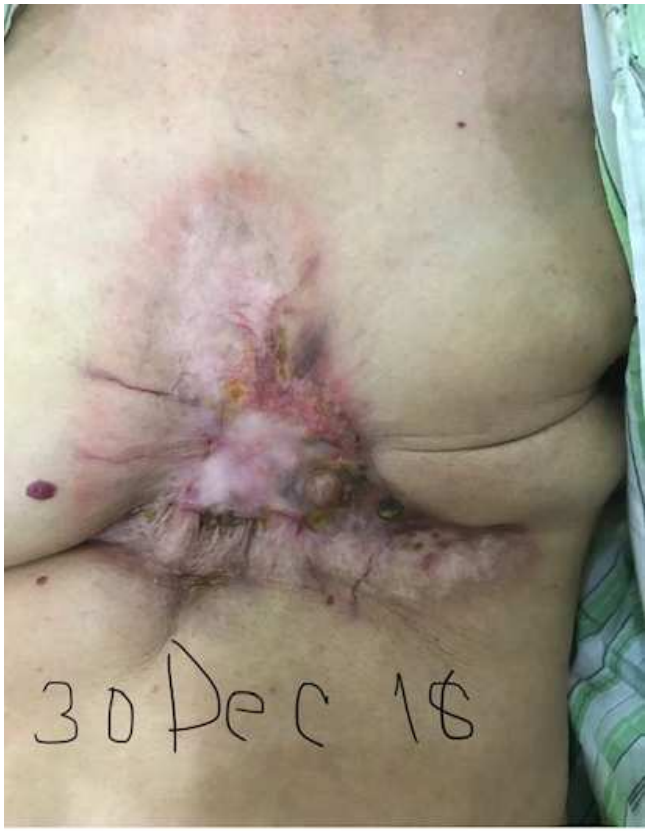




First clinical results: Breast Cancer

Breast cancer patient with ulceration and 4 treatment cycles (last one with Nano-ICG):





First clinical results:

Testimonial (USA):

“We’ve had some exciting results so far:

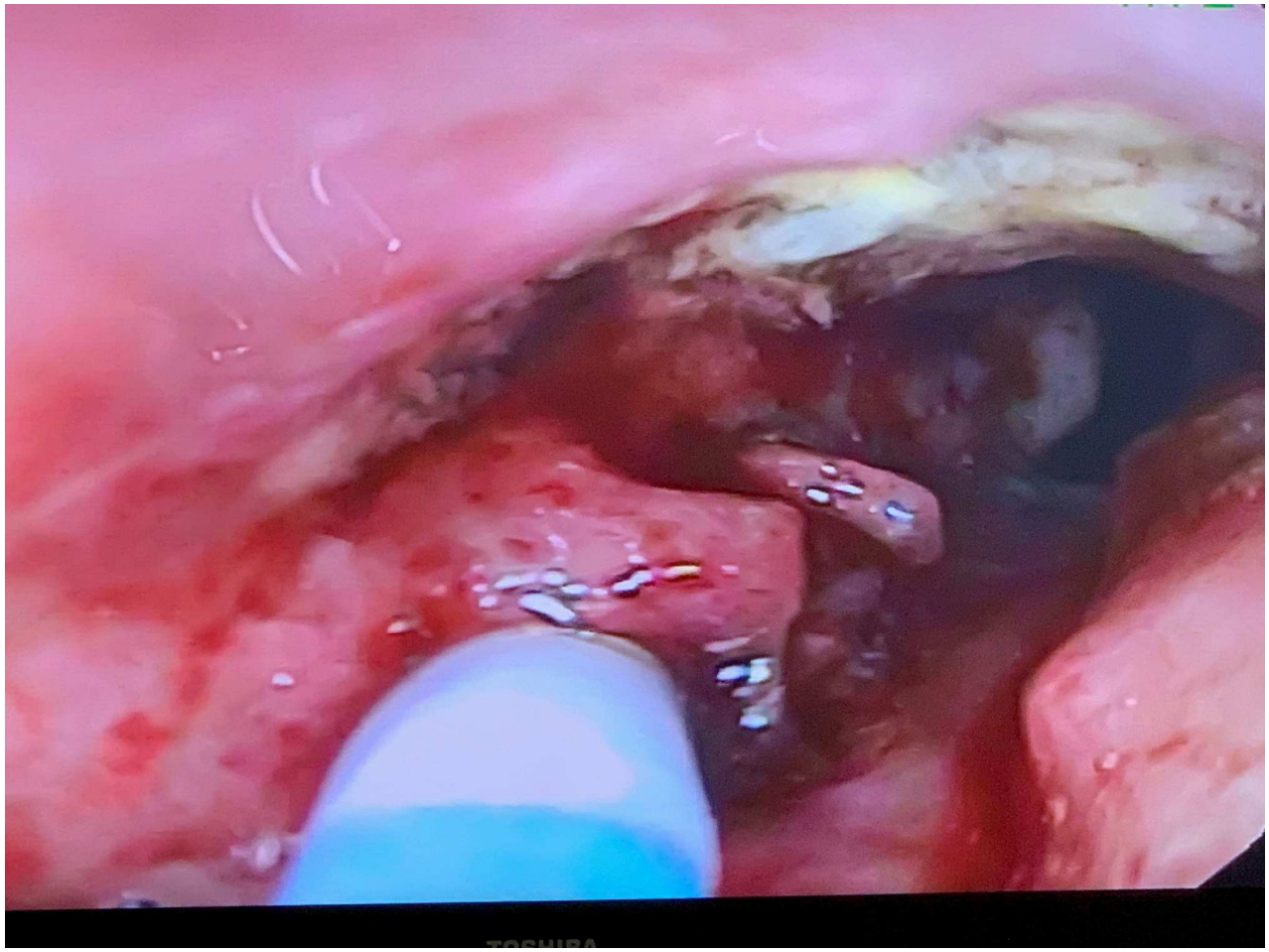
One patient with multiple brain tumors along with metastases through liver, bones had a complete disappearance of all the tumors in her brain other than one that had shrunk substantially and all the cancer markers had greatly reduced indicating that the other tumors were dying off.

Also had a patient with tumors all over her lungs and that completely disappeared.

We’ve seen some great reductions in breast cancers as well where in one of the patients the large tumor completely disappeared.“

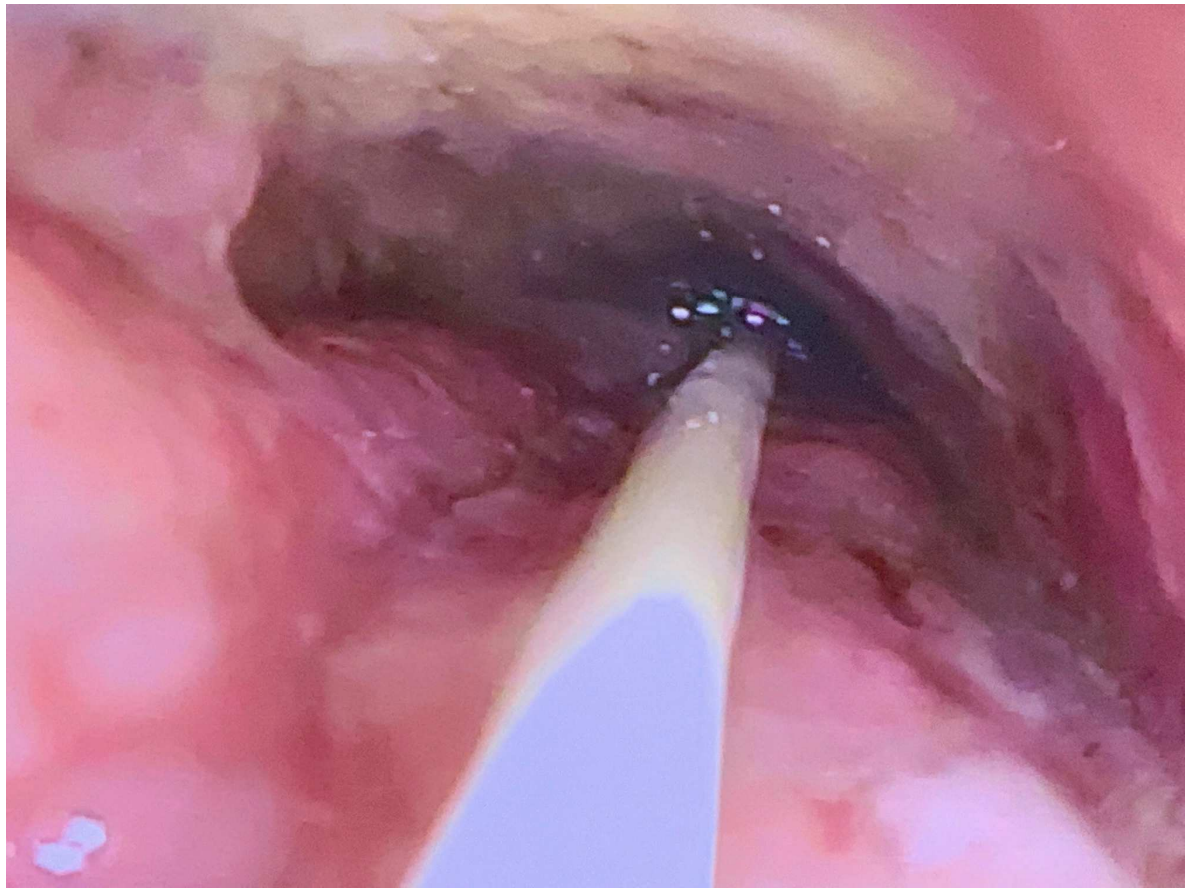
First clinical results: Oesophageal Cancer

Day 1:



First clinical results: Oesophageal Cancer

Day 6:



First clinical results: Squamous Cell Carcinoma

Diagnosis: Base of Tongue squamous cell carcinoma, HPV positive with bi-lateral nodal involvement

"I was very unwell for the first 10 days on my return to the UK. I have no doubt this was a Herxheimer effect of so much dead cancer in my body. My urine was copper coloured for days but gradually cleared. I endured a terrible cough and couldn't sleep for several nights unless fully propped up in bed. I kept bringing up huge amounts of very brown coloured mucus that had a terrible smell. On 3 occasions large lumps of tumour came into my throat and I've attached photos with dates. The long tube (with my wife's finger in the photo for scale) was quite solid and about 6cm long!"

First clinical results: Squamous Cell Carcinoma

"It is now 3 weeks since we were with you and **I no longer have any mucus, am hardly coughing and feel as if there's a lot of space in my throat.** In some ways I feel that everything needs to settle down in me and I'm supporting my health with my diet embracing the Budwig protocol. I have read extensively on her scientific discoveries and approach to cancer. Nevertheless I am so pleased with what's happened to me with your care."

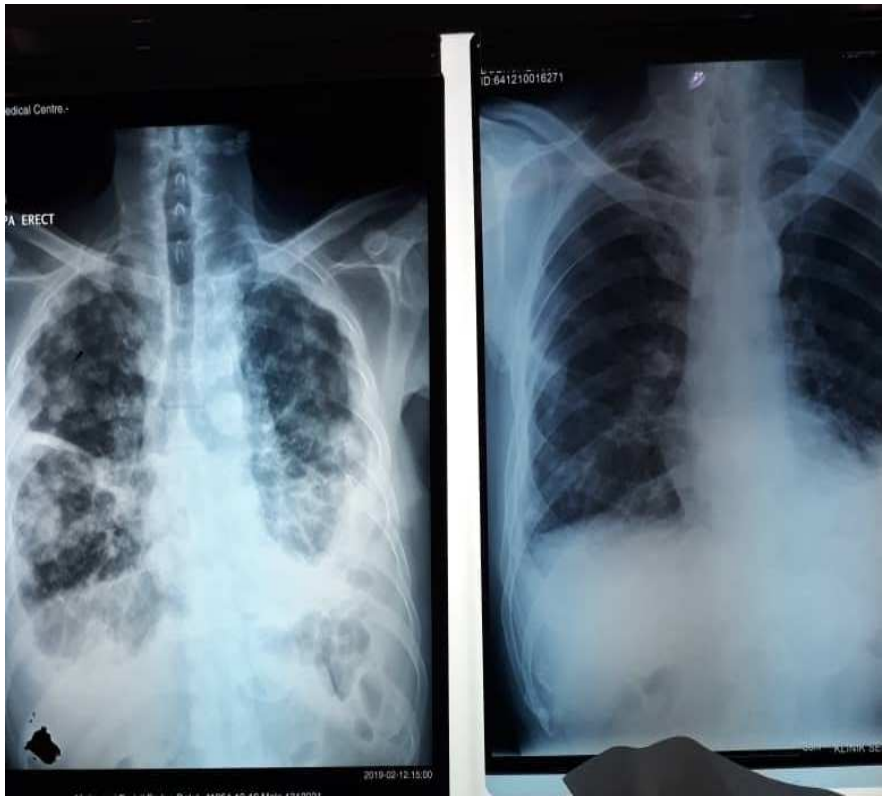
First clinical results: Lung Cancer

Case report from Malaysia:

“Lung Cancer patient did chemo 3 months before. 3 month later massive recurrent involving whole lung and pleura (stage 4).
Surgeons gave no hope. So we tried new Nano ICG.“

“I‘m reporting from Malaysia […] on the success case of my lung cancer patient (stage 4).
[He is] one month after PDT with Nano ICG now near recovery.“

Chest xray specialist said almost complete cure of lung and pleura.



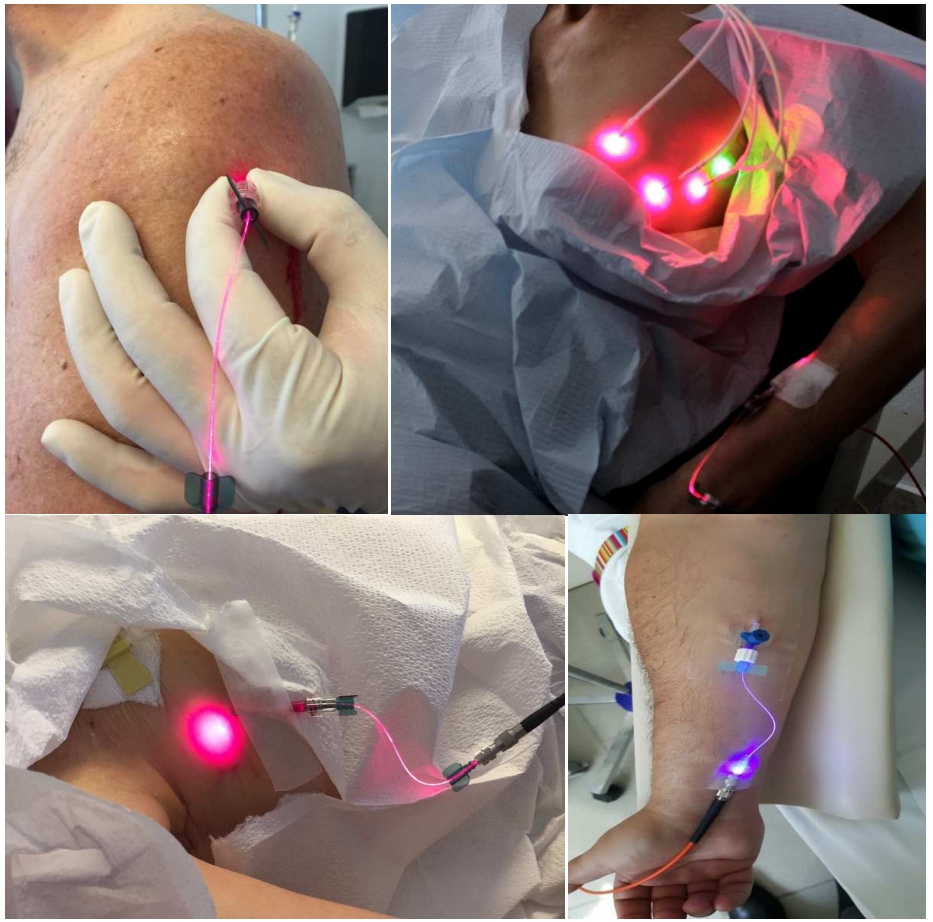
Additional case reports:

BMG - Baja California Mexico (Jennifer Miele):

IMPORTANT INTEGRATION

Laser Therapy and PDT

- Integrating laser therapy and PDT into our clinical practice has shown impressive results. The synergy between therapies has noted increased responses and improvements.
- We continue our research and protocol integration for the results of the individual patient.



Additional case reports:

BMG - Baja California Mexico (Jennifer Miele):

" We have been working with the Nano ICG since late January 2019 with impressive and promising results ranging **from chronic infection, lyme to late stage cancers.** "

64-year old female patient diagnosed with stage four Endometrial cancer. Metastatic disease with peritoneal tumor, liver tumor and right lung taken.

Report from Jan 2019:
Liver tumor 5.2 CM by 5.6 CM
Peritoneal tumor 2.2 CM X 2.8 CM

March 2019:
Liver tumor 2.0 CM X 2.4 CM
Peritoneal tumor 2.7 CM X 0.6 CM

Additional case reports:

BMG - Baja California Mexico (Jennifer Miele):

19-year old Osteosarcoma patient with metastatic disease to liver.

PET CT scan reported SUV uptake of 14.2 in liver mass with 2.8 CM liver mass.

Follow up PET CT, after Nano ICG and PDT protocol, reported liver mass SUV 2.7 and mass size 1.7 X 1.2 CM.

Additional case reports:

BMG - Baja California Mexico (Jennifer Miele):

STAGE IV BREAST CANCER
57 y/o female, diagnosed in 2013
Diagnosis confirmed by biopsy – pathology report

PET CT Scan Diagnostic impression - September 2018
Metabolic tumor activity disseminated in liver and skeleton.
Increased metabolism in Thyroid nodule.
Metabolic activity in zone of the lung as well as mediastinal adenopathies.

Extreme pain due to metastatic activity in the lumbar/sacral area and in hips
Could not walk without assistance of a walker or cane
Abdominal swelling and discomfort
Weakness, weight loss, lack of appetite, dizziness, migraines, abdominal distention

Additional case reports:

BMG - Baja California Mexico (Jennifer Miele):

- March 2018

CA 15-3 and CA 27-29

reported at over 11,000

- July 2018

CA15-3 =1586.8

Ref. range less than 31.3 U/ml

CA 27-29 =1589.8

Ref range less than 38.6 U/ml

-September 2018

CA15-3 = 818.5

Ref. range less than 31.3 U/ml

CA 27-29 = 742.5

Ref range less than 38.6 U/ml

- November 2018

CA15-3 =339.5

Ref. range less than 31.3 U/ml

CA 27-29 =367.1

Ref range less than 38.6 U/ml

-December 2018

CA15-3 = 97.5

Ref. range less than 31.3 U/ml

CA 27-29 = 113.4

Ref range less than 38.6 U/ml

Additional case reports:

BMG - Baja California Mexico (Jennifer Miele):

Comparative Abdominal ultrasound

December 2018

Metastatic liver nodules measuring 9-13-15-18 and 26mm maximum diameter.

January 2019

The classic metastatic nodules have disappeared. There are at present fibroid nodules in liver segment VII and VIII measuring 11-12 and 17 mm maximum diameter. The liver resembles a fibroid liver post-chemotherapy. There are no dilation of intra-nor extrahepatic biliary ducts observed

January 2019 - CT San of Chest

No noted metastatic or cancer activity is observed.

Additional case reports:

BMG - Baja California Mexico (Jennifer Miele):

After therapy:

- Liver enzymes - normal range.
- CA markers decreased.
- C reactive protein returned to normal range.
- Noted improvement in image reports.
- Patient able to walk without assistance.
- No pain – removal of prescribed pain medications.
- Weight stabilized
- Increased energy

Additional case reports:

BMG - Baja California Mexico (Jennifer Miele):

CHOLANGIOCARCINOMA
76 y/o female, diagnosed in 2017
Diagnosis confirmed by biopsy – pathology report

- Extreme abdominal pain and bloating
- Weakness
- Weight loss
- Lack of appetite
- Nausea
- Dizziness
- Jaundice
- Confusion
- Elevated bilirubin, liver enzymes, ammonia…

Additional case reports:

BMG - Baja California Mexico (Jennifer Miele):

CHOLANGIOCARCINOMA

November 2018

CA19-9 = 11295.64

Ref. range less than 37 U/ml

December 2018

CA19-9 = 9003.21

Ref. range less than 37 U/ml

January 2019

CA19-9 = 2742.43

Ref. range less than 37 U/ml

After therapy:

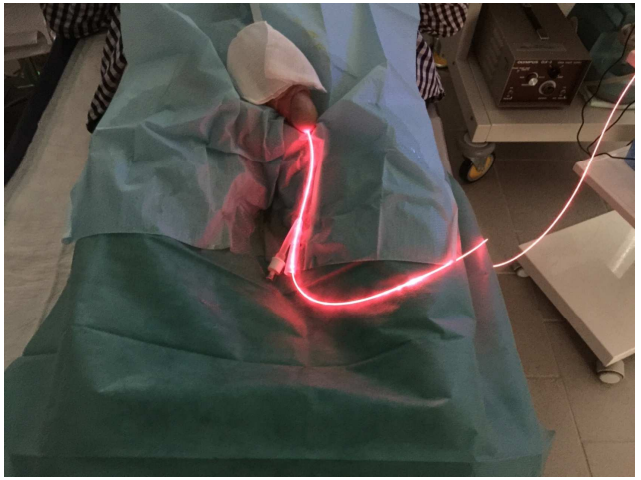
- Jaundice – not present.
- Liver enzymes reduced.
- Bilirubin reducing to normal range.
- CA markers reducing.
- Appetite returned & weight stabilized.
- Patient notes increased energy
- No abdominal distention

Additional case reports:

First results in prostate cancer treatments:

- Until now very limited success with prostate cancer treatments
- 2019: Treatment with Nano-ICG and intraurethral and intrarectal irradiation

→ 4 cases with promising results



Additional case reports:

BMG - Baja California Mexico (Jennifer Miele):

Prostate Cancer

65 Yr Old Male Patient

August 5 2019: PSA 17.31	**Sept 21 2019: PSA 7.03**
August 7th 2019 Transrectal ultrasound 5.27 X 4.2 X 3.8 CM	**Sept 9th 2019** **4.2 X 4.3 X 3.64 CM**
Pereferica right 8 X 6 mm	**Pereferica right 5.8 x 4.6 mm**
Vascularized solid nodule	**Reduced size of vascularized nodule**

Patients Experience and Safety:

- PDT with Nano ICG is usually offered in a 1- or 2-week treatment course with daily treatment
- Safe application without significant side effects (however Photodynamic therapy can lead to local reactions such as pain and inflammation)
- One of the key advantages of Nano-ICG is that there is no increased light sensitivity (as opposed to photosensitizers like Chlorin or Hypericin)

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