# New Developments in Photodynamic and Sonodynamic Cancer Therapy

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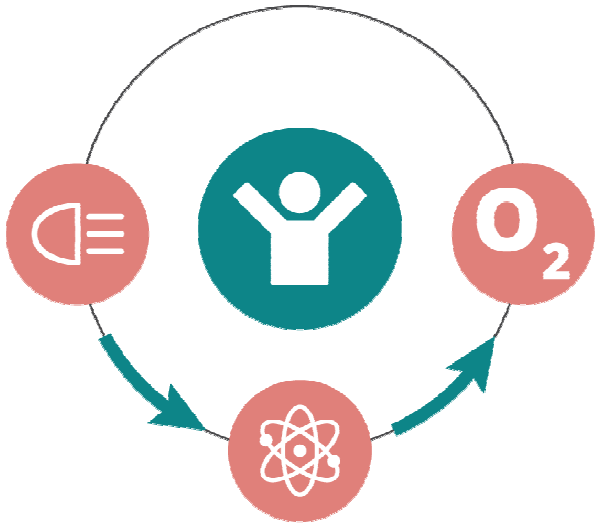


# 1. Introduction and Mechanisms of PDT

# Photodynamic Therapy (PDT)

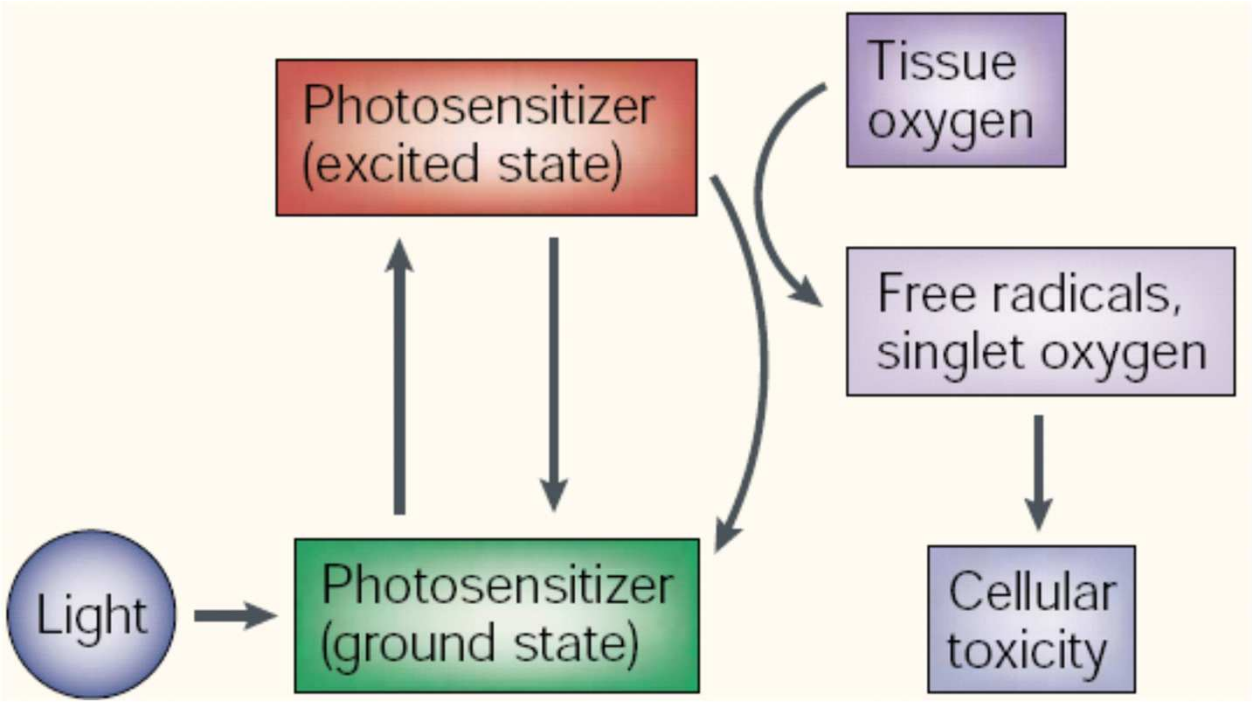
- Photodynamic therapy is one of the most interesting and promising approaches in the treatment of various cancers
- The principle is the stimulation of a light sensitive drug which is injected into the bloodstream and accumulates in cancer cells
- Tumor tissue is subsequently destroyed by irradiation with light of appropriate wavelength according to the absorption spectra of the photosensitizers
- The basic principle behind this mechanism is the development of radical oxygen species

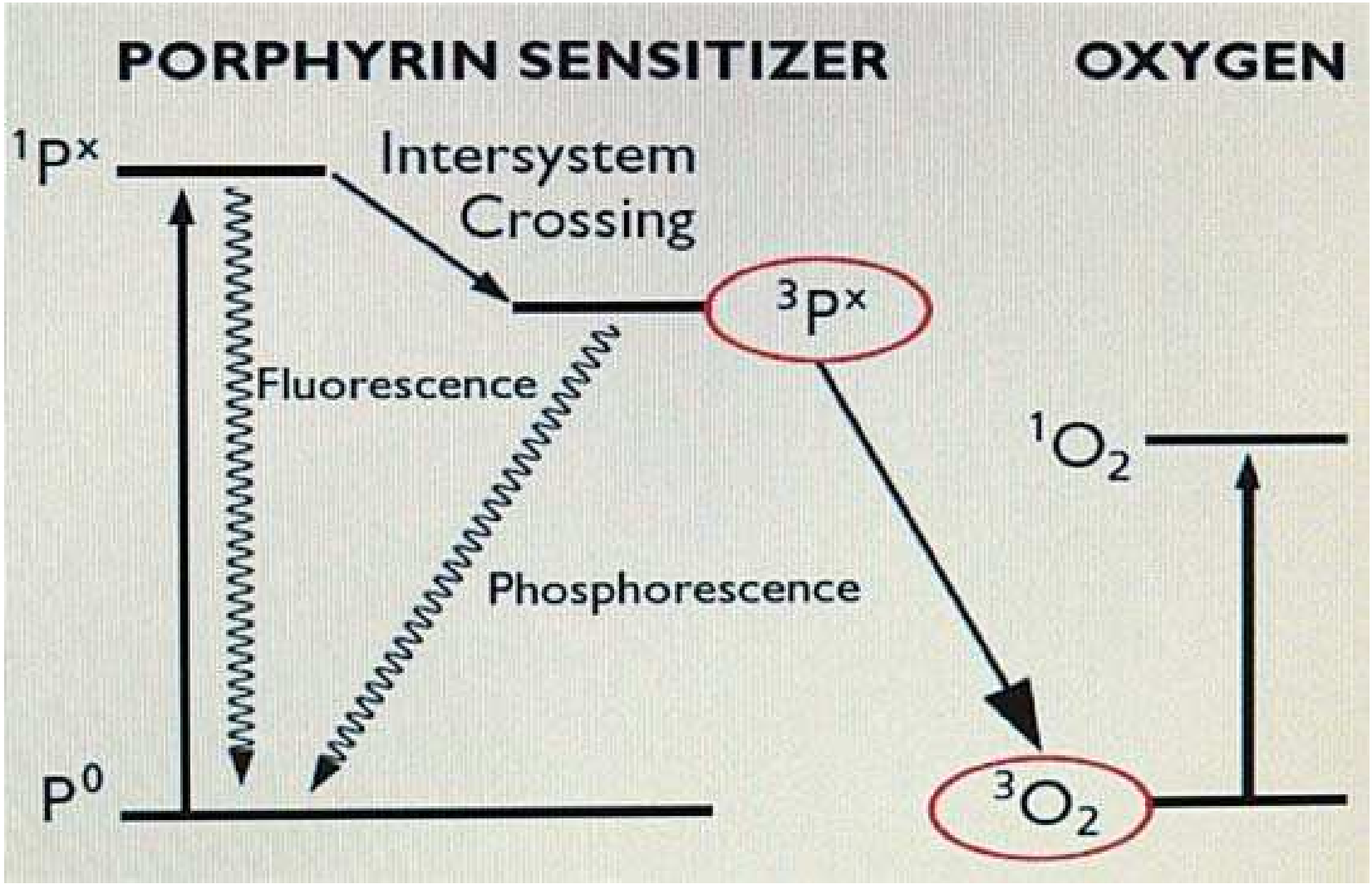
- *Until recently PDT has mainly been used in superficial cancers due to limited light penetration into the body*
- *New development of interstitial laser therapy facilitates treatment of deep tumors now*

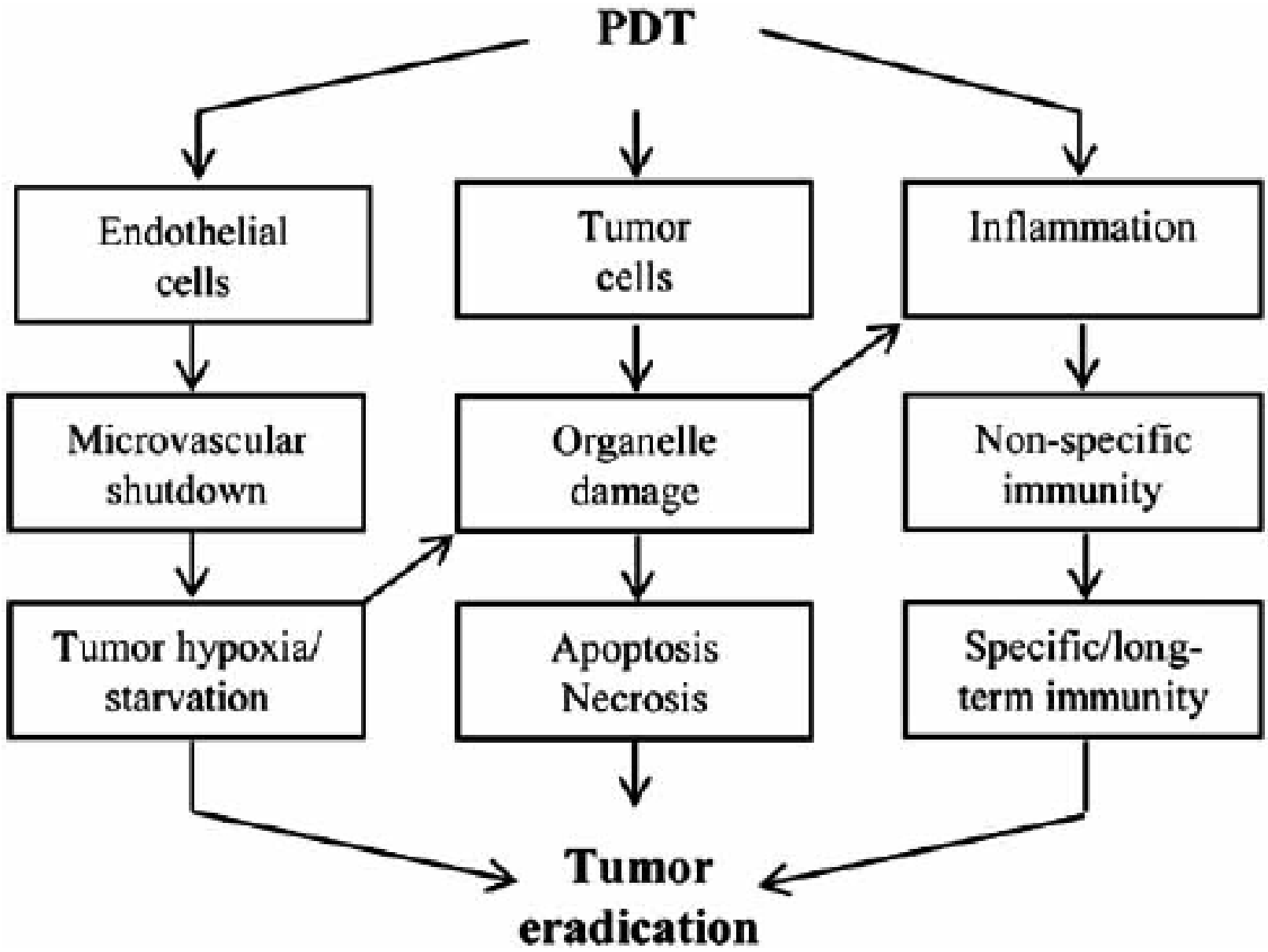
# Mechanism of Photodynamic Therapy

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

1. Photosensitizing agent
2. Light of specific wavelength



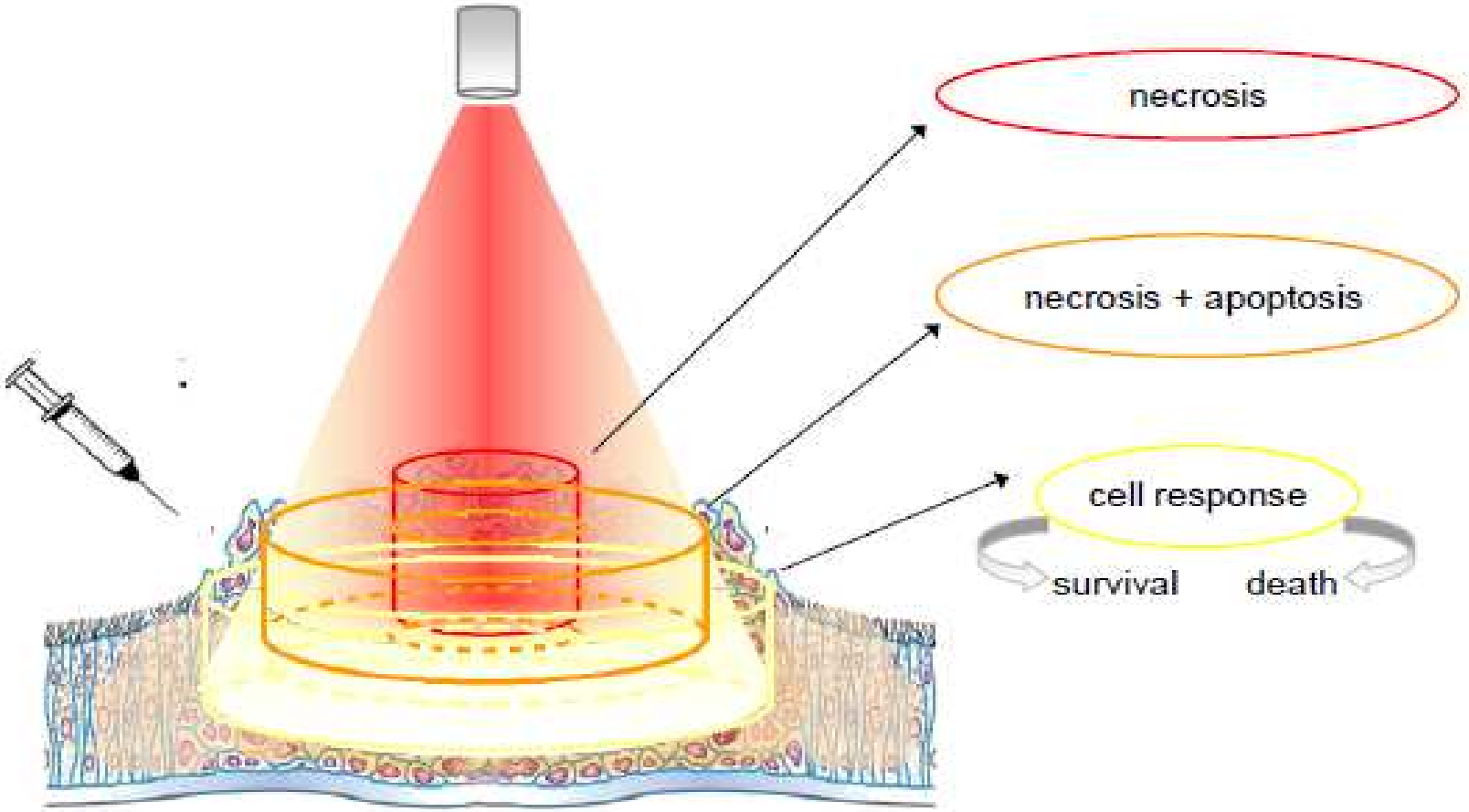

PORPHYRIN SENSITIZER
OXYGEN
$^1P^x$
Intersystem Crossing
$^3P^x$
Fluorescence
Phosphorescence
$^1O_2$
$P^0$
$^3O_2$


PDT
Endothelial cells
Tumor cells
Inflammation
Microvascular shutdown
Organelle damage
Non-specific immunity
Tumor hypoxia/ starvation
Apoptosis Necrosis
Specific/long-term immunity
Tumor eradication

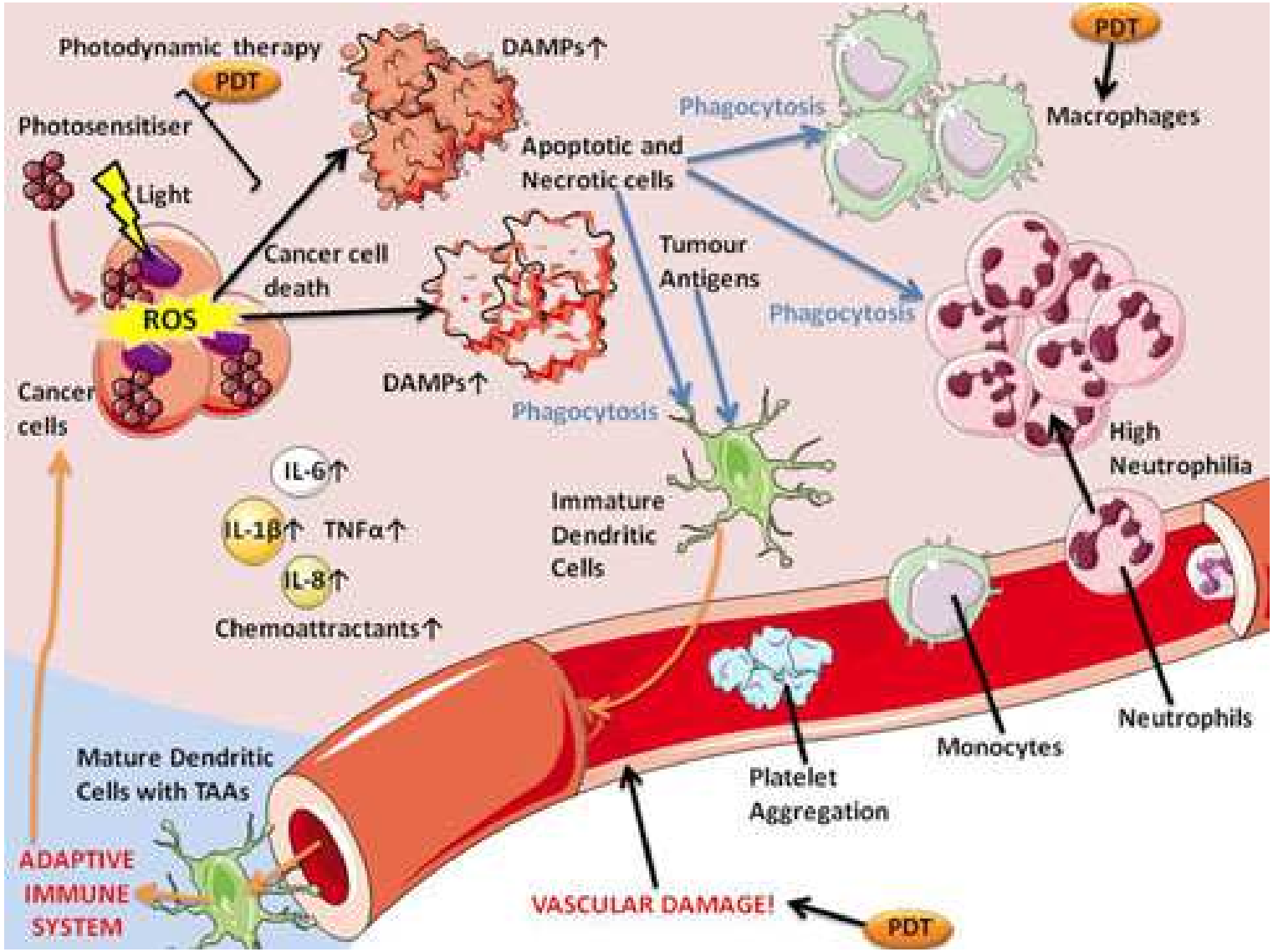
# Mechanisms of PDT

- Selective targeting of tumor cells
- Minimal side-effects
- No resistance after repeated treatments
- Tumor vascular shutdown by thrombosis and haemorrhages
- Induction of local inflammation
- Immune activation

# Light Distribution and Cellular Response During PDT



# Immunological Effects of PDT



# 2. Photosensitizers

# Traditional Photosensitizers:

- Haematoporphyrins, HpD
  - Derivatives of Haem (Photofrine and others)
- Chlorines
  - Derivatives of Chlorophyll
- Porphycenes
  - Synthetic Porphyrines

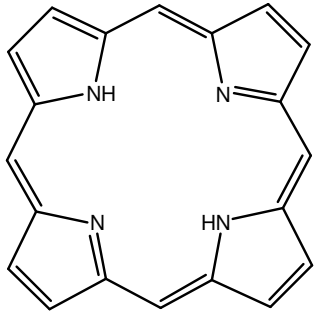



**Table 1** Currently available photosensitizers.

| 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 |

# Approved Photosensitizers and Indications:

| 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. |

# New Natural Derived Photosensitizers:

- Chlorin E6 (Red 660 nm)
- Indocyaninegreen liposomal (Infrared 810 nm)
- Hypericin  (Yellow 589 nm)
- Curcumin  (Blue 447 nm)
- Riboflavin (Blue 447 nm)

# Chemodrug Derived Photosensitizers

- Doxorubicin liposomal (Blue 447 nm)
- Mitoxantron (Yellow 589nm, Red 632nm)
- Paclitaxel (Ultraviolett, 345 nm)
- Cisplatin (Ultraviolett, 345 nm)
- 5-FU (Ultraviolett, 345 nm)

# 5-Aminolaevulinic-acid (5-ALA) for Topical PDT

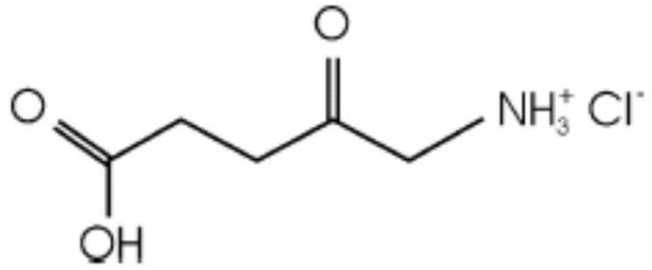
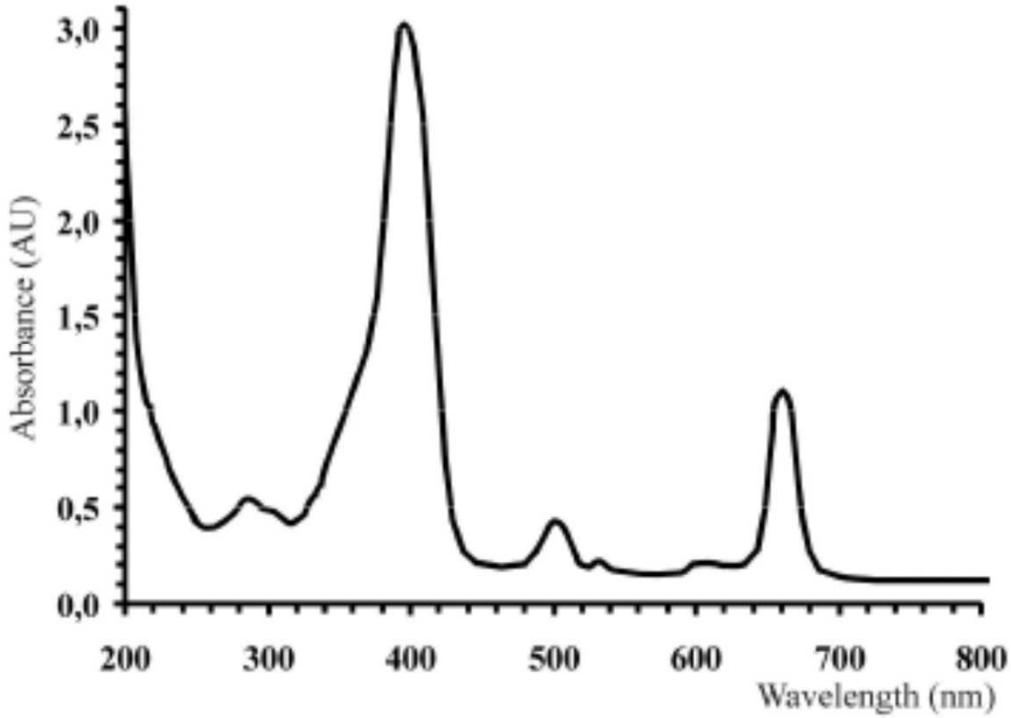



Figure 2 Molecular structure for ALA.

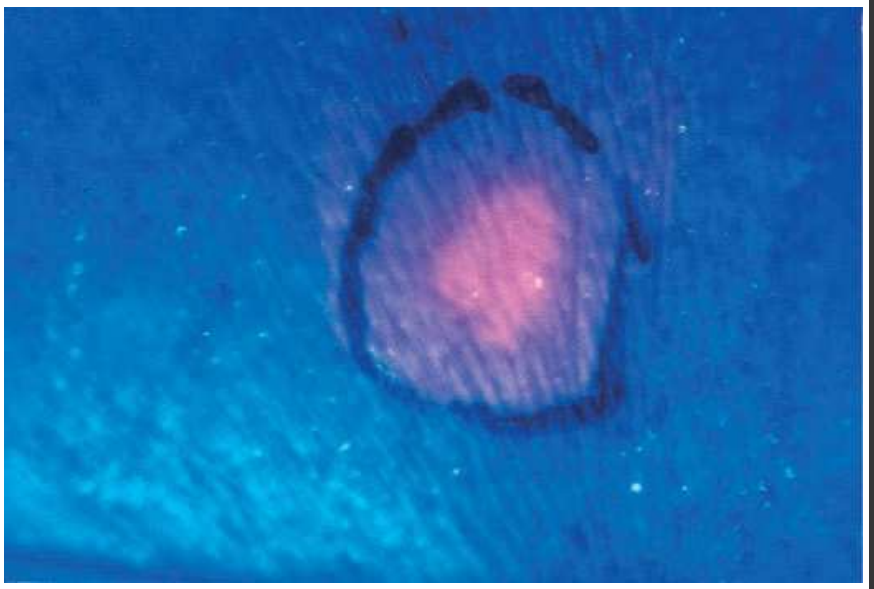


# 3. Topical PDT

# Photodynamic diagnostics PDD

## (Fluorescense diagnostic with blue laser)

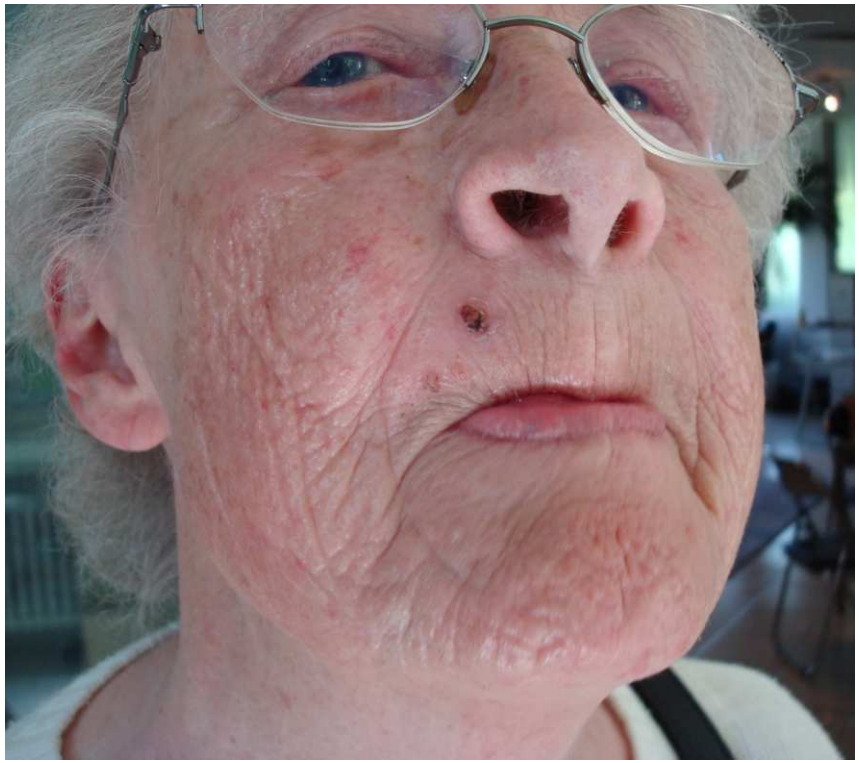
Fuselage skin basal cell carcinoma in daylight



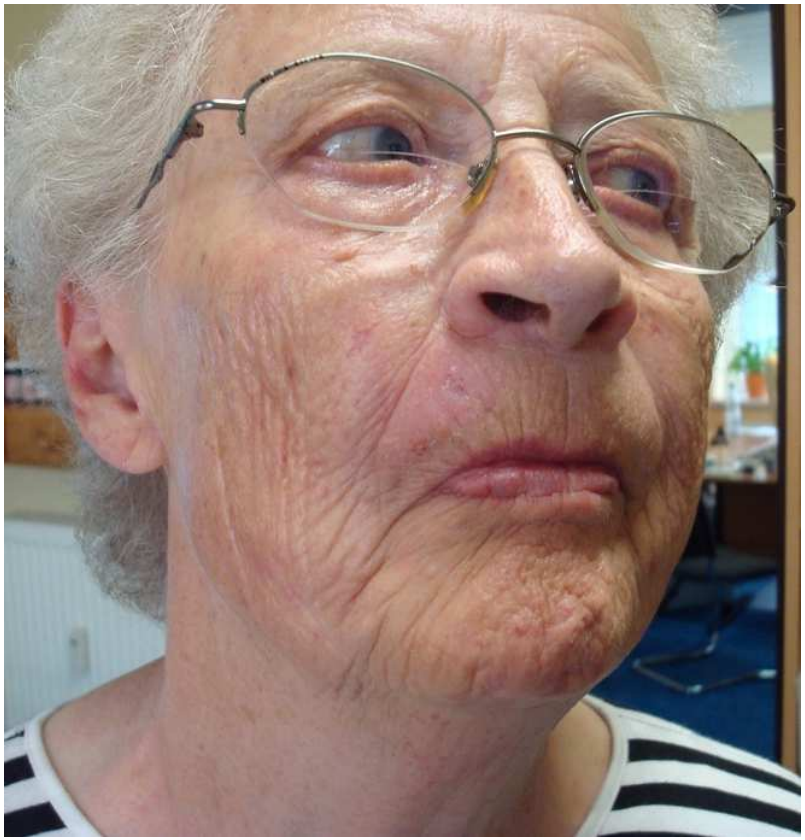
Fuselage skin basal cell carcinoma under wood light

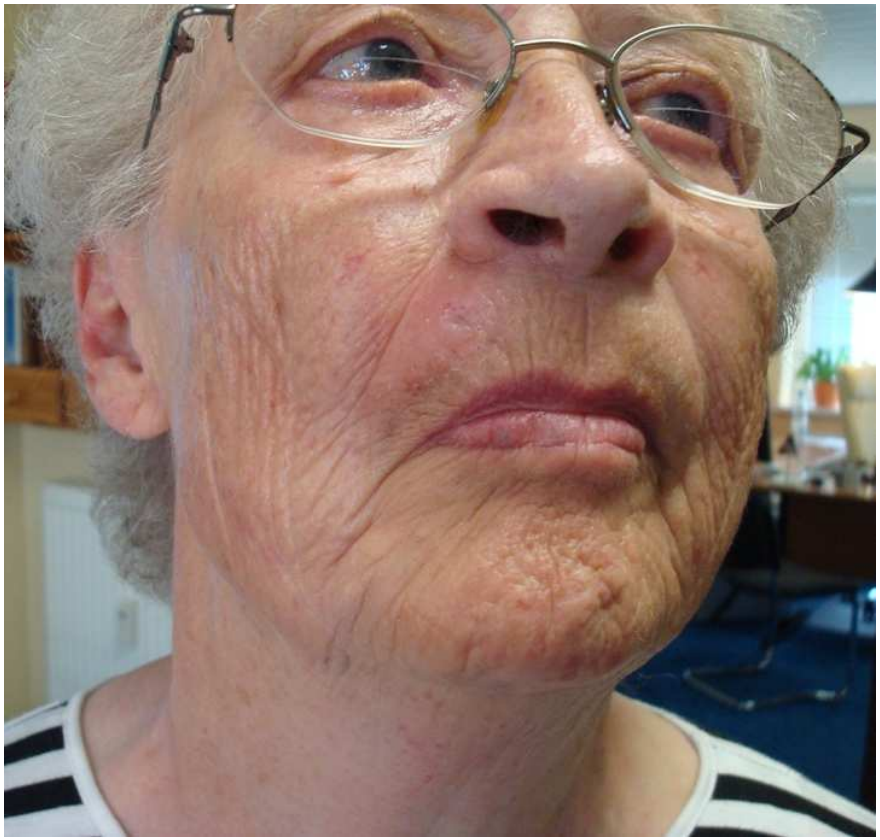
# Photodynamic Therapy of Actinic Keratosis

# Photodynamic Therapy of Basal Cell Carcinoma



# Photodynamic Therapy of Basal Cell Carcinoma





# Photodynamic Therapy of Basal Cell Carcinoma

Ulcerated basal cell carcinoma before treatment

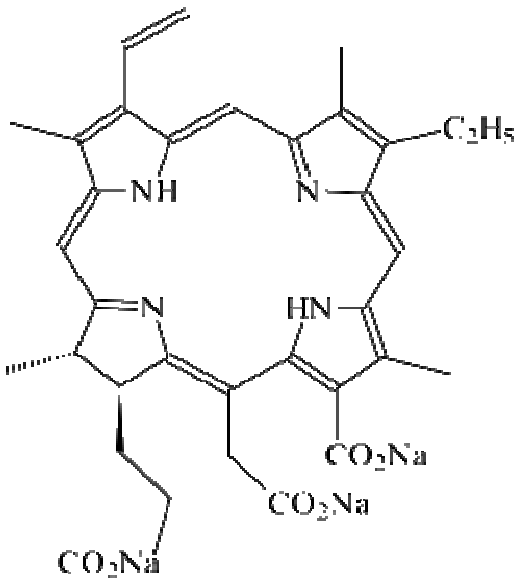
Findings after 1 treatment PDT

# 4. Systemic and Interstitial PDT with Chlorin E6

# Systemic Photodynamic Therapy

## Fotolone (Chlorin E6)

- Trisodium salt of the „green“ porphyrin
- High solubility in water
- Molecular formula: $C_{34}H_{33}N_4Na_3O$
- High stability of the lyophilized API



# Production of Chlorin E6

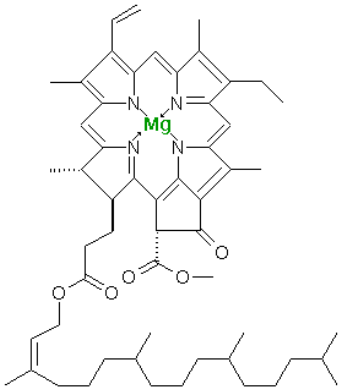
- Natural sources (algae, grass, lucerne etc.)
- FDA approved, GAP
- Inexhaustible availability (different sources/world-market)

# Production of Chlorin E6

**GAP**

Extraction

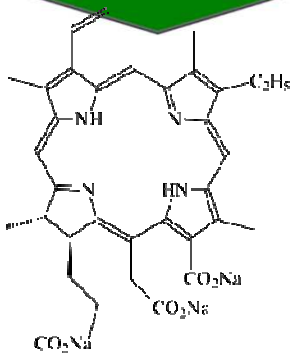
**In accordance to GMP**



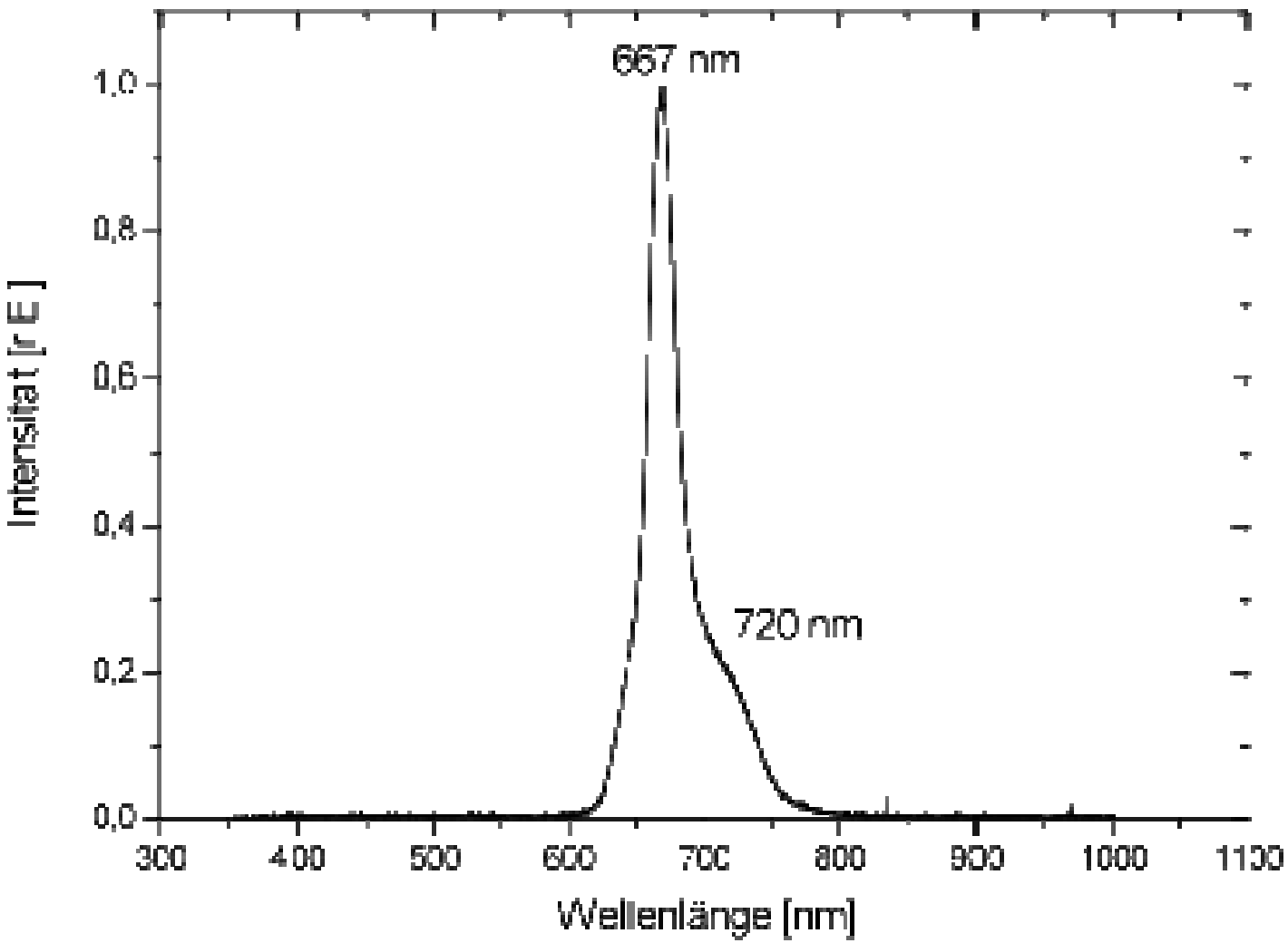

Processing

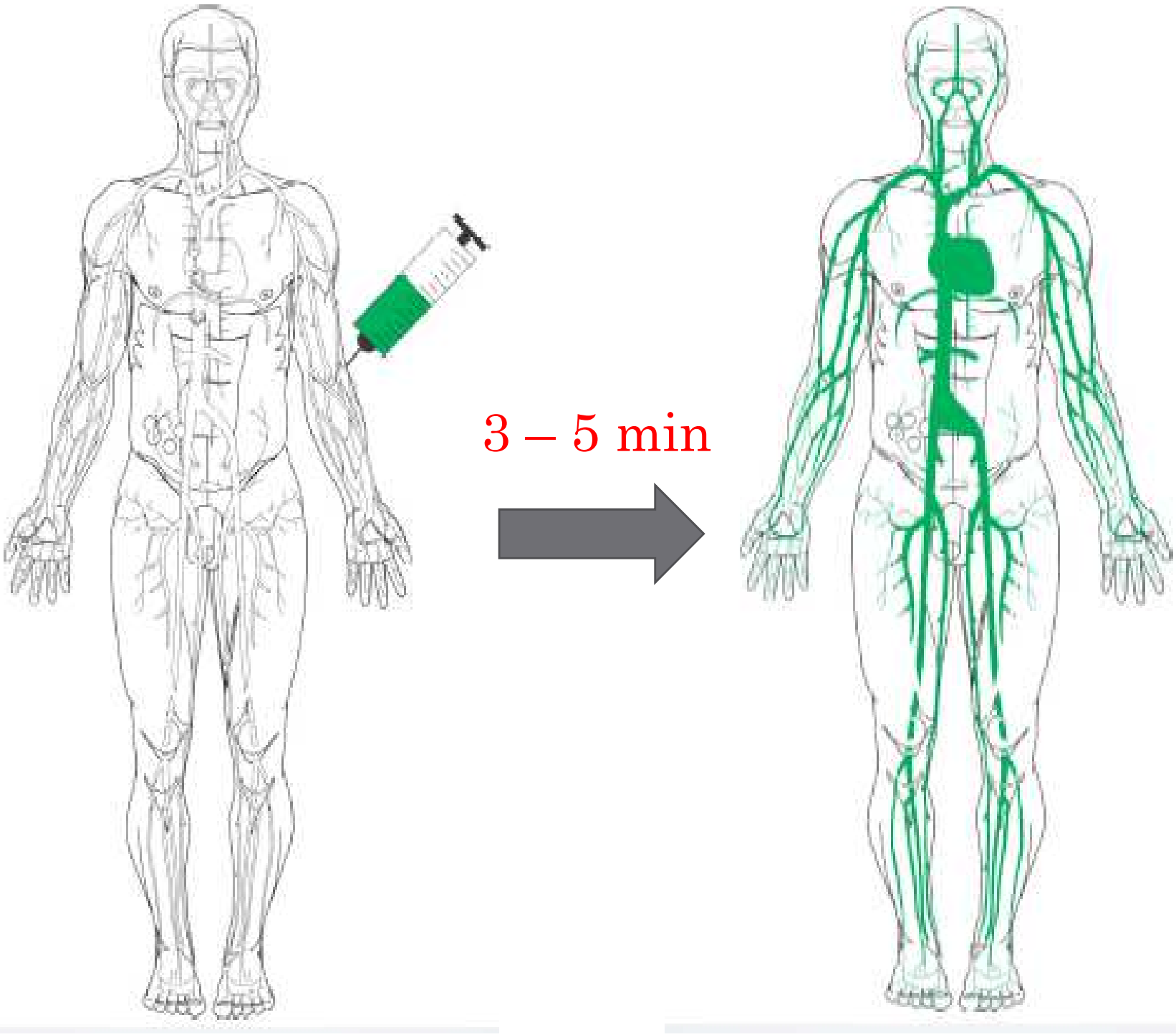
**GMP process:**

- **Unique**
- **Efficient**
- **Highest purity**



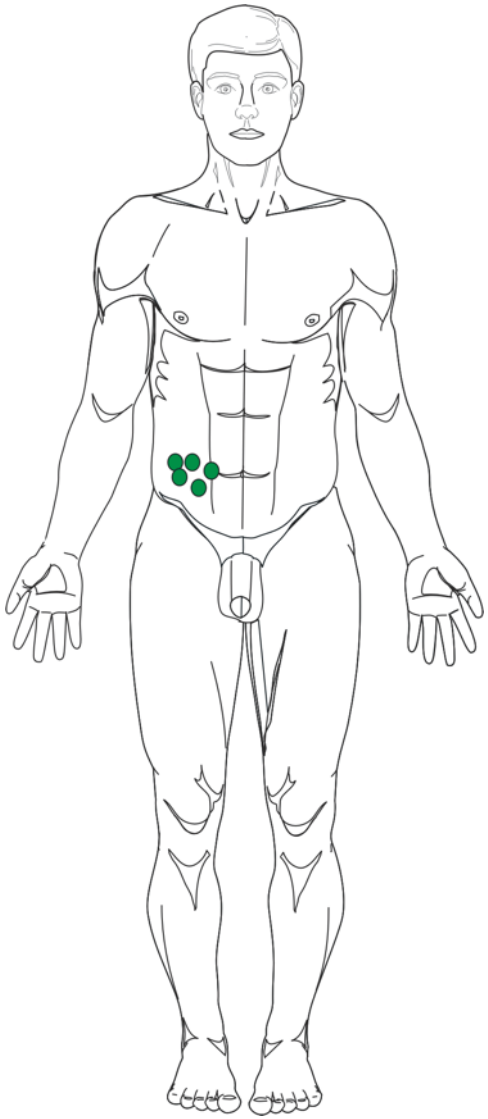
# Absorption Spectrum of Chlorin E6



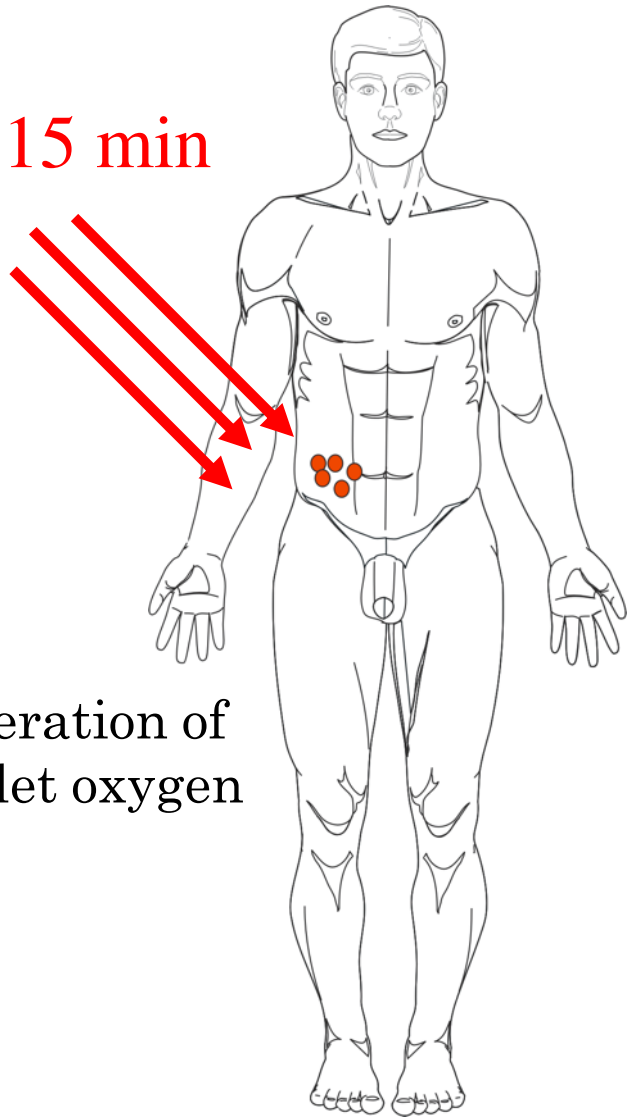

3 – 5 min

# PDT

3 – 4 h

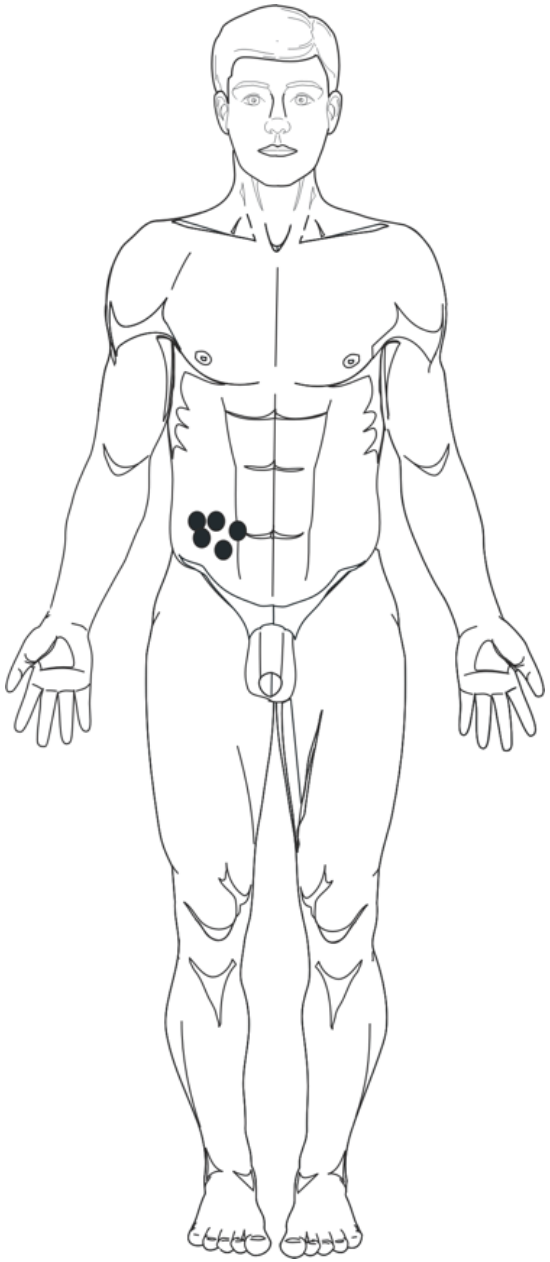


1 – 15 min



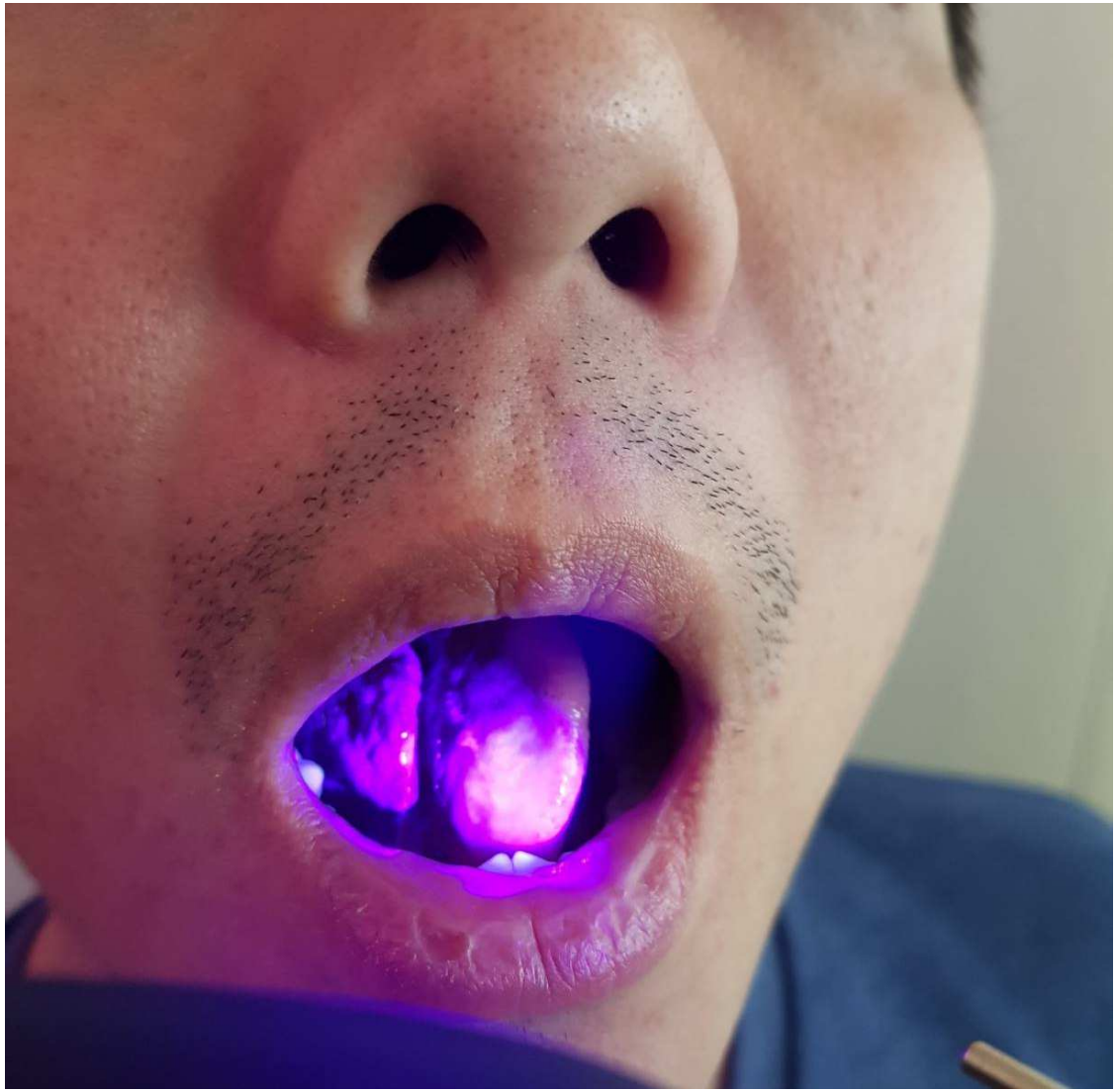
Generation of
singlet oxygen

24 – 48 h



- Apoptosis/ Necrosis
- Elimination of Chlorin E6 from blood

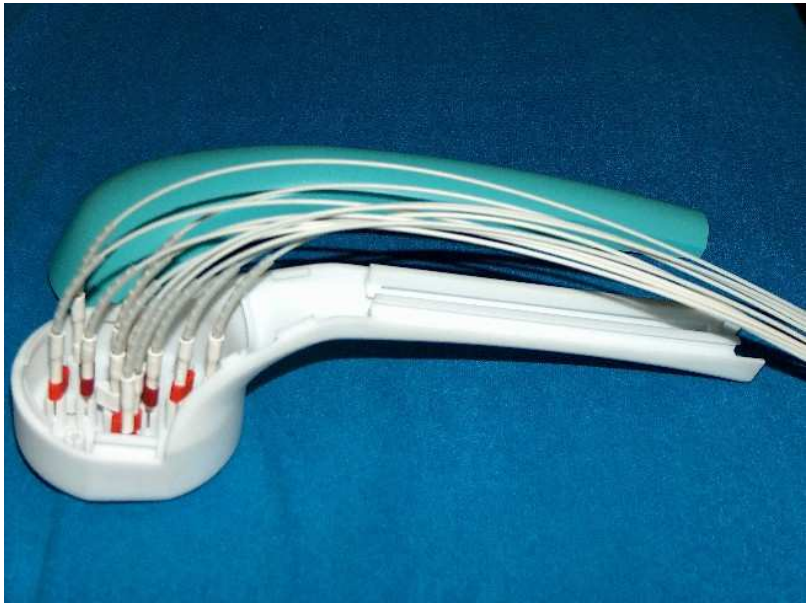
# Tongue Cancer (Fluorescense Diagnostic)



# Tongue Cancer, Intraoral Irradiation

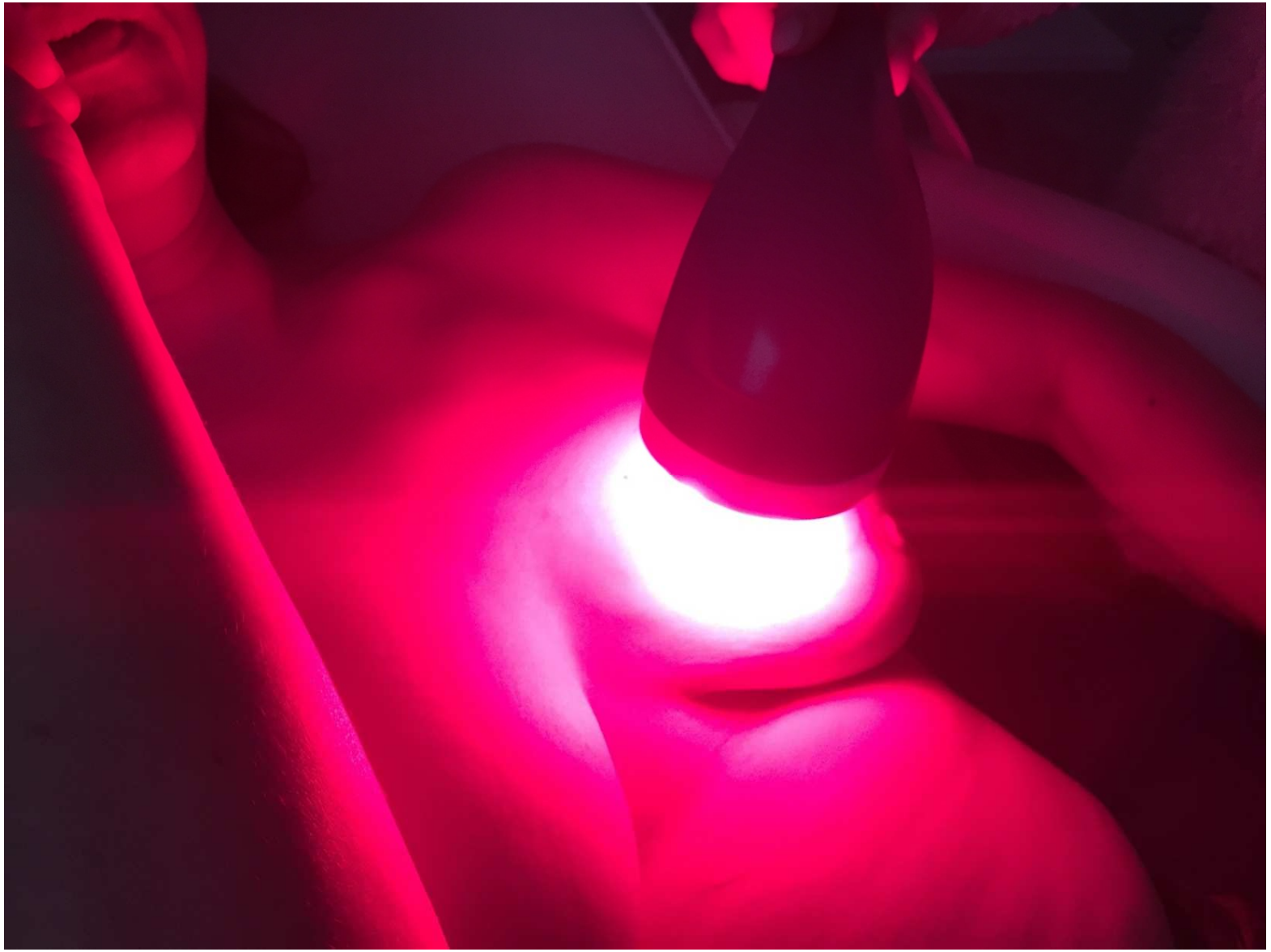
# Tongue Cancer, control after 4 weeks

# External PDT for Treatment of Superficial Tumors:



# External PDT of Lymph Metastases:

# Potential Overdosing with Skin Burning:



# Interstitial Photodynamic Therapy of Liver Metastases

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S. Zangos · C. Herzog · A. Thalhammer
K. Engelmann
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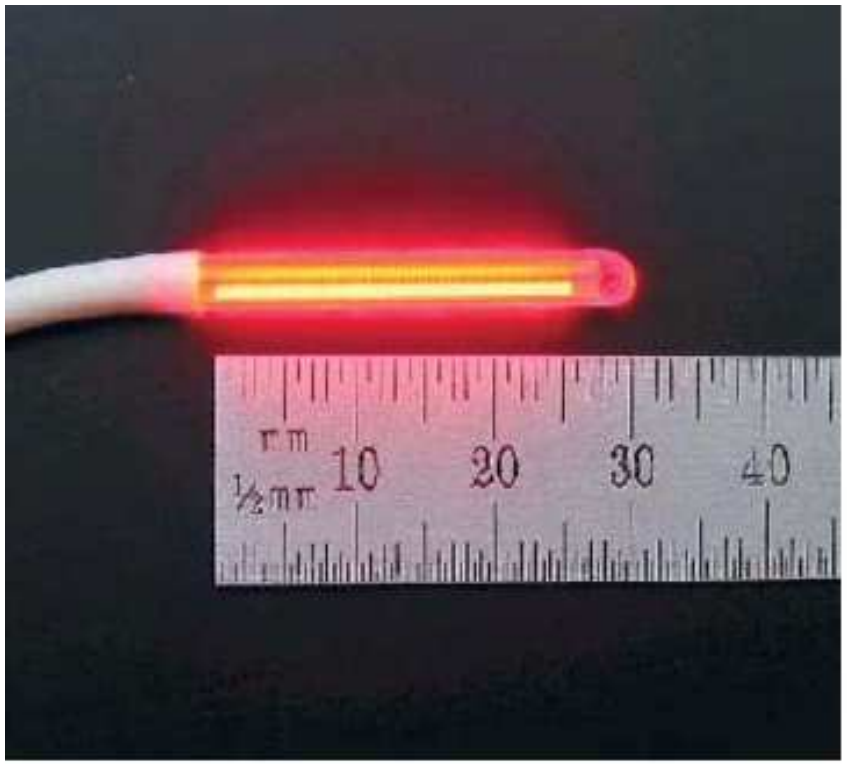
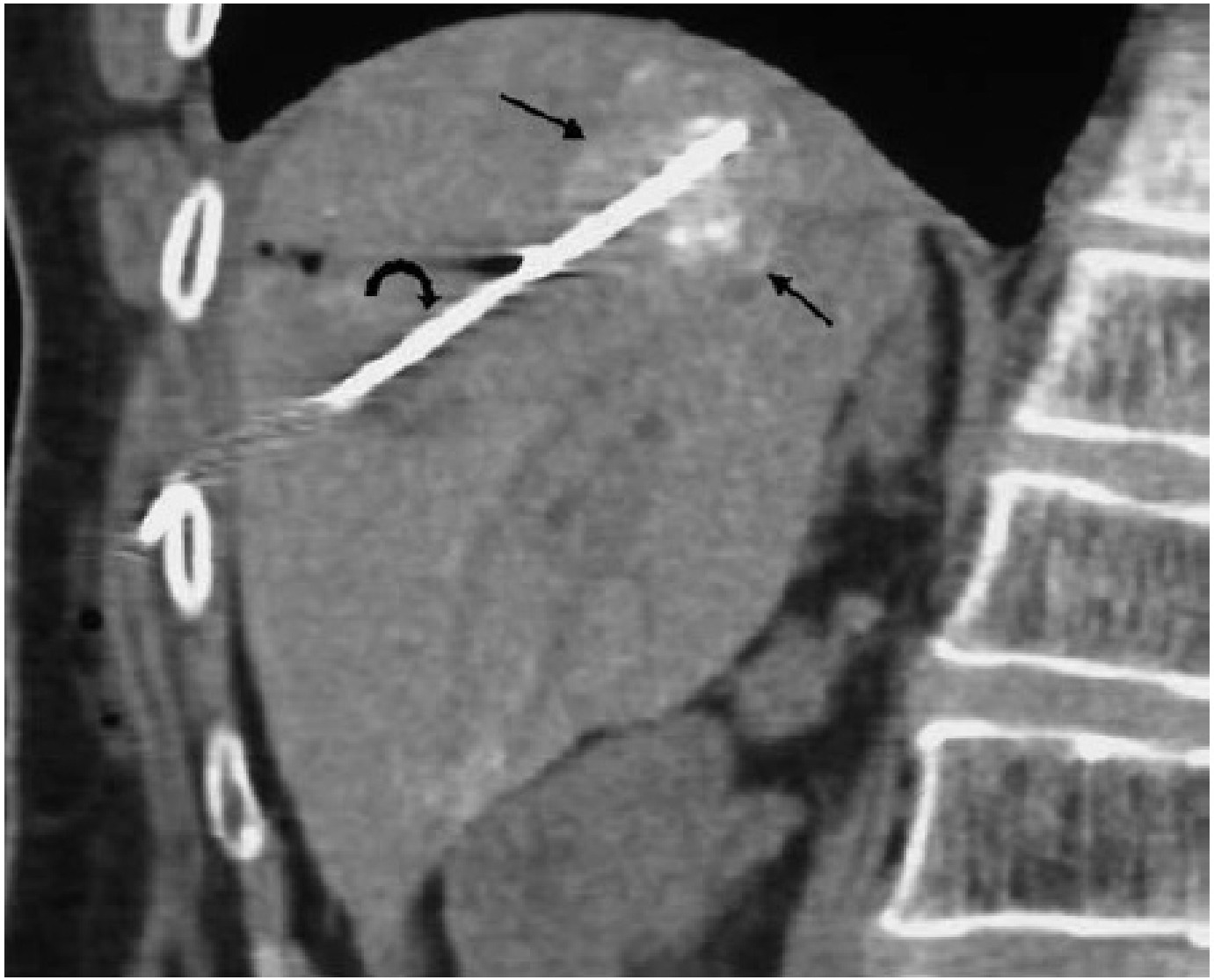
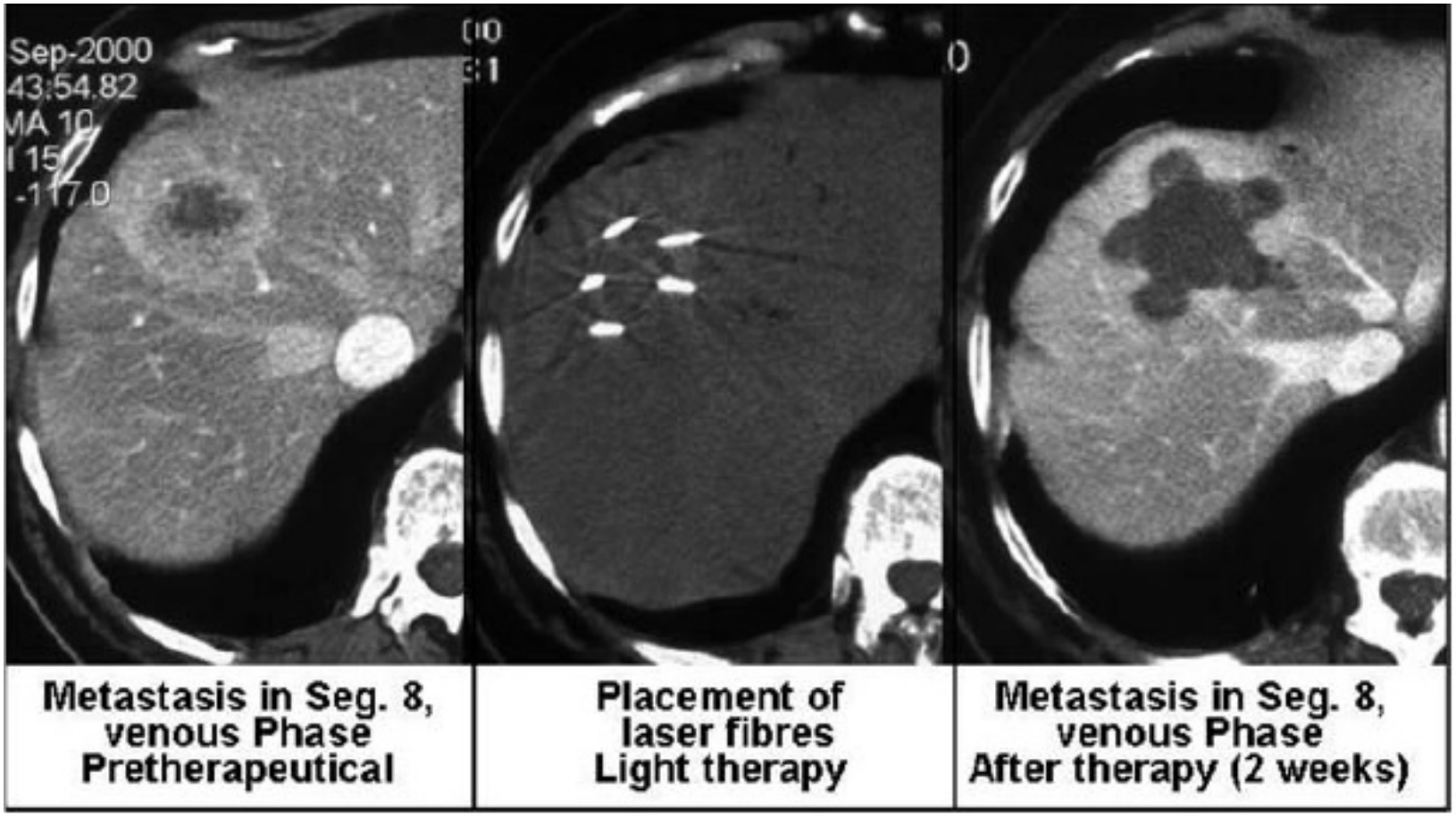


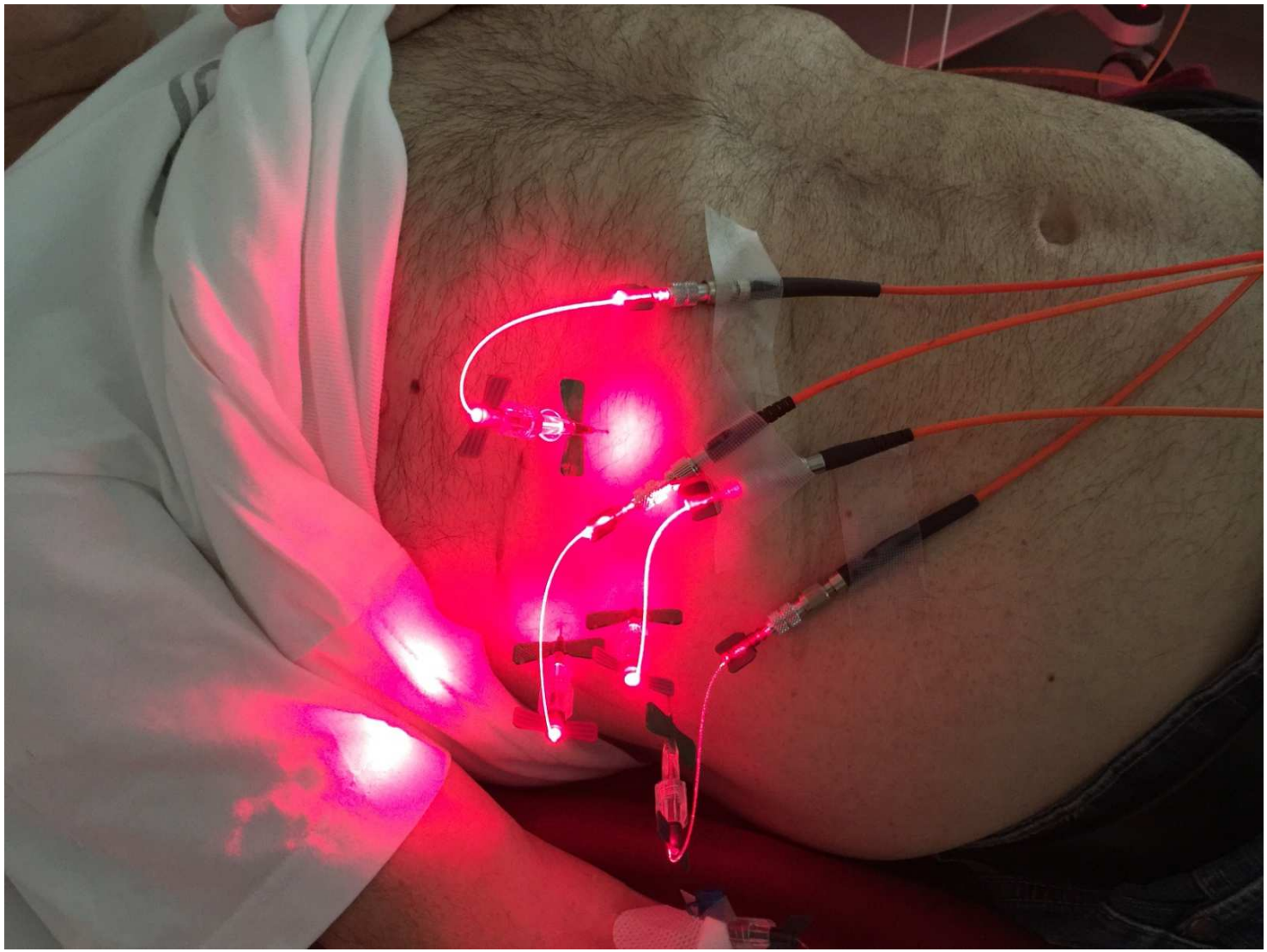

# Interstitial Photodynamic Therapy of Liver Metastases



# Interstitial Photodynamic Therapy of Liver Metastases

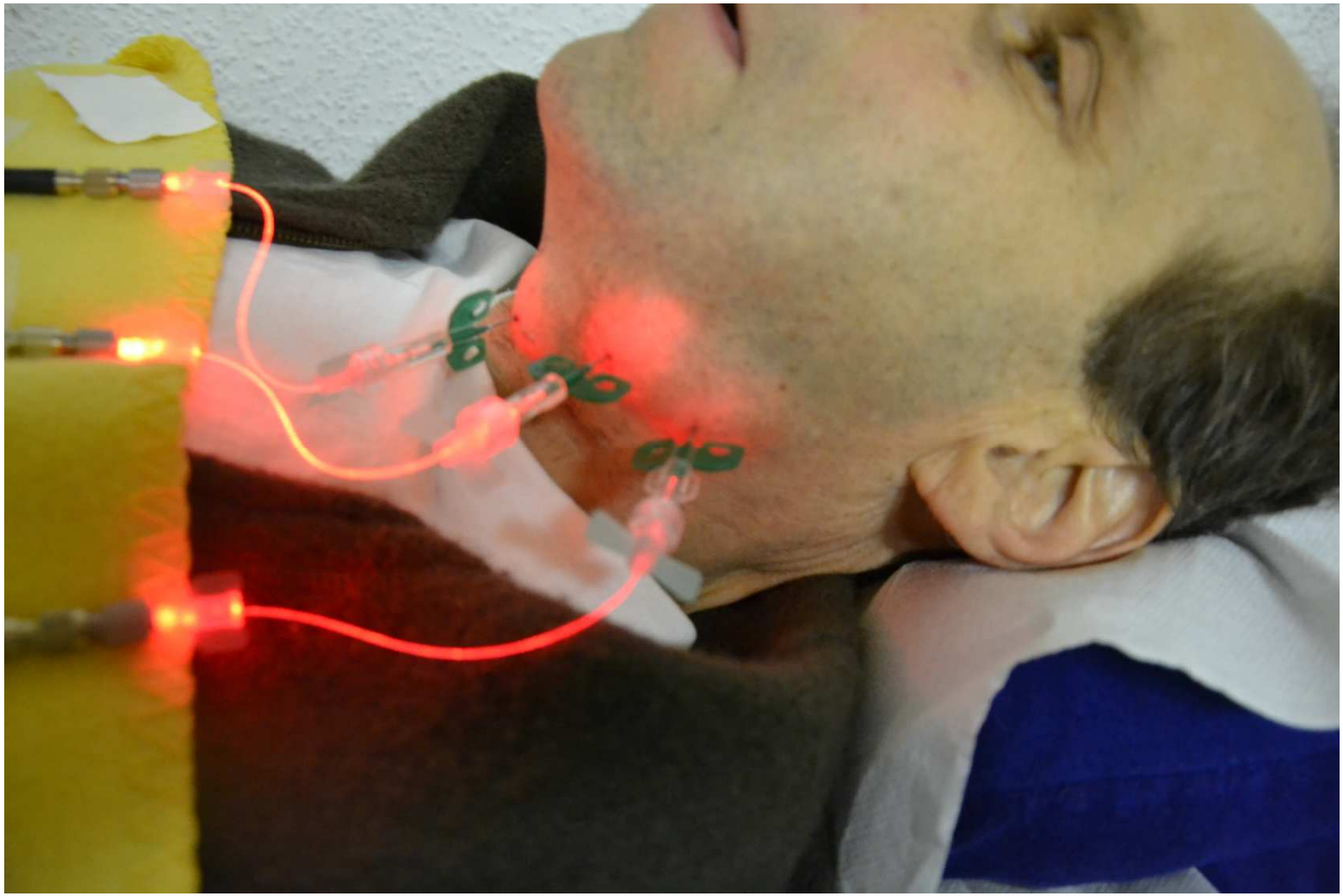


# Interstitial Photodynamic Therapy of Liver Metastases



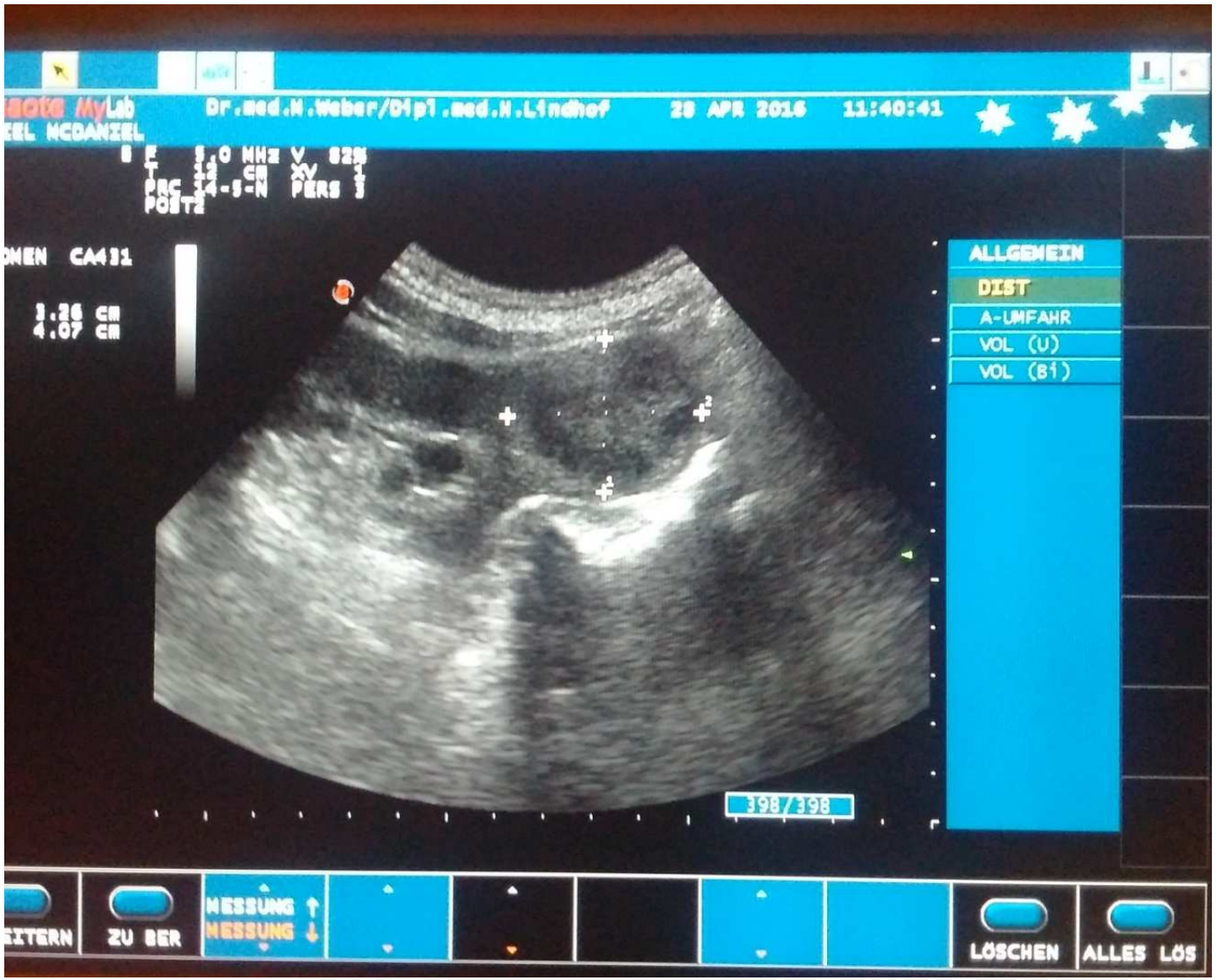
# Interstitial PDT of Lymph Metastases:

# Interstitial PDT of Squamous Cell Carcinoma:

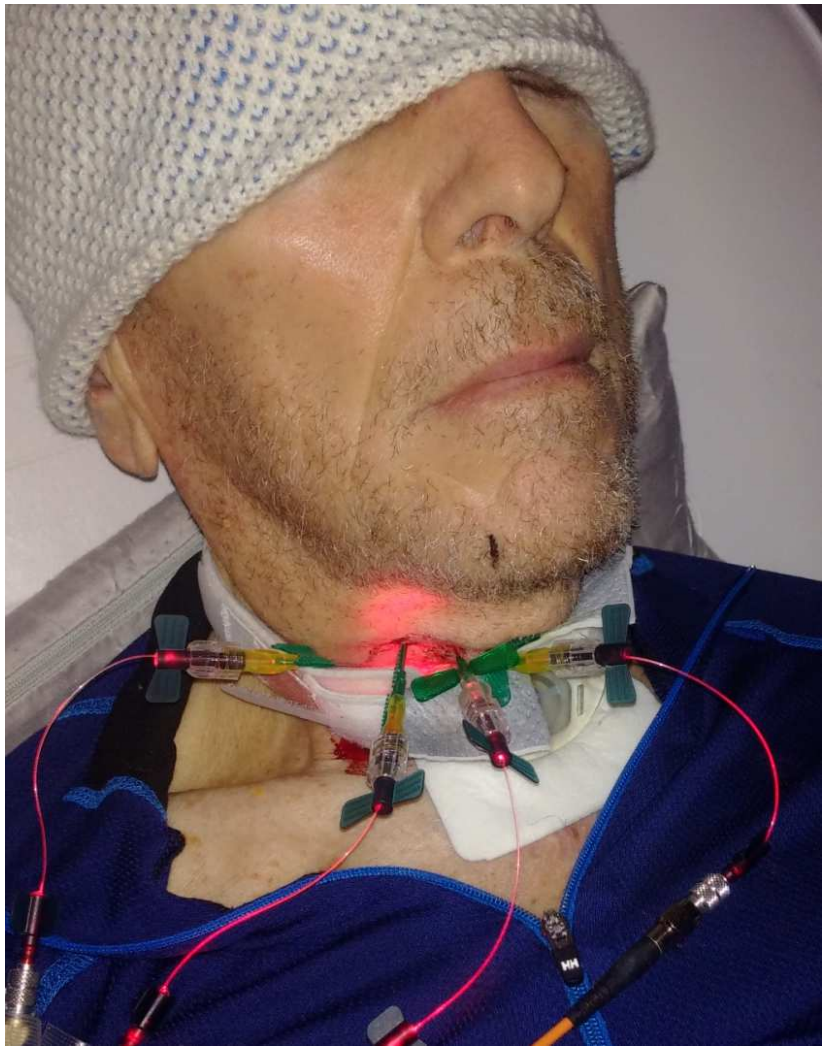


# Interstitial PDT of Mouth Bottom Cancer with Lymph Nodes:

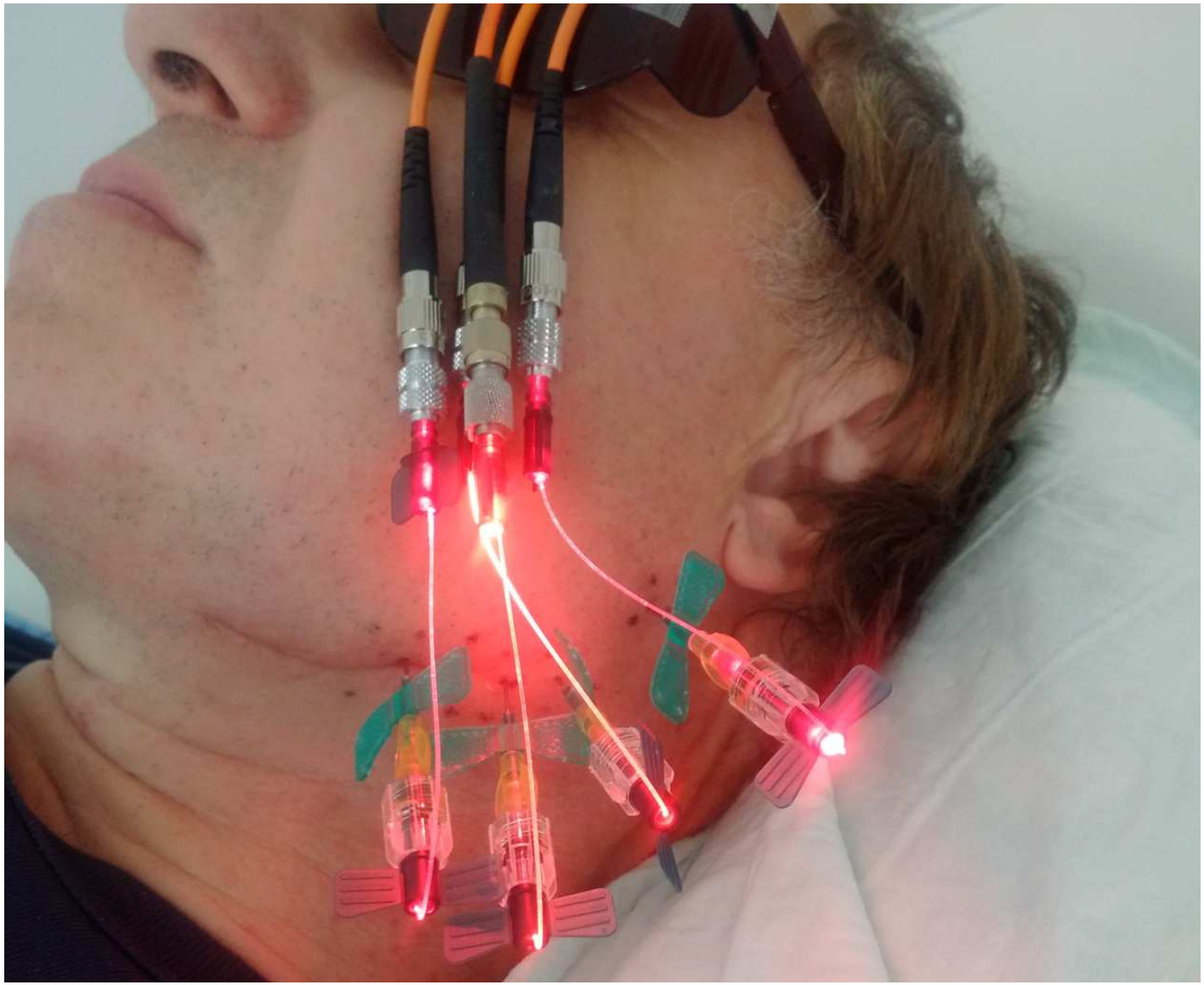
# Larynx Cancer, spreading in the neck:



# Interstitial PDT of Larynx Cancer:



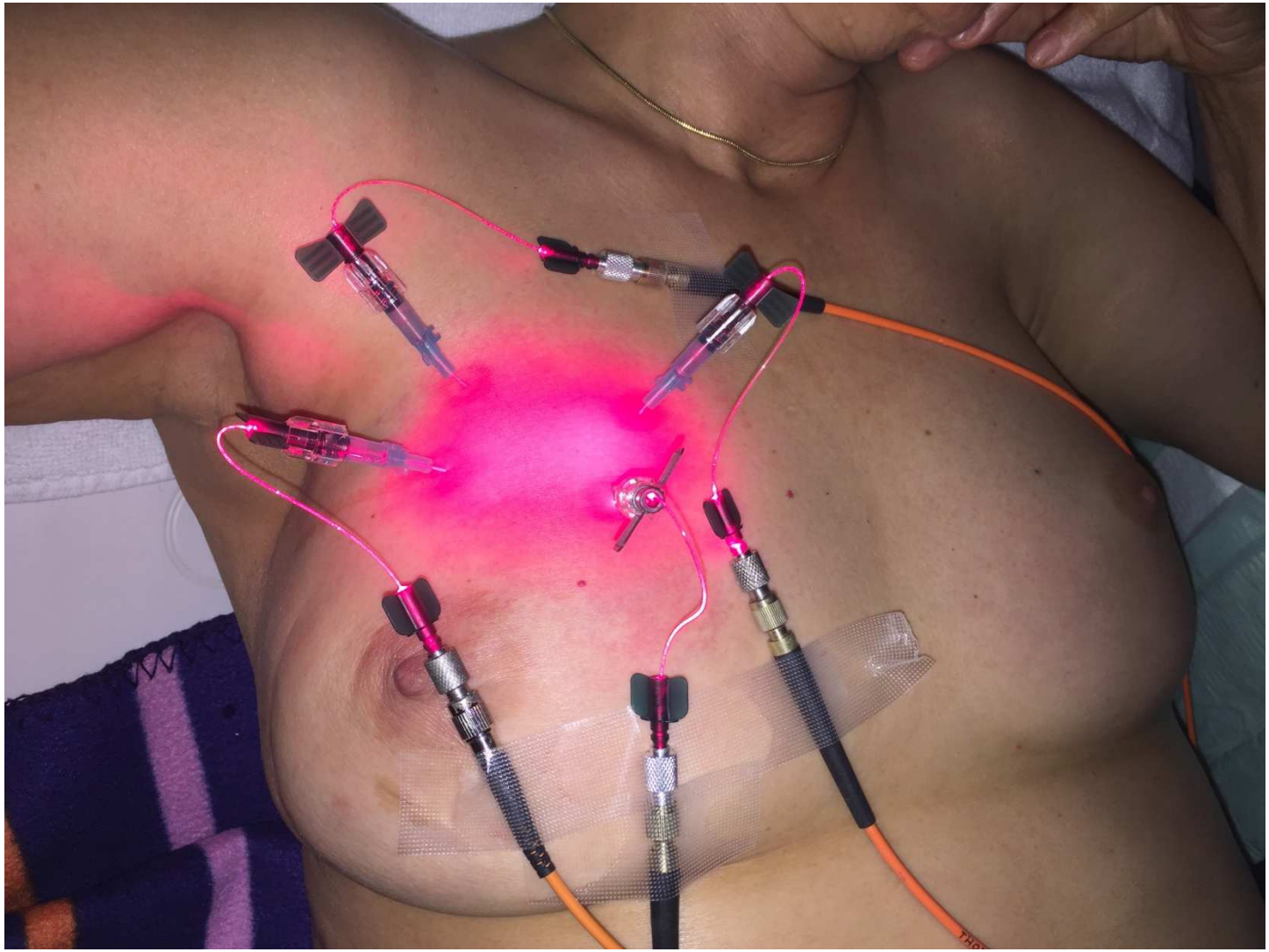
# Interstitial PDT of Neck Lymph Nodes:



# Interstitial PDT of Neck Lymph Nodes:

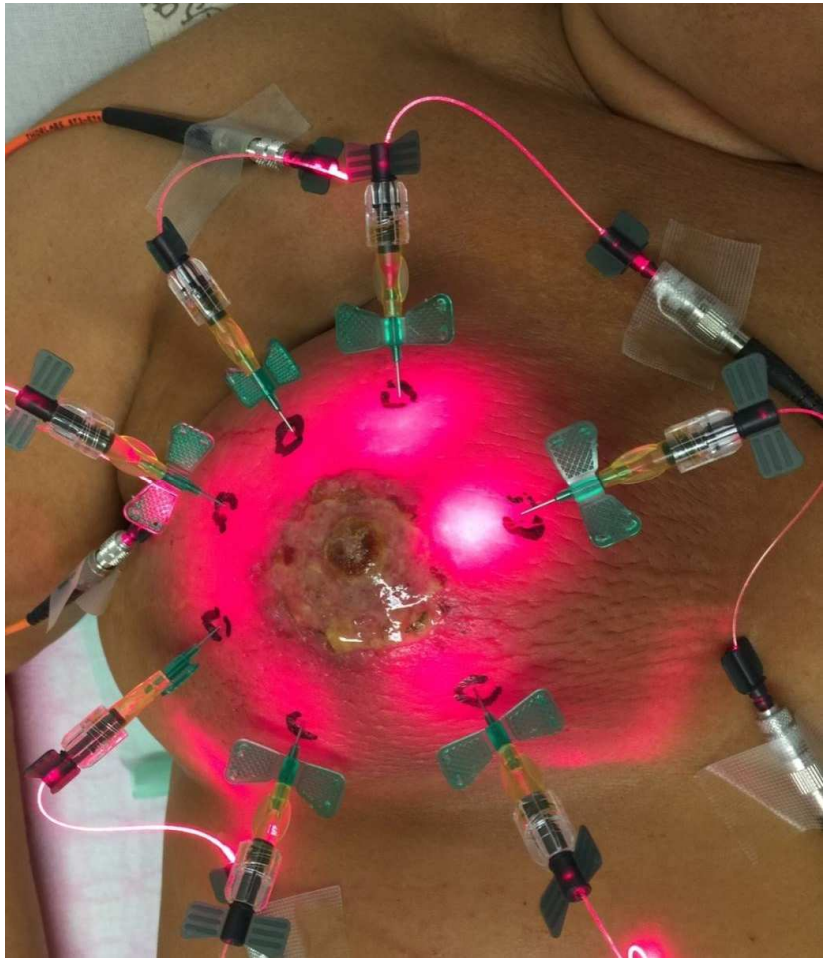
# Interstitial PDT of Thyroid Cancer:

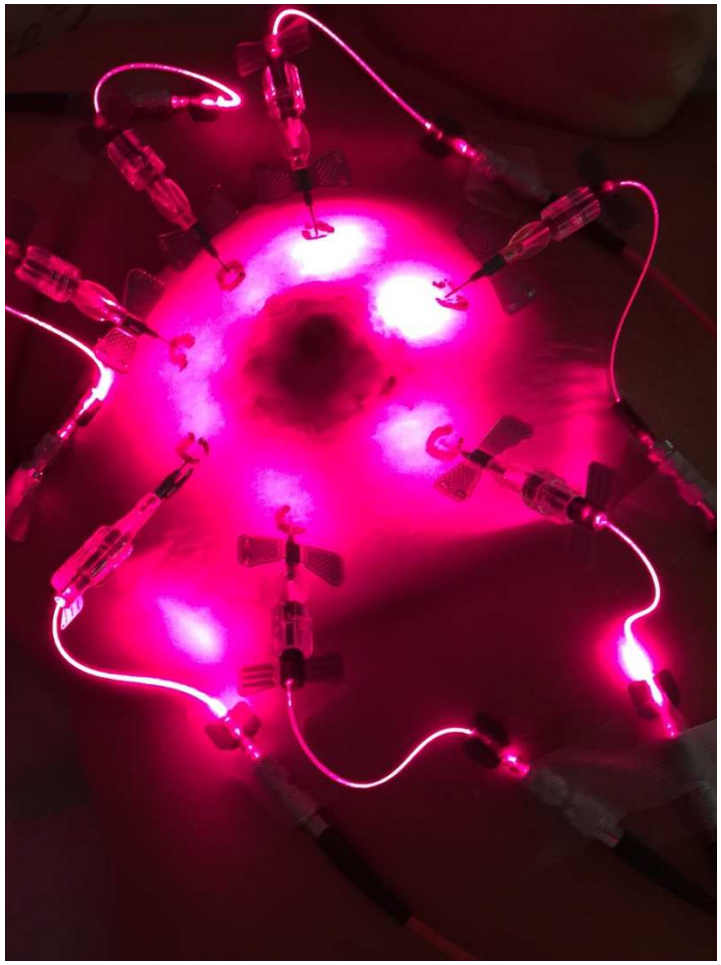
# Interstitial PDT of Breast Cancer:



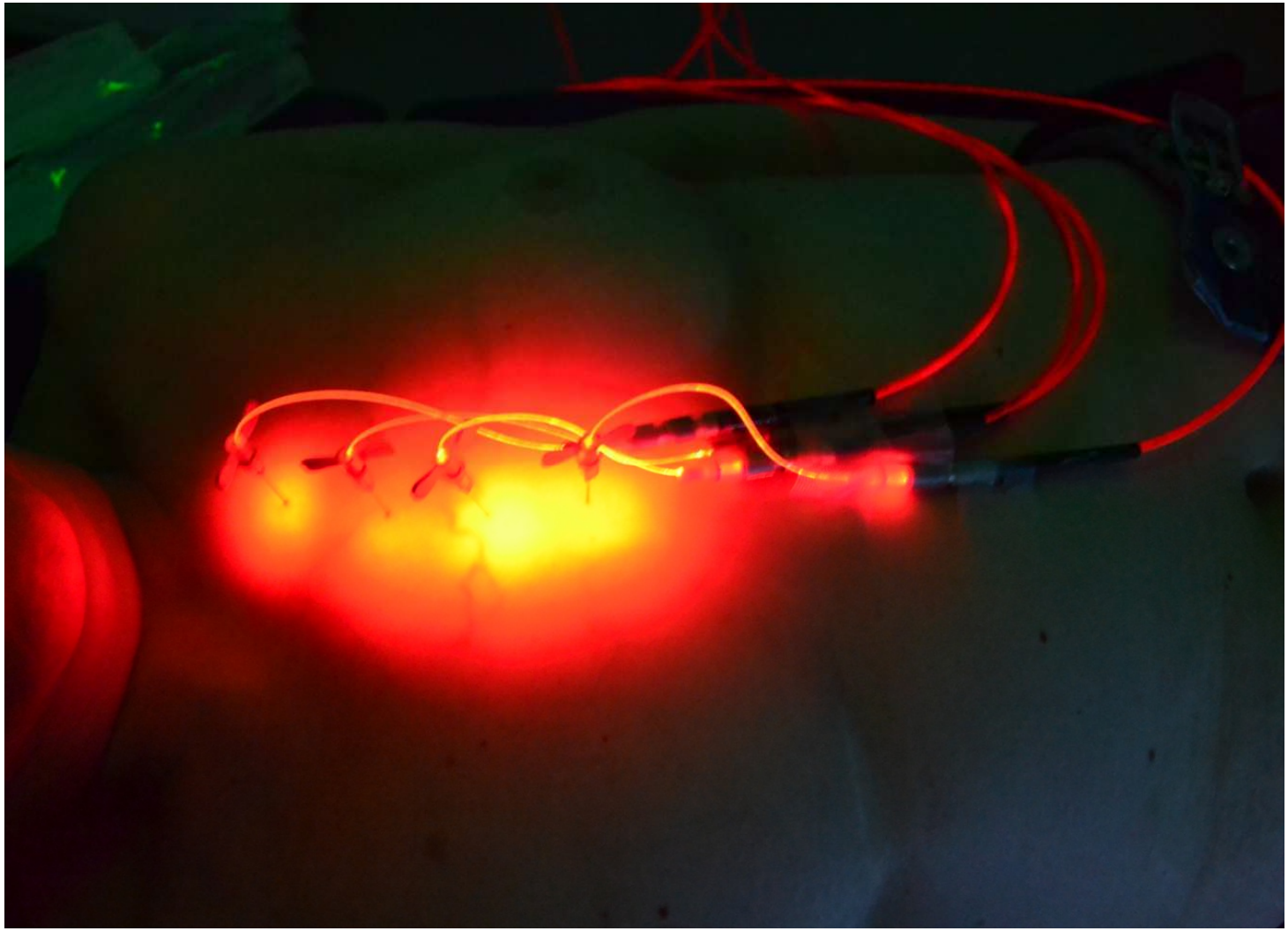
# Interstitial PDT of Breast Cancer:

# Interstitial PDT of Breast Cancer:

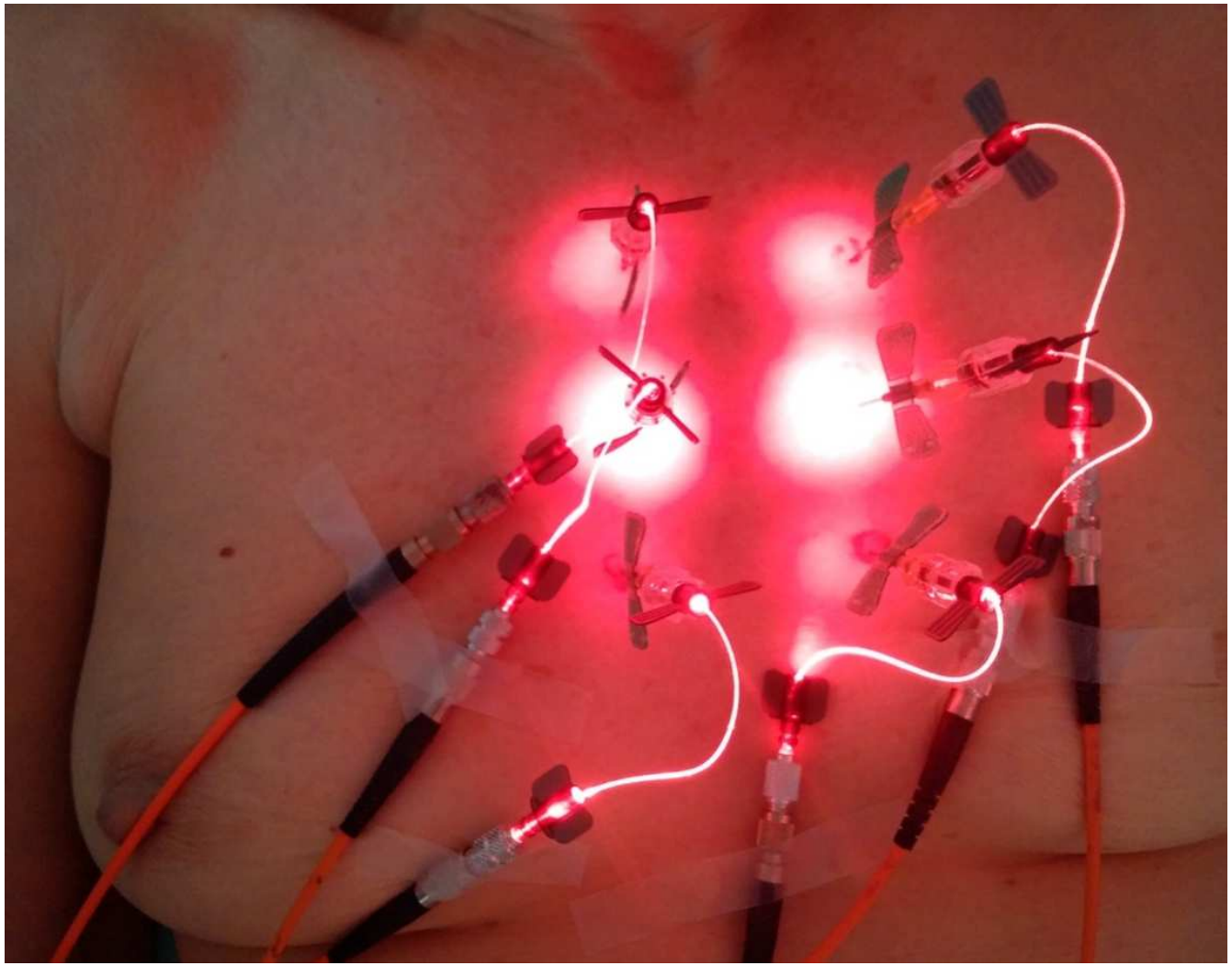




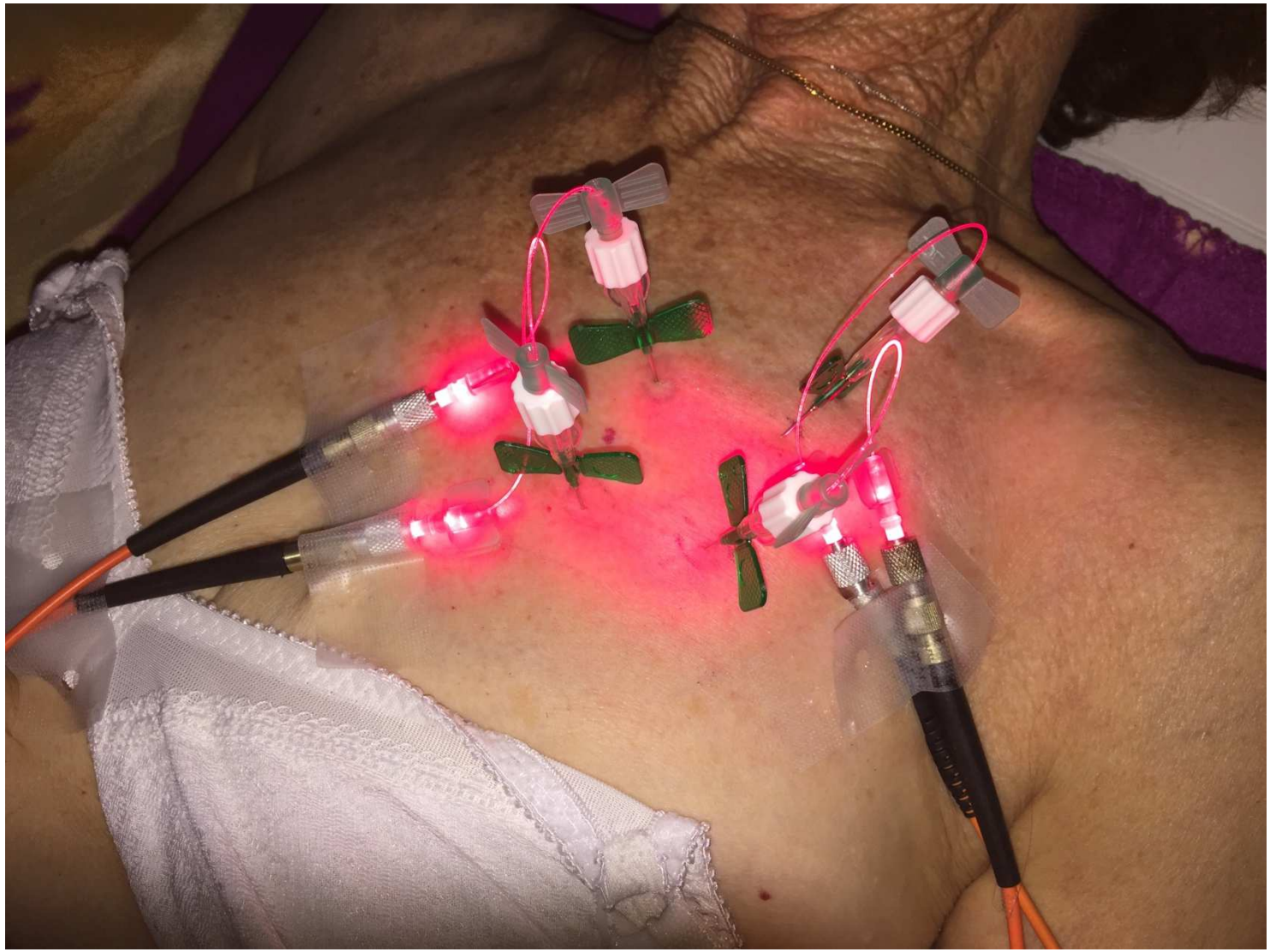
# Interstitial PDT of Breast Cancer with Mediastinal Lymph Metastases:



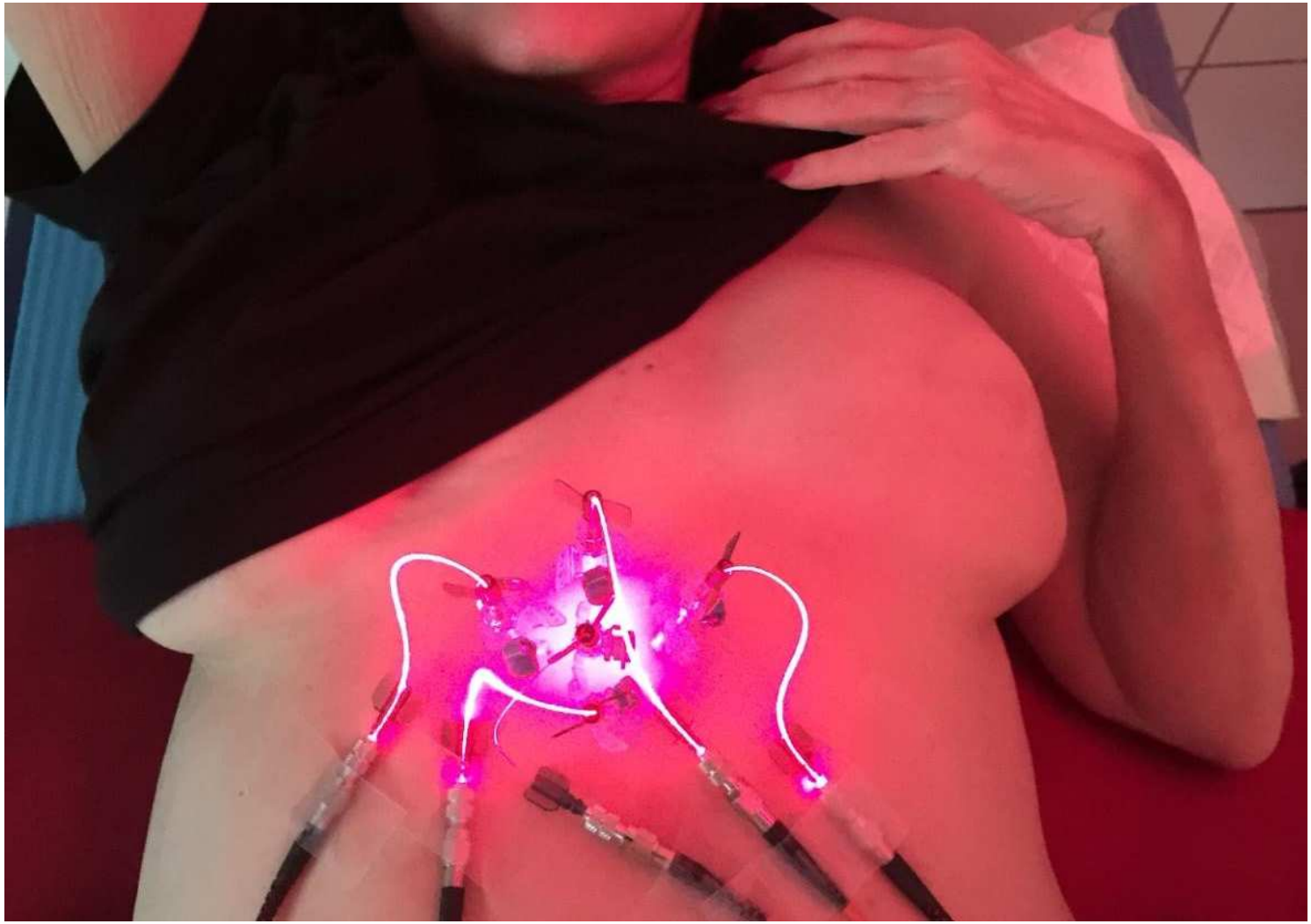
# Interstitial PDT of Mediastinal Metastases:



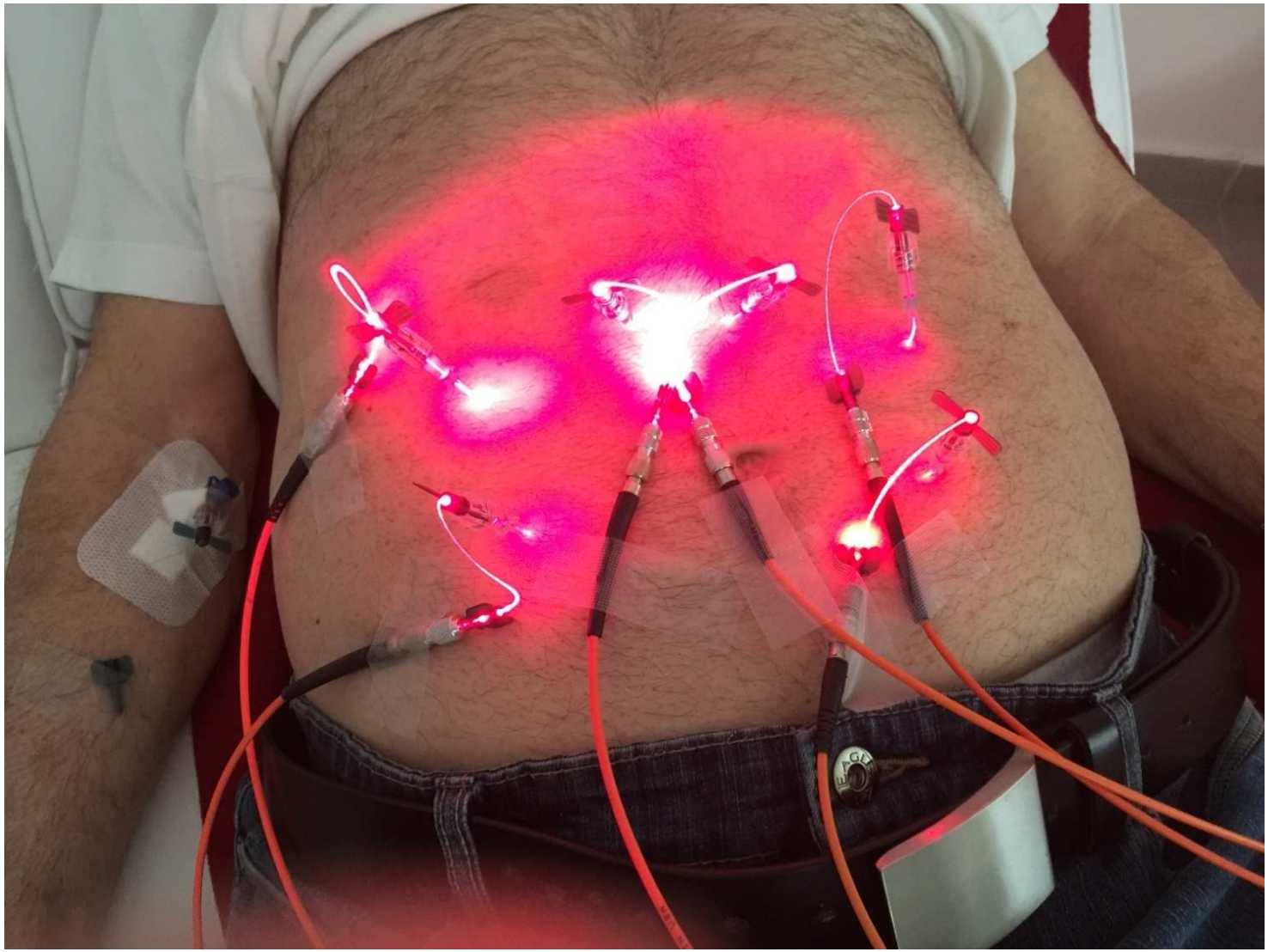
# Interstitial PDT of Lung Cancer:



# Interstitial PDT of Pancreatic Cancer:

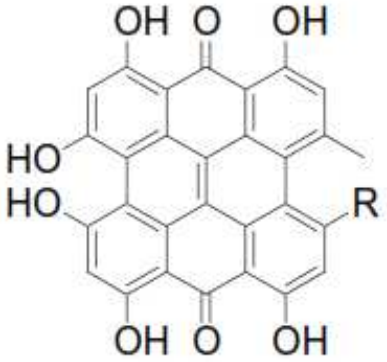


# Interstitial PDT of Peritoneal Carcinosis:

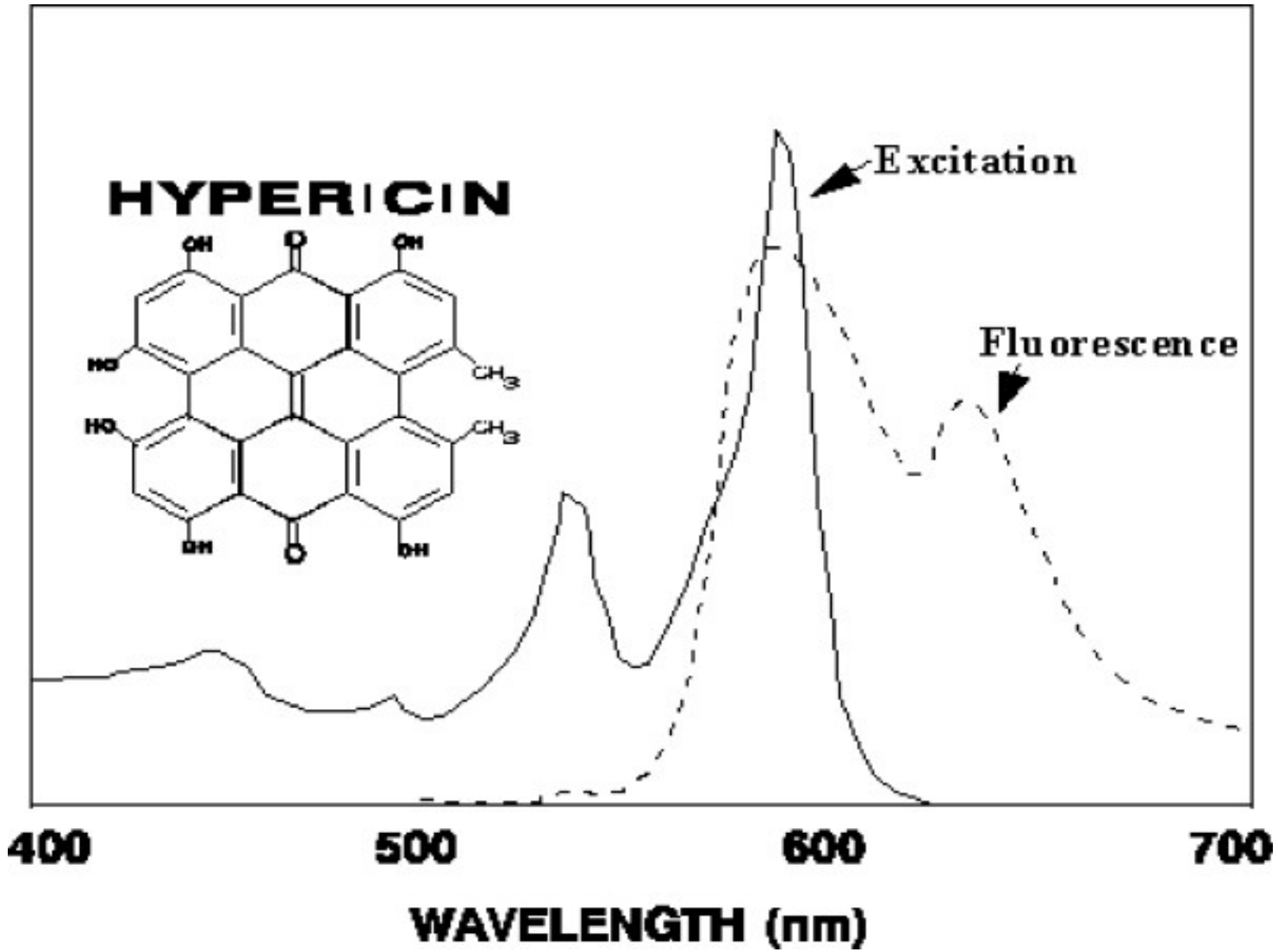


# 5. Other Natural Photosensitizers

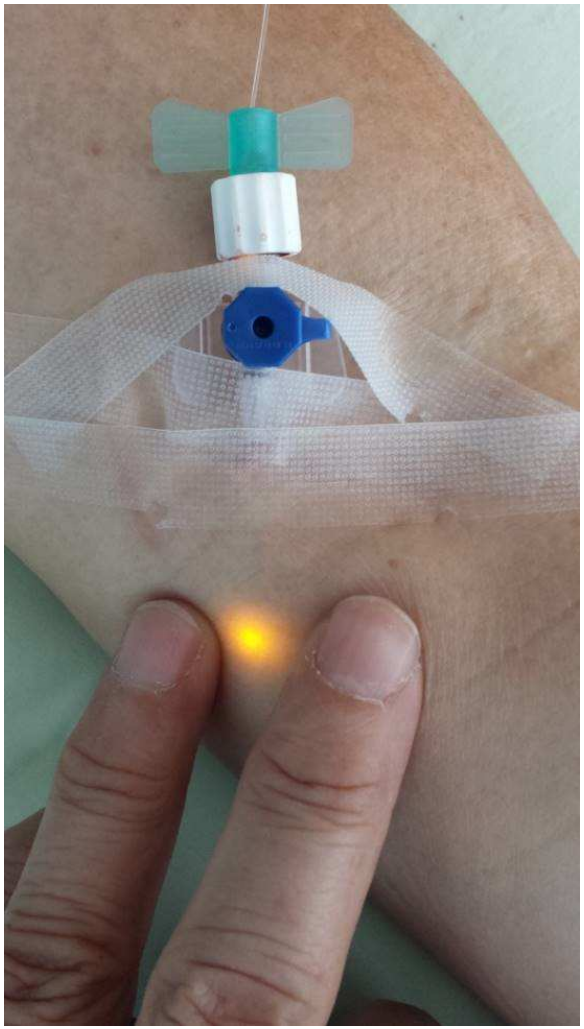
# Hypericin (St. John‘s Wort Plant):

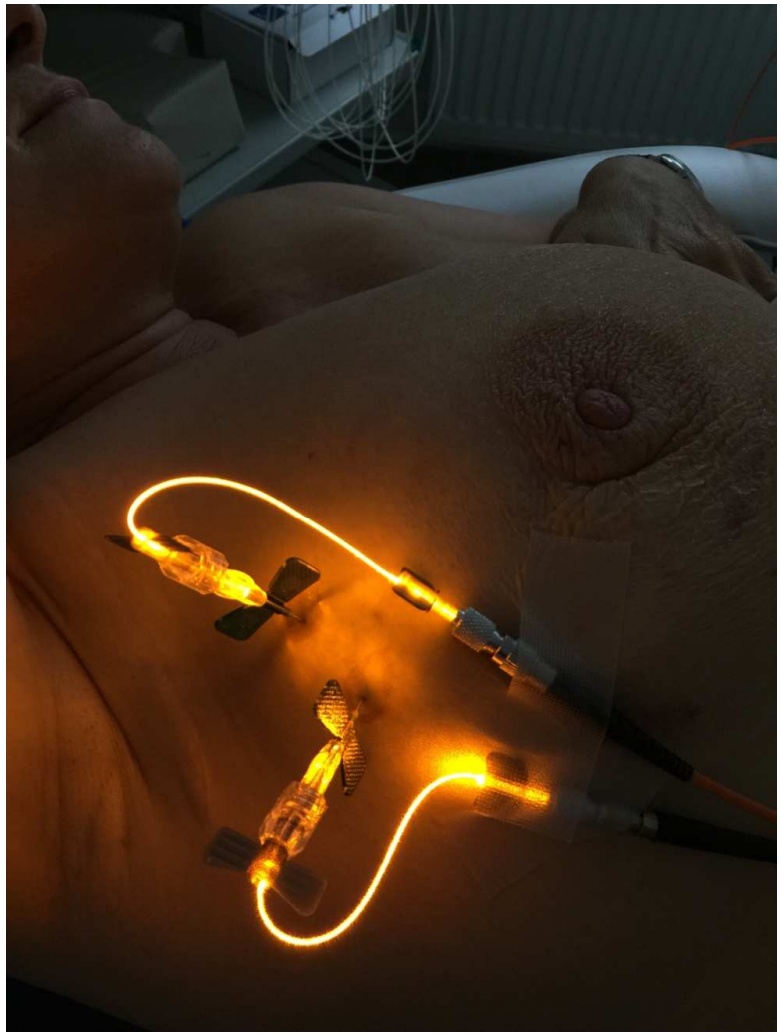



# Absorption Spectrum of Hypericin:

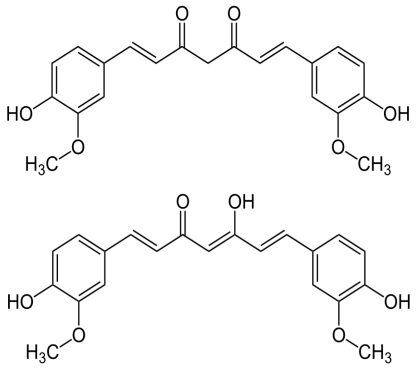


# PDT with Hypericin and Yellow Laser:

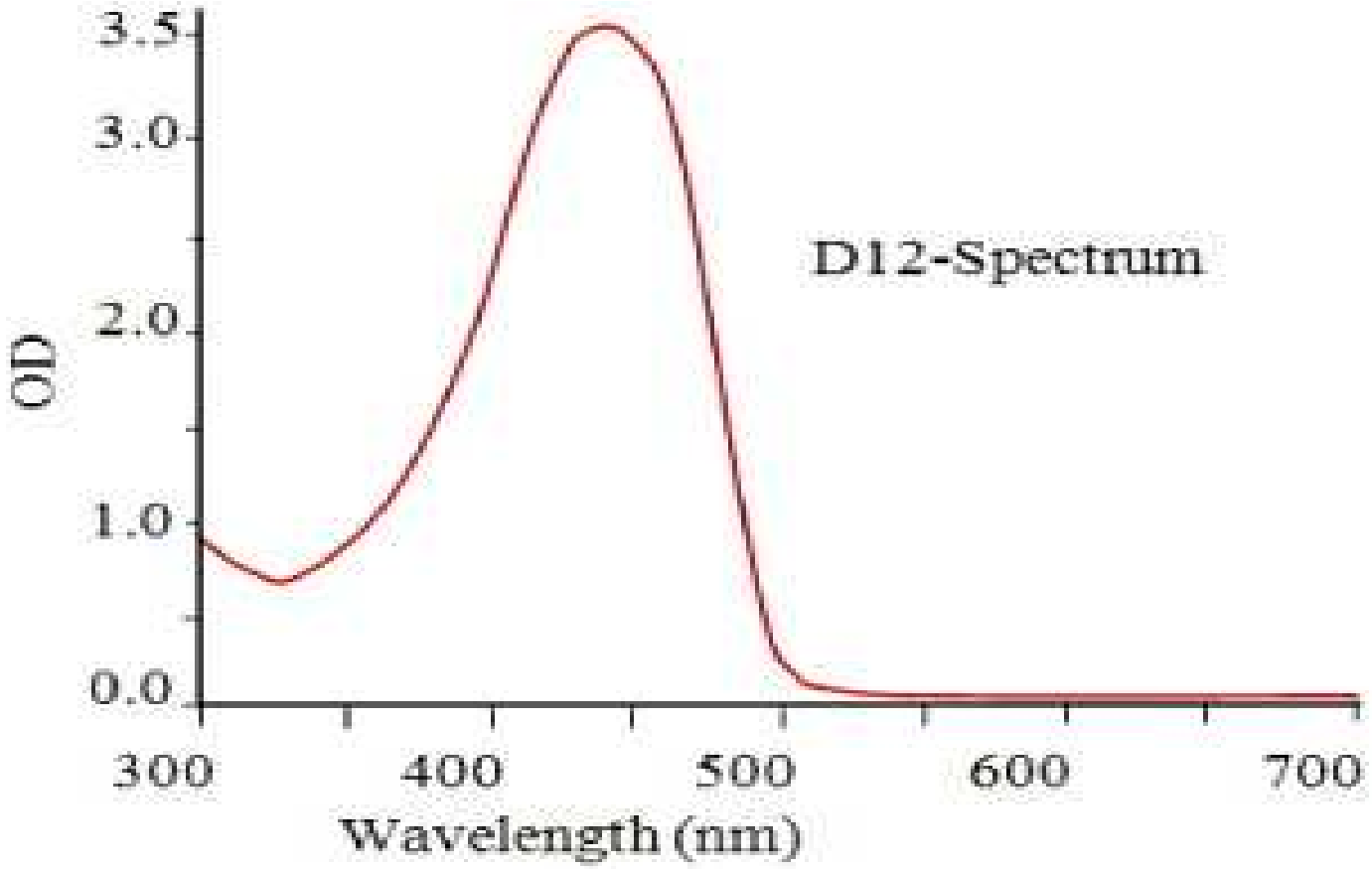




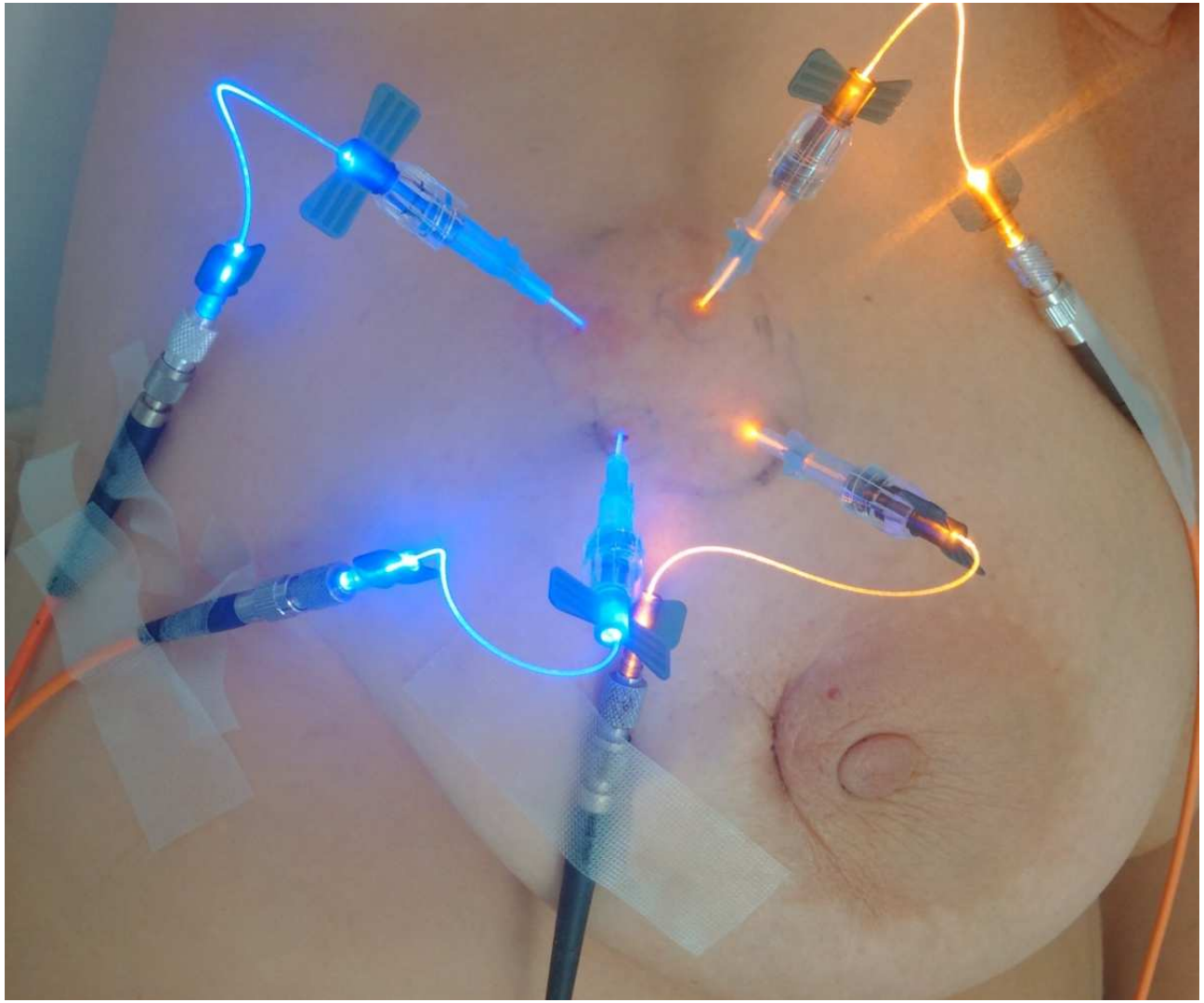
# Curcumin as Photosensitizer:




# Absorption Spectrum of Curcumin:



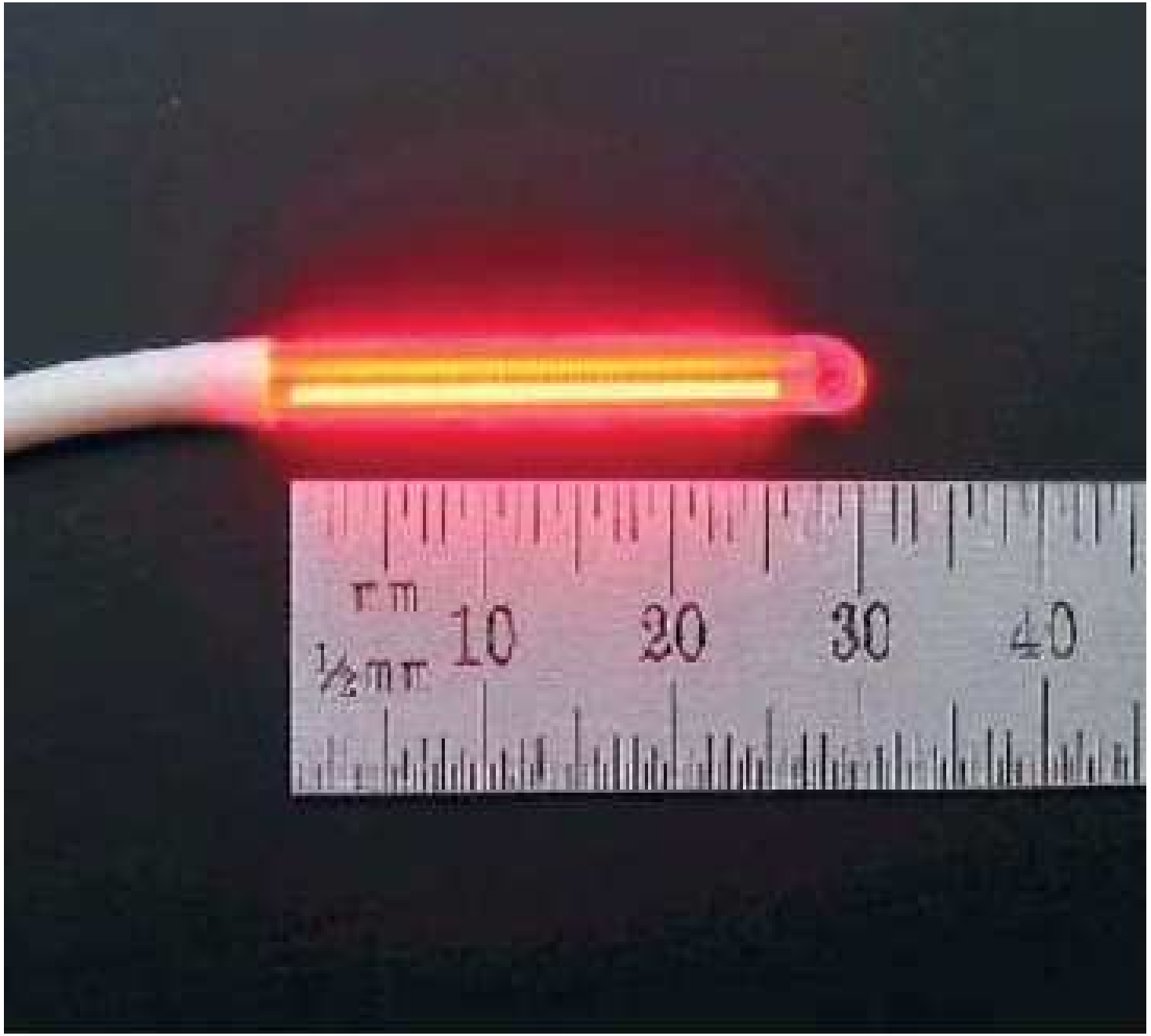
# Interstitial PDT with Hypericin (Yellow Laser) and Curcumin (Blue Laser):



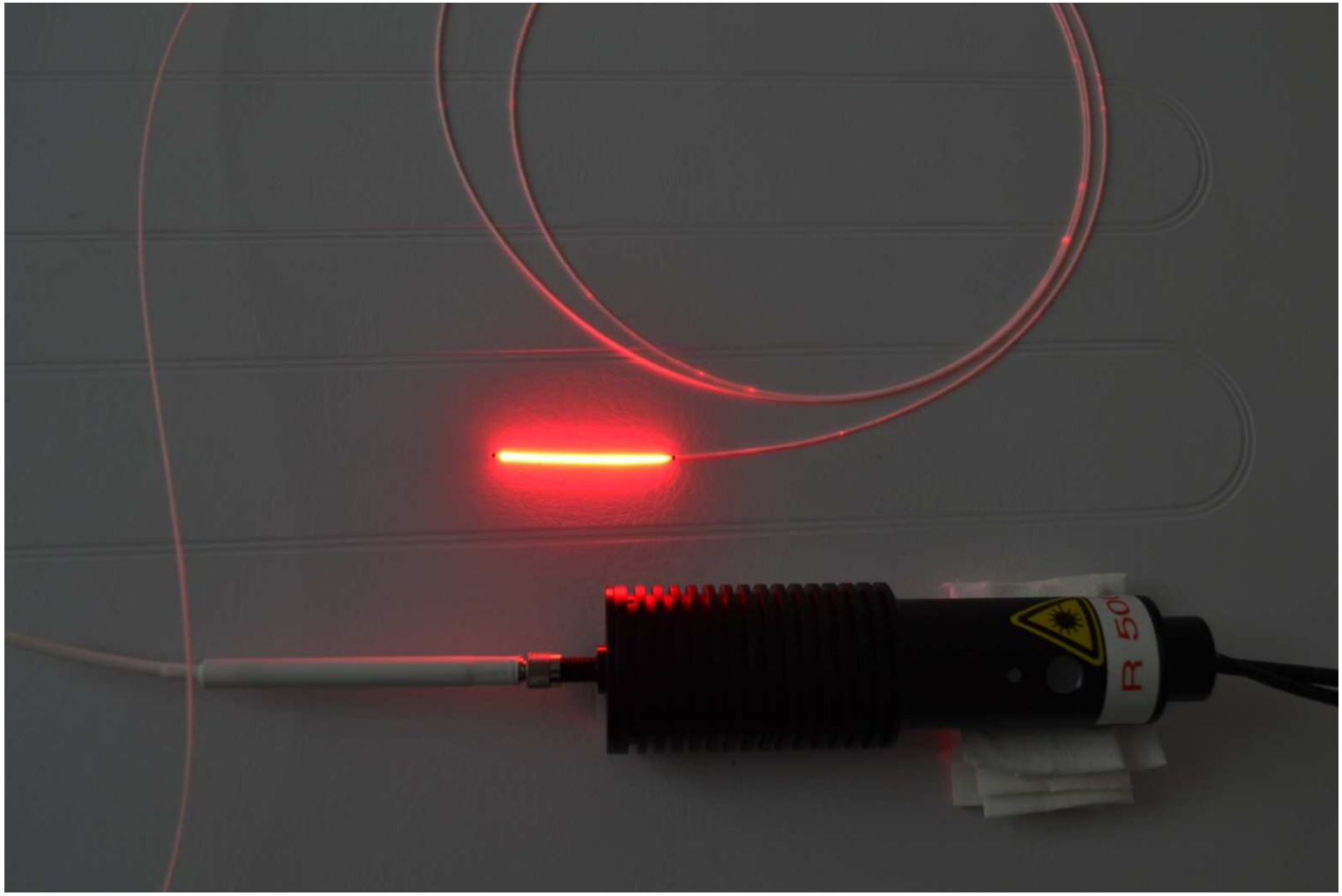
# 6. Applications in Urology

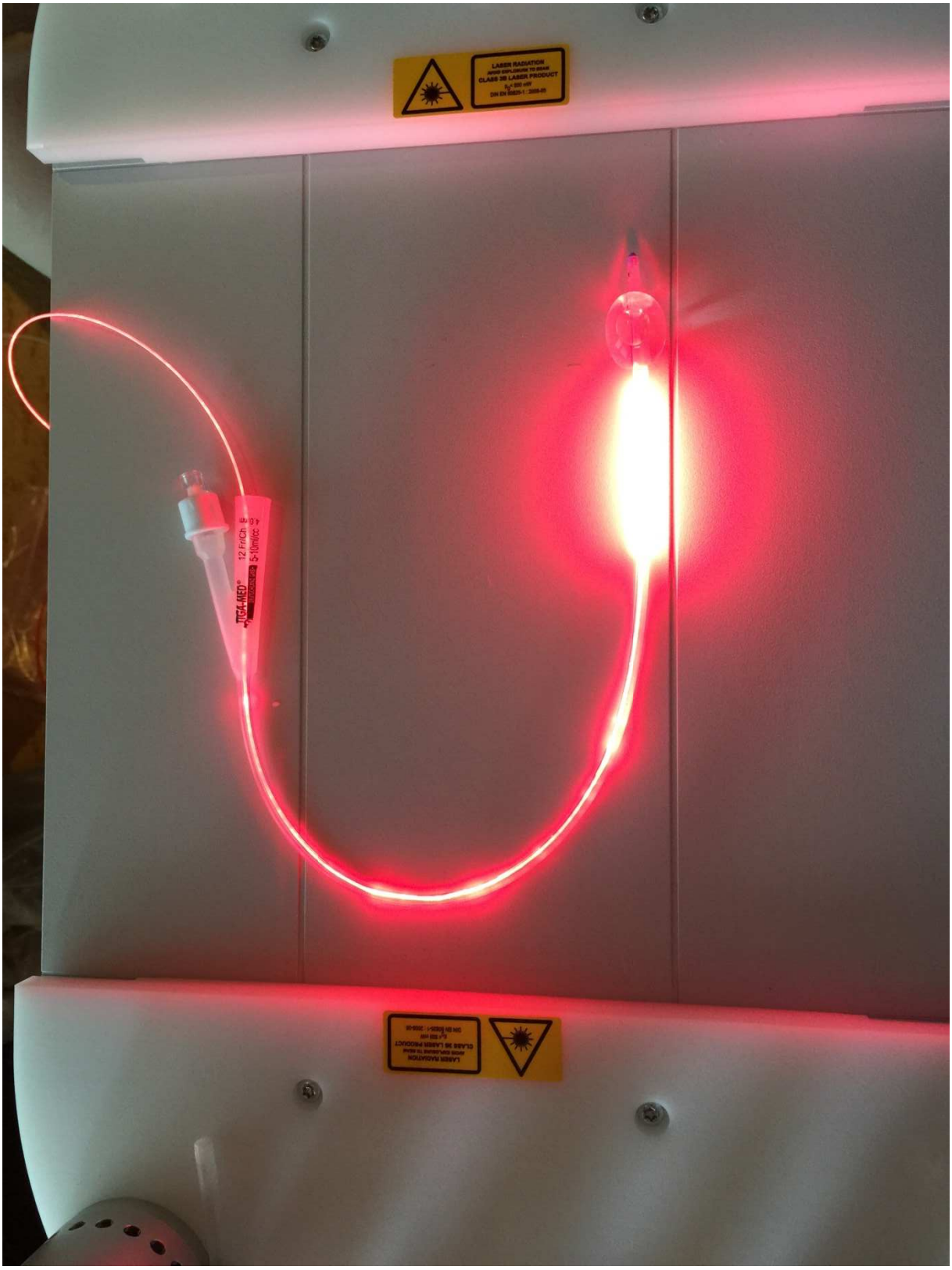

12 Fr/Ch
4.0mm
5-10ml/cc
TIGA-MED

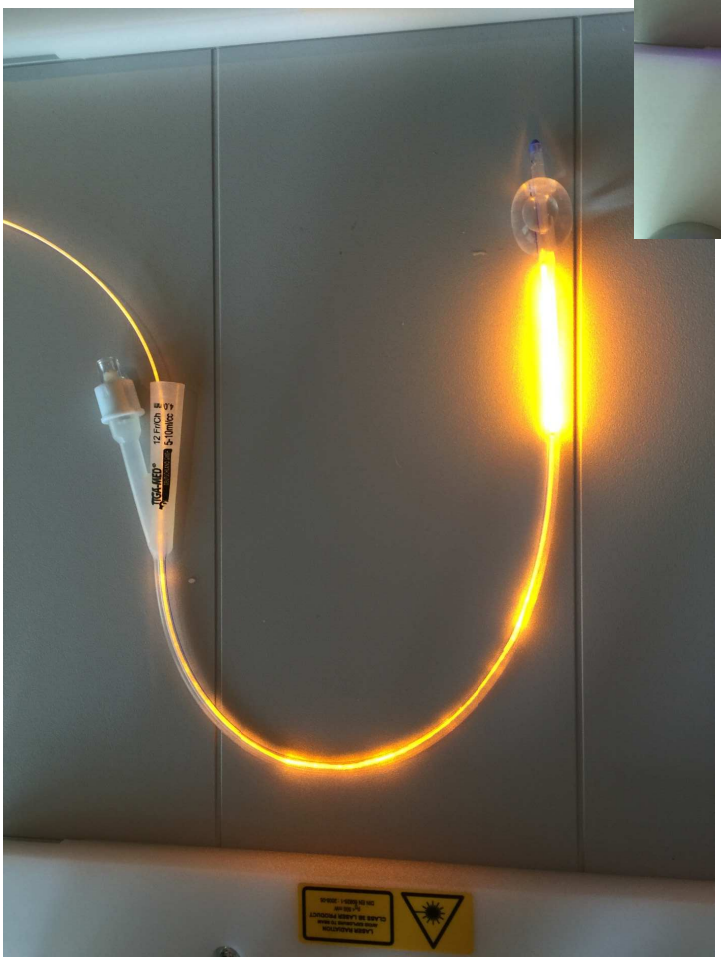
# Fiberoptic Catheter with Circular Irradiation (for prostate cancer):


cm
½ in
10
20
30
40

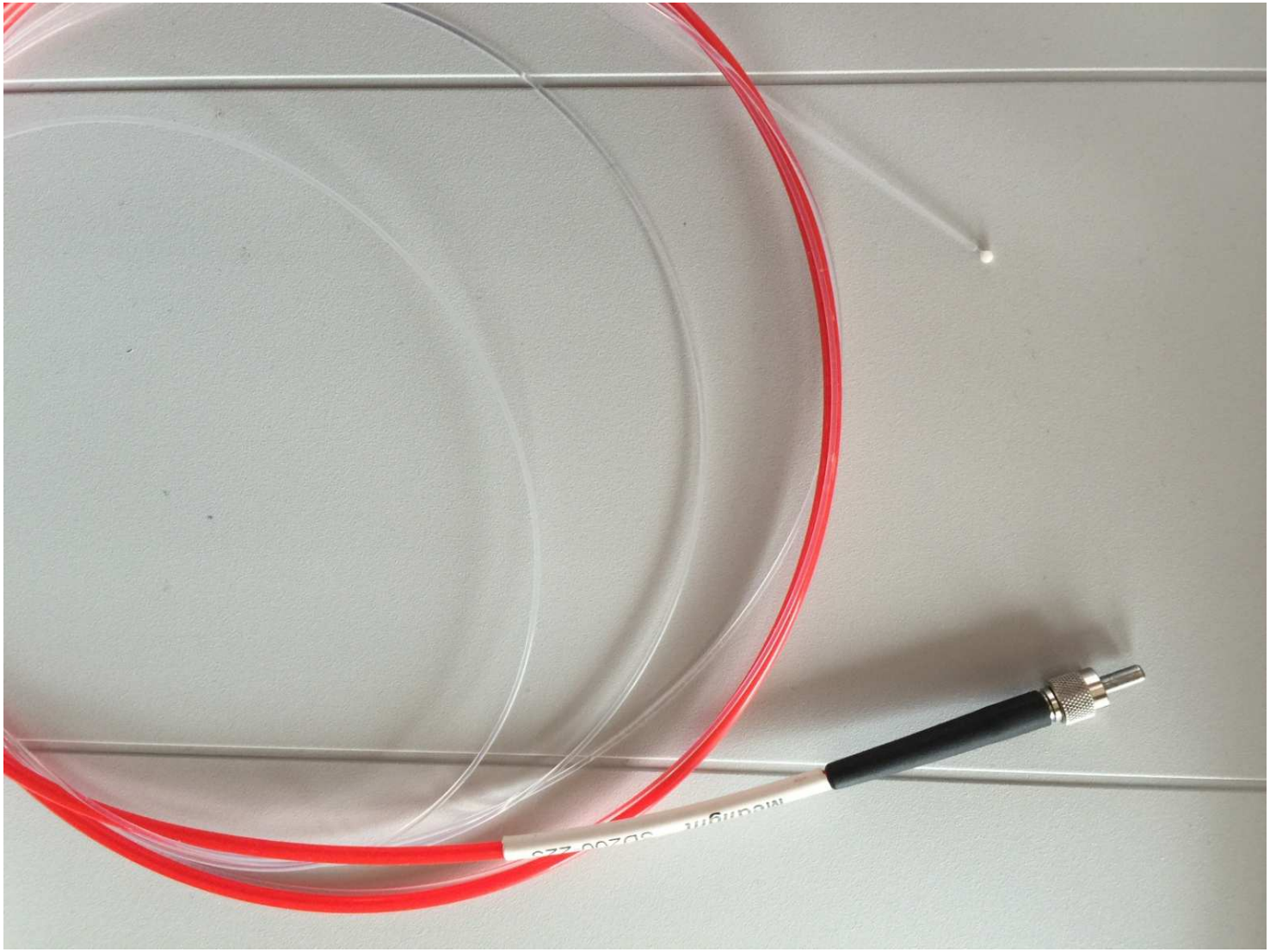
# 500 mW Red Laser 658 nm:

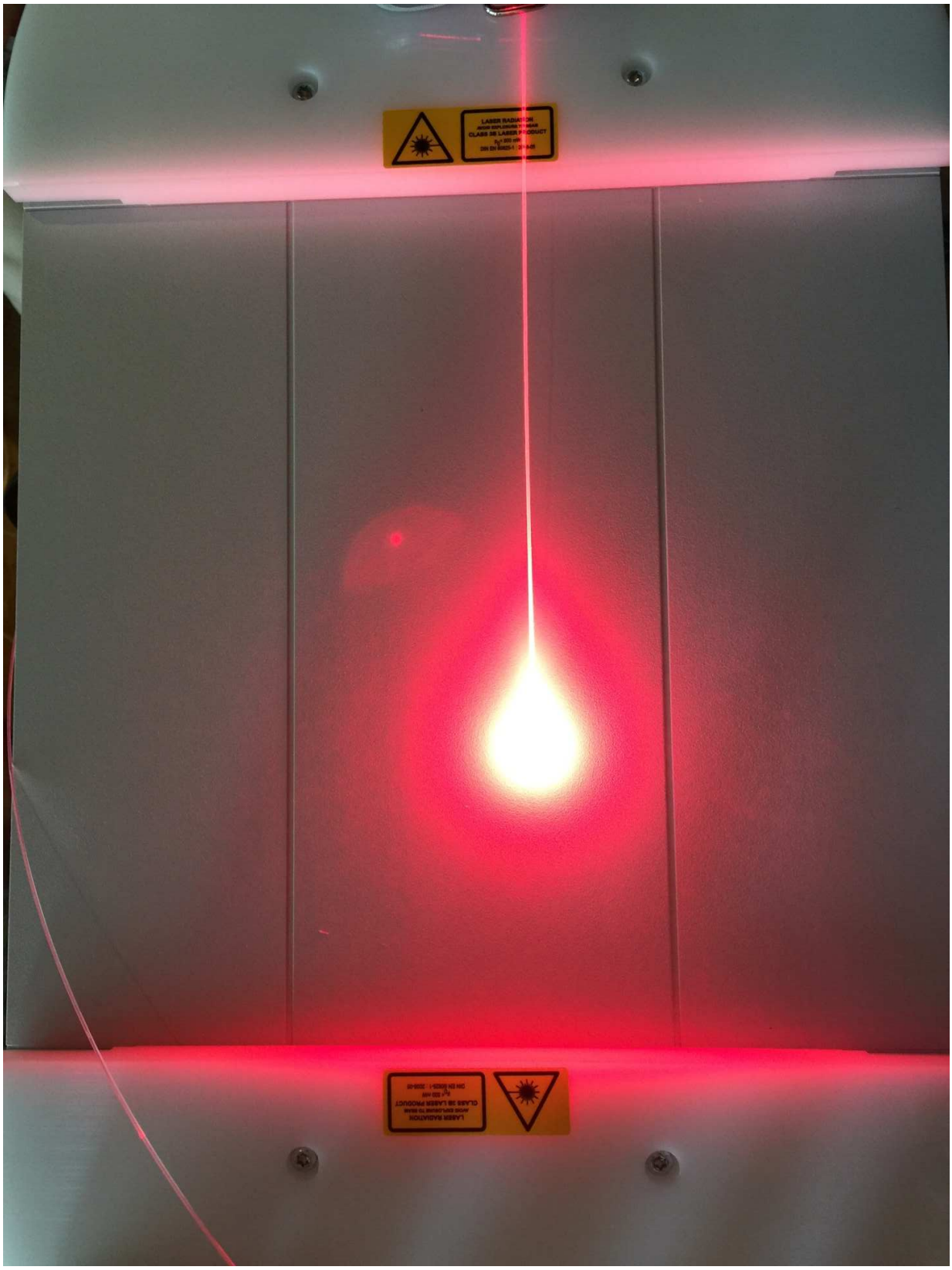


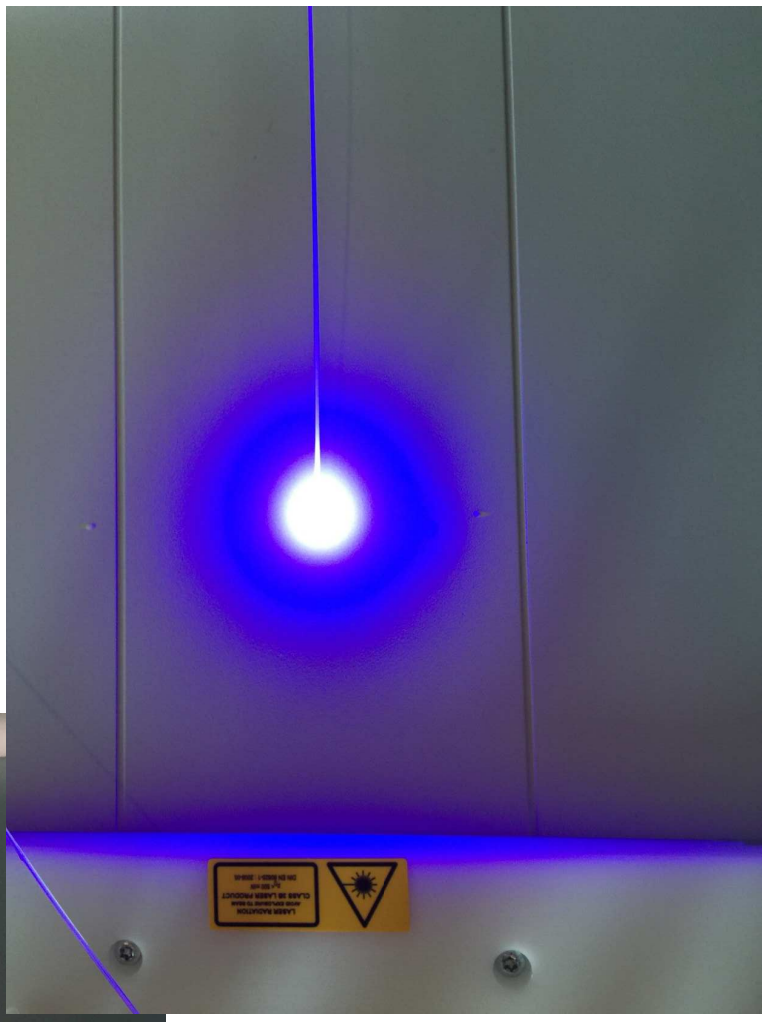

LASER RADIATION
CLASS 3B LASER PRODUCT
TIGA-MED
12 Fr/Ch
5-10ml

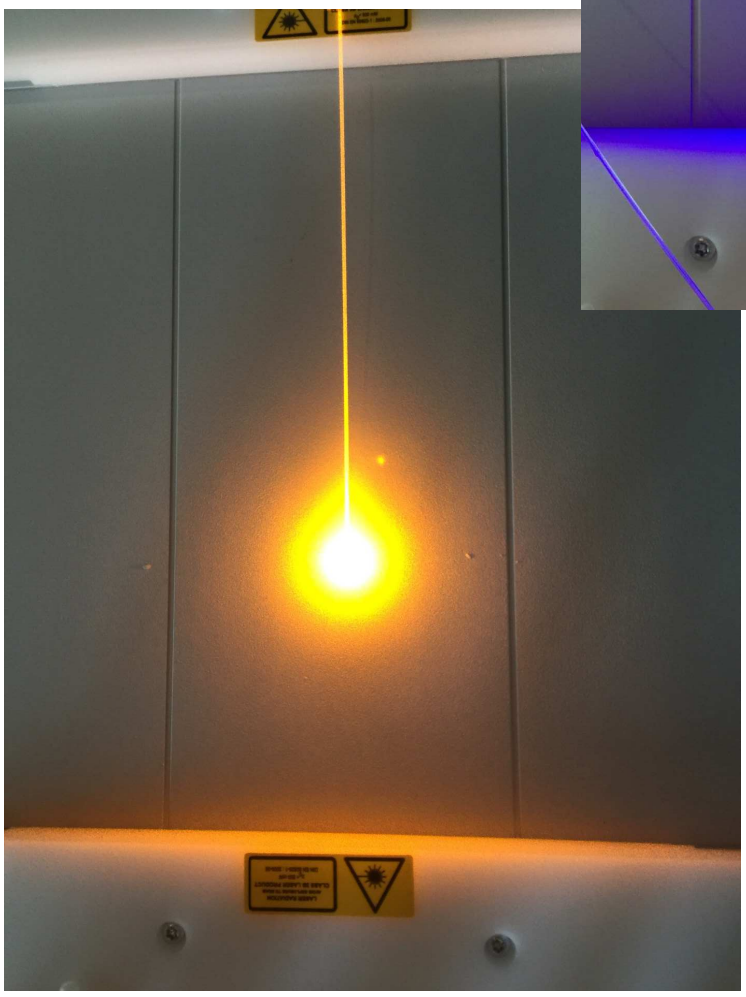


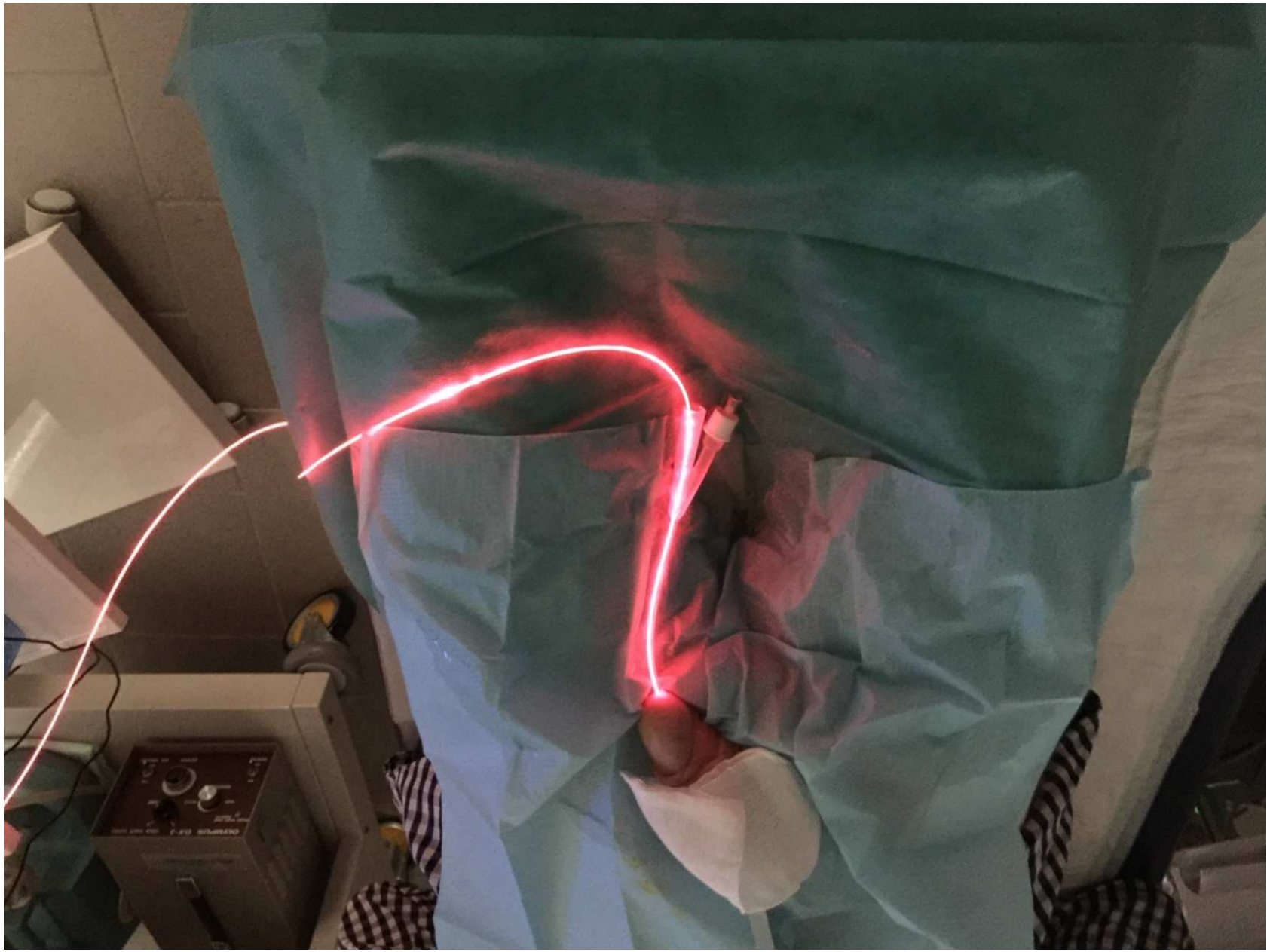
# Fiberoptic Catheter with Spheric Irradiation for Bladder Cancer:




LASER RADIATION
AVOID EXPLOSURE TO BEAM
CLASS 3B LASER PRODUCT

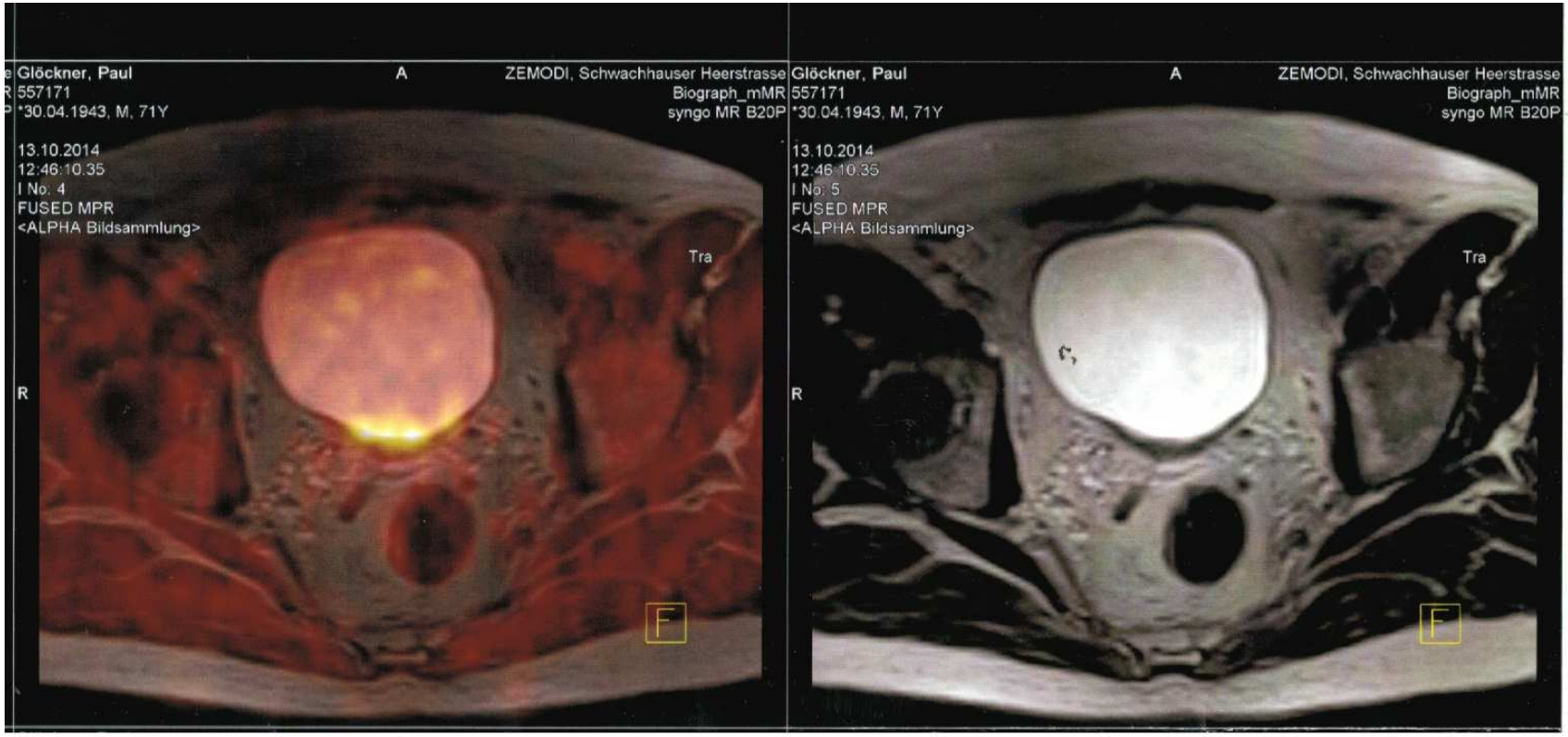




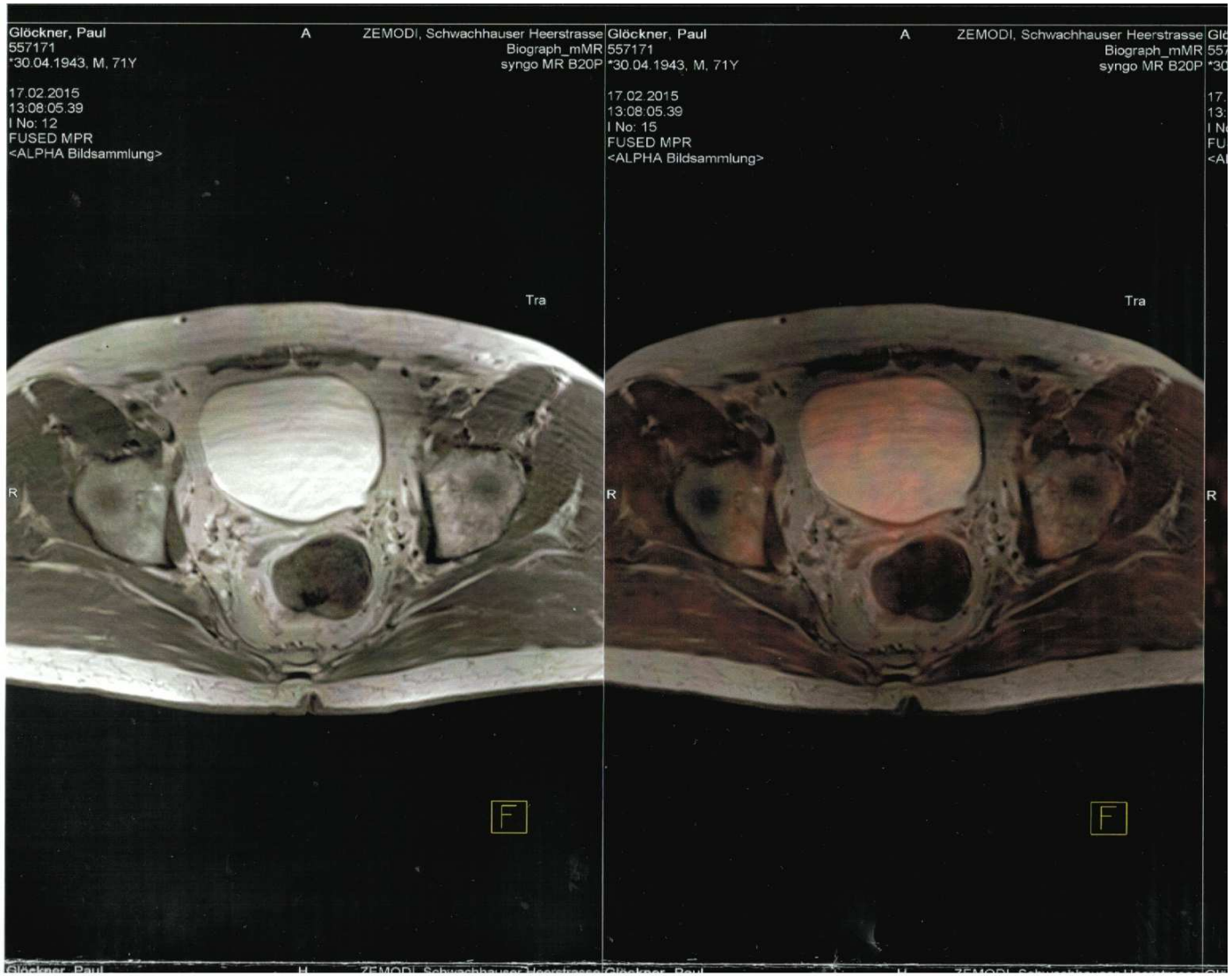


# Bladder Cancer:

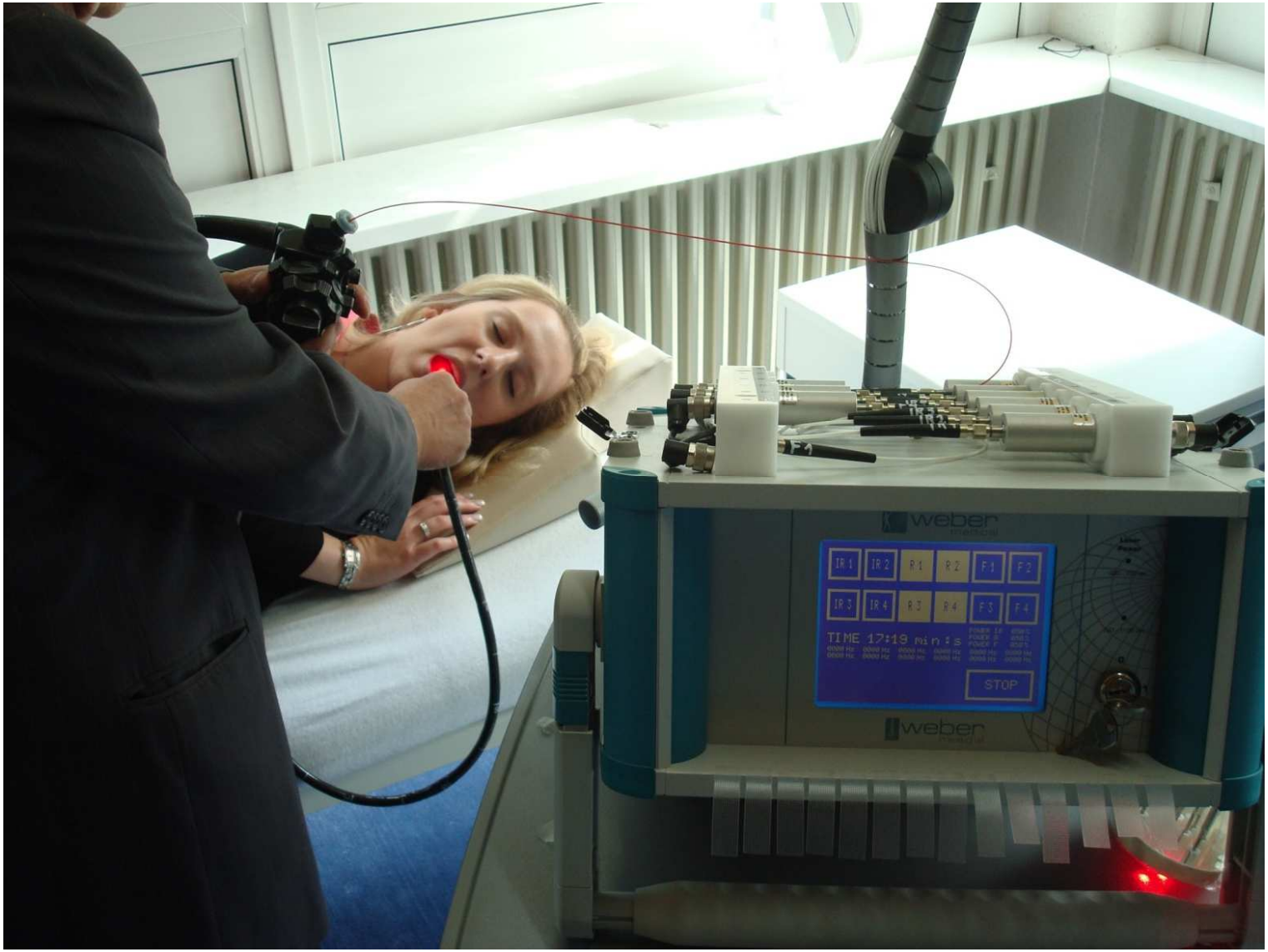
# Bladder Cancer PET 10/2014
# Before Treatment:

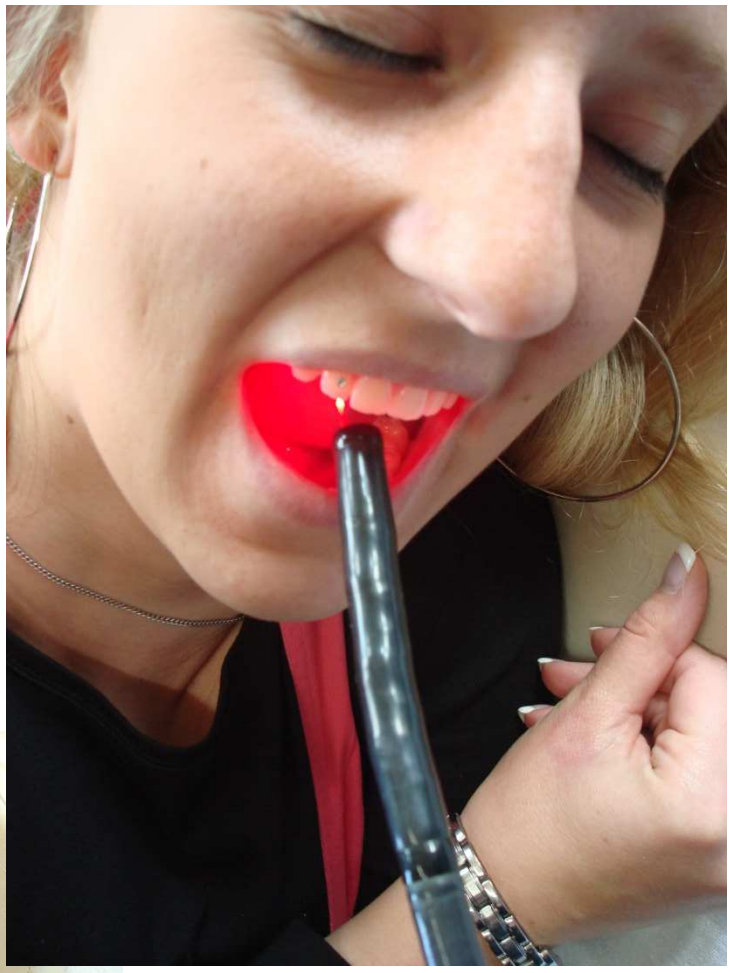


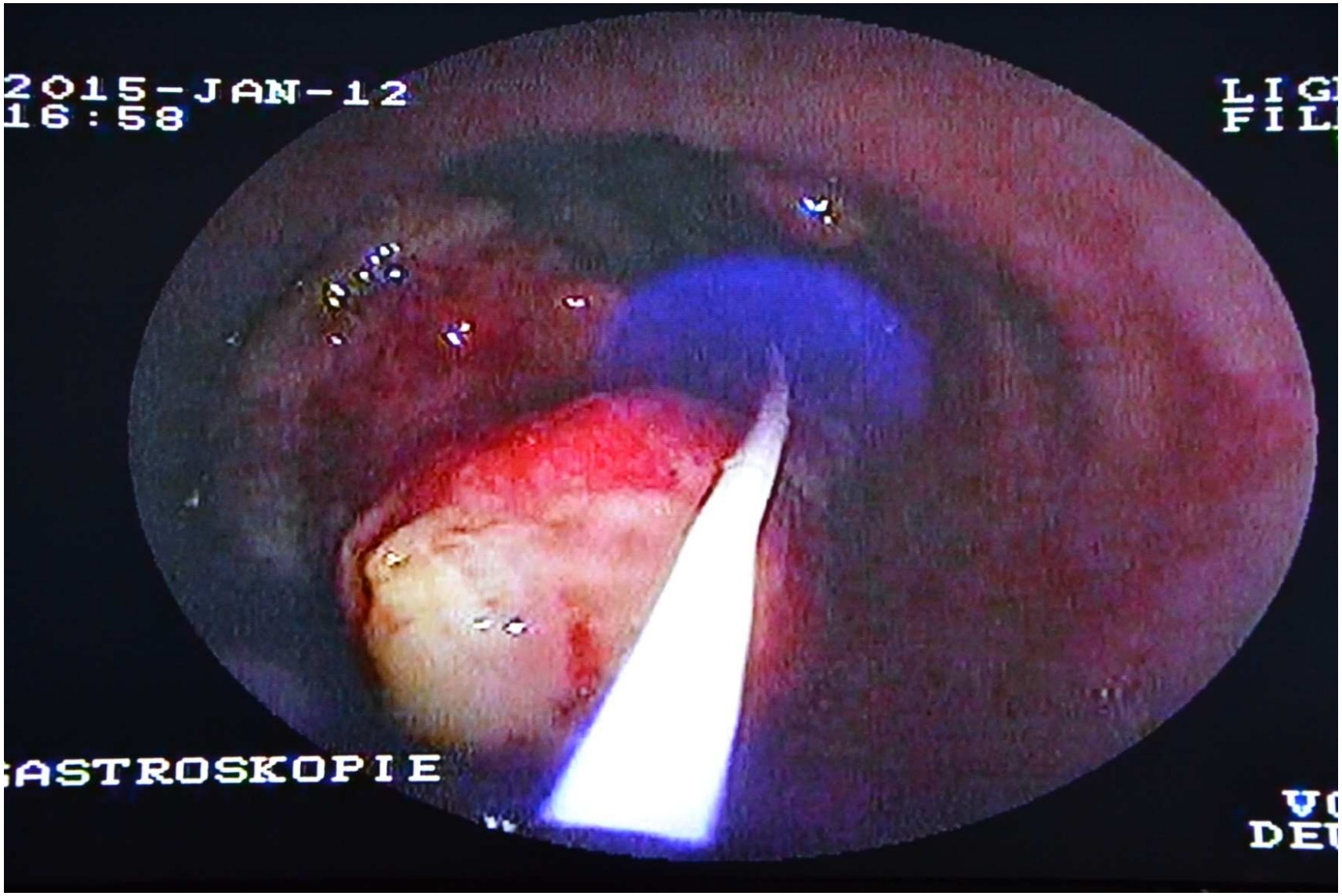
# Bladder Cancer 2/2015 after PDT:

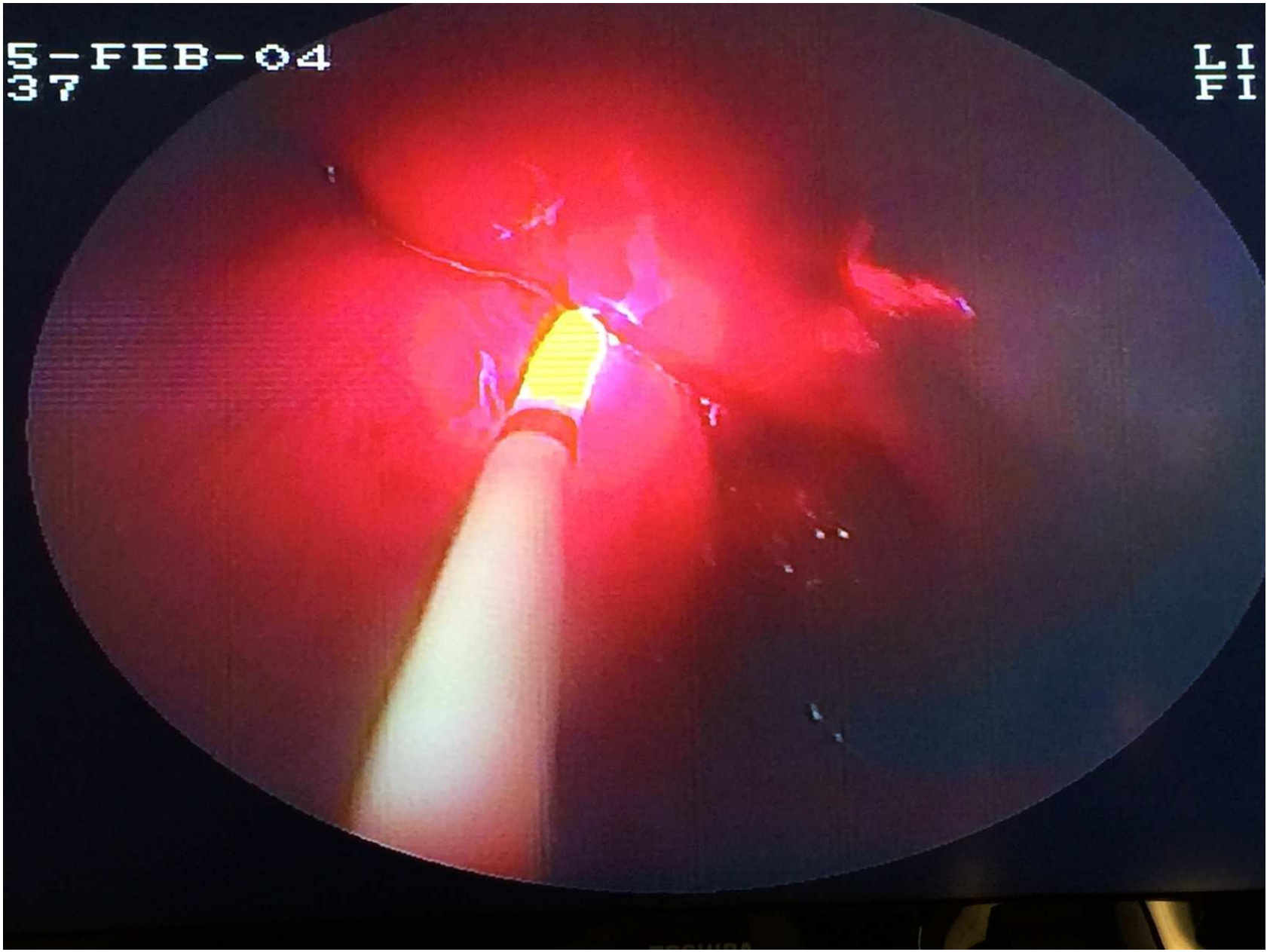


# Endoscopic PDT :



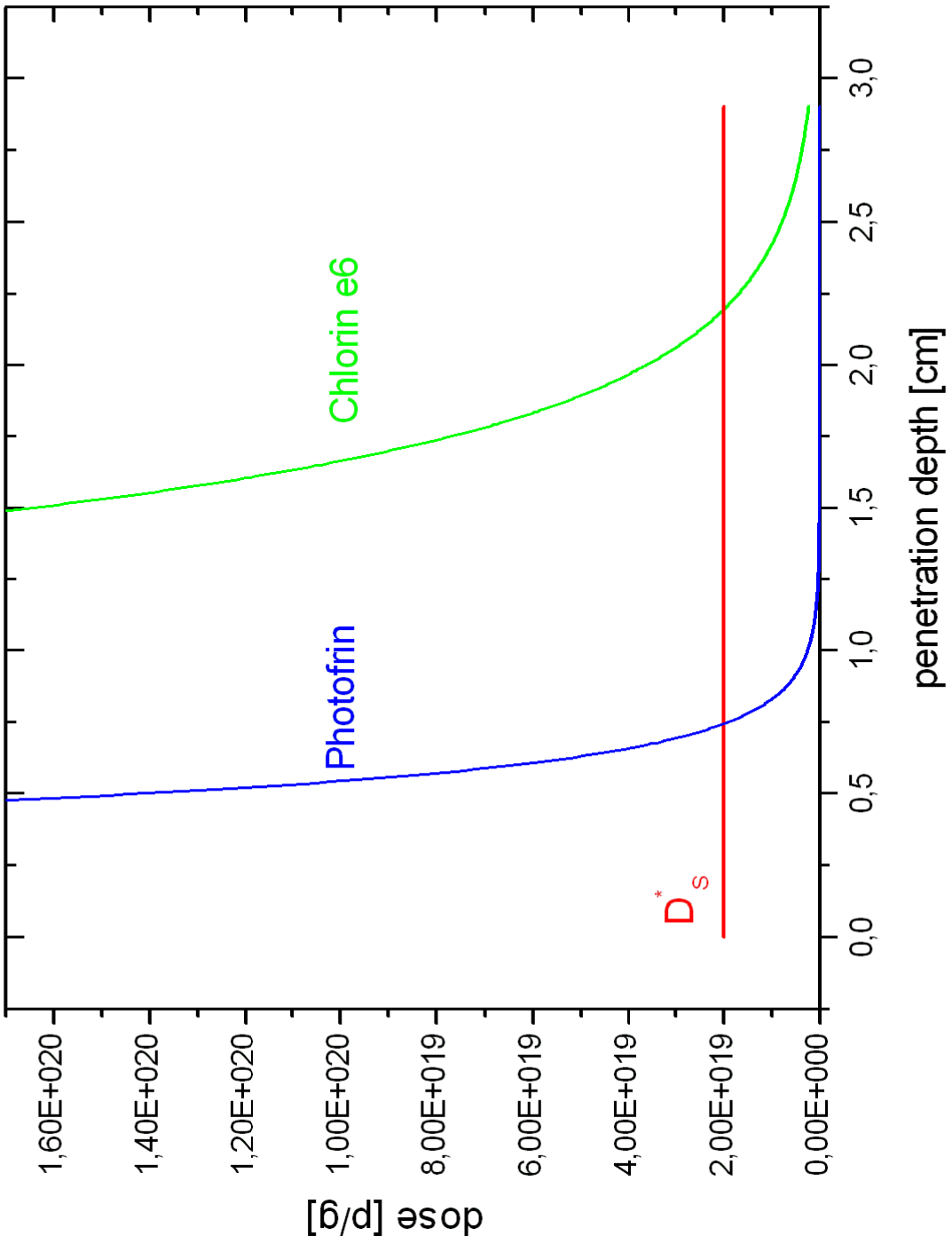



2015-JAN-12
16:58
LIG
FIL
ASTROSKOPIE
DE


5-FEB-04
37
LI
FI

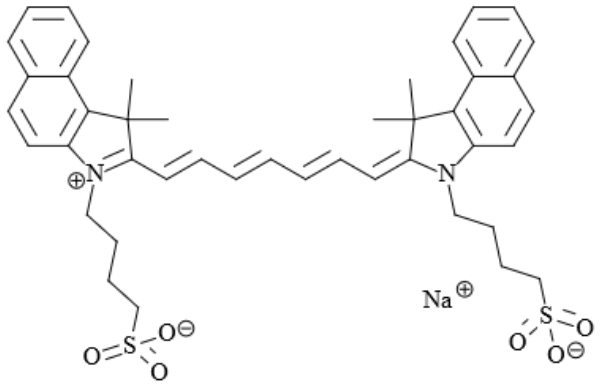
# Limitations of PDT with Chlorin E6, Hypericin and Curcumin:

- Limited succes by using red, blue and yellow lasers due to limited penetration depth (max. 2,5 cm for red laser)
- Limited tumor size: max 2,5 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


dose [p/g]
penetration depth [cm]
Chlorin e6
Photofrin
$D_s^*$
0,00E+000
2,00E+019
4,00E+019
6,00E+019
8,00E+019
1,00E+020
1,20E+020
1,40E+020
1,60E+020
0,0
0,5
1,0
1,5
2,0
2,5
3,0

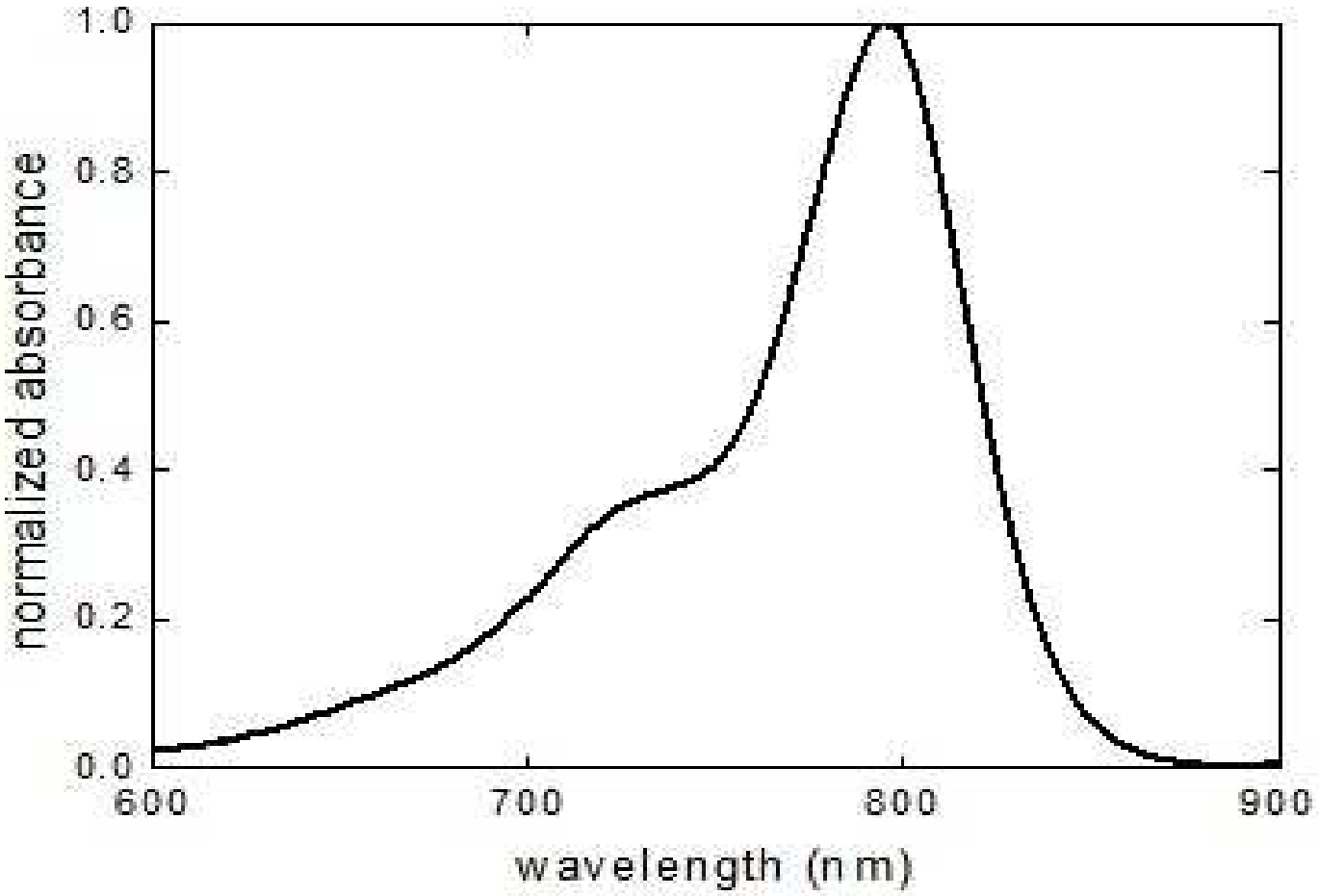
# 7. Systemic and Interstitial PDT with Liposomal Indocyaninegreen (ICG)

# Liposomal Indocyaninegreen (ICG):

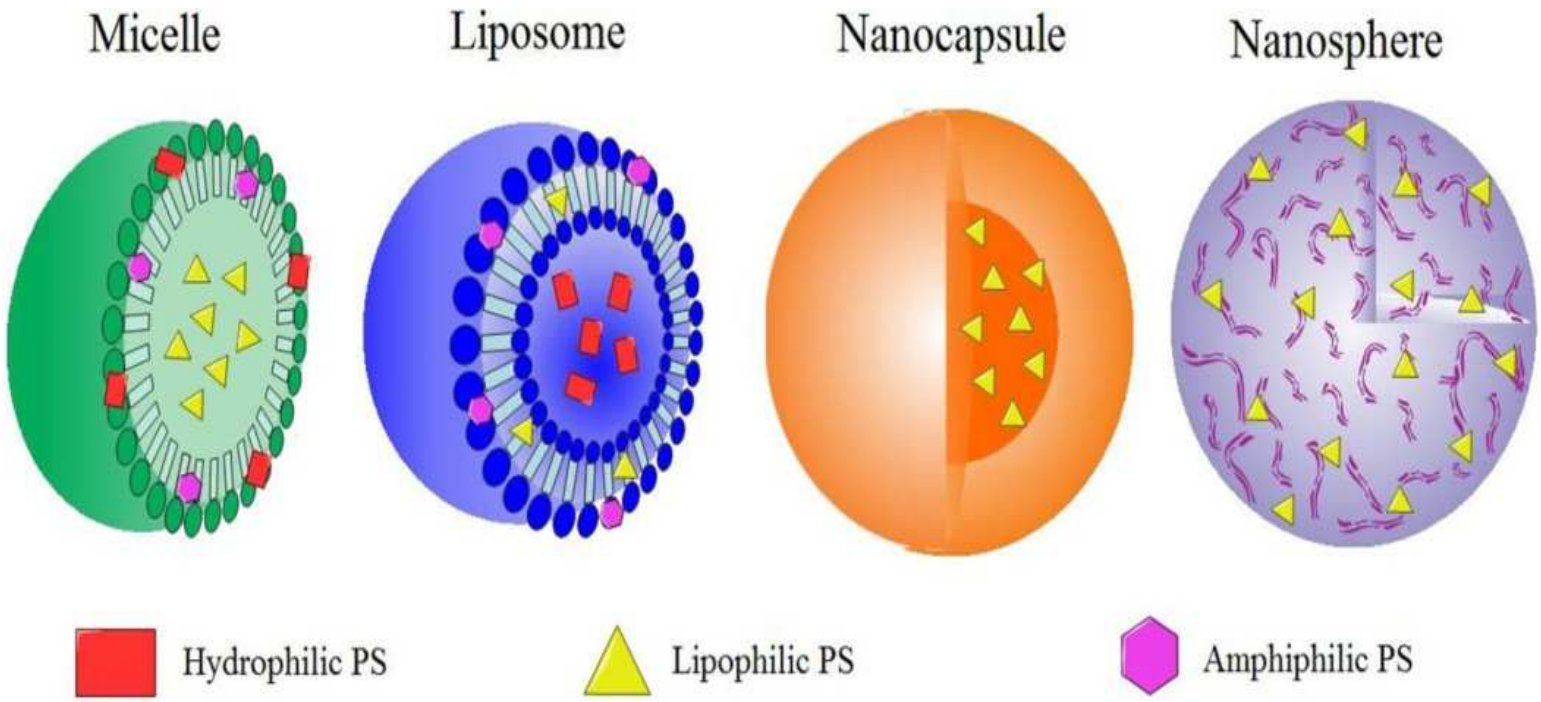


- **Indocyaninegreen** is a fluorecent green dye and absorbs light in the infrared range (810 nm)
- It is applied intravenously
- Indocyaninegreen is an approved drug in fluorescense diagnostics for blood flow in eyes, liver and heart (even FDA-approved in the US)
- Pure Indocyaninegreen binds to plasma proteins and is removed from the body in about 30 minutes (cannot be used as photosensitizer)
- **In liposomal form** it is integrated in tumor cells and can thus be used for PDT with infrared laser

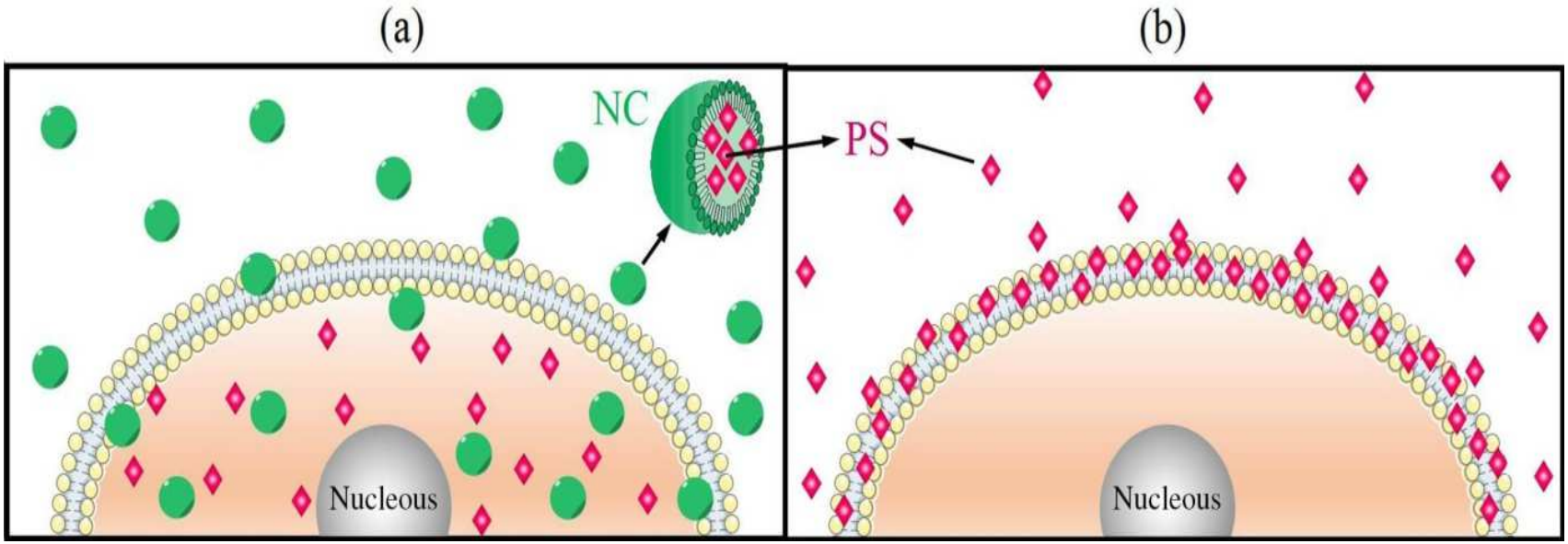
# Absorption Spectrum of Indocyaninegreen:



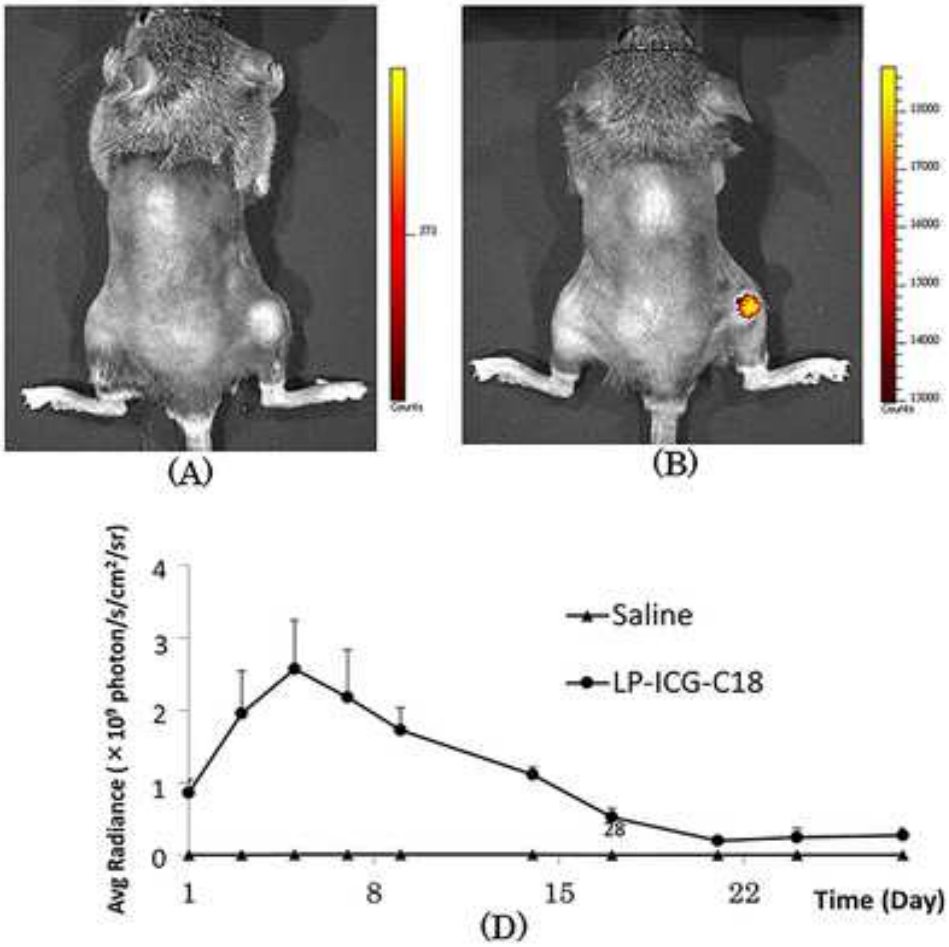
# Nanoparticles for Transport of Photosensitizers:



# Cellular Integration of a Lipophile Photosensitizer:



# Pharmacokinetics of Lip-ICG:



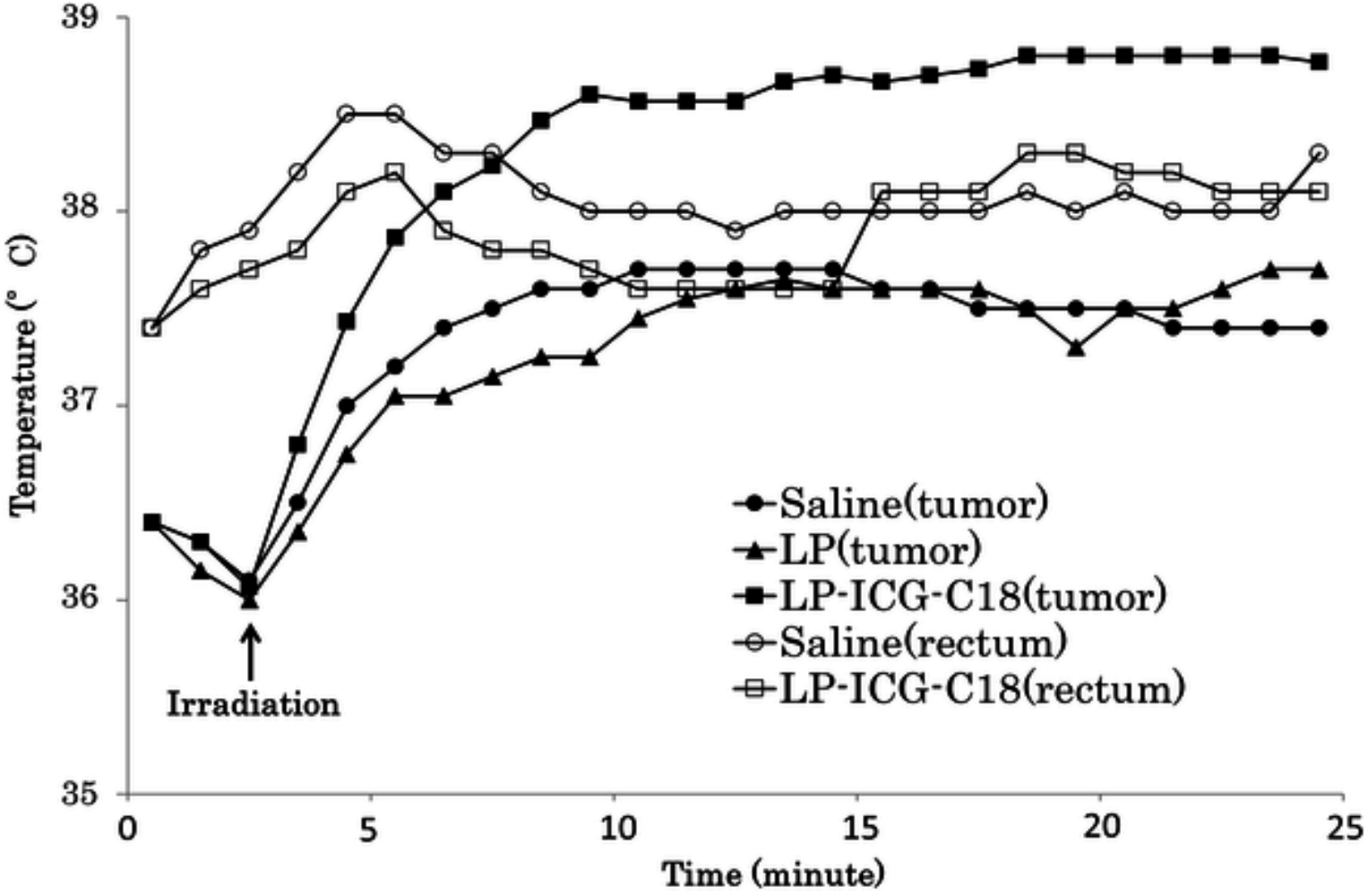

NIR fluorescence images of tumor bearing mice 24 hours after injection of (A) saline and (B) LP-ICG-C18. (C) NIR fluorescence images of the organs 24 hours after injection of LP-ICG-C18. (D) Photon count of tumor bearing mice.

Maruyama T, Akutsu Y, Suganami A, Tamura Y, Fujito H, et al. (2015) Treatment of Near-Infrared Photodynamic Therapy Using a Liposomally Formulated Indocyanine Green Derivative for Squamous Cell Carcinoma. PLoS ONE 10(4): e0122849. doi:10.1371/journal.pone.0122849 http://journals.plos.org/plosone/article?id=info:doi/10.1371/journal.pone.0122849

# Selective “Over-Heating” of Tumor Tissue by Infrared Stimulated Indocyaninegreen:

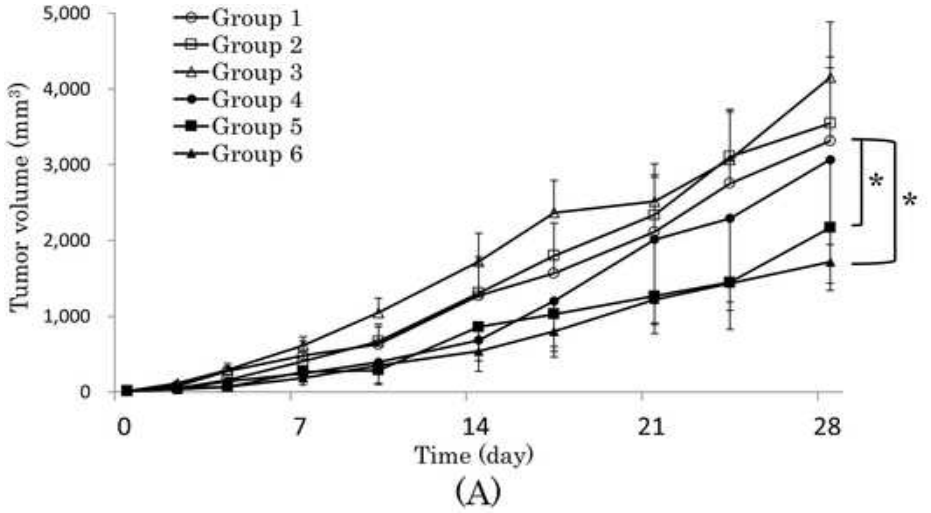
- ICG absorbs infrared light of 810 nm
- Infrared light has the highest penetration depth into tissue
- Besides activation of the ICG with production of **singlet oxygen** tumor tissue will be warmed up (**overheating effect**)
- This effect supports the photodynamic reaction without damage of surrounding healthy tissue
- The combination of overheating and PDT leads to an improved reaction with “tumor melting“
- This is called **“Photothermodynamic therapy (PTDT)“** or **“Photothermoablation“** of tumor tissue

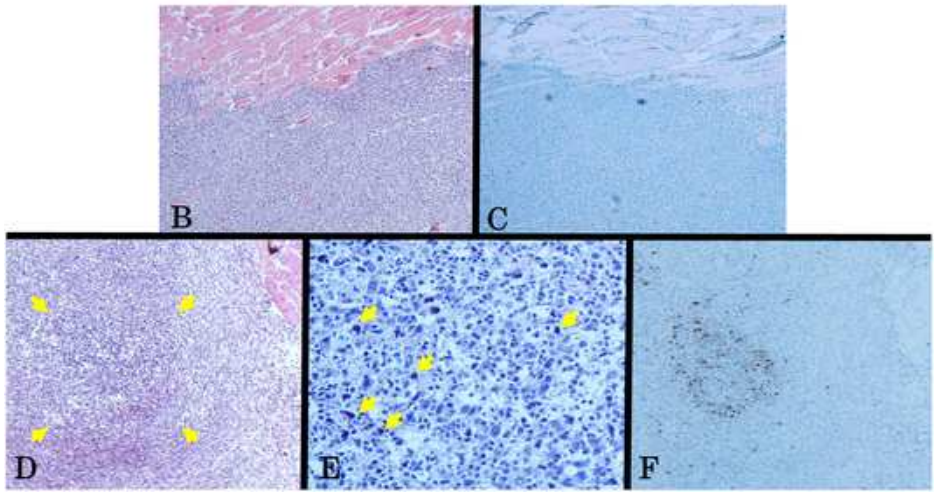
# The Transition of Temperature in the Tumor and Rectum during Irradiation:




Maruyama T, Akutsu Y, Suganami A, Tamura Y, Fujito H, et al. (2015) Treatment of Near-Infrared Photodynamic Therapy Using a Liposomally Formulated Indocyanine Green Derivative for Squamous Cell Carcinoma. PLoS ONE 10(4): e0122849. doi:10.1371/journal.pone.0122849
http://journals.plos.org/plosone/article?id=info:doi/10.1371/journal.pone.0122849

# Antitumor Effect of Lip-ICG-C18 in SCCVII Subcutaneous Mice Model:



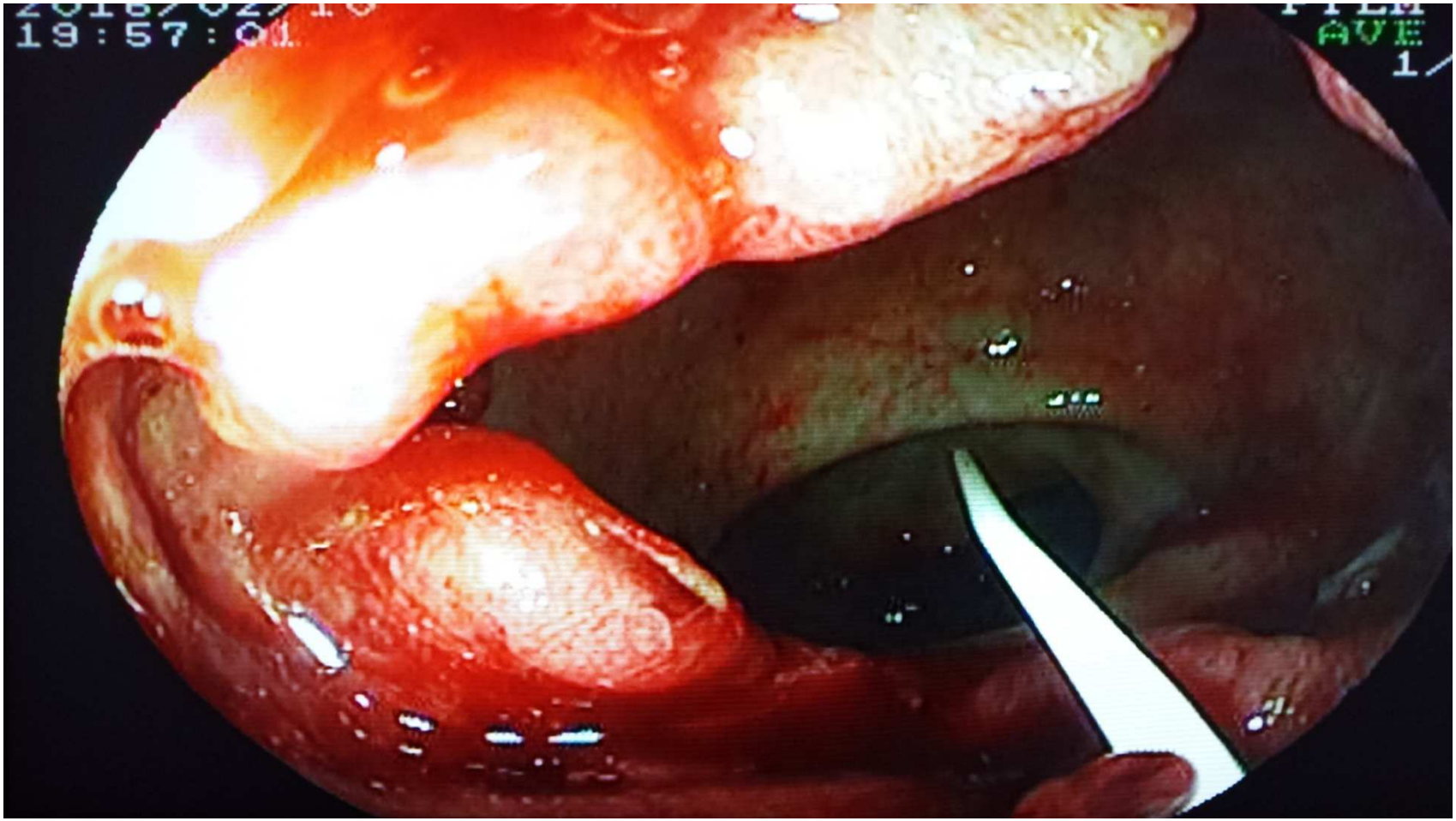




Maruyama T, Akutsu Y, Suganami A, Tamura Y, Fujito H, et al. (2015) Treatment of Near-Infrared Photodynamic Therapy Using a Liposomally Formulated Indocyanine Green Derivative for Squamous Cell Carcinoma. PLoS ONE 10(4): e0122849. doi:10.1371/journal.pone.0122849
http://journals.plos.org/plosone/article?id=info:doi/10.1371/journal.pone.0122849

# Liposomal Indocyaninegreen Infusion:

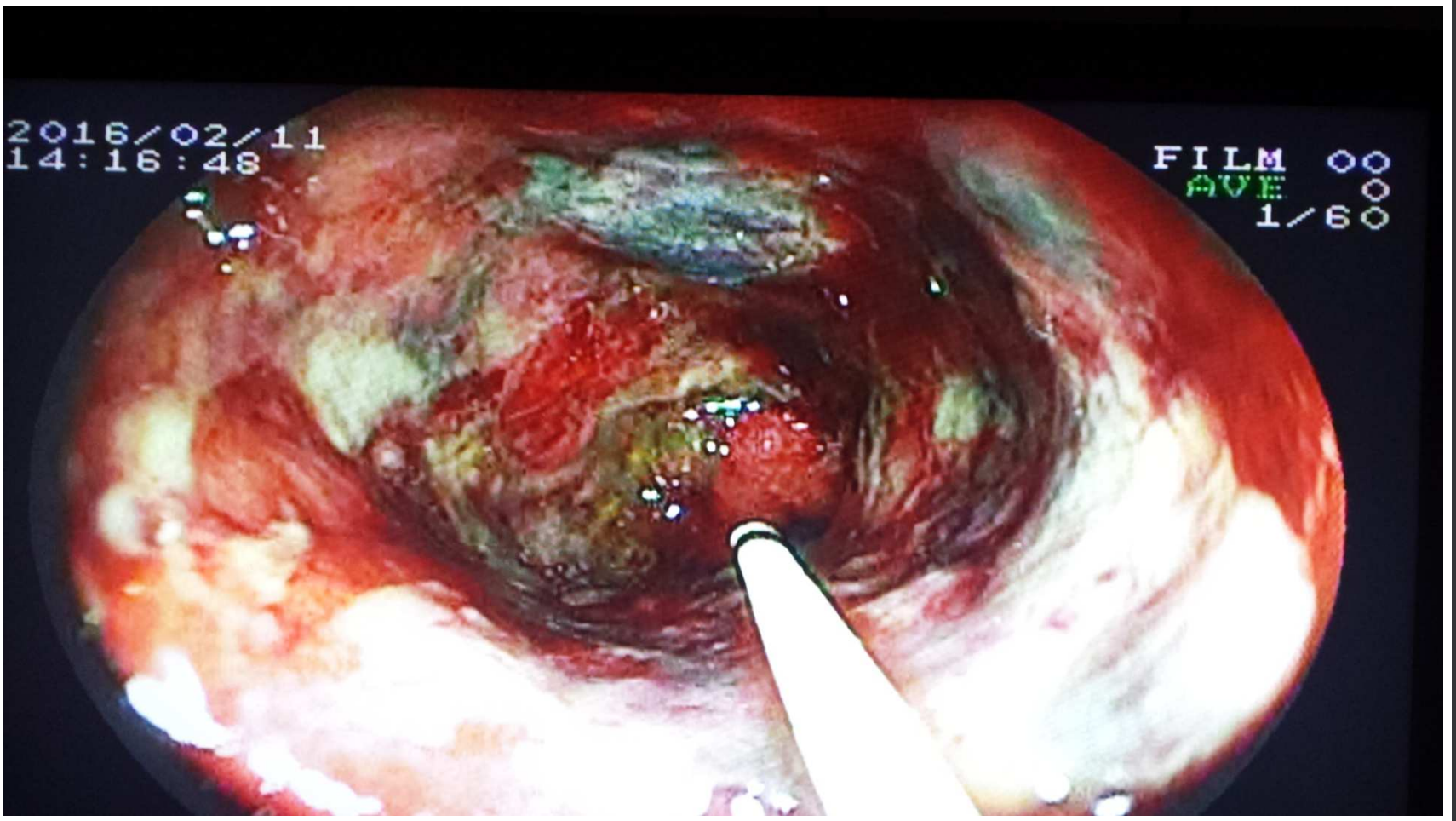
# Lip-ICG-PDT of Rectal Cancer:

# Lip-ICG-PDT of Rectal Cancer:



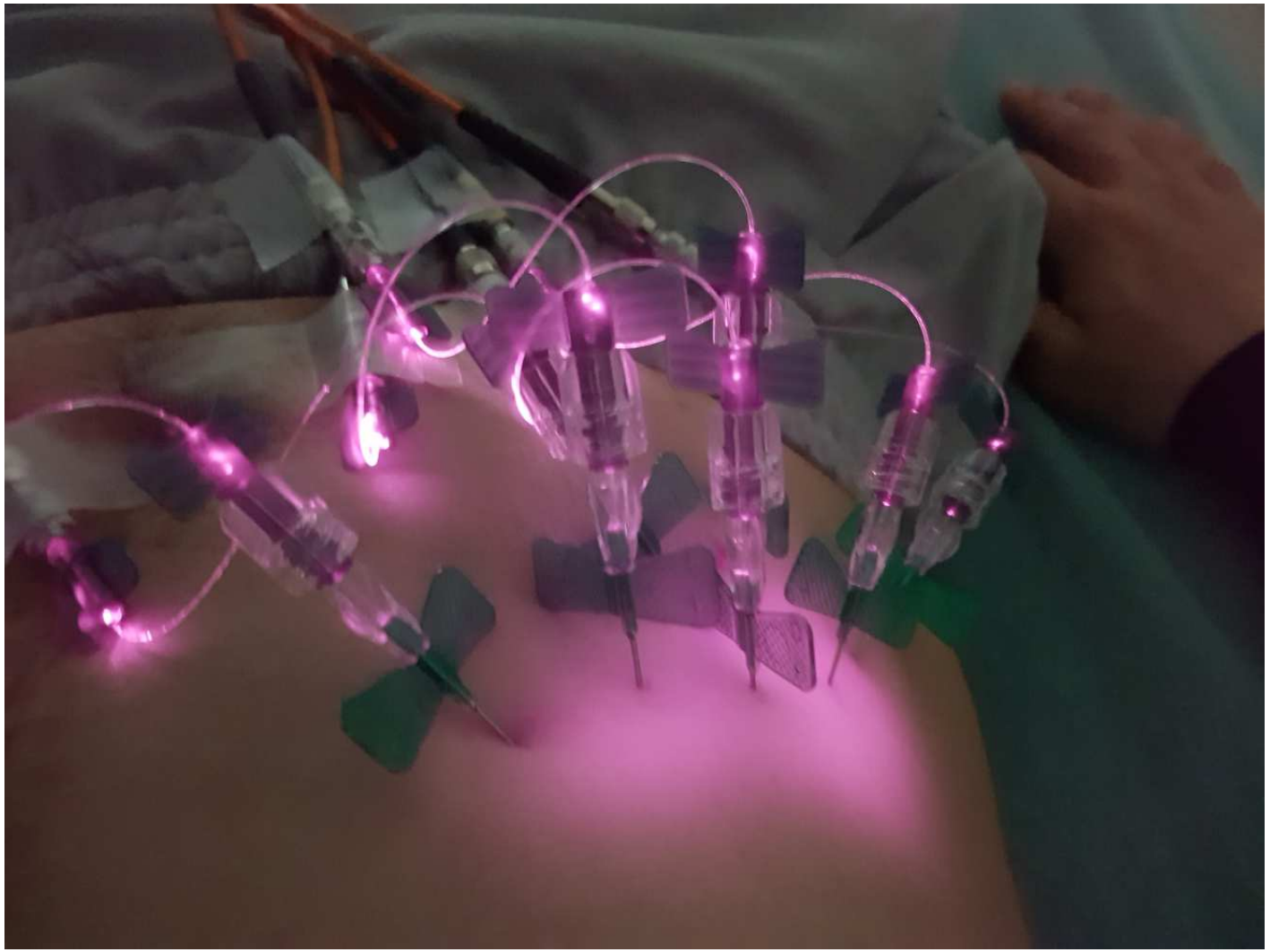
# Lip-ICG-PDT of Rectal Cancer:

# Lip-ICG-PDT of Rectal Cancer:

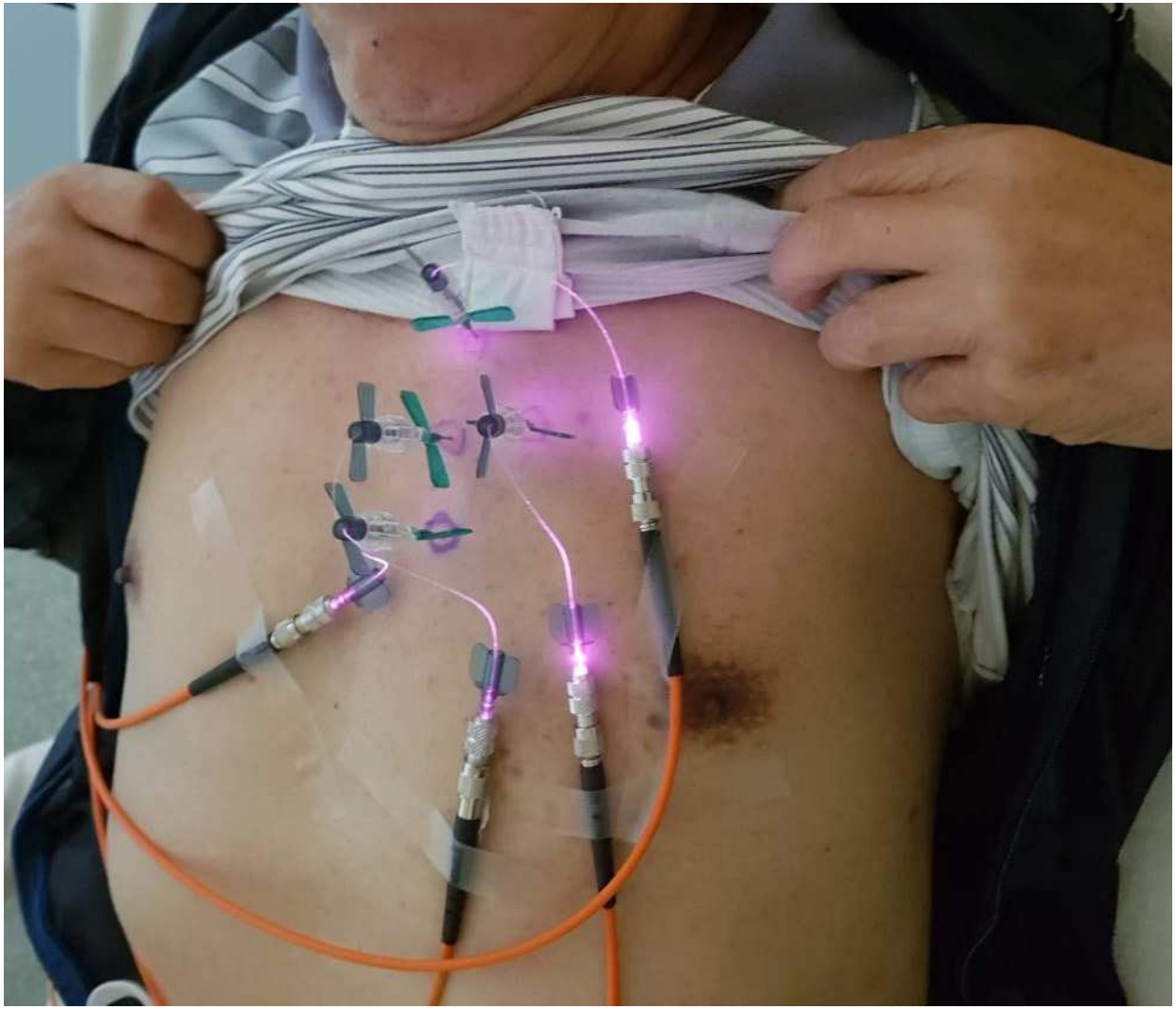


# Interstitial PDT with Lip-ICG:

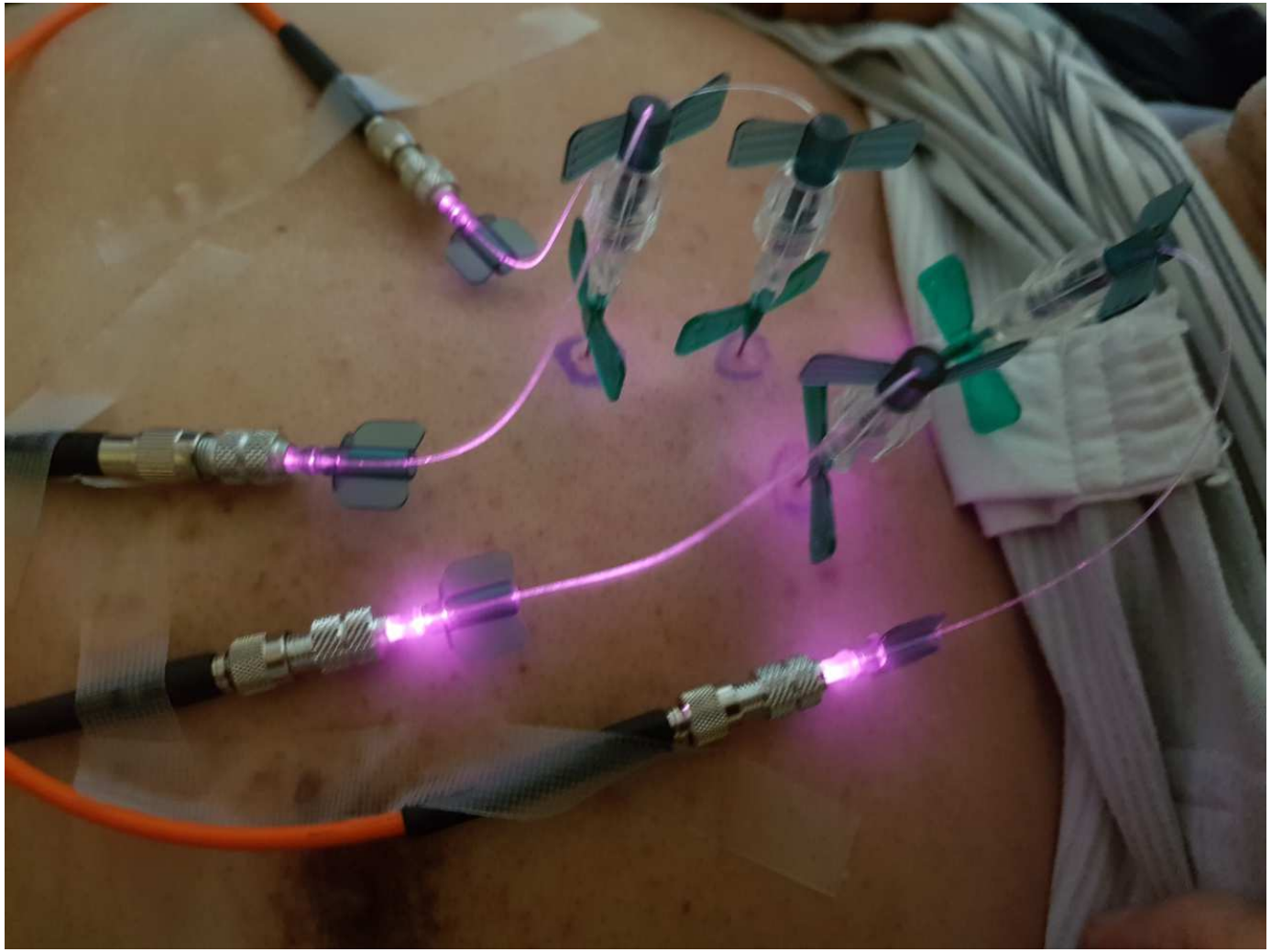
# Interstitial PDT with Lip-ICG and Infrared Laser:



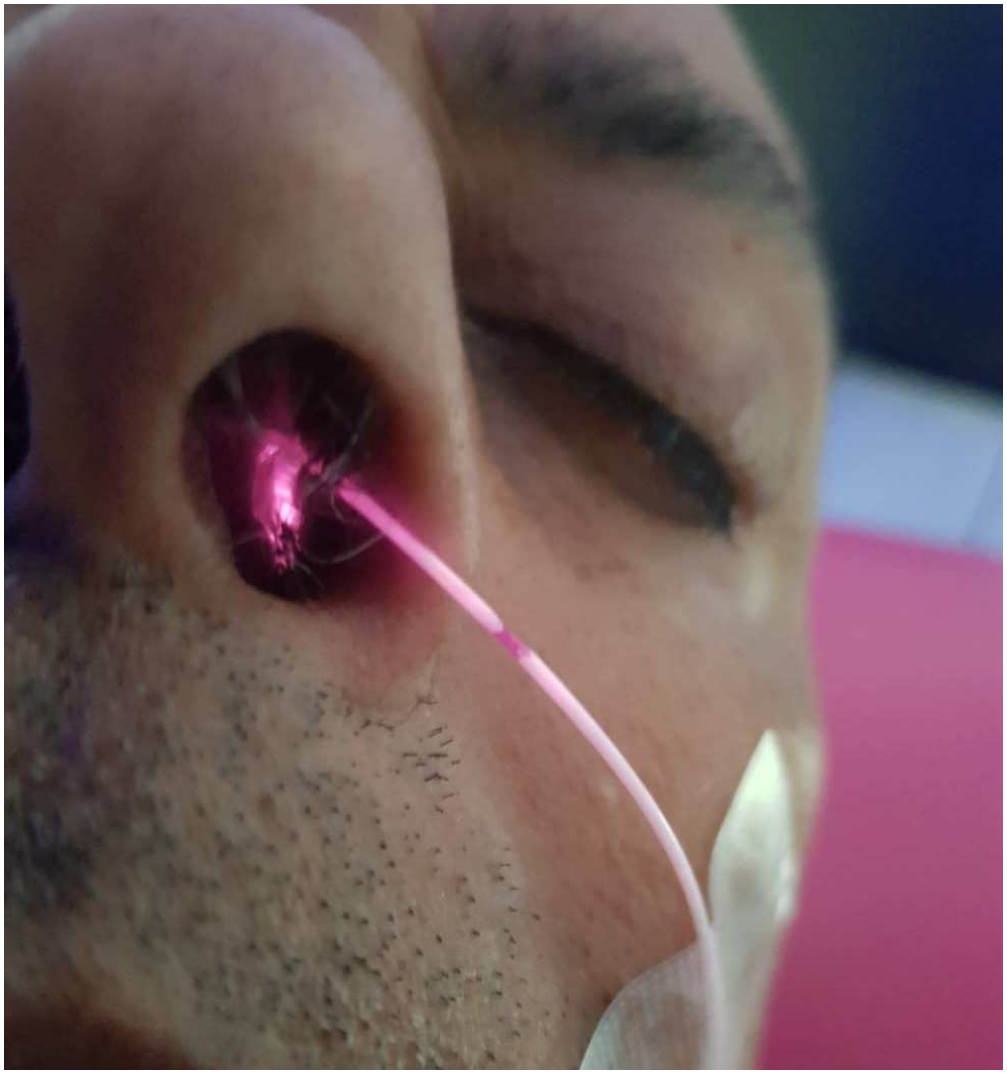
# Interstitial PDT with Lip-ICG of Lung Cancer:

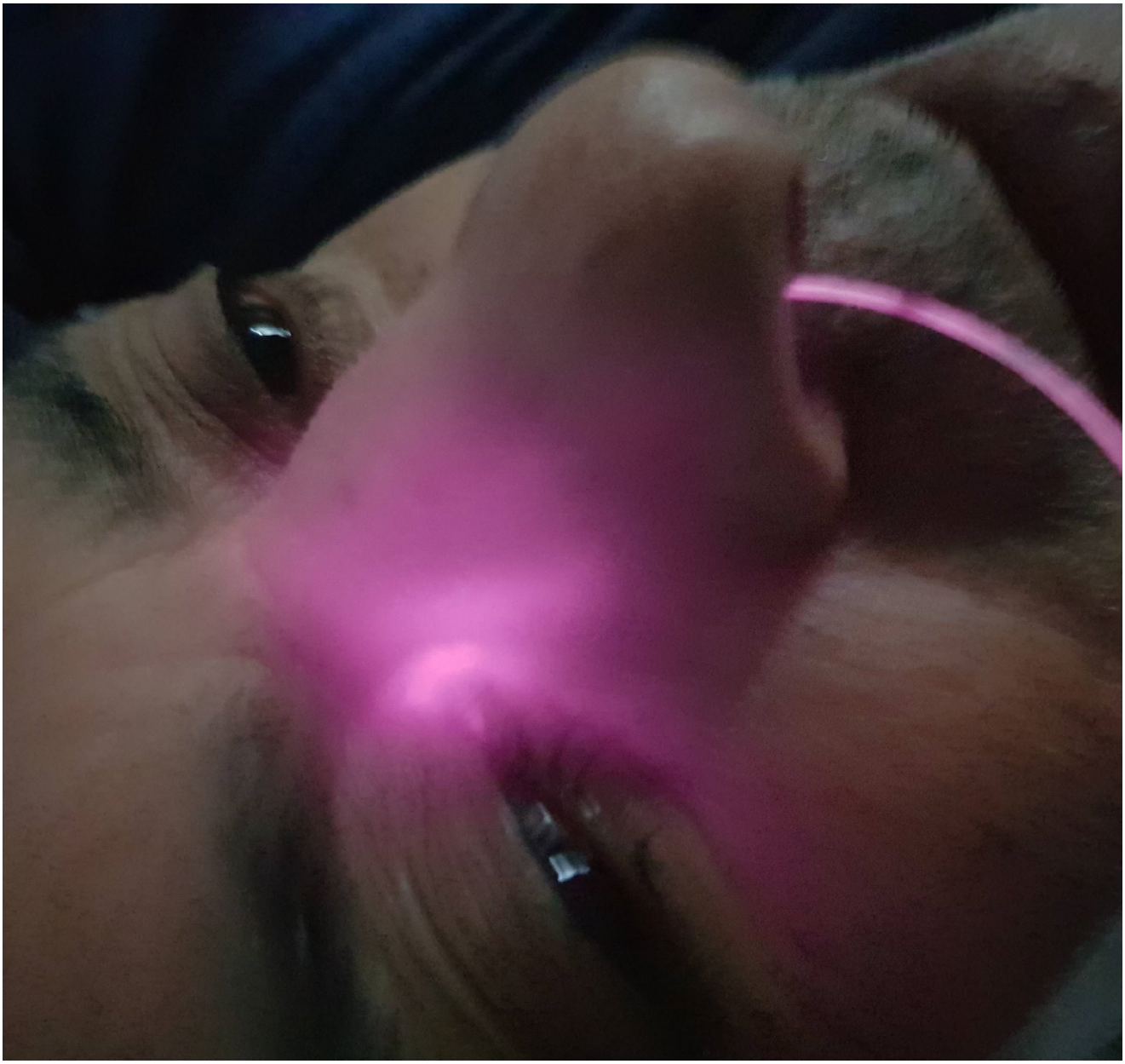


# Interstitial PDT with Lip-ICG of Leiomyosarcoma:



# Interstitial PDT with Lip-ICG of Nasopharyngeal Cancer :





# Absorption Spectra of different Photosensitizers:

| | |
|---|---|
| • Chlorin E6 | 660 nm Red |
| • Indocyaninegreen | 810 nm Infrared |
| • Hypericin | 589 nm Yellow |
| • Curcurmin | 447 nm Blue |
| • Riboflavin | 447 nm Blue |

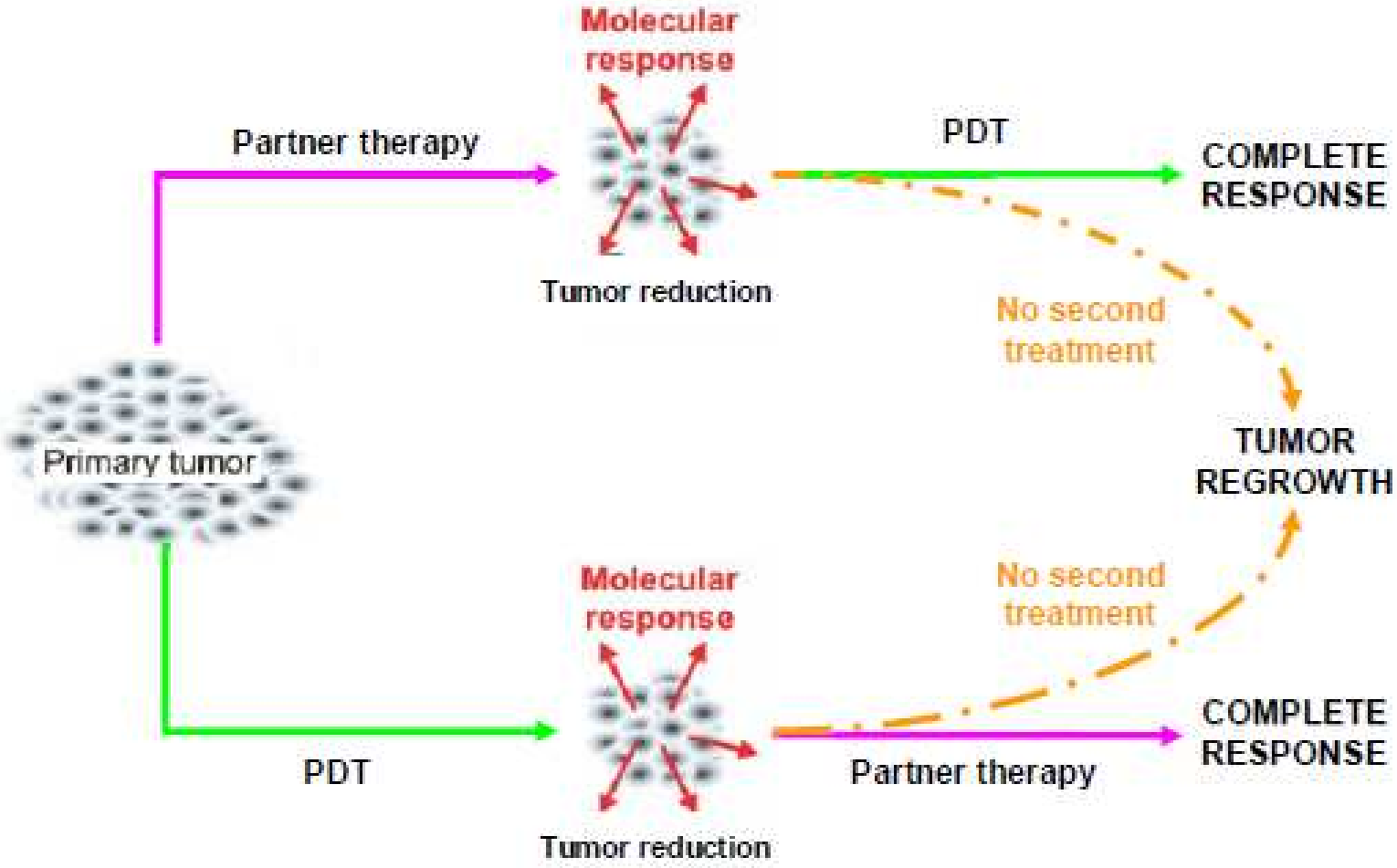
# 8. Cancer Combination Therapy

# Cancer Combination Therapy:

- Small tumors can be treated with PDT alone
- **However, PDT alone is not effective in**
  - big tumors
  - widely spreading tumors
  - multiple metastases

**→ Here we need a combination of PDT with other anti-cancer drugs and methods.**

# Cancer Combination Therapy:



# Cancer Combination Therapies:

1. Combination with traditional chemotherapy
2. **Combination with light sensitive chemodrugs (using chemodrugs as photosensitizers)**
3. **Combination with sonodynamic therapy (using photosensitizers and chemodrugs as sonosensitizers)**
3. Combination with antioxidants
4. Combination with antiangionesis inhibitors
5. Combination with Cox-2 inhibitors
6. Combination with antibodies
7. Combination with different natural compounds
8. Combination with immunotherapy

# 5-Fluorouracil as a Phosensitizer

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*1National Institute for Lasers, Plasma and Radiation Physics,*
*Laser Department, P. O. Box MG-36, Bucharest – Magurele;*
*2Central Military Hospital, Ophthalmology Clinic, Bucharest, Romania*

## Abstract

*5-FU exhibits a high fluorescence after irradiation with UV-vis light. An enhancement of the cytostatic activity of 5-FU under UV-vis irradiation was observed on an in vivo experimental model.*

# The Tautomeric Forms of 5-FU:

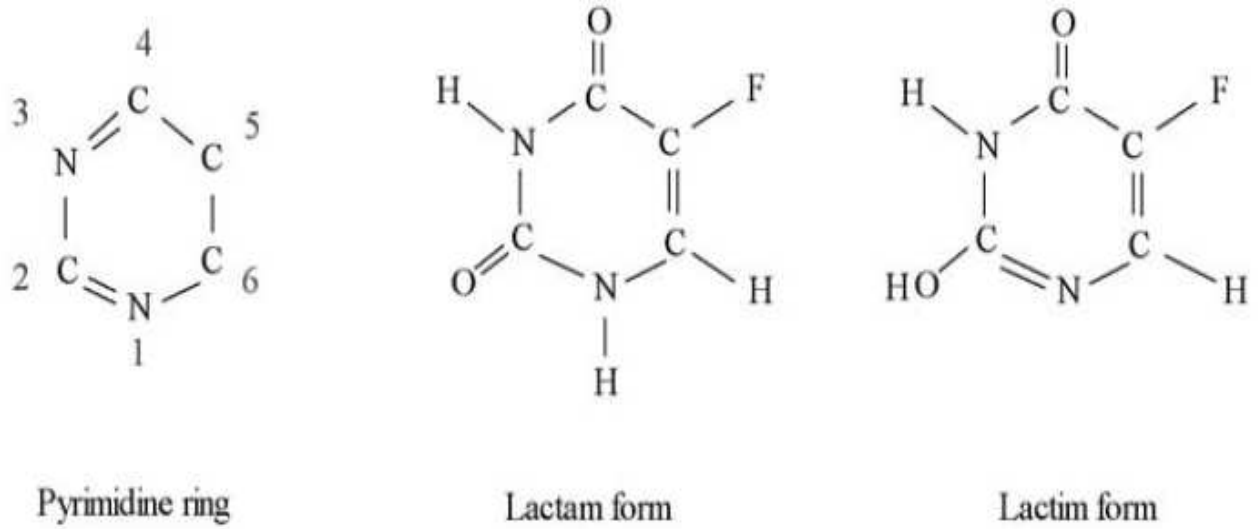
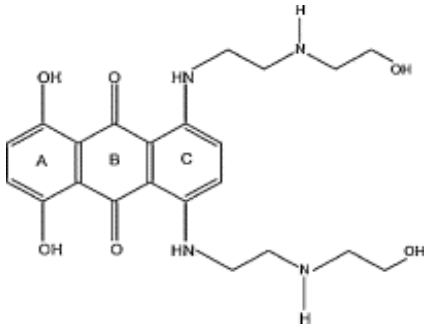
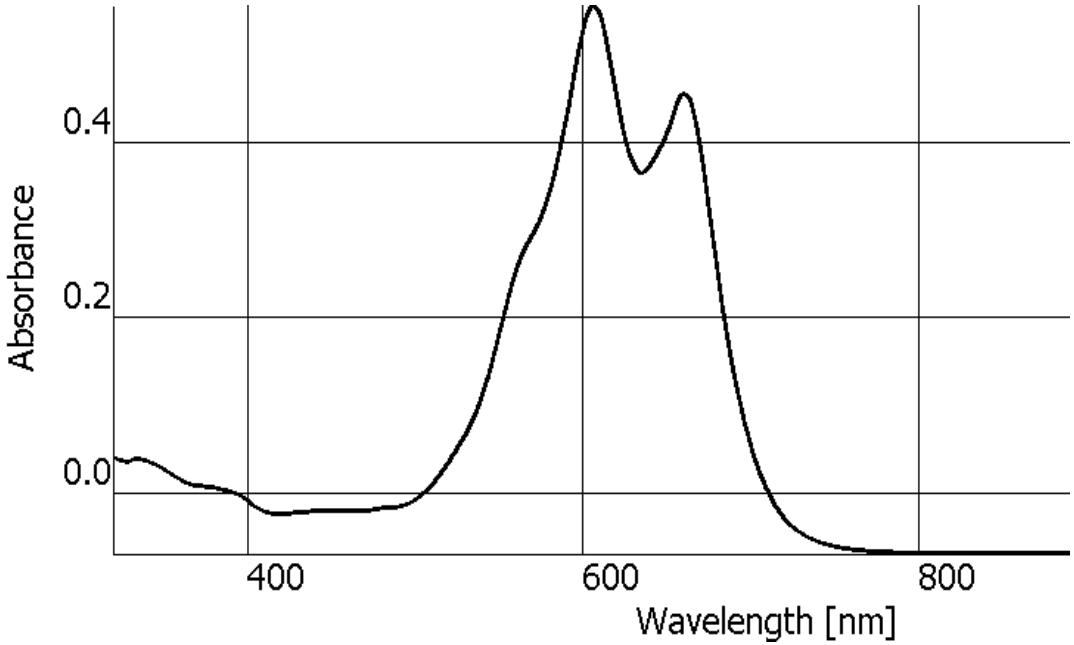



Figure 1. *The pyrimidine ring and the two 5-FU tautomers: lactam and lactim forms.*

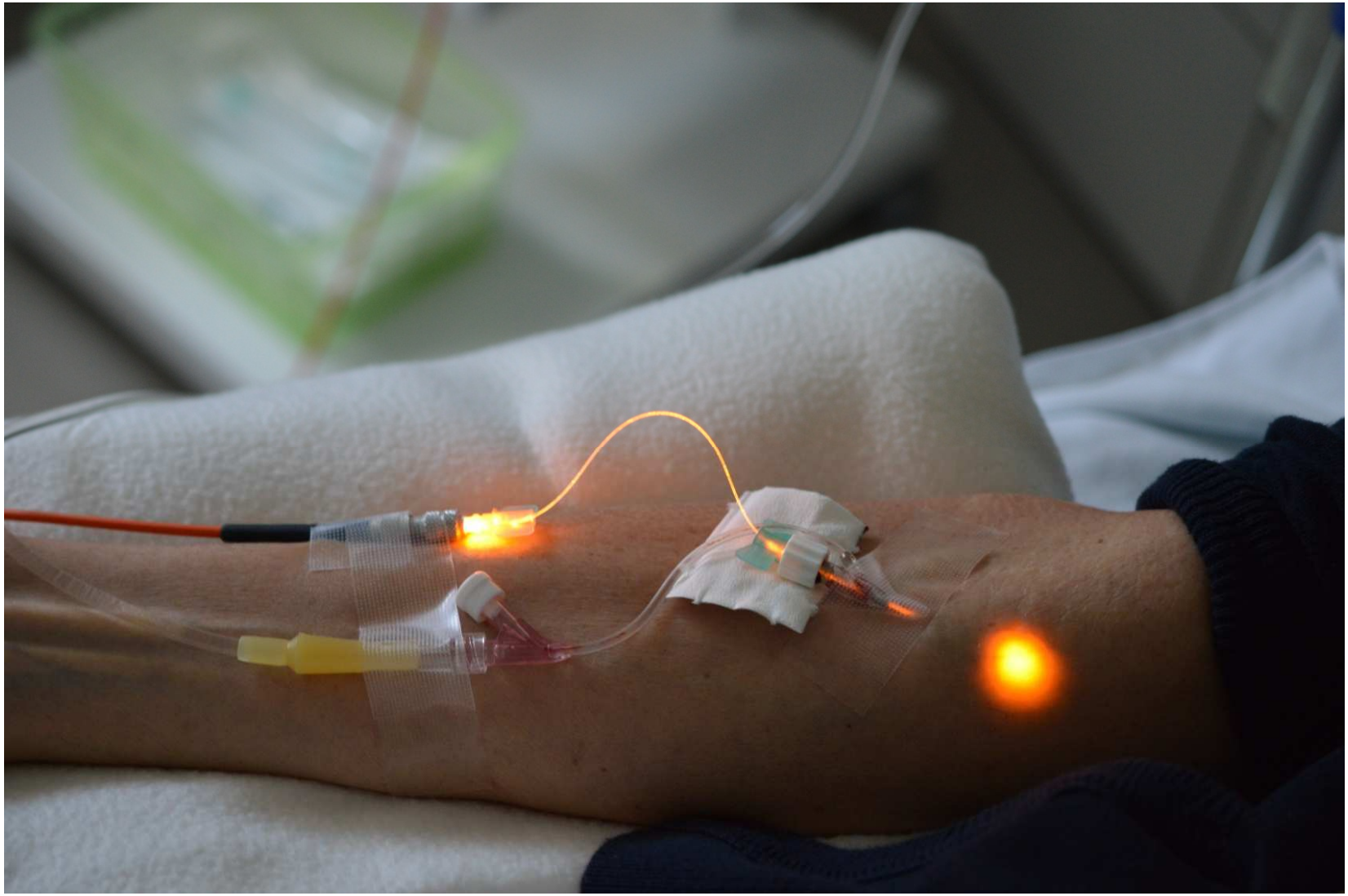
# Mitoxantron as Photosensitizer:

- Mitoxantron is a blue substance
- It is activated by yellow and red light
- It is a strong chemo-photosensitizer
- It is effective in multiple cancers



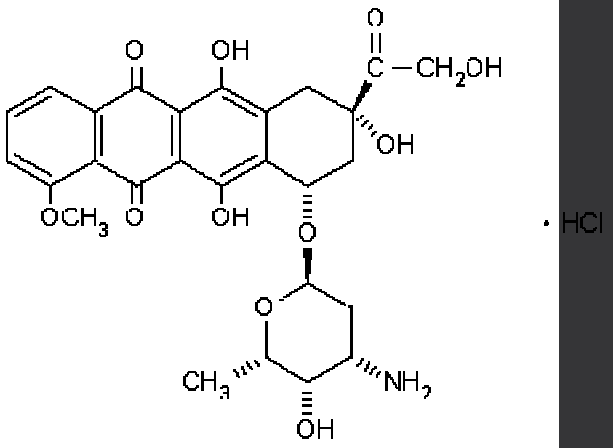



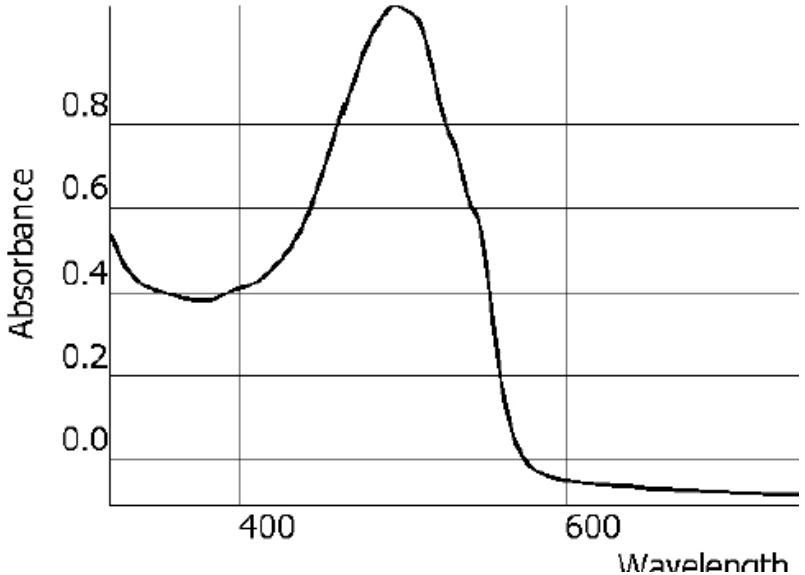

# Mitoxantron Stimulation with Y-cannula

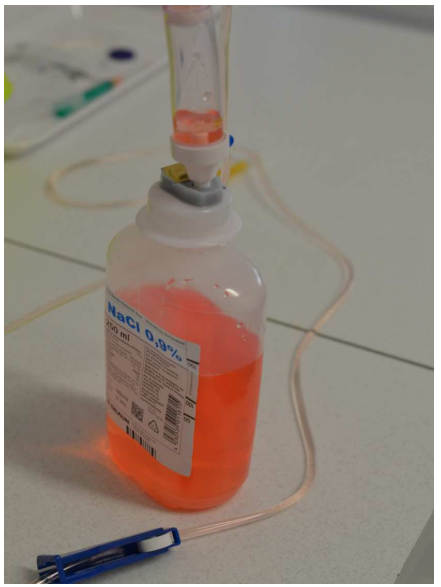


# Doxorubicin (liposomal) as Photosensitizer:

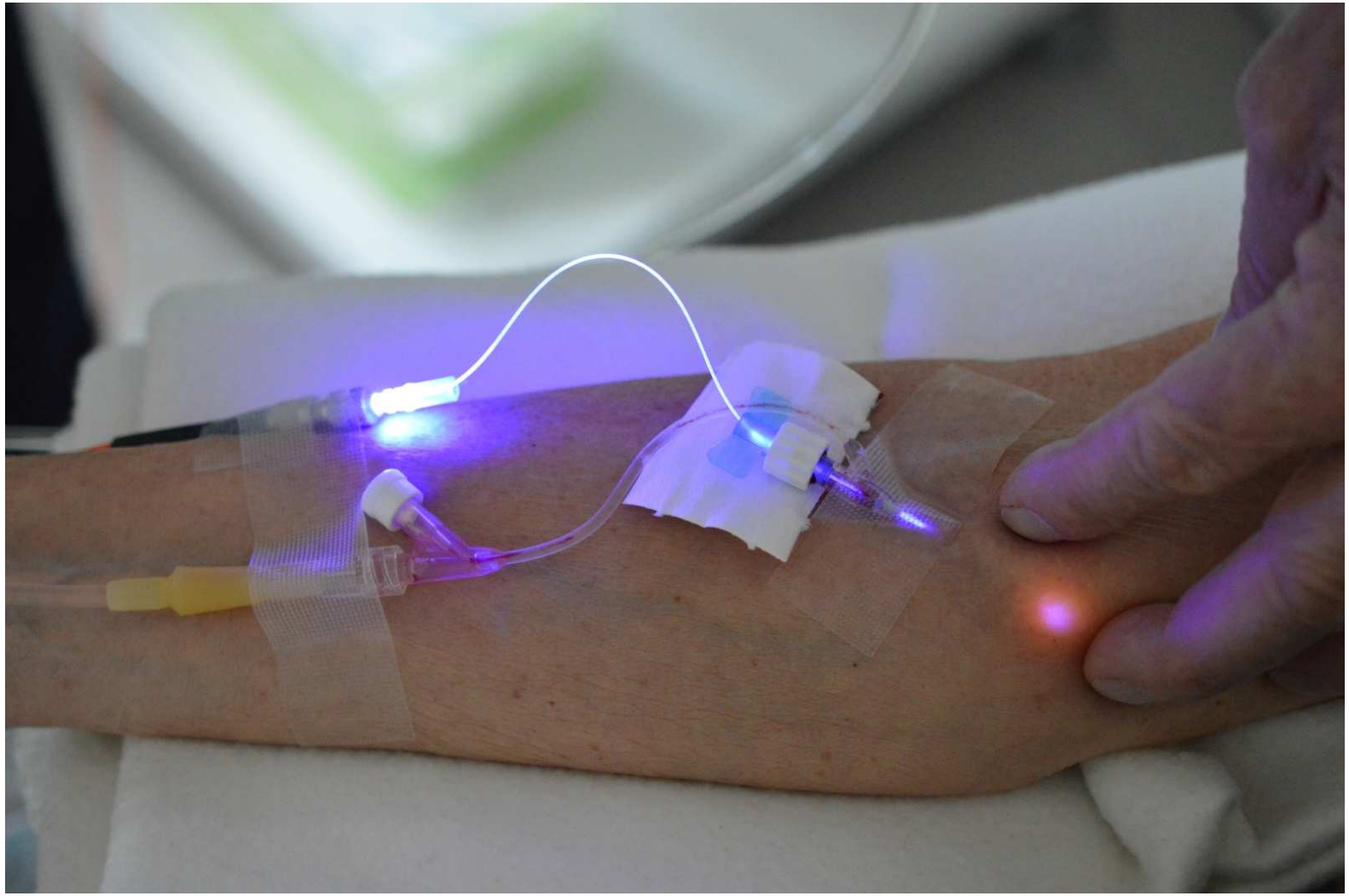
- Doxorubicin is widely used for many different cancers (Anthracyclin antibiotics)
- It is an orange solution and is stimulated by blue-green laser light
- It can be enhanced by liposomal delivery (Doxil)



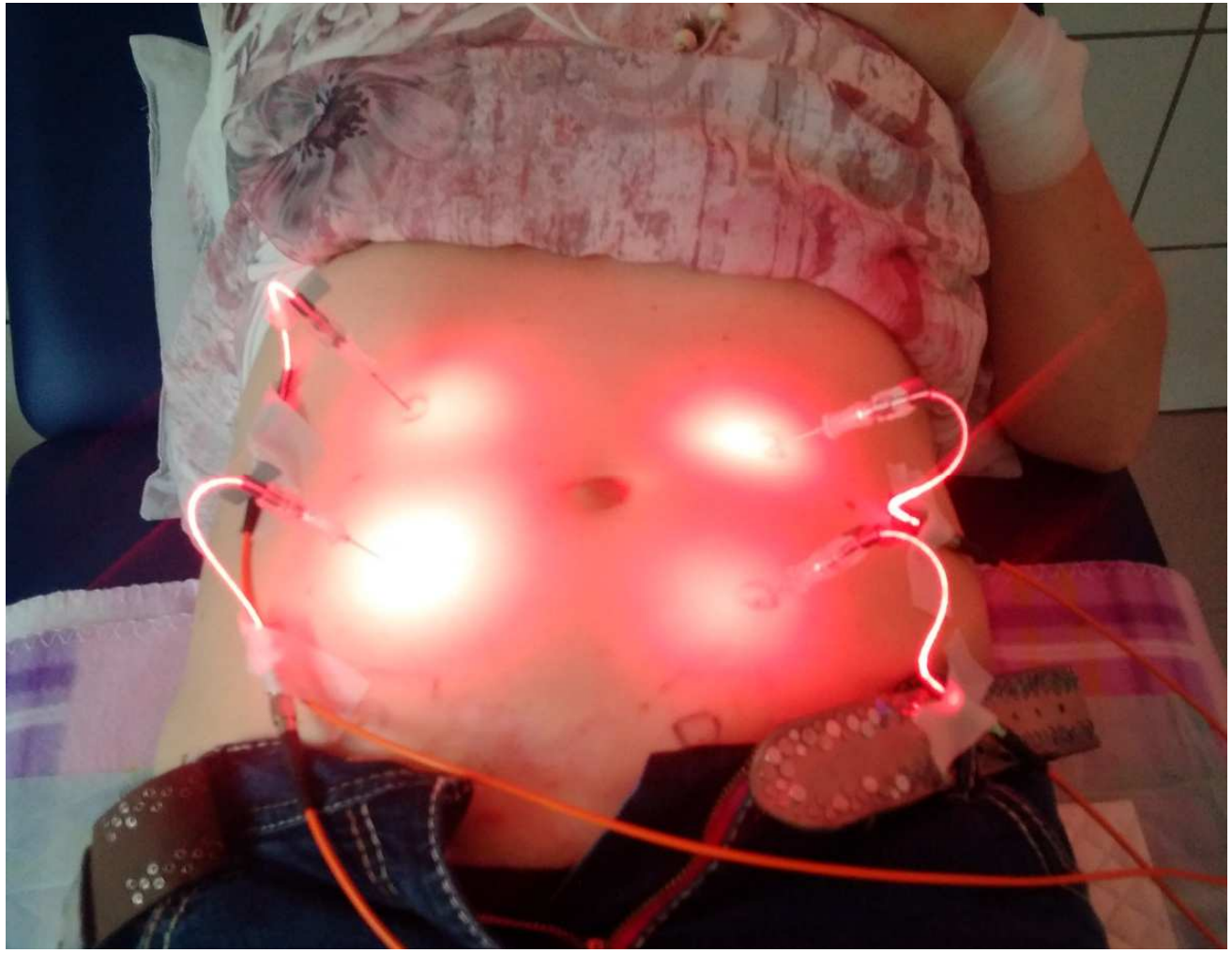
# Doxorubicin Stimulation:



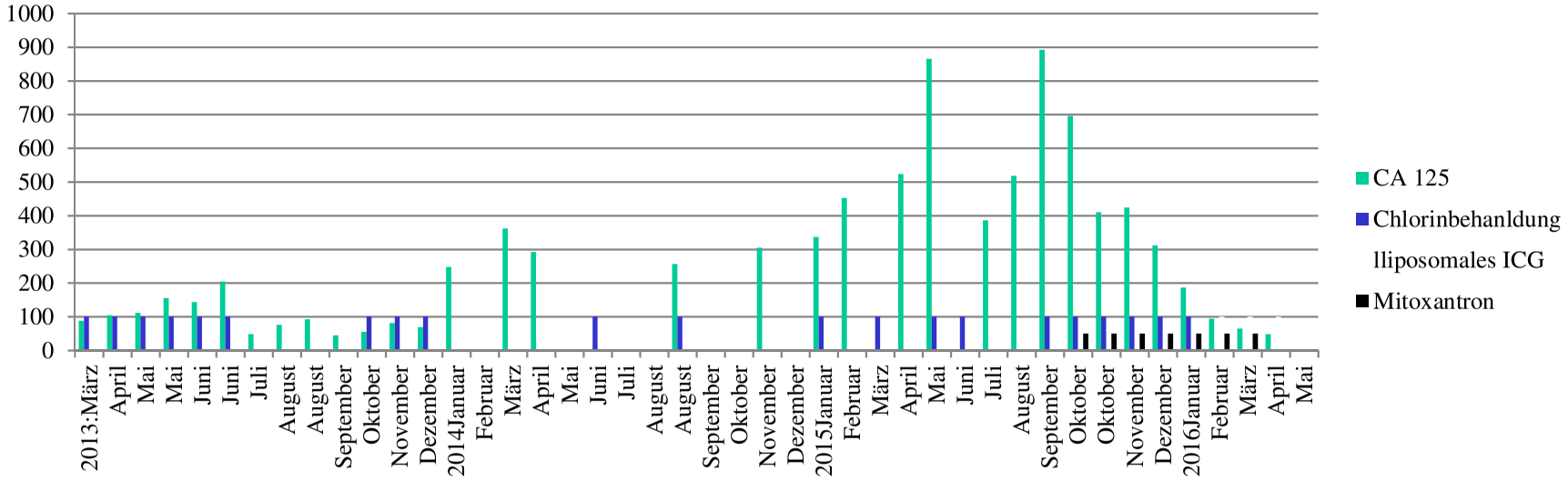
# Case Report: Ovarian Cancer with Peritoneal Carcinosis (patient 45 y.):

- **First check: 19.03.13:** CA 125: 88,4 + ascites in Ultrasound
- **02.04.13: 1st PET-CT Scan:** Ovarial cancer, peritoneal carcinosis, ascites
- **18.06.13: 2nd PET-CT Scan**: Metastases (perihepatic and in pelvis), ascites
- **12.11.13: 1st MRI Abdomen:** Peritoneal carcinosis, subphrenic metastases and in liver and right kidney, ascites
- **08.01.15: 2nd MRI Pelvis**: Cervix carcinoma grade I, ascites, nodular peritoneal carcinosis, no lymph nodes or metastases in bones
- **27.08.15: 3rd PET-MRI scan:** Progredient peritoneal metastases (perihepatic and in pelvis), 2 new big tumors in ovarial area both sides, recurrence of the ovarial cancer, lymph nodes right epiphrenic

# Case Report: Ovarian Cancer with Peritoneal Carcinosis:



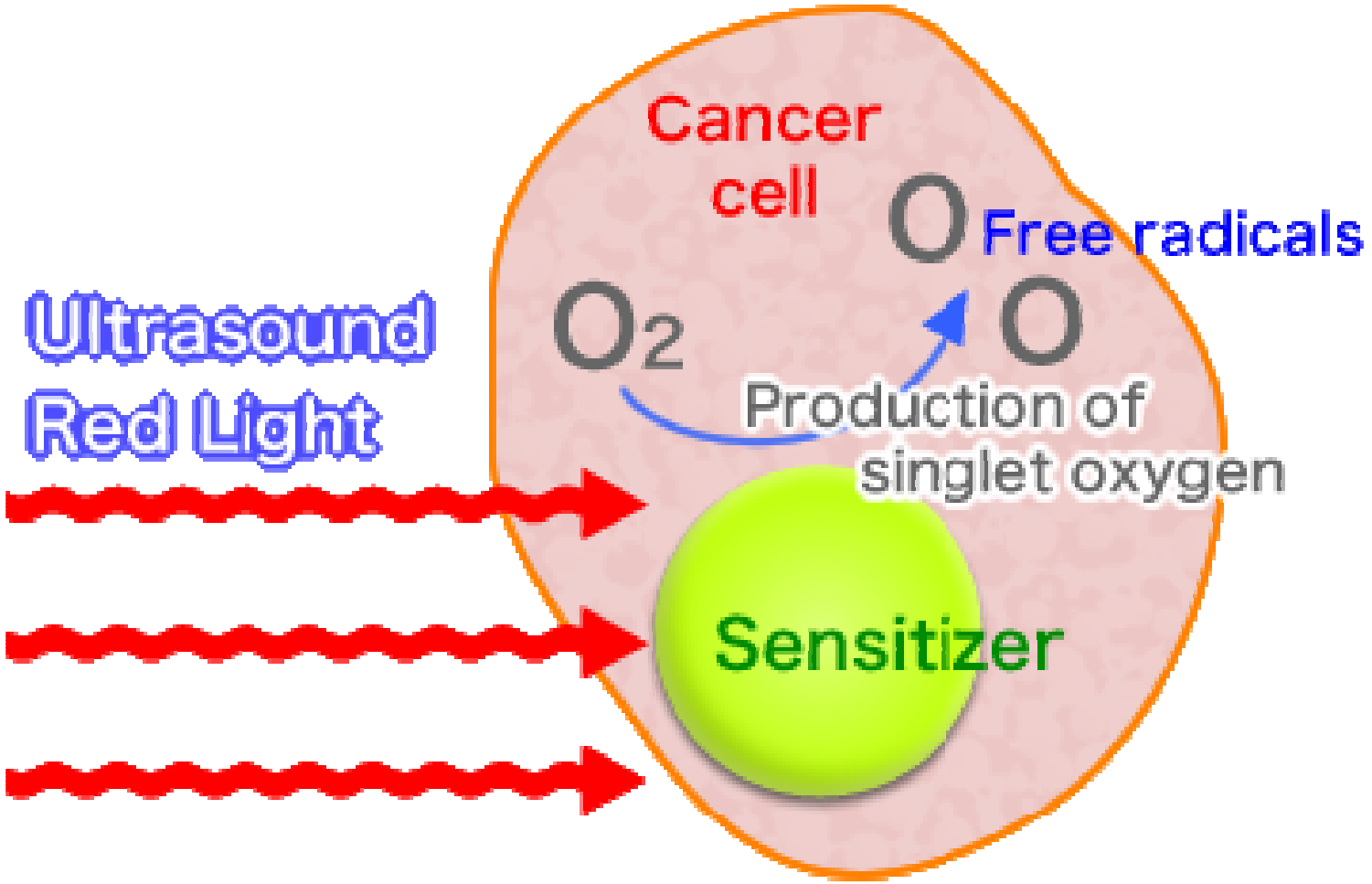
# Case Report: Ovarian Cancer with Peritoneal Carcinosis (patient 45 y.):

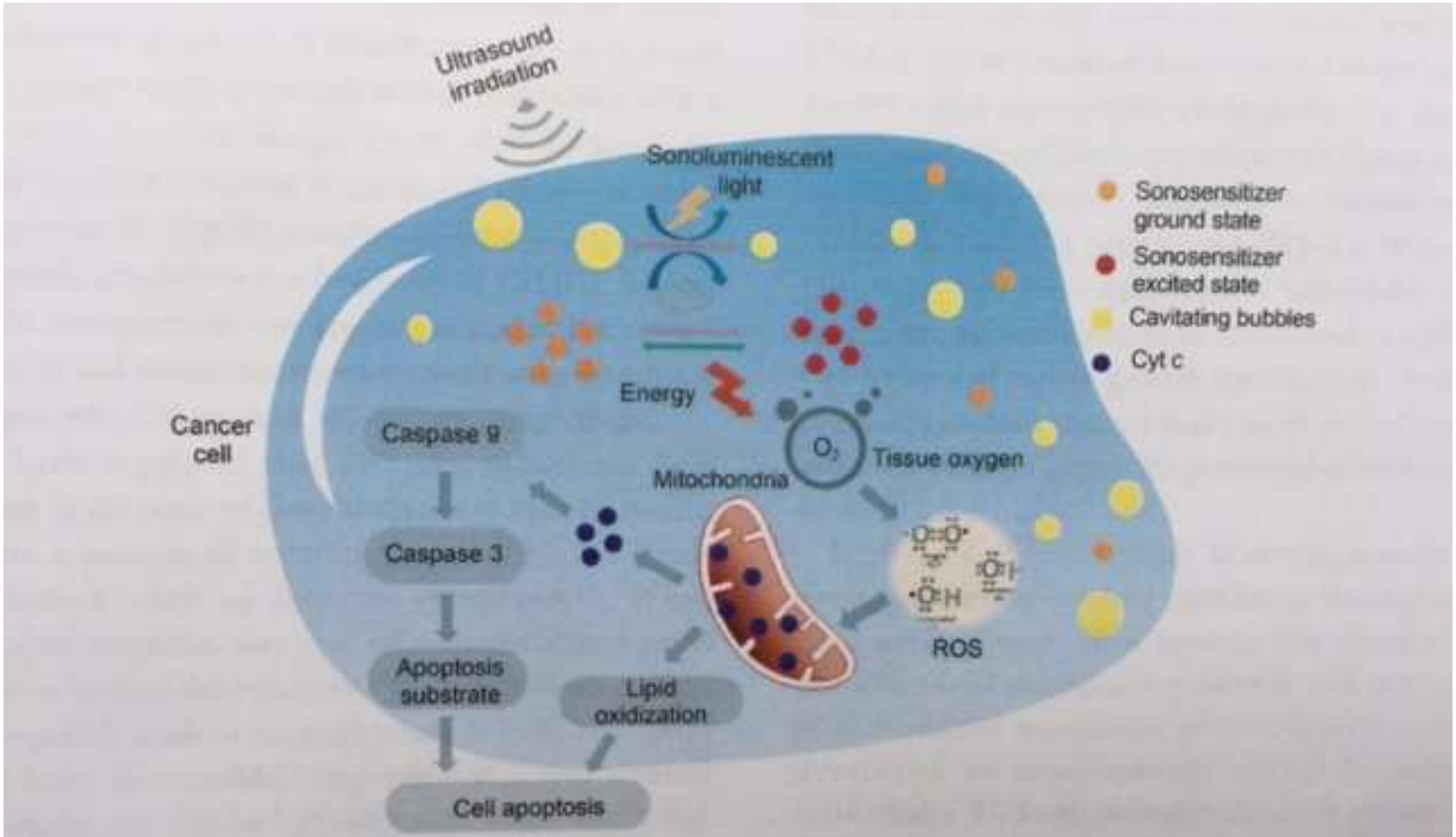


# 9. Sonodynamic Tumor Therapy (SDT)

# Sonodynamic Tumor Therapy:

- Sonodynamic therapy (SDT) is an emerging approach that involves a combination of low-intensity ultrasound and specialized chemical agents known as sonosensitizers
- Ultrasound can penetrate deeply into tissues and can be focused into a small region of a tumor to activate a sonosensitizer which offers the possibility of non-invasively eradicating solid tumors in a site-directed manner
- At the same time, the breath of evidence from SDT-based studies suggests that SDT is promising for cancer treatment


Cancer cell
O
Free radicals
O2
O
Production of singlet oxygen
Ultrasound
Red Light
Sensitizer




Possible mechanisms of SDT. Ultrasound irradiation induces cavitation around the surface of cancer cells. The energy pro
ose of cavitating bubbles initiates the formation of sonoluminescent light in cancer cells. Thus, sonosensitizer is activated
tate into an excited state. As the activated sonosensitizer returns to the ground state, the released energy can be transferre
nbient oxygen to produce a large amount of ROS including oxygen ion, peroxide and singlet oxygen, which subsequently

# Cavitation Bubbles:

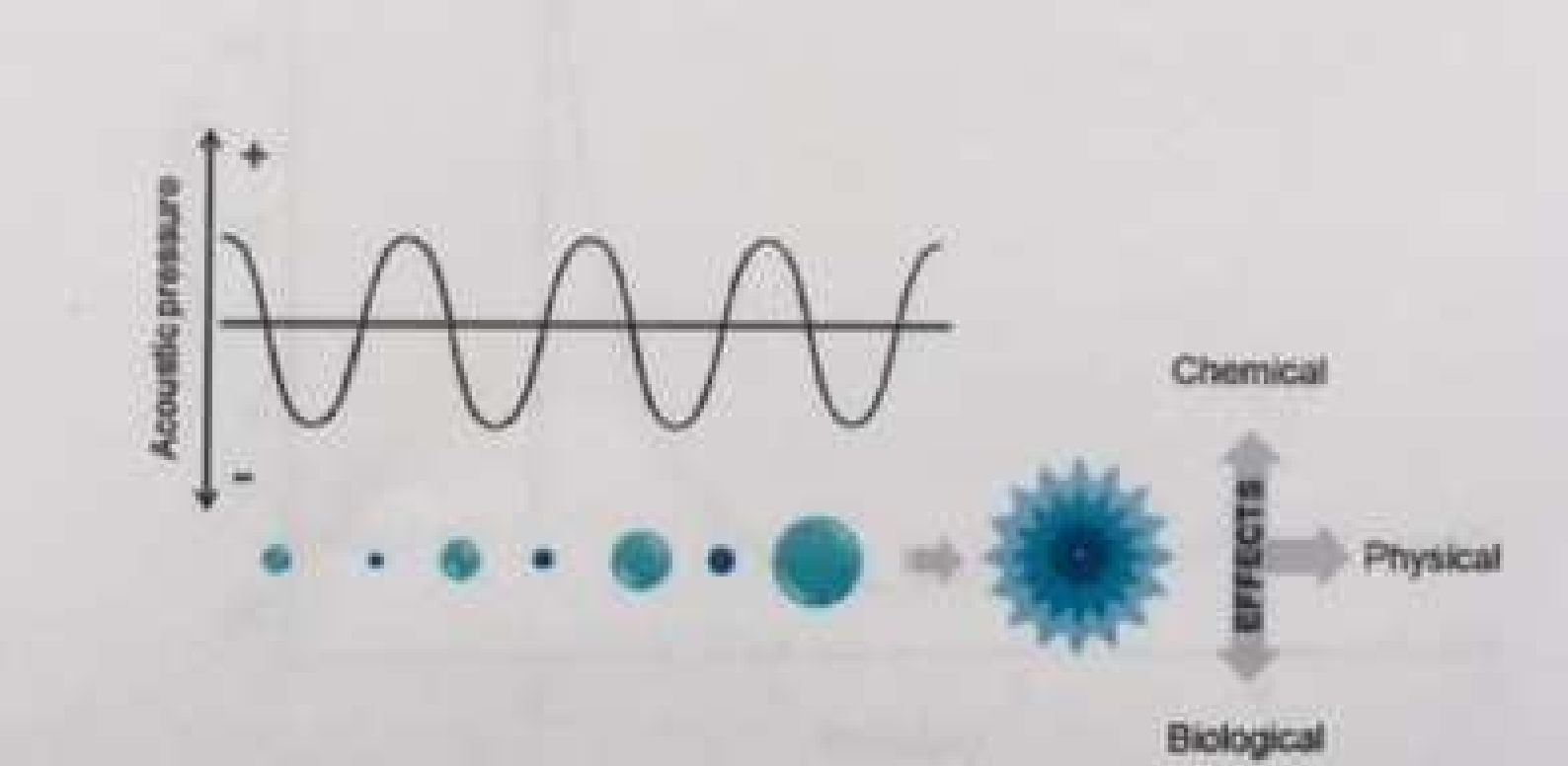
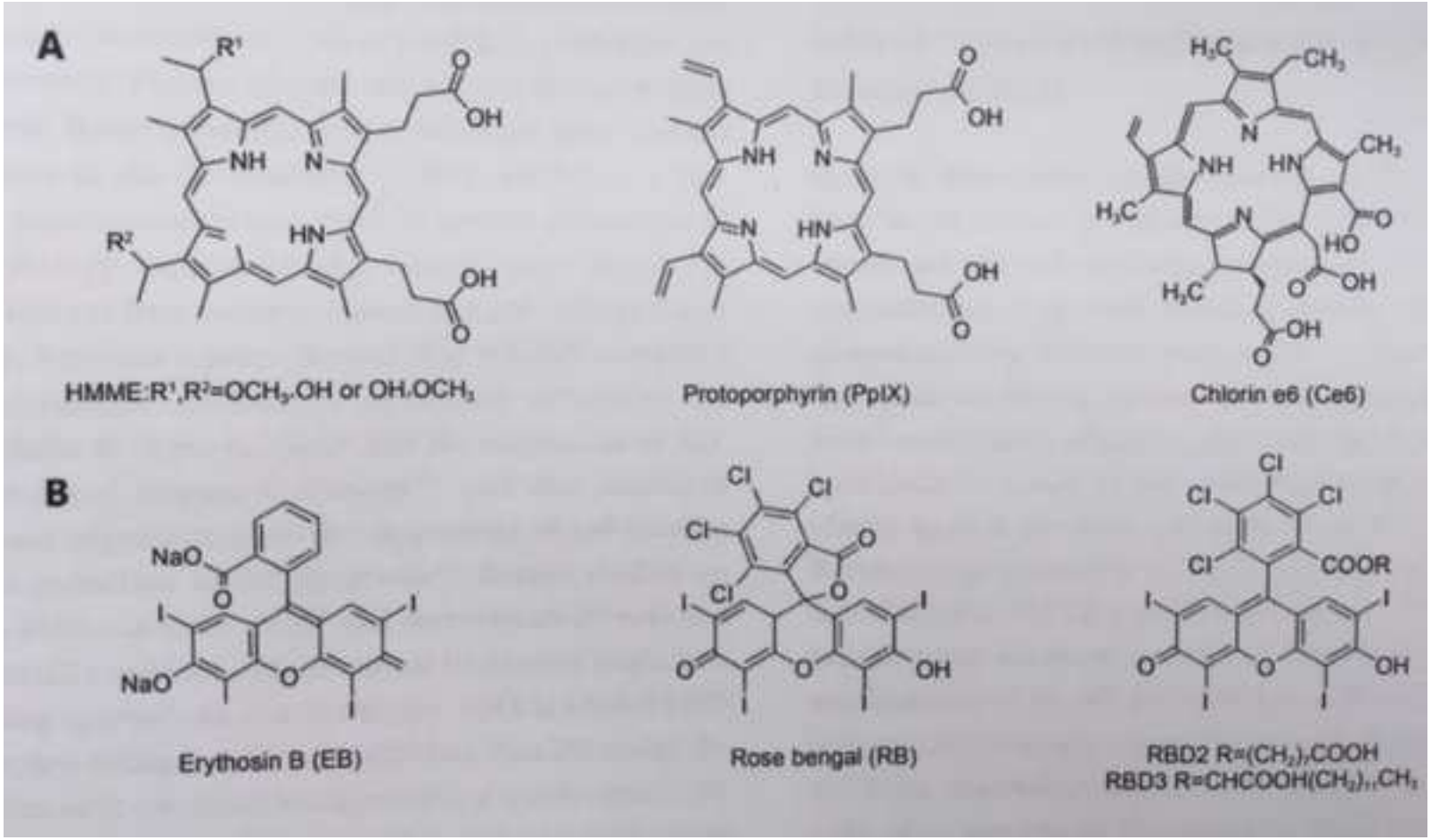



**Figure 1** Drawing showing the formation, growth, and collapse of a cavitation bubble.

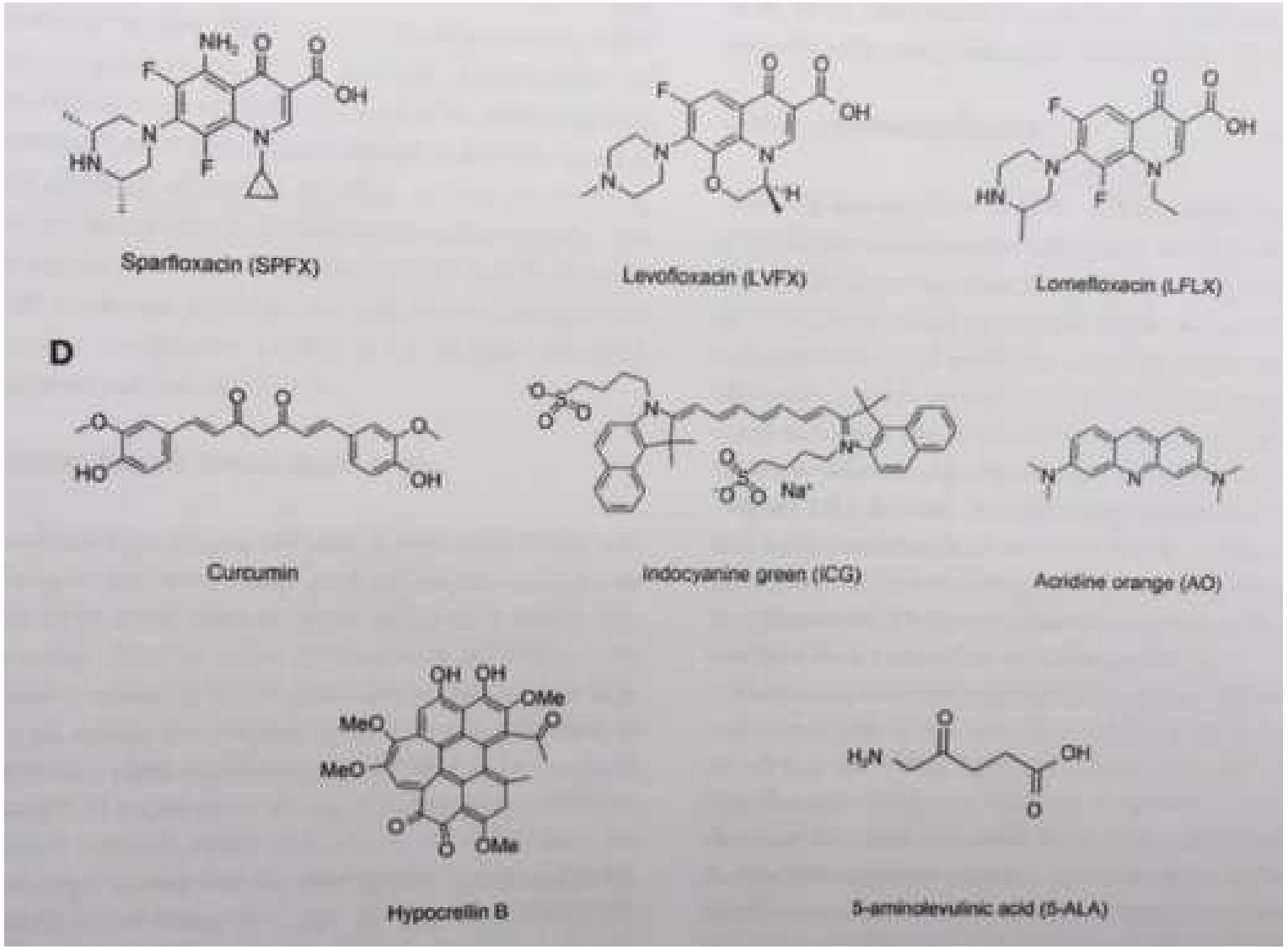
# Ultrasound Application:

- Low power ultrasound ( 1 – 2,2 W/sqcm)
- High frequency ultrasound 300 – 500 W
- Ultrasound Shockwaves

# Sonosensitizers:



# Sonosensitizers:



*Current Drug Therapy*, 2009, *4*, 179-193



# Activated Cancer Therapy Using Light and Ultrasound - A Case Series of Sonodynamic Photodynamic Therapy in 115 Patients over a 4 Year Period

J.N. Kenyon[1,*], R.J. Fuller[1] and T.J. Lewis[2]

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**Abstract:** Activated Cancer Therapy (ACT), also known as Sonodynamic Photodynamic Therapy (SPDT) is a novel therapeutic modality that utilises a non-toxic photosensitive agent with reported ultrasound-activated properties. SPDT has previously demonstrated significant tumour cell inhibition in animal studies. There has been much research into the efficacy of photodynamic therapy and development in understanding of the underlying mechanism of tumour cytotoxicity. Synergistic ultrasound activation represents a promising development to activated sensitiser therapy, as photo-activation is limited by access and penetrance issues. Ultrasound has been demonstrated to activate a number of sono-sensitive agents allowing the possibility of non-invasive targeted treatment of deeper tumour sites than is currently achievable with photodynamic therapy. This case series of 115 patients with a variety of cancer diagnoses reports on experiences of this treatment over a 4 year period using sublingual administration of a new dual activation agent, Sonnelux-1, followed by a protocol of LED light and low-intensity ultrasound exposure. Initial clinical observation suggests SPDT is worthy of further investigation as an effective and well tolerated treatment for a wide variety of primary and metastatic tumours, including those refractory to chemotherapy.

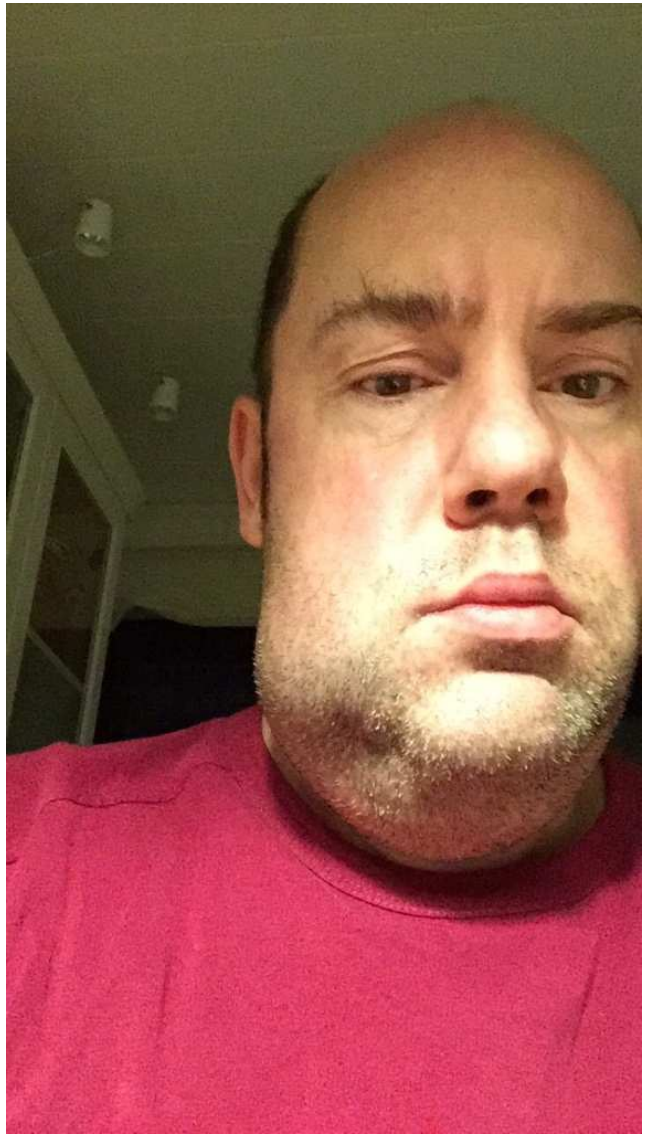
**Key Words:** Sonodynamic therapy, photodynamic therapy, activated cancer therapy, ultrasound activated therapy, metastatic cancer, sonnelux-1, dove clinic, sonnemed.

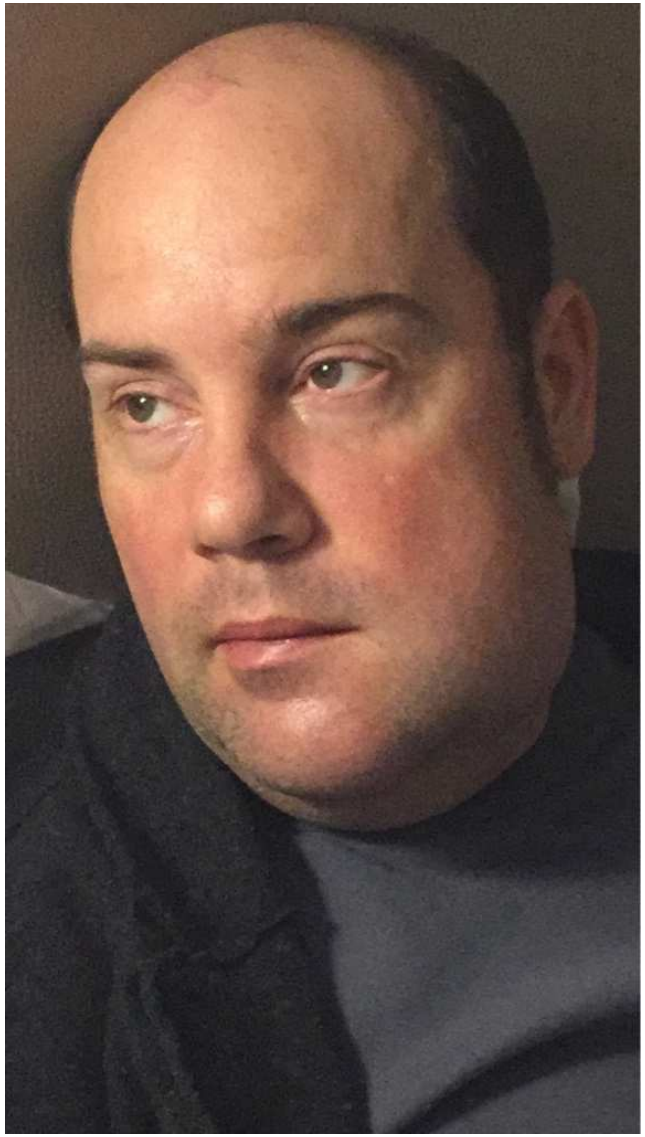
# Low Power Ultrasound (0,2 – 2,2W/sqcm):

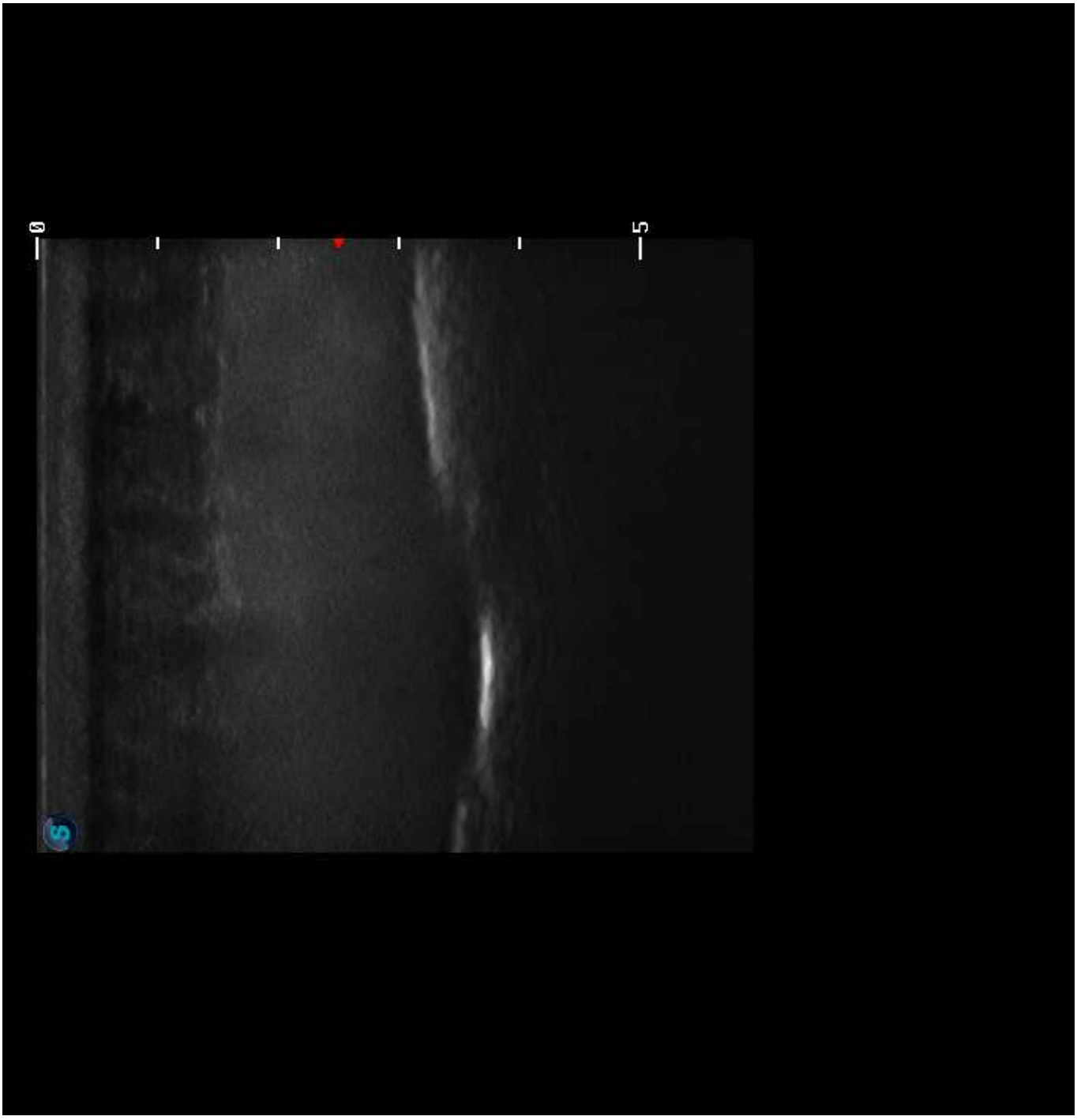

# High Frequency Ultrasound Device:

# Ultrasound Shockwave Device:

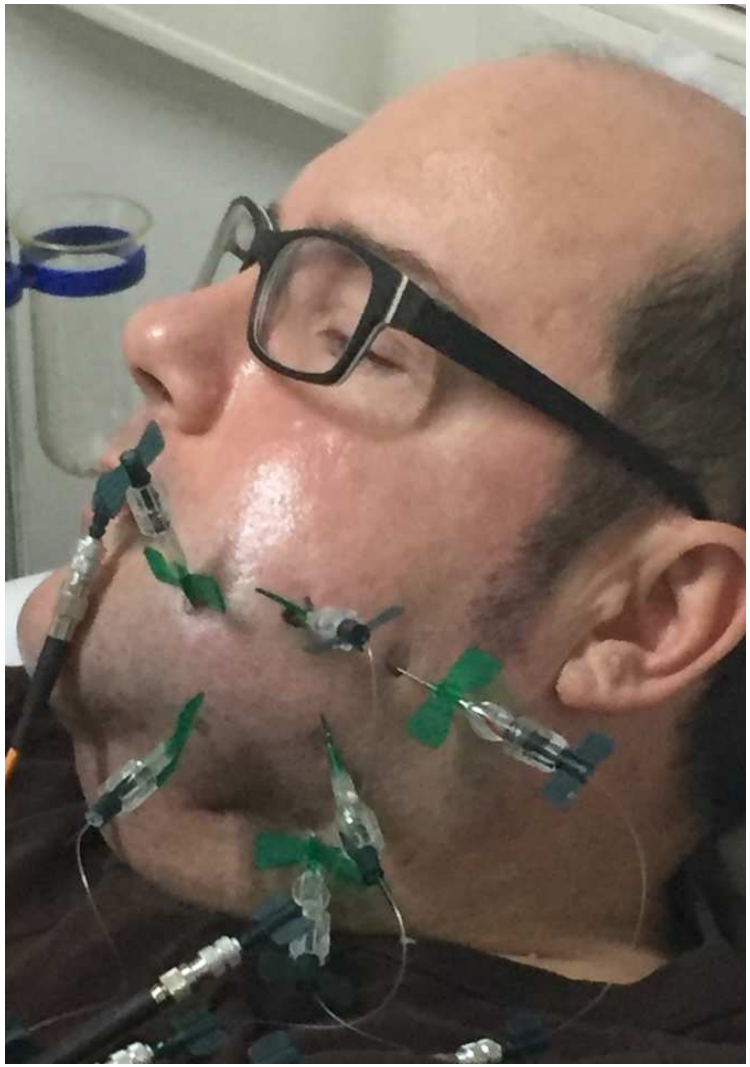
# Case Report: B-cell Lymphoma






6
5

# Case Report: B-cell Lymphoma

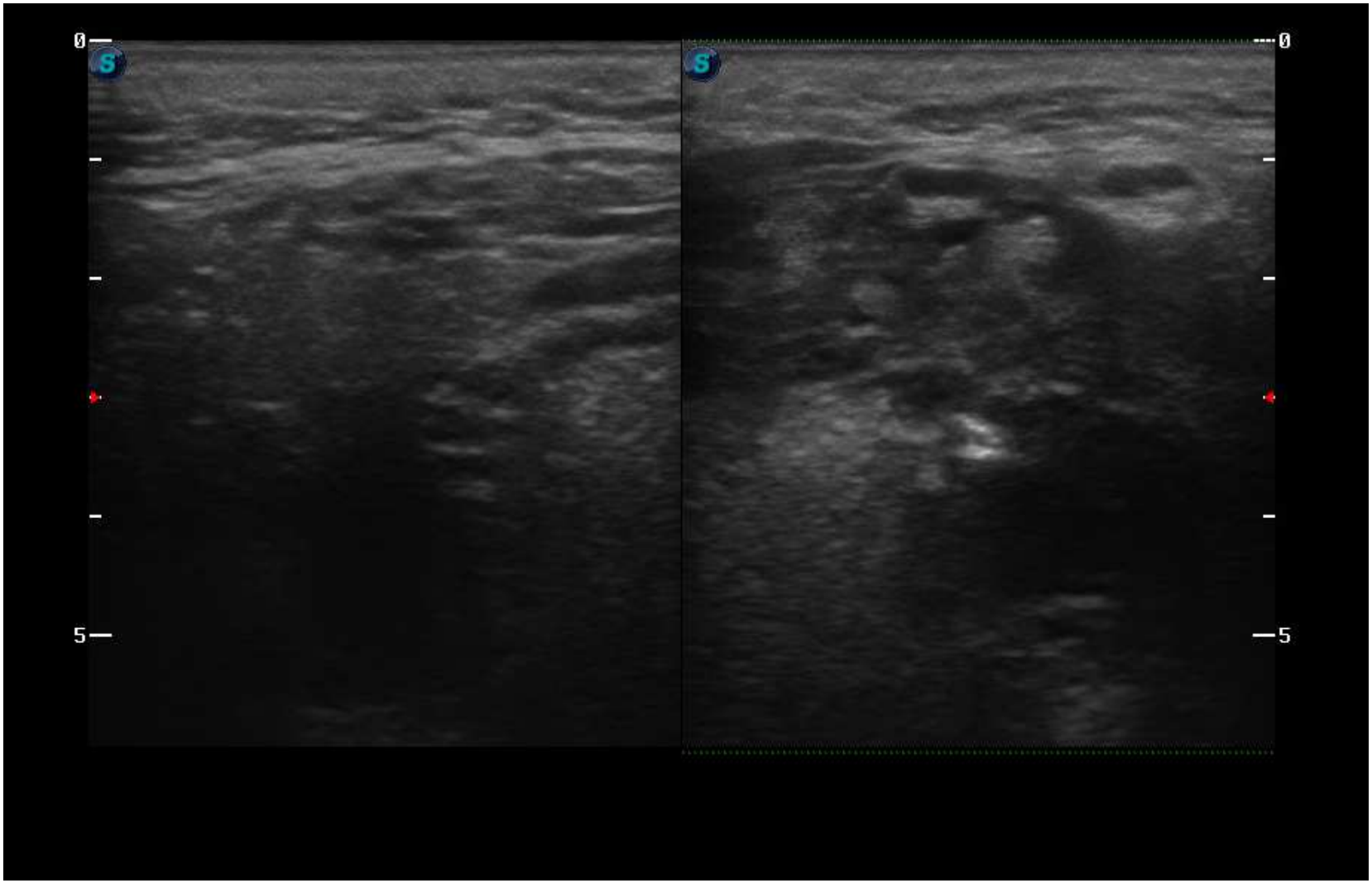



0
1
2
3
4

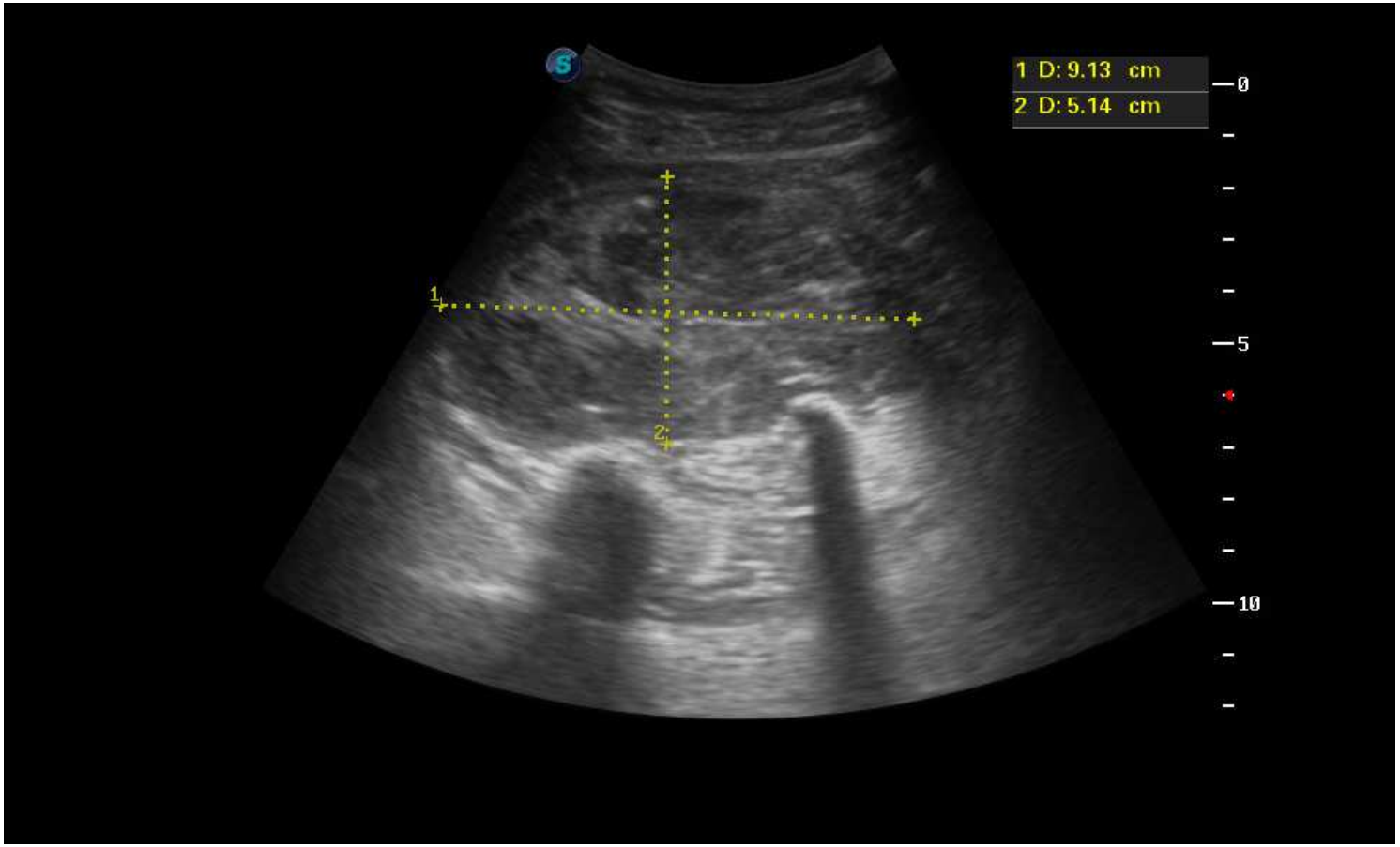

0
1
2
3
4

# Case Report: B-cell Lymphoma (after 10 days)

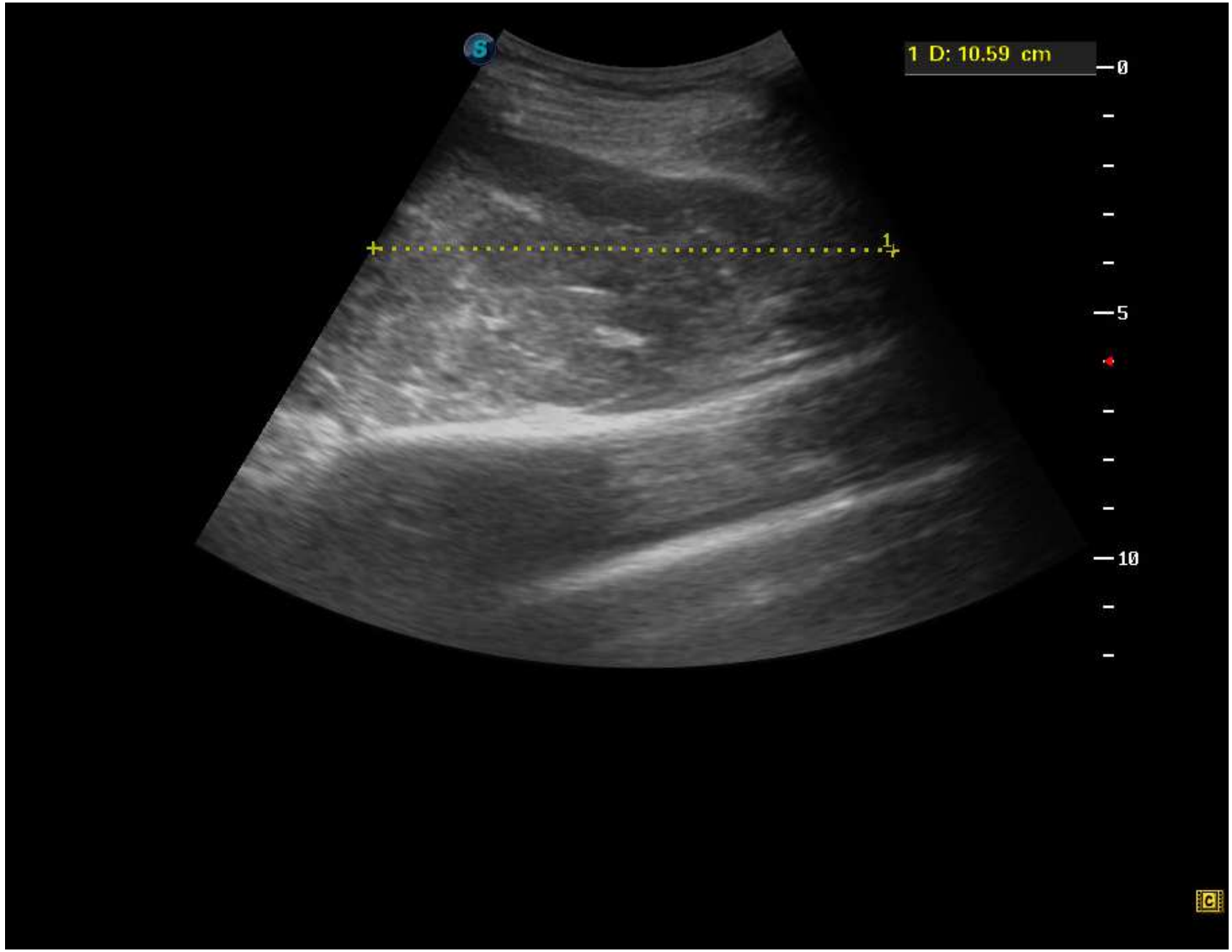

5
5


0
5
0
5

# Case Report: Liposarcoma (12.12.2016)

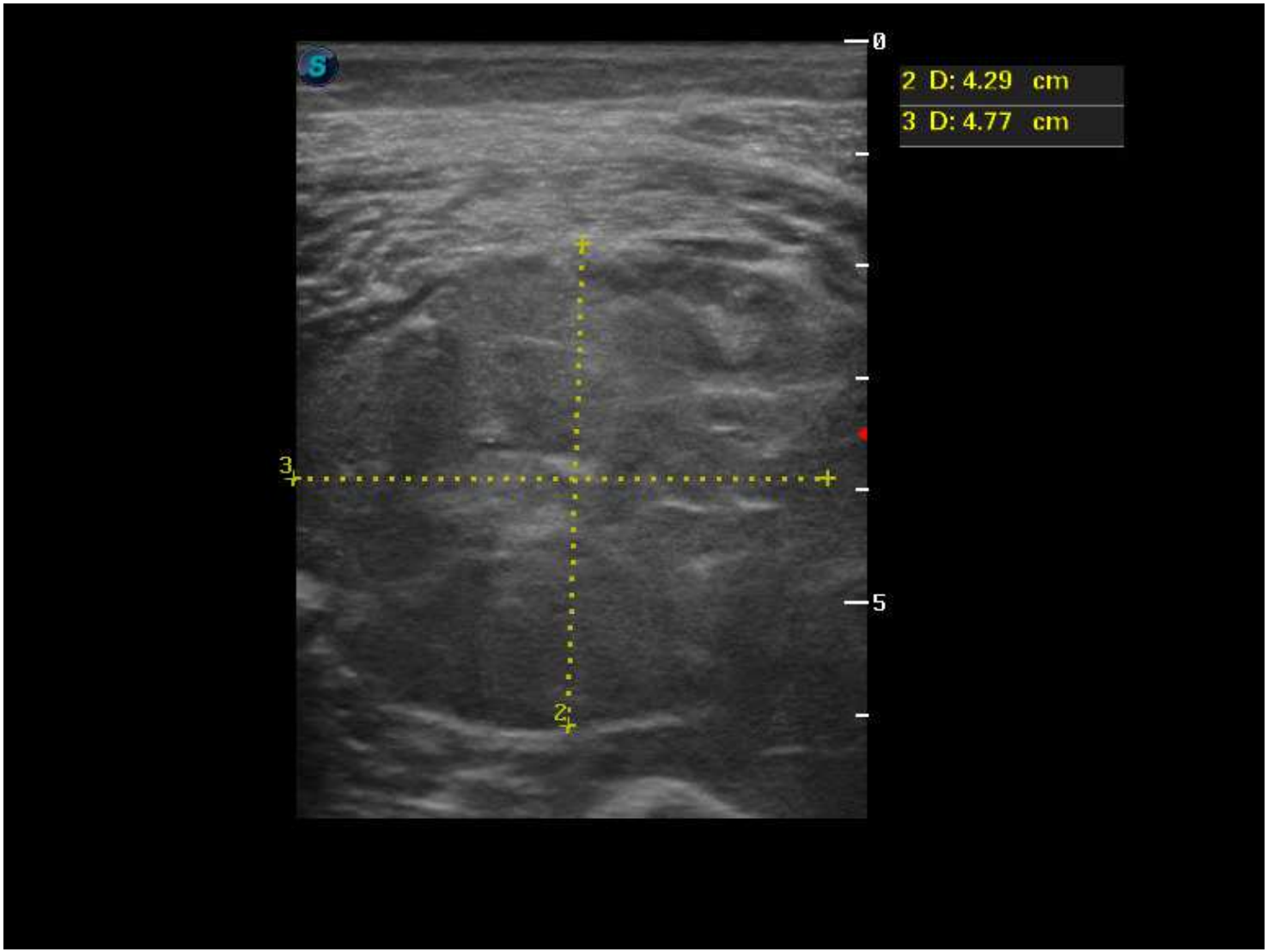


# Case Report: Liposarcoma (16.12.2016)

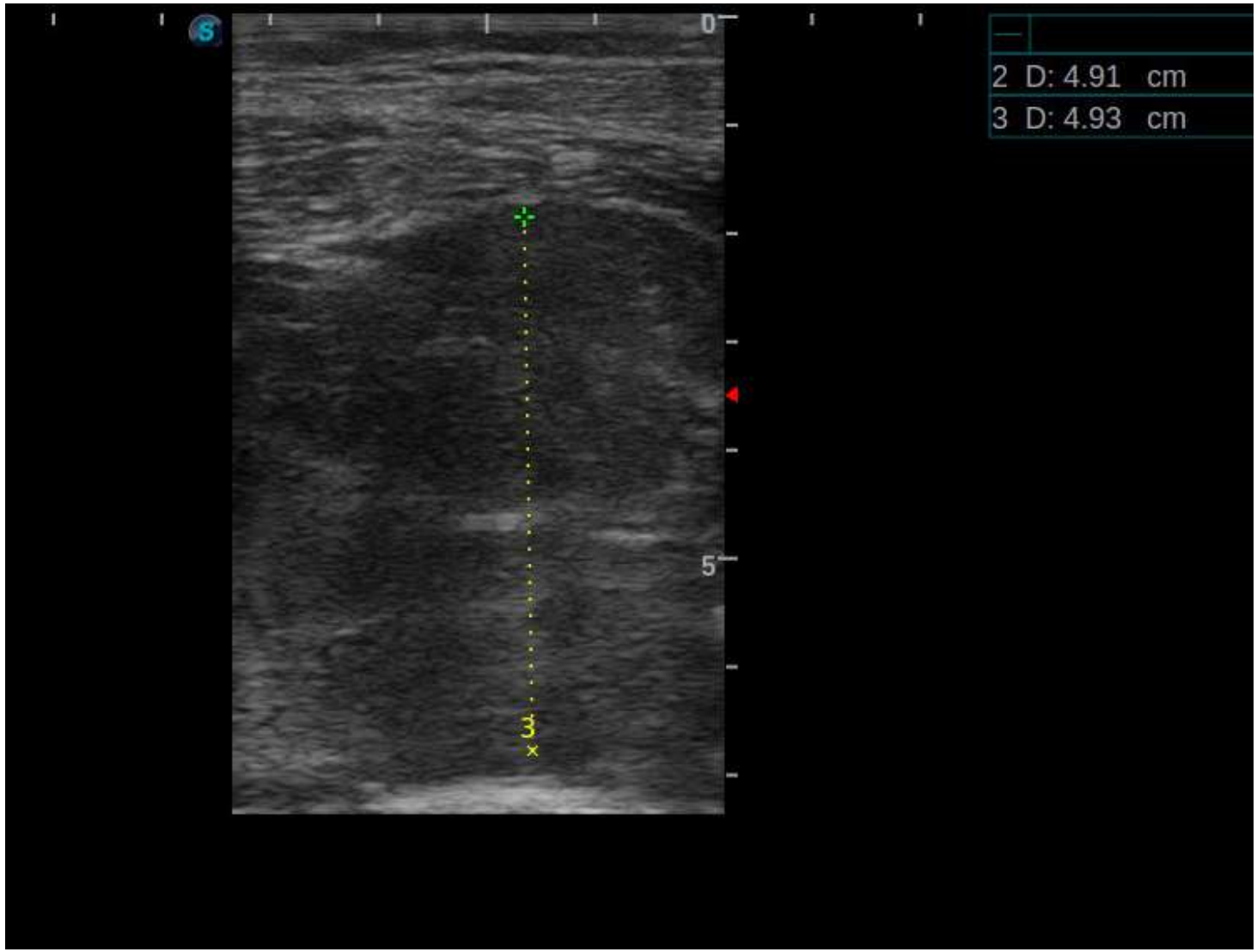


# Case Report: Liposarcoma (19.12.2016)

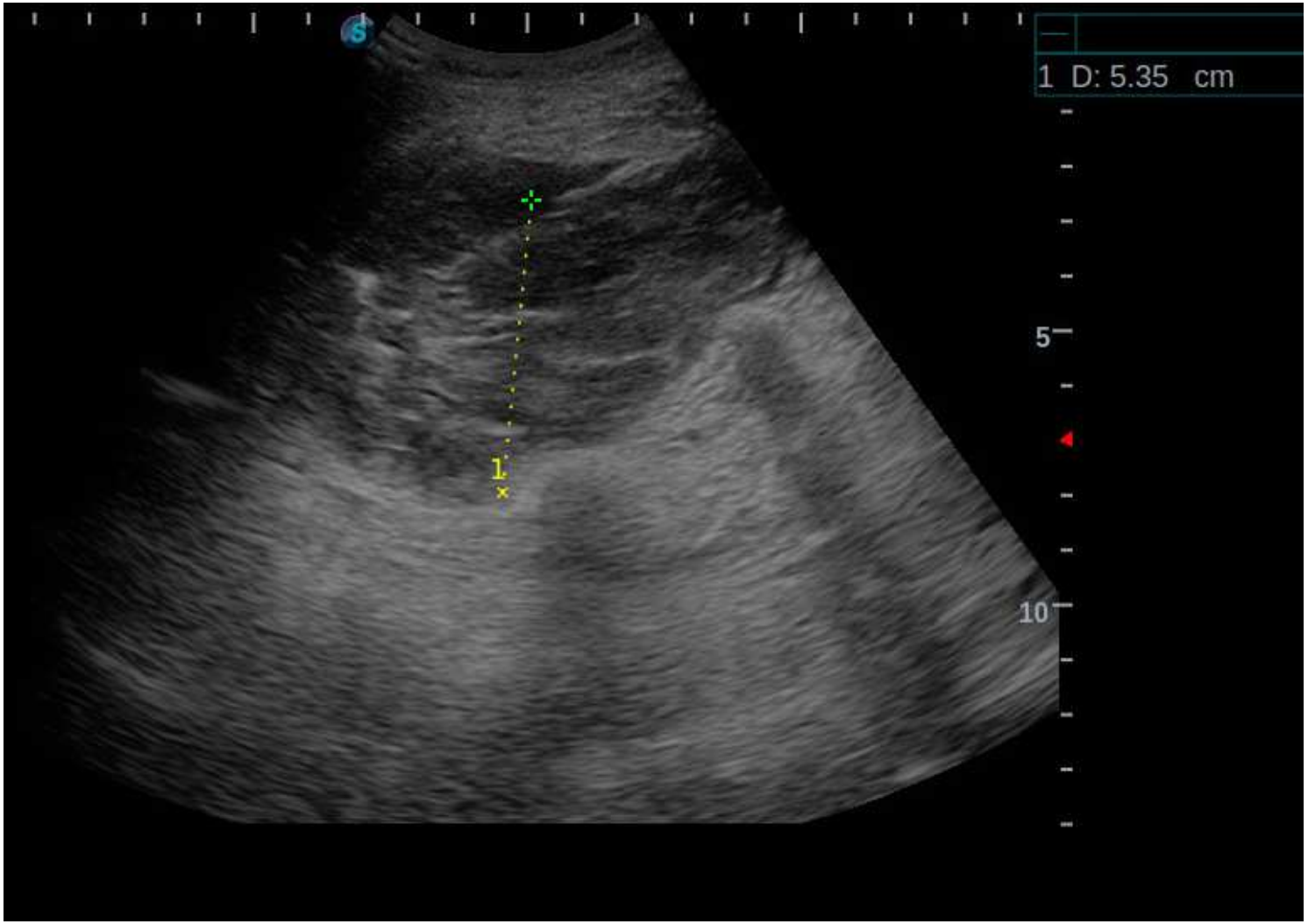
# Case Report: Liposarcoma (22.12.2016)



# Case Report: Liposarcoma (10.02.2017)



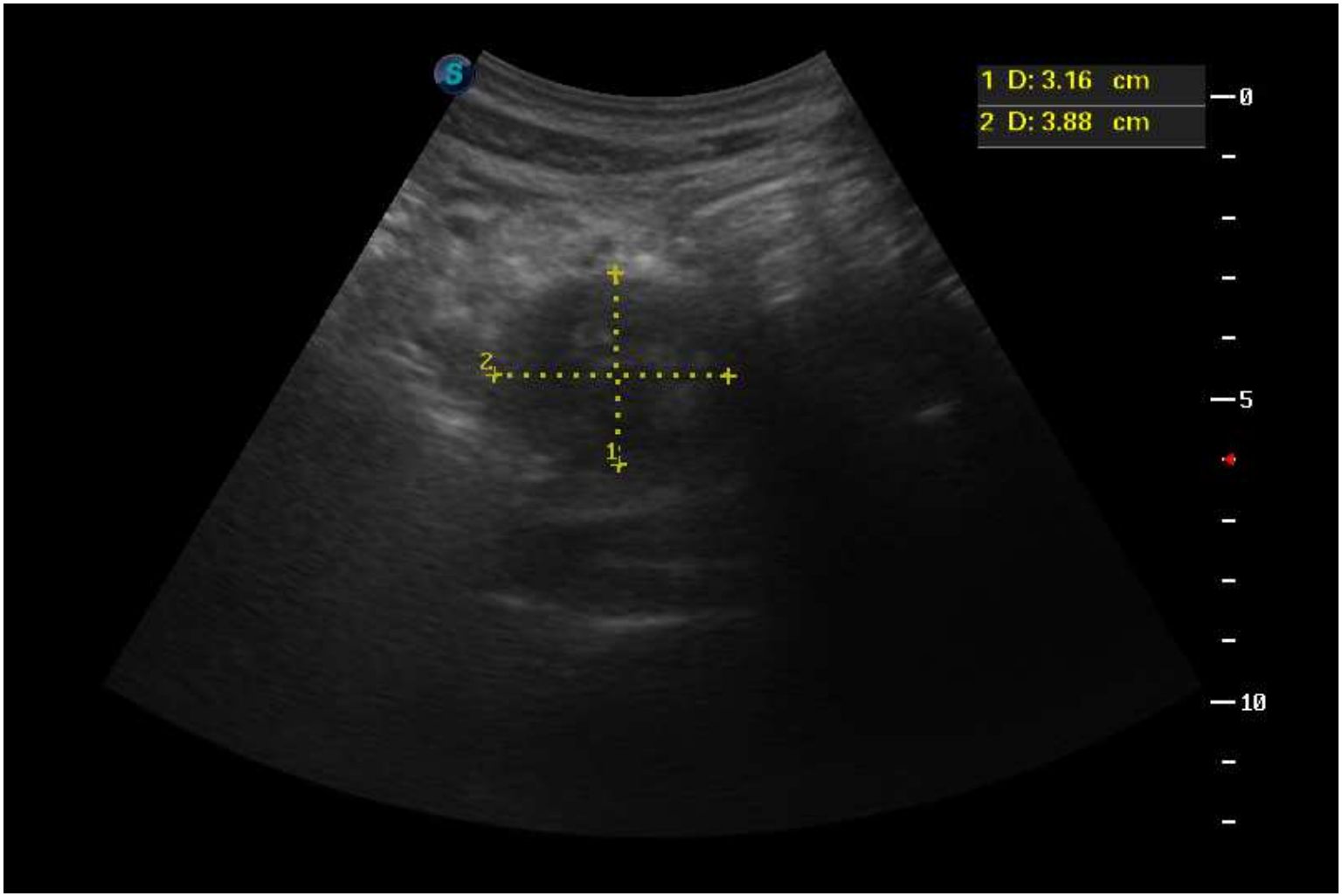
# Case Report: Liposarcoma (10.02.2017)



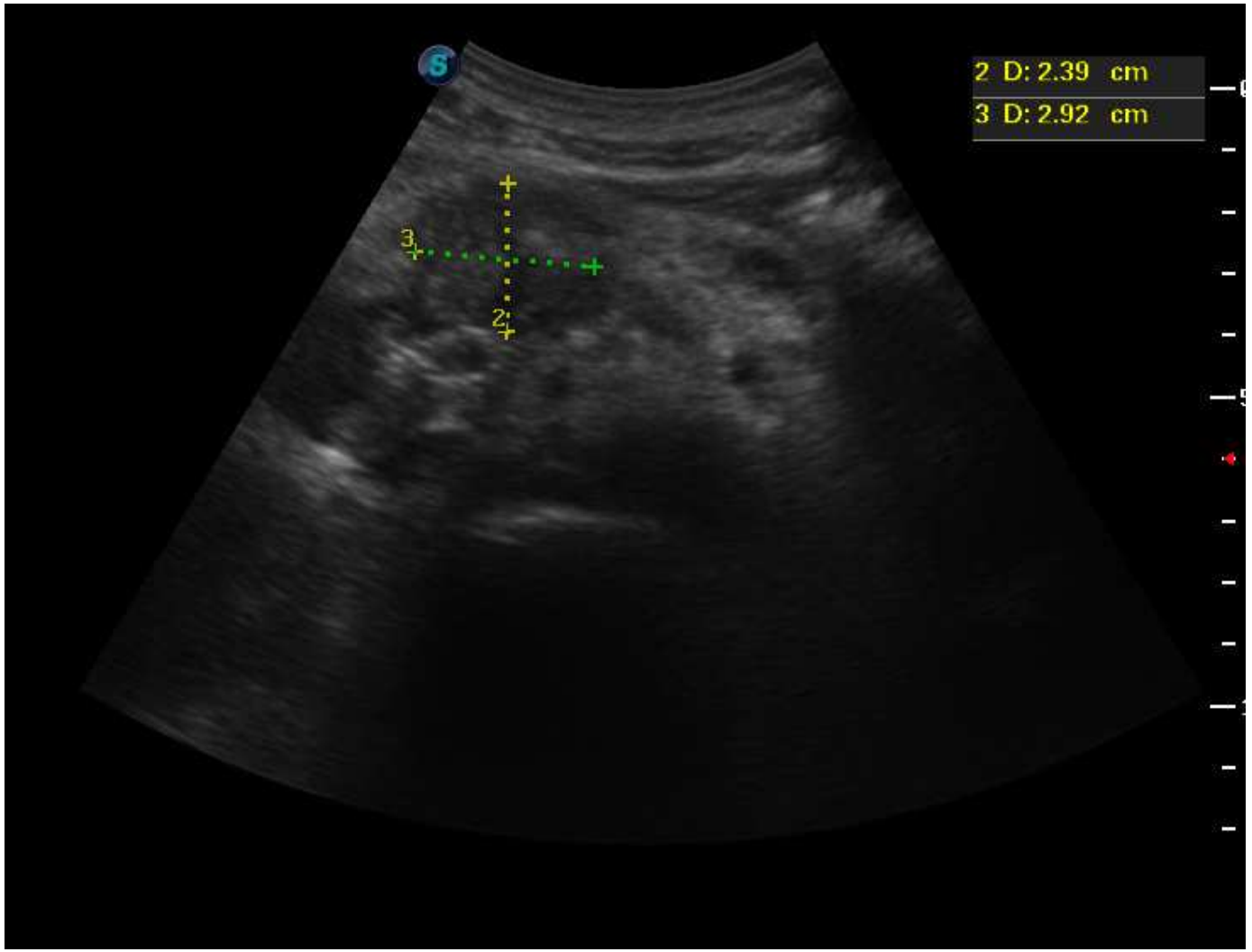
# Case Report: Liposarcoma (10.02.2017)

# Case Report: Liposarcoma (10.02.2017)

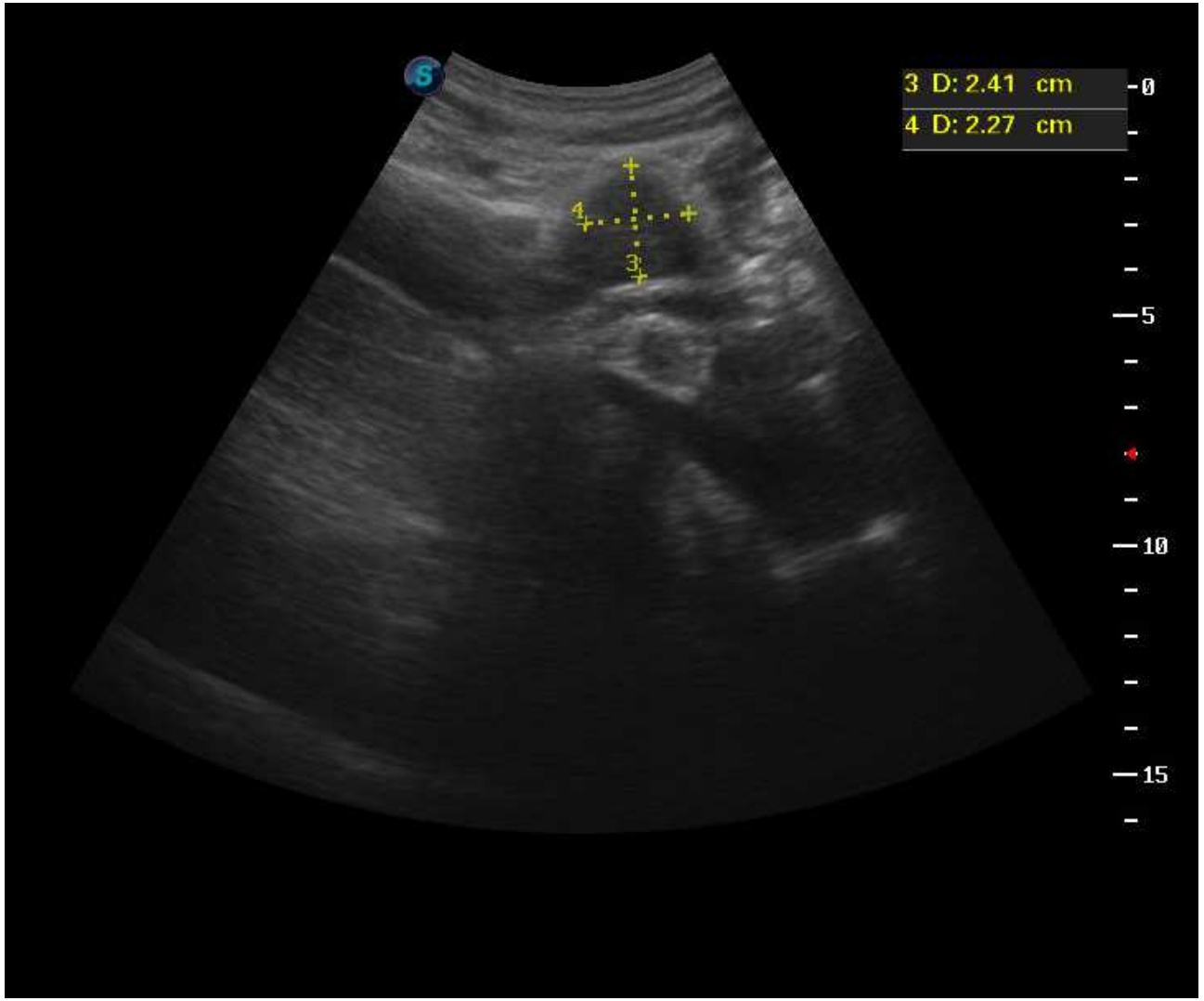
# Case Report: Pancreatic Cancer (10.10.2016)



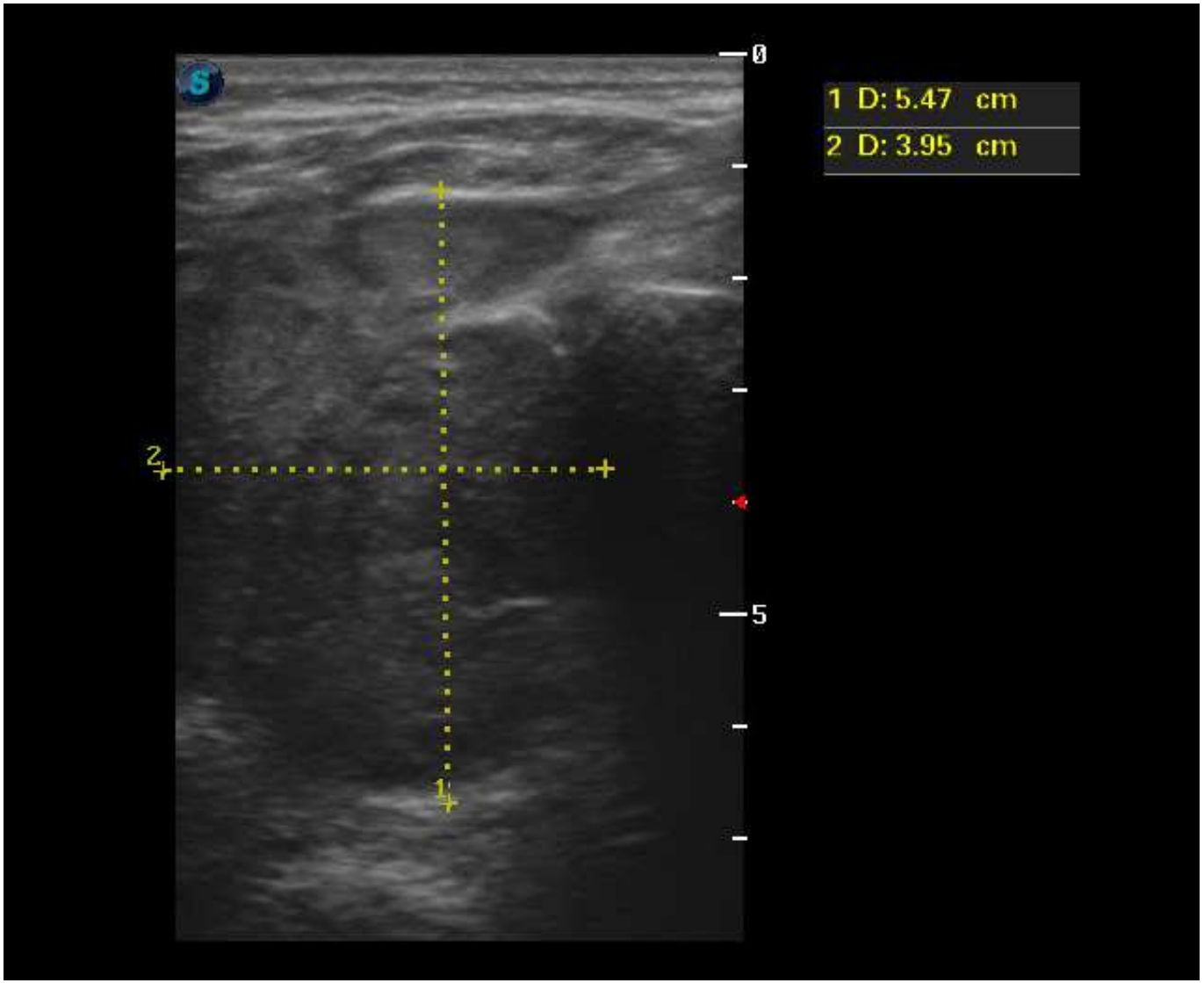
# Case Report: Pancreatic Cancer (13.10.2016)



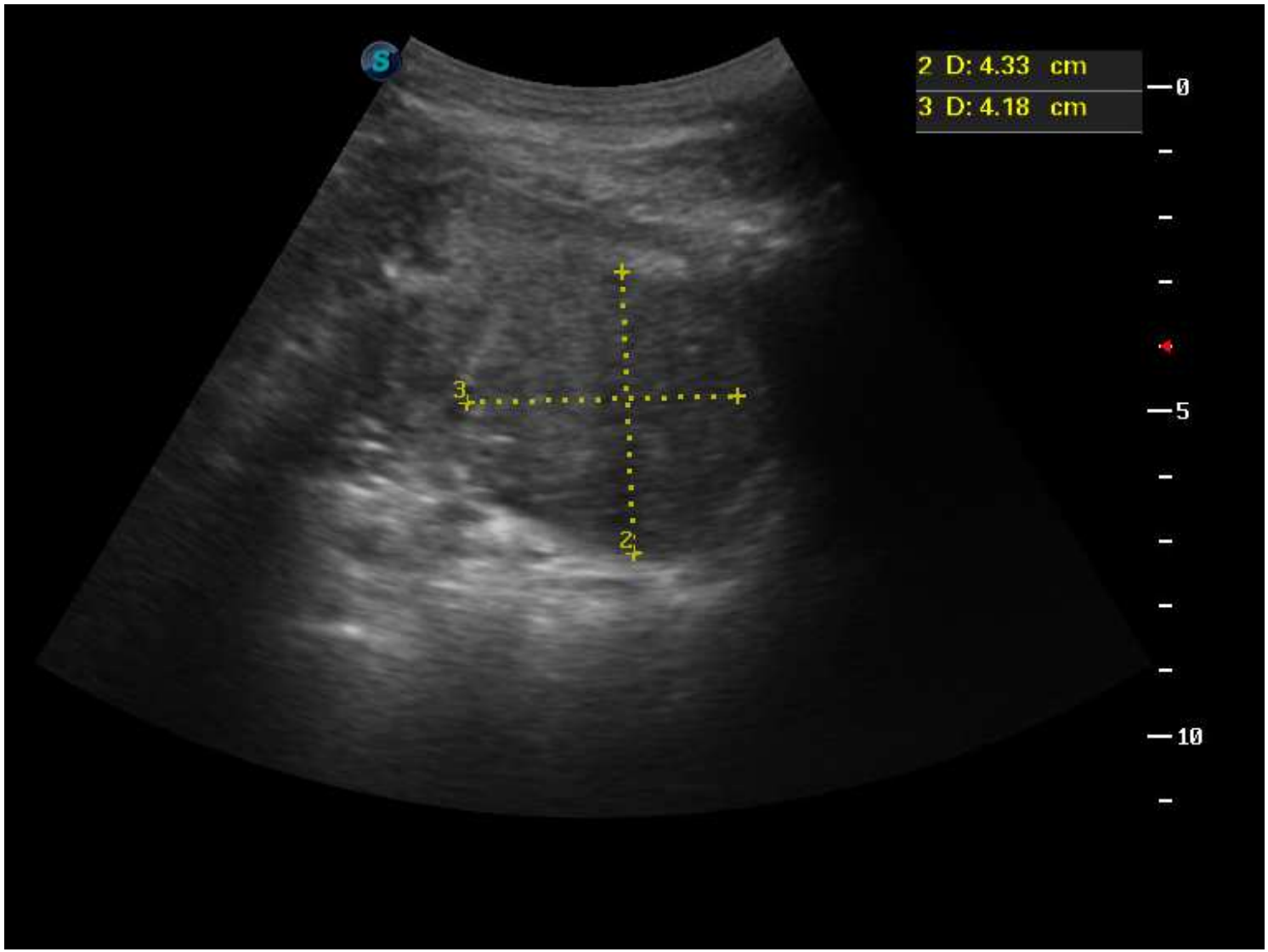
# Case Report: Pancreatic Cancer (21.10.2016)



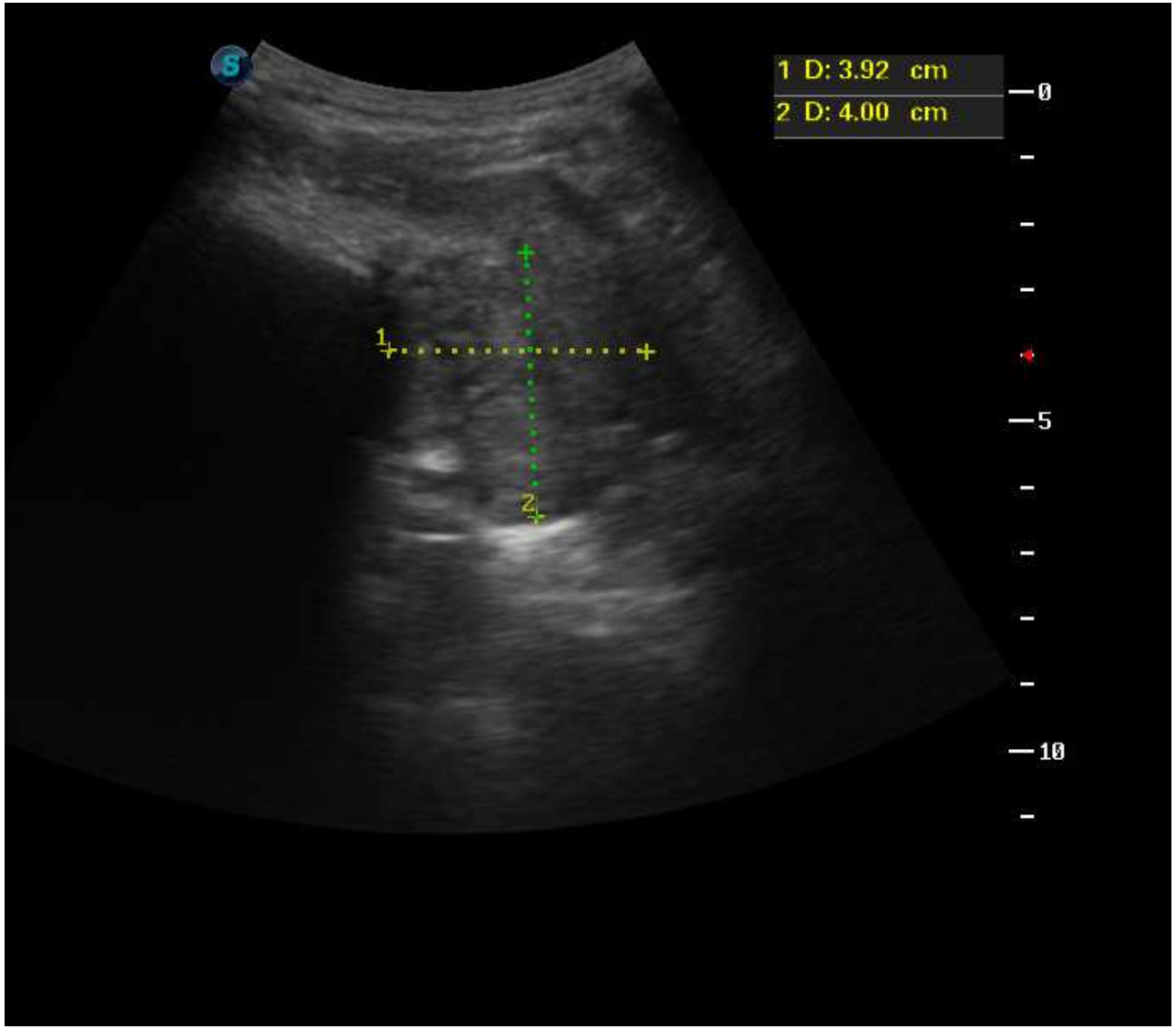
# Case Report: Ewing Sarcoma, sacrum, female, 14 y. (31.10.2016)



# Case Report: Ewing Sarcoma, sacrum, female, 14 y. (02.11.2016)



# Case Report: Ewing Sarcoma, sacrum, female, 14 y. (03.11.2016)



# Case Report: Lung Cancer with 15 Brain Metastases, 45 y., female

Hello Dr Weber,

Yesterday I had review scans at Royal Marsden
and I want to tell you my good news.

The scans showed reduction of tumors both in my lung and lesions in my head. The lung reduced around 40 % in mass (that's my rough calculation based on 2d measurements given) as did the smaller cancer in my lung.

The doctor could not see the other lesions (there were about 14).

# Case Report: Lung Cancer with 15 Brain Metastases, 45 y., female: CT Review

The external CT chest and abdomen scan of 28/12/2016 has been reviewed and compared with the previous scan from 11/11/2016.

The superior right perihilar mass has further reduced in size, measuring 23 x 23mm (series 7 image 37) compared to 29 x 28mm previously. The hilar node inferiorly is now subcentimetre. No other focal lung lesions. No mediastinal or left hilar adenopathy.

No change in the liver cysts. The gallbladder, spleen, pancreas, kidneys and adrenal glands are unremarkable and unchanged. No abdominal lymphadenopathy. No bone lesions.

**Comment: Further reduction in size of the right hilar mass and adjacent adenopathy consistent with further partial response.**

# Patient with Breast Cancer and Multiple Bone Metastases

- 2x therapy with 75 mg lip ICG, Curcumin, low dose chemotherapy with lip-Doxorubicin, 5-FU and Mitoxantron
- Interstitial therapy on the spine, low dose ultrasound and shockwaves
- **90 % reduction of spinal metastases in MRI and nearly pain-free**

# Summary: New Therapeutic Strategies for Cancer therapy

- **Photodynamic and sonodynamic therapy with liposomal ICG, Chlorin E6, Hypericin and Curcumin**
- Low dose chemotherapy using chemodrugs as photosensitizers
- Immunotherapy with intravenous laser blood irradiation
- Immunotherapy with GcMAF, TBL12, dendritic cells, oncolytic viruses and other methods
- Hyperbaric oxygen therapy

# Hyperbaric Oxygen Therapy:

# Thank you!