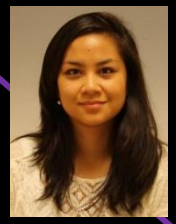
# Optical diagnostics of urinary tract cancer: towards real time finding and grading

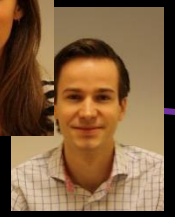
Daniel Martijn de Bruin

**Group leader urological research**

*Dept of urology*

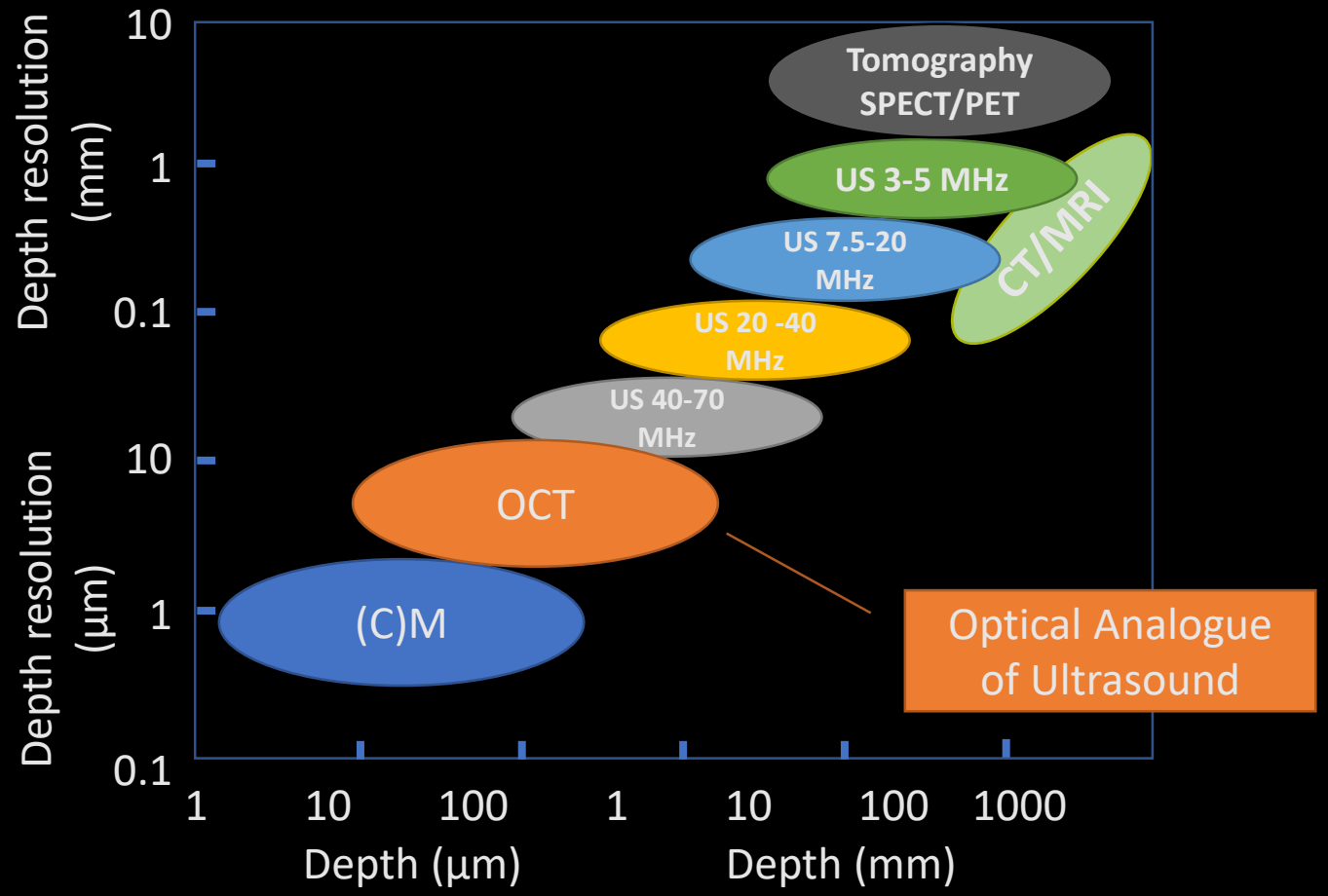
*Dept of Biomedical Engineering & Physics*



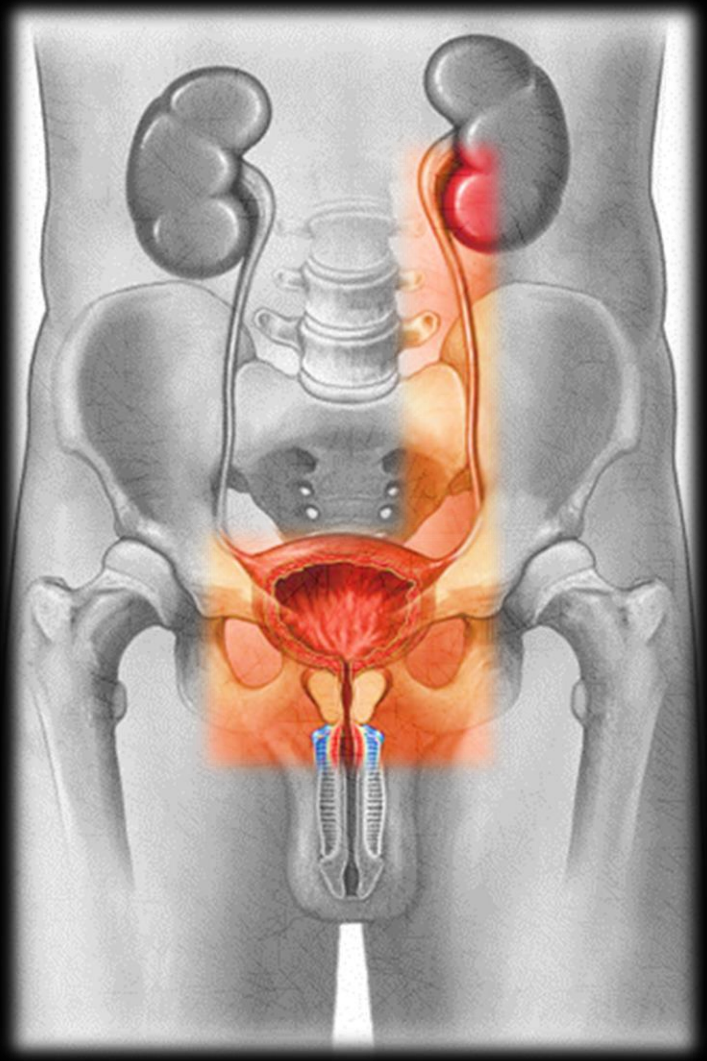


Pathology
Optical endomicroscopy of the bladder
Digital optical pathology
Optical endomicroscopy of the ureter
Optical endomicroscopy during RFA of lungs in asthma patients
Urology
Respiratory Med
Percutaneous optical biopsy /treatment kidney
Percutaneous Optical endomicroscopy of lung nodules
Plastic hand surgery
Optical pathology
Gastro enterology
Percutaneous optical biopsy/ treatment prostate
Surgery
Rad Oncology
OCT in Barret's Esophagus
Optical Visualization of CMC-1 cartilage
OCT Lung and Esophagus During radiotherapy
Optical Perfusion imaging during surgery
Radiology

# Medical Imaging

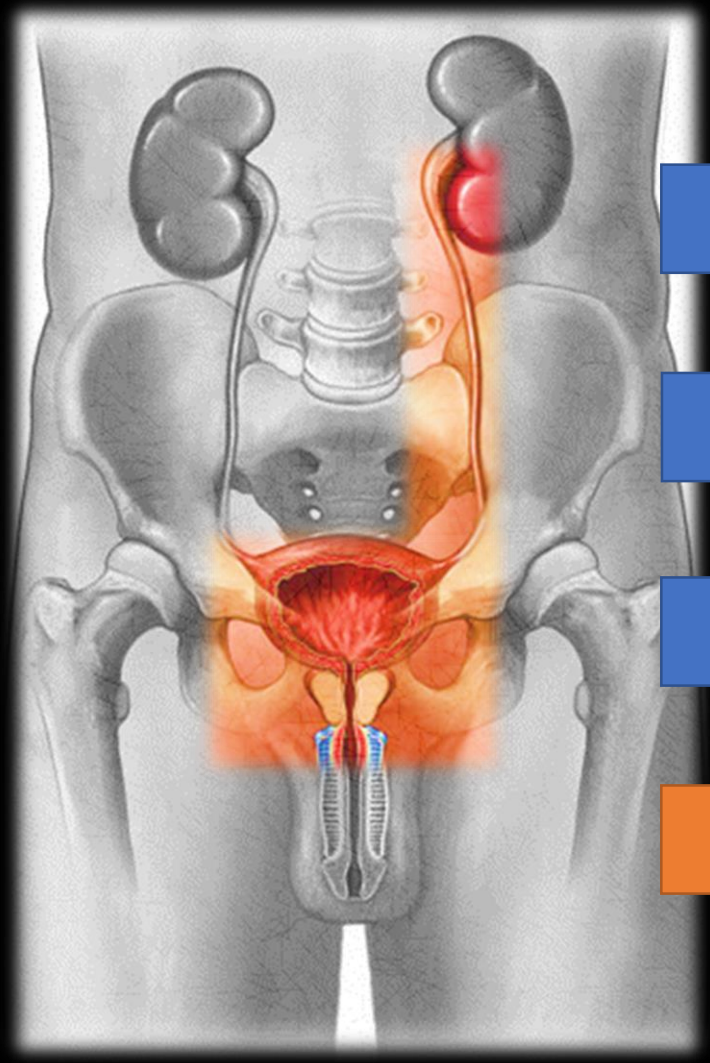


# ENDOUROLOGY - ENDOUROLOGIST

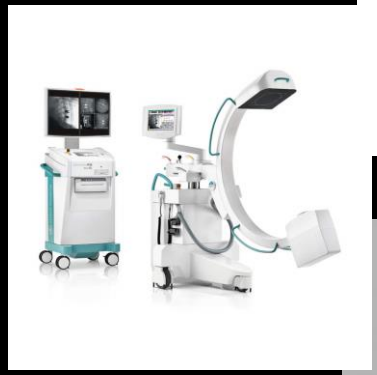


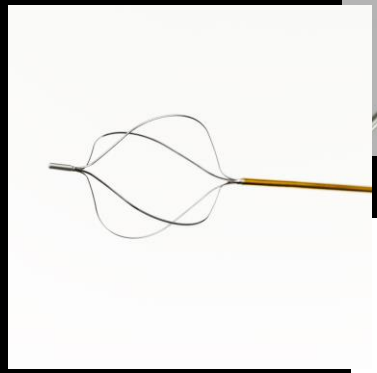
- Urinary tract tumor 4th most common
- 90-95% bladder
- 60% recurrence
- Lifetime follow-up
- Highest economic burden of all cancers

# ENDOUROLOGY - ENDOUROLOGIST



- stones
- enlarged benign prostate
- stricture
- cancer





# (OPTICAL) DIAGNOSTICS IN THE URINARY TRACT

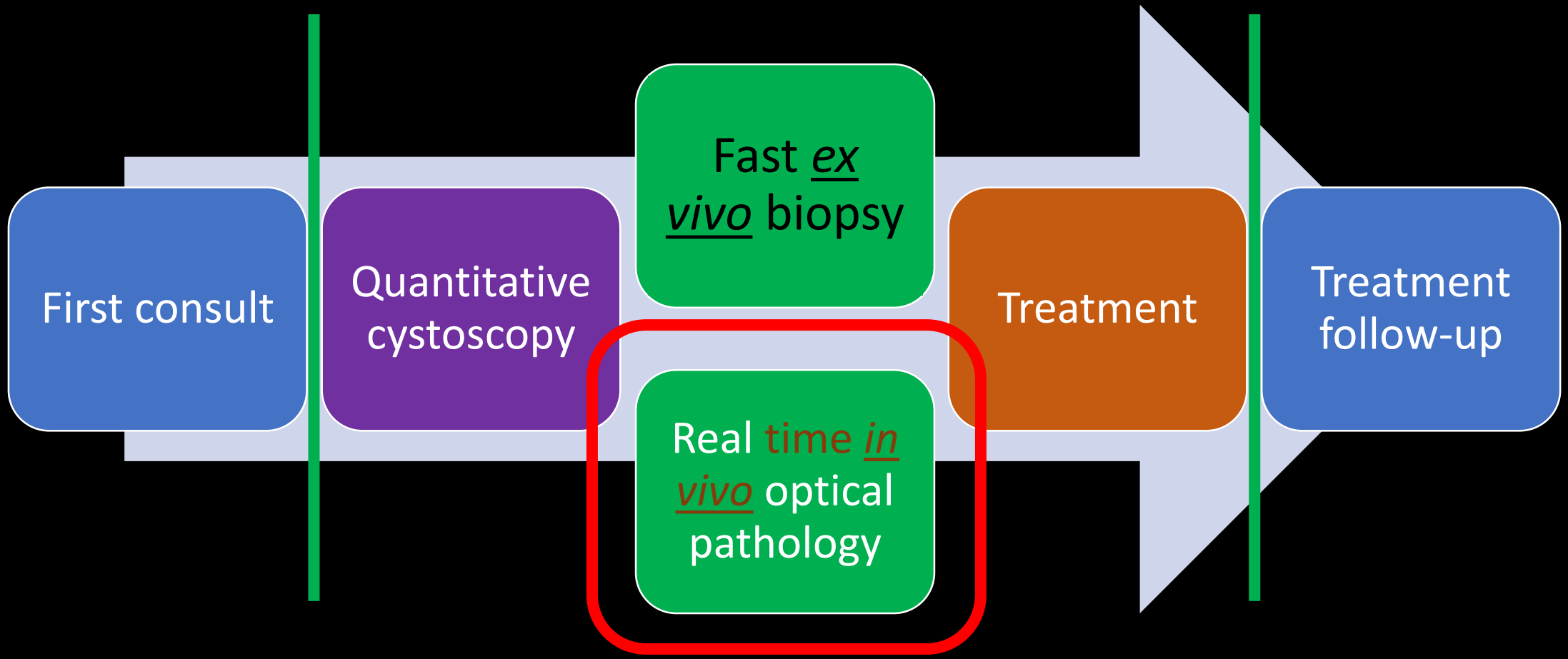
***FINDING A SUSPECTED LESION***

- Narrow Band Imaging (NBI, Olympus)
- Storz Profesional Image Enhancement System (SPIES, Storz)

***DIFFERENTIATING A SUSPECTED LESION***

- Confocal Laser Endomiscroscopy (CLE, Mauna Kea Tech)
- Optical Coherence Tomography (OCT, St. Jude)
- Endoluminal Ultrasound (ELUS, Volcano)

# THE OVER ALL SCOPE



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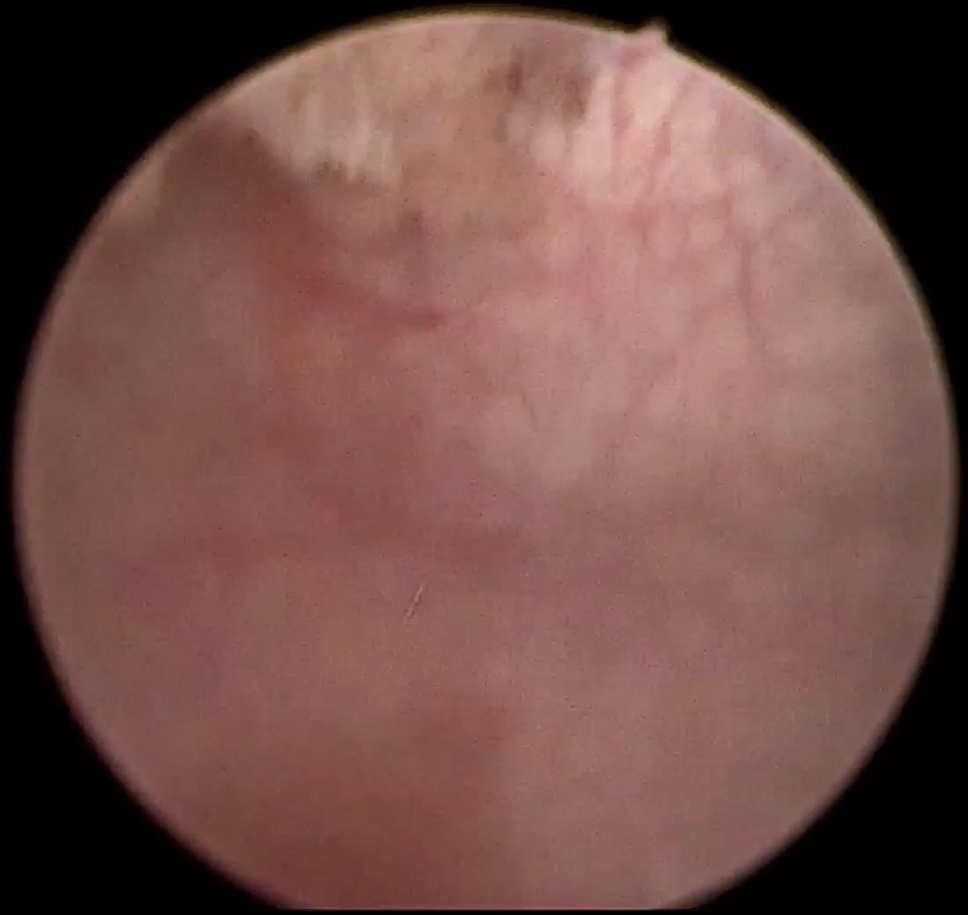
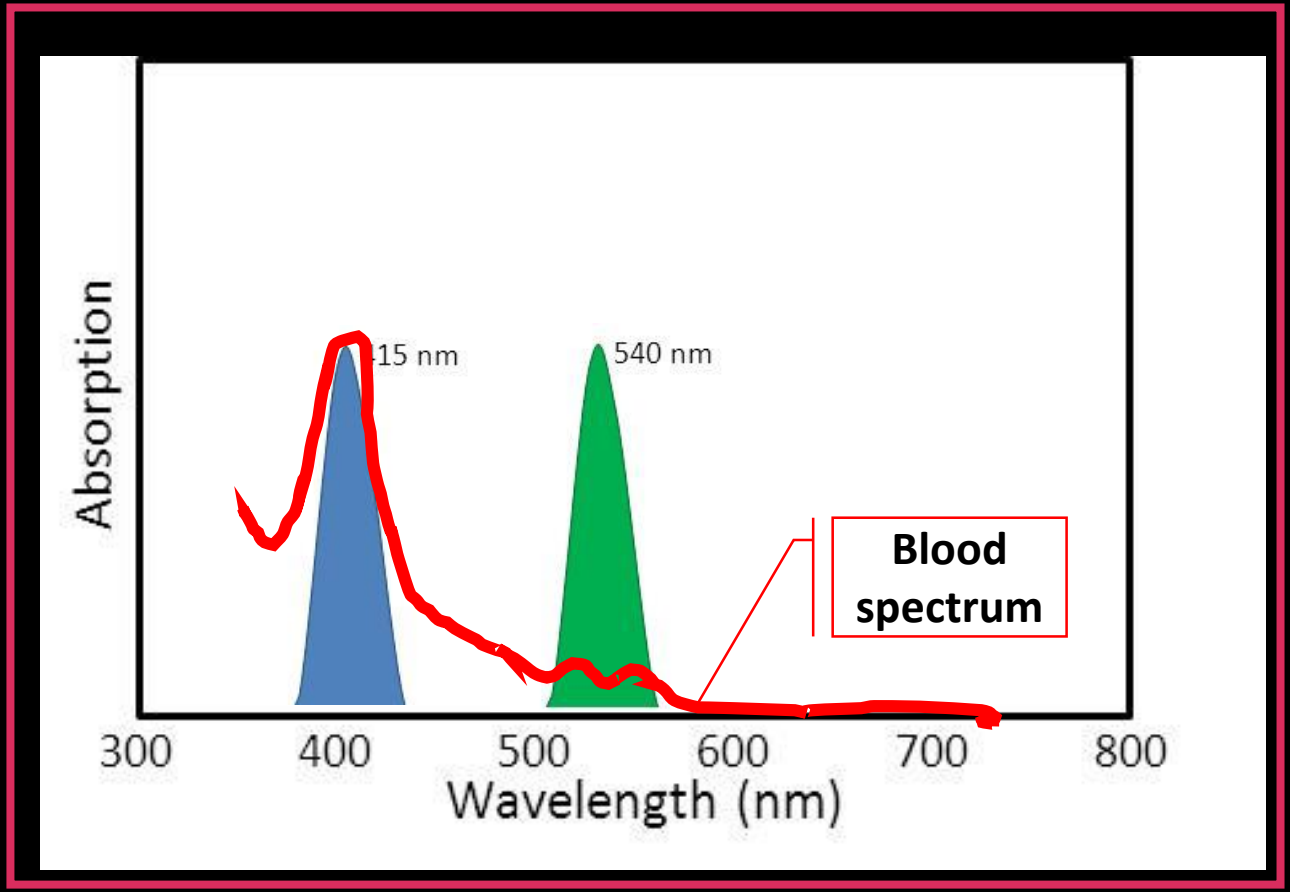
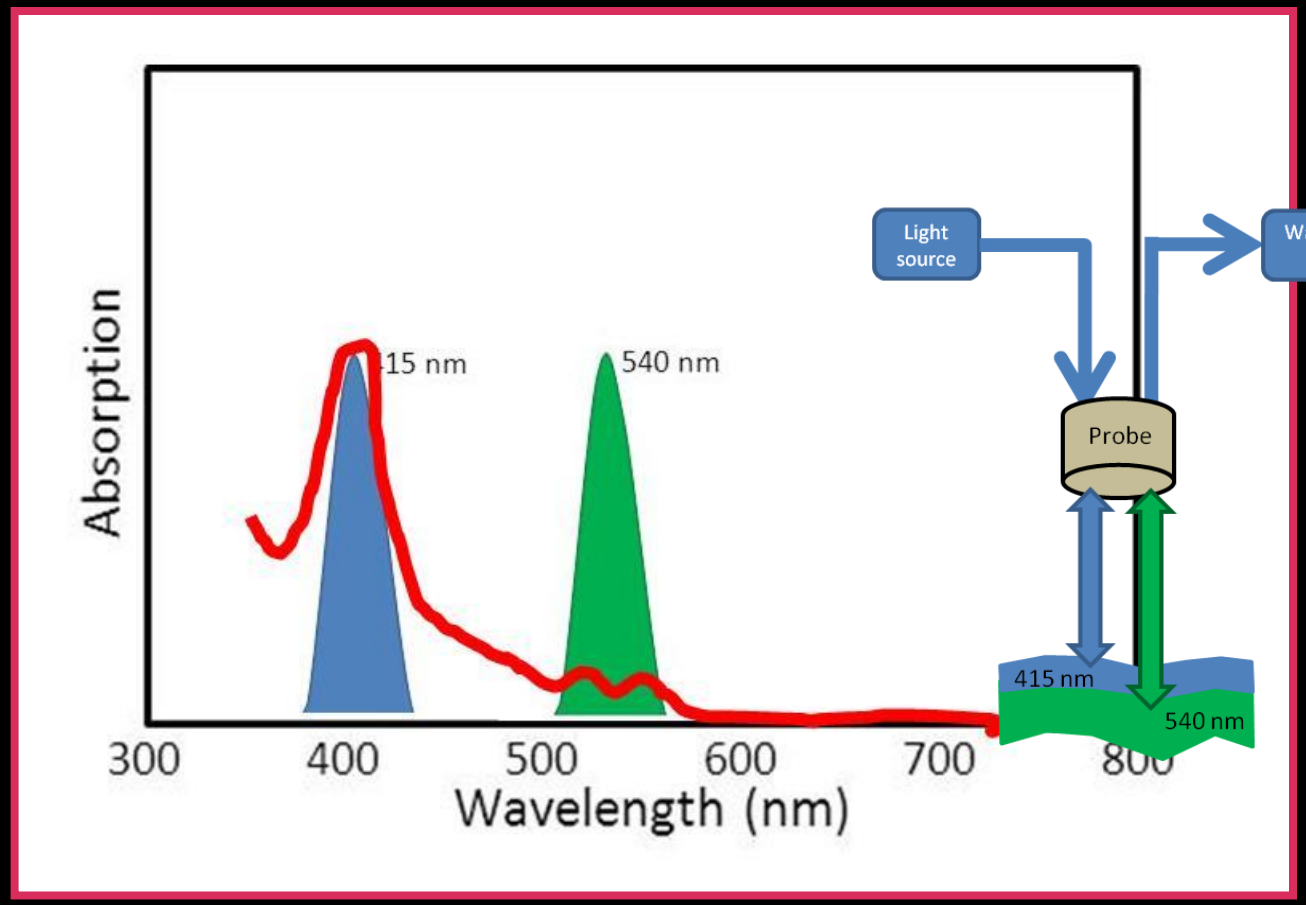


# Narrow band imaging



- Two colors (wavelengths) are used (415 & 540 nm)
- Both colors are absorbed by **Blood**

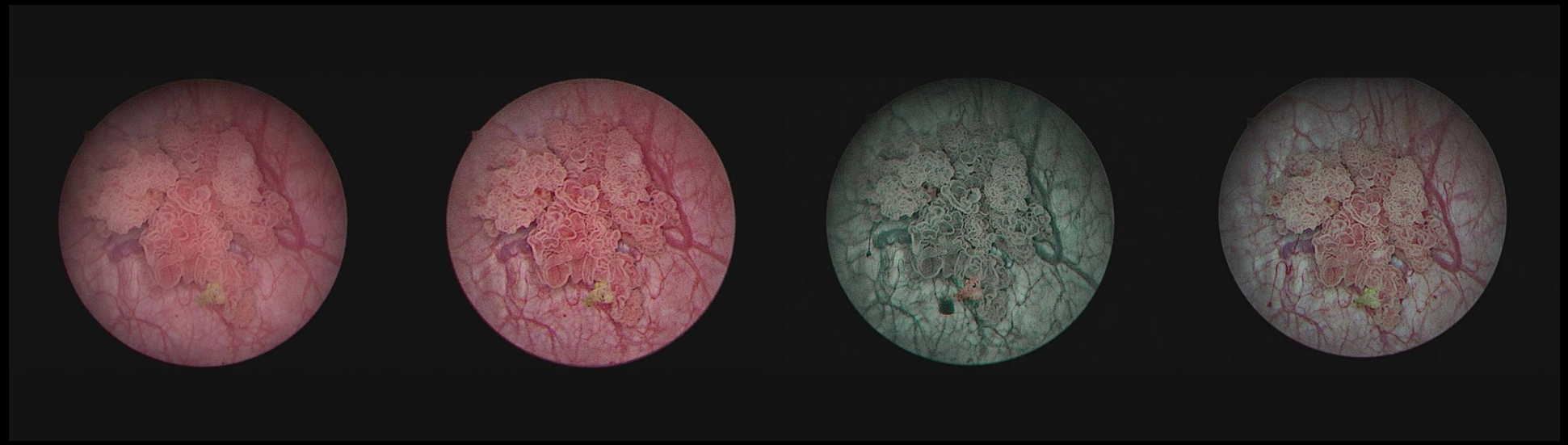
# Narrow band imaging



- Two colors (wavelengths) are used (415 & 540 nm)
- Both colors are absorbed by **Blood**
- Green light penetrates deeper, revealing deeper bloodvessels

# storz profesional imaging enhancment system (SPIES)

Example in the bladder II

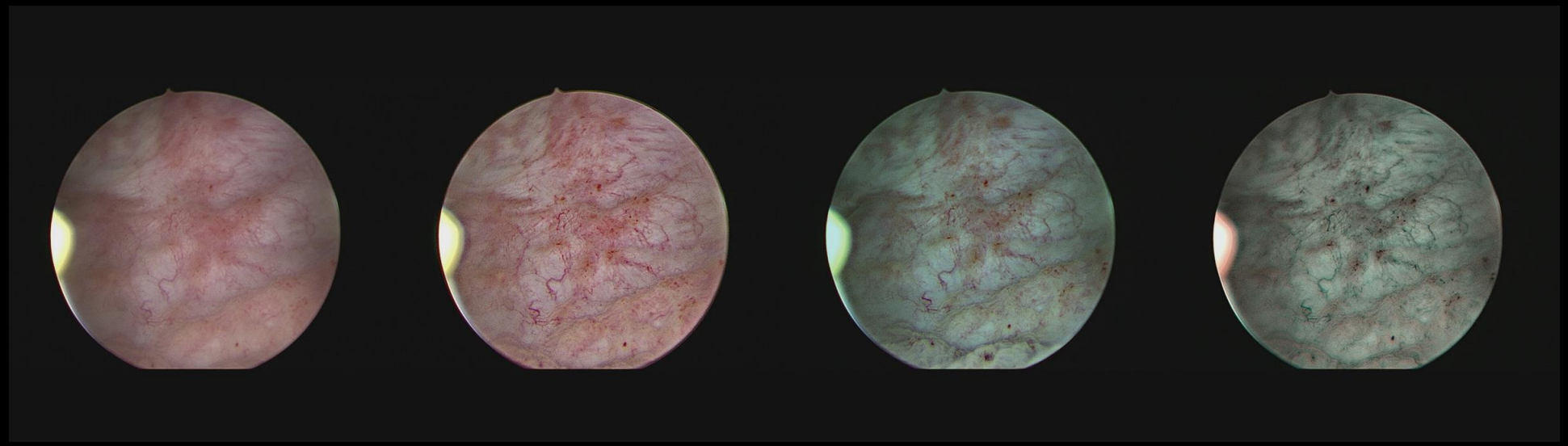


White light | Clara & Chroma | Spectra A | Spectra B

*Guido M Kamphuis et al, Journal of endourology 2016*
*Guido M Kamphuis et al, J Cancer Sci Ther , 2016*

# storz profesional imaging enhancment system (SPIES)

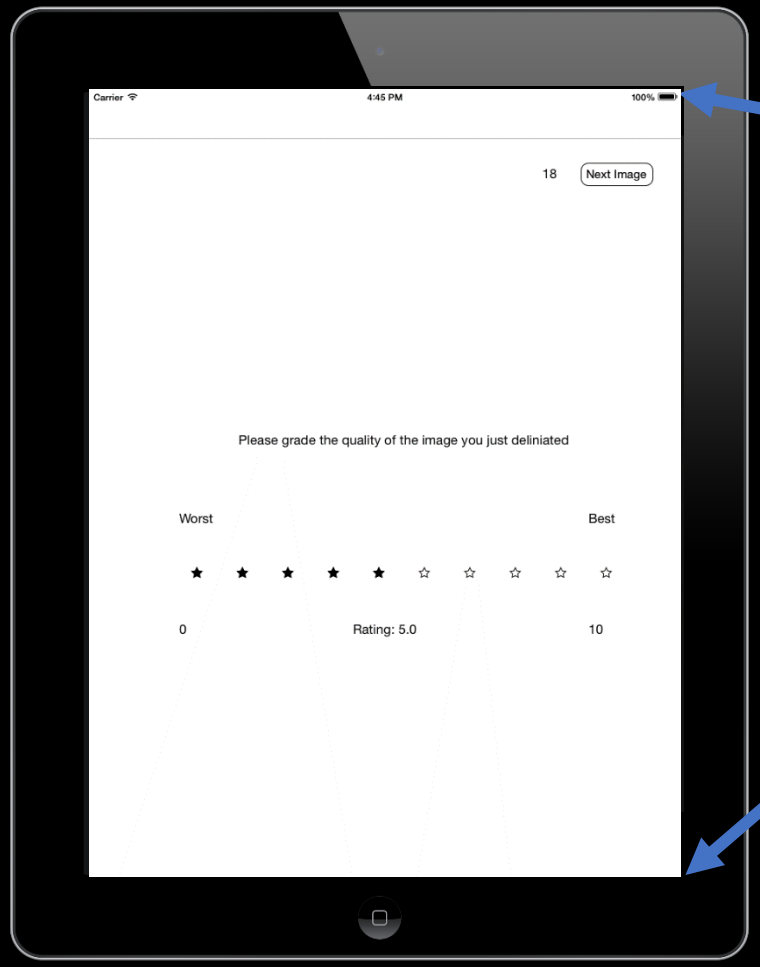
Example in the bladder I



White light | Clara & Chroma | Spectra A | Spectra B

*Guido M Kamphuis et al, Journal of endourology 2016*
*Guido M Kamphuis et al, J Cancer Sci Ther , 2016*

# iSPIES iPAD App



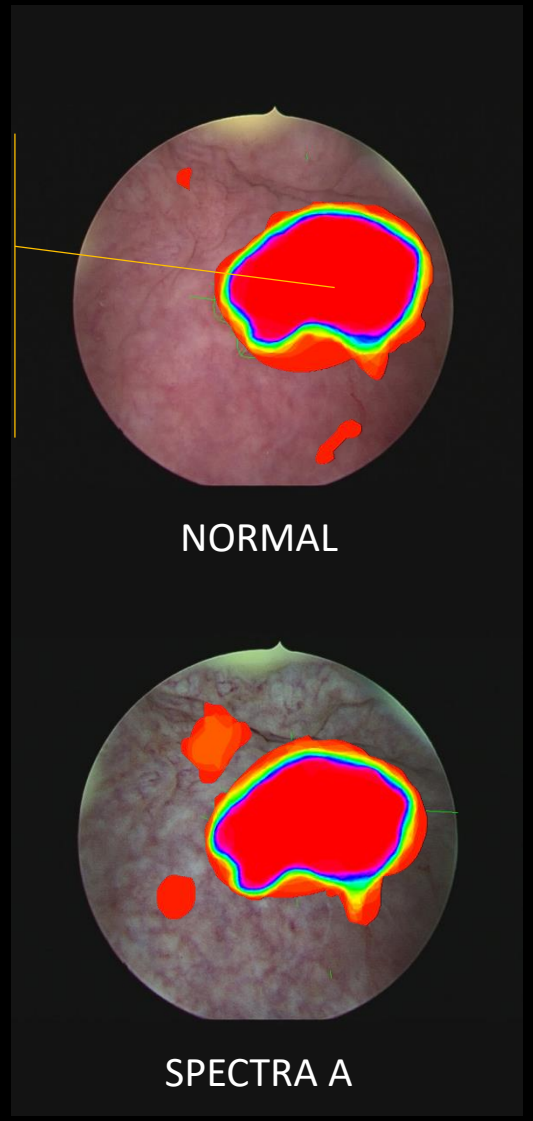
*Guido M Kamphuis et al, Journal of endourology 2016*
*Guido M Kamphuis et al, J Cancer Sci Ther , 2016*

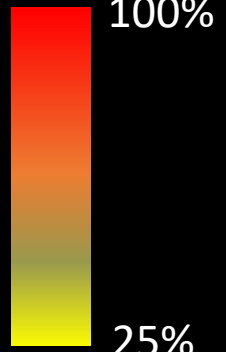
# PARTICIPATION BY ± 90 UROLOGISTS

*Guido M Kamphuis et al, Journal of endourology 2016*
*Guido M Kamphuis et al, J Cancer Sci Ther , 2016*

# DELINEATON RESULTS FROM 90+ UROLOGISTS

From all delineations we calculate the overlap and standard deviation





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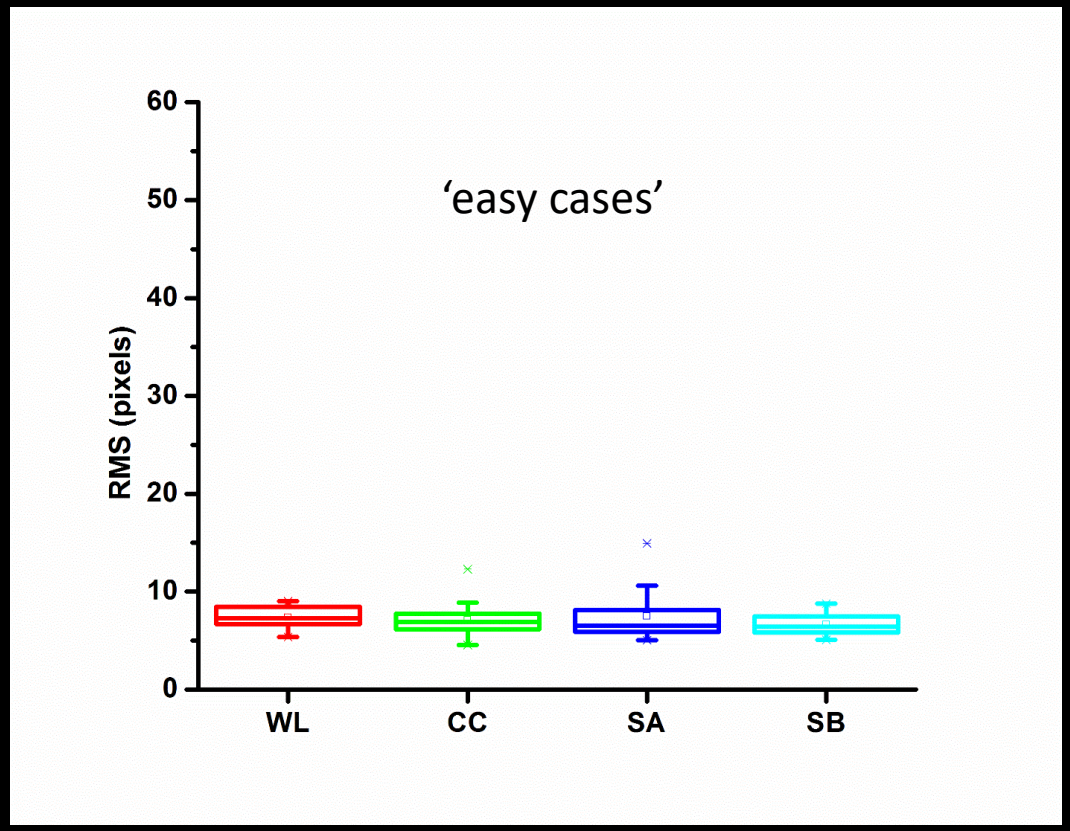
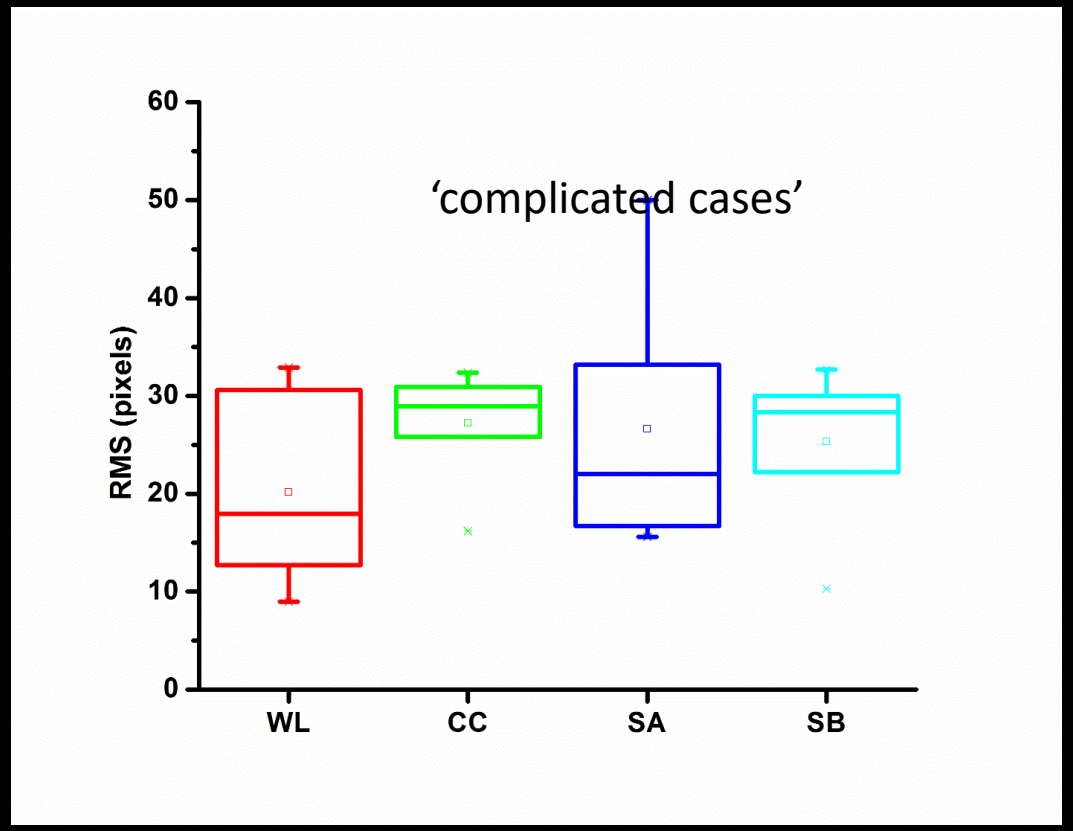



*Guido M Kamphuis et al, Journal of endourology 2016*
*Guido M Kamphuis et al, J Cancer Sci Ther , 2016*

# Automatic recognition

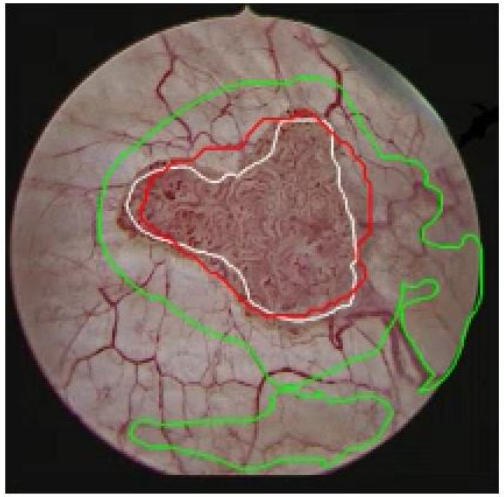
- GOAL: AUTOMATIC regimentation of lesions
  - Support Vector Machine (SVM)
  - Decision Tree (DT)
  - Random Forest (RF) classifier

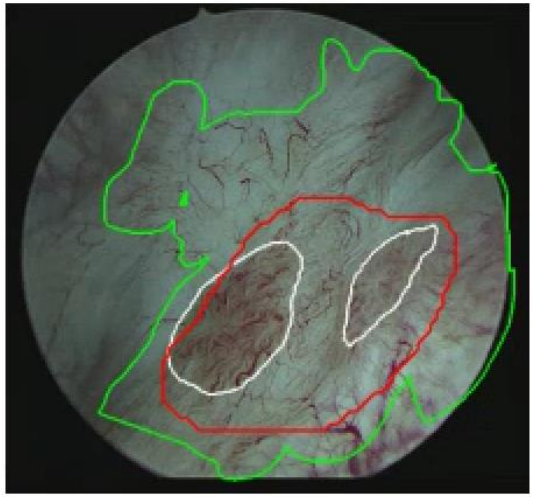
*Bladder cancer segmentation on multispectral imagesJ Van Der Putten, F Van Der Sommen, S Zinger, DM De Bruin, ...*
*Proceedings of the 12th International Conference on Distributed Smart …*

# First results using Automatic recognition

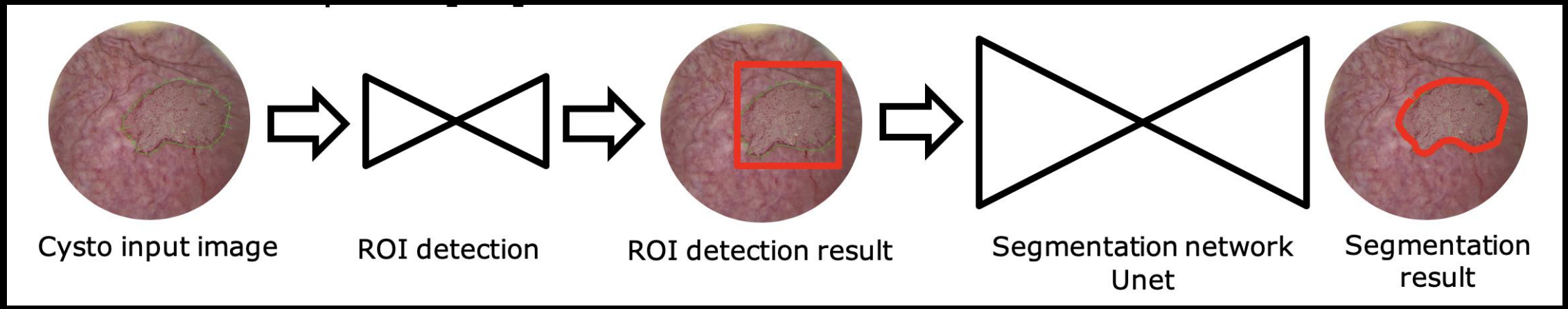
| Metric | "AUC all" | | | "AUC no ambiguous" | | | JIGS | | |
|---|---|---|---|---|---|---|---|---|---|
| Classifier | SVM | RF | DT | SVM | RF | DT | SVM | RF | DT |
| CC | 0.69 | 0.70 | 0.64 | 0.74 | 0.79 | 0.68 | 60% | 56% | 56% |
| SA | 0.66 | 0.59 | 0.52 | 0.74 | 0.64 | 0.57 | 53% | 44% | 48% |
| SB | **0.81** | 0.71 | 0.70 | **0.90** | 0.79 | 0.77 | **65%** | 52% | 59% |
| WL | 0.73 | 0.71 | 0.72 | 0.80 | 0.77 | 0.76 | 61% | 54% | 61% |

**Table 2: Segmentation comparison of the different modalities and classifiers.**





# Neural network for segmentation
# The ENDURO project



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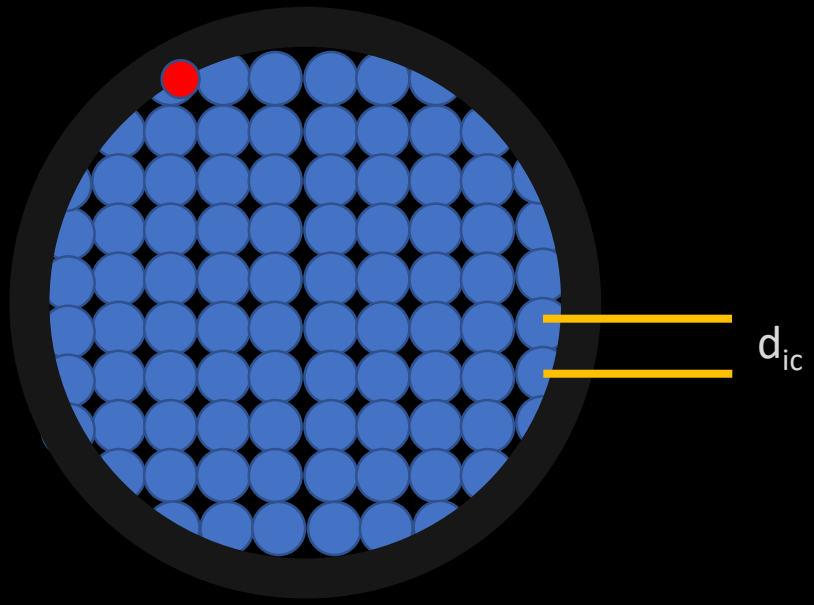
# Background

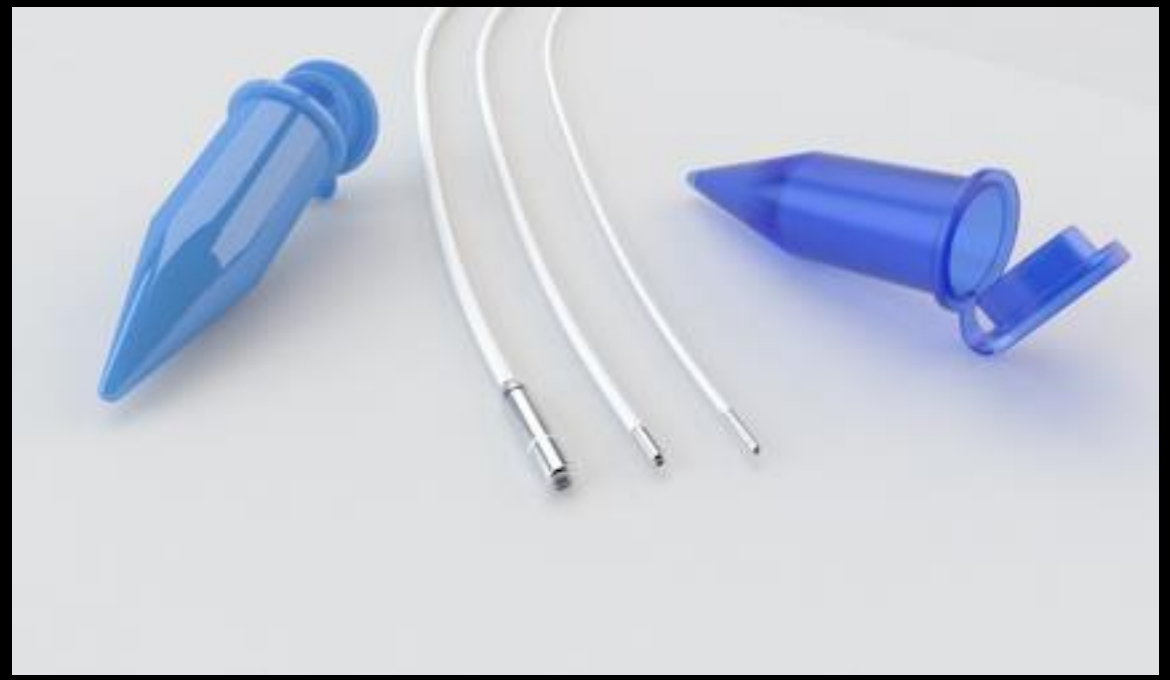


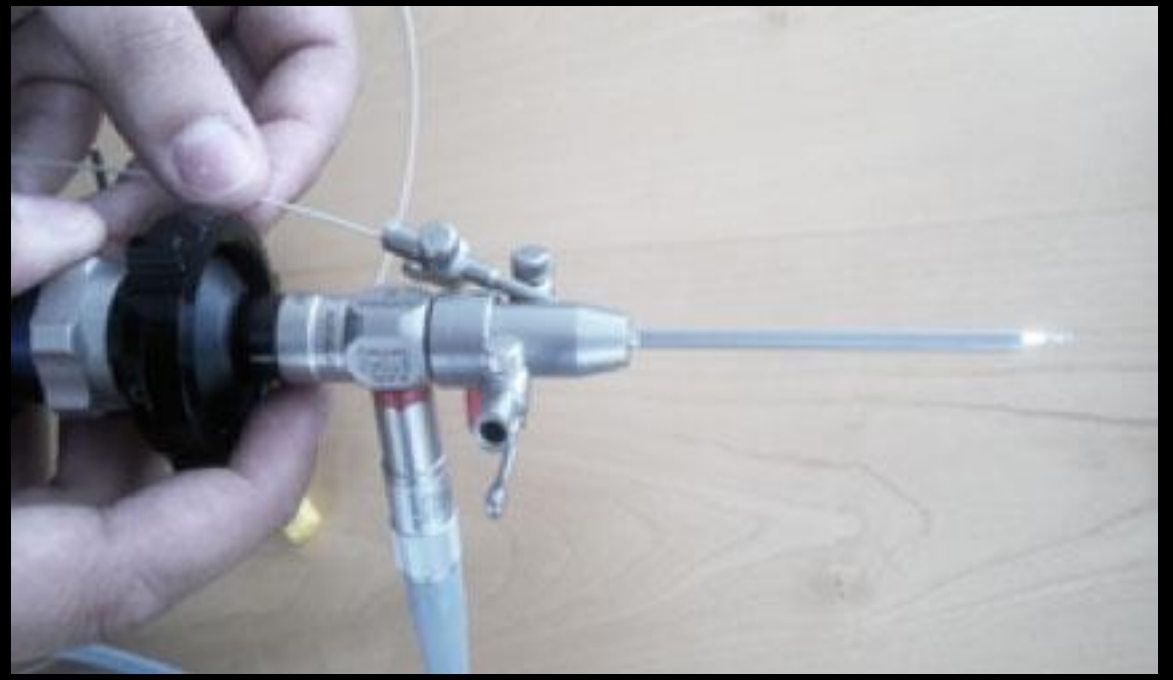

Lateral resolution = $\frac{2 \times dic}{M}$

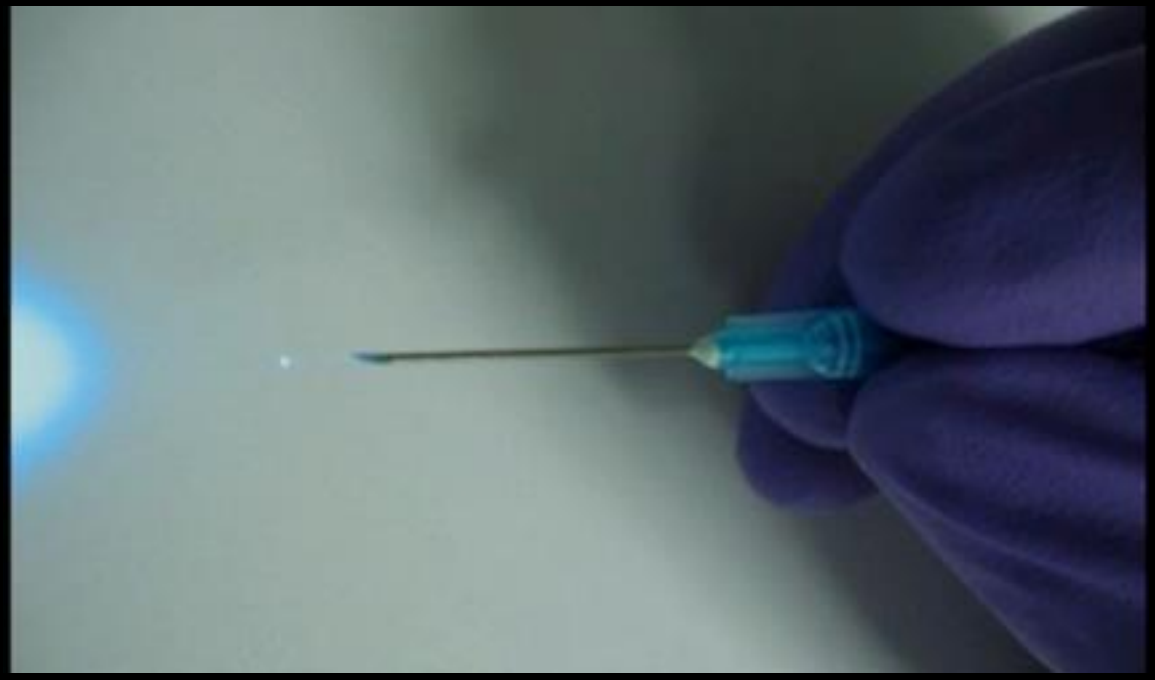
Operating wavelength = **488 nm**

Scanning frequency = **4 kHZ**

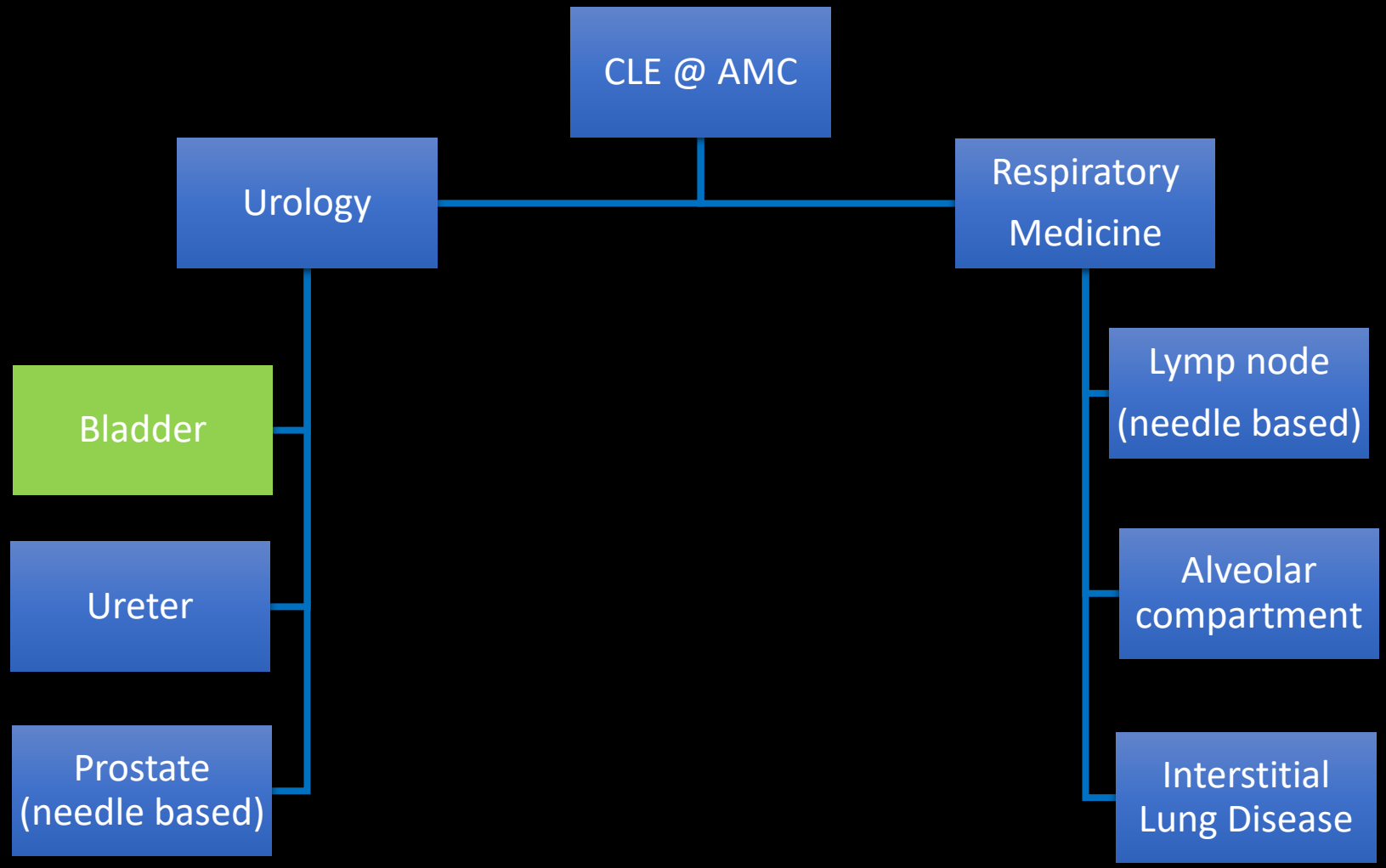
# Background

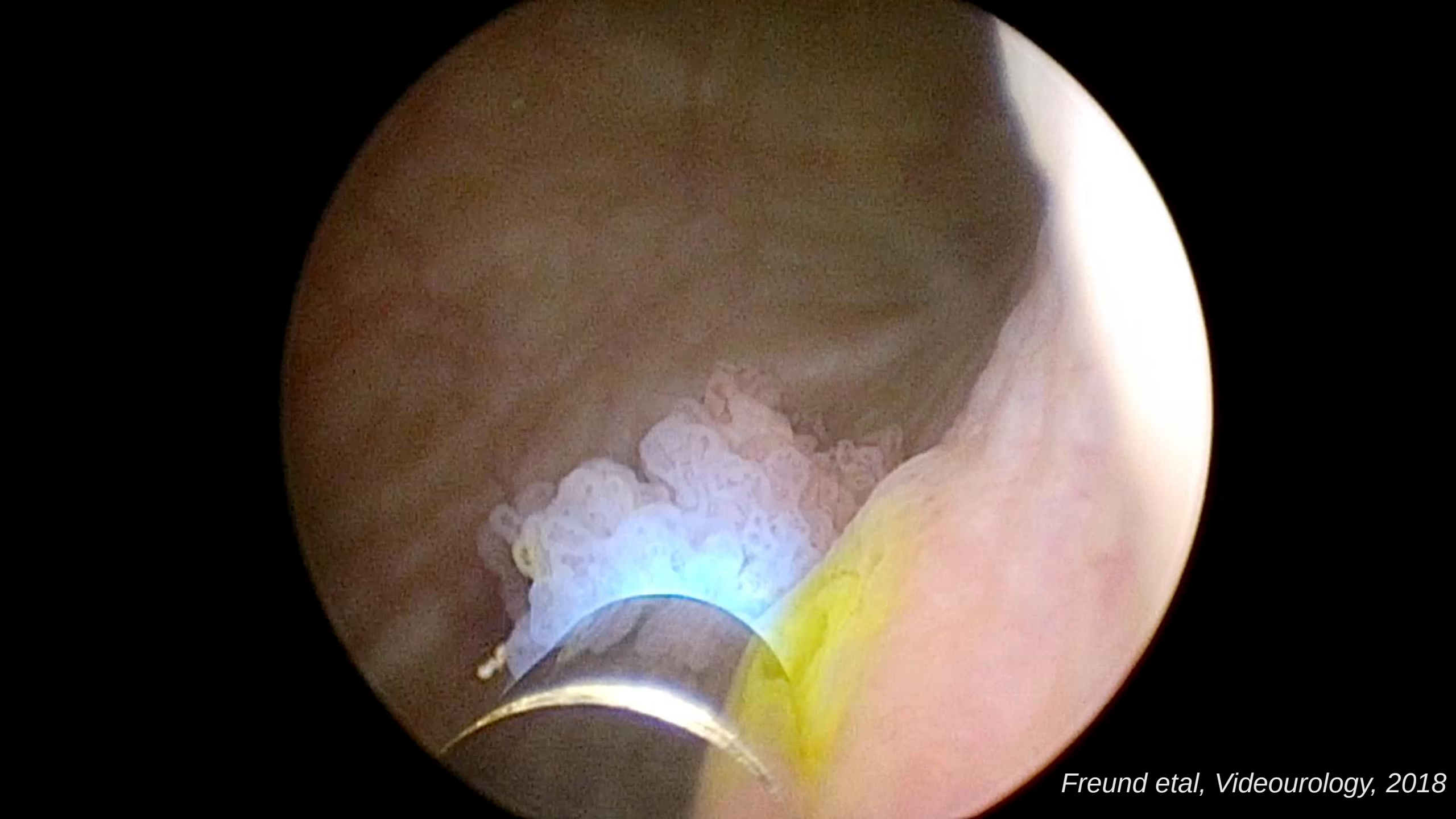






# Studies @ AMC

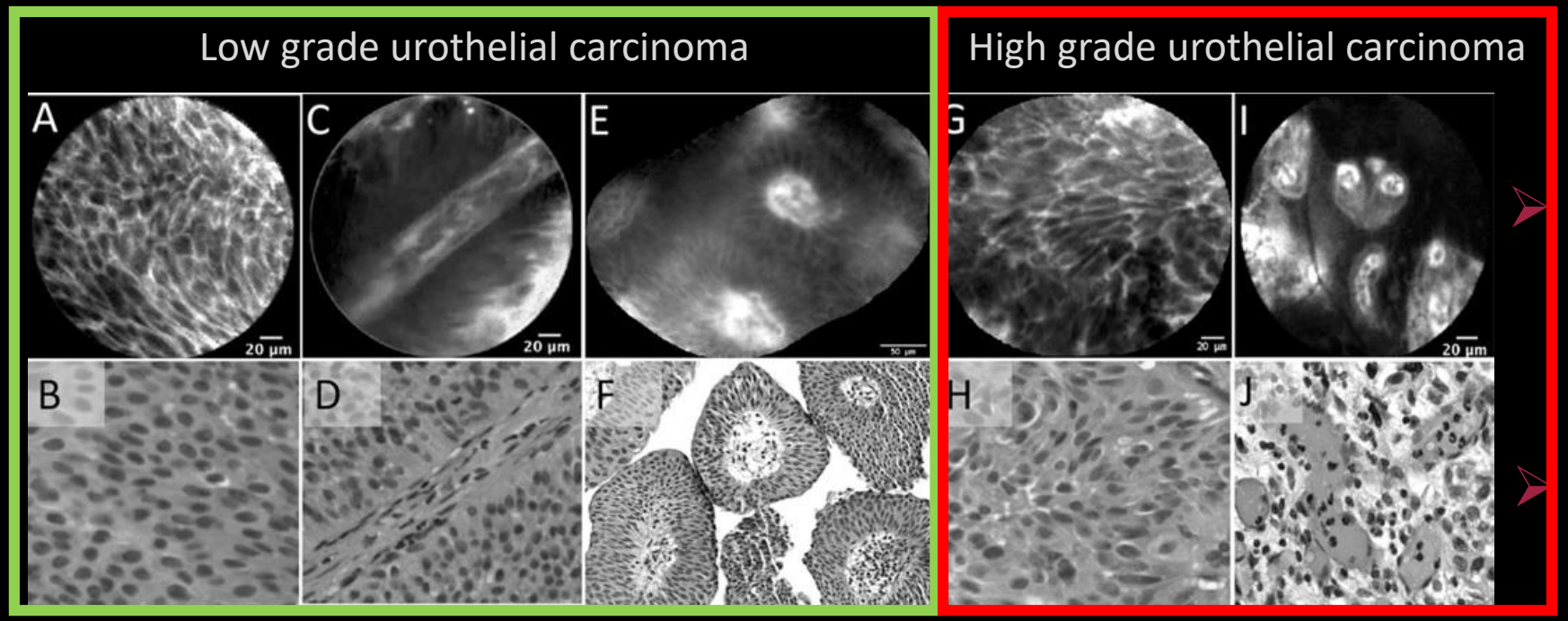

CLE @ AMC
Urology
Respiratory Medicine
Bladder
Ureter
Prostate (needle based)
Lymp node (needle based)
Alveolar compartment
Interstitial Lung Disease



*Freund etal, Videourology, 2018*

# confocal laser endomicroscopy (CLE)

*Liem etal, JMIR research protocols, 2018*
*Liem etal, Eur Uro Focus, 2018*




| Papillary |
| --- |
| Polarity |
| Organisation |
| Cohesiveness |
| Morphology |
| Borders |
| Vasculature |

Yes / No

Crowding of uniform-appearing cells

Fibrovascular stalk with a thickened endothelial layer

fibrovascular stalk containing erythrocytes in the vascular core

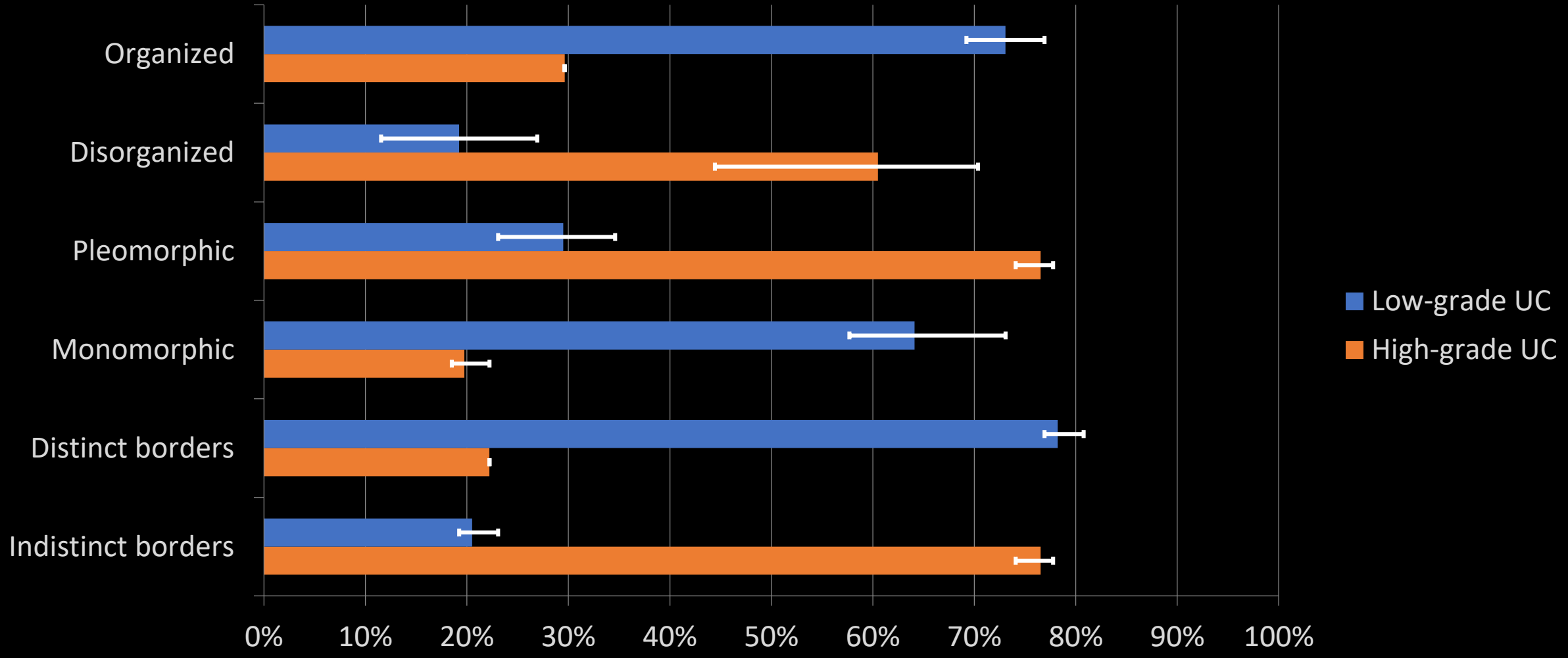
Pleomorphic and distorted sheet of cells

Distorted fibrovascular stalk with variably sized vascular cores.

*Wu etal, Urology. Jul 2011; 78(1): 225–231.*

# Most Prominent features differentiating LG from HG (n=67)

*Liem etal, Eur Uro Focus, 2018*



# Reducing subjectivity: Artificial Intelligence

- All available CLE bladder data is used

1. Image preprocessing
2. Automatic Frame selection
3. Classification using a recurrent neural network (RNN)
   a) Healthy and benign vs tumor
4. Feature extraction using Imagenet pretrained networks
   a) Inception V3
   b) Xception
   c) Inception Resnet V2
5. Sequence analysis using a long-short-term-memory (LSTM)
   a) Low grade vs High Grade

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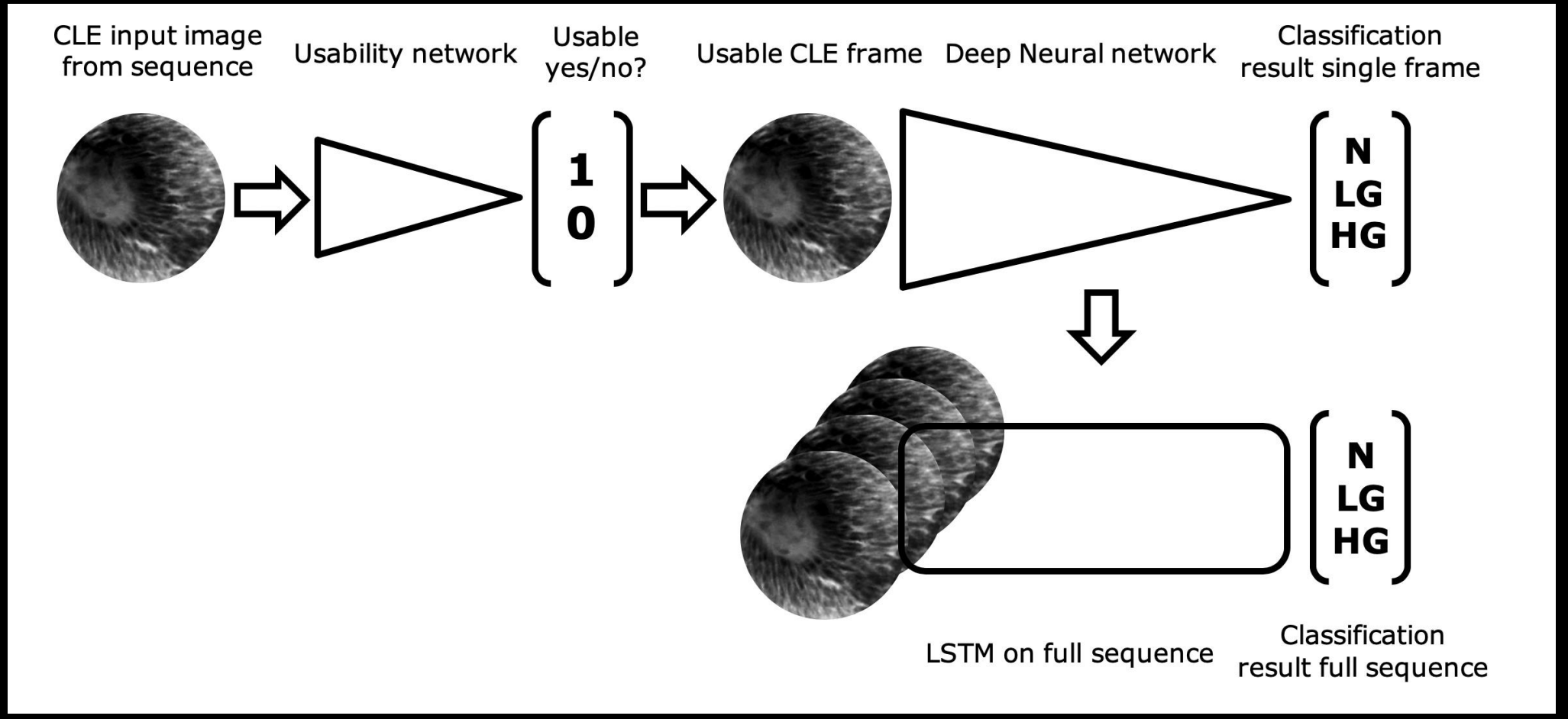

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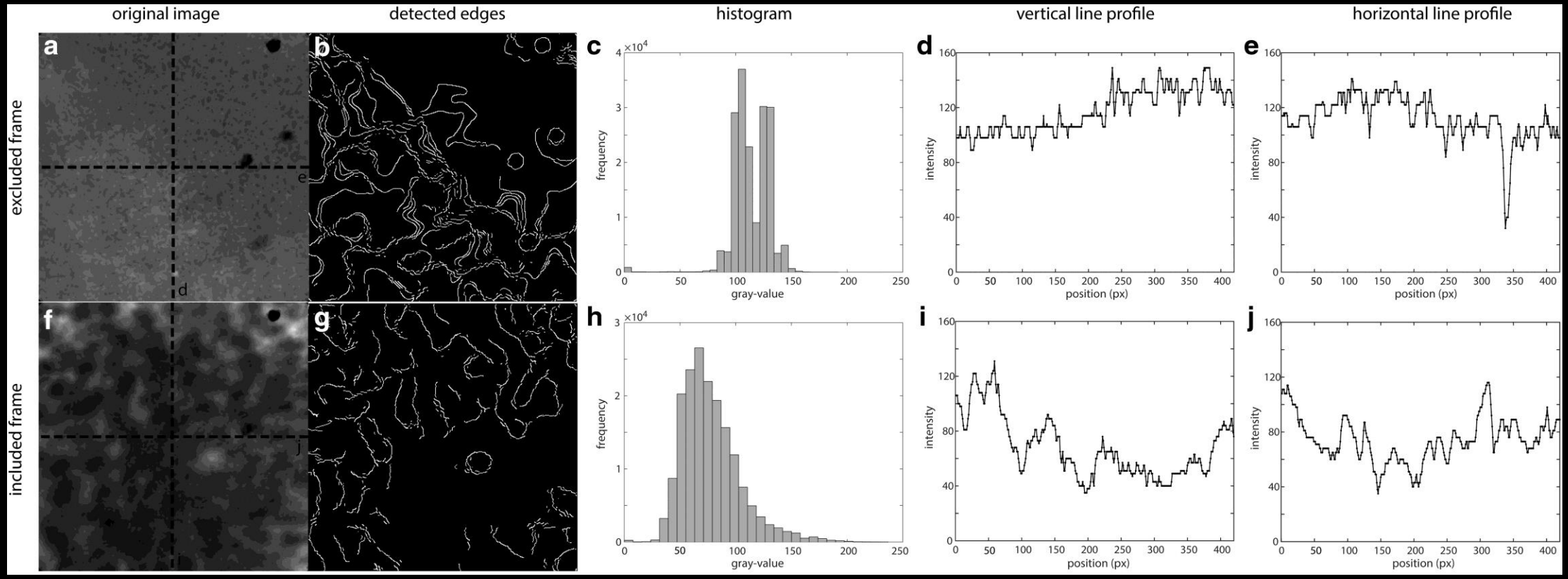

# Reducing subjectivity: Healthy and benign vs tumor

Table 1. Results of Differentiation of Healthy Tissue and Benign Tumors from Malignant Tissue

| | *Sensitivity (%)* | | | *Specificity (%)* | | | *Accuracy (%)* | | | *AUC* | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *#1* | *#2* | *#3* | *#1* | *#2* | *#3* | *#1* | *#2* | *#3* | *#1* | *#2* | *#3* |
| Inception | 82 | 77 | 71 | 55 | 88 | 100 | 68 | 81 | 83 | 0.66 | 0.91 | 0.89 |
| V3 | | 77 | | | 81 | | | 77 | | | 0.82 | |
| Inception ResNet | 82 | 85 | 79 | 55 | 75 | 100 | 68 | 81 | 87 | 0.76 | 0.74 | 0.92 |
| V2 | | 82 | | | 77 | | | 79 | | | 0.81 | |
| Xception | 73 | 69 | 57 | 73 | 88 | 89 | 73 | 76 | 70 | 0.74 | 0.88 | 0.84 |
| | | 66 | | | 83 | | | 73 | | | 0.82 | |

# Reducing subjectivity: Low grade vs High Grade

**Table 2. Results of the Classification of Low-Grade and High-Grade Papillary Urothelial Carcinoma of the Bladder**

| *Experiment (# of lesions)* | *Sens (%)* | *Spec (%)* | *Acc (%)* | *PPV (%)* | *NPV (%)* | *AUC* |
|---|---|---|---|---|---|---|
| 1 (4HG 8LG) | 75 | 88 | 83 | 75 | 88 | 0.94 |
| 2 (4HG 8LG) | 100 | 88 | 92 | 80 | 100 | 0.88 |
| 3 (6HG 8LG) | 67 | 75 | 71 | 67 | 75 | 0.75 |
| **Average** | **81** | **84** | **82** | **74** | **88** | **0.86** |

Sensitivity (Sens), specificity (Spec), and accuracy (Acc) are given for each experiment, together with the PPV, NPV, and AUC. The average of all the experiments is also given.

HG = high-grade; LG = low-grade; NPV = negative predictive value; PPV = positive predictive value.

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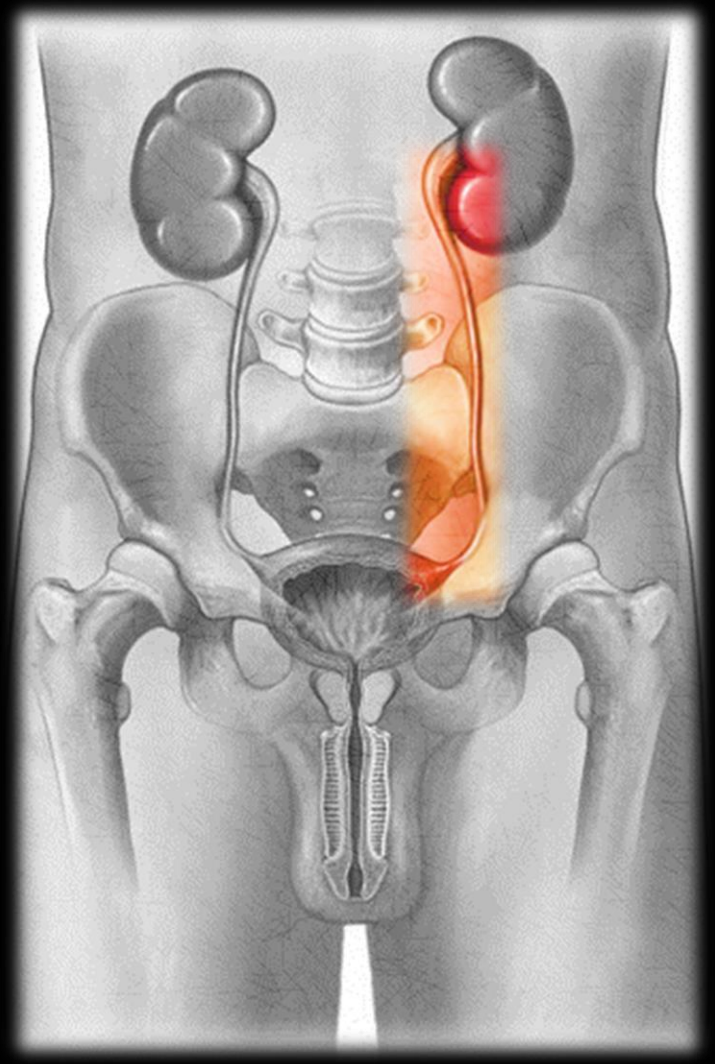
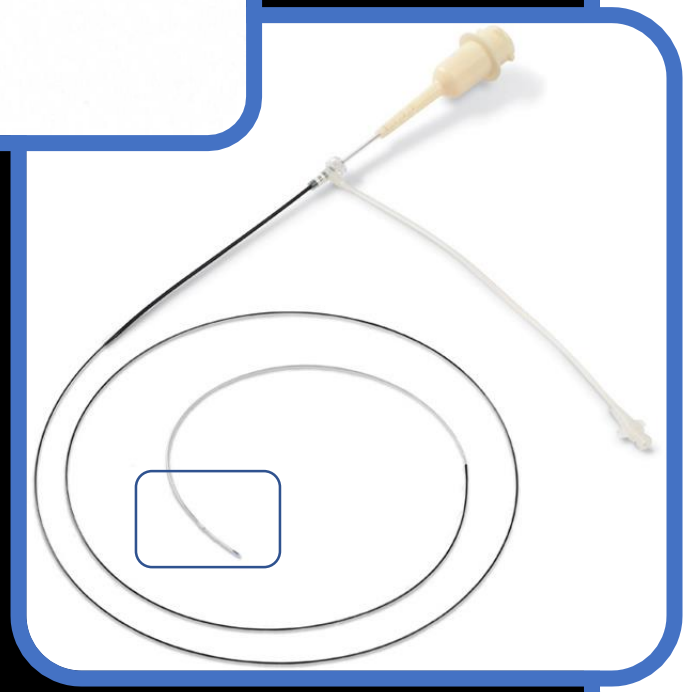
# OCT in Urology: Ureter



*Bus etal, Jour of Uro, 2016*

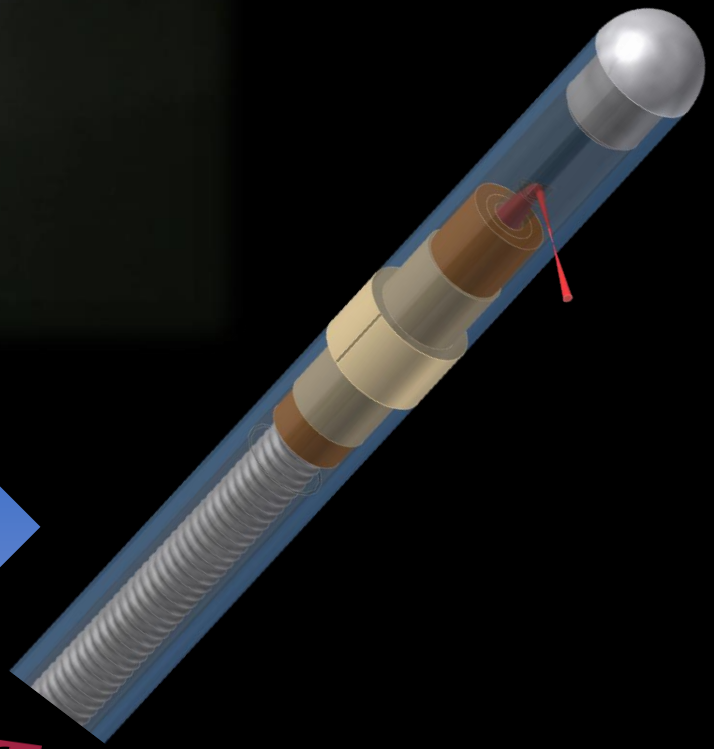
# OCT in Urology: Ureter



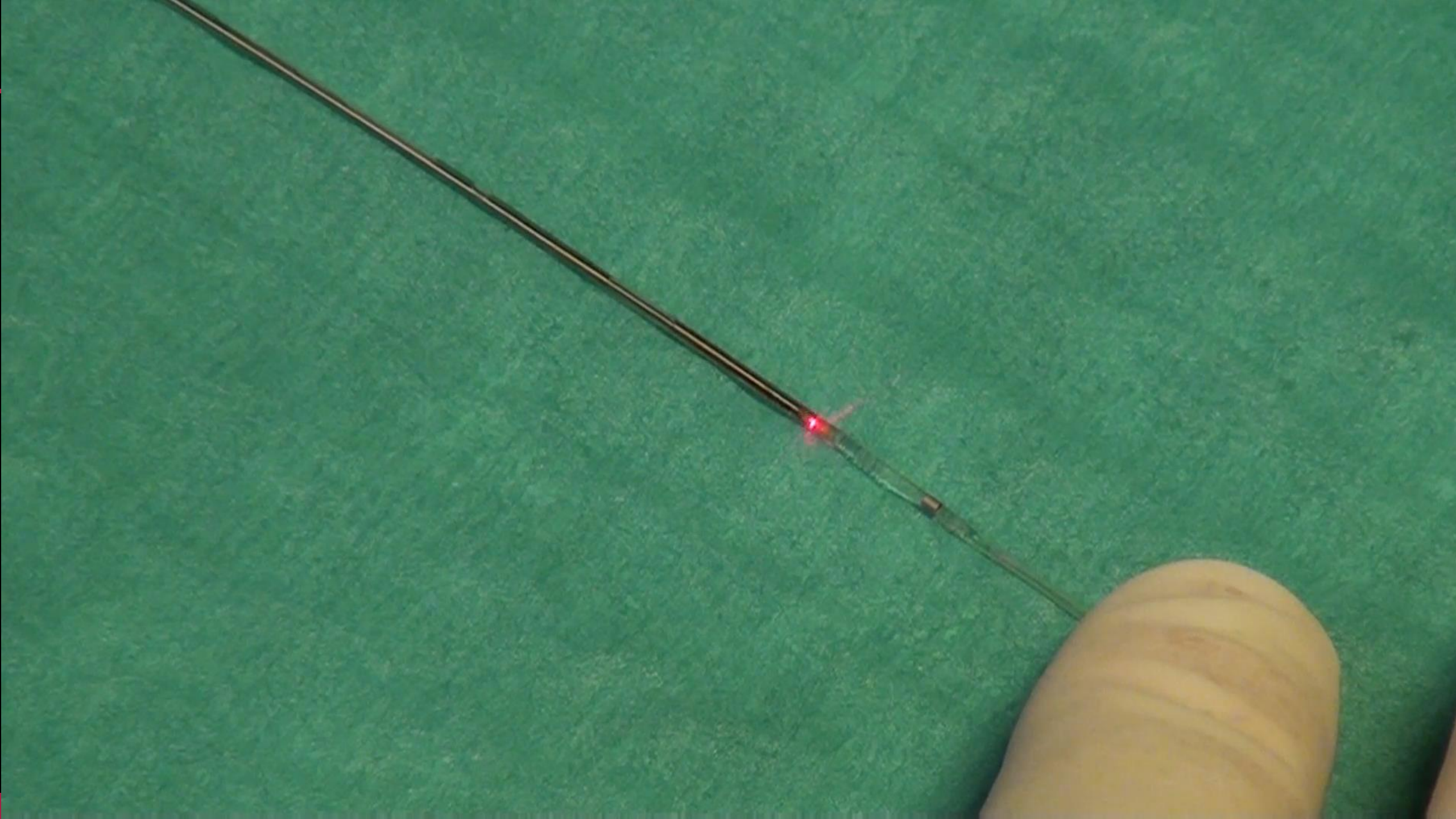
# Going endoscopic

**Development of small scale catheters**

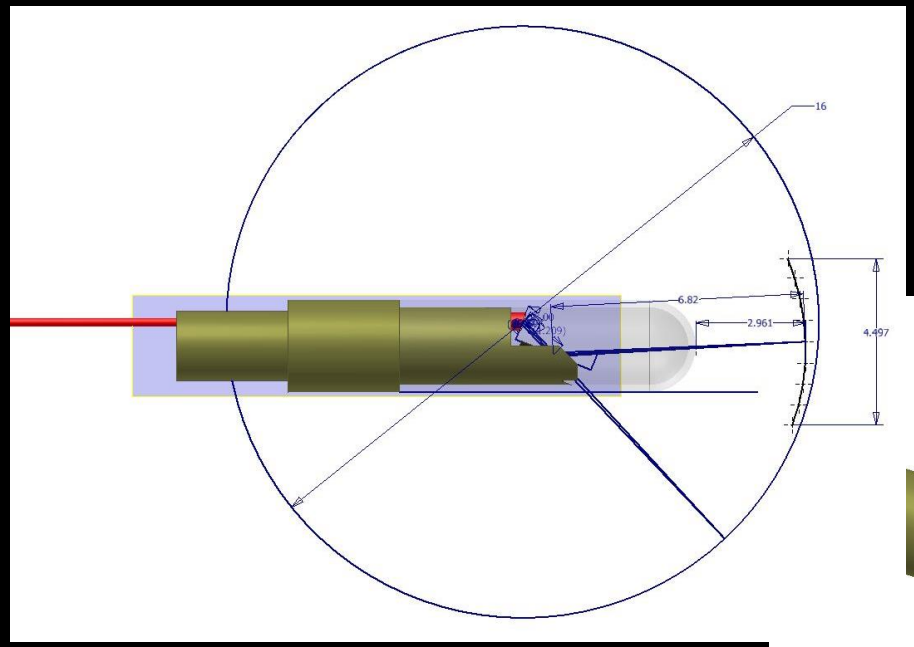
**0.9 mm**

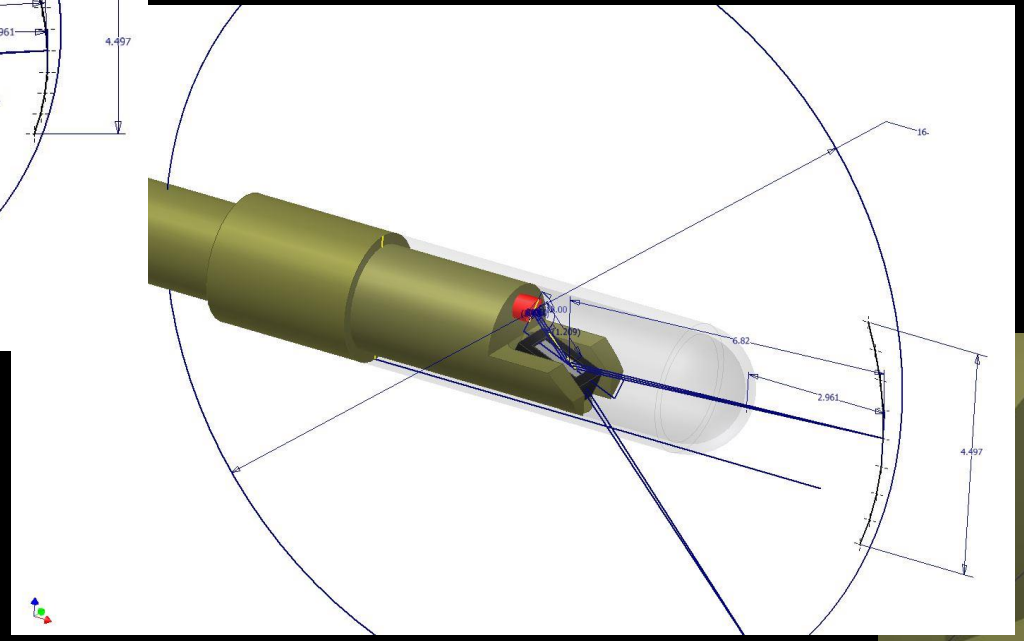


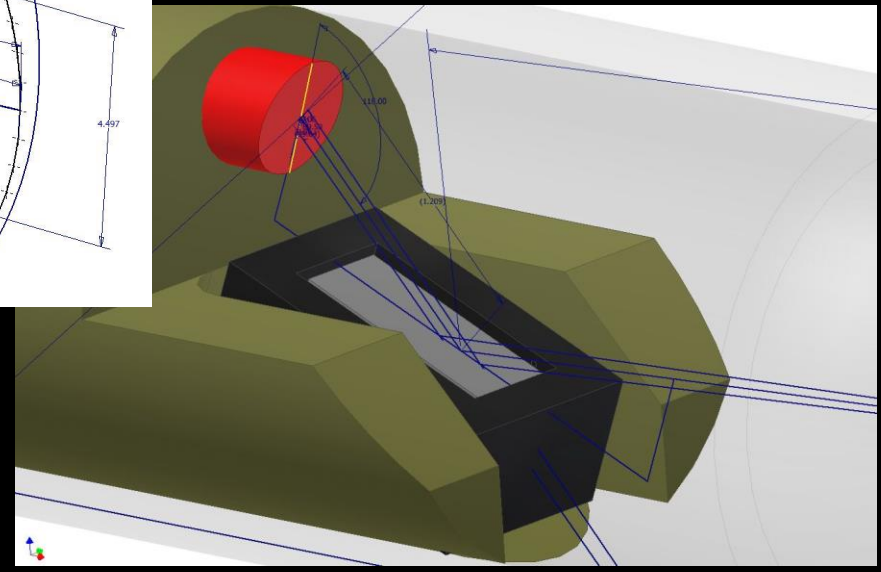
100.000 times smaller
1600 times faster



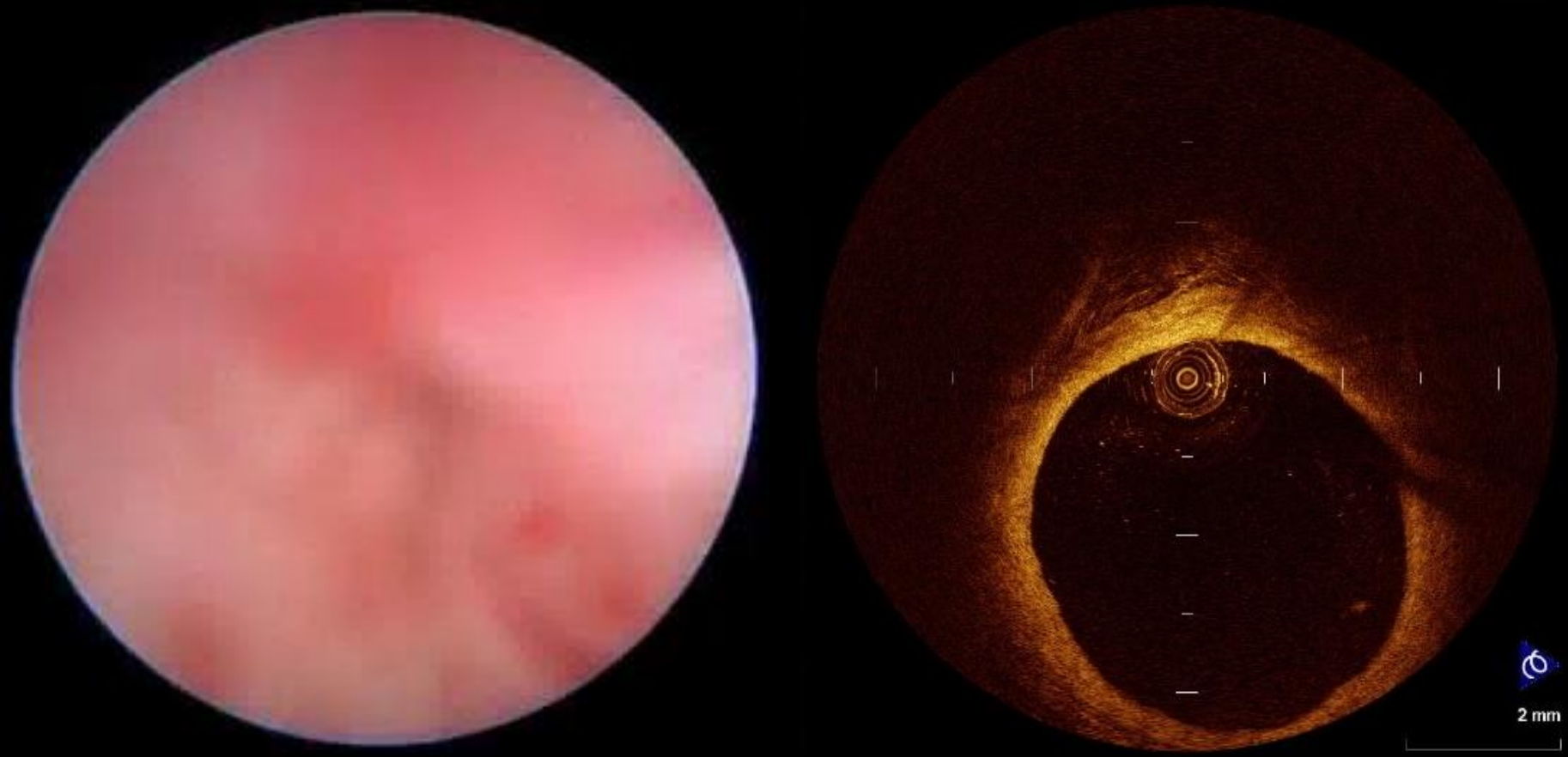
# FORWARD LOOKING PROBE DEVELOPMENT FOR THE BLADDER



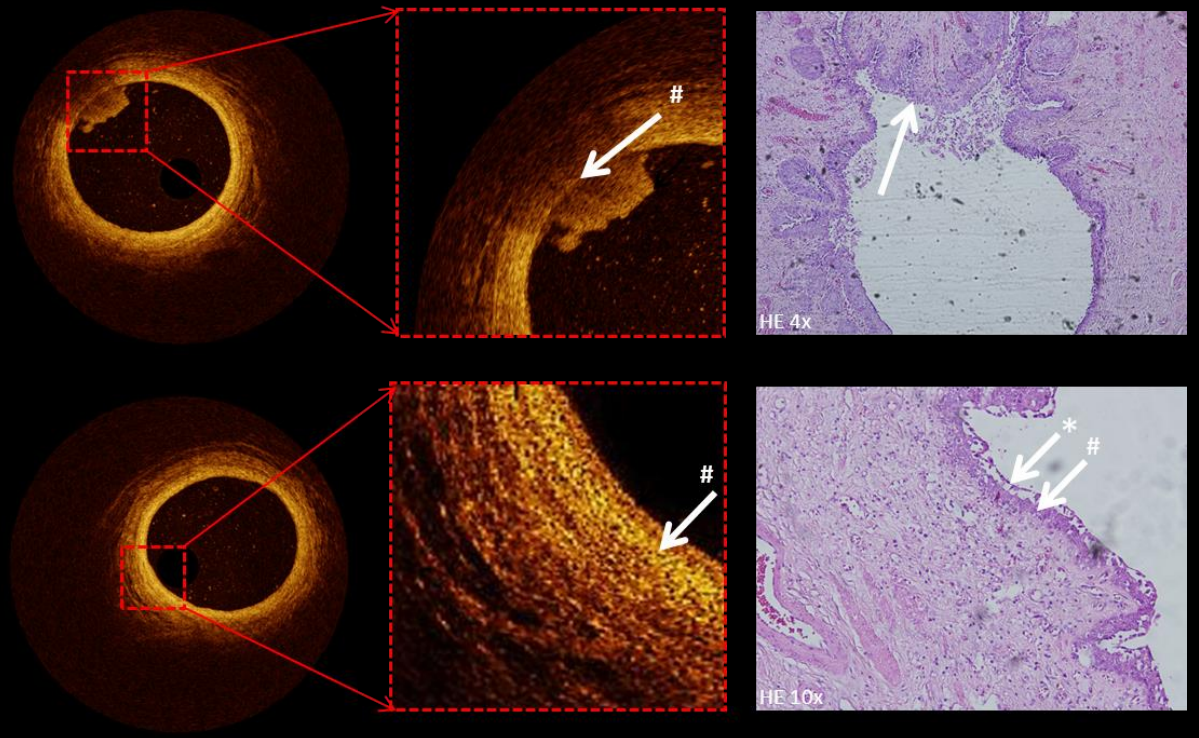



# OCT in Urology: Ureter

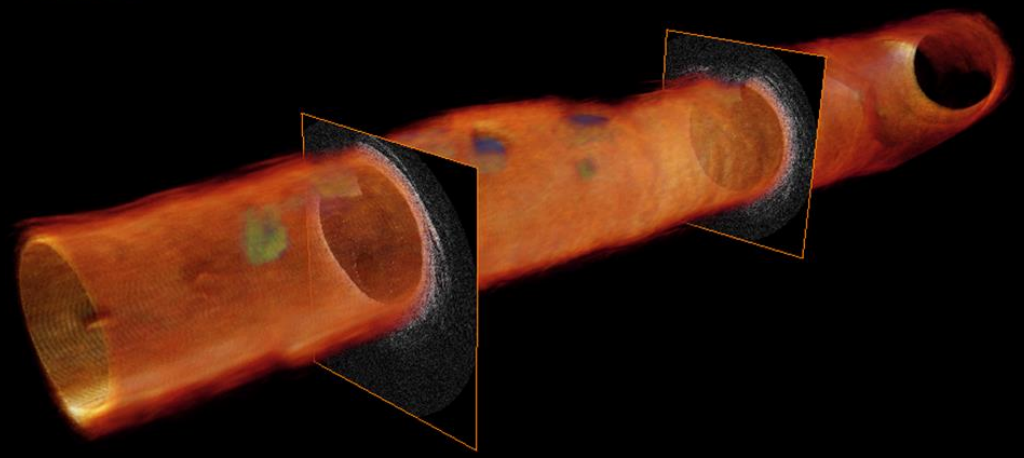



*Bus etal, Jour of Uro, 2016*

# optical coherence tomography (OCT)

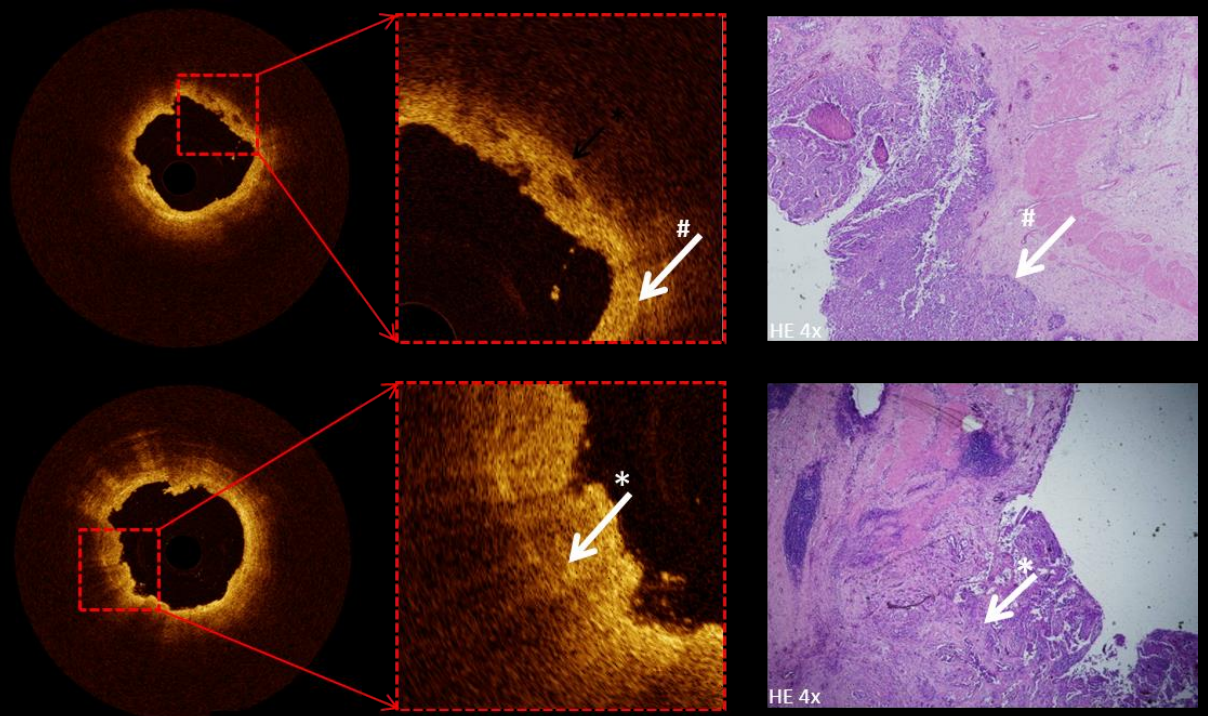



**LOW STAGE: TA, G1-2**

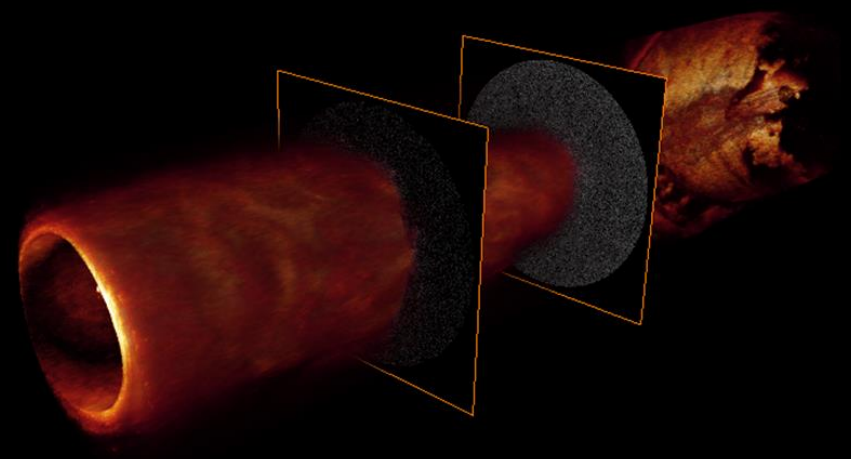


*Bus etal, Jour of Uro, 2016*

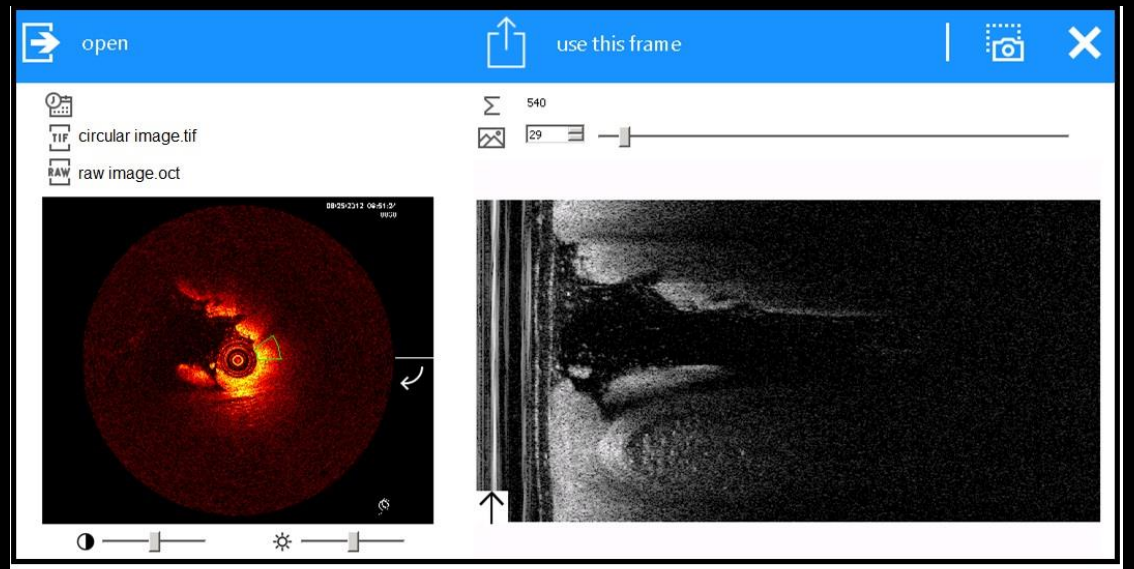
# optical coherence tomography (OCT)

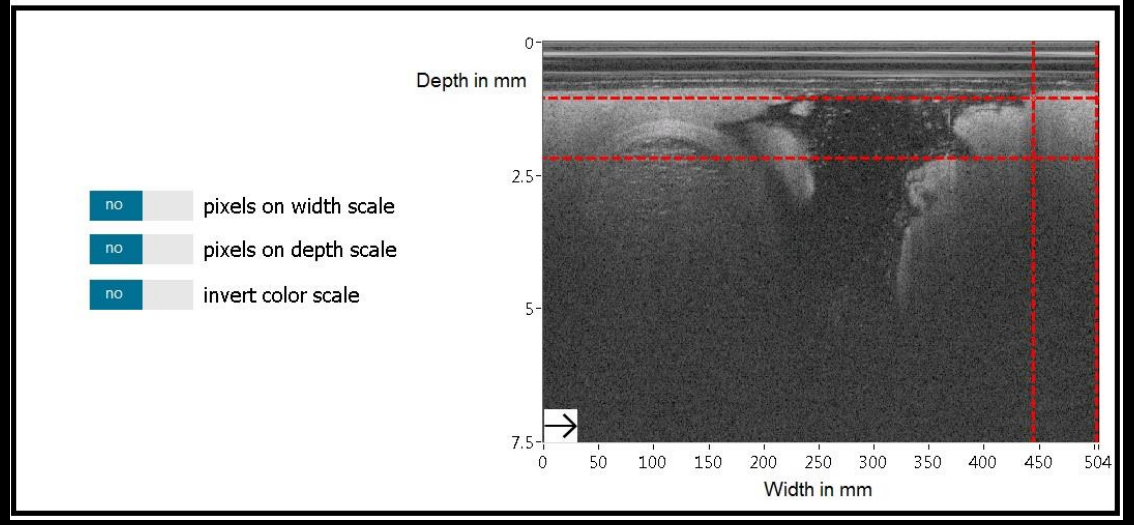


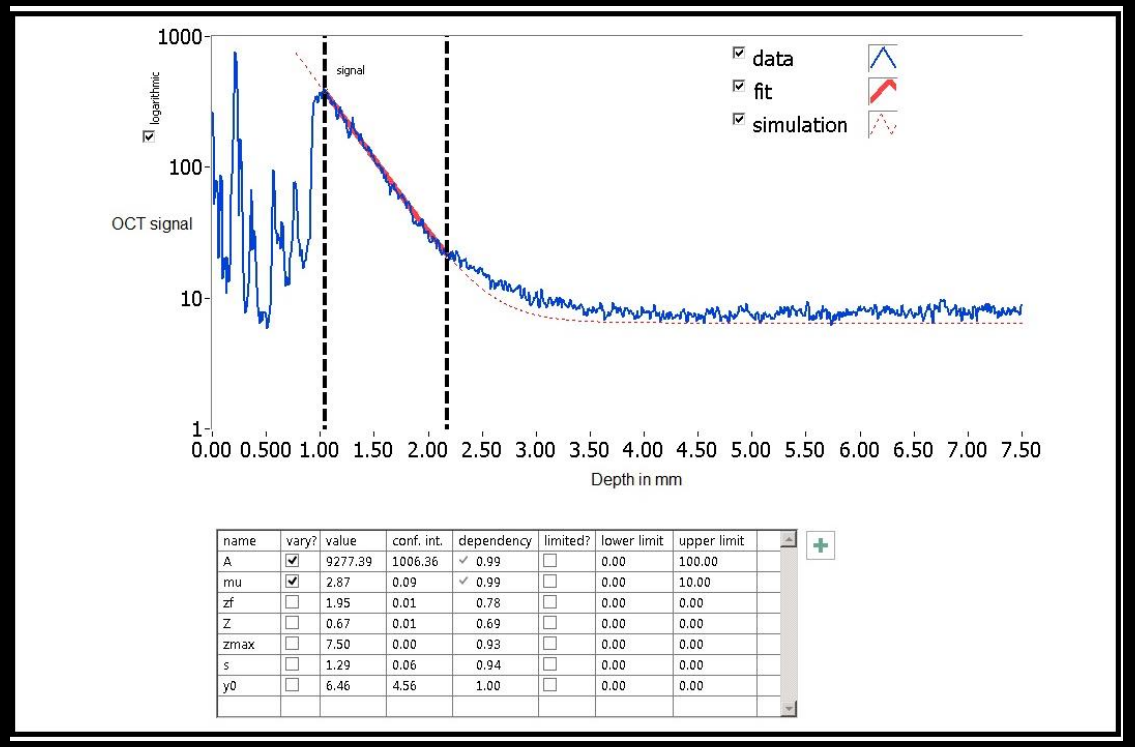

**HIGH STAGE: T3, G3**



*Bus etal, Jour of Uro, 2016*



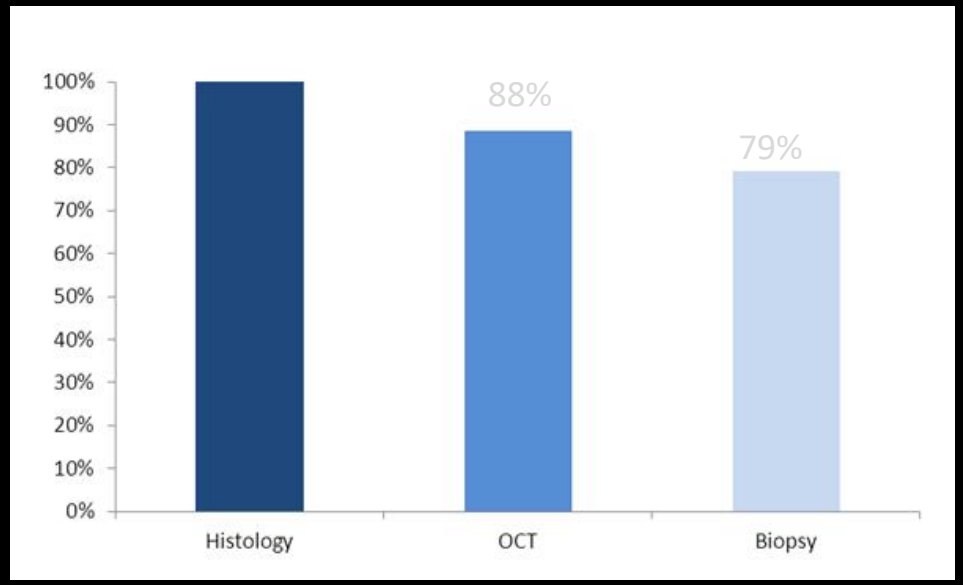



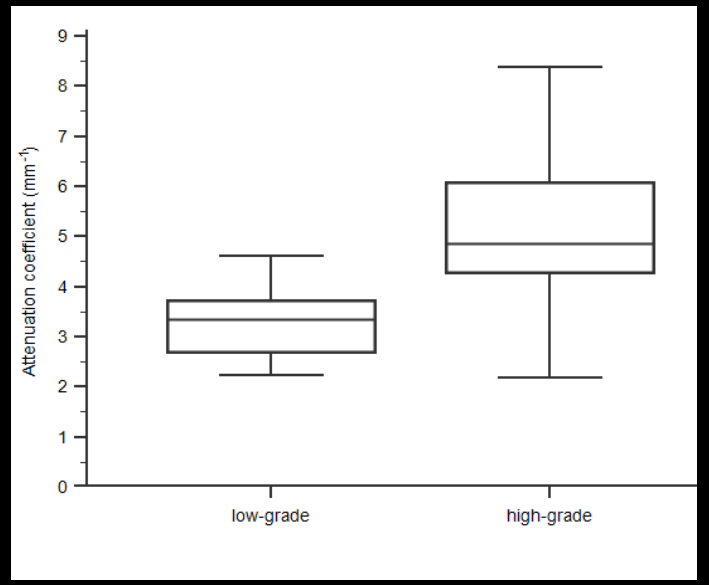

*Bus etal, Jour of Uro, 2016*
*Freund etal, LISM, 2019 inpress*

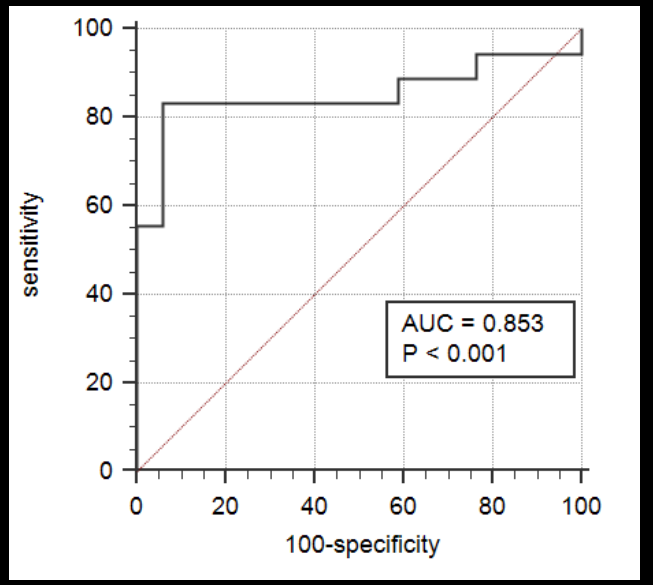
# RESULTS ON GRADING

Non diagnostic vs diagnostic




Low grade vs high grade




*Bus etal, Jour of Uro, 2016*
*Freund etal, LISM, 2019 in press*

# OCT END CLE IN THE EAU GUIDELINES FOR UTUC

Optical coherence tomography and confocal laser endomicroscopy (Cellvizio©) have been used *in vivo* to evaluate tumour grade and/or for staging purposes, with a promising correlation with definitive histology in high-grade UTUC [68,69]. Recommendations are listed in Section 5.5.

# THE END

# This presentation was presented at
# EPIC Meeting on Photonics for Cancer Diagnostics and Treatment 2019

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