Mueller Polarimetric Colposcopy: An Innovative,Label-Free Approach for High-Precision, Real-Time In Vivo Detection of Cervical Precancer

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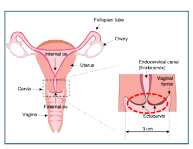
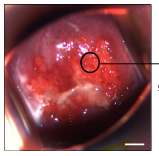
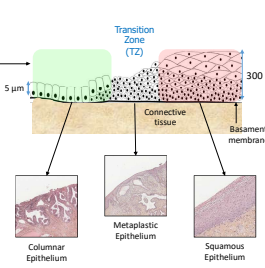
Anatomy and microstructure of cervix

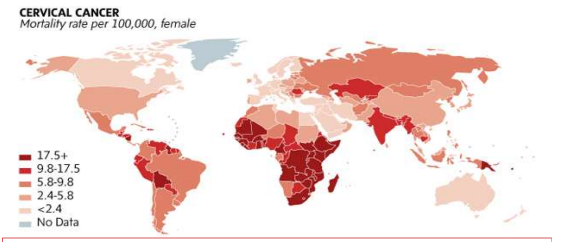


Female reproductive system


Ectocervix

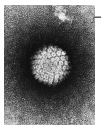


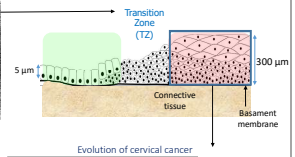
- Ectocervix covered by a non-vascularized epithelium.
- Three main epithelial regions : Squamous, Columnar, and Metaplastic Epithelium or Metaplasia
- Connective tissue composed of collagen I, elastin, and blood vessels
- Collagen represents 90% of cervical volume

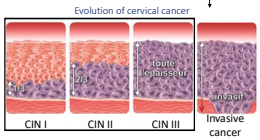


- Major health problem: one of the most common female cancers in the world with 275 000 deaths per year, mainly in low-ressource countries
- Slow evolution (10 - 20 years): ideal case for screening
- Direct access to cancer
- Model for other epithelial cancers

Cervical cancer starts with infection by Human Papilloma Virus (HPV)


HPV

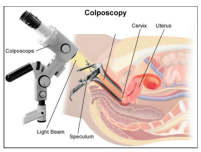




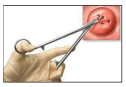
- Detecting lesions at an early stage allows recovery in about 95% of cases with minor surgery
- Detecting these lesions with conventional optical techniques remains a major challenge

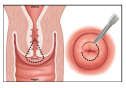
CIN = Cervical Intraepithelial Neoplasia

Colposcopy



Colposcope: low magnification microscope


Guiding biopsies


Guiding conization

Colposcopy: ineffective and costly technique
(low sensitivity and specificity for the detection of precancerous lesions)

Objective: Improve colposcopy using Mueller polarimetric imaging

Mueller polarimetry

Stokes vector
Four-component intensity vector

$$\mathbf{S} = \begin{bmatrix} S_0 \\ S_1 \\ S_2 \\ S_3 \end{bmatrix} = \begin{bmatrix} I \\ I_x - I_y \\ I_{+45^\circ} - I_{-45^\circ} \\ I_L - I_R \end{bmatrix}$$

Mueller matrix
16-component real matrix

$$\mathbf{S}' = \mathbf{M}\mathbf{S}$$

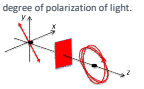
$$\mathbf{M} = \begin{bmatrix} m_{11} & m_{12} & m_{13} & m_{14} \\ m_{21} & m_{22} & m_{23} & m_{24} \\ m_{31} & m_{32} & m_{33} & m_{34} \\ m_{41} & m_{42} & m_{43} & m_{44} \end{bmatrix}$$

$$\mathbf{M} \in \mathbb{R}^{4x4}$$

Comprehensive polarimetric description of a target

Tissue polarimetric parameters

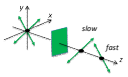
Depolarization (M_Δ)
Depolarization quantifies the ability of a target to reduce the degree of polarization of light.



Stochastic process
(multiple scattering)

Biological origin:
organelles, cytoplasm, ...

Retardance (M_R)
Phase difference between two polarization eigenstates

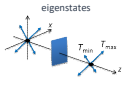


Azimut **(α):** orientation of the slow (or fast) axis

Birefringence: the refractive index varies with polarization

Biological origin:
collagen, elastin, muscle fibers, ...

Diattenuation (M_D)
Difference in attenuation between two polarization eigenstates

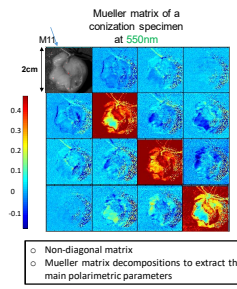


Absorption anisotropy:
The absorption coefficient varies with polarization

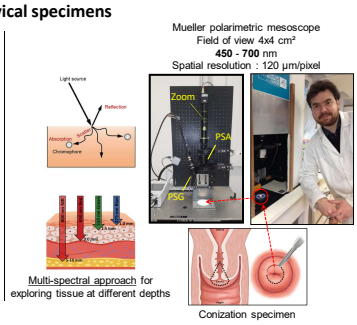
$$\mathbf{M} = \mathbf{M}_\Delta \mathbf{M}_R \mathbf{M}_D$$

Lu-Chipman Decomposition to separate the main polarimetric effects

Ex vivo polarimetric images of cervical specimens

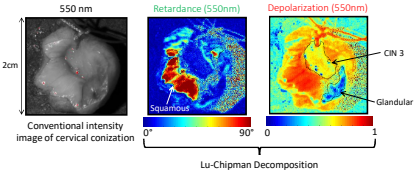


- Non-diagonal matrix
- Mueller matrix decompositions to extract the main polarimetric parameters



Multi-spectral approach for exploring tissue at different depths

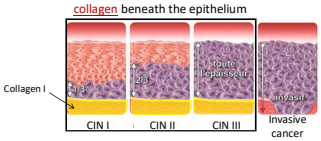
Conization specimen



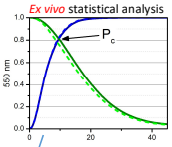
Conventional intensity image of cervical conization

Lu-Chipman Decomposition

Precancerous lesions modify the structure of collagen beneath the epithelium



Ex vivo statistical analysis

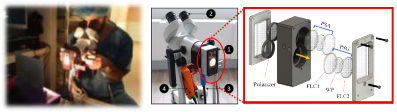


	450 nm	550 nm	600 nm
All pixels	Threshold :10.1° Se:77,6% Sp:77,1%	Threshold :8,9° Se:78,7% Sp:78,8%	Threshold :9.2° Se:78,1% Sp:77,8%
(Depol >0.65)	Threshold :10.6° Se:83,8% Sp:83,6%	Threshold :9,7° Se:81,7% Sp:80,9%	Threshold :9,8° Se:79,7% Sp:79,2%

Statistical analysis on 83 specimens

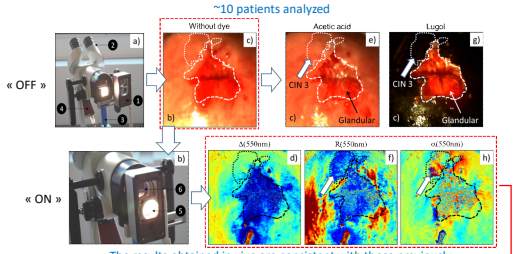
- >80% sensitivity and specificity using retardance at 550 nm alone to discriminate **CIN3** from **healthy squamous epithelium**
- ~90% sensitivity and specificity by combining Retardance and Depolarization at different wavelengths using deep learning algorithms

Mueller polatrimetric colposcopy

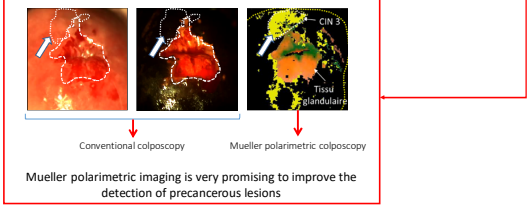


No mechanical movements
Wavelengths : 460, 530 and 630 nm
2 additional wavelengths at 650 and 700 nm
64 images in 1 s
Field of view: 4x4 cm²
Spatial resolution: 50 µm/pixel

~10 patients analyzed

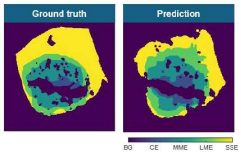


The results obtained in vivo are consistent with those previously observed ex vivo



Mueller polarimetric imaging is very promising to improve the detection of precancerous lesions

A model to accurately characterize healthy cervical tissue is needed to establish a baseline



- The clinical study (COLPOTERME) is conducted at Kremlin Bicêtre University Hospital to probe cervical microstructure for improved prematurity prediction
- **The cervix of pregnant women provides a unique in vivo model to characterize metaplastic transformations**
- ~400 women analyzed to map multiple anisotropy and scattering cervical properties involved in these transformations
- Input: RGB + polarimetric features (multimodal)

- Semantic segmentation of 4 epithelial classes **Columnar Epithelium (CE), Mid Metaplastic Epithelium (MME), Late Metaplastic Epithelium (LME), Stratified Squamous Epithelium (SSE) + background (BG)**

Clinical trial

- Polarimetric analysis of the cervix for a large cohort of patients *in vivo*
- Accurate comparison between polarimetric images and biopsy results

200 patients to analyze

On average 2 biopsies per patient for a total of about 400 biopsies

1. J. Park Digital multispectral Mueller colposcopy for exploring cervical microstructure in vivo, 2022 (PhD Thesis).
2. A. Pierangelo, et al. "Mueller polarimetric imaging for cervical intraepithelial neoplasia detection" In: Polarized Light in Biomedical Imaging and Sensing. Springer, Cham. doi: 10.1007/978-3-031-04741-1_6(2023).