Optical imaging technologies in bladder cancer – Evidence based progress and recent update

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For over 100 years white-light cystoscopy has remained the gold-standard technique for the detection of bladder cancer. Some limitations in the detection of flat lesions (CIS), the differentiation between inflammation and malignancy, the inaccurate determination of the tumor margin status as well as the tumor depth, have led to a variety of technological improvements [1].

Endoscopy coupled with targeted resections represents a corner stone in the diagnosis, staging and treatment of patients with bladder cancer. In this paper we will review contemporary endoscopic technologies and techniques used to improve our ability to safely identify and resect malignant lesions (TURBT) in patients with bladder cancer [2].

Enhanced endoscopic imaging technology may improve detection rates for bladder cancer which may lead to improvements in recurrence and progression rates for non-muscle invasive bladder cancer (NMIBC). New techniques, including photodynamic diagnosis (PDD), narrow-band imaging (NBI), Image 1 S-System (formerly known as SPIES), optical coherence tomography (OCT), and others have shown benefit and may further improve our ability to detect and stage bladder tumors [2].

The precise identification and detection of bladder tumours is a prerequisite for complete transurethral resection and, thus, the reduction of recurrence. White-light cystoscopy (WLC) remains the gold standard and has been further improved by the introduction of digital HD techniques. New digital techniques have been promoted to better visualise suspicious areas. However, fluorescence or photodynamic diagnostics after instillation of hexaminolevulinic acid into the bladder is the only approach supported by good evidence. It is recommended by most guidelines in high-grade tumours or carcinoma in situ, while the value of NBI and the Image 1 S-System is under evaluation. Newer approaches include microscopic techniques such as optical coherence tomography, confocal laser endomicroscopy or molecular imaging. The combination of these methods with macroscopic imaging could be very promising [3].

Gallagher et al compare the recurrence rate at 3 years for non-muscle invasive bladder cancer between good quality PDD resection and same quality white light TURBT. Of 808 patients recruited, 345 had TURBT for NMIBC and were included [4].

The recurrence rate at 3 years was significantly less for PDD overall [RR-3y: PDD: 57/146 (39.0%), WL: 72/135 (53.3%) OR = 0.56 (0.35-0.90) p = 0.02] and on a 1:1 matched pair basis [PDD: 29/118 (24.6) vs. 59/118 (50.0) OR 0.33 (0.19-0.57) p < 0.001)]. Benefit was most marked in high-risk patients: RR-3y in high-risk patients treated with PDD was 25/48 (52.1%) vs. 28/35 (80%) for WL [OR 0.27 (0.10-0.74) p = 0.01] [4].

In a recent study, Kim et al had try to evaluate the efficacy of narrow-band imaging as a diagnostic tool for detecting bladder tumors during cystoscopy compared with white-light cystoscopy. A randomized prospective study was conducted on 198 patients underwent transurethral resection of bladder tumor

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In a recent study, Kim et al had try to evaluate the efficacy of narrow-band imaging as a diagnostic tool for detecting bladder tumors during cystoscopy compared with white-light cystoscopy. A randomized prospective study was conducted on 198 patients underwent transurethral resection of bladder tumor by a single surgeon. The patients were divided into two groups according to diagnostic method. In group I, WLC only was performed. In group II, NBI was additionally performed after WLC. It was analyzed the rate of detection of bladder tumors as a primary endpoint. In addition, rates of recurrence were evaluated in each group. In the analysis of rates of detection, the probability of diagnosing cancer was 80.9% in the WLC group, and the probability of diagnosing cancer using WLC in the NBI group was 85.5%. After switching from WLC to NBI for second-look cystoscopy in the NBI group, NBI was shown to detect additional tumors with a detection rate of 35.1% (13/37) from the perspective of the patients and 42.2% (27/64) from the perspective of the tumors. The 1-year recurrence-free rate was 72.2% in the WLC group and 85.2% in the NBI group (p=0.3) [5].

A paper of Drejer et al has compared findings in NBI to findings in WL and PDD in a high-risk patient population. A total of 171 patients were included in the study from 4 different urology departments in Denmark and Norway. Patients were scheduled for a PDD-guided transurethral tumor resection or cystoscopy-guided biopsy in accordance with Danish guidelines, on the suspicion of primary or concomitant CIS. All patients were examined with WL cystoscopy followed by both NBI and PDD before biopsy.

A total of 136 patients were biopsied due to findings with suspicion of CIS in at least 1 modality (482 biopsies with a mean of 3.5 biopsies per patient). Analysis at patient level showed that NBI and PDD had a significantly higher sensitivity regarding identification of CIS and dysplasia compared with WL (NBI: 95.7%, PDD: 95.7% vs WL: 65.2%, p < .05). Specificity was not significantly different between the 3 methods (NBI: 52.0%, PDD: 48.0%, and WL: 56.8%). When analyzed per biopsy, NBI and PDD had a significantly higher sensitivity than WL (NBI: 72.7% and PDD: 78.2% vs WL: 52.7%, p < .05), whereas the positive predictive values were not significantly different (NBI: 23.7%, PDD: 22.2%, and WL: 19.0%) [6].

In another study, Ma T et al had compared the differential effects of narrow band imaging-assisted holmium laser with transurethral resection on the 1-year recurrence rate of non-muscle invasive bladder cancer, and to evaluate the clinical values of NBI-assisted holmium laser resection for NMIBC (NBI-HoLRBT). 178 cases of NMIBC were randomly divided into NBI-HoLRBT group and white light imaging (WL) assisted transurethral resection of bladder tumor (WL-TURBT) group. In NBI-HoLRBT, all suspicious lesion identified by either WL or NBI were resected with WL and in NBI mode for lesion only visible with NBI. At the end of the procedure, a NBI cystoscopic examination was performed to assess the margins of the resection areas and to identify eventual residual lesions. In WL-TURBT group, only WL and TURBT were applied. All patients underwent routine follow-up with WL and NBI cystoscopy supplemented with cytology every 3 month. The recurrence risk of patients with NMIBC subjected to either NBI-HoLRBT or WL-TURBT was compared at 3 and 12 month. The 3-month and 1-year recurrence rate was 18.48% (17/92) and 38.04% (35/92) respectively in the WL-TURBT group, it was 5.81% (5/86) and 18.60% (16/86) in the NBI-HoLRBT group (both $p<0.05$). In addition, the in situ recurrence rate was less in the NBI-HoLRBT than WL-TURBT group (2.33% vs 14.13%, $p<0.05$) [7].

In an exhaustive study, Schubert et al. aimed to evaluate the impact of these improvements in the diagnosis of this pathology and their effectiveness in clinical practice. A systematic literature search was conducted to identify studies reporting on imaging modalities in the diagnosis of NMIBC between 2000 and 2017. A two-stage selection process was utilized to determine eligible studies. A total of 74 studies were considered for final analysis [1].

Optical imaging technologies have emerged as an adjunct to white-light cystoscopy and can be classified according to their scope as macroscopic, microscopic and molecular. Macroscopic techniques including photodynamic diagnosis, narrow-band imaging and Image 1 S-System are similar to white-light cystoscopy, but are superior in the detection of bladder tumors by means of contrast enhancement. Especially the detection rate of very mute lesions in the bladder mucosa (CIS) could be significantly increased by the use of these methods [1].

Microscopic imaging techniques like confocal laser endomicroscopy and optical coherence tomography permit a real-time high-resolution assessment of the bladder mucosa at a cellular and sub-cellular level with spatial resolutions similar to histology, enabling the surgeon to perform an 'optical biopsy'. Molecular techniques are based on the combination of optical imaging technologies with fluorescence labeling of cancer-specific molecular agents like antibodies. This labeling is intended to favor an optical distinction between benign and malignant tissue [1].

As a conclusions, optical improvements of the standard white-light cystoscopy have proven their benefit in the detection of bladder cancer and have found their way into clinical practice. Especially the combination of macroscopic and microscopic techniques may improve diagnostic accuracy. Nevertheless, hexaminolevulinic acid-PDD guided cystoscopy is the only approach approved for routine use in the diagnosis of bladder cancer by most urological associations in the EU and USA to date.

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