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.

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what has long been a promising technique truly improves outcomes for men undergoing RP. We look forward to keeping your journal and the wider urological community informed of our findings.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.eururo.2020.03.052.

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Uropathologists During the COVID-19 Pandemic: What Can Be Learned in Terms of Social Interaction, Visibility, and Social Distance

Rodolfo Montironi [a,*], *Liang Cheng* [b], *Alessia Cimadamore* [a], *Antonio Lopez-Beltran* [c], *Marina Scarpelli* [a]

We read with great interest the recent series of papers published in *European Urology* related to current uro-oncology practice during the COVID-19 pandemic. The papers report that doctors are doing their best for the patients, with minimal delays in the diagnosis and treatment of urogenital neoplasms [1,2]. This involves what

Fig. 1 – A pathologist uses a multiple-head microscope with a digital camera and a TV screen showing an image of prostate cancer. The equipment is associated with a computer and a monitor showing a remote participant discussing the case. The audience is composed of a resident sitting at a distance from the microscope.

we can call *social interaction*, *visibility*, and *social distance*. These three items, as discussed below, concern clinicians, uropathologists, and patients.

Consider, as an example of a clinician and typical activity, a urologist and the interaction with a patient with prostate cancer. In this context, *social interaction* refers to the fact that the urologist deals with the patient from diagnosis to treatment, and all the steps in between. The urologist has an active role and co-participate with the patient in the diagnostic and therapeutic processes. The patient is not only informed but is also always and constantly part of the discussion and decisions. The urologist's role is not only the mechanical process of removing the prostate in the surgical theater while the patient is asleep. Should the urologist be simply involved in a single step of the process, such as performing the prostate biopsies at the request of the family doctor, the urologist loses what we can call *visibility* as a consequence of the lack of social interaction.

The papers related to COVID-19 published in *European Urology* help readers to understand how clinicians can retain social interaction and visibility while maintaining social distance in these difficult times when dealing with patients whose treatment cannot be postponed [1,2].

The traditional role of a pathologist does not always involve a high level of social interaction and visibility, as addressed in a recent article by some members of our group [3]. The background for this contribution was a paper

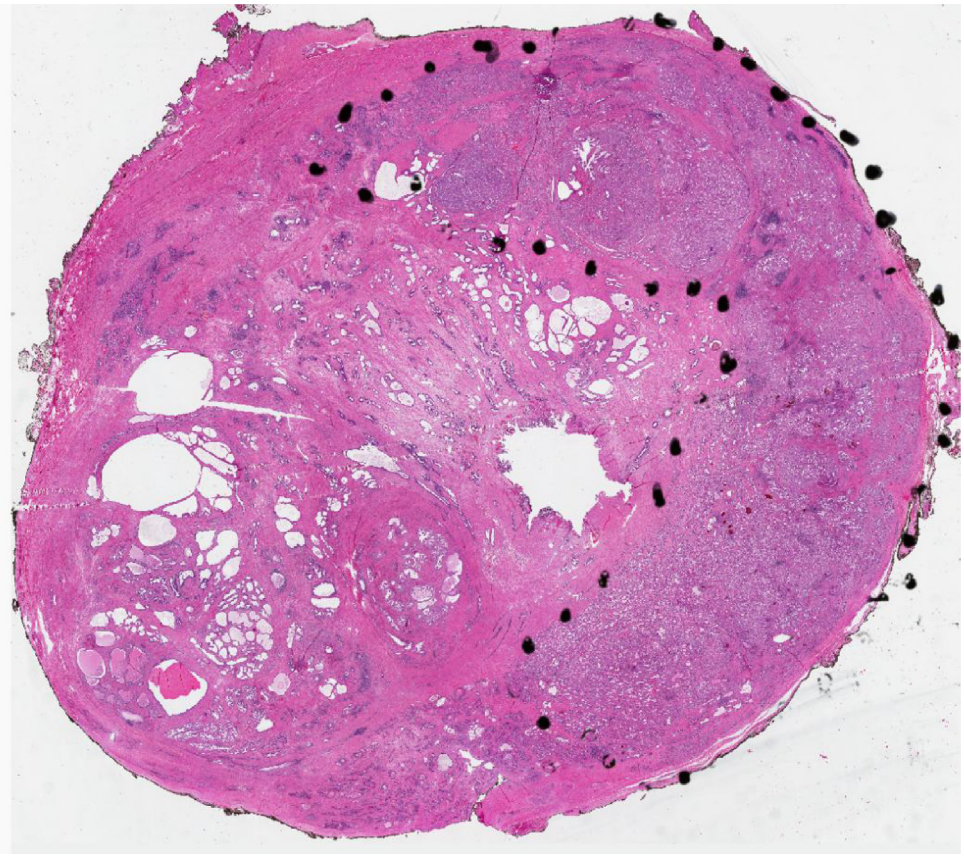

Fig. 2 – Whole-mount section of a radical prostatectomy specimen. The tumor is outlined with black dots. The virtual slide scanned at 20× can be downloaded from https://drive.google.com/file/d/1GK7ph9DV39nTXcSlM9KfoZ_tcRHltl9q/view?usp=sharing.

published in the same journal by Harrold et al. [4], who pointed out that the waning interest in pathology among medical students led to a negative impact on the level of visibility and social interaction of pathologists. Our paper, the aim of which was to reverse this trend, was submitted and accepted for publication months before any hint of the current COVID-19 pandemic. When the article was published, our group suddenly felt that it might have appeared at the wrong time.

Pathologists face the risk of being marginalized because they do not have clinical experience or a role in the diagnostic and therapeutic processes related to COVID-19. At a time of global reductions in clinical activity, they risk being confined to "processing and reporting specimens that did not really deserve to be examined histologically", as mentioned at the end of our paper [3]. This represents a real threat to visibility and social interaction because of the COVID-19 pandemic.

This consideration prompted our transnational group of closely collaborating uropathologists to think about the actual risk of not remaining visible for lack of social interaction. We discussed how to continue to be an integral part of the clinical processes still in place, and how the current experience might influence our future approach to pathology after the pandemic is resolved.

Equipment we all have readily available in our offices and laboratories can have a particular value in maintaining, if not increasing, the level of social interaction and visibility while following the rules for social distance when closely collaborating with clinicians in the diagnostic identification of patients with high-grade urothelial carcinoma, advanced kidney cancer, testicular cancer, or penile cancer who need to be prioritized for treatment [2].

A microscope with a digital camera, a computer with webcam, a TV monitor, an internet connection, and a slide scanner are pieces of equipment we can exploit for sharing images and consulting, teaching, and communicating with clinicians and patients in real time. To some extent these goals can also be achieved via so-called smart working from home. There are basically two ways we can use routinely to meet these goals.

The first is a microscope with a digital camera. The images are shown on a wide TV screen. A computer with a webcam can be added for remote viewing using software that is freely available on the internet. This set-up is basically what we now use for intradepartmental consultation (Fig. 1).

The second is based on virtual slides obtained with a digital scanner. Modern equipment can also scan whole-mount sections (Fig. 2) [5]. Virtual slides are shared among the group (members are located not only in Italy but also in Portugal, Spain, and the USA) or sent over the internet to other colleagues, with no limits as far as institution and country are concerned. For instance, Google Drive can be used to send a virtual slide via a link for downloading images, as in the caption for Figure 2. The procedure is simple and fast, considering that the size of a virtual whole-mount section can be in the range of gigabytes. The viewing and image analysis software can be downloaded from the internet free of charge.

This means that the histological features of both glass slides and virtual slides are shared and their content discussed with pathology colleagues for both consultation and teaching purposes. The same systems are also used to discuss cases with clinicians and even with patients. This approach fulfils the basic requirement of social distance while maintaining social interaction and visibility.

The question is whether we, as pathologists, will return to the routine we followed before the pandemic. It is difficult to foresee. However, considering that we are rapidly moving into an era of global digitalization, most of our future activities may well be based on what we are currently doing during the COVID-19 pandemic.

This is in line with the conclusions of Porpiglia et al. [6] in their paper on traditional and virtual congress meetings. They foresee that "By the end of the COVID-19 emergency, we will enjoy a new reality in which technology and sociality go together in order to offer a more engaging and adaptable scientific congress experience, allowing more flexible and dynamic use of content, modulated to the needs of each attendee."

Finally, in this time of the COVID-19 pandemic, uropathologists can learn a lot from clinicians in terms of social interaction, visibility, and social distancing. Similarly, clinicians can learn from uropathologists not only through a process of interaction [7] but also, above all, by working in a tighter way than we have defined in the past: together we can do it better [8]. And, as mentioned, the patient is always an integral part.

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A Call for Standardized Reporting of Adverse Events

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While definitions and recommendations for reporting of efficacy outcomes have been developed for clinical trials in prostate cancer [1], there is no standard for reporting adverse events (AEs). Although AEs are well defined, most trials only provide AE proportions. This assumes identical follow-up between the different arms and can result in misleading conclusions about the risk/benefit ratio of a drug. Here we illustrate how differences in reporting could significantly influence AE profiles of next-generation androgen deprivation (ngADT) agents including abiraterone acetate, enzalutamide, apalutamide, and darolutamide.

>We performed a systematic review and meta-analysis of randomized controlled trials of ngADT agents in prostate cancer with data on AE (Supplementary material). Out of 1913 reports, we included 11 trials and 11 505 patients, and AE profiles as simple proportions or time-adjusted events were plotted for each study drug (Supplementary Figs. 1 and 2).

Fatigue is the most commonly reported AE for enzalutamide and is reported in 20% for controls and 30% for enzalutamide (Supplementary Fig. 2). However, the observed differences in proportions vanish after adjusting for follow-up (Fig. 1), a result that is also reported in a meta-analysis of individual patient data [2]. This result can be explained by the fact that trials using ngADT have different follow-up times in each study arm. In one example, the median reporting period for AE was more than three times longer in the treatment group than in the control group [3]. Such "over-reporting" of fatigue during treatment might lead to incorrect patient counseling. By contrast, the risk of hypokalemia is significantly higher for men treated with abiraterone, regardless of time adjustment, as this side effect probably occurs early after the start of treatment (Fig. 1) and is clearly linked to the mechanism of action of the drug.

Similar discrepancies can also be observed for cardiovascular events. Previous meta-analyses have simply pooled proportions and concluded, potentially erroneously, that ngADT treatment is associated with an increase in the risk of cardiovascular events [4]. A further problem is the different grouping of cardiovascular AEs, which constrains accurate comparison of individualized cardiovascular AEs. For example, some trials report each single cardiovascular AE diagnosis meticulously, while others pool cardiovascular AEs into nonspecific groups labeled as "cerebrovascular complications" or "cardiac disorder".

We attempted to address the issue of inconsistent AE reporting by performing an individual patient meta-analysis and encountered a further major problem, namely difficulty in gaining access to the data. Thus, to aid in providing better understanding and transparency of the AE profile of drugs, we propose that all AEs should be reported as supplementary material to submissions and that AE rates reported in these trials be determined on the basis of treatment exposure.

In conclusion, proper AE analysis is currently not feasible and we therefore recommend that working groups cover AE reporting in their future recommendations, including important effect modifiers (eg, skeletal-related events and bone protection). From a statistical point of view, numerous superior methods that also account for recurrent events and competing risks are available [5]. Moreover, most trials are underpowered for studying AEs and therefore sharing and meta-analyses of individual-patient clinical trial data including AEs should be encouraged.