PHOTODYNAMIC DIAGNOSIS & THERAPY

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Presentation Plan

- Introduction photomedicine
- Photodetection (PDD)
- Photodynamic Therapy (PDT)
- Conclusion / Perspective
Photodynamic Principle

• Use of a photo-enhancing or photo-sensitizing chemical to aid in the diagnosis or treatment of a target cell
Historical


! LASERS + OPTICAL FIBERS !

1993 First approval (by the canadian health agency) of PDT with Photofrin® for the prophylactic treatment of bladder cancer.
Photophysical Processes

Fluorescence detection

Photodynamic Therapy

$S_0 ightarrow S_1$ Absorption

$S_1 ightarrow S_2$ Fluorescence

$I_{SC} = 1$ ns

$\tau = 10 \mu$s

$T_1$ Phosphorescence

$d = 45$ nm

$\Delta t = 250$ ns

Singlet Oxygen production

Collision energy transfer
PHOTORADIATION THERAPY OF CANCER
(Laser–Hematoporphyrin Derivative)

Cancer

48 - 72 hours

Inject HPD (drug) in vein

Drug selectively retained by cancer cells

Fiber optic bundle

Argon Laser

Dye Laser

514 nm
488 nm
(Blue-Green Light)

625-635 nm
(Red Light)

sens + hv → 1sens*

1sens* → 3sens*

3sens* + 3O₂ → O₂ + sens

O₂ + substrate → oxidation

sens = HPD

O₂ Kills Cells
Photosensitizers

• Porphyrrins
  – Photofrin (PF)
  – "Aminolevulinic acid (ALA)", Protoporphyrin IX (PpIX)

• Chlorins
  – m-Tetrahydroxyphenyl chlorin (mTHPC): Temoporfin (Foscan, Foslip)
  – Benzoporphyrrin derivative mono-acid (BPD): Verteporfin (Visudyne)
  – Tin ethyl etiopurpurin (SnET2)

• Phthalocyanines
Photofrin Approval

• Superficial bladder cancer (Canada 1993)
• Early and late esophageal and lung ca (Netherlands 1994)
• Advanced esophageal ca (USA 1995)
• Early ca of stomach, esophagus, lung, cervix and cervical dysplasia (Japan 1994)
Approvals of second generation photosensitizers

- Temoporfin (Foscan, Biolitec): PDT head and neck cancer (USA 2001)
- Meth-aminolaevulinate (Metvix, Galderma): PDT actinic keratosis, basal cell carcinoma (EU and Australia 2003)
- Verteporfin (Visudyne, QLT, Novartis): macular degeneration of the retina (USA and EU 2002)
PHOTODETECTION
Problematic

Early cancers are easier to treat

Advanced cancer
Difficult to treat

Localized

Radiography, endoscopy, MRI

Early cancer are difficult to detect

Metastases

Contrast
Early lesion / normal surrounding

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Mathieu Zellweger, Février 2000
Principle of fluorescence

- **Excitation Photon**
- **Fluorescence photon**

**Fluorescent molecule**

\[ \Delta E > 0 \]  
\[ \Delta E < 0 \]
Combined Diagnosis System

- White Light
- ALA-Mode
- Autofluorescence-Mode
- Rigid Telescopes
- Fiberscopes
- OP - Microscopes
PHOTODETECTION
Clinical Data

M. Kriegmair,
Ludwig Maximillians-University Munich
Neurosurgery

Special Fluorescence Microscope
Cooperation w/ Carl Zeiss

Early Tumor Detection with Marker Substance

High grade Glioma

Stummer, Reulen
Munich-Großhadern
Figure 1

Common sites of ovarian cancer metastases.
Ovarian cancer spreads fast to the whole abdominal cavity by exfoliation.
Survival by outcome of second look

![Cumulative Survival vs Survival (Months) graph showing survival outcomes for neg second look, microsc pos, and macrosc pos.](image)
PDD in Gynaecology

- Laparoscopic view of ovarian cancer after ip ALA-application

A. Major
Geneva University Hospital
Light micrographs (A) and fluorescence (B) of a peritoneal nodule (size < 0.5 mm) 6 hr after ip ALA administration. Magnification (C) of the peritoneal serosa (boxed area in B) showing a thin layer of tumor matching with the fluorescence.

Blue Light Mode (ALA)
PDD Mode
Blue Light Mode (ALA)
PDD Mode
PDD Mode
Blue Light Mode (ALA)
PDD Mode
CONCLUSIONS

- Photodetection of ovarian cancer peritoneal implants, not visible by other methods, has been shown to be efficient and feasible in patients.

- Survival advantage has to be demonstrated in clinical trials (second look and staging of first stage ovarian cancer).
PHOTODYNAMIC THERAPY
PHOTODYNAMIC THERAPY

Dye (PS) -> Photons

DYE

$0_2$

TOXICITY

ACTIVATED
Methaminolaevulinate (MAL) PDT in Actinic Keratosis

Trond Warloe
Radium Hospital Oslo
MAL-PDT in Basal Cell Carcinoma

Trond Warloe
Radium Hospital Oslo
MAL-PDT in Basal Cell Carcinoma

Trond Warloe
Radium Hospital Oslo
A. Major
Geneva University Hospital
CONCLUSIONS

• Photodynamic therapy (PDT) can be used efficiently in patients who were already treated with surgery, radiotherapy, and chemotherapy.

• PDT heals with better cosmetic results compared to other treatments (surgery, cryotherapy).

• PDT has no long-term side effects and has no limitations in repeating the procedure.