IN VIVO OPTICAL COHERENCE TOMOGRAPHY IN ENDOSCOPIC DIAGNOSIS OF BLADDER DISEASE

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ABSTRACT

Purpose: OCT is a new imaging method which produces a 3 mm wide x 2.5 mm deep 2D picture with a resolution of 15 µm.
Materials and Methods: We utilised the Tomograph Sirius 713, developed at the Medical Laser Centre in cooperation with 4-Optics AG, Lübeck, Germany. This apparatus uses a special Super-Luminescence-Diode (SLD) that produces light within the near infrared wavelength, with a central wavelength of 1300 nm. The coherence length is reduced to 15 µm. The light is introduced into a fiberglass optic which is several meters long and is easy to handle. To measure the depth of invasion and position of urothelial bladder tumours, the fibreglass optic is attached to a regular endoscope (Wolf, Knittlingen, Germany) via an OCT adapter. That way, in parallel to the regular endoscopic view of the bladder mucosa with or without pathologic findings, an OCT picture of the superficial as well as the deeper muscle layers is visible online. OCT was used to obtain 275 images from the bladder of 30 patients.
Results: OCT of normal bladder mucosa produces an image with a cross section of up to 2.5 mm. It is possible to distinguish between transitional epithelium, lamina propria, smooth muscles and capillaries. In cystitis, the thickness of the mucosa is constant, but the distinction between the different layers is blurred. In squamous metaplasia there is thickening of the epithelial layer, with preservation of lamination of the lower layers. In transitional cell carcinoma there is a complete loss of the regular layered structure. Thus, the border between tumor and normal bladder tissue can be easily distinguished.
Conclusions: This method can provide valuable information on tumor invasion and extension in real time and therefore influence therapeutic strategies

Key words: optical coherence tomography, endoscopy, bladder disease

1. INTRODUCTION

Conventional imaging modalities like CT or ultrasonography have a spatial resolution of 70-1000 µm. OCT is a new method by which infrared light is introduced into a fiberglass optic to measue tissue structures of up to 2.5 mm depth with a spatial resolution of up to 10-15 µm. In the early 1990's, the first experimental studies to provide tissue images with resolutions of 10-20µm were accomplished in different centers .[1,2] Using OCT, the transparent tissues of the eye, the skin, the teeth, the brain cortex and cartilages have been visualized.[3-7] König et al presented the first OCT pictures of a bladder carcinoma in an animal model and Zagaynova et al demonstrated 680 OCT–Measurements during TUR-B of 66 patients.[8,9]

We utilised the Tomograph Sirius 713, which uses a special Super-Luminescence-Diode (SLD) that produces light within the near infrared wavelength (1300 nm). The goals of our study were: to test whether OCT is suited for a diagnostic application in conjunction with regular endoscopes and to examine OCT measurements of normal, inflammatory, and malignant lesions of the urothelium. In the following article the OCT photographs of bladder tumors were correlated with histological results.

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2. MATERIALS AND METHODS

From April, 2002 to March, 2003, 30 patients (28 women, 2 men, age 45-81 years) who were suspected to have bladder cancer were endoscopically examined for a primary or recurrent tumor. A total of 275 OCT measurements were carried out in 96 areas of the bladder. (table 1). These were then compared with histology slides.

Table 1: Results of the endoscopic optical coherence tomography

BLADDER AREAS HISTOLOGY	**NUMBER OF EXAMINED AREAS**
Normal bladder mucosa	**31**
Pathological bladder mucosa :	**42**
Cystitis	9
Hyperplasia	3
Dysplasia	2
Tumor:	28
Carcinoma in situ	*2*
TaG1-3	*17*
T1G2-3	*6*
T2-3G2-3	*3*
Borders of pathological bladder lesions	**23**
TOTAL	96

OCT produces a 2D picture, which is 3 mm wide and 2.5 mm deep with a resolution of 15 µm. It takes about 3 sec to generate one image. To prevent the introduction of errors by mechanical pressure of the OCT device onto the mucosa, we use a special adapter that keeps a 2 mm distance from the surface to the fiberoptic. The Medical Laser Center Lübeck (MLL) developed (in cooperation with the Richard Wolf and 4Optics Companys) a rigid OCT-system for endoscopy (fig. 2), which is suitable for applications in urology.

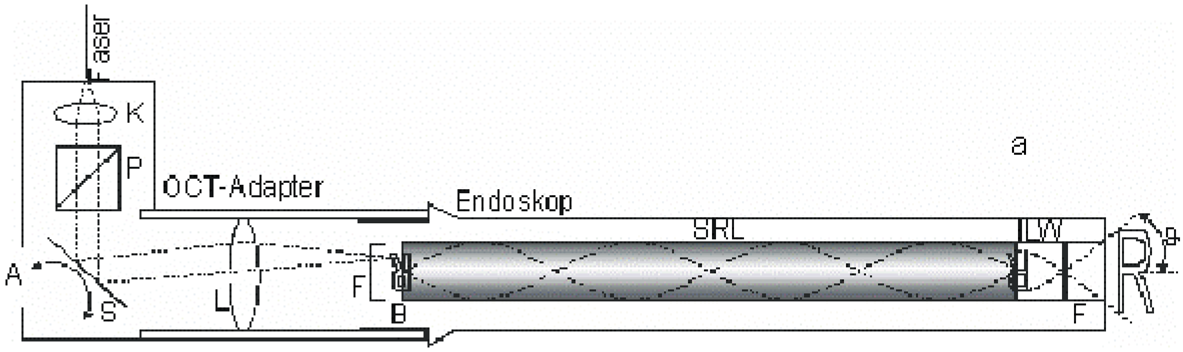

Fig. 1: OCT endoscope. The single mode fiber (LWL) is connected to the modified OCT system from the 4Optics AG. The mirror is driven by a galvanometer for a lateral acan.

This common OCT-system consists of video-based devices and OCT devices. Using the CCD video camera and video adapter,the video signal from the cystoscope of the examined surface is represented on the computer display. The OCT-devices: Thomograf Sirius 713, glass fiber, OCT adapter, computer-basis-turn out Sirius 212, cystoscope and the 2D picture of the computer display are demonstrated (fig.2). For the OCT Sytem, a special endoscope with a more inserted lens was designed. With such a lens, both the normal video and the OCT signal can be transmitted.

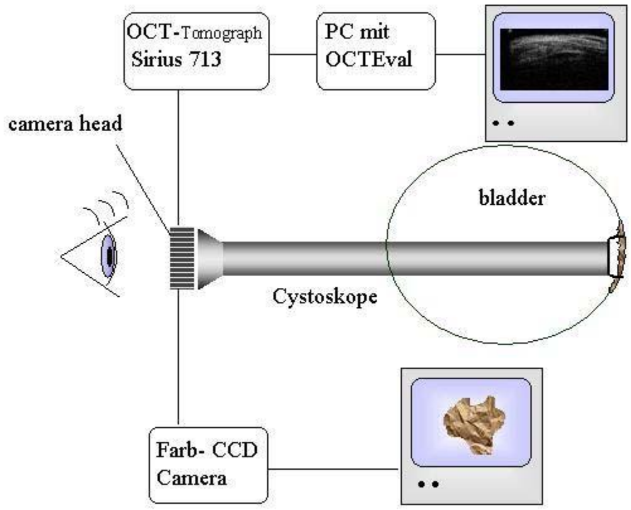

Fig. 2: Schematic overview of OCT-Cystoscopy

The following steps were followed for each patient who underwent OCT. First, a standard 20 Fr cystoscopic sheath was introduced transurethrally through which the special OCT- optics were then placed. By the special design of the optics it was possible to provide permanent OCT- photographs at the same time that the bladder was observed cystoscopically. Cystoscopy was performed in the standard fashion. The procedure was documented on video. Normal and suspicious areas of the bladder were then examined with the OCT system. By placing the optics directly on the bladder surface, movement artifacts were avoided. In order to prevent pressure from being placed on the bladder mucosa with resultant compression of the bladder layers, a measuring rod was used to show the distance between the point of interest on the bladder surface and optics surface. The measuring procedure proved reliable, as artifact-free pictures were produced. The procedure required approximately 5-10 seconds per picture (pure Scan time approx.. 2 seconds).

3. RESULTS

OCT of normal bladder mucosa allows imaging of a cross sectional area of up to 2.5 mm. It is possible to distinguish transitional epithelium, lamina propria, smooth muscles and capillaries (fig.3). Capillaries with red blood cells can be observed in cross section or from an angle. Under OCT visualization, the lamina propria appears as well-reflected strips of small, mostly horizontally-oriented tissue. Small and large capillaries are seen as poorly reflected oval forms with horizontally-oriented marks. The resolution of OCT provides the ability to differentiate the muscularis mucosa in the lamina propria from the true muscle layer of the bladder. With OCT, the muscle layer appears as a homogeneous, poorly-reflected layer.

In cystitis, the thickness of the mucosa is constant, but the distinction between the different layers is blurred. In squamous metaplasia, there is thickening of the epithelial layer, with preservation of lamination of the lower layers. In transitional cell carcinoma there is a complete loss of the regular layered structure. Due to these differences, tumor and normal bladder tissue can be easily distinguished.

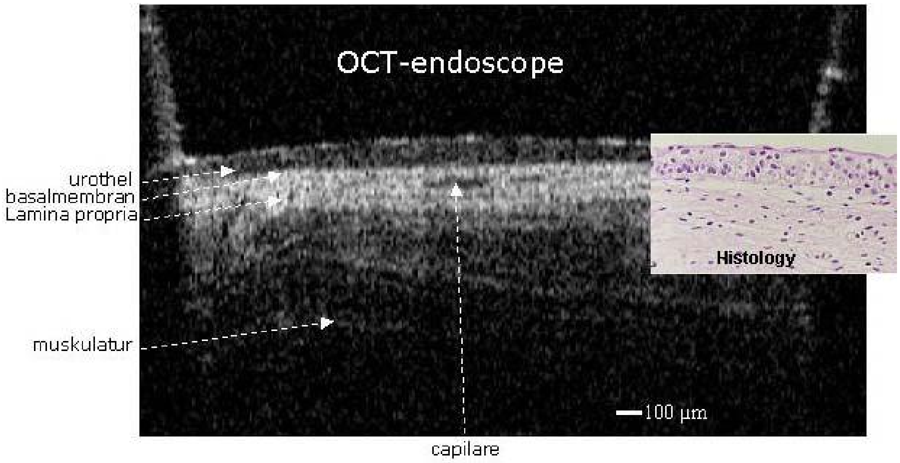

Fig. 3: OCT picture of normal bladder mucosa

The following problems with OCT existed during our research. The OCT- Cystoscope has a limited length of 6 cm and at present only a 0° OCT-Optic is available. No flexible cystoscope is available at present. This means that there are areas of the bladder mucosa which are not accessible for measurements. Capturing the image takes about 2-3 seconds. Mechanical pressure with the head of the OCT-Cystoscope on the bladder mucosa leads to a distorted OCT image of the superficial layers (fig.4).

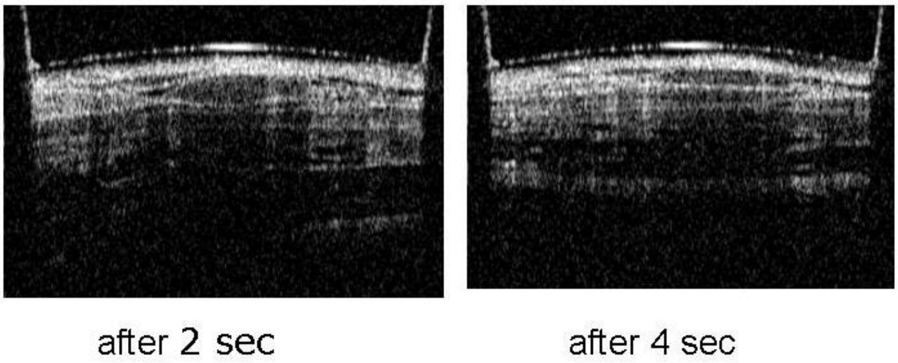

Fig.4: Influence of pressure on the OCT-picture

4. DISCUSSION

OCT has been established within the last ten years as a new imaging method with a resolution of 10-30 µm for the representation of the tissue in vivo.[1, 10] The results published so far, which used the available 830 nm of OCT devices, only exhibited a penetration depth of up to 4mm. The small resolution was used in order to provide a clear picture of the tissue structure of the skin or cornea.[11, 12] The penetration depth and resolution of the OCT pictures depend on the wavelength of light used. Longer light wavelengths are weakened more as they pass through the tissue. Thus, the attainable investigation depth is decreased. With OCT investigation using wavelengths of 830 nm and 1300nm, penetration depths of approximately 4 - 6 mm and 2 - 4 mm can be achieved.

The resolution of the visual system is defined in optical physics as the minimum distance which is necessary so that two objects are still recognizable separately in the video display. The detail recognizability or resolution is higher with more strongly coherent light. The axial resolving power of our equipment Sirius 713 is appropriate for about 15 µm. That means that any structure, which is at least 15 µm large, can theoretically be recognized. Practically, this succeeds only if these structures are accordingly high-contrast in relation to their environment. The lateral resolving power depends on the width of the lens on the end of the cystoscope. Our OCT-system has approximately 10 µm of lateral dissolution. If the tissue size is clearly larger than the resolving power of the light wavelength used, then these boundary surfaces are easily illustrated anatomically. This is clearly demonstrated in our study in the pictures of the urothelium, lamina propria, capillary etc..

Welzel J. et al[11] showed that structures up to a depth by 4mm under the skin surface could be pictured. The OCT-measurements were accomplished ex vivo with intact bladder tumors in animal experiments.[8, 13] In our OCT-system, a new cystoscope lens was developed. This allowed us to transmit the OCT signal while simultaneously viewing the normal cystoscopic image. Interior reflections from the cystoscope lens can disturb the video picture at the edges. In our study, the combination of the new lens and the external OCT adapters provided very high axial resolution and a lateral resolution of approximately 10µm. This makes illustration of the bladder tissue possible during cystoscopy.

5. CONCLUSION:

This study has shown the following important aspects for the application of optical coherency tomography to cystoscopy:

1. Optical coherency tomography (OCT) is a new optical procedure with a resolution of approximately 10µm, which can produce a cross sectional picture of up to 2.5 mm of depth of the bladder during Cystoscopy. It is possible to visualize epithelium, lamina propria, smooth musculature and capillaries.
2. In cystitis, the thickness of the mucosa is constant, but the distinction between the different layers is blurred.
3. In transitional cell carcinoma, there is a complete loss of the regular layered structure. This method can be used to improve the diagnosis of superficial bladder tumors. The border between tumor and normal bladder tissue can be easily distinguished.

4. With OCT measurements, the tumor grade can be determined intraoperatively. Differentiation of hyperplasias, dysplasia and carcinoma by means of OCT can be difficult due to the similar morphologies.

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