CENTER FOR MEDICAL PHYSICS AND BIOMEDICAL ENGINEERING
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Multimodal morpho-molecular early stage bladder cancer assessment using endoscopic optical coherence tomography and Raman spectroscopy

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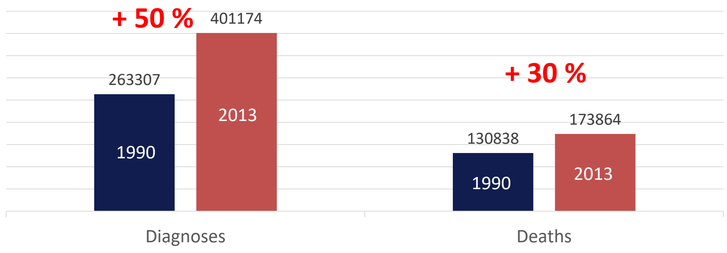
Motivation

Raman spectroscopy (RS) is a non-invasive imaging technique, providing label-free information on the molecular composition of investigated biological tissue.

Optical coherence tomography (OCT) is a non-invasive imaging technique, providing cross-sectional images of biological tissues at a micrometer resolution up to 2 mm in depth.

- OCT gains importance in endoscopic applications such as bladder, esophagus, vessels[1]
- RS extensively used for clinical tissue characterization[2]
- forward-imaging probe: easier positioning of the probe in front of the targeted area[3], e.g. in bladder



Comparison of number of bladder cancer diagnoses and deaths in the year 1990 and 2013 [4]

Results

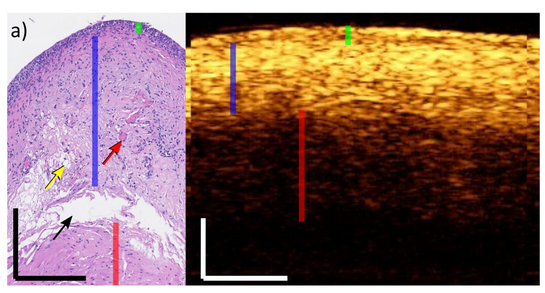
	OCT (%)	RS – T/NT (%)	RS – HG/LG (%)
Accuracy	73.4	92	77
Sensitivity	78	95	81
Specificity	69	88	68
Confidence interval	(72.9-73.9)	(92.2-92.6)	(73-81)

Performance of OCT: texture analysis differentiating non-tumor from tumor (OCT),
Performance of RS: model level 1 for tumor (T) & non-tumor (NT) / model level 2 for high grade (HG) and low grade (LG) [5]

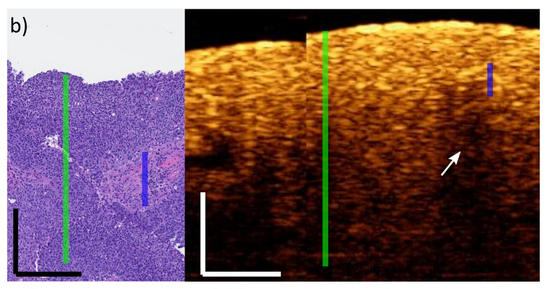
Non-tumor	Cancerous	Total
69 (22)	50 (22)	116 (44)

Stage			Grade	
CIS	pTa	pT1a	High	Low
1 (1)	48 (22)	1 (1)	12 (6)	38 (19)

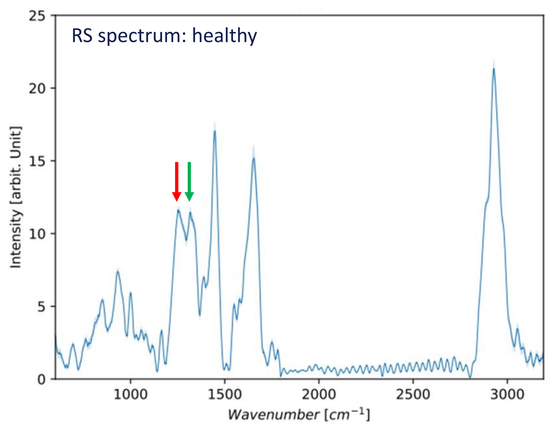
Distribution of biopsies according to the stage and grade information. Histopathological label as gold standard for classification. Number in brackets indicate patient number. [5]

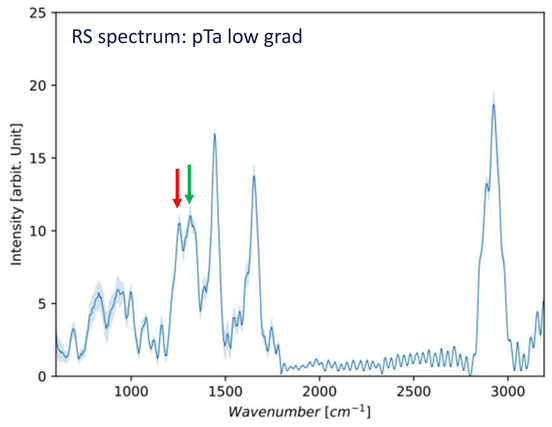


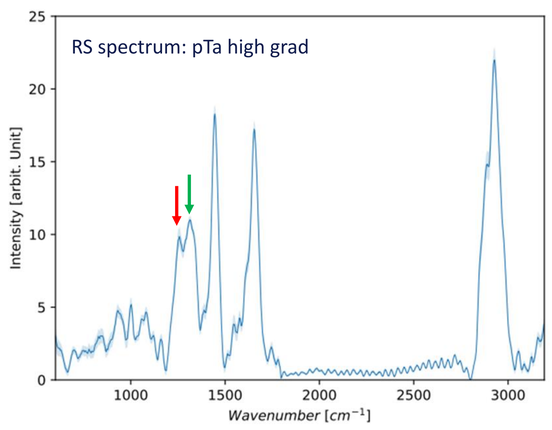
Healthy bladder wall (OCT correlation to histopathological image). The green line indicates the mucosa/urothelium layer, the blue line shows the lamina propria and the red line is the muscularis layer. Scale bars: 250µm. [5]



pTa low grade tumor (OCT correlation to histopathological image). The green line indicates the mucosa/urothelium layer, the blue line shows the lamina propria. Thickened urothelium due to tumor progression. Scale bars: 250µm. [5]



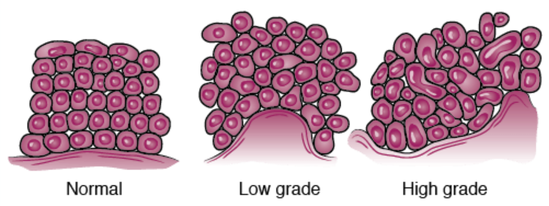




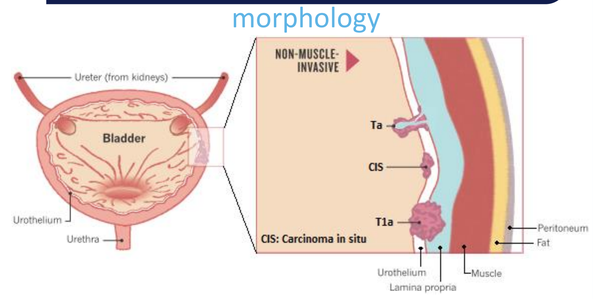
This project has received funding from the European Union's Horizon 2020 research and innovation program under the Marie Skłodowska-Curie grant agreement No 721766 and MIB project No 667933.

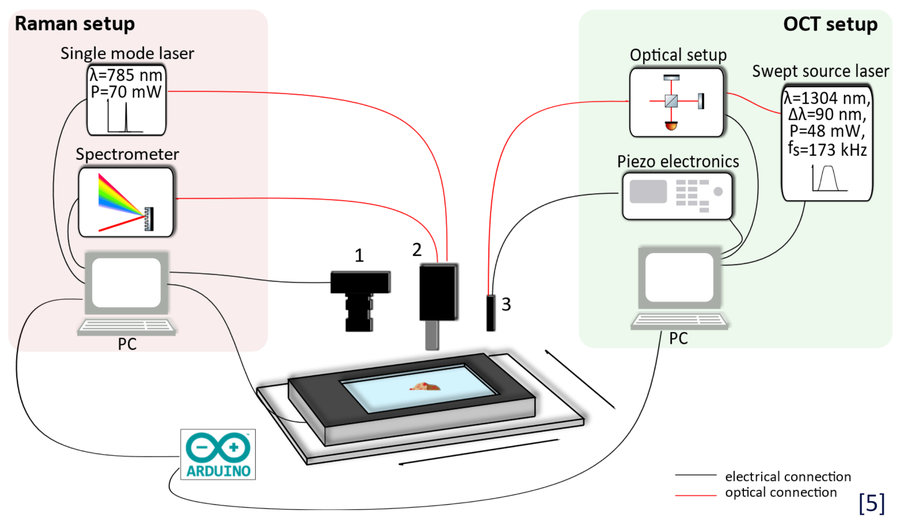
Aim and methods

Raman ⟷ Grade — molecular



OCT ⟷ Stage — morphology

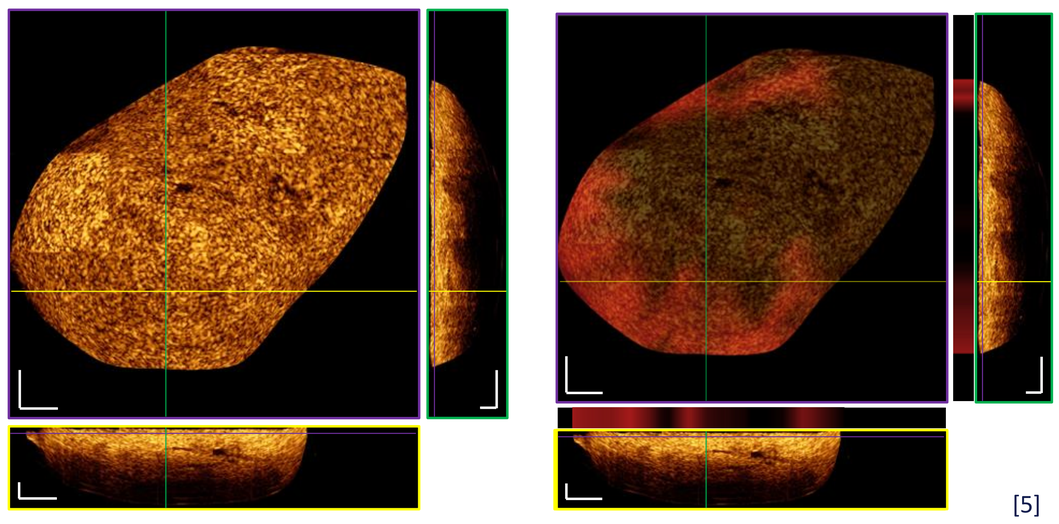




[5]

- Tumor grade by RS & Tumor stage by OCT
- Automated combined setup based on forward view OCT endoscope (3) and RS probe (2)
- White light camera for choosing region of interest (1)
- Automated classification of OCT data and RS data

Co-localized Raman and OCT

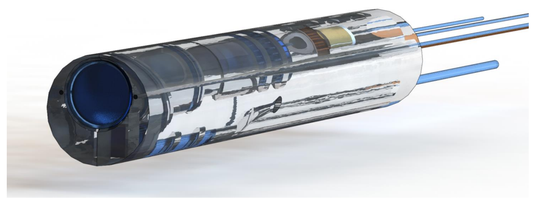


[5]

Heterogeneity of a pTa low grade labelled biopsy. Red arrows: loss of transition between the urothelium and the lamina propria. Blue arrows: regions of present lamina propria. OCT-RS combination: Model level 1 highlights tumor (red) and non-tumor (black) areas and it is overlapped to the OCT image. The lamina propria appears bright in the OCT image and RS predicts the non-tumor tissue (black color within the stripes above the B-scans). Scale bars: 250µm.

Outlook

- Co-localization of OCT and RS
- Apply combined endoscopic probe for in-vivo test (diameter: 4.4mm)
- Approval work for clearance of AGES (Austrian Agency for Health and Food Safety Ltd) using a non-CE-marked device for clinical trial



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