Spectroscopy microsystem for the detection of gastrointestinal dysplasia

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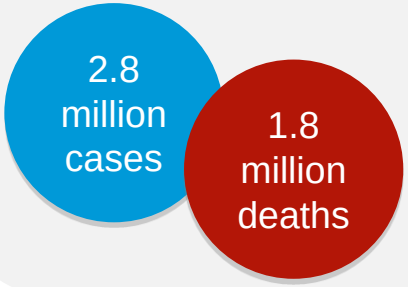
Outline

- **Motivation**
- **Conventional endoscopy**
- **Capsule endoscopy**
- **Goal**
- **Diffuse-reflectance and fluorescence spectroscopy**
- **Miniaturized spectroscopy system**
  - Wavelength reduction simulations
  - Thin-film optical filters: design, simulation, fabrication, and characterization
  - Results
- **Conclusions**
- **Future Work - Spectroscopy imaging**

Motivation

Gastrointestinal cancers - among the fifth most common cancers worldwide, the fifth leading causes of cancer-related deaths



International Agency for Research on Cancer
World Health Organization
(2010)

Early cancer detection

More effective treatment

Improved survival rate

Normal cells

Dysplasia

Cancer *in situ*

Localized invasive tumor

Regional lymph node involvement

Distant metastases

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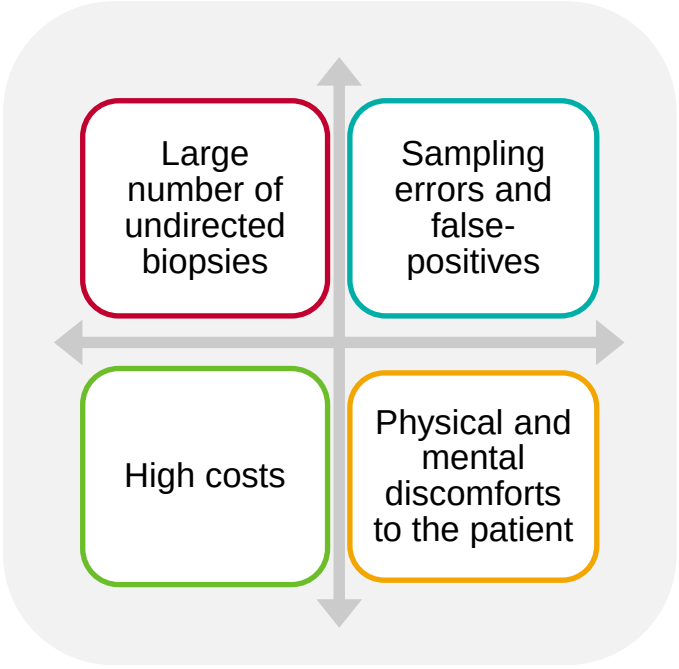
Motivation

- **Early cancerous lesions are invisible**



Optical techniques

- Diffuse Reflectance &
- Fluorescence Spectroscopy

- Morphological &
- Biochemical tissue information

Tissue Diagnosis

Successfully applied in conventional endoscope prototypes for detecting and classifying gastrointestinal dysplasia

Conventional endoscopy

- **These prototypes have several drawbacks**
  - High-cost
  - Complex and bulky
  - Low collection efficiency
  - **Invasive and uncomfortable**
  - **Requires the presence of the physician**
  - **Some parts of the GI tract remain inacessible**

Capsule endoscopy

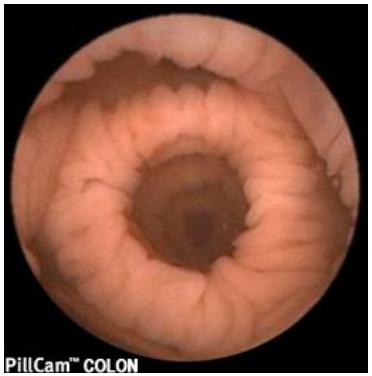
- **The last frontier in gastrointestinal endoscopy has been crossed with the success of**

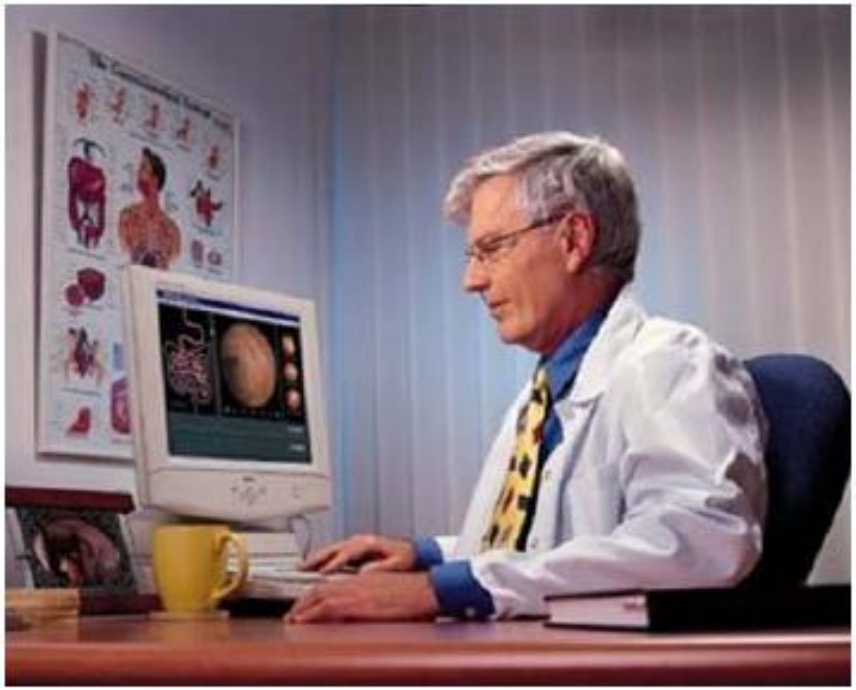
WIRELESS CAPSULE ENDOSCOPY

Capsule endoscopy procedure

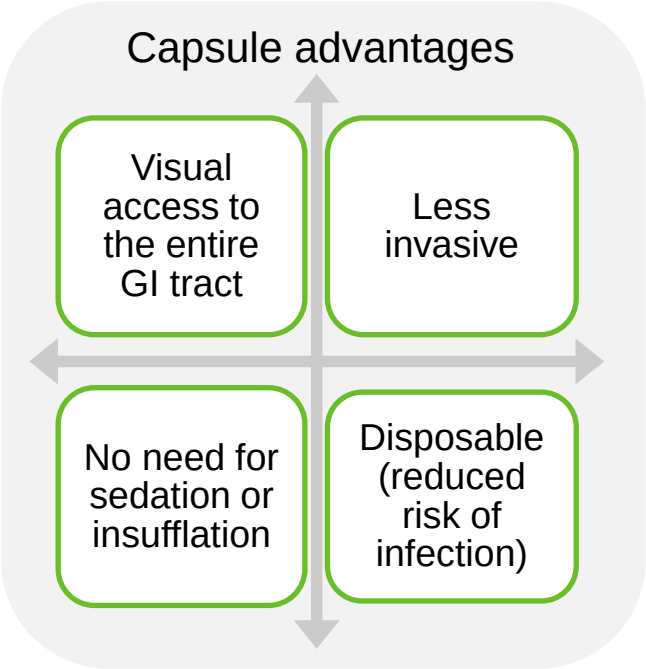
Capsule endoscopy procedure

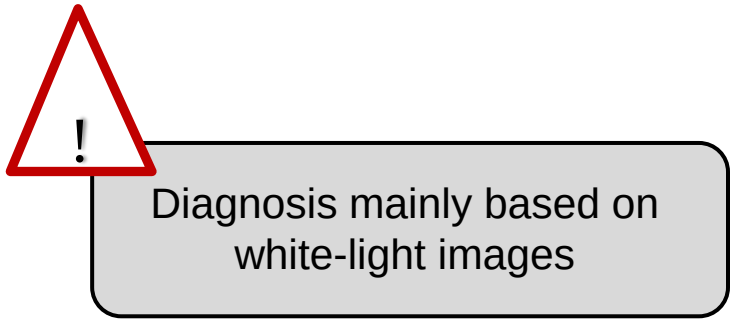
- After 8 h, the data recorder is connected to a computer workstation, the data are downloaded, processed and, finally, high quality endoscopic images can be viewed on a monitor





Capsule endoscopy





Goal

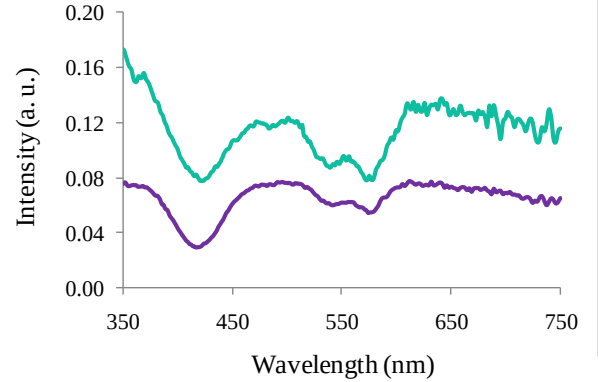
Development of a simple, miniaturized and less costly spectroscopy system to be integrated in less-invasive devices for the detection of gastrointestinal dysplasia

Two main spectroscopy techniques: diffuse-reflectance and fluorescence

Diffuse Reflectance Spectroscopy

- White-light is delivered to the tissue, and photons are absorbed and multiple scattered by tissue constituents before being detected
- Scattered photons provide information about the connective tissue with collagen
- Absorption is mainly due to hemoglobin

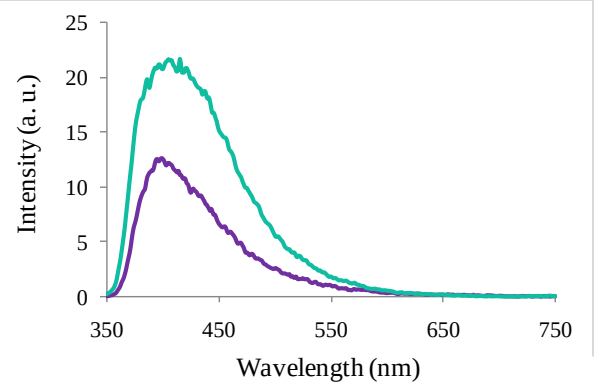
Diffuse reflectance signal is usually lower in dysplastic tissue, when compared with normal tissue: decrease in scattering and increase in absorption



Fluorescence Spectroscopy

- Tissue is illuminated with UV or short-wavelength visible light
- Fluorescence emission depends on the fluorophores present in the tissue
- A modification in the fluorescence emission spectra (intensity and spectral shape) may be correlated to the emergence of pathological conditions

Fluorescence signal is usually lower in dysplastic tissue, when compared with normal tissue: higher absorption (by Hb) and increased epithelial thickness



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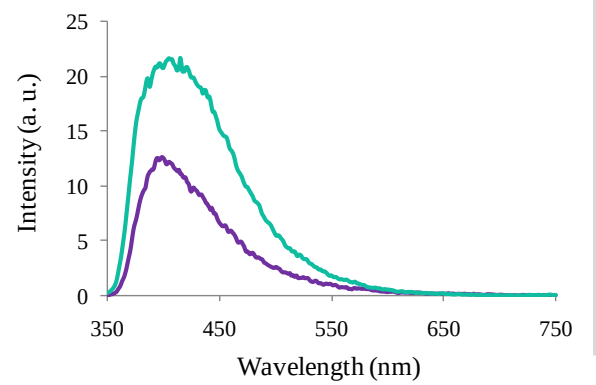
Fluorescence Spectroscopy

- An increase in NADH is associated to an increase in cellular metabolic activity and proliferation, both of which occur with the progression of dysplasia
- A decrease in collagen can be an indicator of loss of structural integrity, and is translated by low fluorescence intensity

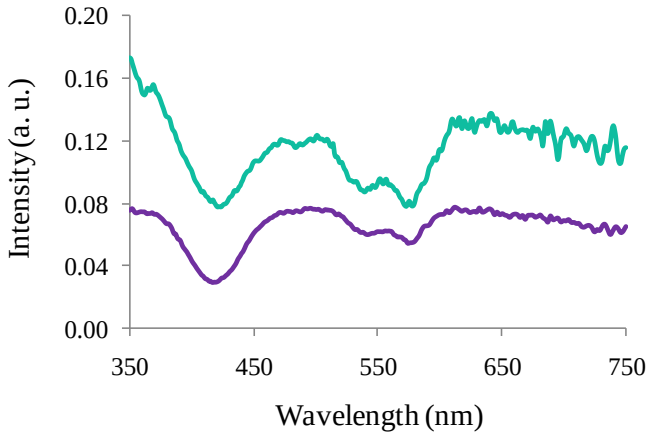
Fluorescence signal is usually lower in dysplastic tissue, when compared with normal tissue: higher absorption (by Hb) and increased epithelial thickness

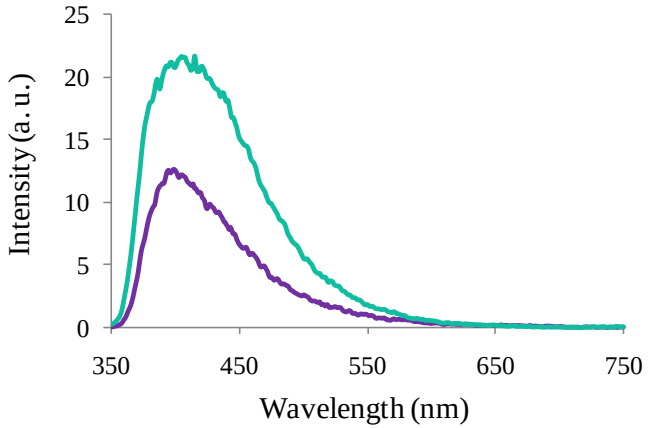


Diffuse-reflectance and fluorescence

- **Quantitative information**
  - Tissues scattering, hemoglobin concentration, oxygen saturation and fluorophores can be obtained using specific models

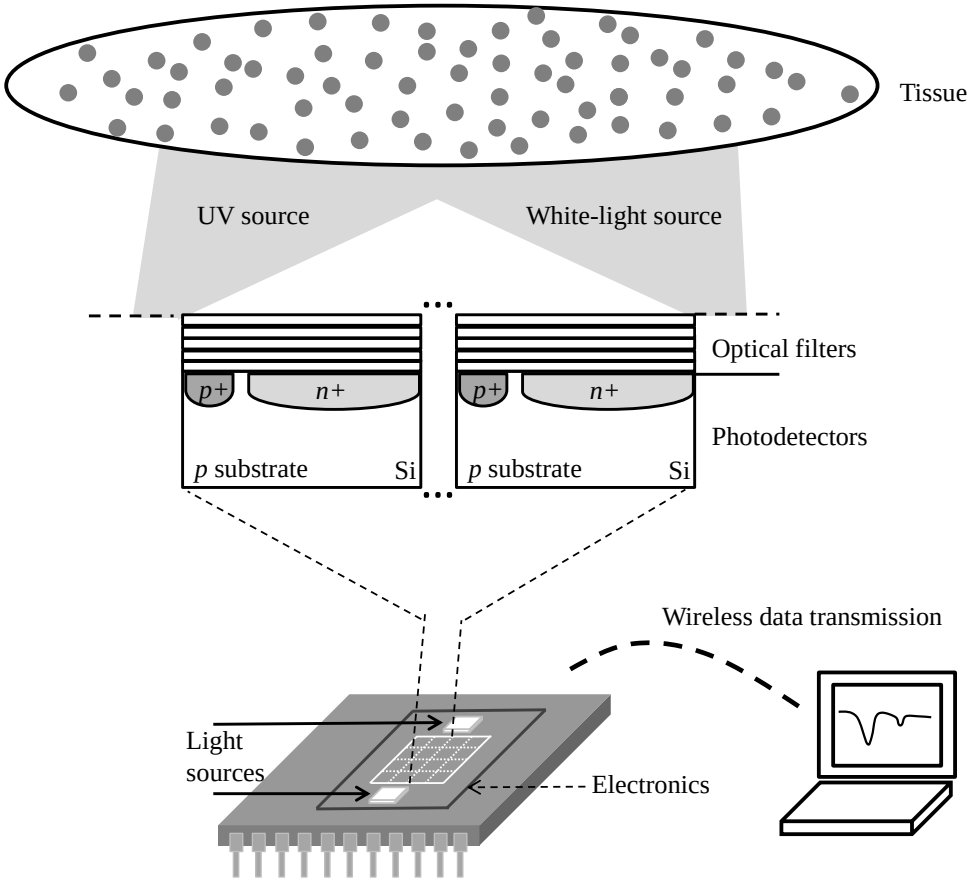
Diagnostic algorithms





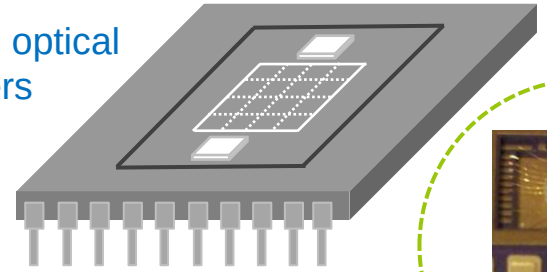
Miniaturized spectroscopy system

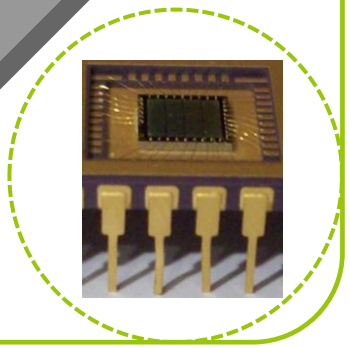
- **Overview**



Wavelength reduction simulations

No. optical filters





Feasibility of using a small number of spectral bands for diagnosis

Miniaturized spectroscopy system

Wavelength reduction simulations

- Spectroscopy data set from GI tissue
- Spectroscopy models implemented using MATLAB tools

- Tissue parameters were determined using a reduced number of wavelengths from which the full spectra were reconstructed - interpolation

- The best results comprises the following discrete points: **350, 370, 380, 400, 420, 450, 480, 510, 540, 560, 580, 600, 620, 650, 700, and 750 nm**

↓

Optical filters designed to be centered at these 16 wavelengths

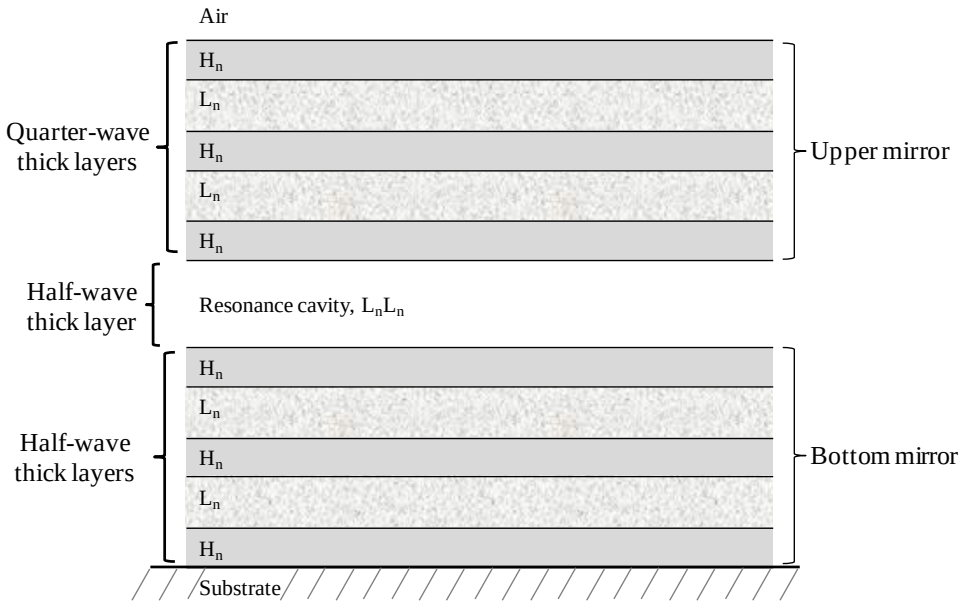
Miniaturized spectroscopy system

Optical filters design

- Fabry-Perot interferometer structure – two parallel mirrors separated by a resonance cavity
- Multilayer structure – 11 layers
- Dielectric mirrors composed of TiO_2 and SiO_2 thin-films

Suitable optical characteristics and fabrication advantages

- Filtering array composed by **3 groups of optical filters** :
  - Near-UV/violet (350 to 450 nm)
  - Central visible spectrum (480 to 600 nm)
  - Red (620 to 750 nm)



Filters are tuned to a different wavelength by changing only one layer

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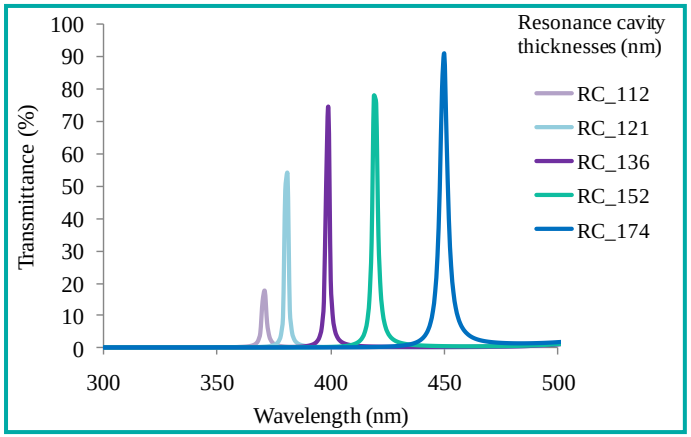
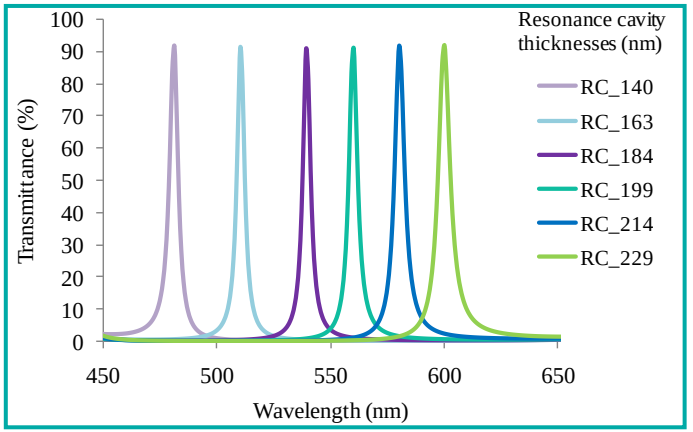
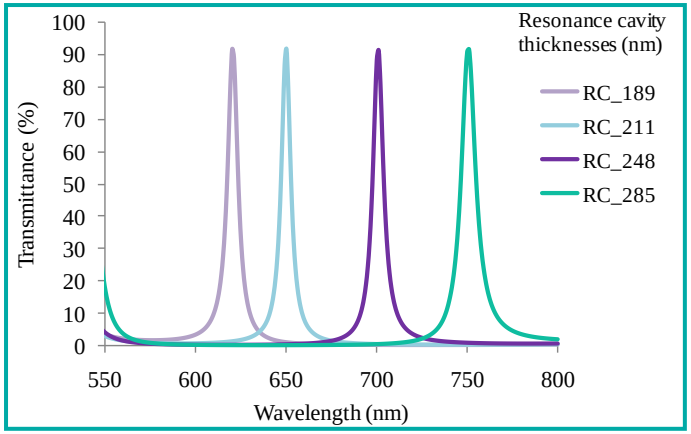
Miniaturized spectroscopy system

Optical filters simulations

- **TFCalc** and **Sopra** materials database were used for the structural optimization of the filters







- Transmittance higher than 90%
- FWHM less than 10 nm (average ~6 nm)

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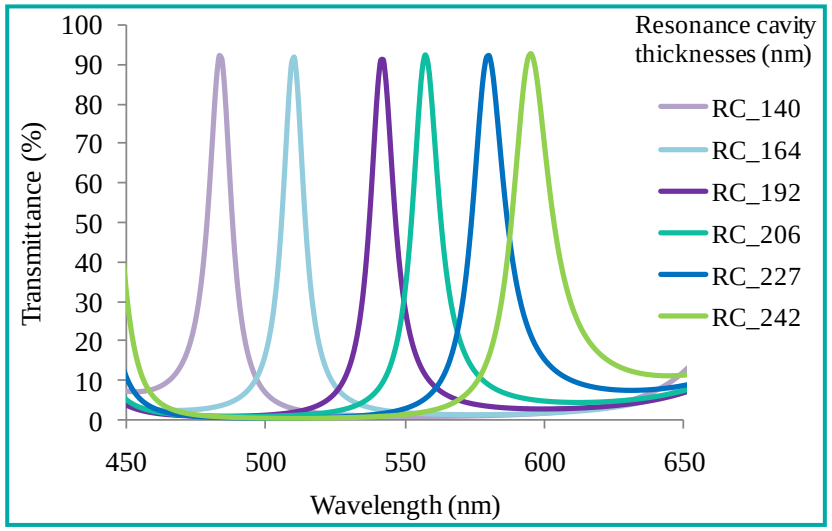
Miniaturized spectroscopy system

- **Layer thicknesses optimization**
  - The TiO_2 refractive indices obtained are smaller - increase TiO_2 thicknesses

Simulation results



- Transmittance higher than 90%
- FWHM less than 17 nm (average ~12 nm)

Filters fabrication

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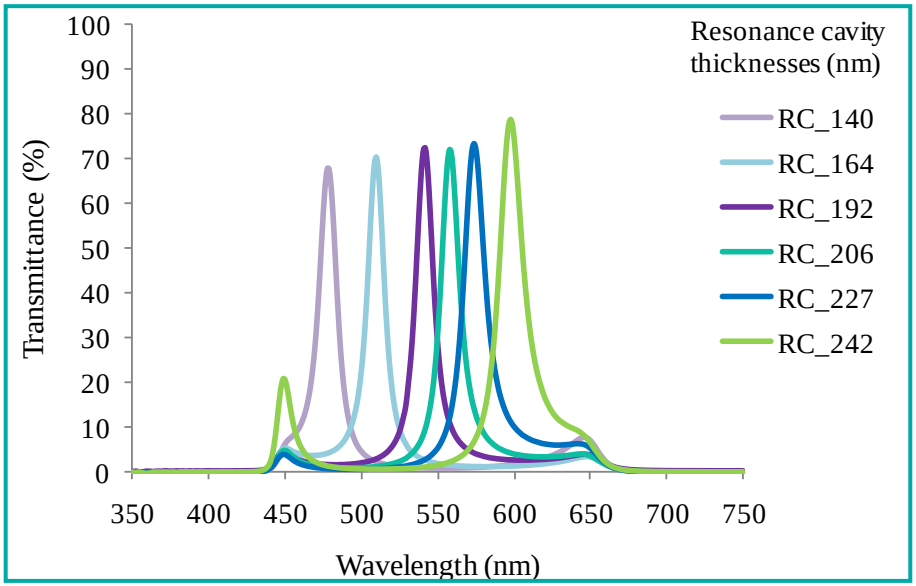
Miniaturized spectroscopy system

Optical filters characterization

- **Optical characterization** – transmittance measurements

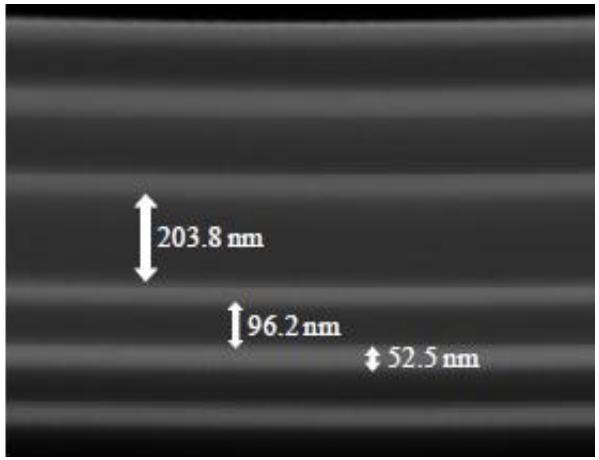


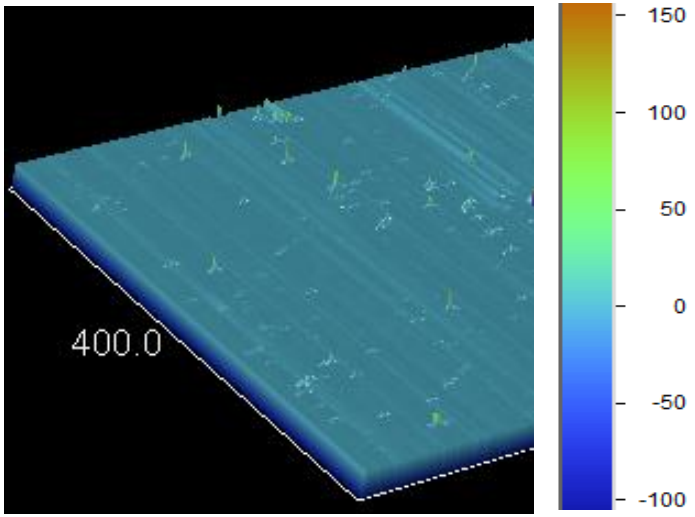
- Transmittance higher than 65%
- FWHM less than 20 nm (average ~15 nm)
- Small peak deviation (~3 nm)

Miniaturized spectroscopy system

Optical filters characterization

- **Structural characterization** – SEM, AFM and profilometer measurements

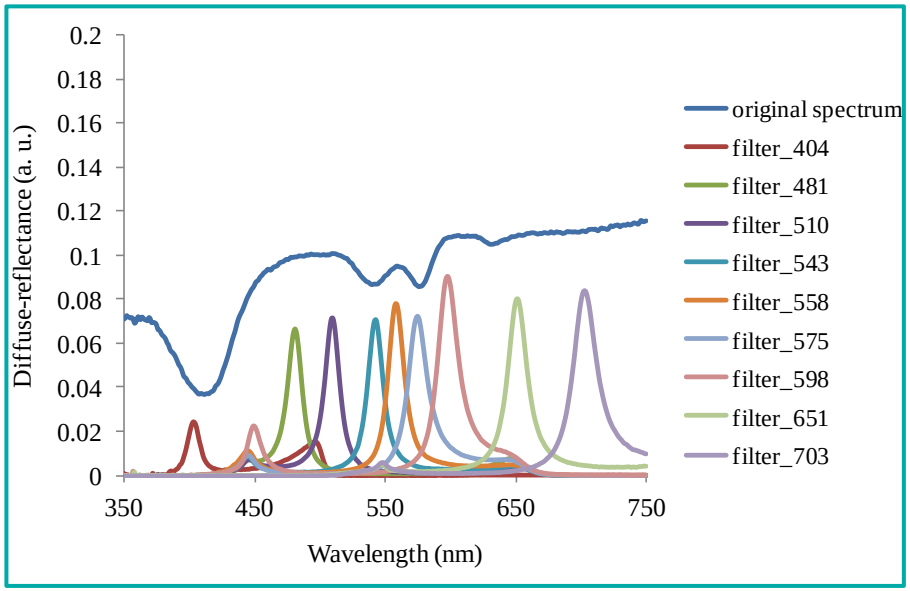


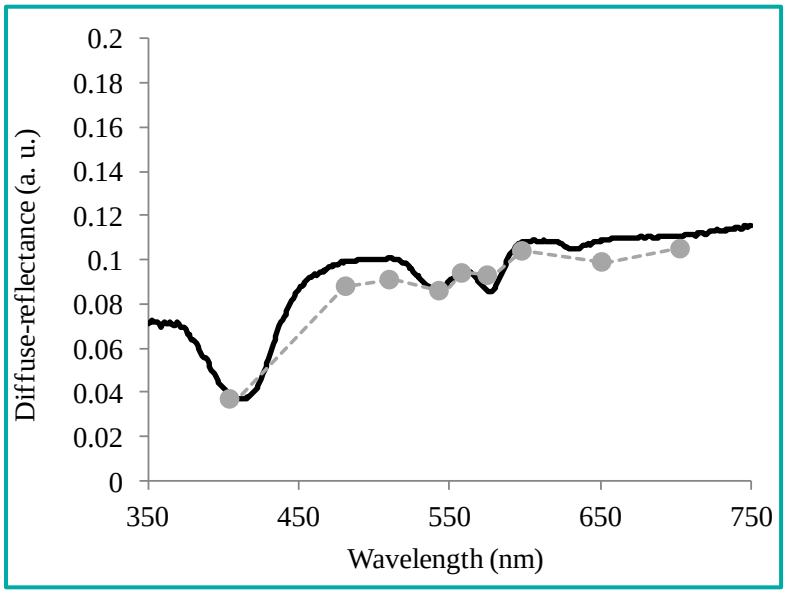


- Clear separation between the SiO_2 and TiO_2 layers
- Thickness measurements in good agreement with the nominal values
- Good film flatness along the entire area

Results

- **Optical filters – ability for diagnosis**
  - **Quantitative diagnosis:** DRS measurements on 5 different phantoms using the fabricated optical filters to verify how accurately each filter is able to select a specific spectral band

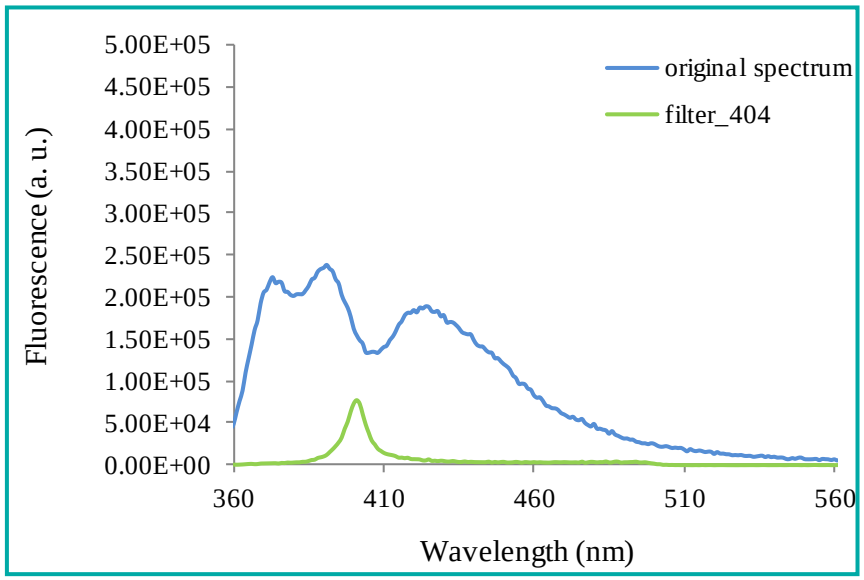


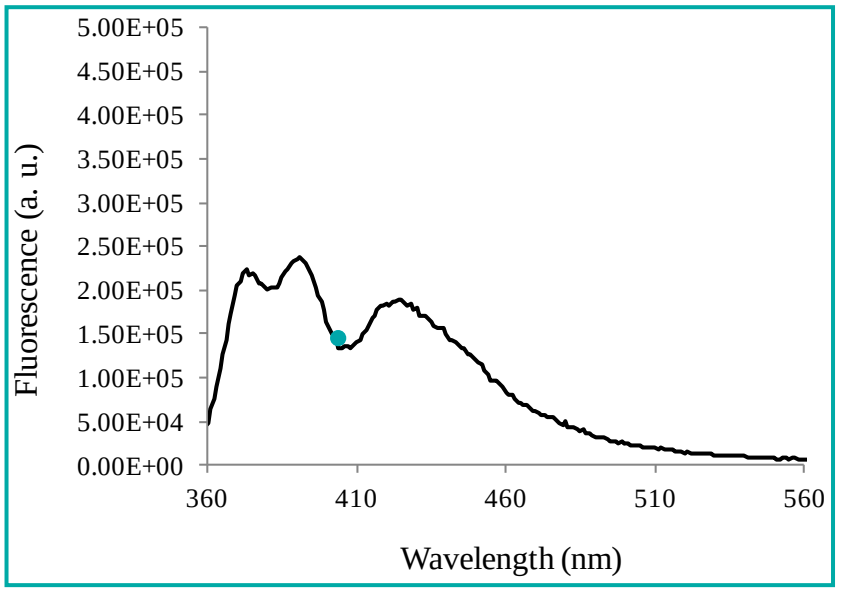


Intensity values obtained with the fabricated optical filters are similar to the originally obtained intensities measured over the full wavelength range

Results

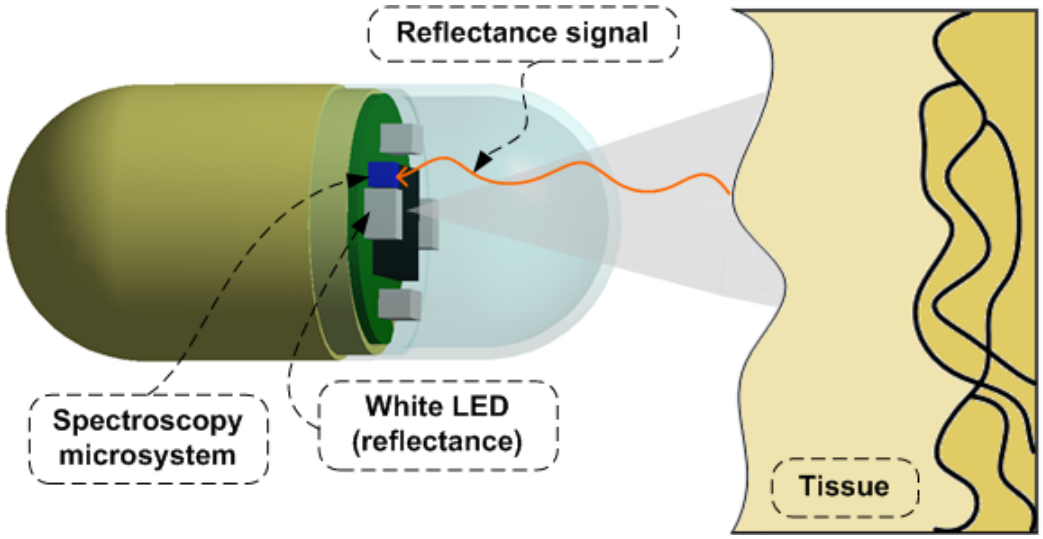
- **Optical filters – ability for diagnosis**
  - **Quantitative diagnosis:** Fluorescence measurements on 2 different phantoms using the fabricated optical filter centered at 404 nm





Intensity value obtained with the fabricated optical filter is similar to the originally obtained intensity

Application in endoscopic capsules



The addition of spectroscopy functions will offer the possibility of detecting the very earliest mucosal changes at the microstructural and biochemical levels

Conclusions

- **Miniaturized spectroscopy system**

  - Accurate reconstruction of the full spectrum using only 16 points
  - Feasibility of using optical filters to establish a quantitative diagnosis

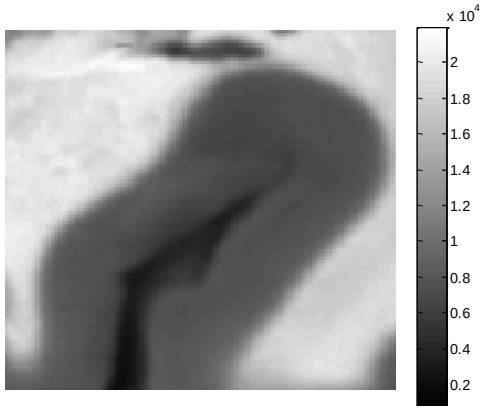
The replacement of the spectrograph by an array of thin-film optical filters was validated

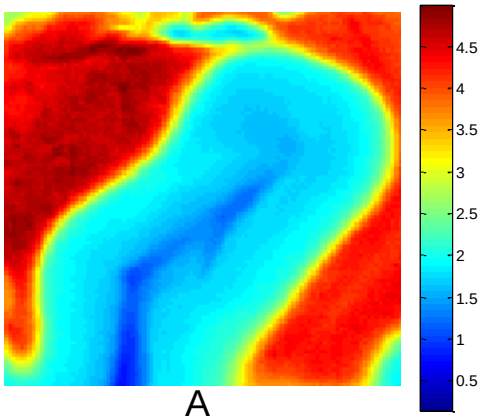
Next Step???

Spectroscopy Imaging

Preliminary results

- **Spectroscopy imaging** – e.g. brain tissue samples





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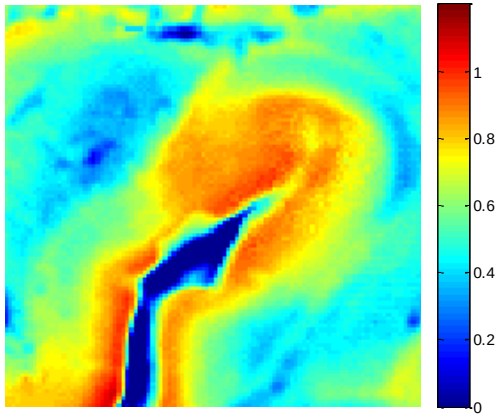

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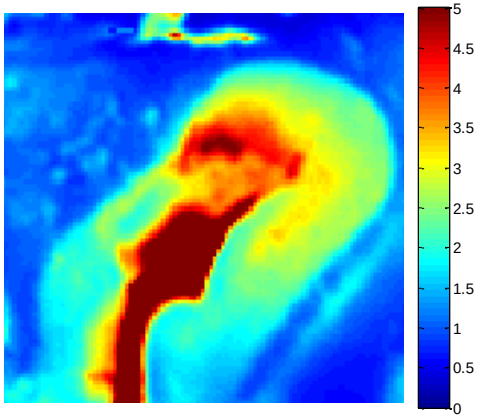

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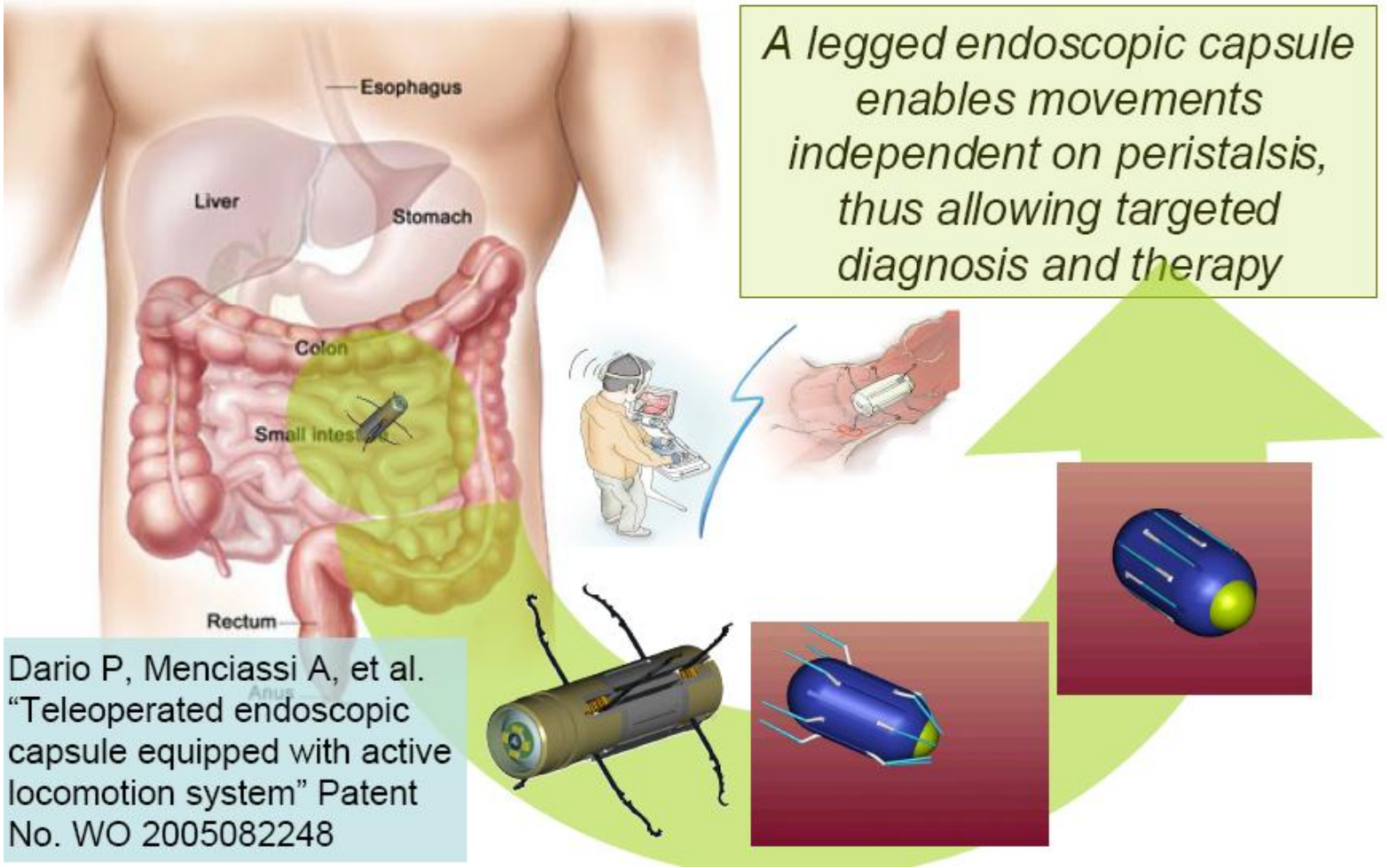
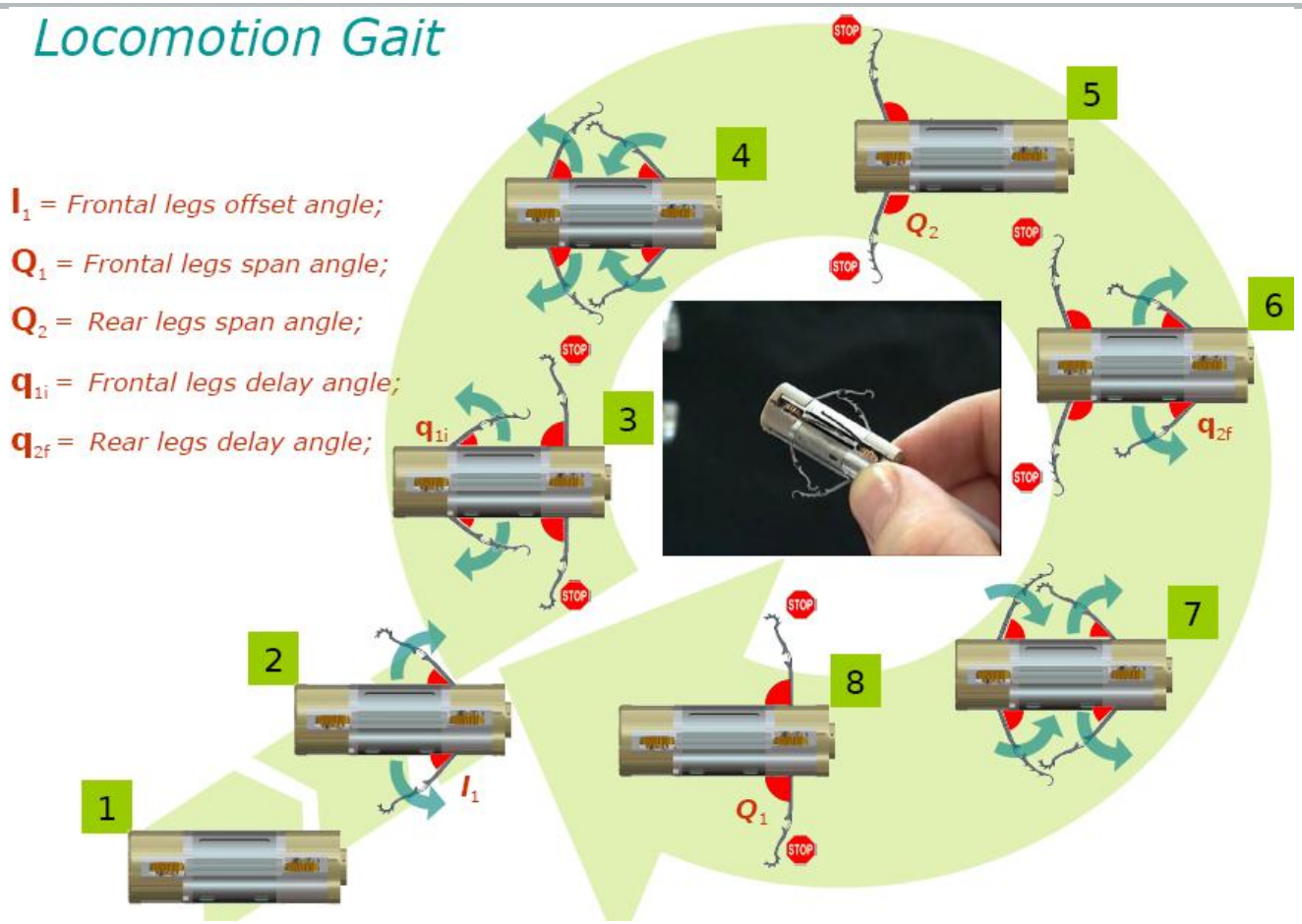
Capsule Locomotion



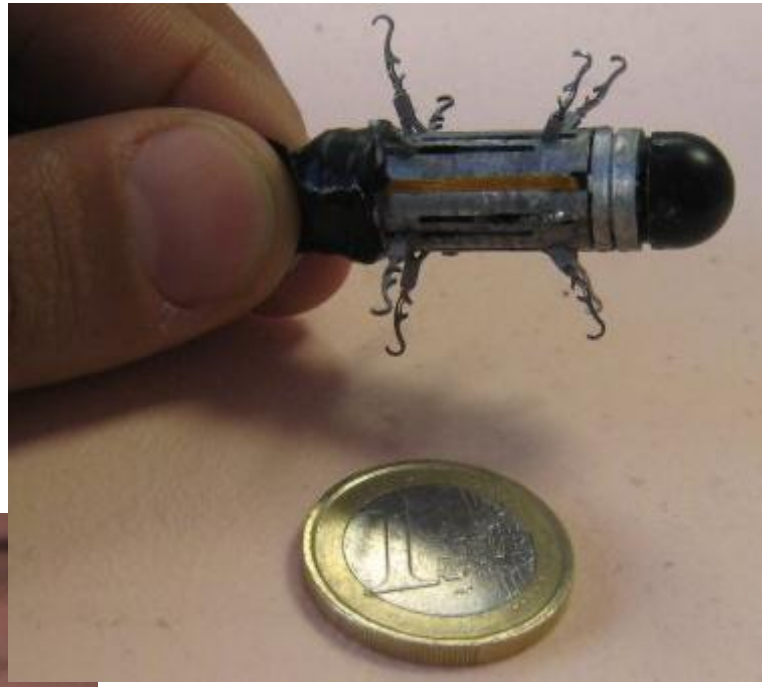
A legged endoscopic capsule enables movements independent on peristalsis, thus allowing targeted diagnosis and therapy

Dario P, Menciassi A, et al. "Teleoperated endoscopic capsule equipped with active locomotion system" Patent No. WO 2005082248

Capsule Locomotion



Capsule Locomotion



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