The role of photomedicine in gynecological oncology

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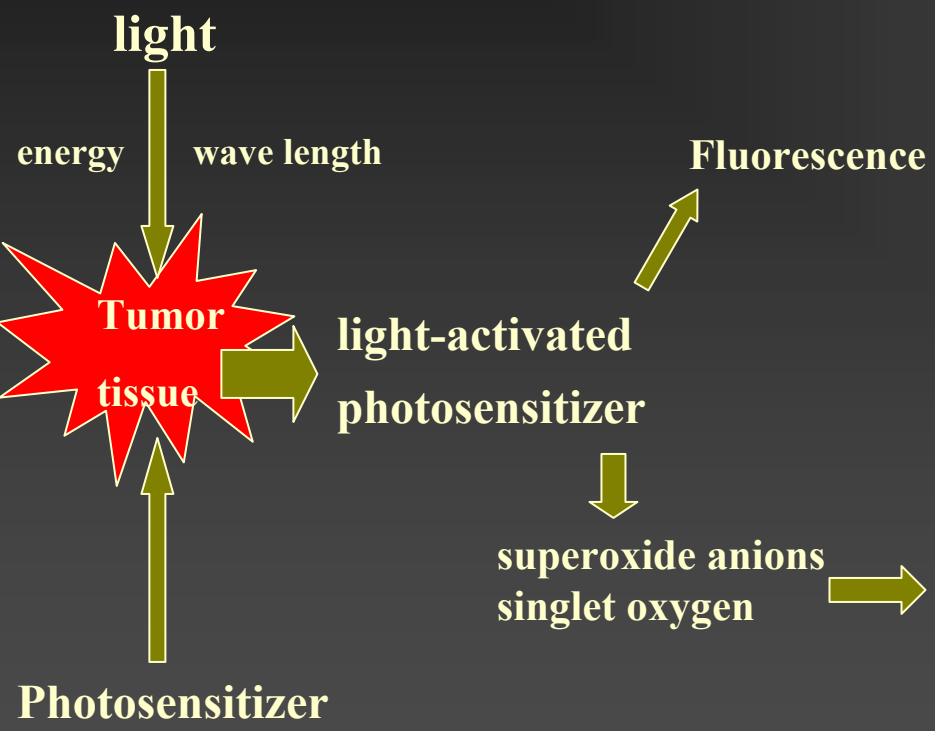
photomedicine

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

Introduction/Mechanism



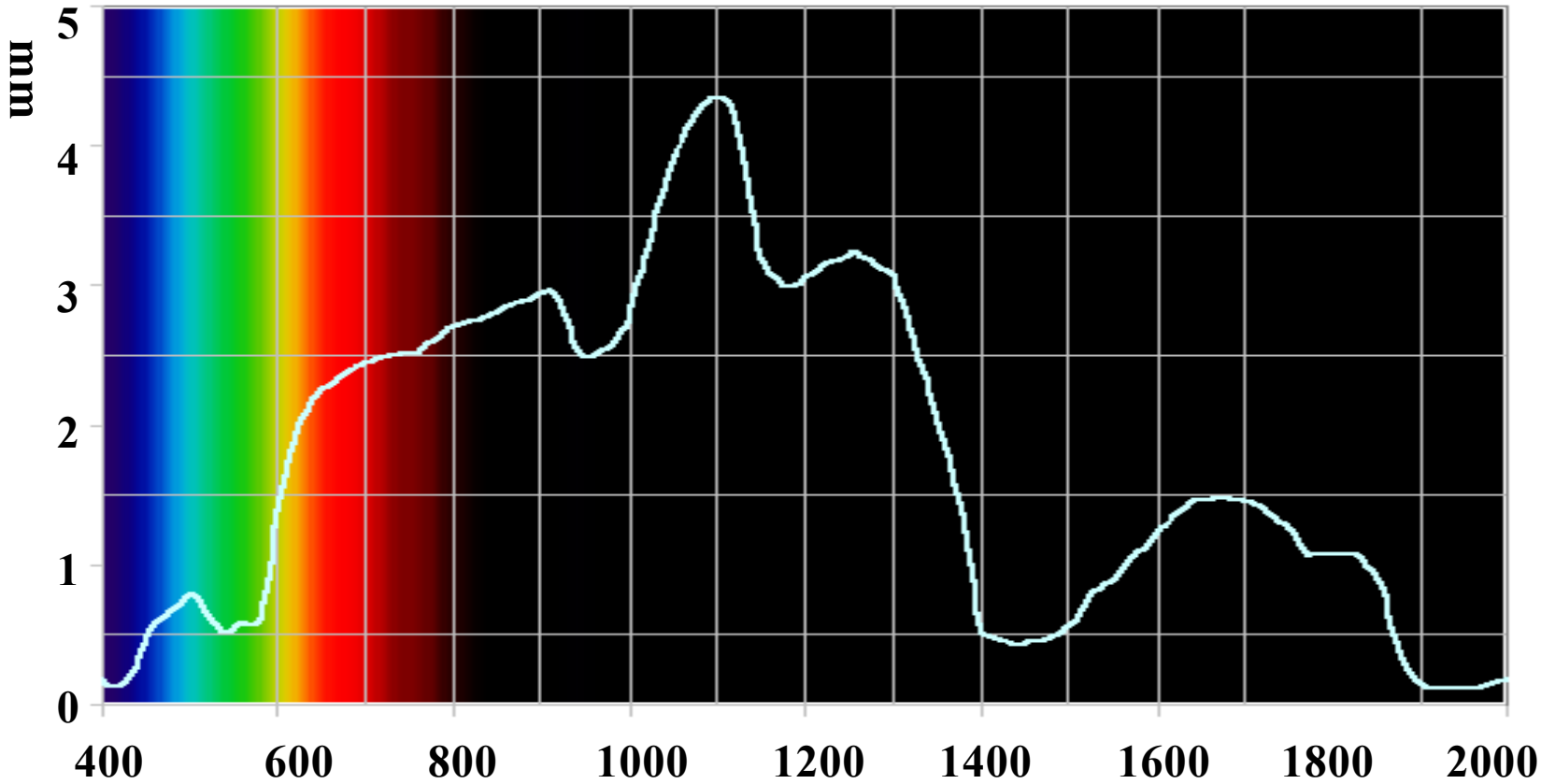
Photodynamic diagnosis

PDD

Photodynamic therapy

PDT

Penetration depth of light in tissue in relation to the wavelength



Photosensitizer

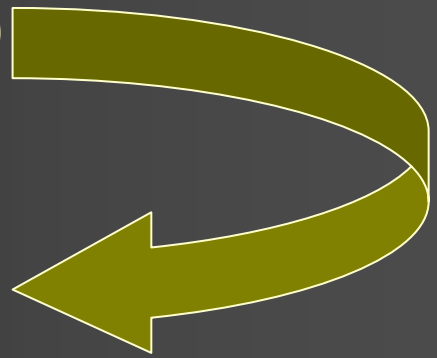
- **PPIX-precursors (ALA and h-ALA)**

  5-aminolaevulinic acid (ALA)

  (endogenous substance)

  protoporphyrin IX (PpIX)

  (endogenous photosensitizer).

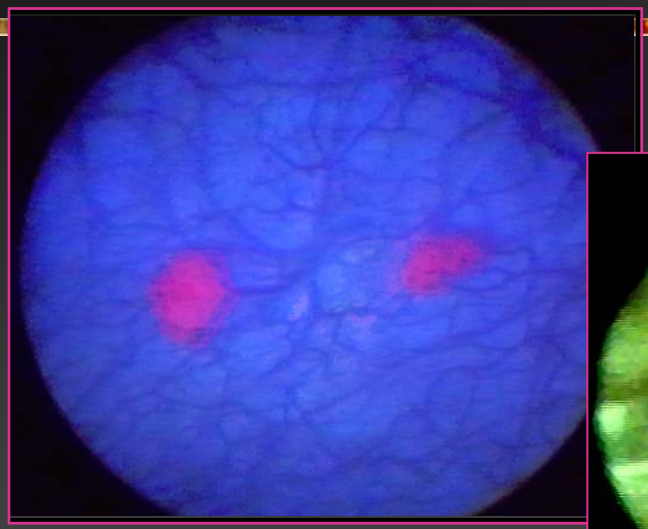


Photosensitizer

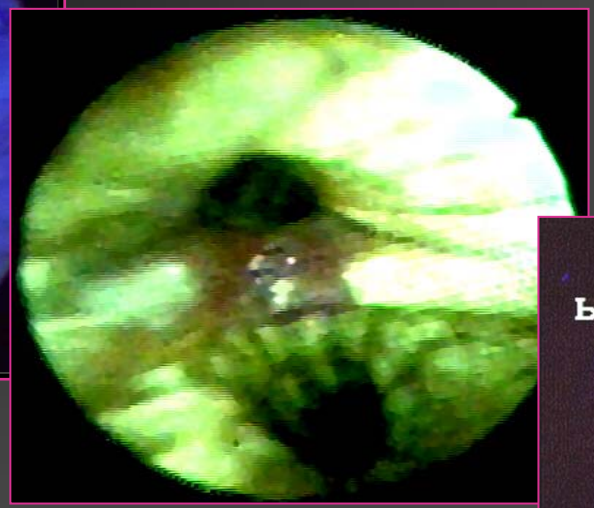
- ALA
  tumor selectivity
  deeper tissue destruction
  fast serum clearance 24-48 hours
  cosmetic effect
  photodection
- h-ALA (ALA-hexylester hydrochloride)
  faster PpIX formation
  25-fold increase in PPIX fluorescence levels
  more pronounced photodamage

PDD

Early Tumor Detection



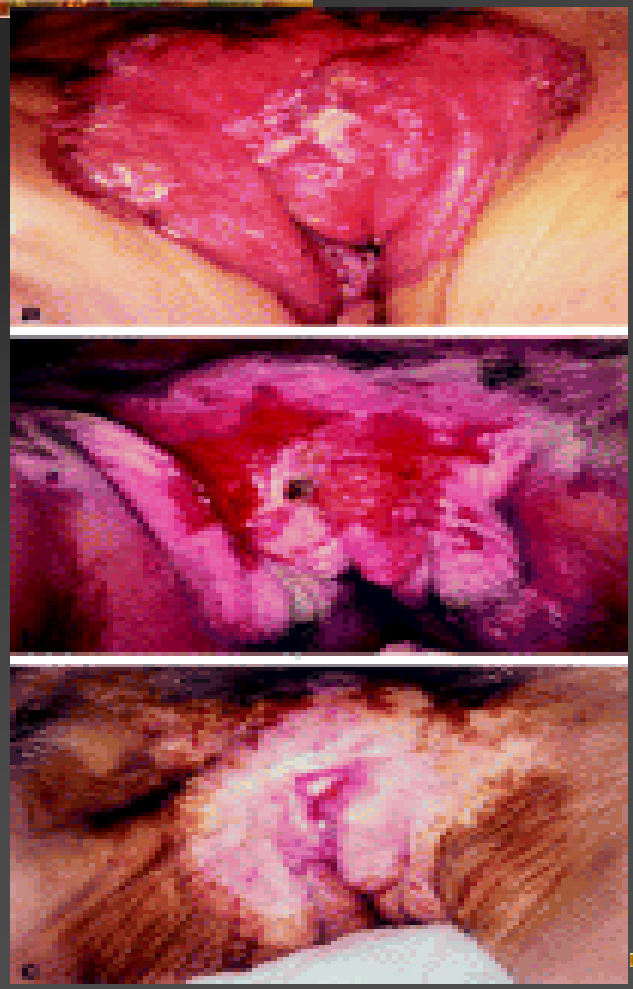
Urology



Pneumology

Neurosurgery

PDT



Henta et.al . British Journal of Dermatology 1999 141(2) 347

PHOTOMEDICINE

GYNECOLOGICAL ONCOLOGY

PDD in gynecological neoplasms

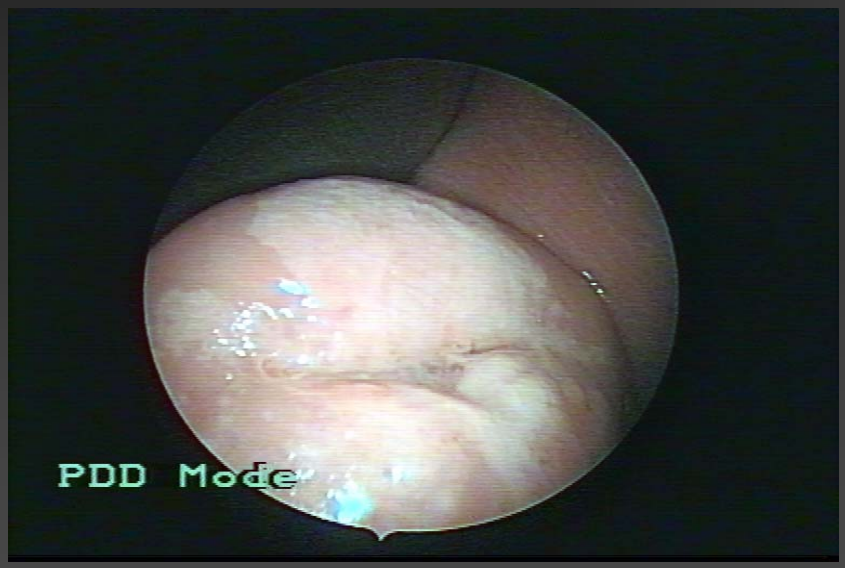
- CIN
- endometrial cancer
- intraperitoneal metastasis of ovarian cancer

PDD in CIN

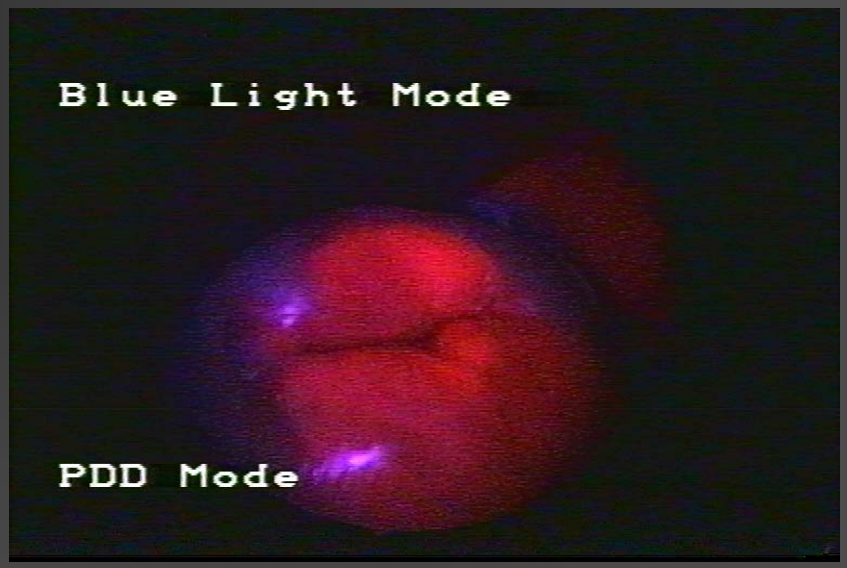
- early detection
- noninvasive staging of CIN

Fluorescence image of the cervix after h-ALA application

White light



Fluorescence



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 :

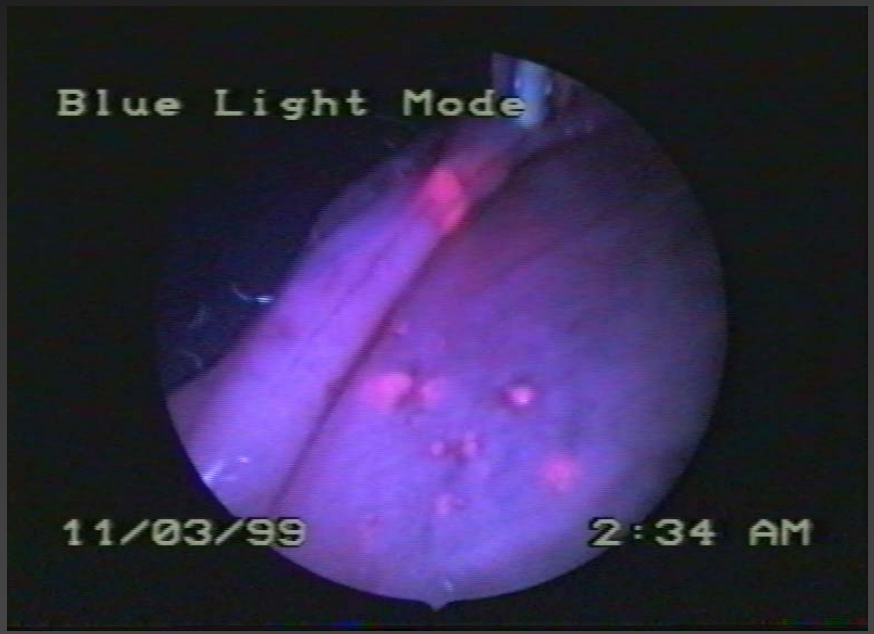
  fluorescence spectroscopy 75%

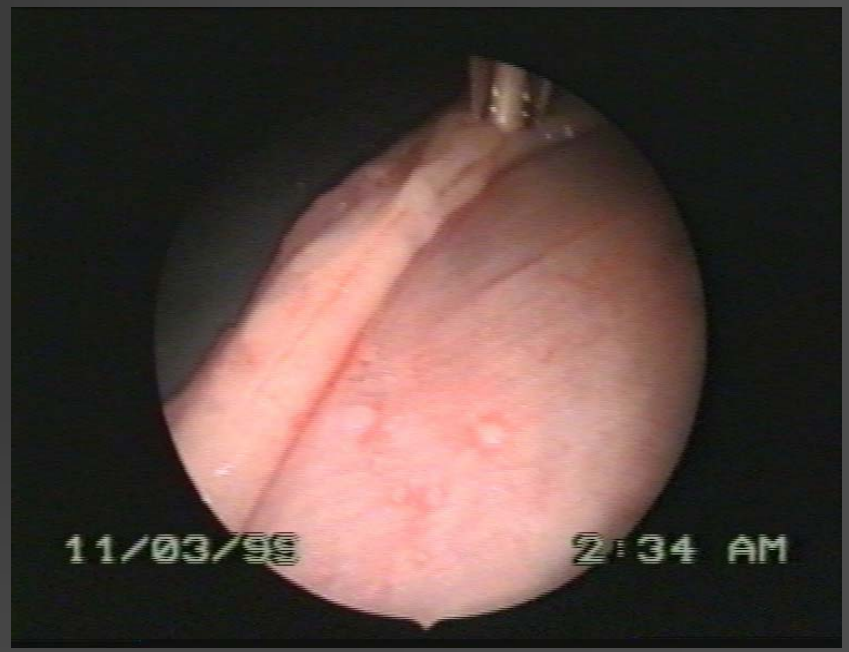
  colposcopy 50%
- sensitivity :95%
- Double ratio (DR) fluorescence imaging technique

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 significant 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 squamocolummnar 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

	Pretreatment diagnosis		Outcome (3 months after PDT)		
Group	I	I/II	Normal	No change	Apparent progression
Placebo	12	1	4(31%)	5(38%)	4(31%)
PDT	10	2	4(33%)	5(42%)	3(25%)

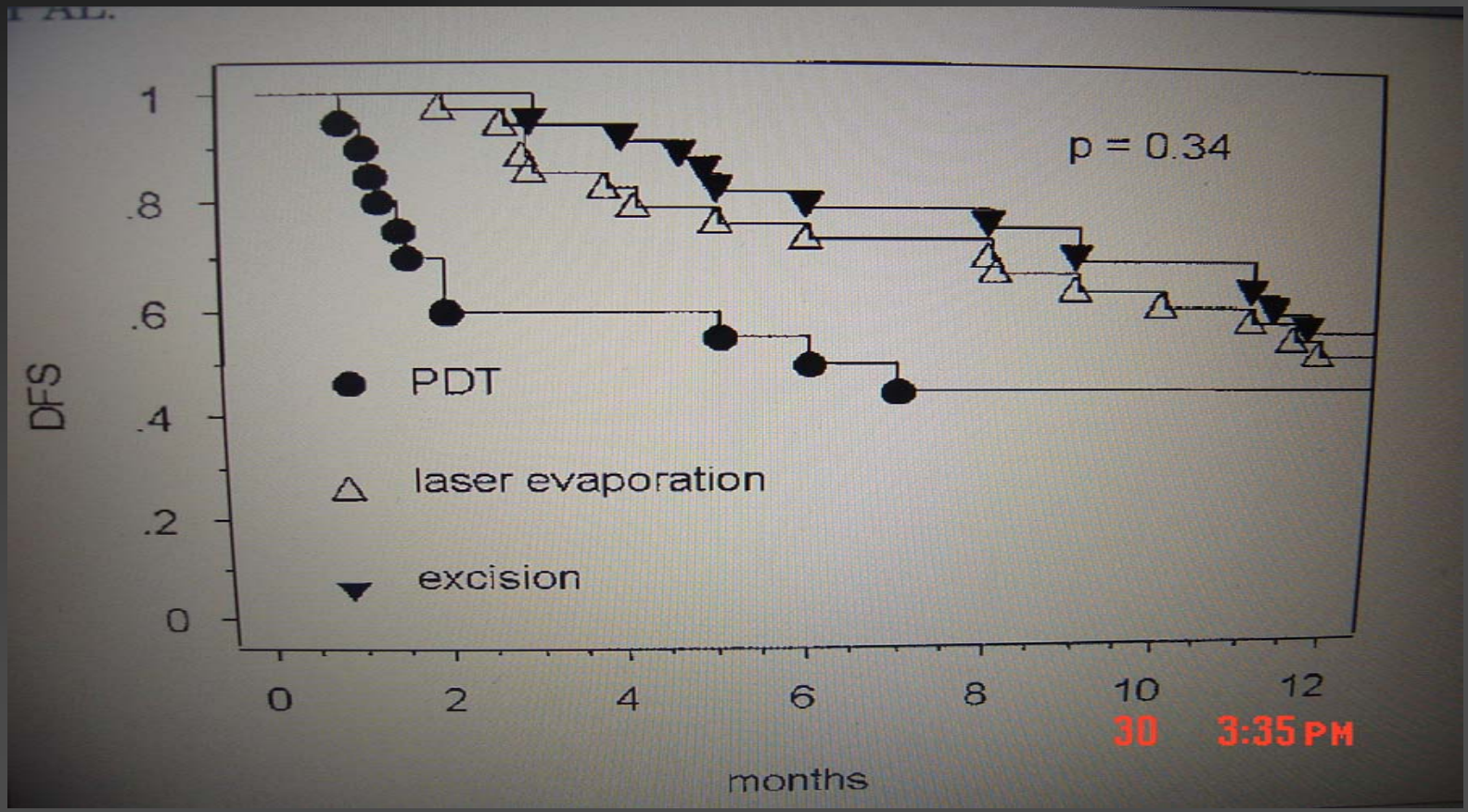
Adrian A 2003

PDT in CIN

- CIN III

  Success rate was 31% (10/32) 12 months after treatment

PDT in vulvar neoplasms



PDT in vular 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 caner 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 phototherapy”
  - photoimmunotherapy
  - photochemotherapy

PDT in endometrial cancer

Koren 1996

	Month after treatment	
	1	12
CR	6	1
CR-REC	-	5
NR	3	-
total	9	6

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 photosensitzers

Discussion

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


Thank You !