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

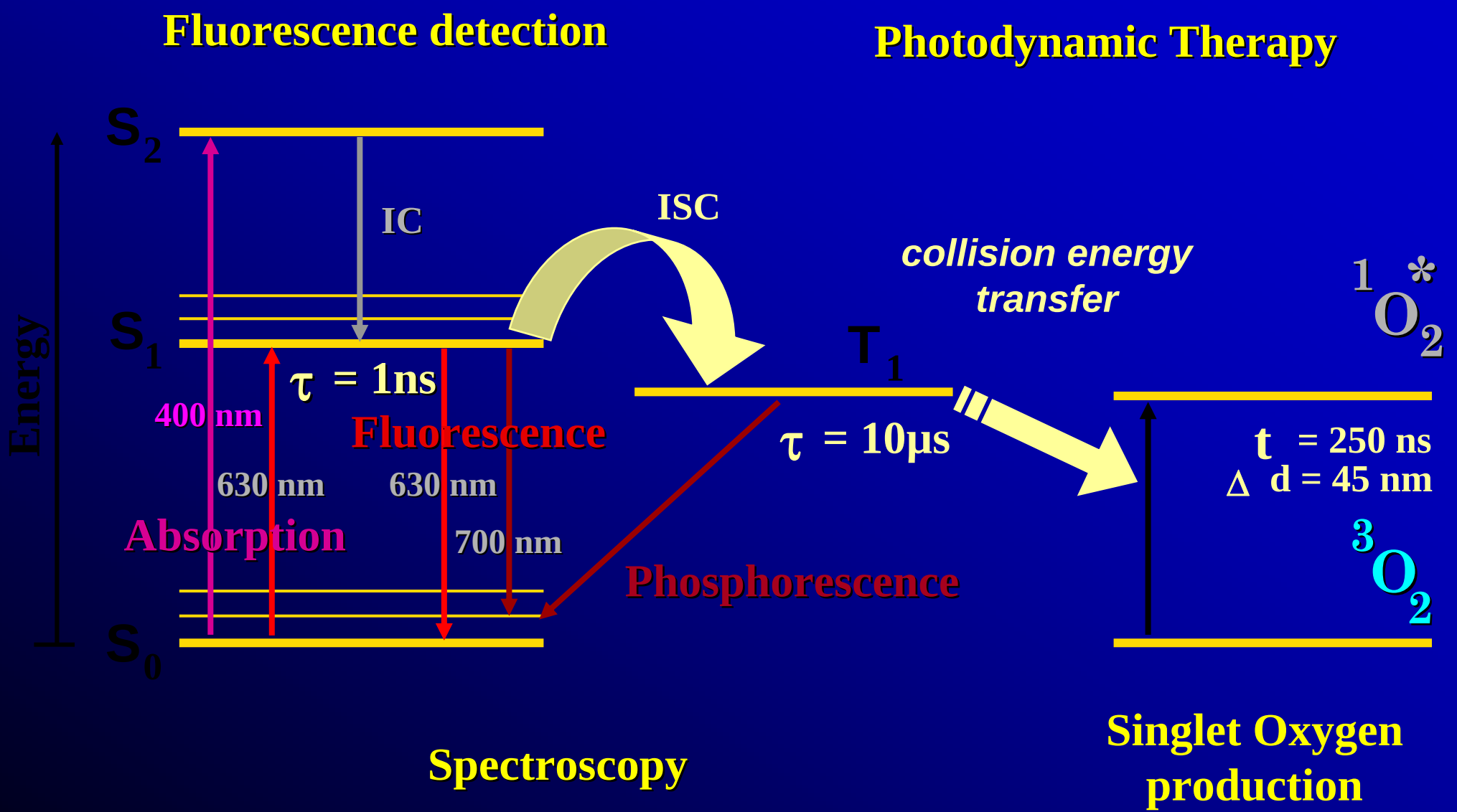
1976 J. F. KELLY + M. E. SNELL - First clinical PDT of a bladder carcinoma with HPD. (J. Urol., 115, 150, 1976).

1978 T. J. DOUGHERTY et al.- Clinical assessment of PDT (Cancer Res., 38, 2628, 1978).

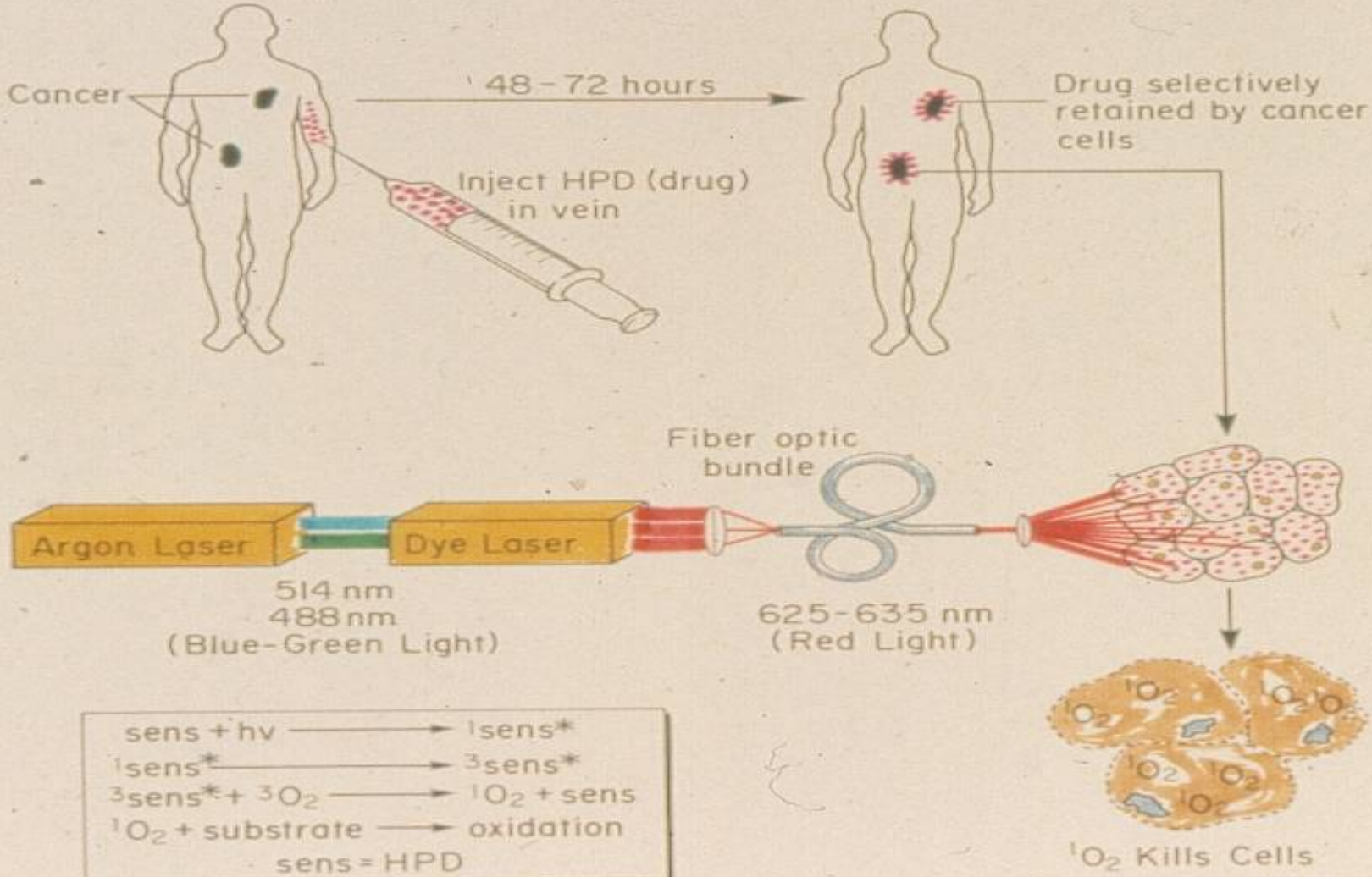
! LASERS + OPTICAL FIBERS !

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

Photophysical Processes



PHOTORADIATION THERAPY OF CANCER
(Laser–Hematoporphyrin Derivative)



$$\text{sens} + h\nu \longrightarrow {}^1\text{sens}^*$$
$${}^1\text{sens}^* \longrightarrow {}^3\text{sens}^*$$
$${}^3\text{sens}^* + {}^3O_2 \longrightarrow {}^1O_2 + \text{sens}$$
$${}^1O_2 + \text{substrate} \longrightarrow \text{oxidation}$$

sens = HPD

Photosensitizers

- Porphyrins
  - Photofrin (PF)
  - "Aminolevulinic acid (ALA)", Protoporphyrin IX (PpIX)
- Chlorins
  - m-Tetrahydroxyphenyl chlorin (mTHPC): Temoporfin (Foscan, Foslip)
  - Benzoporphyrin derivative mono-acid (BPD): Verteporfin (Visudyne)
  - Tin ethyl etiopurpurin (SnET2)
- Phtalocyanines

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)
- Hex-aminolaevulinate: PDD bladder cancer (Sweden 2004, EU 2005)
- Verteporfin (Visudyne, QLT, Novartis): macular degeneration of the retina (USA and EU 2002)

PHOTODETECTION

FLUORESCENCE SPECTROSCOPY OF EXOGENOUS, EXOGENOUSLY-INDUCED AND ENDOGENOUS FLUOROPHORES FOR THE PHOTODETECTION AND PHOTODYNAMIC THERAPY OF CANCER.

Problematic

Early cancers are easier to treat

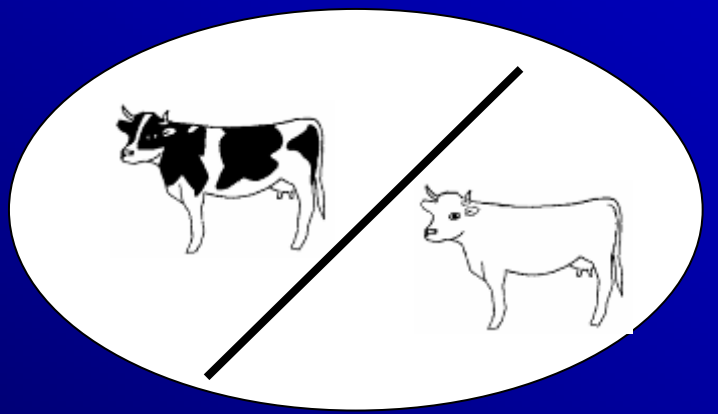
Advanced cancer Difficult to treat

Localized

Metastases

Radiography, endoscopy, MRI

Early cancer are difficult to detect

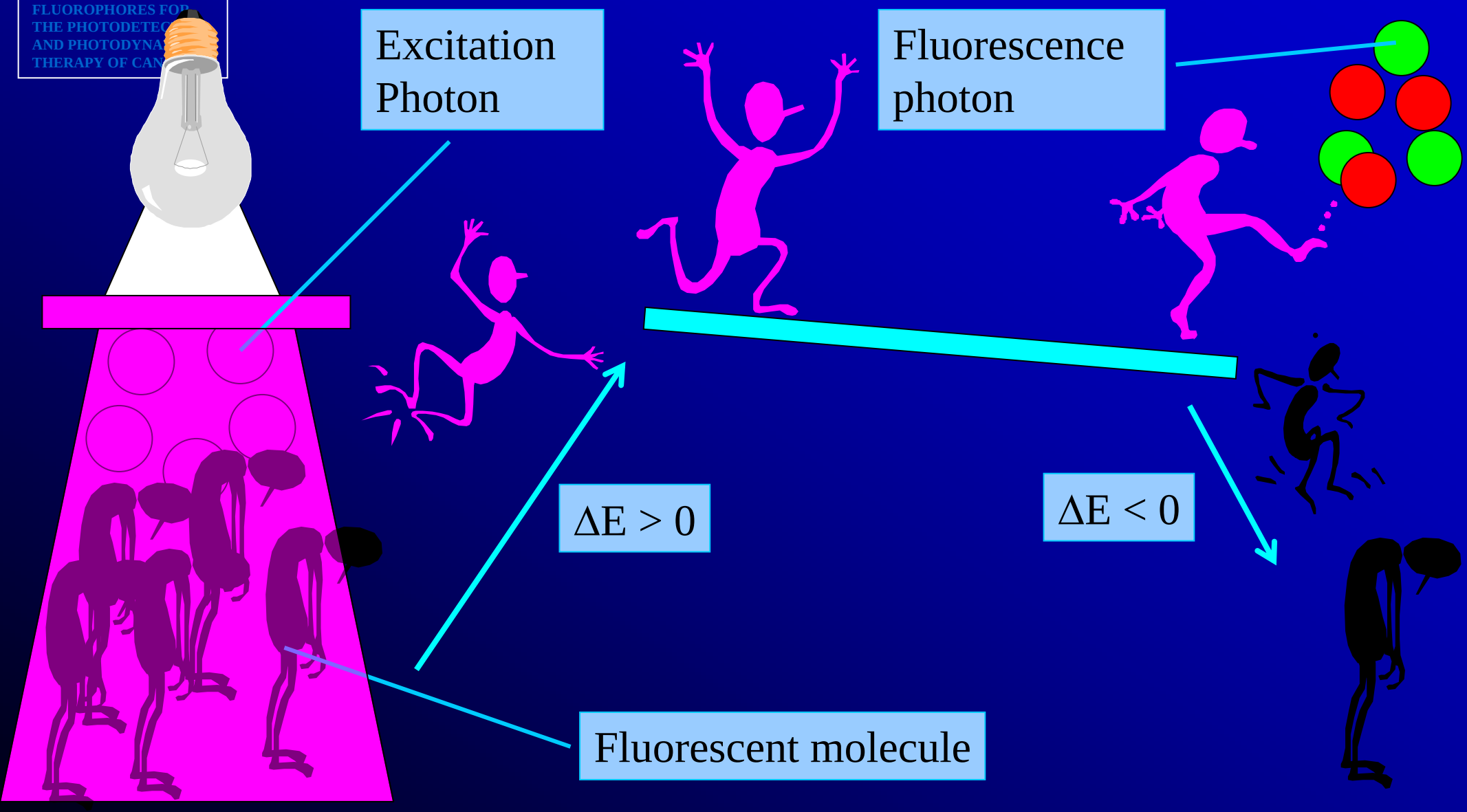


Contrast
Early lesion / normal surrounding

Matthieu Zellweger, Février 2000

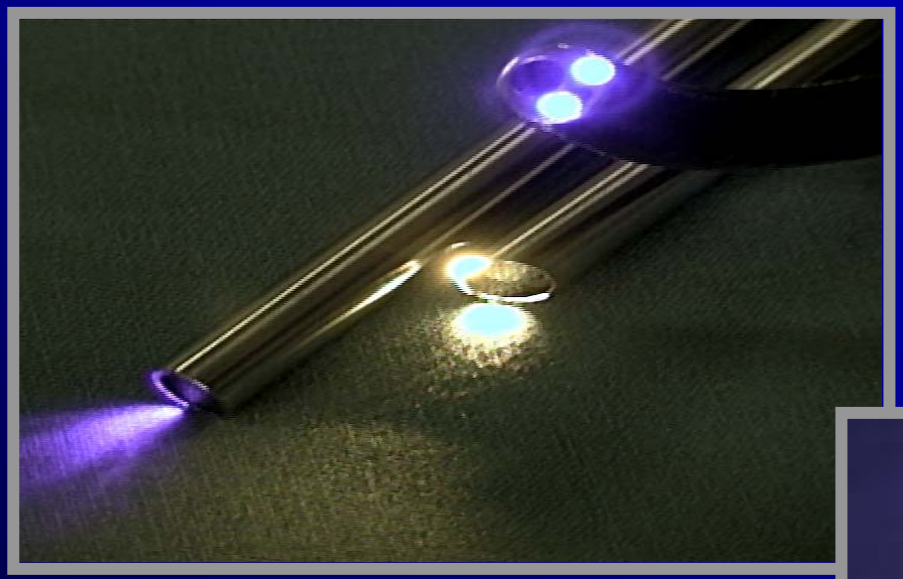
FLUORESCENCE SPECTROSCOPY OF EXOGENOUS, EXOGENOUSLY-INDUCED AND ENDOGENOUS FLUOROPHORES FOR THE PHOTODETEC AND PHOTODYNA THERAPY OF CAN

Principle of fluorescence



Matthieu Zellweger, Février 2000

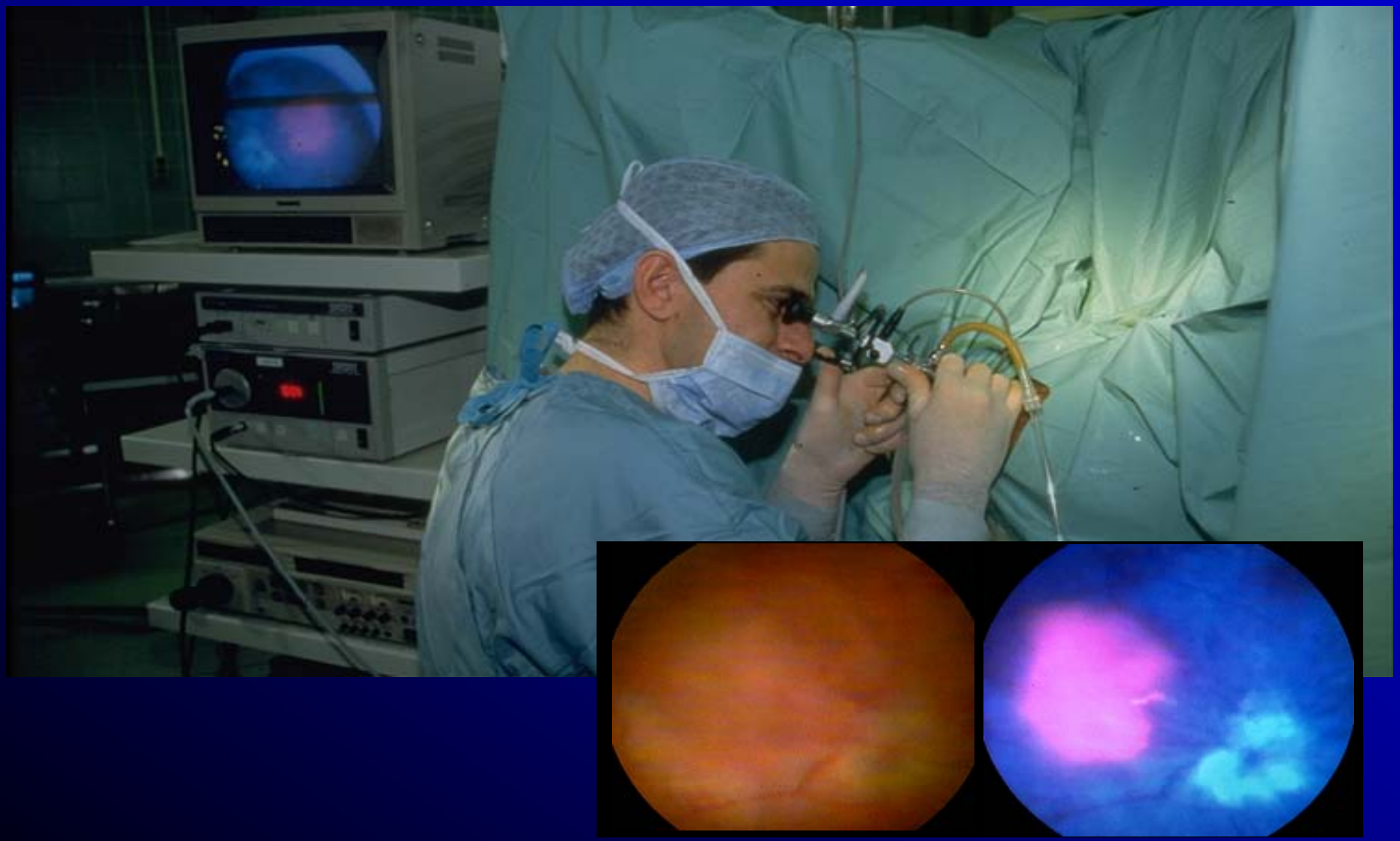
Combined Diagnosis System



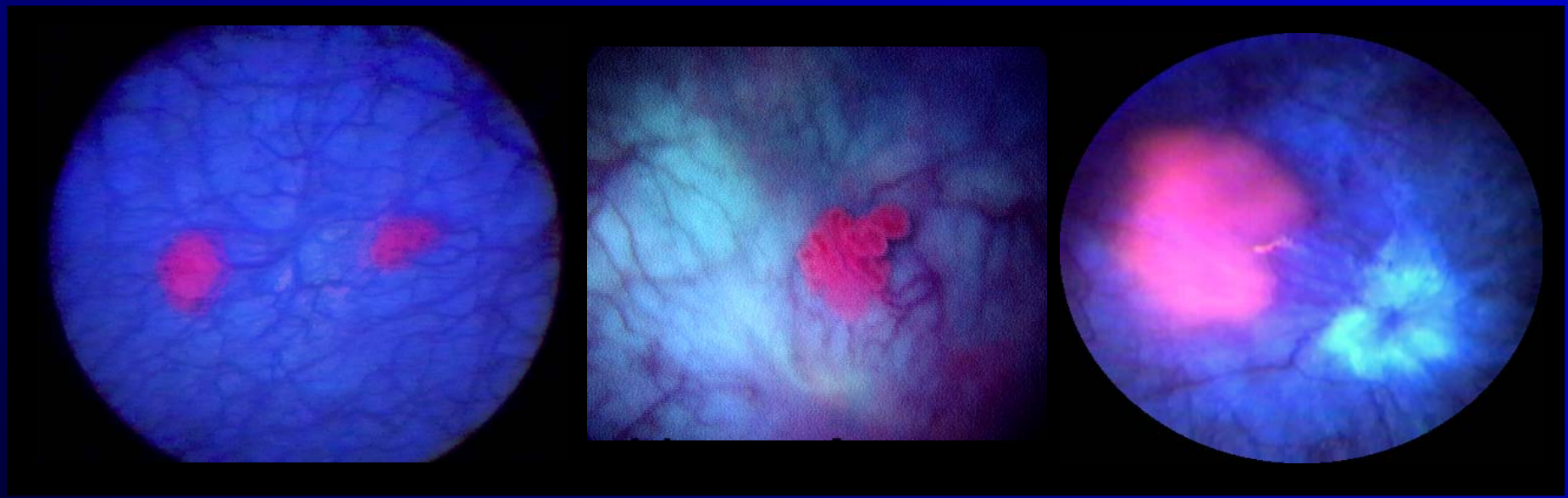
- **Rigid Telescopes**
- **Fiberscopes**
- **OP - Microscopes**

- **White Light**
- **ALA-Mode**
- **Autofluorescence-Mode**

P HOTODETECTION



Clinical Data



M. Kriegmair,

Ludwig Maximillians-University Munich

Neurosurgery

Special Fluorescence
Microscope
Cooperation w/ Carl Zeiss

Early Tumor Detection
<u>with</u> Marker Substance

High grade Glioma

Stummer, Reulen
Munich-Großhadern

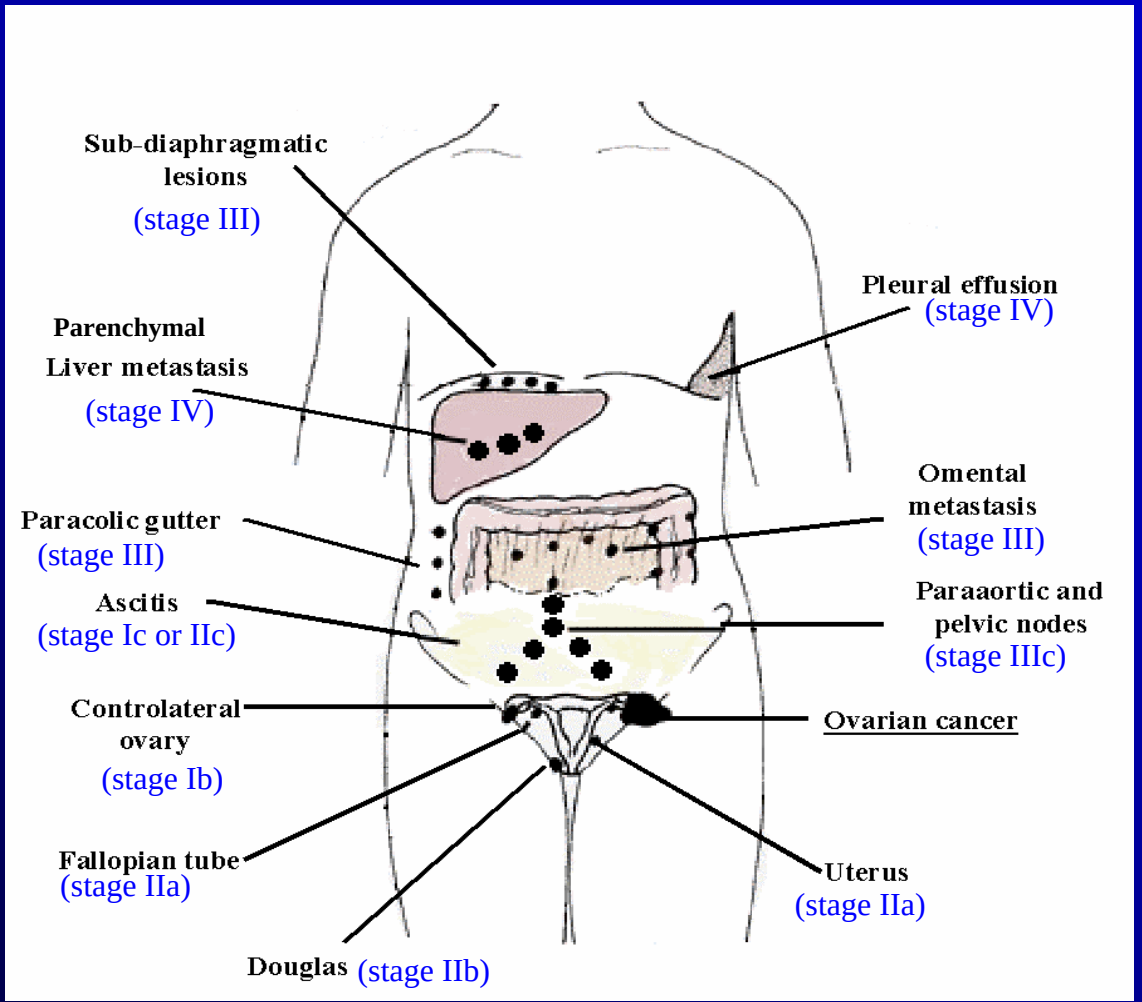
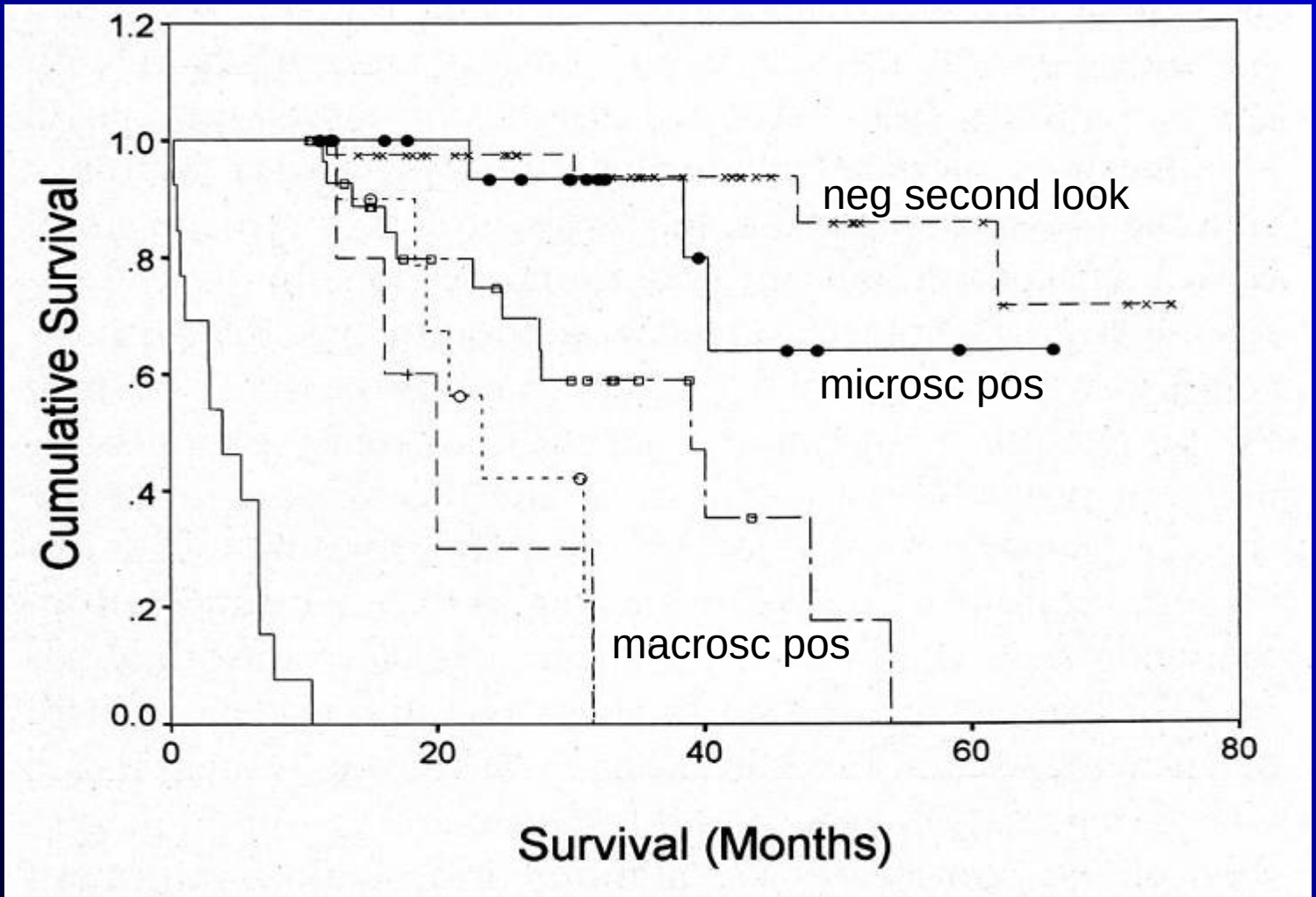


Figure 1

Common sites of ovarian cancer metastases.

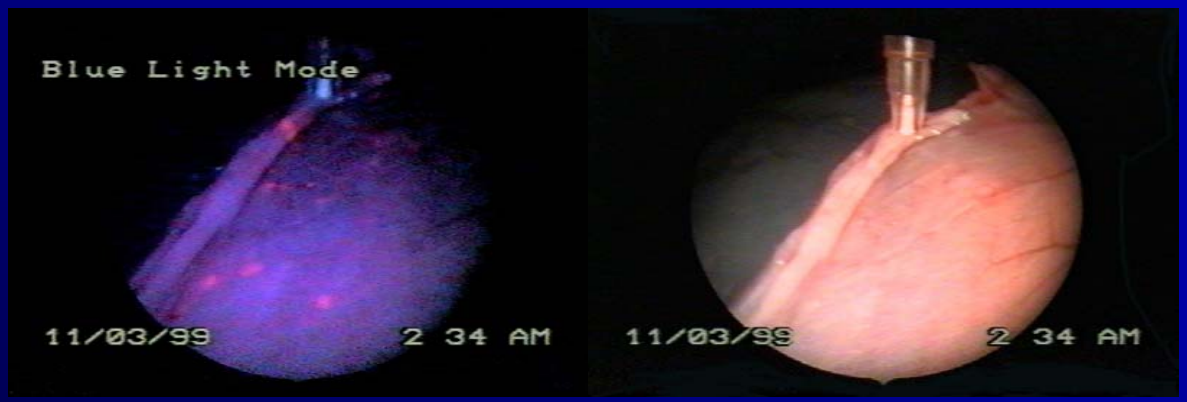
Ovarian cancer spreads fast to the whole abdominal cavity by exfoliation

Survival by outcome of second look

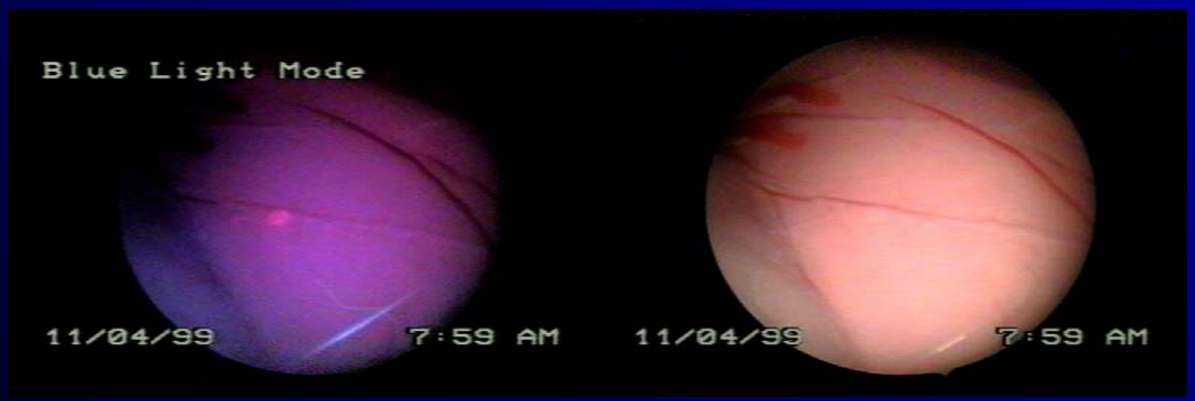


PDD in Gynaecology

- Laparoscopic view of ovarian cancer after ip ALA-application



A

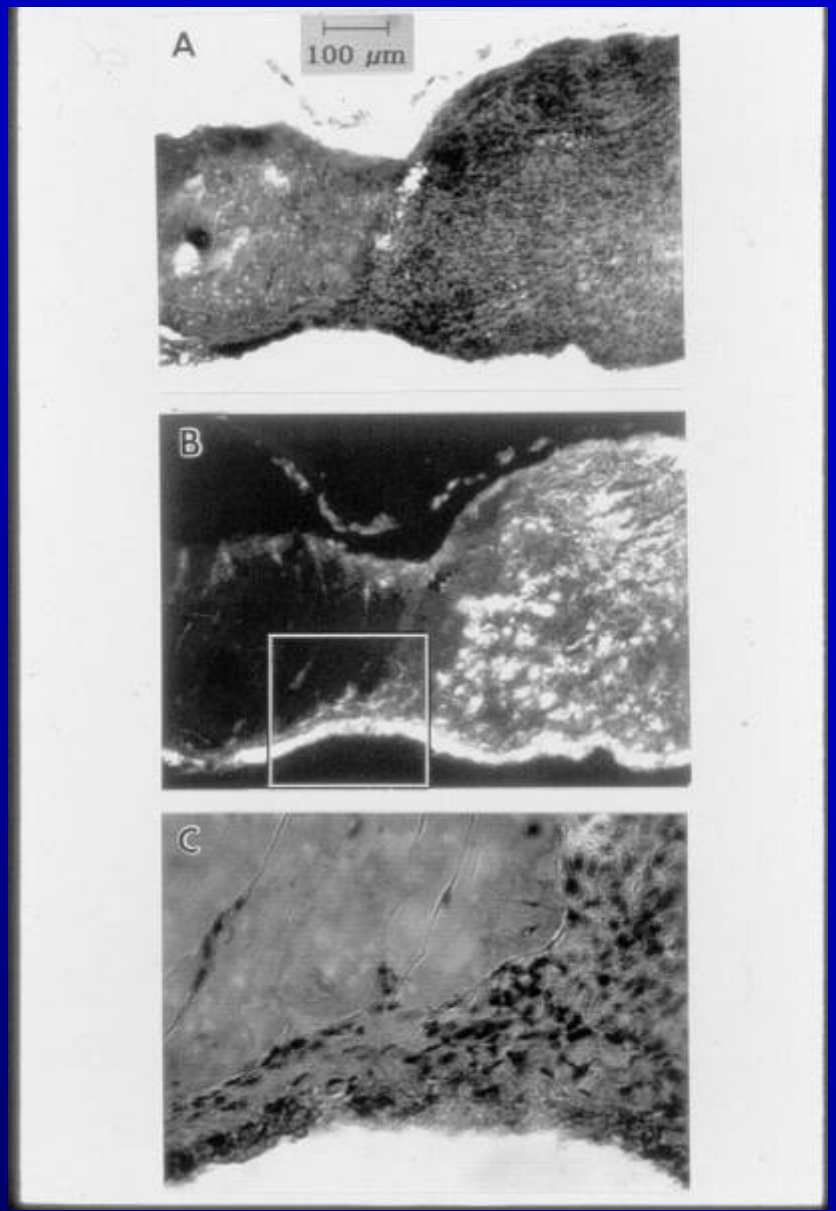


B

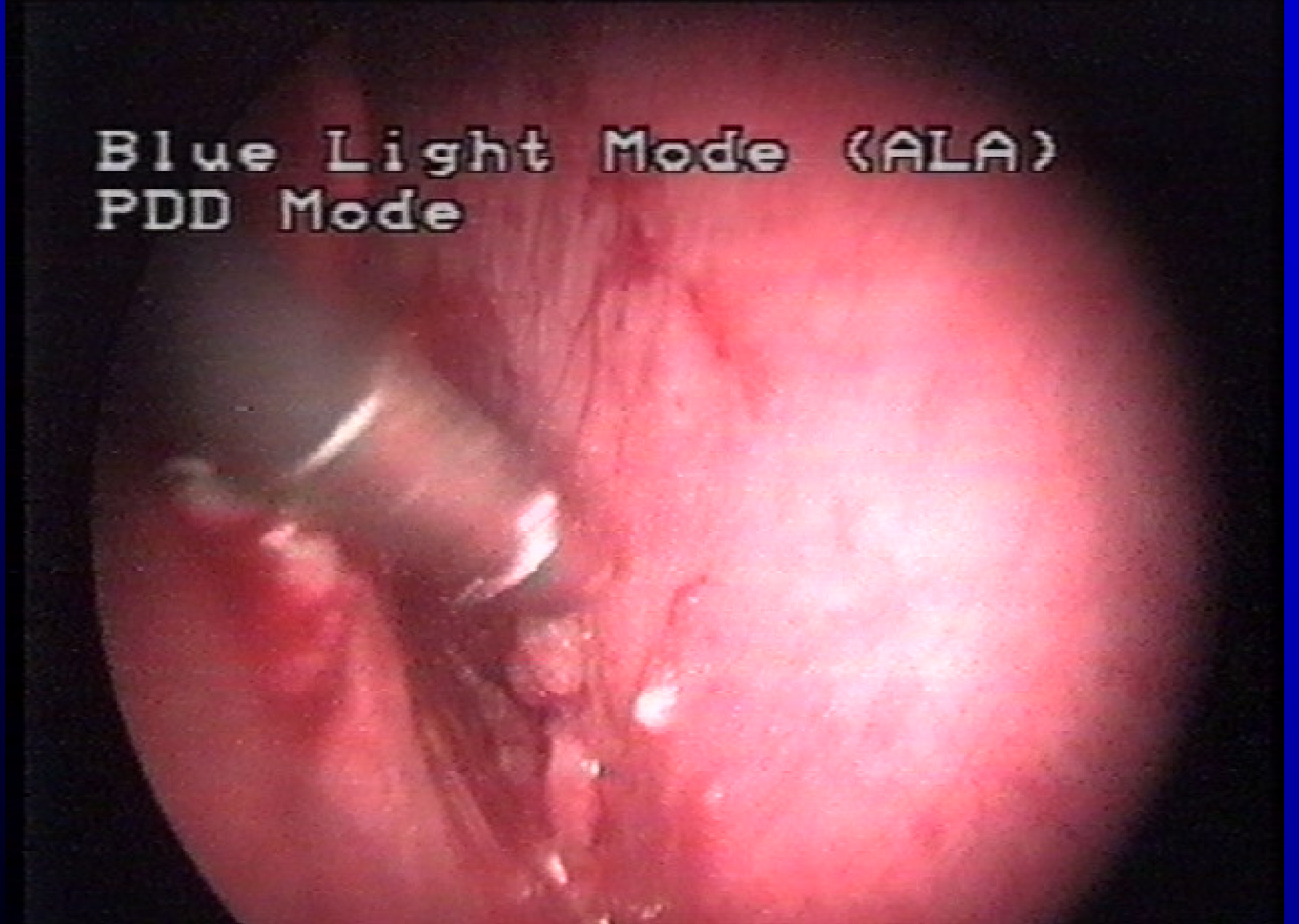
A. Major

Geneva University Hospital

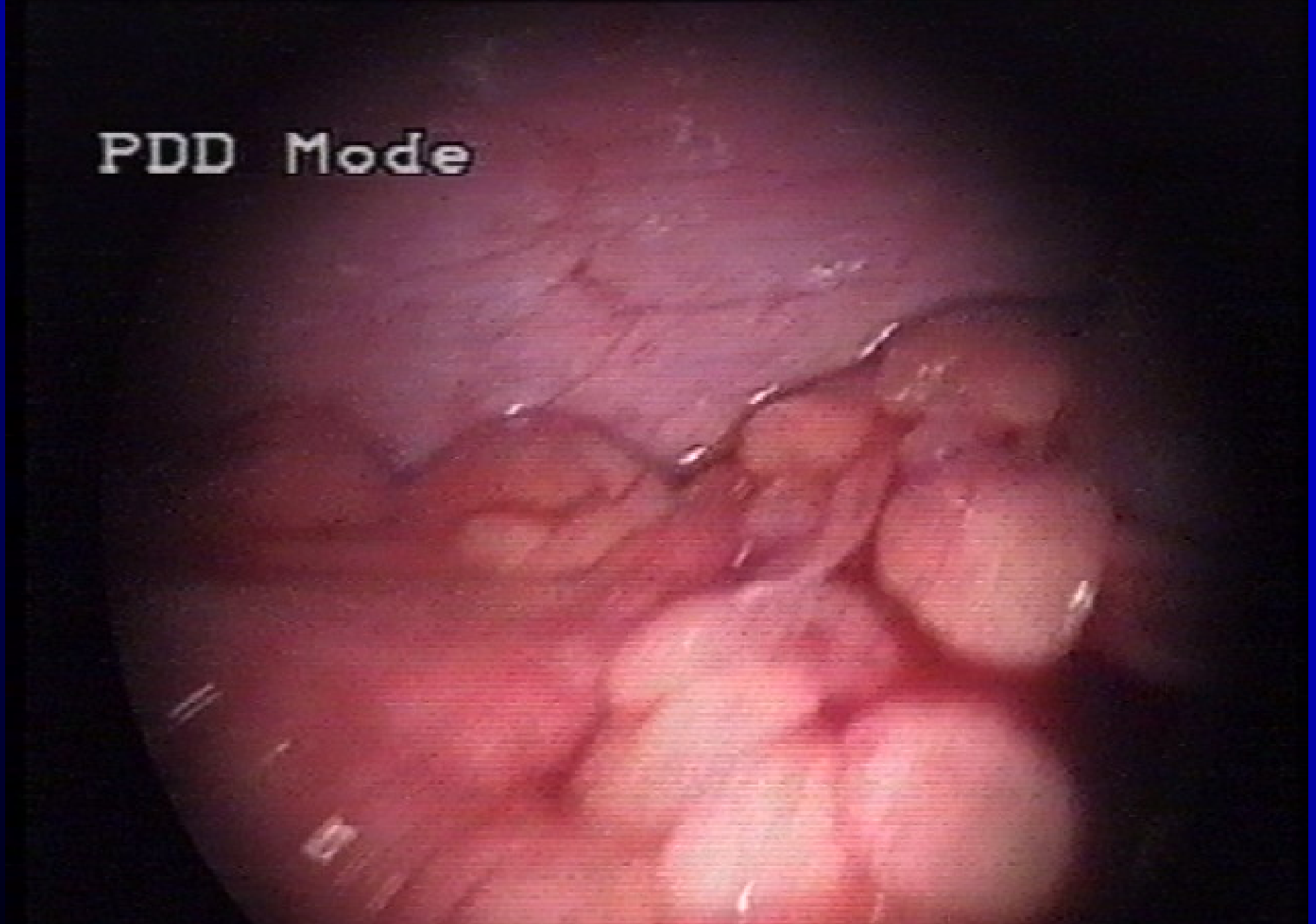
Light micrographs (A) and fluorescence (B) of a peritoneal nodule (size < 0.5 mm) 6 hr after ip ALA administration. Magnification (C) of the peritoneal serosa (boxed area in B) showing a thin layer of tumor matching with the fluorescence



Major A. et al Gynecol Oncol 1996, 66 : 122-32.


Blue Light Mode (ALA)
PDD Mode


Blue Light Mode (ALA)
PDD Mode

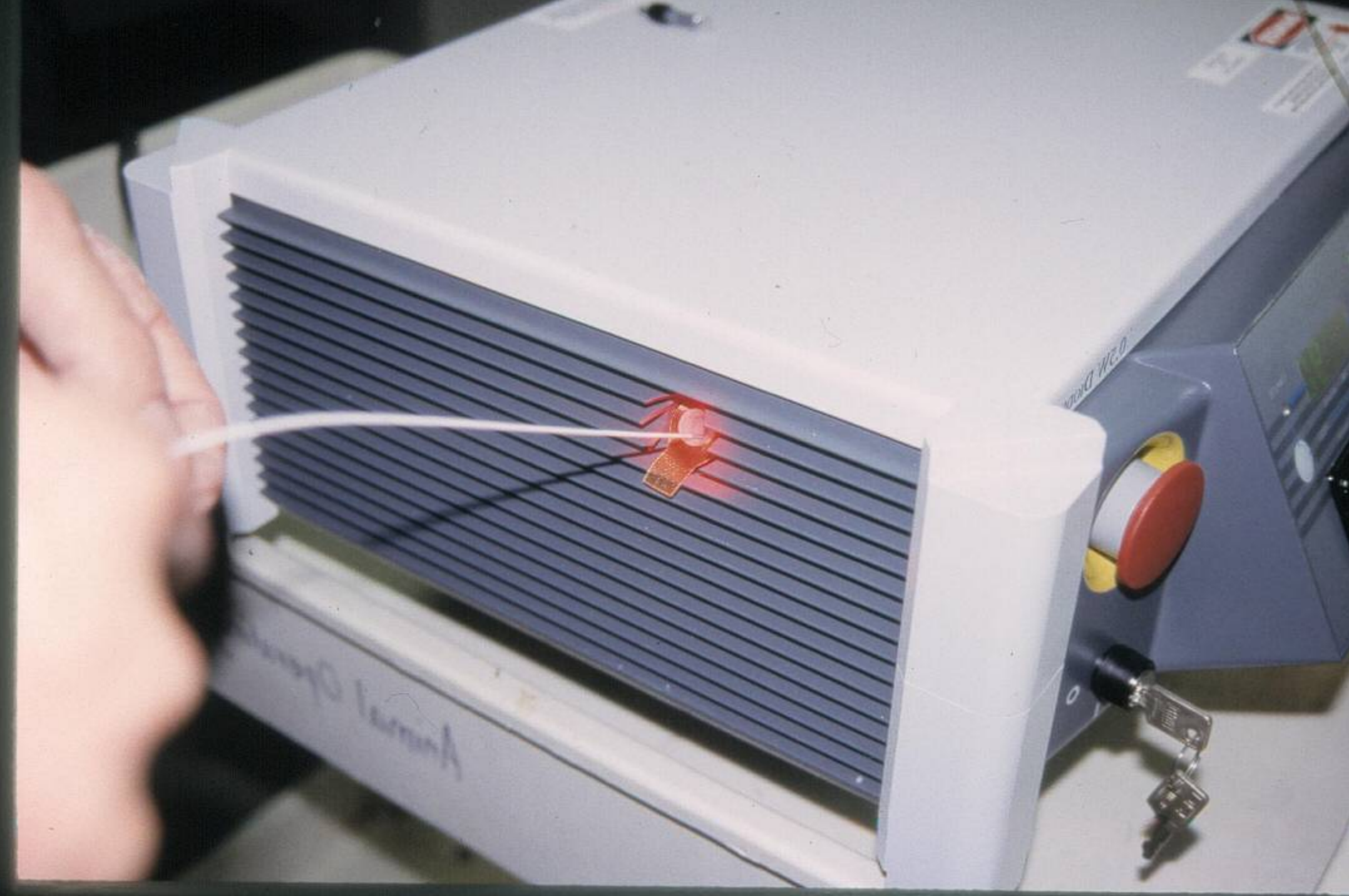

PDD Mode


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



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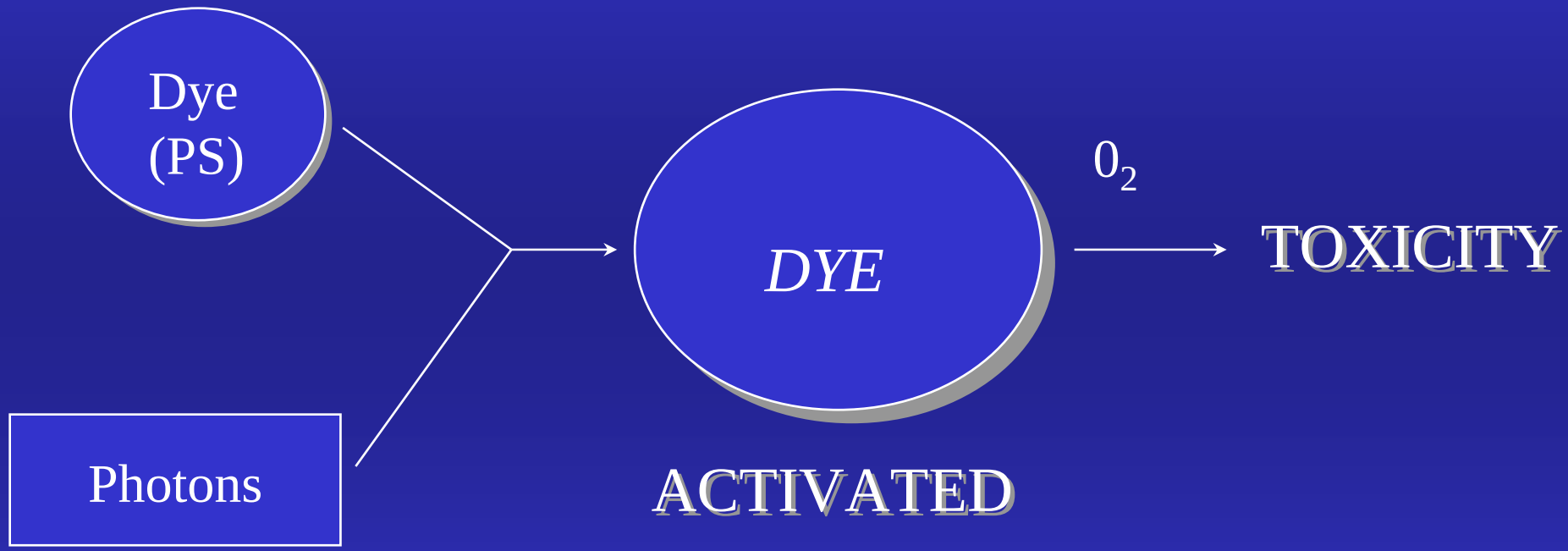
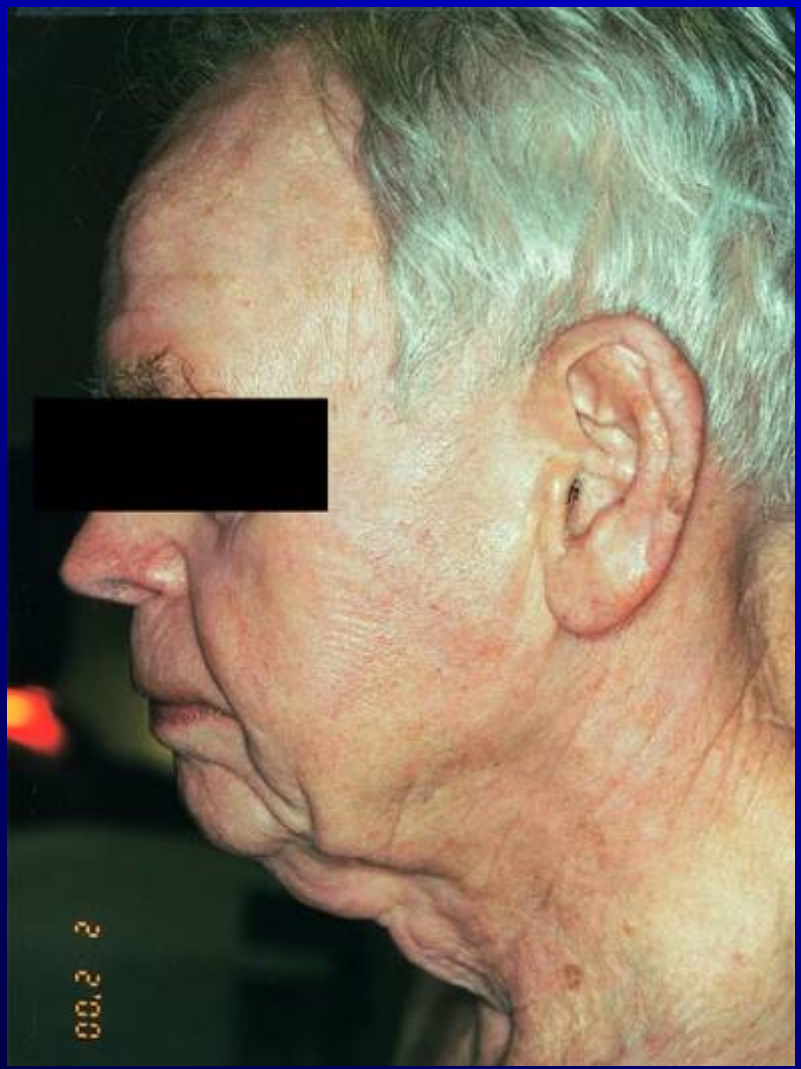


Methaminolaevulinate (MAL) PDT in Aktinic Keratosis



Trond Warloe

Radium Hospital Oslo

MAL-PDT in Basal Cell Carcinoma

Trond Warloe

Radium Hospital Oslo

MAL-PDT in Basal Cell Carcinoma

Trond Warloe

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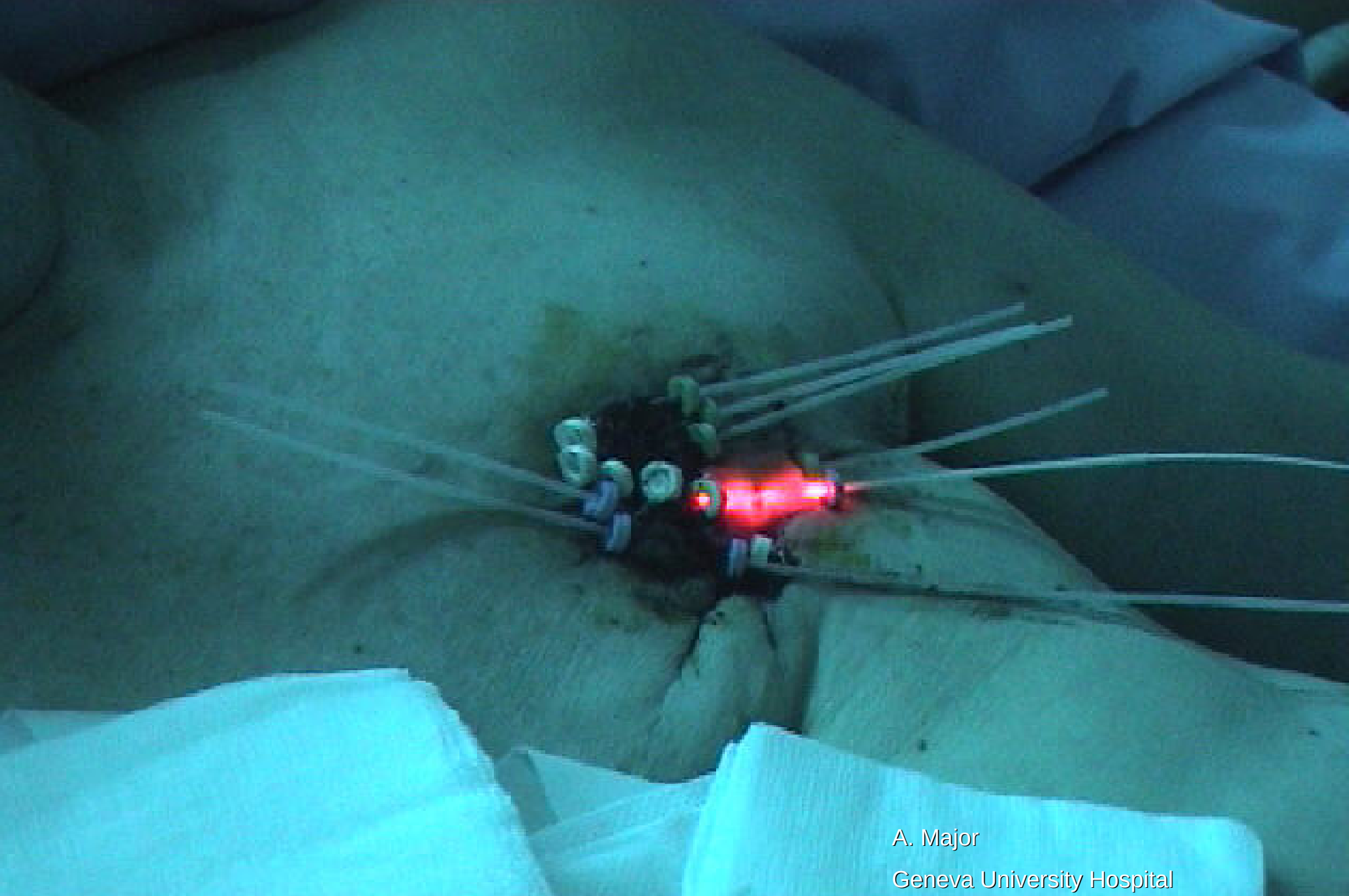
A. Major
Geneva University Hospital



A. Major

Geneva University Hospital

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Geneva University Hospital


HERING

CONCLUSIONS

- Photodynamic therapy (PDT) can be used efficiently in patient 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