# Next-Generation Fiberoptic and Digital Ureteroscopes

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## ARTICLE TITLE

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## KEYWORDS

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## KEY POINTS

• Major technological innovations in ureteroscopy include, but are not limited to bundled optical fibers for flexible image transmission, Rod Lens design for enhanced image quality, active tip deflection and integration of miniaturized digital image sensors.
• Miniaturization of next generation ureteroscopes may decrease primary instrument insertion failure rate.
• Efficacy of ureteroscopy may be improved by warranting constant clear vision. Visibility is intimately related to irrigation flow, which in turn is affected by instruments' and working channel's size.
• Range of motion shall warrant unhindered access to all renal cavities with no exception. Robot-assisted multiple-axis tip defection may achieve this aim.
• Safety of ureteroscopy might be improved by the integration of pressure and temperature control.

## SYNOPSIS

Versatility of ureteroscopy is attributable to tremendous technological innovations over the past decades. An overview on emerging technologies in the light of past achievements, current limitations and possible future directions is provided in this article. Instrument size reduction, pressure and temperature control, active suction of stone dust, multiple-axis tip deflection, variable working channel positions, robotics, ergonomics, image quality, enhanced imaging technology, 3D visualization and the competition between reusable and single-use ureteroscopes are the topics that will be detailed. The 20th century has opened an exciting path for discoveries in ureteroscopy and now, the future is ours.

# Introduction

Ureteroscopy is a widely adopted operation technique for upper urinary tract pathologies. Its current efficacy and safety profile originate from a history of tremendous, continuous and rapid technological innovations. In this article, we present an overview of emerging technologies and current innovations that may possibly define next generation ureteroscopes. Understanding the principles that define current ureteroscopy is key to establish future directions of developments. Therefore, each topic is introduced by a brief summary of current achievements and limitations, before proposing potential solutions.

# From past to present

A chronological summary of the most important past achievements and innovations relating to ureteroscopes is presented in Table 1 [1-15]. Awareness about these developments is essential to help defining next generation ureteroscopes.

# Future directions

## Size reduction

### Anatomical considerations

Retrograde access to the kidney inherently implies to pass instruments within the confinements of the ureter [16]. While this path allows to guide instruments with ease towards the kidney, the ureter also represents a natural bottleneck that dictates the sizing of instruments used in ureteroscopy. Development of the endourological armamentarium has therefore always integrated the necessity of miniaturizing components, with a particular dedication to the design of the tip of ureteroscopes.

### Distal tip design

Several companies provide their ureteroscopes with a tapered tip, allowing a size reduction over a few millimeters at the distal tip (Table 2) (Figure 1-A). Most ureteroscopes are round in cross-section, although some companies have integrated the notion that the ureter is not merely a cylindric tube, but rather a flaccid cavity that may accept any shape of instruments. This observation forms the rationale for providing oval-shaped instruments (Figure 1-B). This design may be advantageous for an optimal and compact orchestration of components within the scope and may also allow for an improved accommodation of the ureteroscope to the angulations of the ureter.

## Scope size

The distal tip of most flexible ureteroscopes is ≤9F (Table 2), which remarkably corresponds to the findings of a study based on CT-scan measurements, where the native ureteral diameter was ≤9F in 96% of all patients [17]. Nevertheless, based on experience from daily practice, most of the currently available flexible ureteroscopes are too large to warrant primary access to the kidney in all patients. Further reducing size of ureteroscopes would therefore lower the rate of ureteroscopic insertion failure, henceforth leading to higher single-session success rates

## Impact of scope size on irrigation flow

Size reduction of ureteroscopes is also key to improve a fundamental determinant for successful ureteroscopy: irrigation flow. To understand this counterintuitive assertion, one should recall the following: an increase in irrigation *inflow* can be easily achieved (e.g. handpumps), but must be compensated by an equal increase in irrigation *outflow* (Figure 2-A) to avoid hazardous increases in intrarenal pressure (Figure 2-B) [18-20]. Most importantly, irrigation *outflow* is dictated by the free space left between the outer contours of the ureteroscope and the inner wall of the ureter. The use of a ureteral access sheath achieves an optimal patency of this free space and therefore achieves a significant improvement in irrigation *outflow* [21-23]. At a constant irrigation *inflow*, this decreases intrarenal pressure (Figure 2-D) [24]. It is not safe to increase the size of ureteral access sheaths as a way to improve irrigation *outflow*, because large-sized ureteral access sheaths entail the risk of serious ureteral wall damages [25]. Henceforth, the ureter must be considered as a fixed anatomical constraint where improved irrigation *outflow* (and therefore overall irrigation fluid turnover in the kidney) goes along with a size reduction of ureteroscopes (Figure 2-C and 2-F).

The necessity of an instrument size reduction as a way of improved irrigation flow becomes particularly valid considering the increasing enthusiasm for high-frequency stone lasering [26,27]. Indeed, when large amounts of stone dust are produced, irrigation is key to maintain uninterrupted clear visibility. This is also valid for conservative management of upper urinary tract tumors, where bleeding from laser vaporization may rapidly preclude visibility if irrigation flow is not sufficient.

## Working channel size

With a few exceptions, the working channel size of currently available flexible ureteroscopes is 3.6F (Table 2). Arguably, reducing the working channel size represents a straight-forward solution to allow an overall size reduction of ureteroscopes. Most certainly, ureteroscopes with a smaller working channel should achieve equally good performance as conventional

3.6F working channel ureteroscopes for stone and tumor treatment. This is exemplified by the fact that pressure levels above 100 cm H20 can be reached despite occupancy of a 3.6F working channel by a laser fiber or a basket [20]. Therefore, it seems that exceeding space should be available to reduce working channel size and still ensure adequate irrigation flow. This assumption becomes particularly valid because ancillary devices such as laser fibers or baskets are expected to become smaller in the years to come. Noticeably, the Thulium fiber laser is being currently explored as an alternative to Holmium:YAG for lithotripsy. This new laser offers the possibility of laser energy delivery through fibers as small as 50 µm, which is substantially smaller than the inferior size limit of fibers for Holmium:YAG (≥ 200 µm) [28].

## Pressure control

### Risks of high pressure

A growing body of evidence suggests high intrarenal pressure as a serious threat for patients undergoing RIRS [29-32]. The underlying physiopathology is not fully understood, but high intrarenal renal pressure has been shown to lead to pyelovenous backflow, forniceal rupture as well as tubular and interstitial intrarenal backflow [18]. Normal intrarenal pressure is approximately comprised between 0 – 10 cm H20 [33]. Gross pyelovenous becomes evident above 40 cm H20 [34]. And forniceal rupture may occur above 80 cm H20, although this has not been verified in humans [35]. Ultimately, high intrarenal pressure has been associated with systemic inflammatory response, septic shock or even death [36,37]. The proposed mechanism is dissemination of pathogens due to backflow.

### Pressure control and irrigation flow

In order to prevent such complications, it appears necessary to integrate pressure control to ureteroscopy. To ensure low intrarenal pressure, one may simply limit irrigation *inflow* pressure. This can easily be achieved by hanging irrigation bags such that the superior limit of saline solution would be less than 40 cm H20 above the level of the kidney. The drawback of this rudimental pressure control is that irrigation flow rate is substantially reduced whenever the working channel is occupied by auxiliary devices, as a direct consequence of pressure loss along the ureteroscope [38]. This explains why irrigation pressure should be modulable in order to maintain sufficient irrigation flow.

### Pressure sensor

A proposed solution for intrarenal pressure control would be to place a pressure sensor within renal cavities during RIRS. Such feedback control would permit continuous modulation of irrigation pressure or irrigation *inflow* rate (“pressure-controlled irrigation”) (Figure 3-A). This concept has already been integrated in a sensor-equipped ureteral access sheath which additionally can control active suction, as a way of increasing irrigation *outflow* [39]. It seems straight-forward that next generation ureteroscopes will be equipped with similar pressure control sensors and will allow pressure-controlled irrigation. The benefit of such devices on operative time and complication rates remains to be demonstrated.

### Pressure control as a limitation

On the short run, pressure-controlled irrigation may be seen as a future limitation to ureteroscopy, since it will most certainly result in an overall reduction of irrigation flow compared to contemporary (possibly excessive) habits of irrigation. This is where size reduction of ureteroscopes will present all its advantages, as it has been exposed above and as it has been illustrated in a study where size-reduction of semi-rigid ureteroscopes achieved an effective reduction of intrarenal pressure [40].

### The hazards of pressure-controlled irrigation systems

A serious hazard of pressure-controlled irrigation systems occurs whenever the urinary tract patency is disrupted (e.g. forniceal rupture or ureteral wall perforation, Figure 3-B). In such cases, irrigation fluid may escape from intrarenal cavities towards the retroperitoneum, leading to a falsely-negative feedback signal from the intrarenal pressure sensor which may in turn result in hazardous excesses of irrigation *inflow*. This may result in unrecognized extravasation of a substantial amounts of irrigation fluid (Figure 3-C).

## Temperature control

### Heat generated by lasers

With increasing power range of newly marketed laser generators, concerns have risen about the risks entailed by temperature dissipation during laser lithotripsy. In several in vitro studies, irrigation fluid temperature rise occurred within seconds after laser activation and reached plateau-phases that were mostly depending on irrigation flow rate and irrigation fluid temperature [41-44]. Damages to tissues (cell death) do not only depend on maximal temperature rise, but also depend on time exposure to high temperature levels [45]. One in vitro study took into account this “thermal dose” effect on tissue and found continuous laser activation during 60 seconds with low power settings (10W) to be safe, even when no irrigation flow was present [42]. At 20W, a minimum irrigation flow of 7-8 ml/min (irrigation fluid at 23°C) was necessary to stay within a safe thermal dose range. At 40W, tissue would theoretically have been put at risk of thermal damage, even if irrigation flow was increased to 14-15 ml/min.

### Temperature sensor to control what?

To date, no reports of thermal tissue damage have been made in conjunction with temperature rise of irrigation fluid during laser lithotripsy in humans, unless laser would be purposely fired in close vicinity with tissue. This raises the question: Should temperature control be recommended for ureteroscopy? Arguably, one may imagine next generation ureteroscopes integrating a temperature sensor at the tip of the instrument. If so, on which parameter would the measured intrarenal temperature impact on and to what extent? Should a feedback control allow for deactivating the laser generator at a given temperature cutoff? Should this control irrigation flow as a way to cool down intrarenal cavities? Should this adapt temperature of inflowing irrigation fluid? An element of response comes from the thermal dose effect theory, which should allow for calculation of a safe laser power range that could be used in conjunction with a given inflowing irrigation fluid temperature and flaw rate. Future studies are warranted to verify the necessity and utility of intrarenal fluid temperature control during ureteroscopy.

## Active suction of stone dust

### What is stone dust?

In recent years, growing enthusiasm for dusting laser lithotripsy techniques has been shared among endourologists, following the observation that stone dust is capable of spontaneous evacuating and therefore discards the necessity of time-consuming stone fragment retrieval [46]. Nevertheless, no study available to date has precisely defined what should be considered to be stone dust. A consequence of this is that clinically significant residual fragments might be left in place after dusting lithotripsy.

### Stone-free dusting

To ensure full clearance of all stone fragments after dusting lithotripsy, it would be desirable to develop a device or a technique capable of active suction of stone dust. The opening diameter of such aspiration device should be in close relation with the size that would define stone dust. At the end of the procedure, active suction of stone dust would allow to identify any remaining residual fragments that would be too large and therefore be at risk not to evacuate spontaneously (Figure 4). We propose this concept as a way of increasing stone-free rates after dusting lithotripsy. Nevertheless, active suction of stone dust through currently available ureteroscopes is not recommended, because clogging of stone dust within the working channel may occur and may cause instrument failure with the necessity of instrument repair. Next-generation ureteroscopes might overcome this limitation and allow safe active suction of stone dust.

## Multiple-axis tip deflection

### One-plane deflection

Historically, flexible ureteroscopes have been developed such that deflection would only be possible in one plane. The rationale for this design comes from the observation that rotation of the instrument's handle permits to orientate the tip of the scope in any other plane. Consequently, for a right-handed operator, posteriorly and anteriorly situated calyces in a right kidney can be visualized by a light supination ~~pronation~~ (Figure 5-A) and extensive supination (Figure 5-B) of the ureteroscope, respectively. The opposite is valid for the left kidney.

### The complexity of renal cavities

Noticeably, the pyelocaliceal system is not to be thought as a system with radiations (calyces) centered on a fixed point (pelvis). Rather, it must be understood as a central cavity (pelvis) with multiple sinusoidal radiations (infundibulum) ending on surfaces (calyces) which may adopt various orientations. This complexity explains why certain renal cavities are not amendable to some ureteroscopes. This has become particularly valid for digital scopes, which have been shown to have a decreased end-tip deflection when compared to fiberoptic scopes [47]. This is caused by the bulky and rigid configuration of the digital camera unit at the tip of digital ureteroscopes. Nonetheless, it appears evident from daily practice that in certain cases, some additional degree of deflection in another plane would have been key for treatment success. The ability of multiple-axis tip deflection therefore appears to be one of the greatest achievements that should be incorporated in next generation flexible ureteroscopes.

## Variable working channel positions

### Anatomical considerations

In line with the consideration outlined above, the success of a given ureteroscopic treatment is dictated by the interrelation between anatomy and proprieties of ureteroscopes. The invariable configuration of the working channel at the tip of the scope remains a problem to be resolved in next generation ureteroscopes. For treatment in a right-sided kidney, gravity will typically displace stones or stone fragments in a 3-o'clock position (Figure 6-A). This location is ideally accessible for accessory instruments inserted in scope with a WC at about 3-o'clock (Table 2). The opposite is valid for a left-sided kidney, where scopes with a WC at about 9-o'clock offer a better access (Figure 6-B). Implementation of the ability to vary the position of the working channel at the tip of the scope would therefore be a major future improvement.

### Memory of the deflection axis

The earlier depicted concept of multiple-axis tip deflection may represent a viable solution for variable working channel positions: if next generation ureteroscopes would be able to memorize and maintain a given position, then a simple rotation of the scope's shaft would make the working channel rotate in the field of view without any change of the position deflectable tip within the kidney. This concept is reminiscent of robotic arms used in laparoscopy, where the needle driver can be rotated such as the position of the arm remains unchanged within the pneumoperitoneum (referred to as EndoWrist® technology by Intuitive Surgical®).

## Robotics

### Definition of a robot

A robot can be either understood as a device capable autonomous or automated operability based on the interpretation of information captured by sensors, or as a device that can mimic, assist or augment human's hand's range of motion and skills. For ureteroscopy, the former can be rudimentary exemplified by an irrigation device capable of intelligent control of intrarenal pressure [39]. The second definition of a robot would correspond to a device capable of influencing the motion and function of a ureteroscope based on tactile, visual or auditive inputs emanating from a human being.

### Limitations of current platforms

Historically, two platforms have been developed for robot-assisted ureteroscopy: The Sensei®-Magellan (Hansen Medical Inc., CA, USA) and the Roboflex™ Avicenna (ELMED®, Ankara, Turkey). The former was initially designed for angiographic purposes. First report about its adaptation for robot-assisted ureteroscopy in humans was made 2008, but any further development of this platform has been discontinued [48]. The Roboflex™ Avicenna has been CE-marketed in 2013, after having proved to ensure feasibility and safety of robot-assisted ureteroscopy feasible [49-51]. The operator sits at a console and steers two joysticks or a central wheel which enable deflection, rotation, insertion and retraction of a ureteroscope. A touch screen and foot pedals additionally allow to change speed of movements and can advance, retract and activate a laser fiber. Improved operator's comfort and reduced radiation exposition have been named as possible advantages, compared to conventional ureteroscopy [49]. Unfortunately, both Sensei®-Magellan and Roboflex™ Avicenna platforms failed to offer any serious advantage in terms of maneuverability. This is because these platforms robotically steer the very same ureteroscopes that can be manipulated by bare hands. In experts' hands, these robotic platforms may therefore even represent a disadvantage, because the tactile feedback of the scope is missing. Other limitations are the acquisition and maintenance costs, as well as the space requirements within operating facilities. These limitations may explain why robotic platforms for ureteroscopy have not been widely adopted by endourologists yet.

### The robotic ureteroscope

Robotic next generation ureteroscopes should aim at offering more sizable advantages over conventional ureteroscopes. Most importantly, this should include an augmented range of motion of the deflectable tip. A scope capable of multiple-axis tip deflection, as proposed earlier, would perfectly exemplify robot-assisted ureteroscopy: the operator would navigate along the upper urinary tract by the means of a hand-held control that could be freely moved in space, then transmitting the positioning information to a software that would transmit the calculated range of movement to the robotic ureteroscope. The latter would then position itself in the intended position, as long as the range of motion of the multiple-axis tip deflection would allow it. Such hand-held controls should also ideally integrate haptics (force feedback) to prevent any hazards such as organ perforation or ureteral avulsion. Alternative or additional controls would be visual or auditive signals. A rudimentary example for an auditive control would be to modulate irrigation flow by vocal orders to the robotic platform. A rudimentary example for a visual control would be to activate narrow band imaging upon a short period of rapid blink of the operator's eyes.

## Enhanced ergonomics

### The look in the eyepiece

The handle of a flexible ureteroscope is conventionally held by the dominant hand at the level of the thorax, with the operating shaft exiting on its lower part. The deflection mechanism is conventionally found at the upper part of the handle and is steered by the thumb [52]. This design originates from the historical necessity of the operator to visualize the image brought by optic fibers through the eyepiece at the top of the instrument's handle. Nowadays, the necessity to look directly in the eyepiece has been waived, as the image can either be caught by a camera fixed at the eyepiece of fiberoptic scopes, or by an image sensor at the distal tip of digital scopes [53]. It thus appears surprising that the design of the handle has remained unchanged for the last decades, with one exception being the PolyScope which is to be held like a syringe [54].

### Weight of ureteroscopes

Despite their similar construct design, weight of currently available ureteroscopes greatly varies: 309 to 352 g (mean 335 g) for fiberoptic ureteroscopes and 278 to 943 g (mean 700 g) for digital ureteroscopes [55]. Another 266 to 798 g (mean 447 g) have to be added to fiberoptic scopes when a camera head is attached to the eyepiece. These weight differences have been associated with decreased muscle activity in favor of lighter ureteroscopes [56]. Ultimately, reduced muscle strain may prevent fatigue of the operator and increase surgical productivity, as has been found in a study on ergonomic stance during laryngoscopy [57]. While such ergonomics-related productivity advantage remains to be demonstrated for ureteroscopy, weight differences between scopes might have represented an element of explanation why digital ureteroscopes led to significantly shorter operative time in several clinical studies [58-60].

Summarily, the design and ergonomics of next generation ureteroscopes could be completely rethought. This becomes particularly valid if robot-assisted ureteroscopy as exposed above was to become available.

## Image quality

### Optical image transmission

Apart from maneuverability proprieties, image quality is a key factor affecting efficacy, safety and versatility of ureteroscopy. The first major advance opening the path to flexible endoscopy was bundling of optical fibers between the distal tip and the proximal eyepiece [2]. This pivotal innovation – along with the Rod Lens construct found in rigid ureteroscopes – has been brought by Harold H. Hopkins [3]. Thin, flexible glass fibers were covered by a cladding with low refraction index, allowing for light transmission over a long distance with minimal losses. For illumination purposes, light is transmitted non-coherently through fiber optics. For image caption, the bundle of glass fibers must be orchestrated coherently in order to produce an identical matrix of glass fibers at both ends of the instrument.

### Electronic image sensors

The next pivotal innovation were electronical image sensors such as charge-coupled device (CCD) or complementary metal–oxide–semiconductor (CMOS) sensors [53]. These sensors transform light (photons) into electron charges that create voltage-depended signals captured by semiconductors. Each sensor is composed of an array of single photo-units (pixels) capturing primary colors: red, green and blue (RGB). After software processing, these pixels finally produce a digital image. One of the greatest advantages of these image sensors is the possibility to transport images for distant projection (e.g. on a liquid crystal display (LCD)). Miniaturization of image sensors has eventually allowed for their integration at the very tip of ureteroscopes, thus palliating any image quality losses conveyed by optical fibers. A parallel development was the replacement of optical fibers by light emitting diodes (LED) for light transmission.

### From fiberoptic to digital technology

The replacement of optical fibers by a few electronic cables within the shaft of the ureteroscope theoretically represents a space sparing which could allow for a size reduction of ureteroscopes. Paradoxically, the smallest currently available ureteroscope is based on fiberoptic technology (Table 2). This is explained by the currently rather bulky design of the digital image sensor unit at the tip of the instrument, which has also been shown to cause significant loss of end-deflection [47].

Comparatively, digital ureteroscopes achieve better image quality than fiberoptic ones [61]. This superiority may represent an element of response as to why digital ureteroscopes achieved significantly shorter operative time in several clinical studies [58-60]. As for detection of upper tract urothelial carcinoma, most authors agree that digital ureteroscopes seem to achieve better tumor detection, although the potential benefits in terms of tumor recurrence rate and survival remains to be established [62].

Next-generation ureteroscopes are likely to integrate ultra-miniaturized digital image sensors with increasing image resolution catching up with current display resolution standards such as “Full HD” (1920×1080 pixels) or “4k” (4096×2160 pixels). The 1:1 ratio of images brought by current digital ureteroscopes might be changed to another format. Finally, one may question whether fiberoptic ureteroscopes may present any residual advantages in future.

## Enhanced imaging technology

Because upper tract urothelial carcinoma (UTUC) is amendable to ureteroscopic management, real-time image enhancement technologies have been integrated to ureteroscopes aiming at a better tumor differentiation. These technologies include narrow-band imaging (NBI), photodynamic diagnosis (PDD) and 1-S technology (formerly SPIES).

### Narrow-band imaging

The concept of NBI was first conceived in 1999 [63]. To understand its mode of operation, three basic principles have to be understood: First, the light source (usually a Xenon lamp) is color-filtered to illuminate tissues with only two bandwidths: 415 nm (blue-violet) and 540 nm (green). These two bandwidths correspond to two distinct absorption peaks of hemoglobin [64], such that poorly-vascularized tissues will reflect a substantially higher proportion of the emitted narrow-band light compared to highly vascular tissue (Figure 7-A). Second, the reflected light is selectively recorded by a camera as follows: 415 nm bandwidth signals (blue-violet light) are assigned to the blue and green color channel; 540 nm bandwidth signals (green light) are assigned to the red color channel [63]. Consequently, the final image on an LCD display has a different color scheme than the actual light that is reflected by tissues. Third, the depth of light propagation in tissues is associated with its wavelength: the longer the wavelength, the deeper the propagation and the less scattering in superficial tissue. Therefore, the 415 nm light will mainly be scattered within and reflected by superficial tissues, thus accounting for the fluorescent-like blue-green shine of the mucosae in the processed image on LCD. In highly-vascularized tissues, the 415 nm light will be mostly absorbed by hemoglobin after scattering, while the 540 nm light will propagate deeper through tissues, thus revealing highly-vascularized tumors in red in the processed image on LCD. This difference in tissue penetration also explains the brownish appearance of superficial capillary networks (e.g. carcinoma in situ) and the cyan appearance of thicker blood vessels in deeper connective tissues. The net result of these three principles is a contrast enhancement that may help in the recognition of highly vascularized tumors [65].

### Photodynamic diagnosis

The PDD also relies on contrasting tumor tissue with normal tissue. For this, a fluorochrome – typically porphyrin-related fluorochrome 5-aminoaevulinic acid (5-ALA) and its derivate hexaminolevulinate (HAL) – is accumulated in cells with high metabolism that are going to be revealed by endoscopic illumination with a blue-violet color spectrum (380-470 nm). This blue-violet light excites the fluorochrome, which will later emit a photon when relaxation of the fluorochrome occurs. This photon is characterized by a longer wavelength, thus producing a different color (red-pink). Consequently, highly metabolic tumor tissue is revealed by its red-pink fluorescence.

### Spectral light modulation

It should be noted that both NBI and PDD are not amenable to ureteroscopes that rely on illumination by LEDs, as the spectral range LEDs cannot be modulated. It remains of interest to point at the three colors emitted by an RGB LED: peaks are typically found at 625 nm (range 620-630) for Red, 525 nm (520-230) for Green and 425 nm (420-430) for Blue [66]. It therefore seems conceivable that specific LEDs could be manufactured to allow tissue enhancement in next generation ureteroscopes.

### 1-S technology

The 1-S technology is based on the re-processing of the image captured by the digital sensor in order to enhance contrast domains that impact on human’s eye interpretation of the rendered image. It does not necessitate a modification of the white light spectrum and therefore any light source can be used for illumination. Of the five available re-processing modalities, the so-called Clara+Chroma mode has been revealed to reach a significantly better subjective image quality score in vitro [67].

### Multimodal image enhancement

Compelling evidence for superiority in terms of tumor recurrence rate and survival is currently not available for any of the image enhancement technologies presented above [68]. Nevertheless, enhanced imaging shall further be explored for next generation ureteroscopes and shall extend their field of application to urinary stone disease (e.g. stone composition analysis). Multimodal approaches integrating differing imaging modalities may present as a solution for better characterization of tissues [69]. Physical integration of auxiliary devices into ureteroscopes might be amenable. Particularly, optical coherence tomography (OCT) and confocal laser endomicroscopy (CLE) for tumor detection may become readily available technologies if integrated in ureteroscopes.

## 3D visualization

Three-dimensional (3D) visualization has not been integrated to any ureteroscope yet. It is not clear whether this is a consequence of physical constrains rendering the development of such scopes difficult, or rather explainable by a lack of interest of end-users. Should 3D visualization be part of next generation ureteroscopes, it would be of great interest to assess whether this might offer any advantage in terms of therapeutic efficacy and safety. One domain that could take advantage of 3D vision would be the detection of papillary upper urinary tract tumor. Of interest, a recent meta-analysis on studies comparing 3D to 2D laparoscopic and thoracoscopic surgeries found significantly short operating time, lower blood loss and shorter hospital stay in favor of 3D imaging systems [70].

## From reusable to single-use

### Current advantages of single-use ureteroscopes

Single-use flexible ureteroscopes represent a decisive milestone for ureteroscopy in the current decade [71]. Rather than a technological innovation, single-use ureteroscopes have led to a complete rethinking of the operative room logistics [72]. Indeed, they offer the advantages to be readily available, always sterile and without traces of instrument wear. This may prevent postponement of interventions, eliminate the risk of nosocomial infection due to instrument contamination and guarantee full operational (deflection) range of instruments for each operation. Also, single-use ureteroscopes do not require a dedicated sterilization process which may be associated with unrecognized supplementary costs and inadvertent breakage of scopes. Additionally, their implementation for treating locations that involve forcing maneuvers may cap the risks entailed by eventual instrument damages and repair costs of reusable scopes. In terms of quality, some of the currently available single-use ureteroscopes have visibility and maneuvering proprieties comparable with contemporary digital reusable flexible ureteroscopes [73].

### Further potential advantages

Further potential advantages of next generation single-use ureteroscopes should be explored: for instance, a given manufacturer could provide his scope in a declination of various working channel positions (e.g. scopes with a 3 o'clock WC for interventions on the right kidney and scopes with a 9 o'clock WC for interventions on the left kidney, respectively (see previous sections and Figure 6)), therefore considerably enhancing versatility for the end-user at no additional price.

### A single-use future

Considering the above, it is conceivable that next generation ureteroscopes are to become single-use-only, therefore entirely replacing reusable scopes. Awareness about sterility issues of reusable scopes and pricing policy will presumably be the pivotal variables determining the timepoint of this shift.

### The hazards of single-use ureteroscopes

The downside of single-use devices is the risk of the appearance on the market of low-cost devices with low built quality. Technical weaknesses of such low-cost devices may become apparent only after repeated use or when facing a challenging case. This might expose the operator at risk of unexpected instrument deficiencies such as spontaneous loss of visions or deflection mechanism failure. Also, because of low instrument replacement costs, surgeons may be tempted to force maneuvering and risk instrument breakage when facing a difficult access to a urinary cavity. Instrument failures may lead to disastrous complications, eventually leading to open surgical extraction of a retained ureteroscope. Therefore, it is of utmost importance to handle single-use ureteroscopes with the same great care as for reusable ureteroscopes. Forcing instruments shall only be done in expert hands.

## Summary

Major achievements and technological innovations from these last decades have shaped what has become ureteroscopy today: a versatile, efficient and safe operation technique for upper urinary tract disease. Necessity for further development of instruments and techniques arises from several domains relating to ureteroscopy: anatomical constraints, intrarenal pressure and temperature, maneuverability and ergonomics of ureteroscopes, image quality, image processing and sterility of instruments. Any addition or improvement to these domains must be ascertained to fulfill its intended advantage with full consideration of its possible secondary hazards. This is an exciting time where emerging technologies are shaping what ureteroscopy will be tomorrow.

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# Tables

**Table 1. Past achievements and innovations relating to ureteroscopes**

| Author(s) | Origin | Year | Achievement or innovation | Details on material | Details on technique |
|---|---|---|---|---|---|
| H.H. Young et al. [1] | US | 1912 (reported 1929) | First ureteroscopy | 9.5F pediatric cystoscope | Inadvertent visualization of the ureter and renal pelvis |
| H.H. Hopkins [2] | UK | 1954 | Bundled optical fibers | A bundle of glass fibers transmits optical images along a flexible axis | Birth of flexible endoscopy |
| H.H. Hopkins [3] | UK | 1959 | Rod Lens design | "Air lenses" are interposed between a series of cylindric ("rod") glass lenses | Substantially enhanced image quality and 4x higher light transmission |
| V.F. Marshall [4] | US | 1960 | First flexible ureteroscopy | 9F fiberoptic ureteroscope, passive deflection, no working channel | Only diagnostic, not therapeutic |
| K. Storz [3] | DE | 1960 | Cold light source | An external light source transmits very bright light through a fiberoptic cable | Solved the previous problem of fragile and heat-generating electric bulbs at the tip of endoscopes |
| H.H. Hopkins [3] | UK | 1961 | Antireflective coating of glass lenses | Coating supporting light to exit lenses instead of being reflected back in the lens | 80x higher light transmission |
| K. Storz [3] | DE | 1967 | Commercialization of Rod Lens cystoscopes | Fully operational cystoscope including a cold light source | - |
| T. Takagi et al. [5] | JP | 1968 | First flexible ureteroscopy with active deflection | No working channel | Only diagnostic, not therapeutic |
| T.M. Goodman, E.S. Lyon [6,7] | US | 1977-78 | First therapeutic ureteroscopy (fulguration of ureteral tumors) | 12-16F dilators, 11F pediatric cystoscope and 14F resectoscope | Limited to the lower ureter |
| H.H. Teichmann [8] | DE | 1979 | First intraureteral lithotripsy | Electrohydraulic and ultrasonic lithotripters | Limited to the lower ureter |
| E.S. Lyon [9] | US | 1979 | First ureteroscopic extraction of urinary stones | 10-16F dilators, 13F pediatric cystoscope, 14.5F resectoscope and stone baskets | Limited to the lower ureter |
| E. Perez-Castro, J.A. Martinez-Pineiro [10,11] | ES | 1980-82 | First therapeutic ureteroscopy including the renal pelvis | 12F rigid ureteroscope, 50cm length, 4F working channel, 0° and 70° | Therapeutic ureteroscopy of the whole upper urinary tract, except for |

| | | | | | |
|---|---|---|---|---|---|
| | | | | Rod Lens optics | lower pole calyces |
| D.H. Bagley [12], G.M. Preminger [13], Y. Aso [14] | US and JP | 1987 | First therapeutic, flexible ureteroscopy | 6.5F up to 13.5F flexible scopes, passive or active deflection, 1.2F up to 6F working channel | Therapeutic flexible ureteroscopy with stone retrieval (basket or forceps) |
| M.R. Humphreys [15] | US | 2008 | First report of about the clinical use of a digital ureteroscope | 8.7F flexible ureteroscope, digital image sensor at the tip, 3.6F working channel, light emitting diode illumination | - |

**Table 2: Characteristics of currently available flexible ureteroscopes**

| Brand | Model | Type | | Tip | | Cross-section | | Scope size* | | Working channel size* | Working channel position* | | | Deflection angulation* (upward/downward) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Fiberoptic | Digital | Flat | Tapered | Round | Ovale | Tip | Shaft | | 3 o'clock | 9 o'clock | Additional working channel | |
| **Olympus** | URF-P5 | x | | | x | x | | 5.3F | 8.4F | 3.6F | | x | - | 180°/275° |
| | URF-P6 | x | | | x | x | | 4.9F | 7.95F | 3.6F | | x | - | 275°/275° |
| | URF-P7 | x | | | x | x | | 4.9F | 7.95F | 3.6F | | | - | 275°/275° |
| | URF-V | | x | | x | x | | 8.5F | 9.9F | 3.6F | | x | - | 180°/275° |
| | URF-V2 | | x | | x | x | | 8.5F | 8.4F | 3.6F | | x | - | 275°/275° |
| | URF-V3 | | x | | x | x | | 8.5F | 8.4F | 3.6F | | x | - | 275°/275° |
| **Storz** | Flex X2 / X2s | x | | x | | | x | 7.5F | 7.5F | 3.6F | | x | - | 270°/270° |
| | Flex Xc | | x | x | | | x | 8.5F | 8.4F | 3.6F | x | | - | 270°/270° |
| **Wolf** | Viper | x | | | x | x | | 6.0F | 8.8F | 3.6F | x | | - | 270°/270° |
| | Boa vision | | x | | x | x | | 6.6F | 8.7F | 3.6F | | x | - | 270°/270° |
| | Cobra | x | | | x | x | | 6.0F | 9.9F | 2 x 3.3F | x | | 12 o'clock | 270°/270° |
| | Cobra vision | | x | | x | x | | 5.2F | 9.9F | 2.4F and 3.3F | | x | 6 o'clock | 270°/270° |
| **Boston Scientific** | Lithovue | | x | | x | x | | 7.7F | 9.5F | 3.6F | x | | - | 270°/270° |
| **Pusen** | Uscope | | x | | x | x | | 9.0F | 9.5F | 3.6F | x | | - | 270°/270° |
| **PolyScope** | | x | | x | | x | | 8F | 8F | 3.8F | x | | - | >250° |

*As given by manufacturer

# Figure Legends

## Figure 1

Comparison of the shape of the distal tip. A: Round and tapered tip (Olympus URF-V2). B: Ovale and flat tip (Storz X$^{c}$). Both ureteroscopes were placed in a 10/12 ureteral access sheath (Coloplast® Retrace®) for demonstration purposes.

## Figure 2

Schematic representation of the relationship between irrigation *inflow*, *outflow*, intrarenal pressure, ureteral access sheath and instrument size. A: Any *inflow* increase must be compensated by an equal *outflow* increase to maintain a stable intrarenal pressure. B: If *inflow* is further increased (e.g. to improve visibility) and *outflow* reaches its maximal transport capacity, then intrarenal pressure will rise. C: At a constant *inflow*, a decrease in intrarenal pressure may be achieved by the use of a miniaturized ureteroscope, because this results in an increased *outflow* transport capacity. D: Alternatively, at a constant irrigation *inflow*, a decrease in intrarenal pressure may be achieved by the use of a ureteral access sheath. E: If *inflow* is further increased (e.g. to improve visibility) and *outflow* reaches its maximal transport capacity, then intrarenal pressure will rise despite the use of a ureteral access sheath. F: Again, at a constant *inflow*, a decrease in intrarenal pressure may be achieved by the use of a miniaturized ureteroscope (analogy to scenario C). UAS = ureteral access sheath.

## Figure 3

The hazards of pressure-controlled irrigation systems. A: As long as the urinary tract patency is conserved, the pump can reliably modulate irrigation inflow according to measured intrarenal pressure. B: In case of disruption of urinary tract patency, irrigation fluid escapes to the retroperitoneum. The pump would then eventually try to compensate a falsely-negative feedback signal from the intrarenal pressure sensor by hazardous increase in irrigation *inflow*. C: This may result in unrecognized extravasation of a substantial amounts of irrigation fluid.

## Figure 4

Aspiration of stone dust. A: Laser lithotripsy of the initial stone mass. B: After a period of lithotripsy, one may find a mixture of stone dust and larger fragments. C: After aspiration of stone dust, larger residual fragments will become apparent. D: These larger residual fragments can now selectively be addressed by laser lithotripsy. E: Residual fragments are now rendered to stone dust. F: Stone-free status could now be achieved by aspiration of stone dust.

## Figure 5

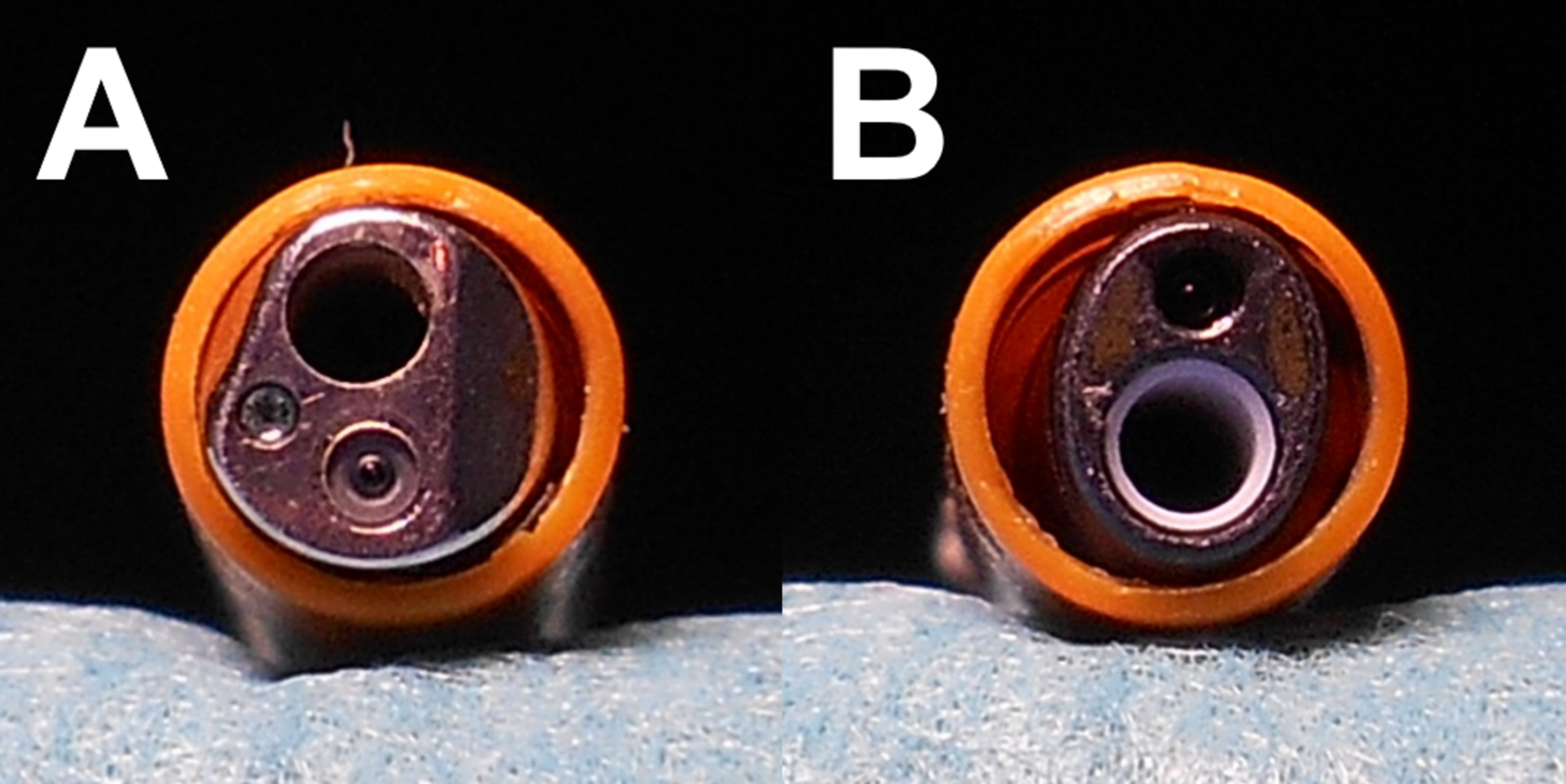
Orienting the deflected scope in another plane. While the deflected scope is within a right-sided kidney, a light supination ~~pronation~~ movement at the scope's handle with give access to posteriorly situated calyces (A), while an extensive supination will give access to anteriorly situated calyces (B).

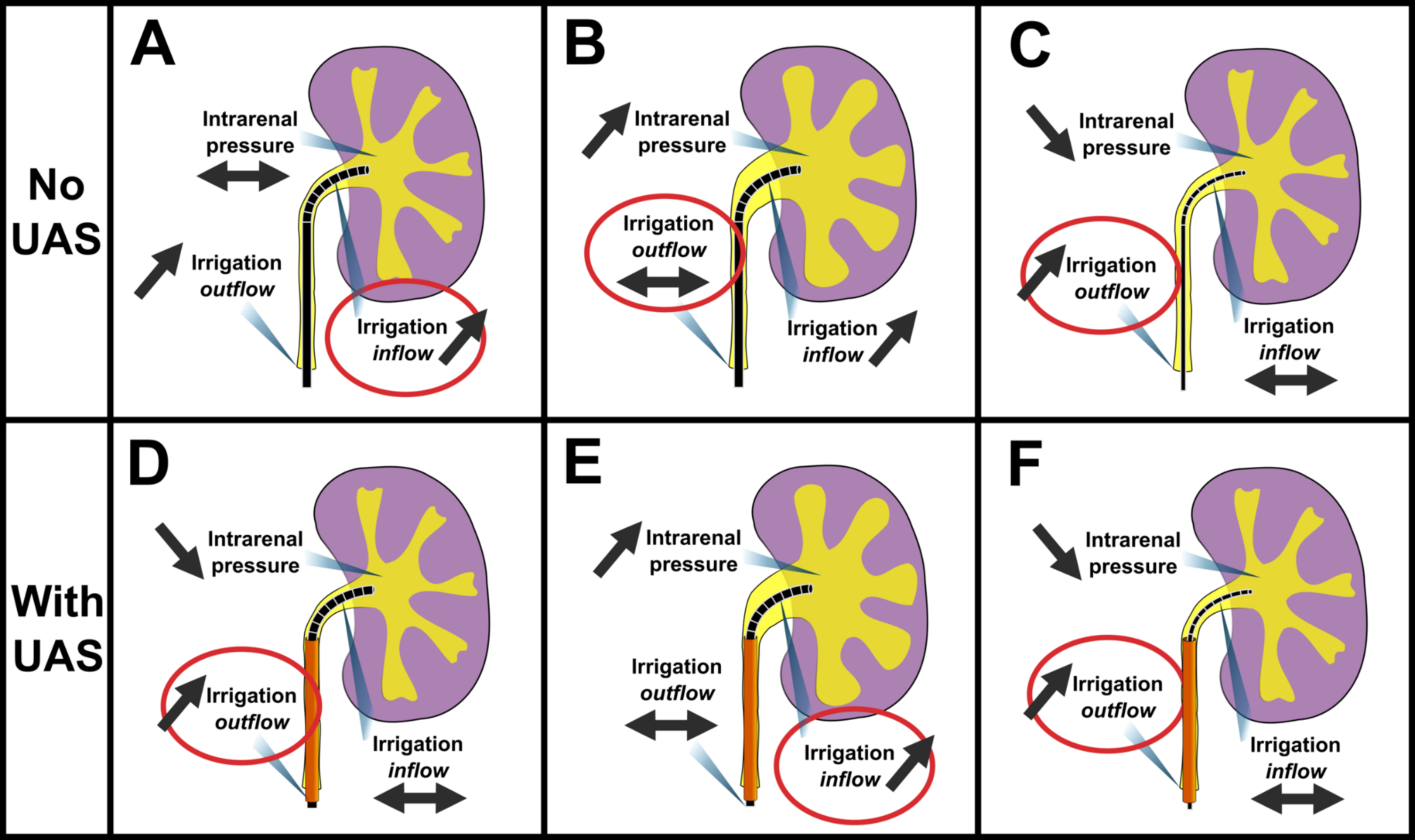
## Figure 6

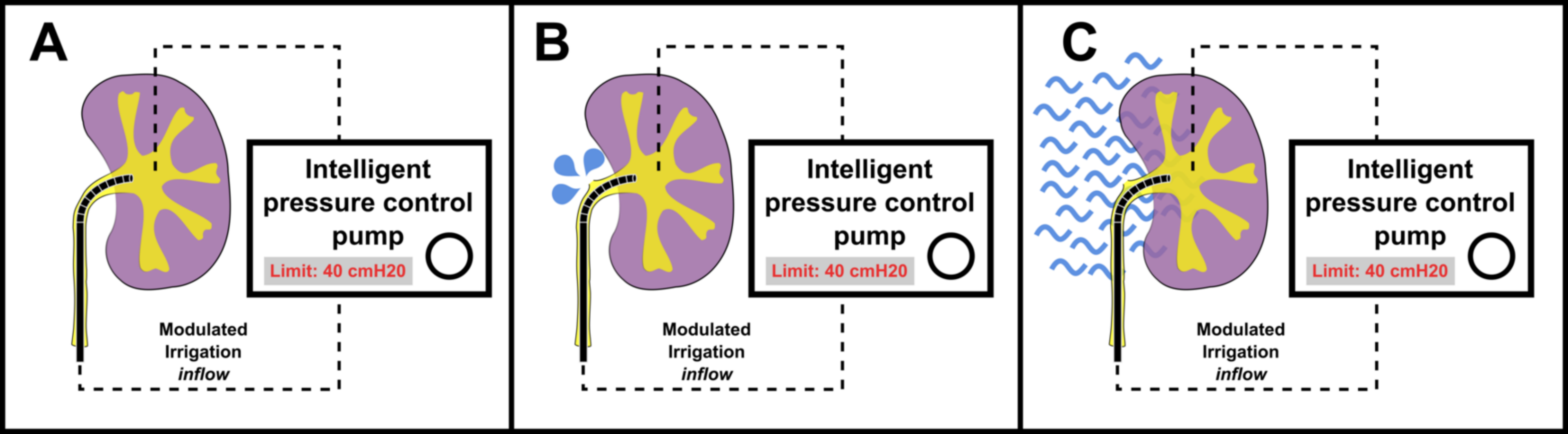
The importance of the working channel position. Gravity will typically displace stones or stone fragments to a 3-o'clock position in a right-sided kidney (A). Stones will be in a 9 o'clock position in a left-sided kidney (B). The respective position of the working channel for a given ureteroscope makes these stones most amenable to laser lithotripsy (blue laser fiber) in either then one or the other side.

## Figure 7

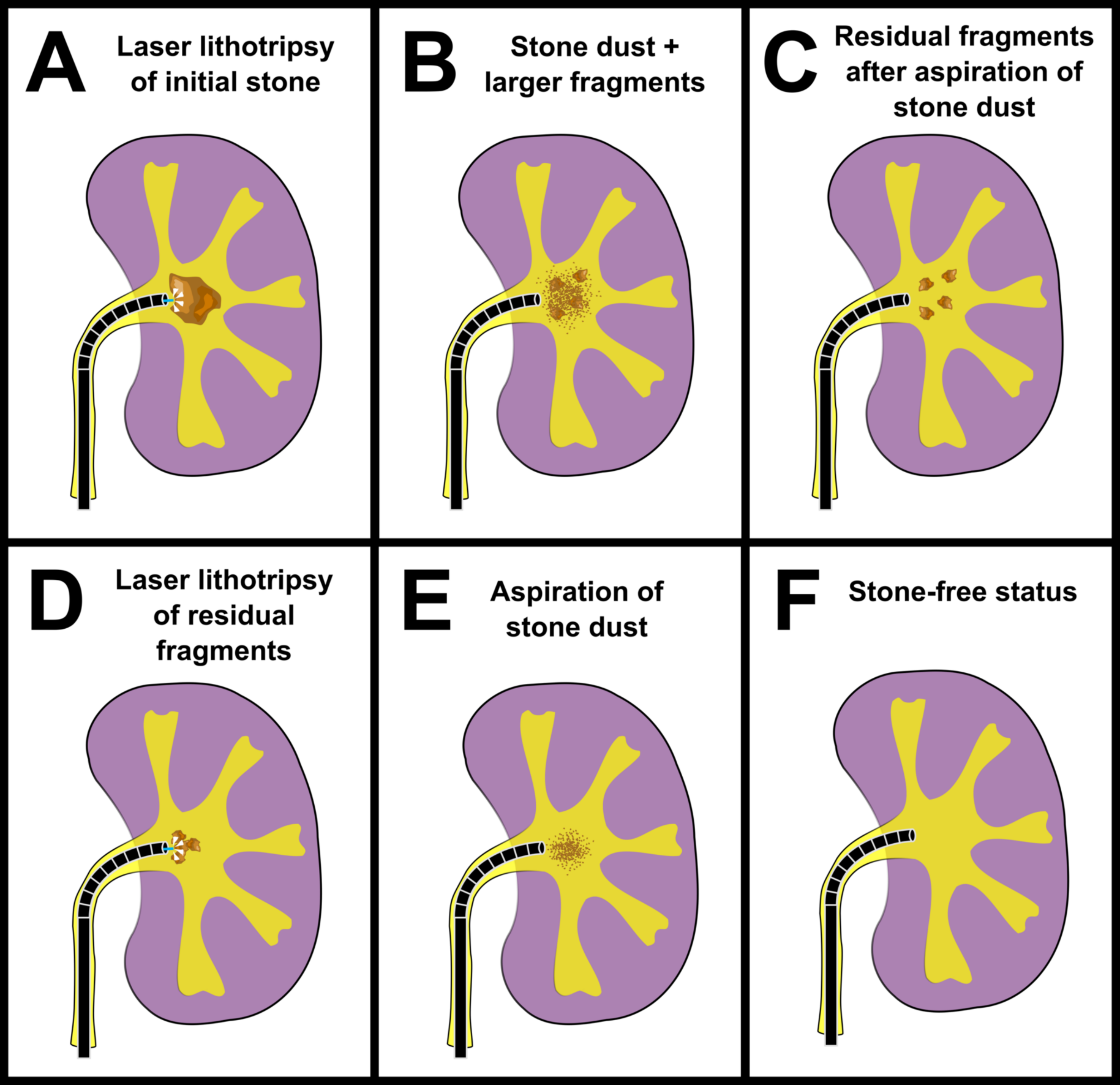
Narrow-band imaging (NBI) and photodynamic diagnosis (PDD): illumination by color-filtered light sources. A: For NBI, two light bandwidths are emitted: 415 nm (blue-violet) and 540 nm (green). These two bandwidths correspond to two distinct absorption peaks of hemoglobin, such that highly-vascularized tissues will reflect a substantially lower proportion of light compared to poorly vascular tissue, especially for blue-violet light which is more subject to scattering in superficial tissues than green light. B: For PDD, light with a spectral range from 380-470 nm is emitted and exits a fluorochrome that accumulates in tissue with high metabolic activity. Upon relaxation of the fluorochrome, a photon with a wavelength corresponding to red-pink is emitted. Highly metabolic tumor tissue can therefore be revealed by its red-pink fluorescence.

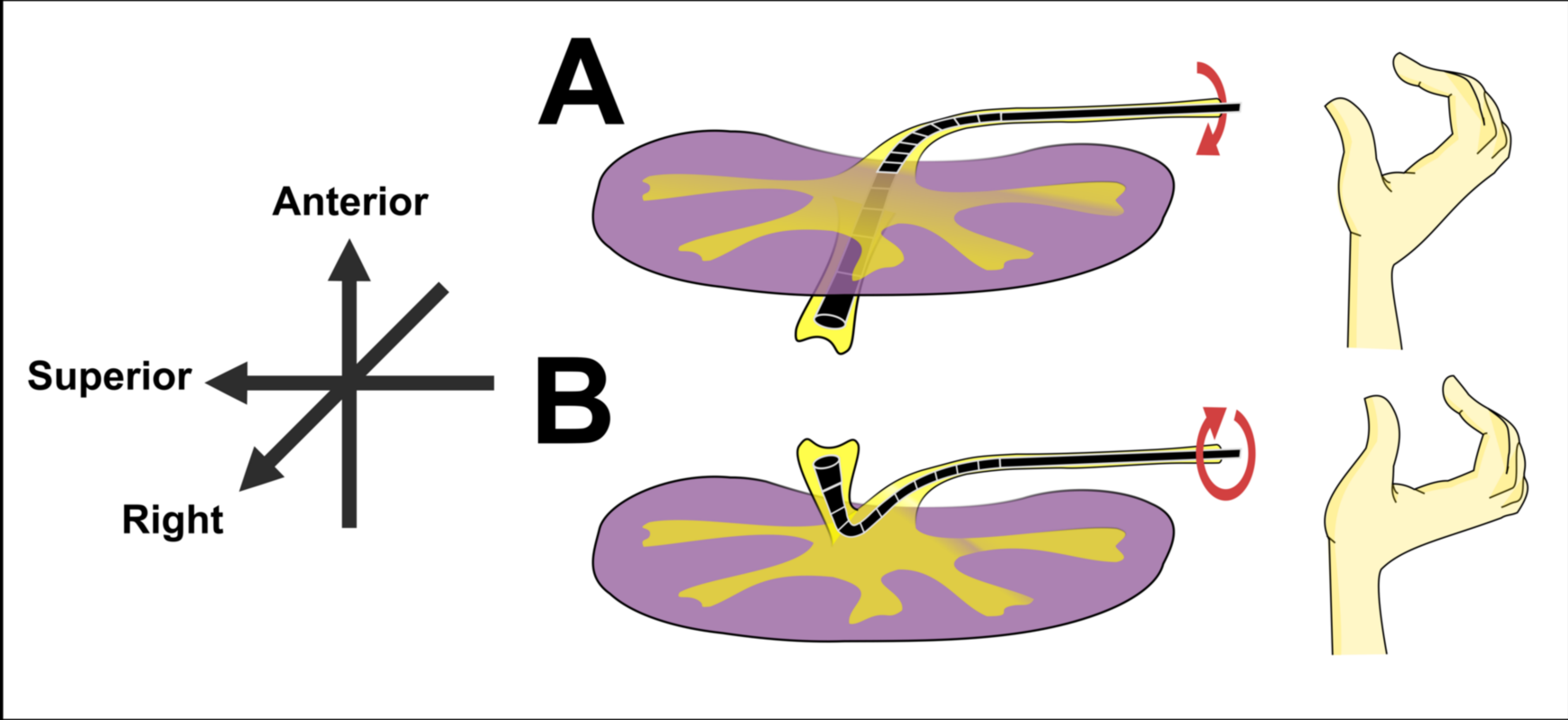

A
B

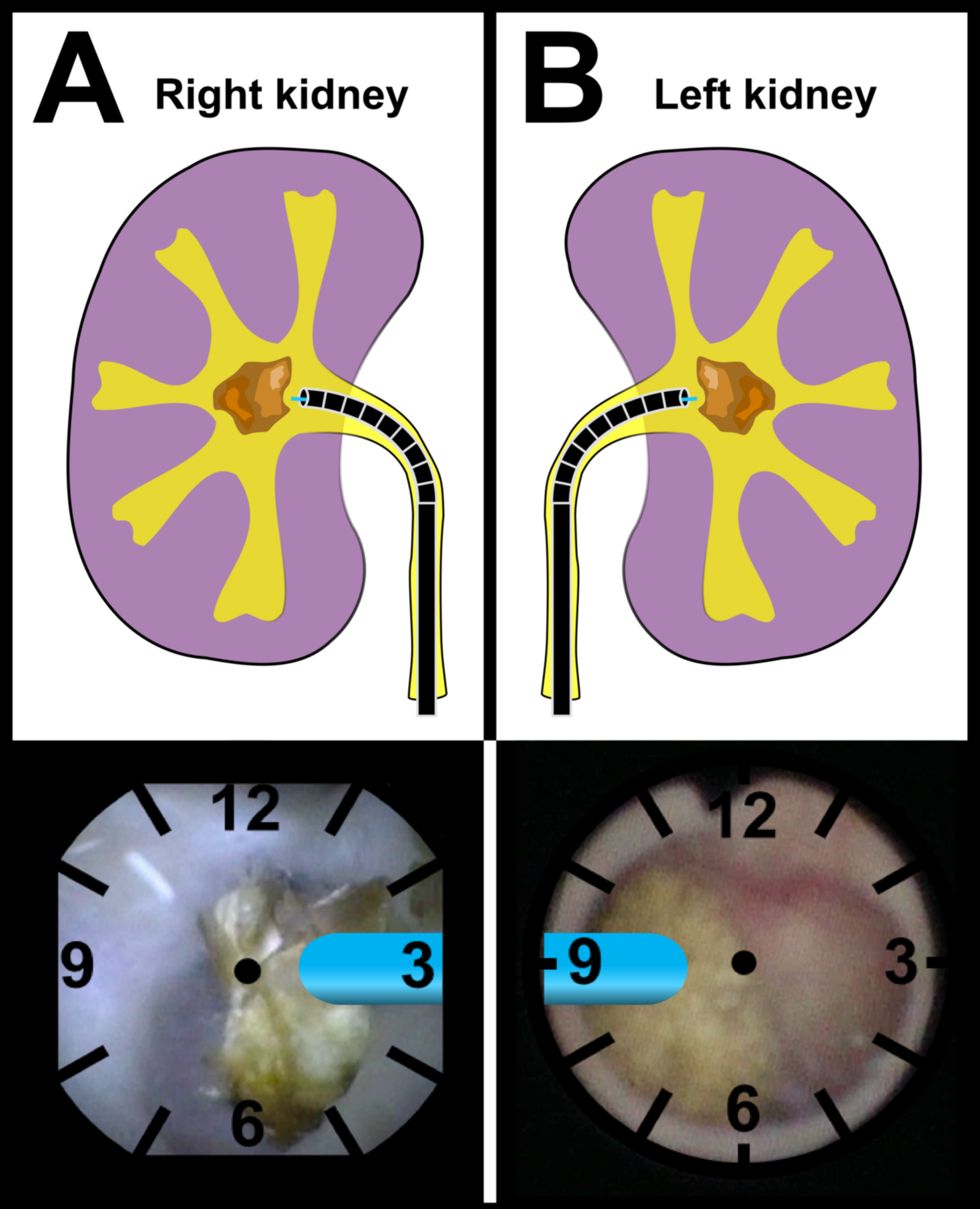

No UAS
With UAS
A
Intrarenal pressure
Irrigation outflow
Irrigation inflow
B
Intrarenal pressure
Irrigation outflow
Irrigation inflow
C
Intrarenal pressure
Irrigation outflow
Irrigation inflow
D
Intrarenal pressure
Irrigation outflow
Irrigation inflow
E
Intrarenal pressure
Irrigation outflow
Irrigation inflow
F
Intrarenal pressure
Irrigation outflow
Irrigation inflow

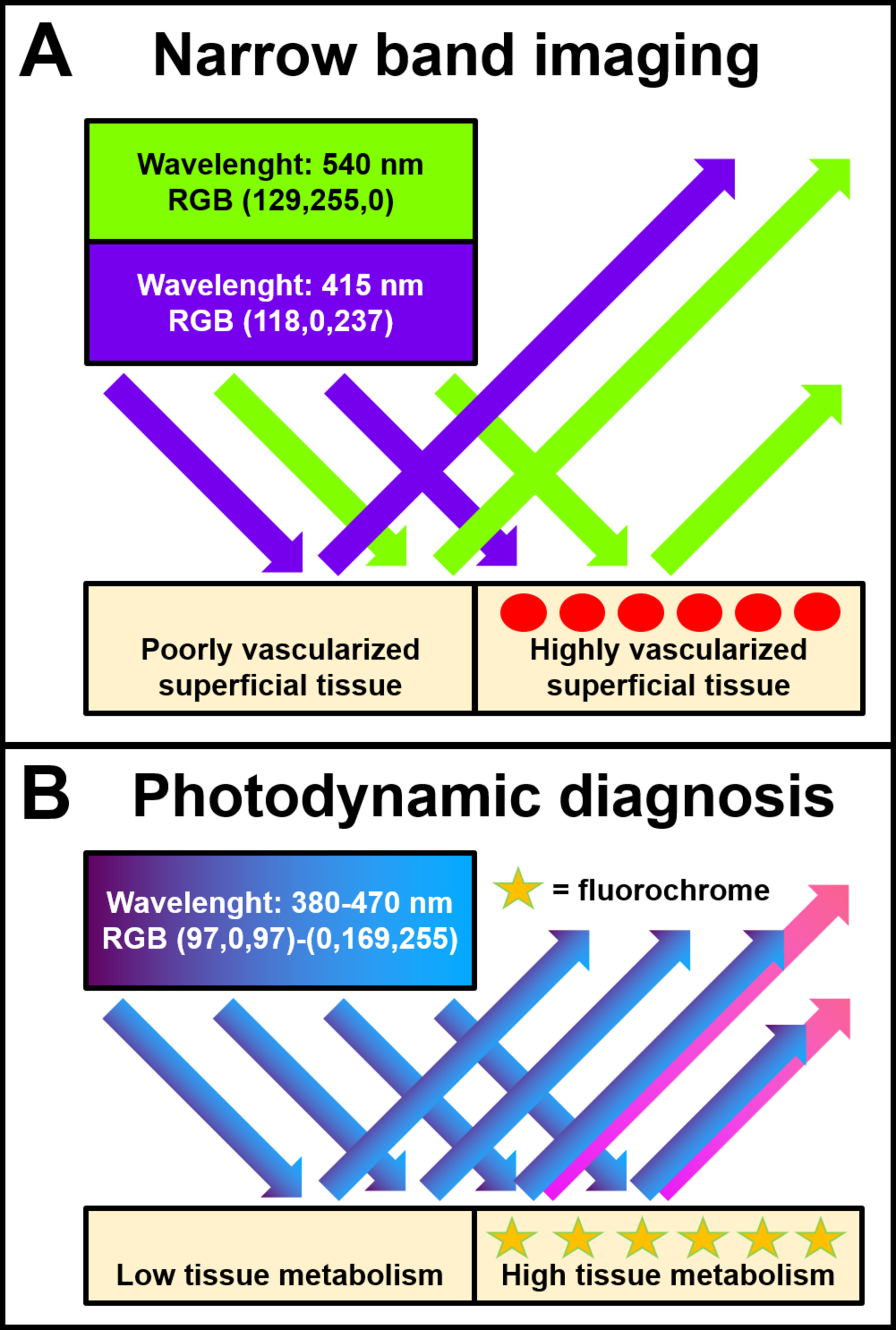


A
Intelligent pressure control pump
Limit: 40 cmH20
Modulated Irrigation *inflow*
B
Intelligent pressure control pump
Limit: 40 cmH20
Modulated Irrigation *inflow*
C
Intelligent pressure control pump
Limit: 40 cmH20
Modulated Irrigation *inflow*


A
Laser lithotripsy of initial stone
B
Stone dust + larger fragments
C
Residual fragments after aspiration of stone dust
D
Laser lithotripsy of residual fragments
E
Aspiration of stone dust
F
Stone-free status


A
B
Anterior
Superior
Right


A
Right kidney
B
Left kidney
12
9
3
6
12
9
3
6


A
Narrow band imaging
Wavelenght: 540 nm
RGB (129,255,0)
Wavelenght: 415 nm
RGB (118,0,237)
Poorly vascularized superficial tissue
Highly vascularized superficial tissue
B
Photodynamic diagnosis
Wavelenght: 380-470 nm
RGB (97,0,97)-(0,169,255)
= fluorochrome
Low tissue metabolism
High tissue metabolism