Photodetection of cervical intraepithelial neoplasia

- Screening, colposcopy, biopsy, treatment
- Optical biopsy
- See and treat
Photodetection of cervical intraepithelial neoplasia

- 5-aminolevulinic acid-induced porphyrin fluorescence
- Autofluorescence
- Life time imaging
Cervix after acetic acid

Pat 10

Cervix
Performance of colposcopy for diagnosis of squamous intraepithelial lesions

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<th>First author</th>
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Photodetection of cervical intraepithelial neoplasia using 5-aminolevulinic acid-induced porphyrin fluorescence

METHODS Sixty-eight women attending our colposcopy clinic underwent a gynecologic examination, including cytology, human papillomavirus (HPV) testing, and colposcopy. They received 10 mL 0.5% or 1.0% 5-aminolevulinic acid (5-ALA) topically. After 30-360 minutes, real-time image analysis was performed, and spectra were obtained from 685 sites.

RESULTS Using 1% 5-ALA, fluorescence imaging after 60-90 minutes achieved similar sensitivity and specificity compared with colposcopy in detecting CIN with 94% and 51% versus 95% and 50%, respectively. However, the specificity was markedly improved by fluorescence spectroscopy, achieving 75%.

Peter Hillemanns et al Cancer 2000, 88 : 2275-82
Haem Biosynthesis

5-ALA synthese

Uptake of exogenous 5-ALA

PBG Deaminase

Cytoplasm

Lower rate in tumour cells

Higher rate in tumour cells

Coproporphyrinogen III

Uroporphyrinogen III

Protoporphyrinogen IX

Protoporphyrin IX

haem

Fe²⁺

Feedback control

Mitochondria

Ferrochelatase

Gycline + succinyl CoA

5-ALA

5-ALA

Porphyrinogen

Porphyrinogen

5-ALA
Transport across cell membrane
A logarithmic plot of the octanol/water partition coefficient $P$ of a series of ALA esters.
Principle of fluorescence imaging tumor depth profiling

Homogenous excitation of the fluorochrome concentrated in the tumoral tissue at two different wavelengths, corresponding to the absorption maxima of the fluorochrome (417, 514 nm)

Detection at the emission maxima (610-720 nm)
Penetration depth of light in tissue in relation to the wavelength

![Graph showing penetration depth vs wavelength]
Cervical squamous carcinoma precursors

- Squamous Intraepithelial Lesion (SIL)
  - Low Grade
  - High Grade
- Condyloma
- Cervical intraepithelial Neoplasia (CNN)
  - Grade 1
  - Grade 2
  - Grade 3
- Normal Dysplasia
- Very Mild-Mild Dysplasia
- Moderate Dysplasia
- Severe Dysplasia
- In situ Dysplasia
- Carcinoma

Microinvasive Carcinoma
Fluorescence analysis of CIN after topical application of 0.1% h-ALA
Pat. 12, 10% ALA in 0.9% NaCl, 3h 15 min application time
Fluorescence analysis of healthy tissue after application of 0.1% h-ALA
Representative spatial distribution of 5-ALA induced porphyrin fluorescence related tissue type

Fluorescence (% of standard)

Tissue depth (mm)

CIN 3

Normal tissue

Epithelium

Cervical stroma