The role of photomedicine in gynecological oncology

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From Research to Practice: Postgraduate Training in Reproductive Health / Chronic Disease  Geneva 2003
photomedicine

- Introduction
- Mechanism
- Application of PDD in gynecological neoplasms
- Application of PDT in gynecological neoplasms
**Introduction/Mechanism**

- **Tumor tissue**
  - **light**
  - energy
  - wave length
  - Fluorescence
  - light-activated photosensitizer
  - superoxide anions
  - singlet oxygen

**Photodynamic diagnosis**
- PDD
- cell necrosis
- induced cell apoptosis
- obstruction of blood vessels
- immune effect
- affect cellular- extracellular matrix interactions

**Photodynamic therapy**
- PDT

**Tumor destruction**
Penetration depth of light in tissue in relation to the wavelength

![Graph showing the penetration depth of light in tissue in relation to wavelength. The x-axis represents wavelength in nanometers (nm), and the y-axis represents depth in micrometers (µm). The graph indicates that the penetration depth increases with wavelength up to a certain point and then decreases.](image-url)
Photosensitizer

- PPIX-precursors (ALA and h-ALA)
  5-aminolaevulinic acid (ALA) (endogenous substance)
  protoporphyrin IX (PpIX) (endogenous photosensitizer).
Photosensitizer

- ALA
  - tumor selectivity
  - deeper tissue destruction
  - fast serum clearance 24-48 hours
  - cosmetic effect
  - photodection
- h-ALA (ALA-hexylester hydrochloride)
  - faster PpIX formation
  - 25-fold increase in PpIX fluorescence levels
  - more pronounced photodamage
Early Tumor Detection

Urology

Pneumology

Neurosurgery
PDT

Henta et al. British Journal of Dermatology 1999 141(2) 347
PDD in gynecological neoplasms

- CIN
- endometrial cancer
- intraperitoneal metastasis of ovarian cancer
PDD in CIN

- early detection
- noninvasive staging of CIN
Fluorescence image of the cervix after h-ALA application

Fluorescence image and white light image of the cervix uteri after the application of 3% acetic acid. Application of 10mg h-ALA in 10ml 0.9% NaCl solution on the cervix during 3 hrs.
PDD in CIN

- Fluorescence ratio
  - CIN-I: normal 1.3
  - CIN-II: normal 1.21
  - CIN-III: normal 2.35
- Porphyrins accumulated in CIN II/III lesions grown into cervical glands
- HPV DNA positive lesions showed significantly higher fluorescence.
PDD in CIN

- specificity:
  - fluorescence spectroscopy 75%
  - colposcopy 50%
- sensitivity: 95%
- Double ratio (DR) fluorescence imaging technique
PDD in ovarian cancer

- improves visualization and guides treatment of small cancerous nodules (0.3 mm)
PDD in ovarian cancer

In vivo fluorescence and light images of peritoneal tumor nodules. Fluorescence was excited using an endoscope (with D-light) after ip administration of ALA in an ovarian cancer rat (Fischer 344) model.
PDD in endometrial cancer

- Malignant endometrial epithelial cells showed significantly higher fluorescence of PpIX than normal epithelial cells after incubation with 1 mg ALA.
- The well-differentiated cancer cells produced significantly more PpIX than the poorly differentiated cancer cells.
PDT in gynecological neoplasms

- Cervical neoplasms
- Vulvar and vaginal neoplasms
- Ovarian cancer
- Endometrial cancer
PDT in cervical neoplasms

- Eliminate intraepithelial lesions without causing profuse bleeding, vaginal discharge, or a change in the location of the squamocolumnar junction.
- Spare young women from conization
- Large or multifocal lesions or those lesions that extend into the endocervical canal could be targeted through selective drug uptake while sparing adjacent normal cervical tissue
# PDT in CIN

<table>
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<th>Group</th>
<th>Pretreatment diagnosis</th>
<th>Outcome (3 months after PDT)</th>
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<tr>
<td></td>
<td>I</td>
<td>I/II</td>
</tr>
<tr>
<td>Placebo</td>
<td>12</td>
<td>1</td>
</tr>
<tr>
<td>PDT</td>
<td>10</td>
<td>2</td>
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*Adrian A 2003*
PDT in CIN

- CIN III
  
  Success rate was 31% (10/32) 12 months after treatment
PDT in vulvar neoplasms
PDT in vulvar neoplasms

- as effective as conventional treatments (laser evaporation and excision) for condyloma and VIN
- shorter healing time (2 weeks)
- less pain
- excellent cosmetic results
- Lower grades (VIN I) vs high grades (VIN II-III)
- monofocal and bifocal vs multifocal
- pigmented and hyperkeratotic lesions respond poorly
PDT in ovarian cancer

- Diffuse intra-abdominal metastases have been successfully treated with PDT in a mouse model. Minimally invasive debulking of nonresectable pelvic tumors was effective in a rat ovarian cancer model.

- Wierrani et al. m-THPC mediated PDT for two recurrent ovarian cancer patients and one patient following surgical tumor debulking. After more than 2 years all three patients remained free of relapses.
PDT in ovarian cancer

- “conjugated phototherap”
- photoimmunotherapy
- photochemotherapy
PDT in endometrial cancer

*Koren 1996*

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<th>Month after treatment</th>
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<td>6</td>
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7 endometrial carcinomas stage Ia
2 with recurrent endomerial carcinoma at vagina
Discussion

- a promising tool for early detection of superficial gynecological neoplasm
- early detection and noninvasive staging of CIN
- detecting intraperitoneal macroscopically invisible ovarian cancer nodules
Discussion

- a better choice for VIN than conventional treatment
- CIN?
- Ovarian cancer?
- Endometrial cancer?
- Conjugated photosensitizers
Discussion

- Further well designed, large sample size clinical trials are needed!!!