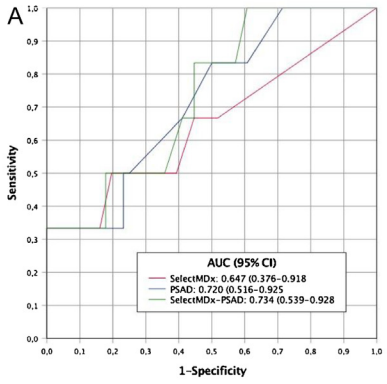
Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

A



B

Parameters of efficacy	SelectMDx	PSAD	SelectMDx-PSAD
Sensitivity, n (%)	4/6 (66.7)	5/6 (83.3)	6/6 (100)
Specificity, n (%)	27/56 (48.2)	28/56 (50.0)	22/56 (38.3)
Positive predictive value, n (%)	4/33 (12.1)	5/33 (15.2)	6/40 (15.0)
Negative predictive value, n (%)	27/29 (93.1)	28/29 (96.6)	22/22 (100)
Accuracy, n (%)	31/62 (50.0))	33/62 (53.3)	28/62 (45.2)
Avoided biopsies, n (%)	29/62 (46.8)	29/62 (46.8)	22/62 (35.5)
csPCa misdiagnosis, n (%)	2/6 (33.3)	1/6 (16.7)	0/6(0)
iPCa overdetection	4/62 (6.4)	2/62 (3.2)	4/62 (6.4)

csPCa =clinically significant prostate cancer; iPCa =insignificant PCa

Fig. 1 – Behaviour of the Select MDx test, prostate-specific antigen density (PSAD), and their combination in detecting csPCa. (A) Receiver operating characteristic curves. (B) Clinical efficacy parameters. AUC = area under the receiver operating characteristic curve; CI = confidence interval.

Conflicts of interest: The authors have nothing to disclose.

Acknowledgments: The authors thank Ferrer for Good for providing the SelectMDx tests.

References

[1] Sathianathen NJ, Omer A, Harriss E, et al. Negative predictive value of multiparametric magnetic resonance imaging in the detection of clinically significant prostate cancer in the Prostate Imaging Reporting and Data System era: a systematic review and meta-analysis. Eur Urol 2020;78:402–14.

[2] Mazzone E, Stabile A, Pellegrino F, et al. Positive predictive value of Prostate Imaging Reporting and Data System version 2 for the detection of clinically significant prostate cancer: a systematic review and meta-analysis. Eur Urol Oncol. In press. https://doi.org/10.1016/j.euo.2020.12.004.

[3] Görtz M, Radtke JP, Hatiboglu G, et al. The value of prostate-specific antigen density for Prostate Imaging-Reporting and Data System 3 lesions on multiparametric magnetic resonance imaging: a strategy to avoid unnecessary prostate biopsies. Eur Urol Focus 2021;7:325–31.

[4] Maggi M, Del Giudice F, Falagario UG, et al. SelectMDx and multiparametric magnetic resonance imaging of the prostate for men undergoing primary prostate biopsy: a prospective assessment in a multi-institutional study. Cancers 2021;13:2047. https://doi.org/10.3390/cancers13092047.

[5] Hendriks RJ, van der Leest MMG, Israël B, et al. Clinical use of the SelectMDx urinary-biomarker test with or without mpMRI in prostate cancer diagnosis: a prospective, multicenter study in biopsy-naïve men. Prostate Cancer Prostat Dis. In press. https://doi.org/10.1038/s41391-021-00367-8.

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SARS-CoV-2 RNA Detected in Abdominal Insufflation Samples During Laparoscopic Surgery

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Since the emergence of COVID-19, new guidelines have been adopted to protect clinical staff from the potential risk of viral aerosolization during laparoscopy without sufficient data supporting these cautions [1]. Elective procedures have resumed after initial cessation in the USA, and in most institutions a negative SARS-CoV-2 polymerase chain reaction (PCR) assay is required within a few days before scheduled procedures to document the absence of infection. There are scant data on the risks of aerosolization during abdominal laparoscopy to inform guidelines during the COVID-19 pan-

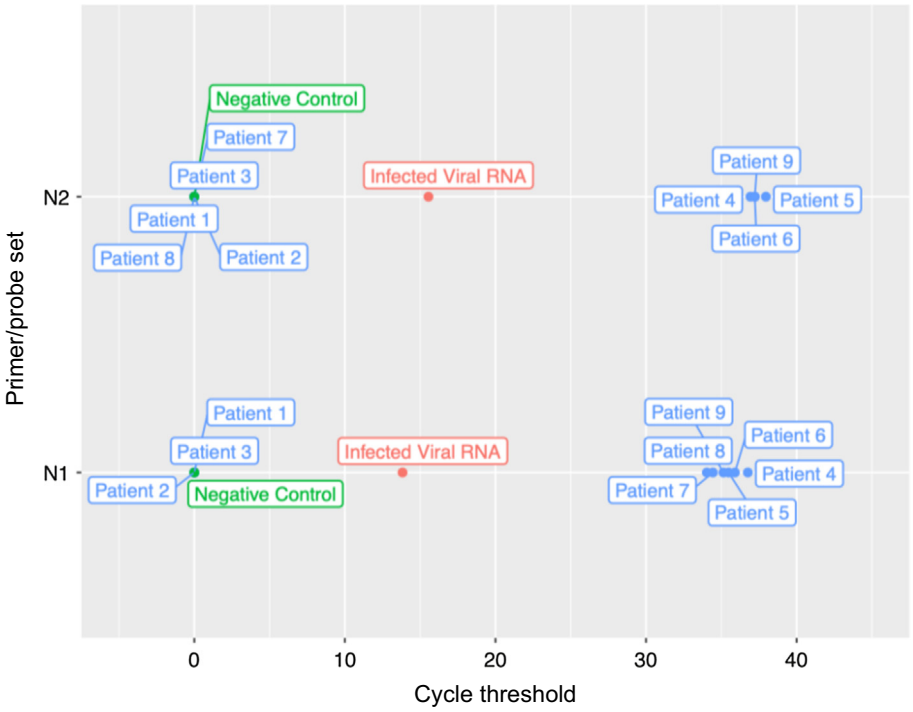

Fig. 1 – SARS-CoV-2 quantitative polymerase chain reaction (PCR) assay for abdominal insufflation samples from patients undergoing laparoscopic surgery. Patients 4, 5, 6, and 9 showed positive PCR results for SARS-CoV-2, all of whom had negative PCR results for preoperative nasal swabs. Our mock SARS-CoV-2 samples (shown in red) confirmed the sensitivity of the N1 and N2 primer/probe sets for SARS-CoV-2 detection. No signal was detected for negative controls.

demic. We sought to evaluate aerosolized plumes from patients undergoing abdominal laparoscopic surgery for the presence of SARS-CoV-2.

Our institutional review board approved this study. Patients undergoing laparoscopic robot-assisted nephrectomy or prostatectomy were selected using nonprobabilistic consecutive sampling between September 2020 and January 2021. For all patients, a SARS-CoV-2 PCR test on a nasopharyngeal swab was carried out 2–3 d before surgery. We used a closed-loop insufflation system (AirSeal; CONMED, Largo, FL, USA) in smoke evacuation mode to filter abdominal CO_2 through a 0.01-μm ultra-low–particulate air filter. RNA was isolated using an exosomal RNA isolation kit (Norgen Biotex, Thorold, ON, Canada; catalog #58000) and RNA extracts were tested using real-time quantitative PCR (RT-qPCR) for the presence of a SARS-CoV-2 genetic signature. The RT-qPCR procedure uses primers and probes from the US Centers for Disease Control and Prevention 2019-nCoV Real-Time RT-PCR Diagnostic Panel (CDC, Atlanta, GA, USA; catalog #2019-nCoVEUA-01) and Mastermix from a Promega GoTaq Probe 1-Step RT-qPCR kit (Promega, Madison, WI, USA; catalog #A6120) for detection of SARS-CoV-2. RNA extraction and qPCR were also concomitantly conducted in the same way for negative controls (no template) and positive controls (viral RNA in vitro spike-in using Vero E6 cells).

Of the nine patients (age range 58–78 yr) in the study, two reported a history of COVID-19, but were well beyond the quarantine period deemed acceptable for elective surgery. All patients had negative preoperative PCR results for nasal swabs. The two primer/probe sets (2019-nCoV N1 and N2) were able to detect (cycle threshold [C_t] <40) SARS-CoV-2 in clinical abdominal insufflation samples (Fig. 1). SARS-CoV-2 was identified via qPCR of the Airseal filter for four of the nine patients (C_t 30–40). We detected viral RNA that was differentiated from the negative controls (no template) for the two primer/probe sets (N1 and N2). Four samples exhibited fluorescence growth curves that crossed the threshold within 40 cycles (C_t <40) for both the N1 and N2 reactions, thus indicating the presence of viral RNA. A further two samples exhibited fluorescence growth curves for the N1 primer/probe alone. Our mock SARS-CoV-2 samples (Fig. 1, shown in red) confirmed the sensitivity of the primer/probe sets for SARS-CoV-2 detection. The four patients who tested positive for abdominal insufflation samples had either prior COVID-19 (n = 2) or high-risk exposure (n = 2) in the months before their surgery.

Viral particles have previously been detected in surgical smoke [2]; however, the theoretical risk of propagation of SARS-CoV-2 particles from pneumoperitoneum has not been reported. Our positive SARS-CoV-2 PCR results for four out of nine patients, despite negative preoperative swab results, represent the first documented finding of SARS-CoV-2 in pneumoperitoneum during laparoscopic surgery. Hypotheses that may explain the discordance between preoperative and intra-abdominal PCR findings include false-negative preoperative tests and a history of prior infection or exposure to the virus with persistent intra-abdominal viral shedding. These phenomena have been demonstrated in previous studies [3,4]. Although our study is limited by its small sample size, the results show that SARS-CoV-2 can be isolated

from pneumoperitoneum. However, the risk of active viral shedding and the potential risk of transmission were not evaluated and will require further investigation.

Conflicts of interest: The authors have nothing to disclose.

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References

[1] Mowbray NG, Ansell J, Horwood J, et al. Safe management of surgical smoke in the age of COVID-19. Br J Surg 2020;107:1406–13. https://doi.org/10.1002/bjs.11679.
[2] Society of American Gastroenterology and Endoscopic Surgeons. SAGES and EAES recommendations regarding surgical response to COVID-19 crisis. www.sages.org/recommendations-surgical-response-covid-19/.
[3] Long C, Xu H, Shen Q, et al. Diagnosis of the coronavirus disease (COVID-19): rRT-PCR or CT? Eur J Radiol 2020;126:. https://doi.org/10.1016/j.ejrad.2020.108961 108961.
[4] Gupta S, Parker J, Smits S, Underwood J, Dolwani S. Persistent viral shedding of SARS-CoV-2 in faeces – a rapid review. Colorect Dis 2020;22:611–20. https://doi.org/10.1111/codi.15138.

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Urinary Extracellular Vesicles in Urology: Current Successes and Challenges Ahead

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Urine contains a variety of membrane-bound vesicles (eg, exosomes, microvesicles, and apoptotic bodies) commonly referred to as urinary extracellular vesicles (uEVs). The molecular composition and cargo of uEVs (proteins, nucleic acids, lipids, and metabolites) strongly resemble their cells of origin in the genitourinary tract. This inherent resemblance, together with the noninvasive availability and abundance of urine as a biofluid, has led to the establishment of a new, highly dynamic uEV field in biomedical and urological research. Currently, uEVs are being broadly investigated not only in different urological and nephrological pathologies as biomarker "treasure chests" in noninvasive liquid biopsies, but also as functional players, therapeutic agents, and targets [1,2].

uEV biomarker research is undoubtedly provoking a great deal of interest. Important steps towards clinic application in prostate cancer have recently been made, with the development and certification of an in vitro diagnostic uEV gene expression assay for high-grade prostate carcinoma [3], and this progress has inspired similar investigations in bladder and renal cancers. The potential of uEVs is now being explored for a much broader spectrum of urological disorders. EVs found in seminal fluid (so-called prostasomes) were already identified as being connected to sexual and reproductive health several decades ago [4]. More recent investigations have addressed the biomarker and therapeutic potential of uEVs in urological infections and lower urinary tract symptoms, as well as after renal injury [2]. Nonetheless, together with new opportunities, the rapid expansion of the EV research field brings several methodological, scientific, and translational challenges that pose barriers to successful exploration of the full EV potential. In response, the establishment of evidence-based guidelines for EV research has become a major objective of the International Society for Extracellular Vesicles (ISEV) [5].

In urology and nephrology research in particular, the increasing interest in uEVs and the pressing need for best practices to translate scientific findings into clinical solutions were recently addressed by a position paper from the Urine Task Force of the ISEV Rigor and Standardization Committee [6]. The position paper presents the consensus view of more than 40 urologists, nephrologists, cardiologists, and biologists with active experience in uEVs research, who provide a detailed overview of the current state of the art of uEV-based analyses for clinical applications, along with an inventory of unresolved challenges and outstanding knowledge and methodology gaps. Of note,