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·*Review*·

Virtual endoscopy of the urinary tract

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Abstract

Technological breakthroughs have advanced the temporal and spatial resolutions of diagnostic imaging, and 3 dimensional (3-D) reconstruction techniques have been introduced into everyday clinical practice. Virtual endoscopy (VE) is a non-invasive technique that amplifies the perception of cross-sectional images in the 3-D space, providing precise spatial relationships of pathological regions and their surrounding structures. A variety of computer algorithms can be used to generate 3-D images, taking advantage of the information inherent in either spiral computed tomography or magnetic resonance imaging (MRI). VE images enable endoluminal navigation through hollow organs, thus simulating conventional endoscopy. Several clinical studies have validated the diagnostic utility of virtual cystoscopy, which has high sensitivity and specificity rates in the detection of bladder tumor. Published experience in the virtual exploration of the renal pelvis, ureter and urethra is encouraging but still scarce. VE is a safe, non-invasive method that could be applied in the long-term follow-up of patients with ureteropelvic junction obstruction, urinary bladder tumors and ureteral and/or urethral strictures. Its principal limitations are the inability to provide biopsy tissue specimens for histopathologic examination and the associated ionizing radiation hazards (unless MRI is used). However, in the case of endoluminal stenosis or obstruction, VE permits virtual endoluminal navigation both cephalad and caudal to the stenotic segment. To conclude, VE provides a less invasive method of evaluating the urinary tract, especially for clinicians who are less familiar with cross-sectional imaging than radiologists. *(Asian J Androl 2006 Jan; 8: 31-38)*

Keywords: computed tomography; three-dimensional imaging; virtual endoscopy; urethral stricture

1 Introduction

Three-dimensional (3-D) reconstruction techniques appeared in published reports in the mid-1990s, but at that time the imaging techniques could not acquire continuous and complete sets of raw data, leading to pronounced artifacts in the final reconstruction. However, recent technological breakthroughs have advanced the temporal and spatial resolutions of diagnostic imaging, and 3-D reconstruction techniques have been introduced into everyday clinical practice.

Virtual endoscopy (VE) is a non-invasive technique that amplifies the perception of cross-sectional images, acquired by axial computed tomography (CT), in the 3-D space, providing precise spatial relationships of pathological regions and their surrounding structures. The use of appropriate software and relative algorithms produces virtual reality images, enabling endoluminal navi-

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gation through any hollow viscous, thus simulating conventional endoscopy. In addition, VE enables the depiction of endoluminal as well as extraluminal adjacent structures in all directions. It may also allow the diagnostic exploration of body regions that are either unaccessible or incompatible with conventional endoscopic procedures. VE has been applied to many hollow anatomical structures, such as trachea, colon, aorta, brain ventricles, nasal cavity and paranasal sinuses [1–8].

Here we reviewed various applications of VE in the urinary tract. A survey of published works on the PubMed database was performed using the following keywords: virtual, three-dimensional, endoscopy, nephroscopy, ureteroscopy, cystoscopy, and urethrosco-py. Seventy-five relevant publications from January 1996 to January 2005 were traced. The selection criteria included: (1) case reports describing the first applications of the technique; (2) novel small series; and (3) prospective clinical studies with well-defined endpoints. Our referred bibliography was confined to 35 articles. The advantages and limitations of VE in each setting were discussed.

2 3-D reconstruction techniques

Spiral computed tomography (SCT) and magnetic resonance imaging (MRI) provide continuous and complete sets of raw data that are transferred to a computer workstation for post-processing and analysis. Once the final 3-D dataset is obtained, a variety of computer algorithms can be used to generate 3-D images, taking advantage of the information inherent in either the SCT or MRI scan. The most commonly applied techniques are shaded surface display, maximum or minimum intensity projection and volume rendering [1–5].

VE is one of the most recent innovations in the field of post-processing techniques and provides supplementary information to those already mentioned. The main goal of VE was to develop a non-invasive diagnostic tool that would be easily tolerated by the majority of patients, by producing images similar to those acquired by the conventional endoscopy.

3 Virtual nephroscopy and ureteroscopy

Renal pelvic and ureteral tumors usually present with gross hematuria and pain. The conventional endoscopic examination used for the diagnosis of these tumors is an invasive and technically demanding procedure which has the potential risks of ureteral injury, hematoma, urinoma, ureteral obstruction and fistula [9, 10]. The use of a flexible ureteroscope makes access easier and can minimize patients' discomfort and complications. However, investigators have explored non-invasive techniques, such as virtual nephroscopy and ureteroscopy, in an effort to overcome the shortcomings of the conventional endoscopic approach.

Published VE studies of the upper urinary tract are still limited. Takebayashi *et al*. [9, 10] pioneered this field by reporting the usefulness of CT nephroscopy and ureteroscopy in the diagnosis of malignancies of the renal pelvis and the ureters. Delayed SCT was performed after intravenous contrast media and a diuretic agent were given in order to achieve the dilatation of the pelvicaliceal system and homogeneous dense opacification of the ureters. CT nephroscopy and renal axial CT were able to detect 92 % and 83 % of tumors, respectively. They showed a good correlation of CT nephroscopic images with the pathological findings and concluded that CT nephroscopy can help in the preoperative planning of endourological treatment. However, CT nephroscopy could not evaluate tumor infiltration of the surrounding structures, renal parenchyma or other adjacent tissues. In the evaluation of ureteral tumors, CT ureteroscopy clearly depicted ureteral stenosis and allowed proximal and distal evaluation of the ureter to the stenotic lesion. Sensitivity for detecting ureteral tumors using CT ureteroscopy was 81 % and the specificity was 100 %. However, neither tumor infiltration beyond the ureteral wall, nor lesion texture or color could be adequately evaluated [10]. Evaluation of the upper urinary tract with VE may also be performed using non-contrast MR urography datasets. Neri *et al*. [11] reported that VE of the renal pelvis and calices was able to be performed in all the 26 cases on the site of the urinary obstruction. VE and optimal depiction of the ureter was able to be obtained from the ureteropelvic junction to the site of obstruction if the ureteral diameter was at least 5 mm. However, VE of MR urography datasets was limited by the degree of dilation of the ureter and by the occurrence of artifacts. Artifacts occurred at low ureteral diameters and the ureter was visualized as narrow or occluded. The non-dilated side could be partly explored in almost half of the cases. The advantage of MR urography, however, is that it does not require the administration of iodinated contrast media and that it avoids radiation hazards.

More recent publications have reported increased resolution of VE images of the upper urinary tract with the use of volume rendering algorithms [12, 13]. In these studies, authors reported their experience with the application of VE to evaluate ureteral patency after the treatment of upper urinary tract obstruction with the use of self-expandable metallic stents. VE findings concurred with the excretory urography findings and VE permitted accurate 3-D visualization of the stented area, and of the proximal ureter cephalad and caudal to the stent, from different angles. The main disadvantage reported by the authors was the inability of the method to differentiate structures with similar absorbing characteristics used in the CT acquisition settings, despite its ability to provide information about the presence of intraluminal stenosis. That is, ureteral wall structures were depicted with similar densities regardless of the underlying histopathology (normal urothelium, luminal encrustation, mucosal hyperplasia or tumoral infiltrations). VE does not differentiate the fine detail in the epithelial lining of anatomical structures, which can be visualized with conventional endoscopic procedures. VE is less invasive compared with endoscopy of the upper urinary tract and is probably superior to excretory urography. We have also recently reported virtual navigation within the pelvis and calices with the efficient depiction of any pelvicaliceal anatomic deformities [14]. Because of the dilation provided by the stent, the quality of data acquisition and VE images of the stented ureter were superior. Metal stents, due to their minimal mass density, caused reduced scattering to the X-rays' quantum energies. Application of specially modified CT reconstruction protocols helps to overcome artifacts from strut reflections [15].

4 Virtual cystoscopy (VC)

The gold standard method for investigating hematuria and detecting bladder tumors is conventional cystoscopy. Although flexible cystoscopy used for surveillance is very well tolerated by patients, the main drawbacks are the failure to evaluate adjacent structures, a 5 % – 15 % risk of urinary tract infection, and patient's discomfort and anxiety [16, 17]. Although conscious sedation is generally not required, it might sometimes be necessary to relieve pain and discomfort. Iatrogenic injury to the urethra and bladder might also occur [18]. Because of these shortcomings, many investigators proposed the use of VC for bladder malignancies. This technique is based on the use of images acquired mainly from CT scanners. The suggested protocols for bladder distension vary from the use of room air, carbon dioxide and, more recently, intravenously infused contrast agents. The use of contrast media is less invasive, more convenient than, and as effective as, the use of air or carbon dioxide insufflations. Although VE has the advantage of providing both endoluminal and extraluminal information, artifacts on virtual images may occur if inadequate mixing of urine and contrast material takes place, or when a metallic hip prosthesis is present [19].

Vining *et al*. [20] were the first to perform VC in 1996. After catheterization of the bladder, drainage of urine and insufflation of the bladder with carbon dioxide, CT of the pelvis was carried out in one healthy volunteer and two patients with already identified transitional cell carcinoma of the bladder. The authors succeeded in correctly detecting bladder tumors and established the diagnostic feasibility of VC. Since then, various investigators have reported on the feasibility, safety and accuracy of VE of the bladder and have suggested that VE may be clinically applied in the long-term surveillance of patients with bladder tumors [18, 19, 21, 22]. VC allows the assessment of tumor size, location and morphology and it has been shown to have a 97 % – 100 % sensitivity rate and a 93 % – 100 % positive predictive value [18–20]. The detection rate of VC depends on tumor size. It has been documented to range from 94 % for tumors larger than 1 cm, to 77 % for tumors less than 1 cm. Depending on the location of the tumor, either the supine or prone position is chosen for the CT scan [22].

In 1998, Merckle *et al*. [23] performed VC with contrast-enhanced CT datasets. Images were acquired in three phases: prior to contrast injection, in the arterial phase during intravenous injection of contrast medium, and in a delayed phase after 30 min. Sedimentation of the contrast medium in the bladder was prevented by the mobilization of the patients. The best visual results were acquired during the delayed phase because of the significant attenuation difference between the bladder lumen and the mucosa. Both conventional and virtual cystoscopy had a 100 % sensitivity rate for tumors greater than 0.5 cm. In 2004, the work of Nambirajan *et al*. [24] and Yazgan *et al*. [25] further strengthened the role of VC with the use of contrast media in the investigation of patients with hematuria and/or bladder tumors. However, the radiation dose, potential allergies to contrast medium, the lack of biopsy specimens, and the reduced sensitivity in detecting tumors (0.5 cm – 1.0 cm) in size remain the primary drawbacks of this procedure [23, 26].

One disadvantage common to all VC methods independent of bladder distension protocol is the inability to precisely depict sessile lesions or wall thickening. Schreyer *et al.* [16] developed an algorithm for color mapping of the thickness of the bladder wall, aiming to ameliorate the accuracy of the detection of subtle masses. To differentiate urine from the bladder wall, contrast medium was given through a catheter. The wall thickness was defined as the shortest distance between a voxel on the inner wall and any voxel on the outer wall. After setting a color scale for the thickness data, the surface could be visualized with different colors depending on the variant wall thickness. The results of this technique were in agreement with those from conventional cystoscopy. Fielding *et al.* [27] used color mapping of bladder wall thickness in an effort to find a correlation between wall thickness detected by VC and the possible presence of tumors [27]. They demonstrated that when VC images showed a bladder wall thickness of less than 5 mm the possibility of tumor on conventional cystoscopy was 10 %, whereas areas of bladder with a wall thickness greater than 5 mm had an 80 % possibility of revealing a suspicious region on conventional cystoscopy. The authors suggested that flexible or rigid cystoscopy would be obviated if virtual CT cystoscopy was negative.

As indicated, one of the major disadvantages of CT VE is the radiation dose. With the aim to minimize the hazard of ionizing radiation, several researchers compared VC at regular (240 mAs) versus reduced (43 mAs–70 mAs) milliampere settings [28, 29]. They demonstrated an almost equivalent rate of sensitivity (94 % – 100 %) and specificity (100 %) regardless of the reduced milliampere settings. They also succeeded in minimizing the effective dose to less than 0.5 mSv [29], making the VE technique appropriate for long-term follow-up studies. In the earlier work of Homer *et al.* [30] the average effective dose of CT urography was 4.95 mSv compared with 1.48 mSv used in intravenous urography.

As far as complications are concerned, Song *et al.* [17] were the first to report a bleeding complication without any clinical sequela during VC, related to catheter removal. This is the only complication traced by our review, which indicates the high safety profile of VE.

The published experience of VC also includes MRI-based studies. A high consistency of MRI-based VC in the depiction of bladder tumors has been reported [31]. A comparison of MRI and CT cystoscopy with axial CT images and conventional cystoscopy for the detection of bladder tumors validated that the findings at MRI cystoscopy concurred with those of conventional cystoscopy [32]. When compared with axial images and CT cystoscopy, MRI cystoscopy did not reveal any significant difference in the detection of polyps that were larger than 1 cm. However, MR cystoscopy showed decreased sensitivity and specificity in the detection of polyps smaller than 1 cm and the entire process turned out to be expensive and protracted.

Frank *et al.* [33] were the first to introduce 3-D CT-based endoscopy of a neobladder. Fifty-four patients undergone bilateral ureteroileal anastomosis were examined with an electron beam CT scanner. The visualization of the pouch, nipple, afferent ileal limb and ureters was feasible, whereas conventional cystoscopy could not reach these structures. Therefore, VC could be used in the evaluation of patients with bladder substitutions and unusual urinary tract symptoms [34].

5 Virtual urethroscopy

Yekeler *et al.* [35] recently reported an evaluation of urethral strictures with contrast-enhanced 3-D MR voiding urethrography. They carried out gadolinium-enhanced MRI of the bladder and urethra during voiding in both five healthy volunteers and 18 male patients with urethral disease. The authors evaluated the visualization of both normal anatomy and the presence of strictures along the prostatic, membranous, bulbous and penile segments of the male urethra. All the pathological findings detected in the virtual reconstructed images were identical to the ones revealed by conventional urethroscopy. Three-dimensional MR urethrography was superior in the depiction of membranous urethral strictures and in the imaging of strictures of the distal urethra that could not be documented by traditional retrograde urethrography. The technique proved to be excellent in visualizing normal urethral anatomy and promising in evaluating the entire male urethra. However, it should be emphasized that overestimation or underestimation of urethral stricture length may occur.

6 VE limitations

We should stress that the application of VE in the urinary tract presents certain limitations. There are dif-

Table 1. Major advantages and principal drawbacks of the application of virtual endoscopy in the urinary tract. CT, computed tomography; EBCT, Electron Beam Computed Tomography; MIP, maximum or minimum intensity projection; mAs, milliampere; MRI, magnetic resonance imaging; SSD, shaded surface display; UPJ, Ureteropelvic Junction; VR, volume rendering.

Study	No. of patients [reference]	VE algorithm	Diagnostic goal	Results summary	Limitations and pitfalls
Virtual nephroscopy	32 [9]	CT and SSD	Renal pelvic tumors	Good correlation with pathology. Sensitivity 92 %.	Incapable of detecting infiltration of peripelvic tissues. No information about lesion color or texture. No biopsy.
Virtual ureteroscopy	16 [10]	CT and SSD	Ureteral tumors	Adequate visualization of ureteral tumors and characterization of ureteral strictures. Sensitivity 81 % and specificity 100 %.	Incapable of evaluating transmural infiltration. No information about lesion color or texture. No biopsy.
Virtual nephroureteroscopy	26 [11]	MRI and SSD	Upper urinary tract	Feasibility study. Adequate morphologic assessment of endoluminal obstructions.	Feasibility is limited by the dilatation of the ureter. Artifacts if ureteral diameter < 5 mm.
Virtual nephroureteroscopy	4 [12]	CT and VR	Follow-up of metallic stents in the UPJ	Small series. Depiction of ureteral lumen both cephalad and caudal of an intraluminal stenosis/obstruction.	Unable to provide information about the nature of recurrent stricture.
Virtual ureteroscopy	6 [13]	CT and VR	Follow-up of ureteral metallic stents		
Virtual cystoscopy	13 [18] 73 [19] 3 [20] 6 [21]	CT and VR	Bladder tumors	Less invasive and more comfortable examination. Sensitivity 95-100 % and specificity 87-100 %.	Ionizing radiation burden. Inhomogeneous filling of the bladder with air, CO_2 or contrast may produce artifacts. No biopsy.
Virtual cystoscopy	12 [23] 18 [24] 33 [25]	Contrast-enhanced CT and VR	Bladder tumors	Excellent depiction of tumors > 0.5 cm. Sensitivity 91-100 %.	Intravenous contrast medium and radiation hazards. No biopsy. Reduced sensitivity for smaller (< 0.5 cm) lesions.
Virtual cystoscopy	5 [16] 31 [27]	VC with bladder wall color-mapping	Mucosal thickening and sessile lesions	Sensitivity 80 % and specificity 90 %.	Adequate distention of the bladder required.
Virtual cystoscopy	24 [29]	VC with reduced mAs CT	Bladder tumors	Reduced radiation hazards. Sensitivity 94-100 % and specificity 100 %.	Potential artifacts (holes) in the bladder wall. No biopsy.
Virtual cystoscopy	24 [29] 25 [31] 29 [32]	MRI and SSD	Bladder tumors	Sensitivity 91 %.	Reduced detection rate of tumors < 1 cm. No biopsy.
Virtual endoscopy of the neobladder	54 [33]	EBCT and SSD	Neobladder evaluation	Pilot study. Non-invasive visualization of postoperative anatomy.	
Virtual urethroscopy	18 [35]	MRI and MIP	Urethral strictures	Small series. Reliable depiction of normal and strictured urethra.	Overestimation or underestimation of stricture length may occur.

ficulties in depicting small and flat lesions or mucosal thickening, and it cannot provide biopsy tissue specimens for histopathologic examination. In addition, the bladder must be sufficiently dilated and analysis of both the axial and virtual images acquired is usually essential for optimal evaluation. Unless MRI is used, CT-based VE bears the risk of radiation. Of note, VE images of the ureter cannot be reconstructed if renal insufficiency or high-grade tumor obstruction hinders contrast excretion into the upper urinary tract. However, in cases of endoluminal stenosis or obstruction, VE may permit virtual endoluminal navigation both cephalad and caudal to the stenotic segment. The major advantages and principal drawbacks of our survey of the published reports are summarized in Table 1.

7 Conclusion

To summarize, VE of the urinary tract is a promising diagnostic technique that could be applied repeatedly in the long-term follow-up of patients with ureteropelvic junction obstruction, urinary bladder tumors and ureteral and/or urethral strictures (Figures 1–3). VE provides a rapid analysis of axial raw data and a more perceptive evaluation of hollow organs, especially for clinicians who are less familiar with cross-sectional imaging than radiologists. Reconstruction of VE images may initially detect tumors and suspicious tissue regions and contribute to the selection of patients who should undergo a more thorough evaluation. The technique can also be used in patients who may be poor candidates for conventional endoscopy, such as those with severe urethral strictures or marked prostatic hypertrophy, or in patients with neobladder where cystoscopy is more complicated. The whole procedure of image processing and the production of VE images depends on the experience of the operator and is usually performed in less than 20 min by the majority of specialists. Nevertheless, comparative studies with larger groups of patients are deemed neces-

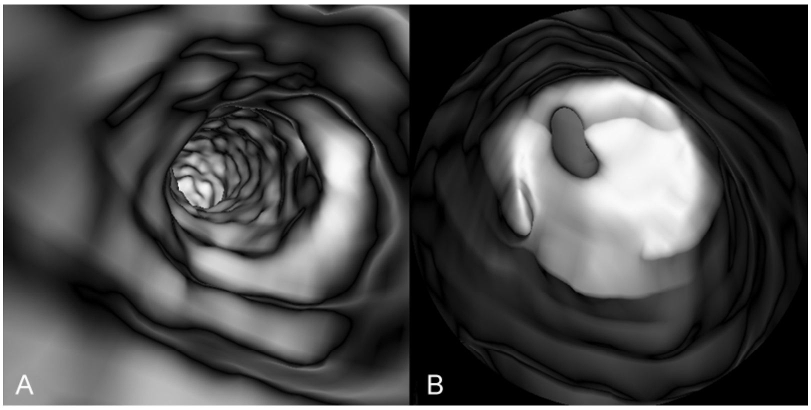

Figure 1. Virtual endoscopy through a ureteral stent. (A): mild hyperplasia of the urethelium protruding through the stent mesh; (B): a virtual endoscopic view towards the proximal end of the stent. A stenosis of the ureter over the stent (trumpet-like functional stenosis) is depicted.

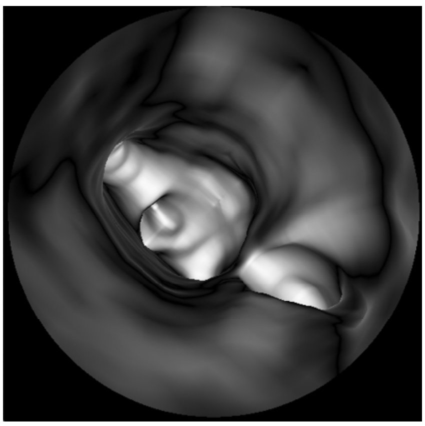

Figure 2. Panoramic virtual endoscopy depicting calyces from the pelvocalyceal system.

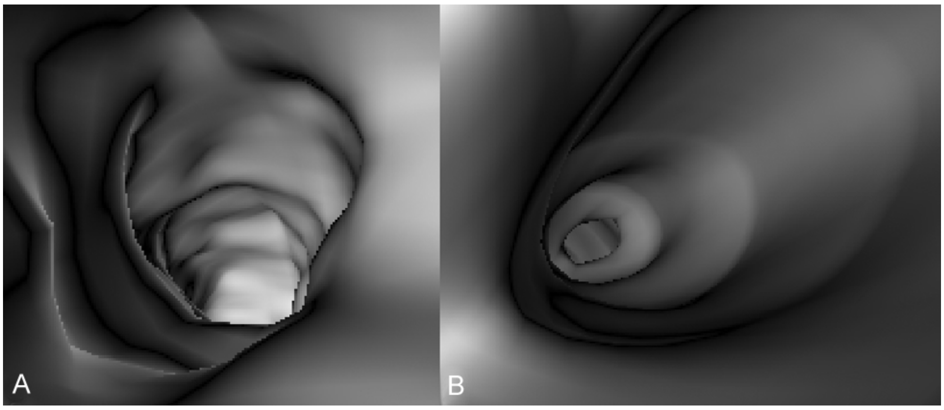

Figure 3. (A): virtual endoscopy of a patent distal urethral lumen; (B): depiction of a concentric distal urethral stenosis.

sary with a view to further validating the diagnostic value and promoting the clinical utility of VE of the urinary tract.

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