Three-dimensional printing technology in urology

3D printing in medicine to expand as research discovers new applications

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Three-dimensional (3D) printing is an additive manufacturing process that has been first introduced in 1984 by Charles Hull, with the invention of stereo lithography apparatus (SLA - a photosensitive resin polymerised by an UV light)[1]. Since the inception of this new concept, technology has significantly evolved allowing the 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, metals to human cells. As one of the fastest areas of industry expansion, 3D additive manufacturing is changing techniques in biomedicine. Therefore, it is not surprising that in the last 15 years 3D printing had a rapid expansion and impacted different areas of medicine and pharmaceuticals, and it has been used to pattern cells; make tissues, organs; construct surgical replicas for planning, counselling and training; build medical devices and prosthetics and in numerous other biomedical applications.

In urology, 3D printing has been used for several purposes and in this article we present the current state of technology as well as its potential impact in translational and clinical medicine.

Surgical planning and patient counselling
It is important to note that even in the age of advanced imaging technology, the pre-operative surgical planning is based on multi-detector computer tomography (CT) allied with conventional techniques of reconstruction such as multi-planar reconstruction (MPR), maximal intensity projection (MIP) and volume rendering or magnetic resonance imaging.

However, these conventional techniques have some limitations. For instance, they are unable to present the reconstruction of all structures at the same time in the same image (intrarenal arterial branches, acquired on the arterial phase and the enhanced collecting system, and obtained at the excretory phase for example), compelling the surgeon to form mental maps based on two-dimensional (2D) images in gray scale. This task is even harder in complex cases, especially for trainees and patient's comprehension.

To address this limitation, several publications using 3D printed physical renal models have been published. The real size of the models, coloured structures and the tactile sensation by touching the 3D printed kidney allowed more fully understanding of the kidney anatomy, especially the interrelationship among the kidney, tumour, vasculature and collecting system. The authors noted that trainees, patients and their family members reported an improved comprehension of the tumour's anatomy and the proposed surgical plan[2-4]. Wake et al. reported 30-50% of surgeons changed the surgical approach after visualisation of 3D models and Maddox reported less blood loss in partial nephrectomies planned with physical models[5-6].

But only small series addressed this topic and the real impact of these models on outcomes need to have a better evaluation with future studies. Our institution is currently constructing 3D-printed models of human kidneys to plan nephron-sparing surgery and the impact of 3D printing, virtual models, and holograms is the topic of an ongoing study (Figure 1)[7]. We also developed an online platform and apps for smartphones to evaluate the role of virtual reconstructions (www.docdo.com.br). Marconi et al. reported no differences in anatomy comprehension comparing virtual model and 3D printing[8]. Our initial impression is that virtual models and holograms may have the same impact in surgical planning compared with 3D printed models.

Other models were developed. Shin et al. reported three-dimensional printed model of prostate anatomy to facilitate nerve-sparing prostatectomy[9]. Srougi et al. reported the use of three-dimensional printers to estimate the resection limits for partial adrenalectomy[10]. Ataley used pelvicalyceal system 3D printed models on residents' understanding of pelvicalyceal system anatomy before percutaneous nephrolithotripsy surgery[11].

Education and training
The advent 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, orthopaedics, vascular, cardiac, neuro, thoracic, and liver surgeries and several others. In urology, simulation-based training is being increasingly used for trainees as a means of overcoming the learning curve associated with new surgical skills and 3D printing presents unique opportunities for the direct ''printing'' of organ structures.

Blankstein et al. designed flexible ureteroscopy course using ureteroscopy model in which bladder, single calyceal and double calyceal models were 3D printed with a translucent, acrylonitrile butadiene styrene (ABS)-like, plastic material and dyed red to simulate internal colour and translucency. The mean post-course task completion times and overall performance scores were significantly better than at baseline and lead to improved short-term technical skills among junior level urology residents[12].

Golab reported the use of 3D personalised silicone replica for partial nephrectomy (PN) training. The authors, prior to each PN, simulated the procedure on laparoscopic trainer with patient-specific silicone model. They concluded that the experience gained during training with silicone models improved the performance on surgery and possibly reduced the need and duration of intraoperative renal ischemia[13]. Ghazi et al. in Rochester developed kidney models for training, which simulates kidney anatomy with tumour and bleeding vessels simulating blood flow for robotic and laparoscopic partial nephrectomy training.

Atalay et al. printed five personalised 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%, the planned surgical procedure by 60% and understanding the complications related to the surgery by 64%[11].

Additionally, Okhunov at the University of California, constructed 3D printed models of human kidneys with extensive urolithiasis and used these models to assist in preoperative planning to determine the optimal percutaneous nephrostomy tract for percutaneous nephrolithotomy (PCNL). By using fused deposition modelling of white thermoplastics, they were able to print kidney parenchyma and staghorn stone separately with anatomically-correct size and shape, and by using polyjet printing they were able to construct a rubber-like kidney. Models were used for residents and fellow's education resulting in a higher familiarity with the shape and orientation of the stone and led toward greater overall confidence in performing PCNL[14].

Kusaka et al. used individual 3D printed models to plan and guide the surgical procedures for laparoscopic donor nephrectomy and recipient transplantation surgery. Replicas obtained using transparent materials allowed for the creation of models with visceral organs, blood vessels, and other details and enabled surgeons and trainees to virtually treat various pelvic conditions, simulate the procedure before they perform the surgery, allowing a shorter operative time and decrease donor risk[15].

Applications in imaging
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. Personalised phantoms were also used for planning interventional imaging-guided procedures and for training fellows to perform laparoscopic ultrasonography[16-18]. 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.

Surgical equipment
In the past few years, several studies have evaluated the feasibility and cost effectiveness of creating surgical instruments using this 3D printing. This technology is capable of manufacturing low-cost and customisable surgical devices. Several institutions have successfully printed and tested basic surgical instruments including retractors, needle drivers, forceps, surgical clips and ureteric stents[19-20]. Initial results are promising; however, vigorous testing will be required to assess the safety, quality, and function compared with those commercially available.

Bioprinting and personalised medicine
Bioprinting is the application of 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. Considered as the holy grail of 3D printing technology, the vision is to have a future where humans can replace damaged and failing organs by simply 3D bioprinting. But despite being a distant reality it has already been utilised for several purposes such as fabrication and modelling of living tissues and organs for medical applications, for drug screening in the pharmaceutical industry, personalised medicine, regenerative medicine, cell-based biosensors and bionics[21-22].

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[23-24]. However, bioprinting more complex tissues consisting of multiple cell types present diverse challenges that must be overcome in order for clinical studies to become a reality.

In urology, there are some initial attempts of tissue reconstruction focused on urethral and bladder tissue engineering using collagen-based scaffolds seeded with urothelial and muscle cells. Zhang et al. recently published their initial results using an integrated bioprinting system to fabricate cell-laden urethra *in vitro* using PCL and PLCL polymers with a spiral scaffold design, which demonstrated mechanical properties equivalent to the native urethra in rabbit[25]. Therefore, 3D printing has the potential to replace traditional tissue engineering. In the near future, 3D bioprinting technology may be useful in designing customisable urethra or bladder shaped scaffolds used in tissue engineering or it may allow physicians to generate entire urethra and bladders for urethral strictures treatment and bladder replacement.

Parallel to an explosion of articles on 3D printing in the medical field, a crescent numbers of researchers with new ideas and applications have emerged; printers continue to improve with higher speed, lower costs and more contemporary printing materials. There is no doubt that in the near future, 3D printing will be more present in medicine. Thus, it is essential that urologists stay up to date and follow the progress of 3D printing and its possible applications.

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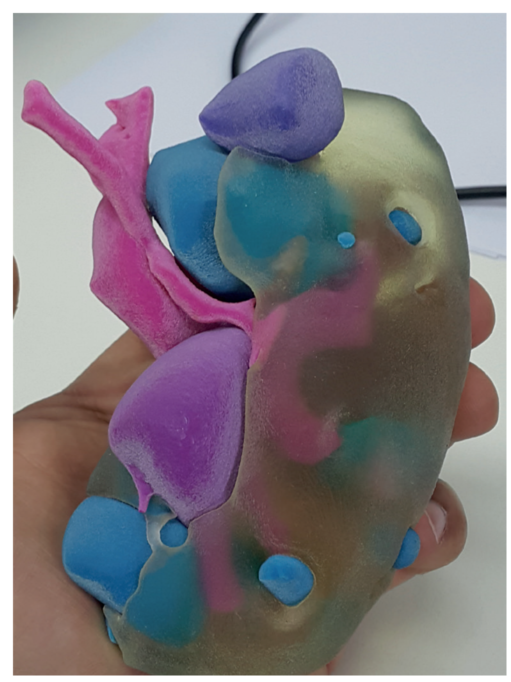

Figure 1: Von-Hippel-Lindau Syndrome. A) Coronal contrast enhanced CT scan B) 3D printed model of the right kidney, posterior view. Blue: tumour; purple: cyst; pink: arteries; violet: collecting system; translucent: kidney surface. Source: www.docdo.com.br