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ORIGINAL ARTICLE

A novel endoimaging system for endoscopic 3D reconstruction in bladder cancer patients

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ABSTRACT

Introduction: The methods employed to document cystoscopic findings in bladder cancer patients lack accuracy and are subject to observer variability. We propose a novel endoimaging system and an online documentation platform to provide post-procedural 3D bladder reconstructions for improved diagnosis, management and follow-up.

Material and methods: The RaVeNNA4pi consortium is comprised of five industrial partners, two university hospitals and two technical institutes. These are grouped into hardware, software and clinical partners according to their professional expertise. The envisaged endoimaging system consists of an innovative cystoscope that generates 3D bladder reconstructions allowing users to remotely access a cloud-based centralized database to visualize individualized 3D bladder models from previous cystoscopies archived in DICOM format.

Results: Preliminary investigations successfully tracked the endoscope's rotational and translational movements. The structure-from-motion pipeline was tested in a bladder phantom and satisfactorily demonstrated 3D reconstructions of the processing sequence. AI-based semantic image segmentation achieved a 0.67 dice-score-coefficient over all classes. An online-platform allows physicians and patients to digitally visualize endoscopic findings by navigating a 3D bladder model.

Conclusions: Our work demonstrates the current developments of a novel endoimaging system equipped with the potential to generate 3D bladder reconstructions from cystoscopy videos and AI-assisted automated detection of bladder tumors.

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KEYWORDS
Bladder cancer; cystoscopy; bladder phantom model; 3D-reconstruction; semantic image segmentation; artificial neural network

Introduction

Bladder cancer (BCa) is the seventh most commonly diagnosed cancer in the male population worldwide and eleventh when both genders are considered [1]. In the European Union (EU), BCa is the sixth leading cause of cancer, accounting for 124,000 newly diagnosed cases annually and 40,465 cancer-specific deaths [2]. In Germany alone, in 2014, BCa represented 6.5% of all new cancer cases in both sexes with 15,850 cases, and 3.2% of all cancer-related mortality with 5,692 deaths [3]. In 2012, the economic burden of BCa for the EU healthcare system was €2.9 billion, with inpatient care as the major cost component accounting for 58% of healthcare expenses [2]. BCa has the highest lifetime treatment costs per patient of all cancers due to high recurrence rates, despite a low stage and grade, and the consequent need for rigorous, long-term surveillance based on the patient́s risk profile [4].

Accurate documentation of all macroscopic tumor features, such as site, size, lesion number and appearance, and mucosal abnormalities found in cystoscopy or transurethral resection is crucial for patient follow-up [5]. Currently, documentation strategies have

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mainly been limited to written reports and two-dimensional diagrams, which lack precision and are subject to observer variability [6]. These methods not only pose a major limitation for patient follow-up but may also play a key role in disease recurrence and progression [6–9]. Therefore, innovative technological solutions are indispensable to assist urologists with the re-acquaintance of previous endoscopic findings and a patient́s clinical history, as an increase in time from the initial presentation makes it progressively more challenging and time-consuming. A novel endoimaging system capable of generating post-procedural 3D bladder reconstructions that accurately depict previous endoscopic findings would make subsequent resections more precise and facilitate patient follow-up. It would additionally pertain to healthcare systems considering the associated BCa prevalence and economic burden.

The RaVeNNA-4pi collaborative initiative strives for a pioneering technological solution to the current endoscopic documentation methods by providing state-of-the-art digital healthcare to BCa patients. The envisaged system seeks to empower patients by closely integrating them into the follow-up program, improve communication between physicians through a tele-medical approach, and provide healthcare systems with cost-effective treatment pathways.

Material and methods

The RaVeNNA-4pi project, funded by the German Ministry of Education and Research (grant number: 13GW0203A), has a three-year duration which began on 02/2018 and will conclude on 01/2021. Project partners were grouped into three working parties (hardware group, software group, and clinical group) according to their professional expertise.

Hardware partners – endoimaging system

The collaboration between Actuator Solutions (Gunzenhausen, Germany), FISBA AG (Berlin, Germany) and KARL STORZ (Tuttlingen, Germany) aims at creating an optimized high-resolution cystoscope that supports post-procedural 3D bladder reconstructions of cystoscopic examinations through a structure-from-motion (SfM) process chain. This approach follows a novel endoscopic principle that involves the integration of various innovative optical, sensor and actuator-based technologies into a cystoscopic endoscanner. The cystoscope is conceived to include an image sensor at its flexible tip and is foreseen to provide a 150° range of movement and a 70° field of view.

Software partners – cloud-based online platform, 3D-reconstruction, semantic image segmentation, 3D model visualization and DICOM format

As the software group coordinator, DORNER (Müllheim, Germany) is in charge of developing an interactive online-platform with a cloud-based centralized database for physicians and patients to objectively visualize cystoscopic findings as 3D bladder models. The electronic patient file was implemented using [i/med]-Web, a PHP-based web application with an underlying n-layer architecture. The electronic patient files are stored in a MariaDB database. This can be run on the same server as the web server, but can also be installed on a separate server. The documents and file attachments are versioned using the Subversion repository. Access to the database is only allowed locally and is protected by a firewall, so that the database cannot be directly accessed by third parties. The web interface of the file accesses the database *via* the web server on which it is based. Online access to the web server is only possible *via* SSL-secured connections. To protect against unwanted attacks, classic web server protection mechanisms as well as two-way authentication procedures were implemented. This protects the electronic data transmission from third parties. The online platform itself has been tested by an OSCP consultant (Offensive Security Certified Professional) and has received a security seal (https://greenhats.com/c/GVRxDmf3) after examination.

QIT Systems (Mannheim, Germany) is establishing a Digital Imaging and Communications in Medicine (DICOM) compatibility format for data processing, implementation, and testing.

INATECH́s (Freiburg, Germany) contribution is twofold: First, developing a 3D bladder reconstruction process chain from cystoscopic video recordings through a SfM approach. Second, implementing semantic image segmentation and deep convolutional neural networks (DCNN) for an AI-assisted detection of bladder tumors and areas suspicious of carcinoma-in-situ (Cis). The SfM pipeline was tested on a 3D printed bladder phantom. The reconstruction process consists of two phases: endoscope calibration and scene reconstruction (Figure 1). To calibrate the endoscope, the non-linear distortions induced by the fish-eye lens are corrected by computing the camera's intrinsic parameters such as projection centre,

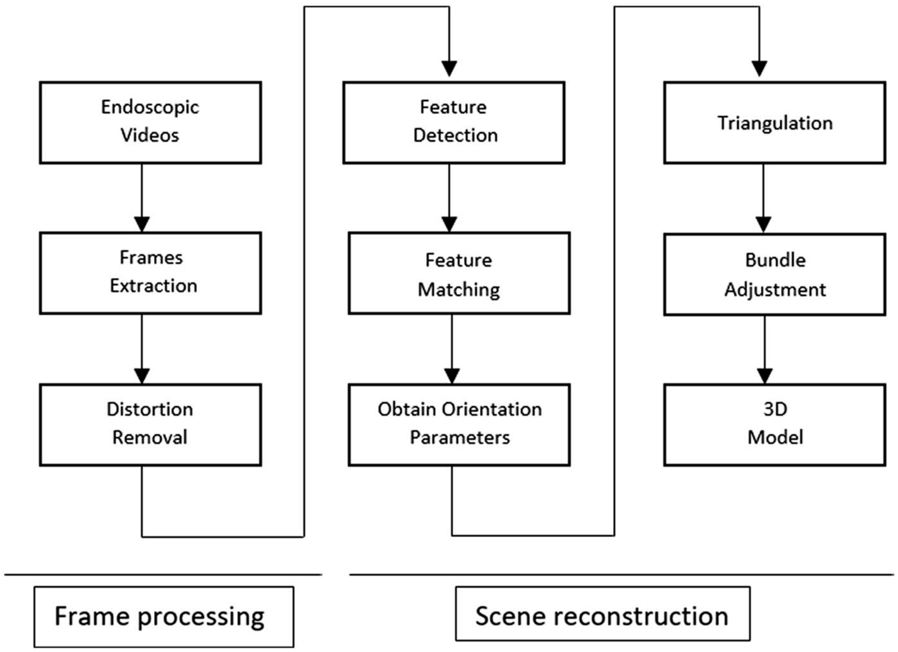

Figure 1. Structure-from-Motion (SfM) process chain.

distortion parameters, and focal length. These parameters are obtained by using an open calibration routine which consists of several images from a predefined chessboard pattern. For scene reconstruction, video frames were first extracted from cystoscopy videos and subsequently calibrated to remove distortions by computing the camera's intrinsic parameters. The frames were further processed with a feature detection algorithm Scale-Invariant Feature Transform (SIFT) to obtain features. Feature matching using Fast Library for Approximate Nearest Neighbours (FLANN) was performed across frames to identify similar features. Once the relation between two frames is established, each corresponding feature point can be triangulated into a 3D point. To initialize the reconstruction, two frames that are likely to provide a stable estimate of relative pose are chosen. Each frame is then added incrementally to complete the reconstruction. Lastly, bundle adjustment is applied to refine the obtained reconstructed structure and motion.

Ethical approval was obtained by the ethics committee of the University of Freiburg – Medical Centre (567/15) to compile cystoscopy videos from consecutive patients who presented to our department and analyze them retrospectively. Frames were extracted from all collected cystoscopy videos, each representing an individual patient, and their annotation performed by trained physicians using label editor software developed at Fraunhofer Institute for Physical Measurement Techniques IPM. The frames´ annotation accuracy was initially confirmed by a board-certified urologist and is to be ratified by a group of urologists from the department to decide on their dataset permanency. Among the classes of interest for AI-assisted automated detection are papillary bladder tumors, carcinoma-in-situ suspicion, resected tumors, bladder diverticulum, bladder stone and left and right ureteric orifices. The segmentation procedure uses U-Net, an encoder-decoder network that has been used successfully in various medical image analysis tasks [10–12]. The network architecture was slightly modified by adding batch normalization after each convolutional layer. For training purposes, 70% of the data were used for training, 10% for validation, and 20% for test.

Furtwangen University provides the software component that allows an interactive 3D visualization/navigation of bladder models and the detailed annotation of cystoscopic findings.

Clinical partners – project coordination, ethical approval, patient data provision, 3D-printed phantom models, animal experiments and clinical trial

By combining 3D printing and polymer molding technology, the Max Planck Institute for Intelligent Systems (Stuttgart, Germany) has previously developed accurate phantom models in partnership with the University of Freiburg [13–15]. For this initiative, in collaboration with the University of Mannheim, a bladder phantom was created based on patients ́ computed tomographic cross-sectional imaging for the SfM pipeline to be tested and to obtain a dense point cloud for preliminary 3D reconstructions. The phantom's physiological properties were investigated with a novel variable-view rigid endoscope (EndoCAMeleon, Karl Storz, Tuttlingen, Germany). The bladder phantoms will play a key role in the new endoimaging systems ́ initial evaluation. The preclinical evaluations performed will help streamline animal experiments, which have already been ethically approved (G-20/05), and may accelerate the possible conduct of a prospective clinical trial to ensure the final practical feasibility of the endoimaging system.

Results

Hardware group

The integration of various sensors successfully carried out orientational tracking of the endoscope's tip to support the 3D bladder reconstruction. As different approaches regarding the position tracking an electromagnetic tracking solution (NDI Aurora) and an inertial sensor-based solution have been compared. The optical design was finalized and the integration of modalities to support optical adaptions of the field of view during the bladder scan is currently in preparation. On the illumination side, a highly effective light source to support improved image contrast is under development. Figure 2 shows the optical and mechanical design of the endoscope's miniaturized distal end.

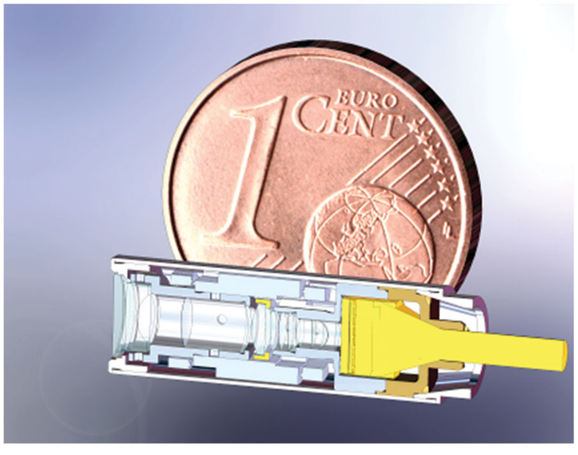

Figure 2. Optical and mechanical design of miniaturized endoscope's distal end.

Software group

The cloud-based online platform ́s administrator rights for physicians were divided into two modalities. The RaVeNNA + version encompasses physicians who are equipped with the endoscopic hardware, grants access to allocated patients and permits the documentation of endoscopic findings on individualized 3D models. Physicians who did not acquire the endoimaging hardware will employ the RaVeNNA – version which allows them to document endoscopic findings on a preconceived 3D bladder model. Patients are provided with read-only access to their medical records and may additionally grant their attending physician entry to their medical history. An administrator account is additionally offered to users involved in administrative activities to access physicians ́ allocated patients. The four versions are web-based and access is granted by logging in with a user profile. Moreover, to separately predict the short- and long-term risks of disease recurrence and progression in individual patients, we provide the European Organization for Research and Treatment (EORTC) BCa risk calculator [16]. The scoring system is based on the six most significant clinical and pathological factors, such as the number of tumors, tumor size, prior recurrence rate, tumor invasion, presence of carcinoma *in situ* and tumor grade.

To date, the semantic segmentation dataset consists of 5,500 endoscopic images which were extracted from 65 cystoscopy videos, each representing an individual patient. Fully convolutional neural networks were used to train, validate and test data achieving an average of 0.67 dice score coefficient (DSC) over all classes. However, the network predictions performed well for the majority of classes that were well-represented in the training dataset such as papillary tumor as shown in Figure 3. Additionally, 93% DSC was achieved for binary segmentation in the detection of papillary tumors when comparing convoluted neural network annotations to the ground truth.

The structure-from-motion (SfM) pipeline has thus far been tested on a bladder phantom using a rigid cystoscope (KARL STORZ, Tuttlingen, Germany) coupled to an inertial sensor, mouse sensor and electromagnetic tracking. These sensors determine the endoscope's rotation and translational movements, and demonstrate that the processing sequence permits a 3D bladder reconstruction. The presence of artifacts in the endoscope ́s field of view such as air bubbles, blood clots, and stone particles have been shown to hamper the acquisition of a dense point cloud for accurate 3D reconstructions (Figure 4). Nevertheless,

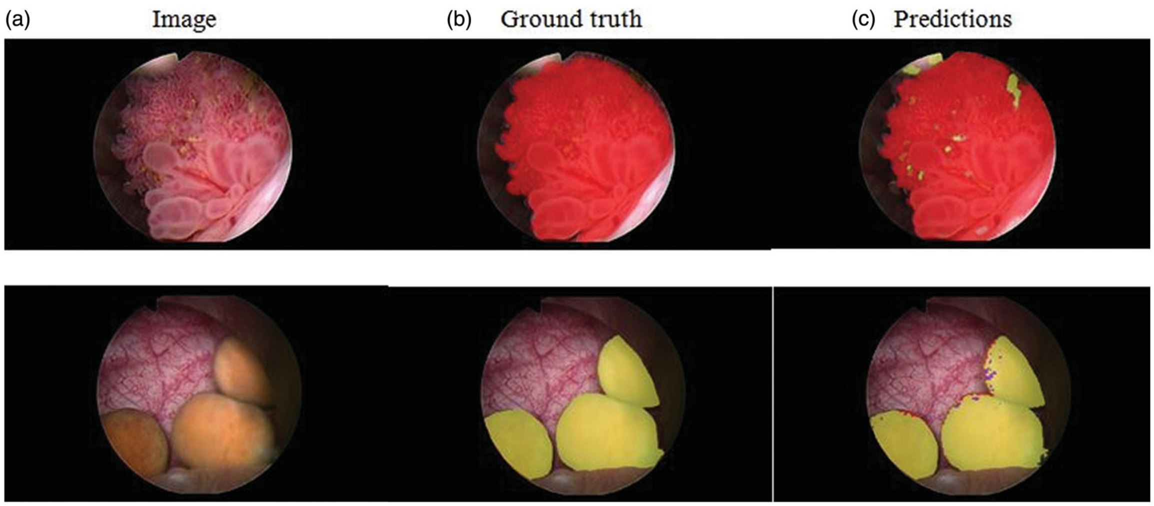

Figure 3. The first and second rows show the visual comparison of example images, ground truth and predictions for class papillary tumor and bladder stones respectively.

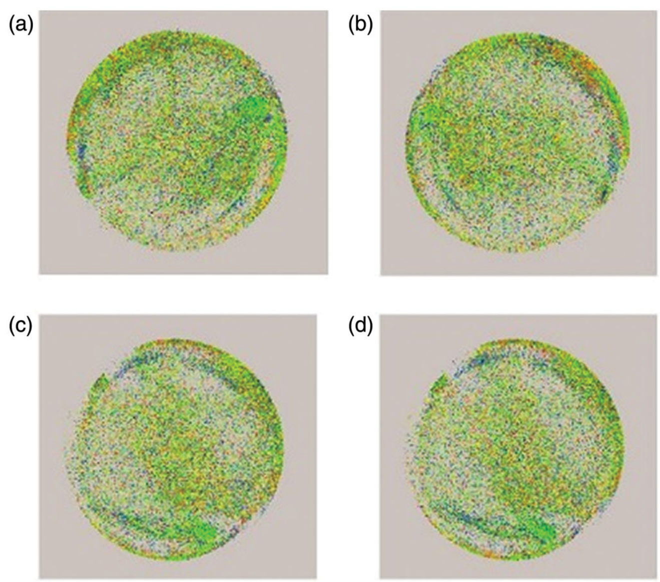

Figure 4. Reconstruction results of a bladder phantom. The first row shows the sparse point cloud from the top (a) and bottom (b) view. Images (c) and (d) show the sparse point cloud from the left and right-side view.

the bladder phantom permitted the acquisition of a point cloud to generate preliminary spherical 3D reconstructions.

For visualization, the point cloud data is converted to textured watertight mesh geometry to improve visualization performance. The developed web-based visualization component runs at least at 30 frames per second on current consumer hardware. The visualization component represents sample data records in the data format that the 3D reconstruction will provide. Initial usability tests have shown that user navigation and visualization meet usability requirements. A sample texturized bladder model depicting correlation accuracy with classes of interest has been integrated into the online platform, allowing users at present to navigate the bladder in a 3D space (Figure 5).

Clinical group

Rigid and expandable 3D-printed bladder phantoms were developed and evaluated to test the SfM pipeline in reproducible preclinical endoscopic procedures. Technical measurements and a practical evaluation by urologists confirmed that the models closely resembled realistic cystoscopic procedures. The

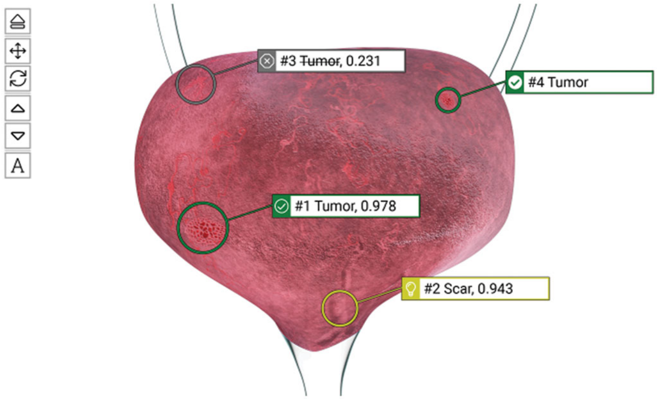

Figure 5. Texturized and navigable 3D reconstructed bladder depicting correlation with classes of interest.

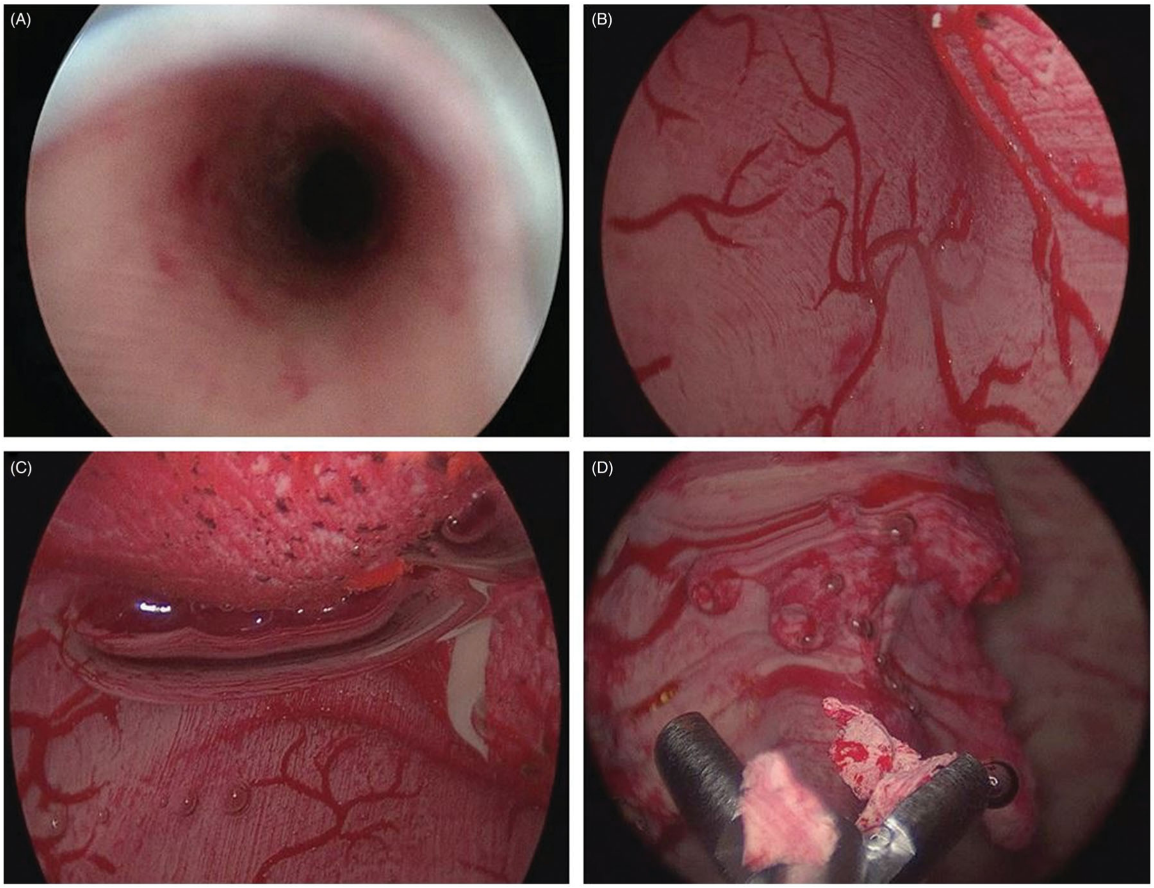

Figure 6. Endoscopic images of the expandable bladder phantom. (A) Urethra. (B) Left bladder wall. (C) Bladder dome. (D) Sham tumor biopsy.

flexible model allows accurate volume expansion, manual compression, visualization of the bladder dome's bubble, and sham tumor biopsy (Figure 6). Lastly, it provided the opportunity for surgeons to gain experience with a novel variable-view rigid endoscope (EndoCAMeleon, Karl Storz, Tuttlingen, Germany), in preparation for animal and preclinical investigations with the novel cystoscope.

Discussion

RaVeNNA 4 pi opens up a wide spectrum of new possibilities for the substantial optimization of BCa diagnosis and management. The envisaged endoimaging system seeks to benefit both patients and physicians in the context of improved diagnostics, treatment, cancer-specific survival, physician communication, patient-empowerment and long-term follow-up. Additionally, health care systems are expected to profit from cost-effective treatment pathways. To the authorś knowledge, a comparable approach to the presented system does not exist and for the first time, endoscopic findings can be objectively presented and compared.

AI-assisted cystoscopy aims to improve lesion detection and achieve diagnosis with high sensitivity and specificity by training deep convolutional neural networks (DCNN) with large data sets of annotated images. Providing physicians with computer-aided diagnostic tools represents a promising approach to revolutionize endoscopic surgical practice by identifying inconspicuous areas of malignancy given the heterogeneous aspect of bladder lesions. Shkoylar *et al.* developed a similar deep learning algorithm for augmented BCa detection [17]. They developed an image analysis platform based on DCNN using a 100 patient dataset of 2335 frames and achieved a tumor recognition sensitivity of 90.9%. In comparison, our database has exceeded the frame number, achieved 93% accuracy when comparing the ground truth to the annotated frame, and it is foreseeable that the patient number will be surpassed by the end of the project, thereby creating a more robust network.

Moreover, 3D bladder reconstructions using a structure-from-motion process chain aim at assisting physicians to navigate and visualize the bladder in multiple angles, and monitor successive resections. Lurie *et al.* presented software that can reconstruct and visualize 3D bladder models from endoscopic videos [7]. Accuracy and robustness were validated with tissue-mimicking bladder phantom videos and the pipeline successfully reconstructed real clinical data stemming from patientś cystoscopy videos during BCa examinations. Nonetheless, our approach differs significantly from these methods in that cystoscopy video recordings obtained from our novel endoimaging system are converted post-procedurally into personalized and navigational 3D bladder models for patients and physicians to access from any remote location with mobile devices. We expect this approach to improve patient compliance, the quality of follow-up care and lead to substantial cost-effective treatment pathways.

Moreover, a telemedical approach coupled to the endoimaging system is envisioned, which makes it possible to discuss findings in the sense of a second opinion and thus strengthen the diagnostic certainty and improve patient care. This way, independent experts could be consulted in challenging cases regardless of their geographical location. Hougen *et al.* developed a telecystoscopy system through transmitted video quality assessment that was validated by experts and non-experts in a method known as 'crowd sourcing' [18]. Several combinations of the telecystoscopy system were tested in a cadaveric specimen to determine the optimal equipment to be selected for the system. There was an overall strong response concordance between both groups; however, out of eight combinations, only two had high enough quality for appropriate medical use. Despite these shortcomings, their contributions provide the scientific rationale for a telecystoscopy system feasibility that can be expanded to BCa surveillance programs.

Our initiative's holistic and standardized digital data acquisition offers the potential for a significant improvement in everyday clinical practice and patient care. The possibility of patientś involvement strengthens their role within the follow-up program with correspondingly expected increased compliance. The separation of healthcare facilities, particularly in BCa management, concerning diagnosis (private practice) and treatment (university hospitals) is common. The digital data sets aimed at in this project offer an essential opportunity to significantly improve the quality of information exchange on endoscopic findings, treatment planning and documentation between healthcare institutions in the future, as well as integrating additional expertise on telemedical diagnostics.

The project development is not devoid of limitations. The legal situation concerning patient files is challenging and therefore security, availability, data protection, and access rights have to be considered in particular aspects. For this purpose, we developed the concept of the rights and carried out a security audit of our web platform. However, in the context of the project, where we are developing a demonstration prototype, this is not yet to be seen as particularly critical.

Conclusion

The RaVeNNA-4pi novel endoimaging system aspires to offer physicians and patients a radically new approach to BCa diagnosis, management, and follow-up. Our work demonstrates the current developments of the conceived endoimaging system which aims to accurately detect bladder tumors through an AI-assisted automated detection approach and to generate post-procedural 3D bladder reconstructions from cystoscopy videos, which can be afterward remotely accessed through an online platform.

Ethical approval

Ethical approval was obtained from the Ethical Committee of the University of Freiburg, Germany.

Declaration of interest

Arkadiusz Miernik: German Federal Ministry of Education and Research, Berlin, DE – research funding, German Association of Urology, Düsseldorf, DE – travel sponsoring, European Association of Urology, Arnhem, NL – travel sponsoring, Walter de Gruyter, Berlin, DE – royalties, RichardWolf GmbH, Knittlingen, DE – speaker, KLS Martin, Tuttlingen, DE – advisor, Avatera medical, Jena, DE – advisor, Lisa laser OHG, DE – proctor, Optimed GmbH, Ettlingen, DE – advisor. The remaining authors have no conflicts of interest to declare.

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Author contribution

R.S: Manuscript drafting and data collection; M.N, U.P: 3D reconstruction, data management and analysis; S.H, A.R, A.M, C.G: project development; M.P, P.I: online-platform; A.S, C.M: graphics visualization; F.W, B.G, M.C.K: 3D-printed phantom models; K.K, J.A.F, L.M, J.Y, H.R, M.K, T.S, N.B: Hardware development and Sensor software; S.B: DICOM data archiving.

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