Review

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# Improving oncological outcomes after robotassisted radical prostatectomy: what novel tools do we have?

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# Abstract

The recent application of novel technologies to the robot-assisted radical prostatectomy (RARP) procedure has provided a new perspective and demonstrated potential usefulness in surgical planning, intraoperative navigation, and education of both patients and healthcare professionals, allowing for a patient-tailored prostate cancer (PCa) treatment. Integration of novel techniques into robotic surgery has improved the accuracy of surgery and has demonstrated a potential benefit in functional and oncological outcomes in patients with PCa. However, further



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randomized and prospective studies are needed to assess and validate the role of these technologies in clinical practice. The aim of this review is to summarize the current evidence on the new emerging techniques, such as three-dimensional (3D) imaging and printing, augmented reality (AR), and confocal microscopy (CM), and their impact on RARP and its oncological outcomes.

**Keywords:** Robot-assisted radical prostatectomy, augmented reality, three-dimensional (3D) imaging, 3D printed models, confocal microscopy

# INTRODUCTION

Radical prostatectomy (RP) represents one of the mainstays of treatment for localized prostate cancer (PCa). The cornerstone of PCa surgery is achieving the balance between complete removal of the prostate gland without jeopardizing oncological results and optimal postoperative functional outcomes<sup>[1]</sup>. In this setting, the nerve-sparing (NS) surgical technique allows preservation of the neurovascular bundles (NVBs), improving functional results, even though it is associated with a higher risk of positive surgical margins (PSMs)<sup>[2]</sup>. Furthermore, PSMs have been identified as predictive factors of biochemical recurrence (BCR), cancer-specific survival (CSS), and overall survival (OS) in PCa patients<sup>[3]</sup>. Consequently, many techniques have been proposed to assist in the intraoperative guidance of RP and evaluate surgical margins in real time, aiming to reduce PSM rates<sup>[4]</sup>.

Currently, PSM rates range from 9%-26% for robot-assisted radical prostatectomy (RARP)<sup>[5]</sup>. In the last decade, entering the era of precision surgery<sup>[6]</sup>, RARP has been adopted as the preferred and most frequently used surgical approach<sup>[7-11]</sup>. Furthermore, robotic surgery allows the integration of novel tools and innovative technologies to plan and guide RP<sup>[6]</sup>.

Moreover, the introduction of imaging techniques for the assessment of the local extent of PCa, such as multiparametric magnetic resonance imaging (mpMRI), aids in predicting and localizing areas of possible extraprostatic extension (EPE) and its proximity to NVBs<sup>[12,13]</sup>. Therefore, mpMRI may have a role in guiding NS surgery, potentially improving the preservation of NVBs and reducing PSM rates<sup>[4]</sup>.

Recently, novel tools integrating mpMRI and robotic surgery have been described for assisting the surgeon during RARP in the real-time evaluation of the main anatomical structures, aiming for optimal oncological and functional outcomes<sup>[14]</sup>. Some authors reported the use of three-dimensional (3D) models in surgical planning and intraoperative guidance<sup>[15]</sup>. Likewise, other techniques such as augmented reality (AR) and confocal laser endomicroscopy (CLE) or fluorescence confocal microscopy (FCM) have recently been introduced as an additional tool in RARP<sup>[14,16]</sup>.

This review summarizes the state of the art of imaging technology (3D models, AR, CLE, and FCM), their emerging role in real-time surgical assessment, and their impact on oncological outcomes in RARP.

# **EVIDENCE ACQUISITION**

This review covers the current scenario of the impact of new technologies (3D imaging and printing, AR, CLE, and FCM) in surgical planning and intraoperative assessment of RARP. We conducted a comprehensive literature search for original and review articles using Medline and PubMed databases from February-March 2022. We searched for the following terms: "robot-assisted radical prostatectomy", "augmented reality", "3D imaging", "3D printed models", "confocal microscopy", and "prostate cancer" alone or in combination. The search period ranged from 2012 to 2022. We included studies in English,

original articles, systematic reviews, and metanalysis. Studies in other languages, case reports, and abstracts in congresses were excluded. The combination of terms is found in more than 1500 related articles. Studies with the highest level of evidence and relevance to the discussed topics were selected with the consensus of the authors, and 39 papers were finally included in this review [Table 1].

# **EVIDENCE SYNTHESIS**

## Three-dimensional imaging and printed models

Three-dimensional (3D) imaging reconstruction, whether in digital modeling or 3D printing, has appeared as an emerging technology in urology in recent years. 3D printing was first described in 1986 by Hull<sup>[17]</sup>, and since then, its application has demonstrated remarkable potential in surgical planning, patient counseling, training, and intraoperative guidance<sup>[18]</sup>. 3D visualization techniques allow a better understanding of the organ's anatomy, the identification of the tumor lesions in each patient, and its relationship with adjacent anatomical structures<sup>[17]</sup>, thus enabling patient-tailored surgery. In the context of RP, a 3D-printed prostate model may help to identify NVB and lesions in their vicinity and, consequently, improve the oncological and functional outcomes by assisting NS surgery whenever possible<sup>[14]</sup> [Figures 1 and 2].

Ukimura *et al.*, described a novel 3D surgical navigation model based on transrectal ultrasound (TRUS)guided prostate biopsies, which was displayed on the TilePro<sup>™</sup> function of the da Vinci Surgical System<sup>\*[19]</sup>. The TilePro function allows for direct and simultaneous visualization of 3D reconstruction and intraoperative endoscopic images on the robotic console screen. The main purpose of the 3D navigation system was to assist NS surgery by facilitating surgical dissection in areas adjacent to biopsy-proven index lesions. Negative surgical margins were achieved in 0 of 10 patients included in the study. Subsequently, Shin *et al.* created life-sized 3D-printed prostate models based on MRI, including the transparent prostate gland, index lesion, and bilateral NVBs<sup>[20]</sup>. They described the advantages of using 3D models in preoperative planning and intraoperative guidance, achieving negative surgical margins in all five reported cases. Jomoto *et al.* presented a new 3D system based on magnetic resonance angiography<sup>[21]</sup>. The study included six PCa patients and suggested a potential benefit of the 3D system in the identification of accessory pudendal arteries and NVBs during RARP. Chandak *et al.* conducted a phase 2 study evaluating the impact of using a 3D-printed model based on MRI in preoperative planning, intraoperative guidance, and postoperative outcomes<sup>[22]</sup>. They reported only 1 PSM among the 10 patients studied.

Recently, Wang *et al.* performed a systematic review of the currently available evidence including 27 nonrandomized studies, nine of which refer to the use of 3D reconstructed images or printed models, demonstrating a promising role for 3D visualization in preoperative planning, intraoperative navigation, and education and training, while noting that prospective studies are needed to validate these technologies and their clinical impact on RARP outcomes<sup>[18]</sup>. Checcucci *et al.* performed a prospective study including 160 PCa patients undergoing RARP with mpMRI-based 3D reconstruction and compared them to a control group of 640 patients in whom 3D technology was not applied<sup>[23]</sup>. In the 3D-assisted RARP group, a more conservative NS approach (full NS 20.6% *vs.* 12.7%; P = 0.02) and a lower rate of PSM (25% *vs.* 35.1%; P = 0.01) were observed.

Moreover, in the setting of surgical planning and physician/patient education, Ebbing *et al.* evaluated a 3Dprinted model based on MRI in a non-surgical setting, comparing the impact on interpreting PCa lesion location by medical personnel of different levels of expertise<sup>[24]</sup>. The study showed that 3D models were more accessible to evaluate than MRI results presented in a multidisciplinary conference, especially by less experienced professionals. Porpiglia *et al.* assessed the use of 3D-printed models in physician education and preoperative surgical planning<sup>[25]</sup>. The survey showed high patient satisfaction with preoperative counseling

### Table 1. Summary of the most relevant studies included in this review

Author	Year	Technique	Image acquisition	Procedure	Application	Study design	Study objective	Results
Simpfendörfer et al. <sup>[31]</sup>	2011	AR	US	Laparoscopic RP	Surgical navigation	Case report/series	To describe an ultrasound-based AR navigation system	Real-time assessment using tracking needles inserted into the prostate surface (visualization error 0.55 0.28 mm)
Ukimura et al. <sup>[19]</sup>	2014	3D model	TRUS/MRI	RARP	Surgical navigation	Case report/series	To evaluate the use of a 3D model based on biopsy-proven index PCa lesions for NS-RARP	9/10 (90%) patients achieved negative surgical margins
Shin et al. <sup>[20]</sup>	2016	3D model	MRI	RARP	Surgical planning and navigation	Case report/series	To describe the advantages of using a life-size 3D printed prostate model with index lesions pre- and intraoperatively	5/5 (100%) patients achieved negative surgical margins
Jomoto et al. <sup>[21]</sup>	2018	3D model	MRI angiography	RARP	Surgical planning and navigation	Case report/series	To assess the benefit of using a 3D printed model during RARP	Improved detection of accessory pudendal arteries and NVB
Chandak et al. <sup>[22]</sup>	2018	3D model	MRI	RARP	Surgical planning and navigation	Non- randomized trial	To investigate the use of a 3D printed prostate model with PCa lesions in RARP	9/10 (90%) patients achieved negative surgical margins. Continence 100% at 12 months, 40% no erectile dysfunction at 24 months
Porpiglia et al. <sup>[16]</sup>	2018	AR	MRI	RARP	Surgical navigation	Case report/series	To evaluate the use of AR-assisted RARP	NS-RARP with selective biopsies if EPE is suspected (positive rate of 78%, 11/14 patients)
Harrison et al. <sup>[37]</sup>	2018	AR	-	Ex vivo RARP	Physician training	Non- randomized trial	To analyze the impact of an AR robotic training module on novice surgeon's learning curves	Improvement in performance of bladder dissection and vesicourethral anastomosis (surgical time, instrument collisions, injury to bladder or urethra and total time instruments were out of view; $P < 0.05$ )
Porpiglia et al.	2018	3D model	MRI	RARP	Surgical planning and patient education and physician training	Non- randomized trial	To assess the use of 3D printed models for RARP based on a survey	High level of patient satisfaction with preoperative counseling (scored 9-10/10). Perceived by surgeons as a useful tool in surgical planning (8/10), training (9/10) and anatomical representation (10/10)
Wake et al. <sup>[26]</sup>	2019	3D model	MRI	RARP	Patient education	Non- randomized trial	To evaluate the role of 3D models in patient preoperative counseling	Using 3D models vs. standard imaging, patients better understood the disease, cancer location, size and surgical plan (scores $4.6-4.78/5$ vs. $4.06-4.49/5$ ; $P < 0.05$ )
Porpiglia et al. <sup>[33]</sup>	2019	AR	MRI	RARP	Surgical navigation	Non- randomized trial	To introduce an elastic 3D AR real-time navigation system	Improved capsular involvement identification vs. 2D cognitive group (100% vs. 47%; $P < 0.05$ ). No significant reduction in PSM rate ( $P = 0.73$ )
Samei et al. <sup>[5]</sup>	2020	AR	TRUS/MRI	RARP	Surgical navigation	Case report/series	To describe a combined MRI-TRUS- based AR guidance system for RARP	The average error between US and da Vinci system was 1.4 $\pm 0.3 \mbox{ mm}$
Shee et al. <sup>[36]</sup>	2020	3D model	-	<i>Ex vivo</i> RARP	Physician training	Non- randomized trial	To develop a 3D-printed vesicourethral anastomosis model for RARP training	Superior rate of completion of the anastomosis in the pre-trained group of residents (54% vs. 20%; $P$ < 0.0001)
Saba et al. <sup>[27]</sup>	2021	3D model	MRI	RARP	Surgical planning and physician training	Non- randomized trial	To investigate the use of 3D computed- aided designs and 3D-printed models as preoperative tools for urologists	Improved accuracy, faster and more confident identification of PCa lesions by urologists comparing 3D visualization with mpMRI
Schiavina	2021	AR	MRI	RARP	Surgical navigation	Case	To describe the impact of 3D AR	Improvement in index PCa lesion identification and change

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et al. <sup>[15]</sup>					report/series	technology to guide NS-RARP	in NS surgical planning in 38.5% of patients (appropriate decision in 94.4% of cases)
Bianchi et al. <sup>[4]</sup>	2021 AR	MRI	RARP	Surgical navigation	Non- randomized trial	To assess a novel technique of IFS targeted to the index PCa lesion by using AR-3D models for NS-RARP	Comparable overall PSM rate but a lower rate of PSMs at the level of the index PCa lesion in patients who underwent IFS (5% vs. 20%; $P = 0.01$ )
Rocco et al. <sup>[13]</sup>	2021 FCM	-	RARP	Surgical navigation	Case report/series	To describe a technique for intraoperative evaluation of margin status using FCM analysis	PSMs were found intraoperatively in 4/24 patients, performing a secondary resection. Final histopathology showed negative surgical margins in all patients
Checcucci et al. <sup>[23]</sup>	2022 3D model	MRI	RARP	Surgical navigation	Non- randomized trial	To evaluate the role of 3D models on PSM rate	Lower rate of PSM (25% vs. 35.1%; $P = 0.01$ ) and more conservative NS approach (full NS 20.6% vs. 12.7%; $P = 0.02$ ) in the 3D-assisted RARP-group

AR: Augmented reality; EPE: extraprostatic extension; FCM: fluorescence confocal microscopy; IFS: intraoperative frozen section; mpMRI: multiparametric magnetic resonance imaging; MRI: magnetic resonance imaging; NS: nerve-sparing; NVB: neurovascular bundles; PCa: prostate cancer; PSM: positive surgical margin; RARP: robot-assisted radical prostatectomy; RP: radical prostatectomy; TRUS: transrectal ultrasound; US: ultrasound; 3D: three-dimensional.

(Likert scores 9-10/10). Moreover, the surgeons perceived 3D visualization as a useful tool in procedure planning (score 8/10). Subsequently, Wake *et al.* performed a study including 200 patients randomized to receive a preoperative assessment with a routine imaging test or with a 3D model (printed, visualized in AR, or viewed on a computer monitor)<sup>[26]</sup>. The results show that patients better understood the disease, cancer localization, size, and surgical plan using 3D models versus standard imaging (scores 4.60-4.78/5 *vs.* 4.06-4.49/5; P < 0.05). Recently, Saba *et al.* evaluated 3D prostate computer-aided designs and 3D-printed models as preoperative planning tools<sup>[27]</sup>. Comparing 3D visualization with mpMRI in the pre-RARP evaluation of ten PCa patients, urologists showed improved accuracy, with faster and more confident identification of prostate lesions. Finally, Cipollari *et al.* introduced the new approach of applying histological tissue clearing techniques to 3D technology, demonstrating the role of 3D imaging in molecular and histopathological assessment of prostate volumes and its correlation with mpMRI<sup>[28]</sup>.

Nevertheless, although an increasing trend in the use of 3D modeling has been reported over the last decade, there are still limitations to these techniques. Firstly, 3D models are based on image acquisition from MRI or ultrasound, thus assuming the risk of missing some PCa lesions not visible on these imaging tests<sup>[18]</sup>. Secondly, 3D-printed models can reproduce the same size as the real organ, although the material does not reproduce the consistency and elasticity of normal tissue<sup>[18,22]</sup>. Thirdly, 3D models add an additional cost to the RARP procedure. Therefore, a cost-effectiveness analysis of the implementation of these technologies in the routine surgical process in the future would be necessary<sup>[14,18,22]</sup>. Lastly, all currently available studies evaluating the role of 3D technology are based on small, single-center cohorts. Therefore, the overall level of evidence remains suboptimal, and further prospective randomized trials will be needed to assess the potential benefit of novel technologies and validate their use in clinical practice<sup>[14,18]</sup>.

#### Augmented reality

In the era of patient-tailored surgery, another innovative technique has been developed to implement 3D reconstruction in real-time assessment during



Figure 1. 3D prostate rendering (image courtesy of Medics). The tumor lesion is highlighted in green, the urethra in yellow, and the prostatic limits in blue. 3D: Three-dimensional.



Figure 2. QR-code that links to a YouTube video of the 3D prostate model designed for robot-assisted radical prostatectomy (image courtesy of Medics). QR: Quick response; 3D: three-dimensional.

surgical procedures. Augmented reality (AR) is a technology that overlays objects or images onto the real world. Superimposing 3D models on the robotic vision enhances intraoperative navigation and accuracy in the identification of essential anatomical structures during the surgical procedure<sup>[4,18,29]</sup> [Figures 3 and 4].

The first clinical application of AR in RP was described in 2008 by Ukimura and Gill<sup>[30]</sup>, introducing a realtime fusion system of TRUS with intraoperative laparoscopic vision. The system enabled synchronization of



Figure 3. AR images during RARP (courtesy of Prof. Porpiglia). AR: Augmented reality; RARP, robot-assisted radical prostatectomy.



Figure 4. AR images during RARP (courtesy of Prof. Porpiglia). AR: Augmented reality; RARP: robot-assisted radical prostatectomy.

the TRUS 3D images with the surgical view through a high-speed computer workstation and the use of optical tracking systems for the dynamic motion of the surgical instruments. The authors concluded that AR is a valuable tool in intraoperative guidance, providing increased accuracy and confidence to the surgeon and a better understanding and interpretation of the tumor lesions and surrounding anatomy. Subsequently, Simpfendörfer *et al.* described the *in vivo* application of an ultrasound-based AR navigation system for laparoscopic RP<sup>[31]</sup>. The system used tracking needles inserted into the prostate surface and traced their movements and locations in real time with a 3D ultrasound probe. Furthermore, Porpiglia *et al.* introduced an AR technique based on preoperative MRI<sup>[16]</sup>. The MRI-based 3D imaging was superimposed on the real anatomy in the robotic view. The NS strategy was based on local staging and reconstruction obtained from MRI, including 16 clinical T2 (cT2) patients who underwent the intrafascial NS technique and 14 cT3 patients in whom standard NS and AR-guided biopsy of suspected EPE were performed. Final pathology confirmed clinical staging and all the intraprostatic lesions. Selective biopsies in patients with suspected EPE showed a positive rate of 78% (11/14 patients). The discrepancy between the surgical specimen and the 3D reconstruction ranged from 1 to 5 mm. Despite the potential advantages of using the

AR technique, the authors described some limitations: the need for manual orientation and the rigidity of the virtual models. In this setting, the group improved the AR technique by implementing hyper-accurate 3D reconstruction technology (HA3D)<sup>[32]</sup> and further developed a 3D elastic AR system, which allowed simulating the prostate deformation caused by the robotic instruments in the dynamic phase of the surgery and, therefore, to better adapt the imaging overlay during the surgical procedure<sup>[31]</sup>. Porpiglia et al. conducted a prospective study including 40 PCa patients, 20 undergoing 3D AR RARP and 20 undergoing 2D cognitive RARP<sup>[33]</sup>. In the 3D AR group, capsular involvement was correctly identified in 100% of cases versus 47% in the 2D cognitive group (P < 0.05). Moreover, a 10% reduction in PSM rate was noted in the 3D AR group, although no statistical significance was demonstrated (25% vs. 35%; P = 0.73). The authors concluded that the introduction of an elastic system allowed a more accurate surgical simulation and a better adjustment to the dynamic reality of tissue manipulation during surgery. However, this model still had the limitation of requiring manual segmentation and overlapping of the images. Schiavina et al. evaluated the impact of 3D AR technology to guide NS RARP<sup>[15]</sup>. The study included 26 patients who underwent 3D AR-assisted NS RARP, showing an improvement in index lesion identification and a change in NS surgical planning in 38.5% of patients, resulting in an appropriate decision in 94.4% of cases. Samei et al. presented a novel MRI-TRUS-based image guidance system for RARP consisting of a preoperative MRI non-rigidly registered to intraoperative TRUS<sup>[5]</sup>. This technology offered the surgeon a combination of the two imaging tests simultaneously on the robotic console, potentially improving intraoperative tailoring to the specific prostate anatomy and PCa location. Kalia et al. proposed a markerless AR guidance system for RARP, which coordinated the TRUS image with the robotic camera image without the requirement for external calibration markers before or during surgery<sup>[34]</sup>. The focus can thus be changed during surgery, allowing for a re-estimation and adaptation of the image without stopping the procedure. Borgmann et al. introduced the use of wearable computing smart glasses in combination with AR in urological surgery<sup>[35]</sup>. The study demonstrated a high usefulness of this technology, as reported by the surgeons, considering applications in taking photographs, recording videos, reviewing patients' medical records and images, searching for online information, and hands-free teleconsultation. Recently, Roberts et al. conducted a systematic review of the current evidence on AR applications in urology, including 15 studies on prostate surgery which demonstrated a potential value of AR in intraoperative guidance, identification of PCa lesions, detection of capsular involvement, and patient counseling<sup>[29]</sup>. Finally, some authors have assessed the impact of new technologies on surgical training. Shee et al. developed a 3Dprinted model of the vesicourethral anastomosis (VUA) for ex vivo RARP training, showing a superior rate of completion of the anastomosis in the pre-trained group of residents compared to the untrained resident group (54% vs. 20%; P < 0.0001)<sup>[36]</sup>. All participants considered the 3D model a useful tool in the setting of surgical training. Harrison et al. analyzed the impact of an AR robotic training module on novice surgeon's learning curves, demonstrating a significant improvement in performance of bladder dissection and VUA in terms of surgical time (P < 0.0001 and P = 0.0135, respectively), instrument collisions (P = 0.0013 and P =0.066; respectively), total time instruments were out of view (P = 0.0251), and injury to the urethra and bladder (P = 0.032 and P = 0.0189, respectively)<sup>[37]</sup>. Nevertheless, despite the increasing use of robotics in urological surgery, there are currently no standardized training programs for novice urologists. Several authors have presented different training methods, some of them including 3D or AR simulation models to optimize the teaching of RARP. In this setting, Anceschi et al. recently proposed a new system for assessing the quality of RARP learning curves based on pathologic and perioperative outcomes<sup>[38]</sup>. They defined a score to evaluate the RARP procedures performed by trainees, which was established as a predictor of early trifecta achievement (P < 0.05). Conclusively, although the use of new technological tools in surgical training is promising, further studies are needed to define standardized training programs and validate their evaluation methods.

In summary, the development of AR passed through different phases, from the use of ultrasound initially to the inclusion of MRI and the emergence of elastic models. The major limitation of this technique was the rigidity of the 3D virtual models, which failed to adapt the image overlay to the tractions and tissue manipulations involved in the surgical procedure. This barrier was overcome by Porpiglia *et al.*, who described an elastic AR model in 2019. However, all current MRI-based AR systems still have the limitation of requiring manual adjustment of the image by another urologist during surgery<sup>[33]</sup>. Therefore, the development of new automated models in this field will be necessary. In this setting, the advent of artificial intelligence and its application in robotic surgery may play a key role in addressing the technological limitations described to date<sup>[39]</sup>. Finally, as with 3D modeling, further randomized trials are needed to assess the oncological and functional improvement related to these new technologies<sup>[6,14,18]</sup>.

### **Confocal microscopy**

In the precision surgery setting and to improve the identification of the main anatomical structures and PCa involvement, different histopathological and optical imaging techniques have been developed<sup>[14,40,41]</sup>. Real-time assessment of surgical margins and extracapsular extension allows for accurate intraoperative guidance of NS surgery, potentially improving the oncological and functional outcomes of RP<sup>[40]</sup>.

In this context, intraoperative frozen section (FS) analysis is considered the gold standard approach for assessing surgical margin status during surgery. However, the role of FS during RP is debatable due to the lack of benefit in BCR-free survival, the time-consuming nature of the procedure, and the heterogeneity of the technique described in the studies available to date<sup>[13,39,42]</sup>. In 2012, Schlomm *et al.* presented the neurovascular-adjacent frozen section examination (NeuroSAFE) technique<sup>[43]</sup>. The NeuroSAFE approach involves complete dissection of the neurovascular tissue surrounding the prostate and assessment via FS, allowing real-time monitoring of oncological safety in NS surgery. Nevertheless, the use of this technique failed to progress due to the complexity of its application and low reproducibility, requiring the availability of a specific and fully equipped laboratory, a trained pathologist present on-site, and a total time exceeding 30 min<sup>[13,44,45]</sup>. Recently, Bianchi *et al.* conducted a prospective study evaluating a novel technique consisting of intraoperative index PCa lesion FS using 3D AR models in patients undergoing NS RARP<sup>[4]</sup>. The results show a comparable overall PSM rate between the group of patients who received intraoperative FS and the control group, although a lower rate of PSMs at the level of the index lesion was demonstrated in those patients who underwent intraoperative FS (5% *vs.* 20%; *P* = 0.01).

In this scenario, López *et al.* introduced confocal laser endomicroscopy (CLE) in the RARP procedure<sup>[46]</sup>. CLE is an imaging technology based on a fiber-optic system that provides high-resolution cellular images using a blue laser (488 nm) in combination with fluorescein<sup>[14,40]</sup>. The study demonstrated the intraoperative applicability of CLE and the feasibility of identifying NVBs and performing an optical biopsy of periprostatic tissue during RARP<sup>[46]</sup>. Subsequently, Panarello *et al.* developed an atlas of CLE images of prostatic and periprostatic tissues, thus providing the basis for identifying and interpreting histological patterns during RARP<sup>[47]</sup>.

Recently, Rocco *et al.* presented a novel technology to assess real-time pathological examination: fluorescence confocal microscopy (FCM)<sup>[45]</sup>. FCM is an optical technique that allows the acquisition of immediate digital hematoxylin-eosin-like images from freshly excised tissue<sup>[13,40,45]</sup>. FCM analysis has shown 91% concordance with the conventional hematoxylin-eosin technique in discriminating PCa from normal prostatic tissue<sup>[48]</sup>. The group conducted a subsequent prospective study<sup>[13]</sup>, including 24 patients undergoing RARP with intraoperative FCM control of margin status. Digital images from the surgical margins were obtained immediately via FCM. PSMs were found intraoperatively in four patients, and a secondary focal

resection was performed. Final histopathology showed the absence of PSMs in all patients. The authors concluded that FCM might provide a feasible alternative to the NeuroSAFE technique due to the ability to digitalize hematoxylin-eosin-like images and report them in real time remotely and without the need for specific image processing. Further, Bertoni *et al.* developed an *ex vivo* tissue atlas based on FCM images and reported a short learning curve of this novel technique for pathologists<sup>[49]</sup>.

In summary, optical imaging techniques have shown promising results in the assessment of surgical margins and the potential improvement of oncological and functional outcomes of RP. However, further studies are required to define their possible applications in PCa treatment.

# CONCLUSIONS

The advent of novel imaging technologies and their application to RARP procedures has led to a new understanding of surgical planning, intraoperative navigation, professional training, and patient education. Despite the current limitations of the different techniques and the low quality of the available evidence, the new tools have shown a promising role in potentially improving the oncological and functional outcomes of RARP. Nevertheless, further randomized and prospective studies are needed to assess and validate the clinical utility of these technologies.

# DECLARATIONS

### Authors' contributions

Acquisition of data: Dilme RV, Rivas JG Analysis and interpretation of data: Dilme RV, Rivas JG, Hernández LF, Vázquez LI Drafting of the manuscript: Dilme RV Supervision and critical revision of the manuscript: Rivas JG, Cacciamani GE, Puliatti S, Taratkin M, Checcucci E, Belenchón IR, Kowalewski KF, Serrano A, Moreno-Sierra J

## Availability of data and materials

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