Advances in Image-Guided Urologic Surgery

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Springer

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ISBN 978-1-4939-1449-4 ISBN 978-1-4939-1450-0 (eBook)
DOI 10.1007/978-1-4939-1450-0
Springer New York Heidelberg Dordrecht London

Library of Congress Control Number: 2014950792

Printed on acid-free paper

Springer is part of Springer Science+Business Media (www.springer.com)

In loving memory of my father Lienjin, who taught me audacity

Joseph C. Liao

Preface

Advances in imaging technologies have been a key source of innovation in modern medicine and surgery. In the preoperative setting, computed tomography (CT), magnetic resonance imaging (MRI), and ultrasound (US) play indispensable roles in clinical diagnosis and surgical planning. Modern endoscopy and minimally invasive surgery can trace their foundation to the invention of *Lichtleiter* by Bozzini in 1806 and the first laparoscopic procedures a century later. In urological surgery and beyond, patients and their surgeons today strive for precise surgical treatments in the least invasive manner while minimizing collateral damage to surrounding organs.

Advances in Image-Guided Urologic Surgery is a compendium of the emerging field of image-guided surgery and intervention in urology. The book is divided into four sections. The first section focuses on optical imaging technologies including wide-field fluorescence, optical coherence tomography, and endomicroscopy. The second section addresses the current applications of intraoperative ultrasound. The third section focuses on the integration of CT- and MRI-guided surgical interventions, particularly for prostate and kidney cancer. The fourth section introduces other emerging applications including augmented reality, simulators, and molecular imaging.

The intended audience of this book includes urological surgeons and trainees, biomedical engineers, and imaging scientists interested in technology translation. We are grateful for the contribution of a group of international experts who are among the foremost leaders in this emerging field. Ultimately, we share the common goal that by being able to "see" better, we will deliver better surgical outcomes for our patients.

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Gainesville, FL, USA — Li-Ming Su, MD

Acknowledgments

We are indebted to our families for their love and support. We thank our mentors and students for their inspiration. We are grateful to the many authors for their time and dedication in the preparation of their chapters. A special acknowledgment goes to Margaret Burns at Springer for her expert assistance in making this book a reality.

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Part I

Optical Imaging Technologies

Endoscopic Fluorescence Imaging of Bladder Cancer: Photodynamic Diagnosis and Confocal Laser Endomicroscopy

1

Mark Hsu and Joseph C. Liao

Bladder cancer is the second most common genitourinary cancer and the fifth most common cancer overall in the United States. In 2014, there are projected 72,570 new cases and 15,210 cancer-related deaths [1]. Modern white-light cystoscopy (WLC), the standard approach to evaluate the lower urinary tract and manage non-muscle-invasive bladder cancer (NMIBC), has been the result of sequential landmark innovations over the last two centuries [2]. Despite significant advances, WLC and WL-guided transurethral resection (TUR) have numerous limitations that can affect accurate detection and staging of bladder cancer, including differentiation of nonpapillary urothelial carcinoma from inflammatory lesions and delineation of tumor borders [3]. While histology is the standard for definitive cancer diagnosis, it is not available intraoperatively in real time to guide surgical intervention. The inherent subjective nature and operator dependence of WLC can lead to incomplete resection, thereby increasing the risk of tumor persistence, recurrence, and progression [4]. Thus, there has been great interest in developing optical imaging technologies that can enhance the diagnostic accuracy of WLC, improve completeness of TUR, and thereby improve surgical and cancer outcomes.

Fluorescence imaging that utilizes exogenous contrast agents is emerging as a useful adjunct for intraoperative guidance across different surgical disciplines, including urology [5]. With ease of access, the bladder is a well-suited target organ amenable to intraoperative fluorescence imaging. Imaging strategies typically combine a fluorescence illumination source in combination with exogenous contrast agents. Currently, three fluorescent contrast agents are approved for clinical use: protoporphyrin IX precursor hexaminolevulinate (HAL), fluorescein, and indocyanine green (ICG). This chapter focuses on the approved endoscopic fluorescence imaging technologies for bladder cancer: photodynamic diagnosis (PDD) and confocal laser endomicroscopy (CLE). Considerations including optical specifications, ease of OR integration, available clinical evidence, and suggested future directions will be highlighted.

Photodynamic Diagnosis

PDD provides wide-field fluorescence imaging of the bladder mucosa with a field of view comparable to WLC (i.e., ~cm). Also known as fluorescence cystoscopy or blue-light cystoscopy,

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J.C. Liao, L.-M. Su (eds.), *Advances in Image-Guided Urologic Surgery*,
DOI 10.1007/978-1-4939-1450-0_1, © Springer Science+Business Media New York 2015

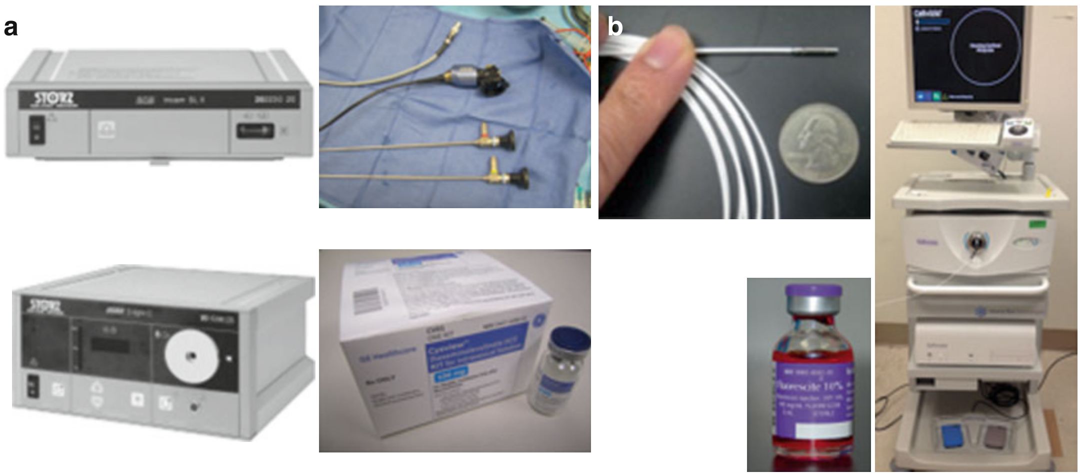

Fig. 1.1 Endoscopic fluorescence imaging systems for bladder cancer. (**a**) Photodynamic diagnosis (PDD) composed of a blue-light source, specialized camera head and lens, and hexaminolevulinate as the contrast agent. (**b**) Confocal laser endomicroscopy (CLE) composed of a 2.6-mm fiberoptic imaging probe, fluorescein as the contrast agent, and the laser scanning unit

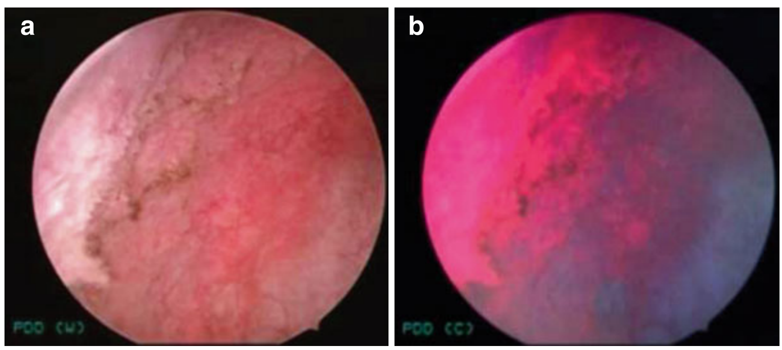

Fig. 1.2 PDD of bladder cancer. (**a**) White-light image of a large flat lesion at the right bladder wall showing indistinct borders and (**b**) the corresponding PDD image. The region was confirmed to be carcinoma in situ (*CIS*) (From Hsu et al. [27], with permission)

PDD uses photosensitive protoporphyrin IX precursor as the contrast agent, a blue-light source that illuminates at 375–440 nm, and a specialized lens and camera (Fig. 1.1a). The protoporphyrin, introduced intravesically, accumulates preferentially in neoplastic tissues and emits red fluorescence under blue light (Fig. 1.2). In the bladder, two protoporphyrin analogues, 5-aminolevulinic acid (5-ALA) and hexaminolevulinate (HAL), have been investigated. HAL is the more potent lipophilic ester analogue of 5-ALA and is approved for clinical use in Europe and the United States for patients with suspicion for or known bladder cancer. Due to increased potential for increased false positives, it is currently approved for single administration after 90 days following intravesical bacillus Calmette-Guerin (BCG).

Integration in the OR environment is overall straightforward. HAL is solubilized and instilled intravesically by either the surgical team or nursing staff via a catheter 1–3 h prior to cystoscopy and TUR. Fluorescence imaging is switched on and off dynamically through the press of a button on the camera head. Fluorescence imaging is used for generalized survey of the urothelium as well as in conjunction with standard TUR, with improved contrast-enhanced visualization of both papillary and flat (i.e., carcinoma in situ, CIS) lesions.

In diagnostic cystoscopy, PDD is reported to have a sensitivity and specificity ranging from 87