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ORIGINAL ARTICLE

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A Joint Action in Times of Pandemic: The German BioImaging Recommendations for Operating Imaging Core Facilities During the SARS-Cov-2 Emergency

Steffen Dietzel,[1*] Elisa Ferrando-May,[2*] Hans Fried,[3] Christian Kukat,[4] Angela Naumann,[5] Roland Nitschke,[5] Pawel Pasierbek,[6] Jan Peychl,[7] Tobias Manuel Rasse,[8] Britta Schroth-Diez,[7] Martin Thomas Stöckl,[2] Stefan Terjung,[9] Roland Thuenauer,[10] Silke Tulok,[11] Stefanie Weidtkamp-Peters,[12] German BioImaging-Society for Microscopy and Image Analysis[13]

[1]Core Facility Bioimaging at the Biomedical Center, Ludwig-Maximilians-Universität München, Planegg-Martinsried, Großhaderner Straße 9, 82152, Germany

[2]Bioimaging Center, University of Konstanz, Konstanz, Universitätsstrasse 10, 78464, Germany

[3]German Center for Neurodegenerative Diseases (DZNE), Light Microscopy Facility, Bonn, Venusberg-Campus 1, Gebäude 99, 53127, Germany

[4]FACS & Imaging Core Facility, Max Planck Institute for Biology of Ageing, Cologne, Joseph-Stelzmann-Str. 9b, 50931, Germany

[5]Life Imaging Center and BIOSS Centre for Biological Signaling Studies, Albert-Ludwigs-University Freiburg, Freiburg, Habsburgerstr. 49, 79104, Germany

[6]Biooptics Core Facility, Institute of Molecular Biotechnology of the Austrian Academy of Sciences (IMBA), Vienna BioCenter (VBC), Vienna, Dr. Bohr-Gasse 3, 1030, Austria

[7]Light Microscopy Facility (LMF) Max Planck Institute of Molecular Cell Biology and Genetics Dresden, Dresden, Pfotenhauerstrasse 108, 01307, Germany

[8]Scientific Service Group Microscopy, Max Planck Institute for Heart and Lung Research, Bad Nauheim, Ludwigstraße 43, 61231, Germany

[9]European Molecular Biology Laboratory, Advanced Light Microscopy Facility, Heidelberg, Meyerhofstraße 1, 69117, Germany

[10]Advanced Light and Fluorescence Microscopy Facility, Centre for Structural Systems Biology (CSSB), Hamburg, Germany and Department of Biology, University of Hamburg, Hamburg, Germany

[11]Technische Universität Dresden, Faculty of Medicine Carl Gustav Carus, Core Facility Cellular Imaging, Dresden, Fetscherstrasse 74, 01307, Germany

[12]Center for Advanced Imaging, Heinrich-Heine University Duesseldorf, Duesseldorf, Universitätsstr. 1, 40225, Germany

[13]GerBI-GMB, c/o University of Konstanz, Konstanz, Universitätsstrasse 10, 78464, Germany

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*Correspondence to: Steffen Dietzel, Core Facility Bioimaging at the Biomedical Center, Ludwig-Maximilians-Universität München, Großhaderner Straße 9, 82152 Planegg-Martinsried, Germany Email: dietzel@lmu.de
Elisa Ferrando-May, Bioimaging Center, University of Konstanz, Universitätsstrasse 10, 78464 Konstanz, Germany Email: elisa.may@uni-konstanz.de

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Abstract

Operating shared resource laboratories (SRLs) in times of pandemic is a challenge for research institutions. In a multiuser, high-turnover working space, the transmission of infectious agents is difficult to control. To address this challenge, imaging core facility managers being members of German BioImaging discussed how shared microscopes could be operated with minimal risk of spreading SARS-CoV-2 between users and staff. Here, we describe the resulting guidelines and explain their rationale, with a focus on separating users in space and time, protective face masks, and keeping surfaces virus-free. These recommendations may prove useful for other types of SRLs.

Key terms

virus; COVID-19; light microscopy; disinfection; droplets; physical distancing

In situations of commonly perceived uncertainty and stress, individuals may come together to elaborate strategies for better coping with an upcoming crisis. This type of collective behavior became manifest at Trends in Microscopy 2020, the first edition of the German BioImaging (GerBI-GMB) imaging school held in Germany in the Swabian Alb from 9th to 13th of March 2020, in the week immediately preceding the nationwide shutdown in response to the COVID-19 pandemic. On the last morning of the meeting, a group of attendees, in majority managers of microscopy shared resource laboratories (SRLs), anticipating the further developments, spontaneously met for a "Corona workshop" to brainstorm about procedures to ensure safe working conditions in their facilities. The outcome of this workshop, the first version of the "German BioImaging recommendations for operating Imaging Core Facilities in a research environment during the SARS-CoV-2 pandemic," was published on the GerBI-GMB website a few days after the meeting. A revised version (Supplementary Material 2) followed on April 1, 2020, which was widely acknowledged by national and international imaging communities. The aim of these recommendations is to help protecting users and staff working in a low-safety environment (mostly biosafety Level 1) from accidental contagion by yet unidentified, asymptomatic SARS-CoV-2 carriers, and are based on our current still fragmentary knowledge of this virus. They do not include high-risk research environments (e.g., biosafety Level 3) where specifically trained scientists work with samples or persons known to be infectious. It is to be expected, that our

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recommendations—as well as all analogous documents and publications from other organizations that followed (see Supplementary Material 1)—will evolve with our knowledge of the virus, its mechanisms of transmission, and the epidemiology of the disease. To document this updating process, we have deposited our recommendations in an open-access repository with version control (1). The summary of a recent virtual meeting organized by the Royal Microscopical Society and Bio-Imaging North America reflects the status of the discussions as of May 13, 2020 (see Supplementary Material 1 for link).

Whether and how strictly the described precautionary measures are implemented will depend on the current local situation, such as the infection rate in the local population and the assumed number of asymptomatic carriers. Any locally enacted guidelines should comply with regulations set by local authorities. Also, it is mandatory to explain the rationale behind each measure to the users to gain their cooperation. Most of the suggested measures can and have been transferred to other types of SRLs, for example, to flow cytometry facilities headed by German BioImaging members. They also could be adopted in case of outbreaks of other, comparably hazardous Coronaviruses, while other types of pathogens may have a very different risk profile and may require different disinfection approaches.

Keeping Distance

According to current evidence, SARS-CoV-2 is primarily transmitted through respiratory droplets and direct contact (2). Keeping distance is thus of utmost importance to cut infection chains. As of May 2020, the majority of SRLs were in one of two situations: (1) the institution is in full lockdown or (2) the institution allows limited/restricted operation. We will discuss keeping distance separately for these scenarios.

(1) In a full lockdown, SRLs are closed, equipment is shutdown, and no users are allowed to enter the facility rooms. SRL managers should communicate with the institute's management that SRL staff can still be productive working from home. We recommend offering user support in terms of project discussions, advice on image analysis, and microscopy-related education via remote tools. Analysis PCs and software should be made available for remote access (see below). Projects related to COVID-19 or other critical topics may be exempted from lockdown regulations. In this case, we recommend that only the independent and fully trained users access the SRL since no on-site support will be available. Otherwise, SRL staff could offer microscopy experiments as a service. Handover of samples must occur contact-free, for instance via a sample dropbox. All these exceptional cases need to be resolved in accordance with local management and safety regulations. The actual work conditions for those projects should follow the recommendations given for scenario 2.

(2) If an institution allows limited/restricted operation, it is strongly advisable to limit the number of people present in the facility at any given time. Staff and users must keep temporal and spatial distance both between and among each other. The latter can be achieved by introducing shift work, that is, alternating between working at home, and presence on-site. Possible concepts consist in having small teams rotating every 14 days (corresponding to the incubation time of the virus and therefore preferred) or on a daily or half-daily basis, or a combination thereof. Communication and assistance via video/telephone and remote computer access should be established. Several commercial and open source solutions exist. We recommend discussing with the local IT department as institutions often offer their own solutions or have restrictions with respect to data security.

Most important is keeping physical distance as regulated by local authorities. In the United States, 6 feet (~1.8 m) are recommended (3). In Austria, the official recommendation changed from 2 to 1 m, in Germany it is stated as "at least 1.5 m." It can be helpful to indicate the distance with tape on the floor. Aspects that can influence a potential transmission of SARS-CoV-2 are the size of the room, the air turnover rate, and the airflow patterns. For example, Universities in the German state of Bavaria required a minimum of 9 m^2 per person (4), whereas the University of Freiburg (Germany) sets this limit to 15 m^2. If a reasonably safe distance between individuals cannot be guaranteed, the SRL should limit the access to one person per room.

SARS-CoV-2 can remain viable in aerosols (particle size <5 μm) for several hours under controlled conditions, with a half-life of about 1.1 h and it appears that aerosols can transmit SARS-CoV-2 (5). An infected person can generate a significant amount of airborne infectious particles during an extended microscope session which can potentially represent a risk (6,7). This effect is mitigated by the automated ventilation system with which SRL rooms are usually equipped and which enforces a several-fold air exchange per hour. Nevertheless, it may still be advisable to introduce a break between users, its duration depending on the intensity of the automated ventilation. If, as common in German laboratories, rooms have four to eightfold air exchange per hour, then 15-min should be sufficient for one complete air volume turnover. Such a break has also the advantage to reduce encounters between users in corridors and at the doors. It can be implemented in the booking software, or with the help of post-it notes on the door.

If staff members need to assist through open doors to keep a safe distance, airflow should be considered: a pressure difference might cause a directed flow of potentially contagious air in one direction. If multiple people work in a room at different instruments, covering their nose and mouth (see mask section below) and keeping the recommended physical

distanceis strongly encouraged. As it is impossible to keep this distance while working at the same microscope, traditional interactive face-to-face training are to be avoided or postponed. GerBI-GMB will report on remote instrument introductions and training in more detail elsewhere.

Wearing Protective Face Masks

The topic of wearing masks in SRLs was challenging at the time when the first version of these guidelines was prepared. Wearing protective face masks in public spaces was not yet officially endorsed by German authorities. Meanwhile, the situation has changed. Many countries, including Germany, as well as the WHO (update on June 5, 2020), promote or require wearing masks or equivalent forms of nose–mouth covering in public spaces as an important additional safety measure (8). Our recommendations follow this rule. The basic idea is simple: my mask protects you, your mask protects me. Masks reduce the number of droplets which are exhaled while speaking, coughing, sneezing, or simply breathing. Therefore, masks help to control the spread of viral infection by reducing the shedding of droplets into the environment from asymptomatic individuals. This is consistent with the experiences of countries that have adopted this strategy, according to the Royal Society DELVE Initiative document (6,9).

Ideally, SRL staff might consider using professional personal protective equipment (PPE) of the FFP2 (N95) or even the FFP3 (N99) category. Filtering face piece (FFP) comes from the European norm EN 149:2001. In the current situation, only non-valved respirators should be used, so that the exhaled air is filtered. This PPE is specified to greatly reduce transmission of viral particles through the route of inhalation. However, especially at the beginning of the COVID-19 pandemic, we were confronted with a global shortage of PPE. It was and still might be hard to obtain professional PPE for people who are not involved in patient care. If users and staff of SRLs respect all other guidelines, that is, coming to work only if symptom-free, respecting social distancing, and minimizing personal contact, simple face masks (textile nose–mouth coverings) should warrant sufficient additional protection.

There are also potential risks associated with wearing masks. They might give users a false sense of security and might become a source of infection when not used properly. Therefore, proper training on how to handle masks is required. Several descriptions as how to make simple masks at home are widely available online (e.g., the website of the US Center for Disease Control and Prevention). The WHO also provides online educational materials on how to handle PPE correctly (see Supplementary Material 1 for links). We propose to use masks made from high-density cotton which can be used repeatedly and easily sterilized by boiling, washing, and ironing. To conclude, we suggest that SRLs staff together with their local safety officer consider introducing masks in public areas including work in SRLs, supposing that wearing masks is in-line with government guidelines.

Preventing Exposure to SARS-CoV-2 VIA Frequently Touched Surfaces

Under normal circumstances, many SRLs have a policy restricting the usage of gloves in their rooms to avoid contamination of instruments by dirty gloves. During the current COVID-19 pandemic, however, potential virus transmission via frequently touched surfaces presents a more pressing concern. Such surfaces include computer mouse, keyboard, power buttons, and controls like focus wheels or stage controllers. Under these circumstances, users are requested to put on fresh laboratory gloves when entering the SRL, in addition to regular thorough hand washing. Persons with sensitive skin may consider wearing cotton gloves underneath. If during work in the SRL, users have to handle hazardous samples they may choose to put on a second pair of differently colored gloves specifically for that purpose. It is recommended to disinfect the gloves in between from time to time as described in the disinfection part below. People should avoid touching their face or mobile phone with gloves. Disposal of gloves and washing hands immediately afterward is the last step when leaving the SRL. A waste bin for used gloves should be placed close to the exit.

Some SRLs normally provide shared lab coats for their users. Under the current situation, however, sharing lab coats must be avoided and shared lab coats must be removed. Each SRL user and staff member should have his/her personal clean lab coat. If coats are used repeatedly before washing, they should be labeled and stored in the facility premises without touching each other to prevent cross contamination.

Keeping microscope eyepieces clean is important, since SARS-CoV-2 potentially may be transmitted via the conjunctiva (10). Ocular usage should be avoided where focusing is possible with camera or using hardware autofocus options such as finding the focus via reflection mode. If using the oculars is necessary, these and the neighboring microscope body should be covered with cling film (Fig. 1). Users are encouraged to bring and wear their own safety glasses for further protection. Frequently touched surfaces that are easy to disinfect, like lab benches, washable keyboards, and mice should be disinfected regularly (see below). Cling film (plastic wrap for household use) can be used to cover those surfaces which are difficult to disinfect, such as microscope eyepieces, nonwashable computer peripherals, touch panels, switches, and similar parts. Cling film should be renewed for each user.

Disinfection

A person infected with SARS-CoV-2 will unknowingly spread the virus to surfaces. Like other coronaviruses, SARS-CoV-2 can persist on inanimate surfaces, such as plastic and stainless steel, for several days (11). Thus, all surfaces that might get touched by different users during operating a microscope are to be disinfected before and after each usage to avoid potential spread of SARS-CoV-2 via this route. This precaution applies in particular for those frequently touched surfaces on the microscope body and add-on equipment, which cannot be covered easily with cling wrap like focus knobs, push

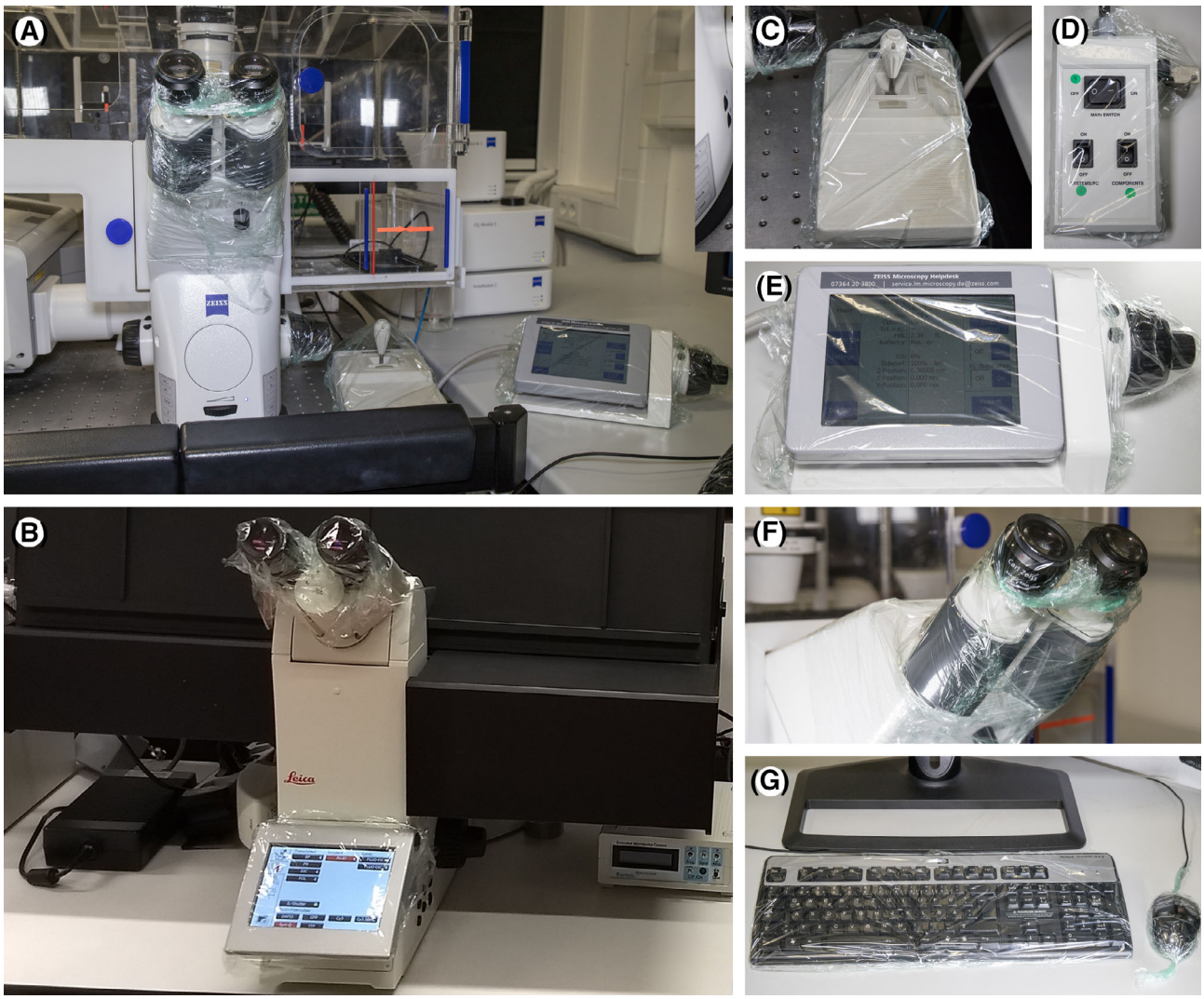

Fig 1. Examples of frequently touched surfaces at microscopes enveloped in cling film: **A**,**B**, microscope stands; **C**, joystick; **D**, laser switches; **E**, touch screen; **F**, eyepieces and tube; and **F**, computer keyboard and mouse. [Color figure can be viewed at wileyonlinelibrary.com]

buttons, condenser, sample holder, joystick, etc. But also cling wrap protected surfaces should be cleaned regularly after unpacking.

The ability of several disinfectants to neutralize SARS-CoV-2 has been tested (12) with the result that formulations containing ethanol or 2-propanol are efficiently able to deactivate the virus within 30 s of exposure. Considering (1) its compatibility with typical materials from which microscope and computer controls and cases are made of and (2) the widespread availability in research laboratories, the common recommendation for all microscope brands is using soft tissue well moistened with 70% ethanol/30% water without any further ingredients. The disinfectant solution should be applied to the tissues using a wash bottle and the disinfectant-soaked tissue then used to thoroughly rub surfaces. An excessive amount of fluid has to be avoided to prevent electric damages. Always consider the necessary exposure time (approx. 0.5–1 min) for the disinfection. Do not use spray bottles to avoid aerosol or mist formation, which is a hazard (lower explosive limit 3.3% ethanol in air) as well as a health problem when inhaled (see safety data sheets for ethanol). As cleaning with 70% ethanol can occur frequently, sufficient air exchange is required, especially in small rooms. During cleaning, proper PPE (gloves, lab coat, mask) should be worn. Materials as well as PPE used for cleaning should be treated as potentially infectious and disposed of in suitable waste bins. These procedures comply with recommendations of the major manufacturers of research microscopes. A respective link is in Supplementary Material 1.

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Author Contributions

Steffen Dietzel: Conceptualization; writing-original draft; writing-review and editing. **Elisa Ferrando-May:** Conceptualization; writing-original draft; writing-review and editing. **Hans Fried:** Conceptualization; writing-original draft; writing-review and editing. **Christian Kukat:** Conceptualization; writing-original draft; writing-review and editing. **Angela Naumann:** Conceptualization; writing-original draft; writing-review and editing. **Roland Nitschke:** Conceptualization; writing-original draft; writing-review and editing. **Pawel Pasierbek:** Conceptualization; writing-review and editing. **Jan Peychl:** Conceptualization; writing-original draft; writing-review and editing. **Tobias Rasse:** Conceptualization; writing-review and editing. **Britta Schroth-Diez:** Conceptualization; writing-original draft; writing-review and editing. **Martin Stöckl:** Conceptualization; writing-review and editing. **Stefan Terjung:** Conceptualization; writing-original draft; writing-review and editing. **Roland Thuenauer:** Conceptualization; writing-original draft; writing-review and editing. **Silke Tulok:** Conceptualization; writing-original draft; writing-review and editing. **Stefanie Weidtkamp-Peters:** Conceptualization; writing-review and editing.

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