

High resolution microendoscope to improve early detection of bladder cancer

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Introduction

- Bladder cancer is the 6th most common cancer in the United States.¹
- High rates of recurrence require frequent surveillance and make bladder cancer the most costly to treat.²
- Standard cystoscopy has difficulty distinguishing benign lesions from small, subtle, cancerous lesions, necessitating many biopsies.²
- New endoscopic techniques such as narrow-band imaging can improve sensitivity, but there is a need to improve specificity.²
- We are evaluating a high-resolution microendoscope (HRME) to help identify and characterize bladder lesions with high specificity during cystoscopy.
- The HRME is a low-cost (<\$3000) fiber-optic microscope that provides images with subcellular resolution in real time, revealing detail traditionally only available following biopsy and histology.

Methods

- Patients scheduled to undergo standard of care cystoscopy were recruited for *in vivo* imaging at Lyndon B. Johnson Hospital in Houston, Texas.
- In addition, bladder specimens were obtained for *ex vivo* imaging to aid in the development of an automated diagnostic algorithm.

High-Resolution Microendoscope (HRME)

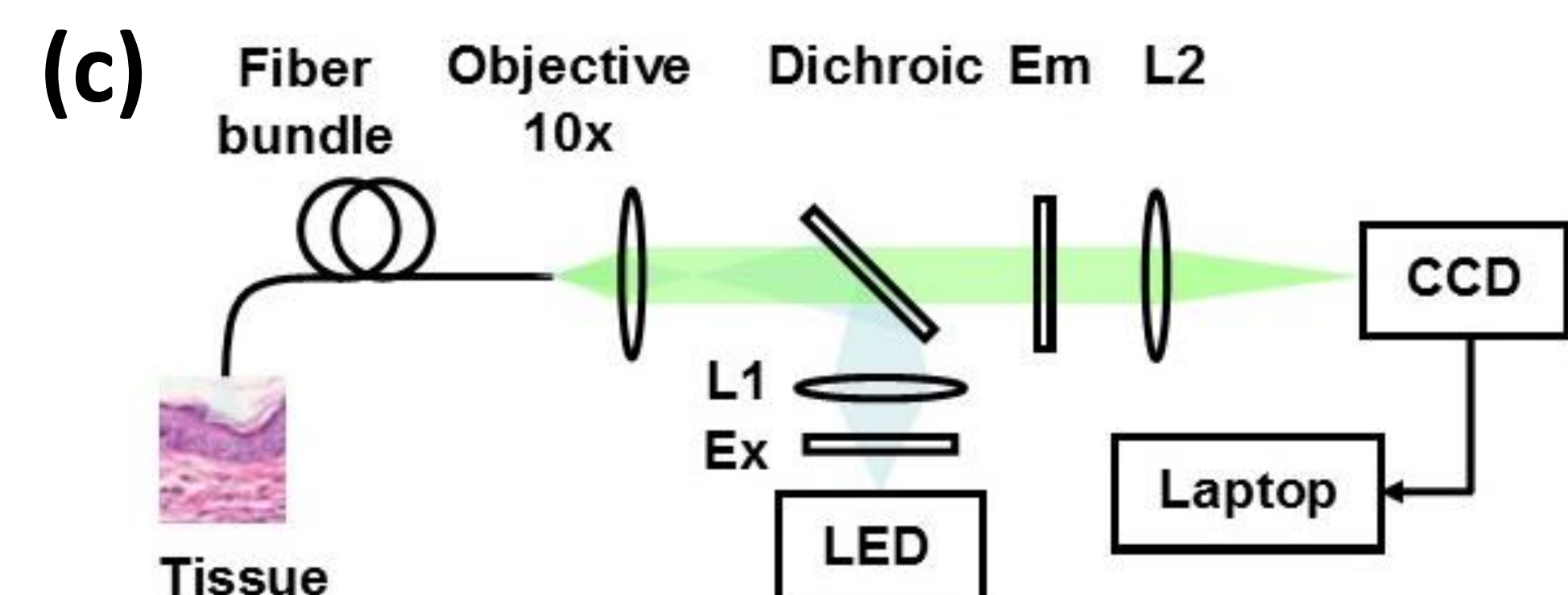
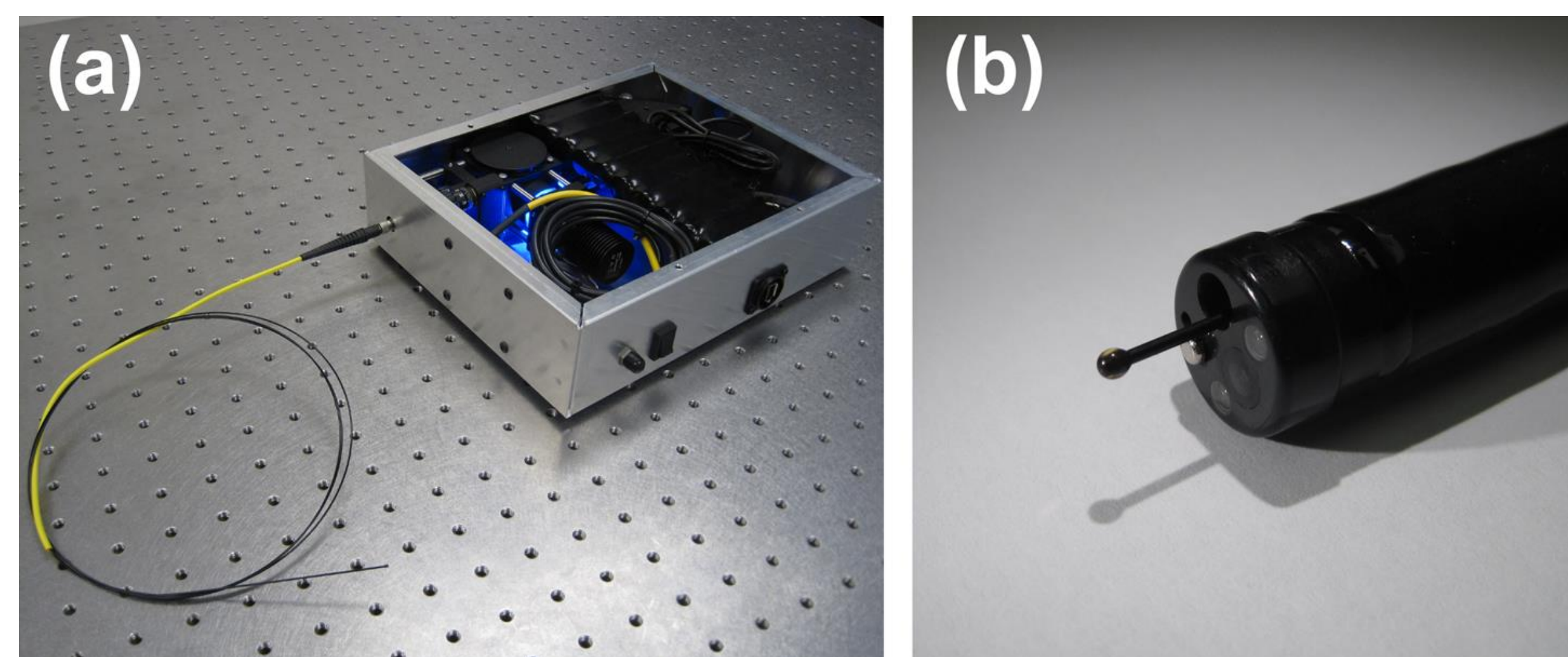


Fig. 1: (a) High-resolution micro-endoscope (HRME) with fiber-optic probe. (b) HRME probe inserted through working channel of an endoscope for esophageal imaging. During bladder imaging, the HRME probe is inserted through the working channel of the cystoscope. (c) Schematic of high-resolution microendoscope (HRME)

Results

- To date, 12 patients have been accrued and imaged in the operating room at LBJ Hospital using the HRME system and 7 *ex vivo* bladder specimens have been imaged at Rice University.
- Types of lesions imaged to date include erythematous lesion/cluster, papillary lesion/cluster, tumor, scar, bullous edema, and post-stent inflammation
- Normal bladder tissue sites have been imaged for comparison.

HRME probe during *in vivo* imaging

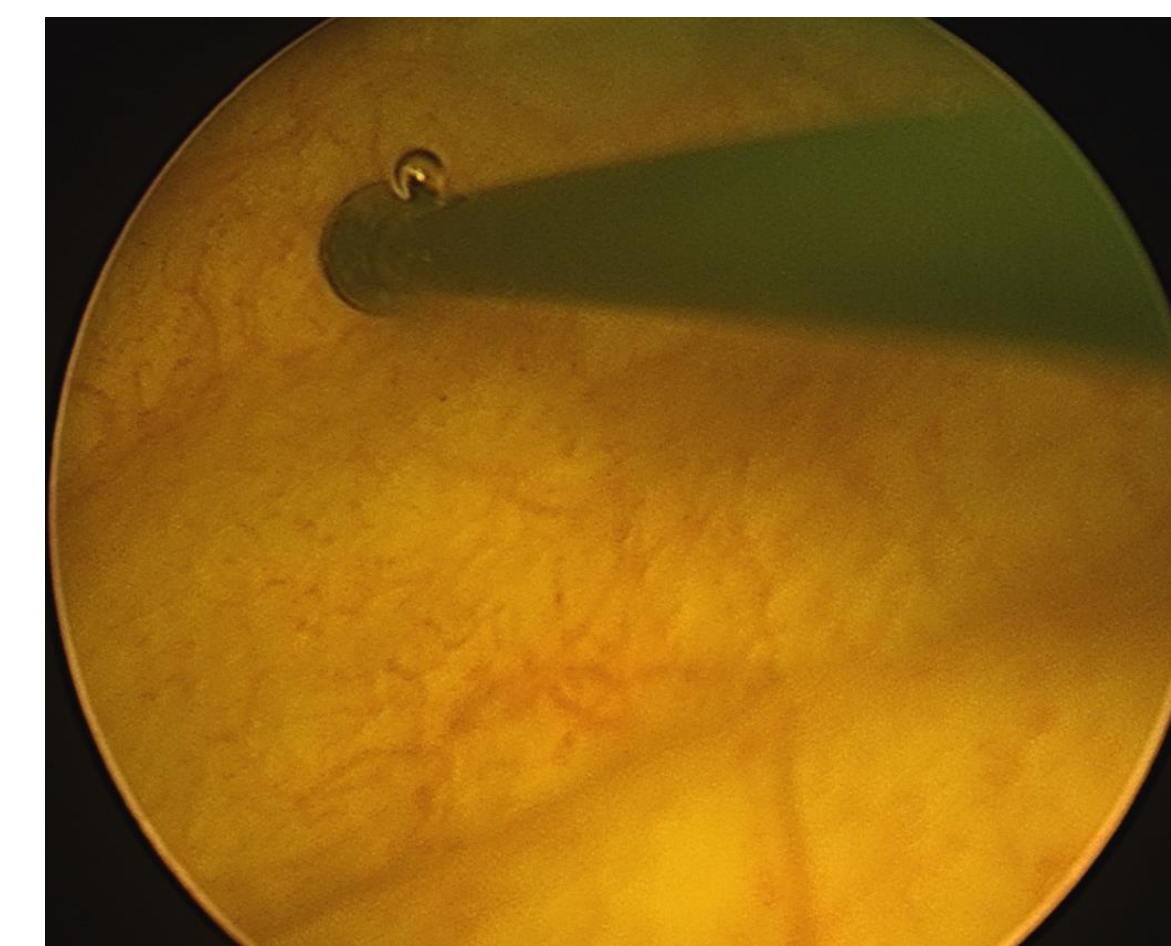


Fig. 2: *in vivo* HRME imaging of a bladder lesion with the HRME probe inserted through the working channel of the cystoscope. Yellow color is due to instilling fluorescent contrast agent proflavine.

- A preliminary analysis was performed to explore the microscopic appearance of bladder lesions and to develop methods to distinguish precancerous and cancerous lesions from non-neoplastic tissue.
- Initial results indicate that cell nuclei are larger, more crowded, and more erratically shaped at lesion sites than in normal bladder tissue.
- This is consistent with our previous clinical studies conducted in other organ sites, such as the esophagus, cervix and oral cavity.

ex vivo HRME Images

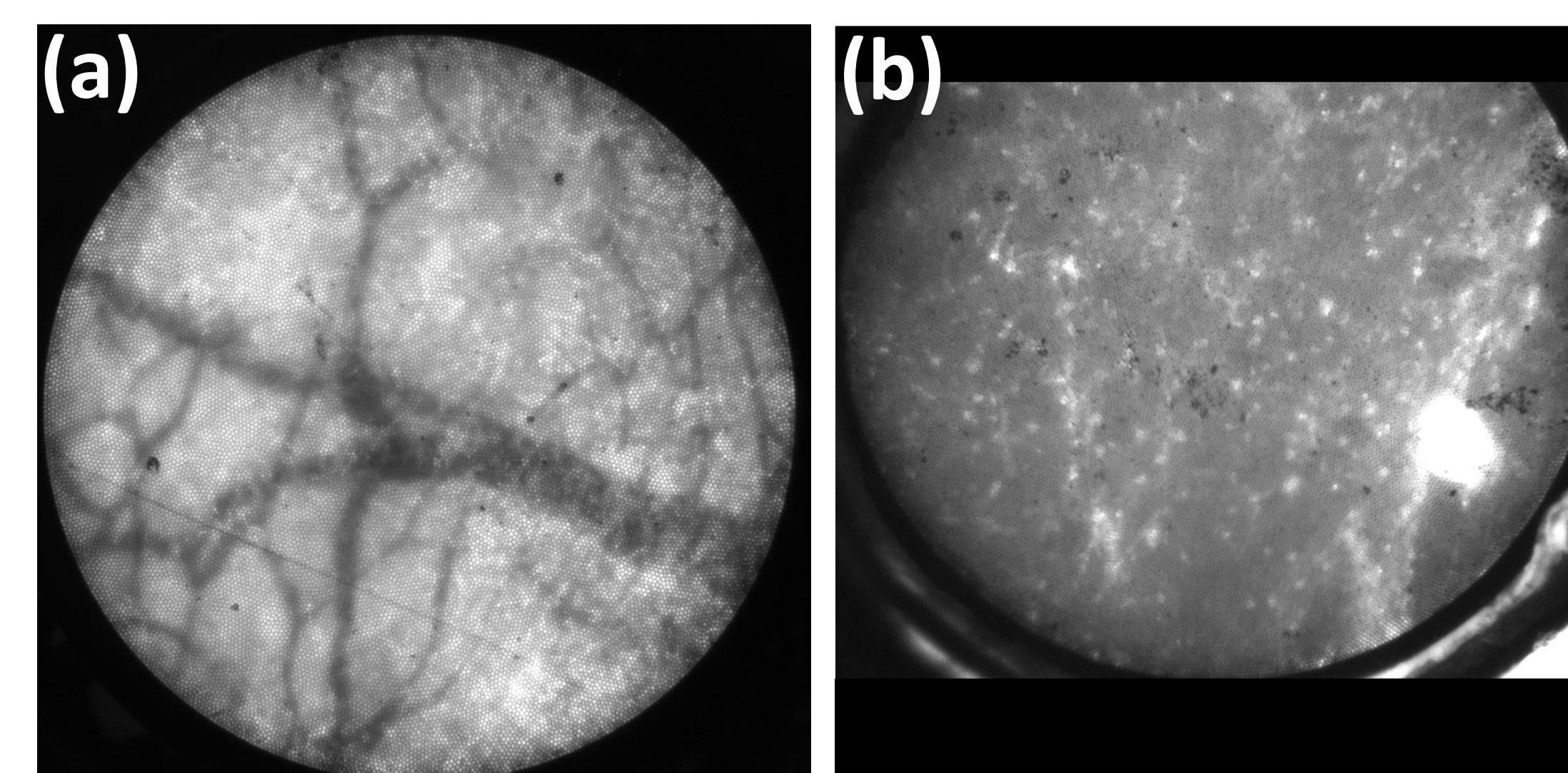


Fig 3: *ex vivo* bladder HRME images with 720 μm field of view. Bladder specimens supplied by Tissue for Research®. (a) Blood vessels clearly visible. (b) Nuclei visible.

in vivo Cystoscopy Images

in vivo HRME Images

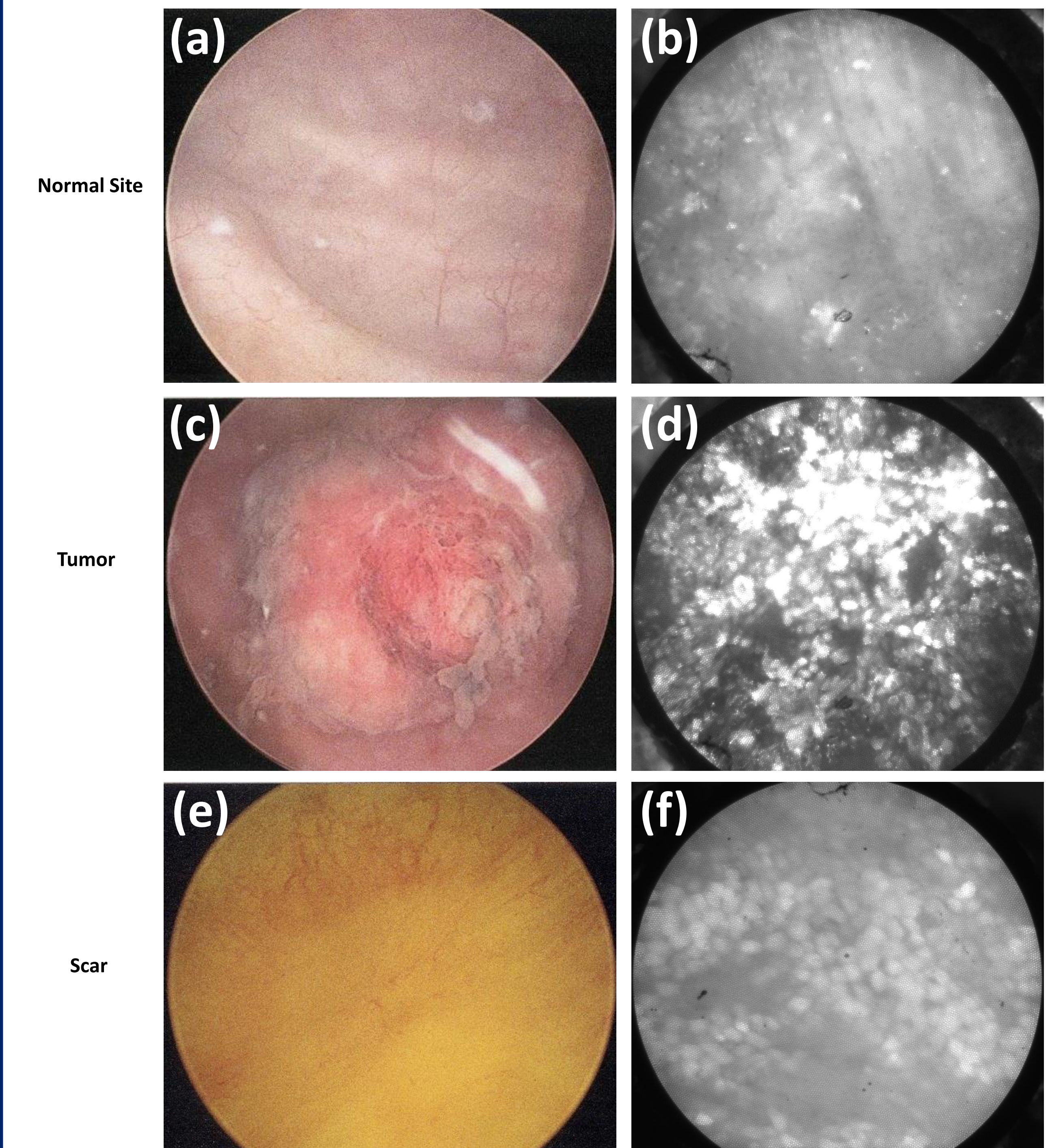


Fig 4: *in vivo* images of bladder taken during cystoscopy. Standard cystoscopic images on left and corresponding HRME images on right. (a, b) Normal bladder wall site at left ureteral orifice. (c, d) Tumor at right lateral dome. Histopathology result for tumor was high grade urothelial carcinoma (e, f) Scar at left posterior bladder wall. Cystoscopic image (e) taken after instillation of proflavine, causing yellow appearance.

- We will continue recruiting patients in order to develop an image analysis algorithm to classify lesions as benign or cancerous.
- Develop a second generation HRME system that incorporates real time image analysis and diagnosis based on the algorithm.

Conclusion

- To the best of our knowledge this ongoing study represents the first use of a low-cost imaging system to image the human bladder *in vivo* with subcellular resolution.
- The ability to image microscopic morphologic features to characterize bladder lesions in real time may have the potential to assist in the early detection of bladder cancer.

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References

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