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Review – Education

Impact of Three-dimensional Printing in Urology: State of the Art and Future Perspectives. A Systematic Review by ESUT-YAUWP Group

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Abstract

Context: Three-dimensional (3D) printing has profoundly impacted biomedicine. It has been used to pattern cells; replicate tissues or full organs; create surgical replicas for planning, counseling, and training; and build medical device prototypes and prosthetics, and in numerous other applications.
Objective: To assess the impact of 3D printing for surgical planning, training and education, patient counseling, and costs in urology.
Evidence acquisition: A systematic literature review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.
Evidence synthesis: After screening, 4026 publications were identified for detailed review, of which 52 were included in the present systematic review: two papers reported the use of 3D-printing modeling for adrenal cancer, two papers for urethro-vesical anastomosis, 24 papers for kidney transplantation and renal cancer, 13 papers for prostate cancer, seven papers for pelvicalyceal system procedures, and three papers for ureteral stents, and three papers reported 3D-printed biological scaffold development.
Conclusions: Three-dimensional printing shows revolutionary potentials for patient counseling, pre- and intraoperative surgical planning, and education in urology. Together with the "patient-tailored" presurgical planning, it puts the basis for 3D-bioprinting technology. Although costs and "production times" remain the major concerns, this kind of technology may represent a step forward to meet patients' and surgeons' expectations.
Patient summary: Three-dimensional printing has been used for several purposes to help the surgeon better understand anatomy, sharpen his/her skills, and guide the identification of lesions and their relationship with surrounding structures. It can be used for surgical planning, education, and patient counseling to improve the decision-making process.

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1. Introduction

Three-dimensional (3D) printing is an additive manufacturing process that has been introduced first in 1986 with photosensitive resin polymerized by a UV light [1]. Since the inception of this new concept, technology has significantly evolved allowing engineers and designers to make 3D models using digital objects. In the following years, several types of manufacturing technologies were developed, enabling the production of 3D objects with different printable materials, ranging from different types of polymers, ceramics, wax, and metals, to human cells [2]. As one of the fastest areas of industry expansion, 3D additive manufacturing profoundly impacted biomedicine. It is not surprising that in the last 15 yr, 3D printing had such a rapid expansion to be considered as a truly disruptive technology in different areas of medicine and pharmaceuticals. Indeed, it has been used to pattern cells; replicate tissues or full organs; create surgical replicas for planning, counseling, and training; and build medical device prototypes and prosthetics, and in numerous other biomedical applications. Moreover, in the era of precision surgery, it is mandatory to find technologies that keep up with surgical improvement [3] to meet surgeons' and patients' expectations. In urology, 3D printing has been used for several purposes to help the surgeon better understand anatomy, sharpen his/her skills, and guide the identification of lesions and their relationship with surrounding structures [4–6].

The aim of the present systematic review is to assess the impact of 3D printing for surgical planning, education, and patient counseling in the urological field as well as its potential impact in translational and clinical medicine.

2. Evidence acquisition

We performed a systematic review of articles limited to the English language, published until December 2017. A full update was performed in January 1, 2019 (Fig. 1). A specific search on MEDLINE, Scopus, and Web of Science databases included "3D printing OR Three-dimensional printing." All studies reporting data of interest were collected. Editorials, commentaries, meeting abstracts, reviews, book chapters, and experimental studies on animal or cadaver were not included in the review. References were manually reviewed to identify additional studies of interest. Two of the authors (G.E.C. and Z.O.) independently reviewed the literature using inclusion and exclusion criteria. Disagreement about

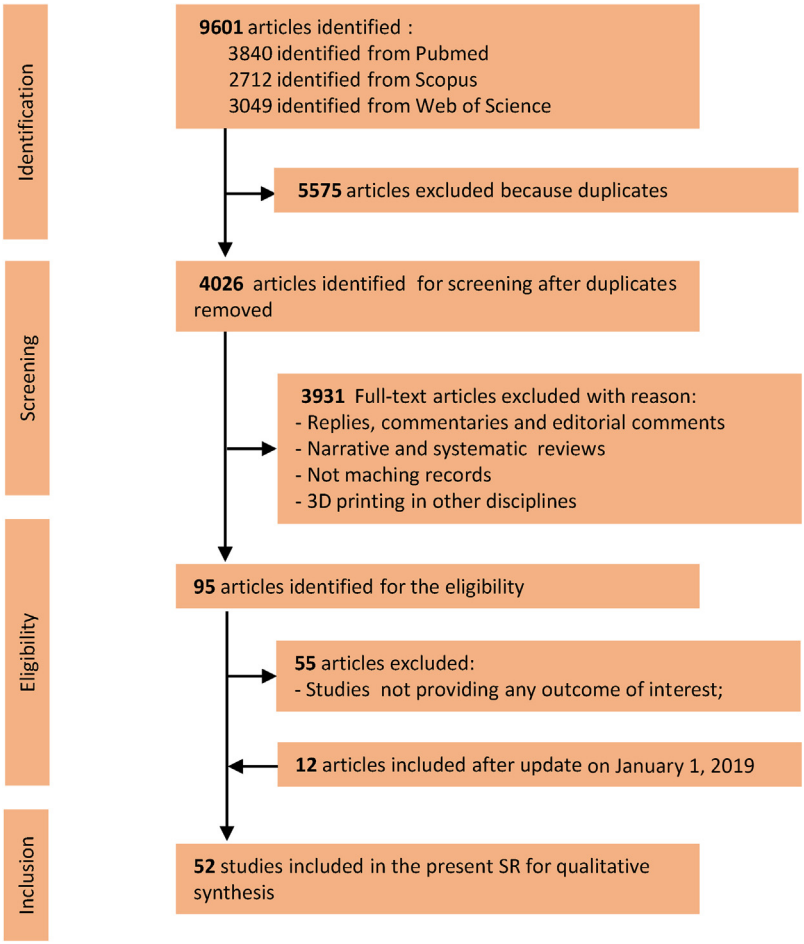

Fig. 1 – Flowchart of the study according to the PRISMA statement. PRISMA = Preferred Reporting Items for Systematic Reviews and meta-analysis; SR = systematic review.

eligibility was resolved by a discussion until a consensus was reached. This study was performed using guidelines set by the Preferred Reporting Items for Systematic Reviews and meta-analysis (PRISMA) statement [7].

All the papers were distinguished according to the 2011 Oxford Centre for Evidence-based Medicine level of evidence for therapy studies: systematic review of randomized or *n*-of-1 trials (level 1); randomized trials or observational studies with dramatic effects (level 2); nonrandomized controlled cohort/follow-up studies (level 3); case series, case-control studies, or historically controlled studies (level 4); and mechanism-based reasoning (level 5) [8]. All data retrieved from systematically reviewed studies were recorded in an electronic database. The protocol was registered in Prospero (CRD42017075886; https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=75886).

3. Evidence synthesis

Our electronic search identified a total of 9601 papers in PubMed, Scopus, and Web of Science (Fig. 1). Of these, 4026 publications were identified for detailed review, of which 52 were included in the present systematic review: two papers reported the use of 3D-printing modeling for adrenal cancer [9,10], 24 papers for kidney transplantation and renal cancer [11–34], 15 papers for prostate cancer [30,34–45] of which two for urethrovesical anastomosis [39,45], seven papers for pelvicalyceal system procedures [46–52], and three papers for ureteral stents [53–55], and three papers reported 3D-printed biological scaffold development [56–58]. Fig. 2A–D depict the studies included in the present systematic review, and the number of correlations found in the literature between organs printed and assessment of the outcomes of interest. This diagram

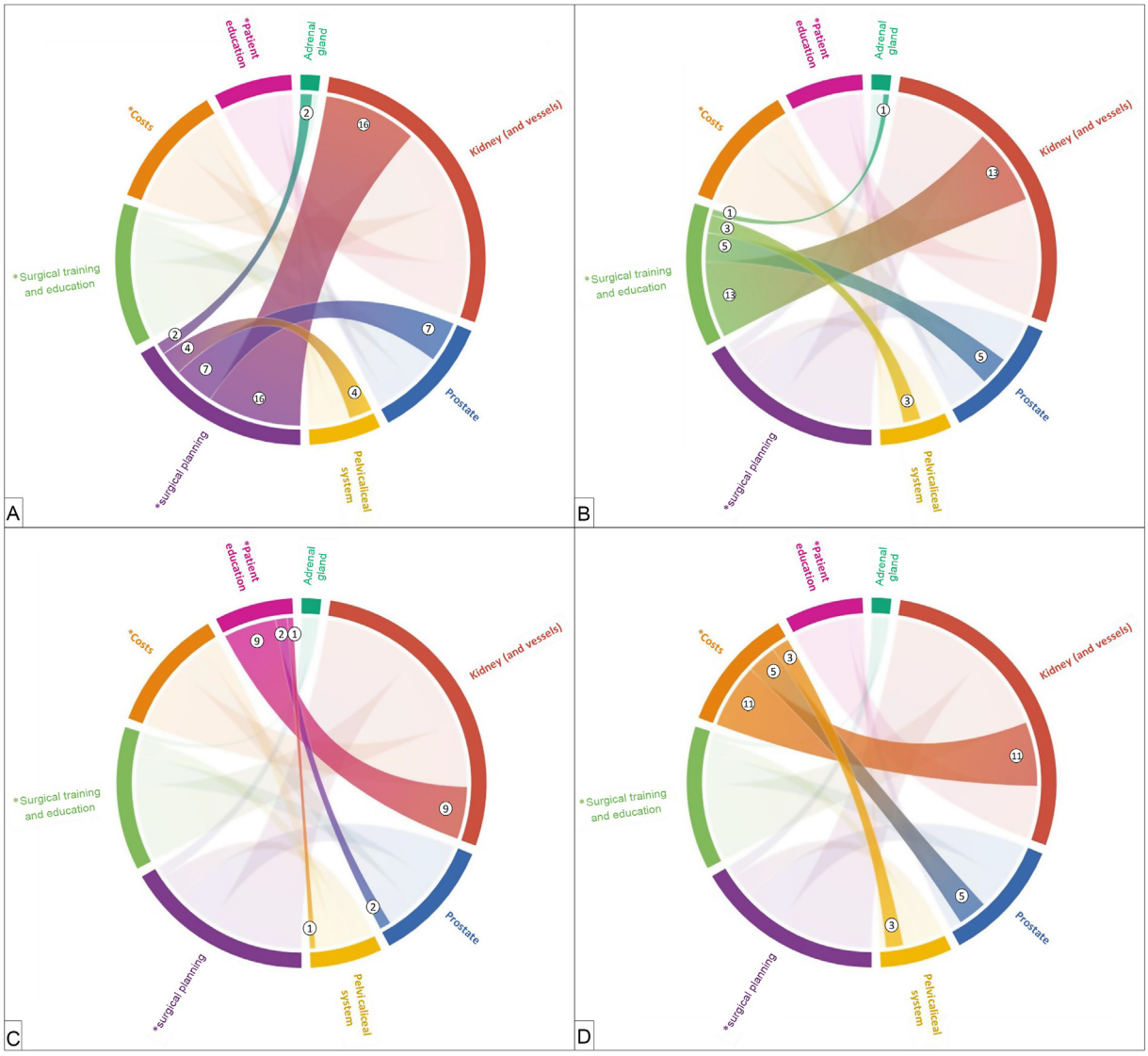

Fig. 2 – Chord diagram of studies associated with 3D-printed organs and outcome domains (*) included in the current systematic review. Connections between 3D-printed organs and outcomes domains (*) represent association. Size of archers represents number of times that associations were studied. (A) Surgical planning. (B) Surgical training and education. (C) Patient education. (D) Costs. An interactive graphical representations of the evidence synthesis chord chart is available at https://public.flourish.studio/visualisation/265059/. 3D = three dimensional.

visualizes inter-relationships between entities. Connections between metrics are used to display that they share outcomes in common. Nodes are arranged along a circle, with the relationships between points connected through the use of Bézier curves. A number of studies reporting a specific comparison represent the values that are assigned to each connection, which is represented proportionally by the size of each arc. An interactive diagram is available at https://public.flourish.studio/visualisation/265059/.

3.1. Pre- and intraoperative surgical planning assessment

Globally, 29 papers reported the "surgical planning" as outcome of interest, of which two evaluated adrenal gland diseases [9,10], 16 kidney disease conditions [11,13,15,16,19–28,30,32], seven prostate cancer [30,35,36,38,40–42,44], and four pelvicalyceal system [47–50] (Fig. 2A). Shin et al. [38] reported that preoperative 3D-printed prostate models facilitate robotic surgeon's understanding of the proximity of the tumor to the prostatic capsule and neurovascular bundles, thereby enhancing both the perceived intraoperative precision and confidence. Souzaki et al. [9] assessed preoperative surgical simulation of laparoscopic adrenalectomy for neuroblastoma (NB) using a 3D-printed model based on preoperative computed tomography (CT) images. The multidetector CT images were transferred to a 3D workstation, and 3D volume data were obtained by reconstructing the sections. Pneumoperitoneum, insertion of trocars, and laparoscopic view were all attainable in this model. This model was applied in three cases with adrenal NB, discussing the port layout before the operation and to simulate the laparoscopic view and range of forceps movement, and all three cases with NB were completely resected without any surgical complications. Golab et al. [15] reported the use of 3D printing for complex renal masses with atrial thrombus. In this case, a 3D mold was used as a valuable interdisciplinary tool to prepare for removal of a giant renal tumor and atrium neoplastic mass. Jomoto et al. [42] reported a surgical navigation system using magnetic resonance angiography and a 3D printer for robot-assisted radical prostatectomy. The combination of these two technologies has been found useful in identifying prostate surrounding structures. The 3D technology has been tested in the stone disease field [59,60]. Li et al. [59] constructed a 3D model of renal stones (RSs) to facilitate comprehensive planning for percutaneous nephrolithotomy (PCNL) and to assist in surgery. A virtual, safe, and reliable percutaneous renal access route was established for each patient by comprehensive planning based on the 3D model of RSs. The 3D models accurately represented the interrelationships between the intrarenal arteries and veins, collecting system, stones, and adjacent anatomical structures. They concluded that building of a 3D model of RSs to minimize the risks of PCNL and achieve higher one-stage stone-free rates is feasible for surgery planning and assistance in patients with complex RSs. The 3D-printing models have been shown to be helpful also in testing new surgical devices to prevent the migration of stone fragments during PCNL [48]. Holding a replica of a patient's anatomy allows the surgical team to be better prepared before entering the operating room. The model presents the pathology that may reveal a solution or possible complication that could not be seen when evaluating a 2D representation [11,16,19,24,25]. Wake et al. [6,25] reported that 30–50% of surgeons changed the surgical approach after visualization of 3D models, and Maddox et al. [23] reported less blood loss in partial nephrectomies planned with physical models. Komai et al. [16] reported their initial experience with a novel style of 3D-printed kidney, which they called "4D" surgical navigation, in 10 patients with a R.E.N.A.L. nephrometry score $\geq$8 renal mass who underwent minimally invasive off-clamp partial nephrectomy. To enhance the advantage of a printed organ, 3D-printed kidneys were herein designed so that the tumor and its margin could be removed. This tumor removability allowed surgeons to preoperatively visualize both pre- and post-tumor resection kidney status, which was termed "4D" surgical navigation. The 3D-printed tumors together with their margins were nearly identical to the surgical specimens. Depending on a 3D printer's ability to match the clinical environment, the model may be used to practice a procedure that involves one or more medical specialties. Often reserved for complicated cases, this can better prepare the team to address risks and difficulties, resulting in more efficient procedures and improved clinical results. Transplant surgery is one of the examples of the multidisciplinary approach of end-stage renal disease. Kusaka et al. [13] developed a 3D kidney graft and a pelvic cavity replica evaluating the usefulness of surgical simulation and navigation of living kidney transplantation. Patients' individual 3D-printed models were used to plan and guide the surgical procedures for laparoscopic donor nephrectomy and recipient transplantation surgery. The details of each patient's anatomy may enable the surgeons to reduce the length of the operation, and provide better anatomical reference tools for tailor-made simulation and navigation of kidney transplantation surgery.

3.2. Education and training assessment

In aggregate, 22 studies reported the use of 3D-printed organs for surgical training and educational purposing, of which one evaluated adrenal gland [9], 13 kidney diseases [11–13,15,17,19,23,24,27–32], five prostate cancer [30,36,37,43,45], and three pelvicalyceal system [46,50,52] (Fig. 2B and Table 1).

Blankstein et al. [61] designed a flexible ureteroscopic model in which bladder, single-calyceal, and double-calyceal models were 3D printed with a translucent, acrylonitrile butadiene styrene-like plastic material, and dyed red to simulate internal color and translucency. The mean postcourse task completion times and overall performance scores were significantly better than those at baseline, and led to improved short-term technical skills among junior-level urology residents. Several studies report the creation of models by casting silicone into a 3D-printed mold, following a process inspired by practical effects for movie productions [21,46]. Adams et al. [50] described the

Table 1 – Studies retrieved from literature research reporting the impact of 3D printing in urology

Author	Year	No. of cases	Organ	Pathology	Procedure	3D imaging	3D printer	Material	Surgical planning	Surgical training and teaching	Patient counseling	Costs	Manufacturing costs
Silberstein et al [11]	2014	5	Kidney	Kidney cancer	Partial nephrectomy	CT scan	NA	Translucent resin	×	×	×		
Knoedler et al [12]	2014	6	Kidney	Kidney cancer	Partial nephrectomy	CT scan	NA	Translucent resin		×			
Cheung et al [46]	2014	27	Pelvicalyceal system + ureter + kidney	Ureteropelvic junction obstruction	Pyeloplasty	NA	Spectrum Z510 3D printer (3D Systems, Rock Hill, SC, USA)	Silicone material		×			
Priester et al [35]	2014	1	Prostate	Prostate cancer	Radical prostatectomy	MRI	Replicator 2 device (MakerBot Industries, LLC)	Polylactic acid plastic	×			×	$4
Souzaki et al [9]	2015	3	Adrenal gland	Adrenal tumor, kidney, renal vein and artery, inferior vena cava, aorta	Adrenalectomy	CT scan	Objet 500 Connex 3 3-D printer (Stratasys, Eden Prairie, MN, USA)	Acrylic ultraviolet curable resin	×	×			
Srougi et al [10]	2015	2	Adrenal gland	Adrenal hyperplasia	Adrenalectomy	CT scan	3D Form 1 printer (Formlabs Inc.)	Translucent resin	×				
Bernhard et al [14]	2015	7	Kidney	Kidney cancer	Partial nephrectomy	CT scan	Objet 500 Connex 3 3D printer (Stratasys)	Photopolymer			×	×	$560
Zhang et al [19]	2015	10	Kidney	Kidney cancer	Partial nephrectomy	CT scan	LaserCore5300 3D printer (Longyuan Rapid Prototyping Ltd, Beijing, China)	Thermoplastic plastics	×	×	×	×	$150
Kusaka et al [13]	2015	2	Kidney and pelvic cavity	Nephropathy	Kidney transplant	CT scan	Objet 500 Connex 3 3-D printer (Stratasys)	TangoPlus/ VeroMagenta	×	×			
Marroig et al [47]]	2015	150	Pelvicalyceal system	Kidney stones	Flexible ureteroscopy	NA	NA	Resin	×				
Wang et al [36]	2015	16	Prostate	Prostate cancer	Target biopsy	MRI	iSLA-450 Pro Stereolithography 3D Printer (Shining 3D Tech Co., Ltd)	Translucent resin	×				
Del Junco et al [53]	2015	6	Ureteral stents	NA	NA	NA	EOSINT P 395 (EOS e-Manufacturing Solutions, Krailling, Germany)	Thermoplastic plastics					
Park et al [54]	2015	1	Ureteral stents	NA	NA	NA	Objet 500 Connex 3 3-D printer (Stratasys)	TangoPlus					
Komai et al [16]	2016	10	Kidney	Kidney cancer	Partial nephrectomy	CT scan	Objet 500 Connex 3 3-D printer (Stratasys)	Biotexture Modeling	×		×		$450–680
Smektala et al [17]	2016	5	Kidney	Kidney cancer	Partial nephrectomy	CT scan	Replicator 2 device (MakerBot Industries, LLC)	Silicone material		×		×	$14.4
Golab et al [15]	2016	1	Kidney	Kidney cancer to the heart atrium	Radical nephrectomy + IVC thrombectomy	CT scan	NA	NA	×				

Table 1 (*Continued*)

Author	Year	No. of cases	Organ	Pathology	Procedure	3D imaging	3D printer	Material	Surgical planning	Surgical training and teaching	Patient counseling	Costs	Manufacturing costs
Woliner-van der Weg et al [18]	2016	1	Kidney and pancreas	Nephropathy	NA	MRI	Objet Eden250 printer (Stratasys)	NA					
Atalay et al [49]	2016	5	Pelvicalyceal system	Kidney stones	PCNL	CT scan or MRI	NA	Acrylonitrile butadiene styrene	×			×	$100
Antonelli et al [48]	2016	1	Pelvicalyceal system	Kidney cancer	PCNL	NA	Stratasys Dimension BST 1200es 3D printing machine (Stratasys Dimension, Eden Prairie, MN, USA)	Acrylonitrile butadiene styrene	×				
Adams et al [50]	2016	NR	Pelvicalyceal system + kidney	NA	NA	CT scan	3Z pro (Solidscape, NH, USA)	UV curable photopolymer VeroClear	×	×		×	Low cost (amount not reported)
Javan et al [37]	2016	1	Prostate	NA	NA	MRI	NA	Polyamide (nylon) material		×		×	$40–100
Shin et al [38]	2016	5	Prostate + NVB	Prostate cancer	Radical prostatectomy	MRI	NA	Translucent resin	×			×	$500
Chu et al [20]	2017	15	Kidney	Kidney cancer	Partial nephrectomy	CT scan	NA	Fommlab Form1	×		×		
Golab et al [21]	2017	3	Kidney	Kidney cancer	Partial nephrectomy	CT scan	Replicator 2 device (MakerBot Industries, LLC)	Silicone material	×	×		×	€100
von Rundstedt et al [24]	2017	10	Kidney	Kidney cancer	Partial nephrectomy	CT scan or MRI	NA	Silicone material	×	×			
Wake et al [25]	2017	10	Kidney	Kidney cancer	Partial nephrectomy	MRI	Connex 500 (Stratasys)	Clear, transparent, flexible material	×			×	$1000
Dwivedi et al [26]	2017	6	Kidney	Kidney cancer	Partial nephrectomy	MRI	Projet 3512HD (3D Systems)	NA	×			×	$161
Atalay et al [51]	2017	5	Pelvicalyceal system	Kidney stones	PCNL	CT scan or MRI	NA	Acrylonitrile butadiene styrene			×	×	
Ghazi et al [52]	2017	1	Pelvicalyceal system	Kidney stones	PCNL	NA	NA	Hydrogel polymer		×			
Wong et al [39]	2017	13	Prostate	Prostate cancer	Urethrovesical anastomosis	NA	Lulzbot Taz 4 3D printer	Polymer		×			
Denizet et al [32]	2018	4	Iliac vessels	Kidney failure	Kidney transplant	CT scan	NA	Elastomeric resin and acrylonitrile butadiene styrene	×	×			
Monda et al [29]	2018	1	Kidney	Kidney cancer	Partial nephrectomy	MRI	Object 260 Connex 3 (Stratasys,)	Silicone material		×		×	$3.90
Uwechue et al [31]	2018	1	Kidney	Kidney failure	Kidney transplant	CT scan	NA	NA		×		×	$1000
Glybochko et al [27]	2018	5	Kidney	Kidney cancer	Partial nephrectomy	CT scan	NA	Polylactic acid	×	×		×	$150–450
Lee et al [28]	2018	10	Kidney	Kidney cancer	Partial nephrectomy	CT scan or MRI	Object 260 Connex 3 (Stratasys)	Photopolymer	×	×		×	$650

Table 1 (*Continued*)

Author	Year	No. of cases	Organ	Pathology	Procedure	3D imaging	3D printer	Material	Surgical planning	Surgical training and teaching	Patient counseling	Costs	Manufacturing costs
Libby and Silberstein [22]	2017	1	Kidney	Kidney cancer	Radical nephrectomy+ IVC thrombectomy	MRI	NA	NA	×		×		
Maddox et al [23]	2018	7	Kidney	Kidney cancer	Partial nephrectomy	CT scan	NA	Photopolymer material	×	×			
Porpiglia et al [30]	2018	18 (10 + 8)	Kidney and prostate	Kidney cancer and prostate	Partial nephrectomy and radical prostatectomy	CT scan or MRI	NA	Photopolymer material	×	×	×		
Wake et al [34]	2018	55	Kidney and prostate	Kidney and prostate cancer	Partial nephrectomy and radical prostatectomy	CT scan or MRI	J750 (Stratasys)	NA			×		
Chandak et al [40]	2018	10	Prostate	Prostate cancer	Radical prostatectomy	MRI	Objet 500 Connex 3 3-D printer (Stratasys)	VeroClear FullCure 810 (UK)	×			×	£250
Wei et al [44]	2018	12	Prostate	Prostate cancer	Radical prostatectomy	MRI	Replicator 5 device (MakerBot Industries, LLC)	Acrylonitrile butadiene styrene	×				
Jomoto et al [42]	2018	6	Prostate + NVB	Prostate cancer	Radical prostatectomy	MRI	MUTOH personal 3D printer MF 2000 (Mutoh, Inc., Osaka, Japan)	NA	×				
Guo et al [55]	2018	1	Ureteral stents	Nutcracker syndrome	NA	CT scan	SLM-250S (EOS, Krailling, Bayern, Germany)	NA					
Schmit et al [33]	2019	1	Kidney	Kidney cancer	Cryoablation	CT scan	Objet350 Connex printer (Stratasys)	Photopolymer			×	×	$400
Qiu et al [43]	2018	1	Prostate	Prostate cancer	Radical prostatectomy	MRI	NA	Silicone material		×			
Ding et al [41]	2019	1	Prostate and bladder	Prostate cancer	Radical prostatectomy	CT scan and MRI	NA	NA	×				
Shee et al [45]	2019	1	Urethra and bladder neck	Prostate cancer	Radical prostatectomy (VUA)	NA	Mojo Desktop 3D printer (Stratasys)	Silicone material		×		×	$50–100

CT = computed tomography; IVC = inferior vena cava; MRI = magnetic resonance imaging; NA = not available; NR = not reported; NVB = neurovascular bundle; PCNL = percutaneous nephrolithotomy; UV = ultraviolet; VUA = vesicoureteral anastomosis; 3D = three dimensional.

print of inner and outer molds of a kidney with a collecting system. A polymer was poured between the two molds and degassed, to create a patient-specific training phantom. Ghazi et al. [52] validated a high-fidelity, full-task trainer for inanimate PCNL within a full-immersion simulation environment. They used the simulated inanimate model that is composed by hydrogel polymer (polyvinyl alcohol) and multiple patients' imaging as a reference to construct an idealized pelvicalyceal system with staghorn calculus. The model has been shown to have excellent face and content validity, providing a complete tool for increase and evaluation of surgical skill before hands-on exposure. The same team developed kidney models for training, which simulates kidney anatomy with tumor and bleeding vessels simulating blood flow for robotic and laparoscopic partial nephrectomy training [62]. Atalay et al. [51] printed five personalized pelvicalyceal system models, which were used for patient information in percutaneous nephrolithotripsy surgery. Patients demonstrated an improvement in their understanding of basic kidney anatomy by 60%, kidney stone position by 50%, planned surgical procedure by 60%, and complications related to the surgery by 64%. Smektala et al. [17] showed the advantages of creating a low-cost silicone replica for surgical training. The authors presented a complete workflow process to create molds that included imaging segmentation, mold design, manufacturing, and replica casting in the silicone material. They conclude that their models reproduce shape and elasticity of the living organ, have similar mechanical strength, and could be used for laparoscopic surgical training. Golab et al. [21] reported the use of a 3D personalized silicone replica for partial nephrectomy training. The authors, before each procedure, simulated the laparoscopic trainer with patient-specific silicone model. They concluded that the experience gained during training with silicone models improved the performance of surgery, and possibly reduced the need and duration of intraoperative renal ischemia. Kusaka et al. [13] reported the creation of 3D models of the pelvic cavity and donor kidney for surgical training and planning to reduce cross-clamp time, blood loss, and their impact on perioperative morbidity and mortality.

3.3. *Patient counseling assessment*

A total of 10 papers reported the impact of 3D-printing technology during patient counseling, including seven for kidney diseases [11,14,16,19,20,30,34], two for prostate cancer [30,34], and one for pelvicalyceal system stones [51] (Fig. 2C and Table 1).

Guarino et al. [63] asked 13 physicians to evaluate a 3D-printed model and rate how beneficial it was to various preoperative activities. In this study, nine of the 13 physicians stated that it was of great benefit in communicating with pediatric patients and guardians about the procedure. Zhang et al. [19] evaluated patients reporting their overall satisfaction of their 3D model augmented consultation. The patients rated the model an average of 9 on a 1–10 scale for the overall satisfaction of conversation, usefulness for understanding their disease, usefulness for understanding the upcoming procedure, and how much they liked being able to discuss their disease characteristics with the urologist. Personalized organ models aided in the patients' understanding of their anatomy, lesion traits, and surgical risks more thoroughly than the physician could normally do in the allotted time. This accordingly led to a more efficient and straightforward discussion over consent. They also reported that the patients surveyed were fascinated by this innovative communication method. Atalay et al. [49,51] further attempted to quantify the benefits of 3D reconstruction for patient counseling. They designed a questionnaire for patients to assess how personalized 3D models affected the patient understanding of their disease before PCNL. One day before their surgery, the patients were seen by their urologist to review the surgery. Questionnaires surveying factors such as understanding of kidney anatomy, kidney stone position, and their planned surgical procedure were given to patients before and after a demonstration of the 3D models and were compared. The authors found that the patients demonstrated an improvement in their understanding of "basic kidney anatomy" by an average of 60%, "kidney stone position" by 50%, "planned surgical procedure" by 60%, and "complications related to surgery" by 64% after examining their personalized 3D kidney model. Interestingly, in these studies, despite patients being provided with extensive verbal and written preoperative information, their initial survey responses showed an extremely low level of understanding of their condition, kidney anatomy, and the procedure they would have undergone. These studies revealed how 3D models can further improve understanding by allowing patients to fully realize what questions they have so that they can have them answered by both the model and the physician. The models seem to have the greatest effect on the patient understanding of basic organ anatomy; therefore, this application would be most appropriate for organ-confined disease patient counseling [11,14]. Porpiglia et al. [30] tested with a survey the face and content validity of 3D virtually rendered printed models, used before robot-assisted prostatectomy for prostate cancer and nephron-sparing surgeries. All patients reported favorable feedbacks (from 9 to 10 out of 10) about the use of this technology during case discussion with the surgeon.

3.4. *Cost assessment*

Globally a total of 19 studies reported the cost of making 3D printing: 11 papers reported kidney diseases [14,17,19,21,25–29,31,33], five papers prostate cancer and treatments [35,37,38,40,45], and three papers pelvicalyceal diseases [49–51] (Fig. 2C and Table 1).

Reported costs are between $460 and $1000 for kidney models [14,16], $40–100 for prostate [36], and $100 for pelvicalyceal system stones [49]. Surprisingly low-cost models were reported by Smektala et al. [17] (silicone kidney replica was $14.4) and Monda et al. [29] (silicone kidney replica was $3.9).

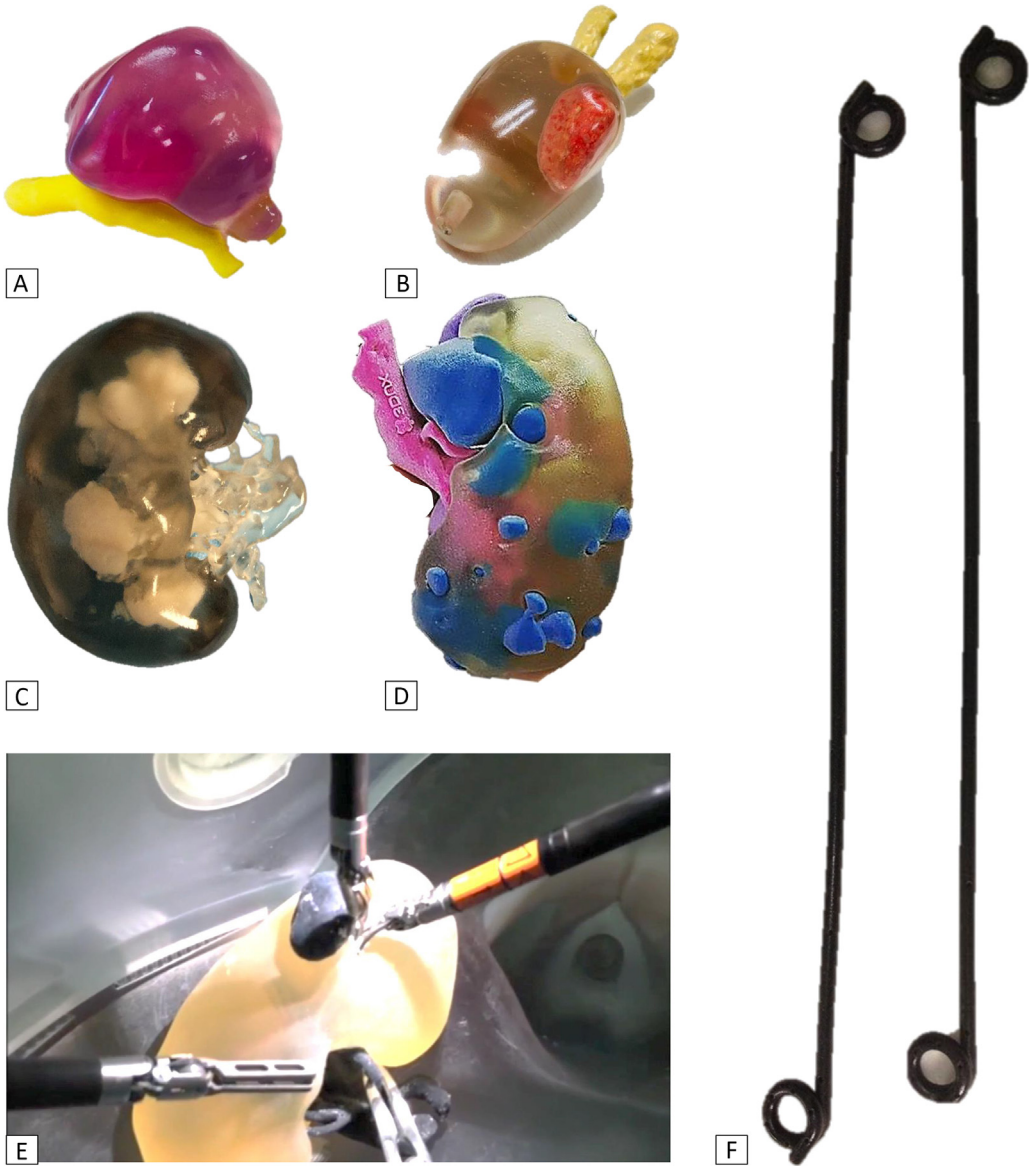

Fig. 3 – Examples of 3D printing in urology. (A) Prostate with lesion and neurovascular bundles used for surgical planning. (B) Prostate with visible lesion used for patient education. (C) Kidney with staghorn stone used for surgical planning. (D) Kidney with multiple lesions and its vascular ramifications in patients with Von Hippel-Lindau syndrome used for both patient education and surgeon planning. (F) Novel 3D-printed stents. (E) Kidney silicone model used for surgical training. 3D = three dimensional. (A and B) Courtesy of USC Institute of Urology, Los Angeles, CA, USA; (C, E, and F) courtesy of Department of Urology, University of California Irvine, CA, USA; (D) courtesy of Department of Urology, Camargo Cancer center, Sao Paulo, Brazil.

3.5. Future perspective

Our systematic search found three initial attempts of tissue reconstruction-focused tissue engineering using collagen-based scaffolds seeded with vital cells [56–58].

Huang et al. [56] evaluated the properties of urethral reconstruction with a novel 3D porous bacterial cellulose sponge scaffold seeded with lingual keratinocytes in a rabbit model showing macro and histologically the urethral tissue regeneration. Zhang et al. [58] recently published their initial results using an integrated bioprinting system to fabricate cell-laden urethra in vitro using polycaprolactone (PCL) and PLCL polymers with a spiral scaffold design, which demonstrated mechanical properties equivalent to the native urethra in rabbit. Yu and Park [57] investigated the feasibility of a PCL scaffold fabricated by 3D printing for tunica albuginea. After seeding the scaffold with fibroblast, mechanical properties of two types of 3D-printed scaffolds were measured using a scanning electron microscope. Microscopy images revealed that human fibroblast cells covered the entire scaffold surface, and cells remained viable and proliferated.

4. Conclusions

The present systematic review methodically analyzed for the first time the impact of 3D-printing technology in the

urological field. Patient counseling, and surgical training and planning seem to take advantage of these new technological opportunities. Three-dimensional–printed anatomical models for surgical planning have a wide array of applications in the hospital inpatient setting (Fig. 3A–D). Coupled with the benefits, they have fuelled growing clinical interest in surgical applications, as indicated by the number of published papers addressing the use of 3D printing in preparation of surgical cases. The benefits of 3D-printing result from the clarity provided by patient-specific anatomical models that illustrate structure and pathology, which may be vague, obscure, or hidden in X-ray, CT, magnetic resonance imaging (MRI), or ultrasound images. The information communicated by a physical model could be translated to numerous advantages starting with better insights, which might lead to better surgical outcomes. Although most of the literature on this topic is regarding retroperitoneal organs, less common today, but potentially more impactful, is the use of patient-specific models to determine the viability of procedure (rule-in/rule-out) and appropriate selection of a surgical approach and device. Using the model, the surgical team may ascertain that an entirely different approach is required or that a more suitable device would better accommodate the patient's anatomy [11,20].

The impact of surgical planning with 3D models may impact patient outcomes, leading us to a better understanding of the anatomy, reducing learning curves and possibly reducing complications. It is important to note that even in the age of advanced imaging technology, preoperative surgical planning is based on multidetector CT allied with conventional techniques of reconstruction such as multiplanar reconstruction, maximal intensity projection, and volume rendering or MRI. However, these conventional techniques have some limitations.

The 3D-printing technology could be a game changer in the field of surgical simulation. The possibility of translating 3D data into real objects is indeed very useful when it comes to rapid prototyping of novel simulators as well as developing molds for model casting. Development of experimental surgical educational tools is a pretty new application of 3D printing, and there are few reports in the literature about it. The introduction of 3D printing to develop training devices and simulation models for surgical training and education proved to be a valuable tool in several medical fields, namely, maxillofacial, orthopedics, vascular, cardiac, neuro, thoracic, and liver surgeries and several others. In urology, simulation-based training is increasingly being used for trainees as a means of overcoming the learning curve associated with new surgical skills, and 3D printing presents unique opportunities for direct “printing” of organ structures.

Moreover, a 3D printable replica of the UCi trainer has been developed in 2016 with the aim of wide-spreading basic hands-on training in laparoscopy [64]. Veneziano et al. [65] described a different use of 3D printing in 2015, developing the C-arm trainer at the University of Minnesota. One of the early large-volume printers at the time by Stratasys (Eden Prairie, MN, USA) was adopted to build the two preliminary versions of the simulator described in the paper, replicating a C-arm with fluoroless visualization technology.

In a world where urologists in training are offered several different tools, in the name of unstandardized surgical training, 3D printing is today representing a possible pathway of feasible standardization.

There is growing interest in utilizing this technology to aid in patient education by using 3D-printed models to help patients comprehend their disease and understand their optimal management options. Often during consultations, 2D imaging is the only graphic representation available from physicians to patients. However, many studies have shown that this may not be the best option to convey information fully to patients regarding their disease, surgery, or risk of complications [66]. Physicians, therefore, need a more effective means of imparting information to patients that would provide better patient comprehension. The creation of individualized 3D models from patient diagnostic imaging can now help bridge the gap in patient knowledge of their condition. This is allowing physicians to inform patients in novel and more comprehensive ways [49,51].

The 3D-printed technology has been used successfully to design and create patient-specific phantoms of several organs based on DICOM files from CT and MRI for dosimetry analysis and planning of radioactive seed implantation. Personalized phantoms were also used for planning interventional imaging-guided procedures and for training fellows to perform laparoscopic ultrasonography [67]. Patient-specific phantoms may offer the potential advantage of increased targeting precision of radiation therapies, which might well result in improved outcomes and diminished complications. There has always been a significant difference between the information that patients get from their doctors and what they would have perceived about the upcoming procedures and disease characteristics. Three-dimensional models have been shown to offer a proficient approach to minimize the gap by allowing patients to visualize their organ and foresee how the physician might approach their case in the operating room. The increase in patient satisfaction, as well as awareness of their condition, illustrates how impactful widespread 3D modeling can be.

Costs remain major concerns when a new technology comes out. The reported cost is variable. Following the initial cost of the 3D printer, the costs of a 3D-printed model mainly depend on the amount of material used [9] and the scale of production. The use of monocolor and monomaterial, as well as big production numbers, could help make it cheaper.

In addition, parallel to an explosion of articles on 3D printing in the medical field, a crescent number of researchers with new ideas and applications emerge. The next generation of additive manufacturing continues to improve with higher speed, lower costs, and more contemporary printing materials, capable of designing objects with high resolution, multiple materials, and sometimes multifunctionalities. New processes have been

developed (micro-/nanoscale 3D printing, bioprinting, and 4D printing), as well as advanced functional materials that have exhibited great potential for the fabrication of 3D structures with multiple functions, leading to improvements in the accuracy of manufacturing and enhancing the functional complexities of the printed structures [68].

Bioprinting is the application of an additive manufacturing process to the biomedical field, defined as the layer-by-layer deposition of biologically relevant material, cells, and supporting components into complex 3D functional living tissues. Up to the present, 3D bioprinting has been used to generate skin, cartilage, bone, and vascular tissues, successfully transplanted in humans in some reconstructive surgeries [69,70]. However, bioprinting more complex tissues consisting of multiple cell types presents diverse challenges, which must be overcome for clinical studies to become a reality. Future development of bioprinting materials would focus on various aspects, including printability, mechanical properties, biocompatibility, degradation, and biomimicry [71]. Developing novel composite biomaterials with different ingredients to obtain reprogrammed mechanical properties and functionality (4D printing) may be a promising approach to fabricating various tissues and organs with different mechanical requirements [72]. Therefore, 3D printing has the potential to replace traditional tissue engineering. In the near future, 3D-bioprinting technology may be useful in designing customizable urethra- or bladder-shaped scaffolds used in tissue engineering, or it may allow physicians to generate the entire urethra and bladders for urethral stricture treatment and bladder replacement, respectively.

Limitations of the present systematic review are related to the heterogeneity between studies. First, different materials, printers, and software used to prepare the models impacted the cost analysis. Next, no validated questionnaires are available to standardize the impact on patient counseling. Moreover, only one study compared the use of 3D-printing modeling with 3D virtual reconstruction [34]. Further comparative investigations are needed to assess the impact of 3D printing and virtual reality on patient and surgeon education.

Three-dimensional printing showed revolutionary potentials for patient counseling, pre- and intraoperative surgical planning, and education in urology. Together with "patient-tailored" presurgical planning, it puts the basis for 3D-bioprinting technology. Although costs and "production times" remain the major concerns, this kind of technology represents a step forward to meet patients' and surgeons' expectations. Further investigation comparing three-dimensional printing with three-dimesional virtual reality are needed.

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Analysis and interpretation of data: Cacciamani, Okhunov, Meneses, Rodriguez-Socarras, Rivas, Veneziano.
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