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EDUCATION

Implementation of a fully digital histology course in the anatomical teaching curriculum during COVID-19 pandemic

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A B S T R A C T

Background: During the COVID-19 pandemic, many medical schools are forced to switch courses of the mandatory curriculum to online teaching formats. However, little information about feasibility and effectiveness is available yet about distance teaching in anatomy. The aim of this study was to evaluate the implementation of a histology course previously taught in a classroom setting into an online-only format based on video conference software.

Methods: Our course design included theoretical introductions, an online-adaptation of virtual microscopy used previously in the classroom, and active learning elements such as collaborative learning in breakout rooms, annotation assignments and multiple-choice questions. Two preclinical semester cohorts of around 400 second and third semester students were taught in histology in parallel courses, using the Zoom software platform. We analyzed data about student attendance during the course, summative quantitative and qualitative evaluation of the students and results of a written test required to pass the course.

Results: We observed that student attendance was high and stable during the 19 course days for both second and third semester, and only few students reported technical problems. There were no significant differences in examination results of second semester compared to the third semester, an unexpected result as the third semester already participated in the dissection course before. Similarly, no significant gender-related effects on the examination performance could be noted in both semesters. However, the age of students was negatively correlated with test scores in the second and third semester. Importantly, the overall evaluation of the digital version of the histology course was at least as positive as the in-person version over the past years.

Conclusion: Together, we experienced that the implementation of a curricular histology course in an online-format is technically realizable, effective and well accepted among students. We also observed that availability and prior experience with digitized specimen in virtual microscopy facilitates transition into an online-only setting. Thus, our study supports the positive potential of distance learning for teaching anatomy during and after COVID-19 pandemic but also emphasizes the need for a synchronous learning environment with partially personnel-intensive small group settings to overcome passivity and inequality aspects, and to foster active learning elements.

1. Introduction

Current COVID-19 pandemic is persisting for more than twelve months now and has already led to severe disruptions in medical education around the world. Even though the infection curve has flattened and increased again in most European countries, it seems that our society needs to cope with the virus and the regularities to prevent spreading in the long term. In response to the virus' outbreak and the necessity of physical distancing, medical schools were constrained to adapt their teaching from face-to-face classes completely or partially towards web-based formats to ensure continuity of teaching (Roy and Cecchini, 2020).

There is a gradual but continuous trend of anatomical educators to adopt new technology into their repertoire (Hopkins et al., 2011). However, anatomy includes practically-oriented dissection courses and microscopy classes that are traditionally taught in face-to-face settings. The transition into online-only teaching forced by SARS-CoV-2 posed a notable challenge for the anatomical community. Innovative approaches as instructional online videos (Barry et al.,

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2016; Langfield et al., 2018), digital self-learning tools (Appaji et al., 2010; Rinaldi et al., 2017), radiology tools (O'Rourke et al., 2020; Royer, 2016), VR-technology (Birbara et al., 2020; Bork et al., 2020; Chytas et al., 2020), video feedback (Donkin et al., 2019), 3D-printed anatomical models (Smith et al., 2018) and social media elements (Maske et al., 2018), have already been proposed, yet there is only little experience with online-only anatomy teaching. Considering the special requirements of anatomical teaching with regard to practical application of knowledge (Schoeman and Chandratilake, 2012), the implementation of general recommendations derived from those studies turn out to be difficult and subject-specific solutions are necessitated. As a result, quite different formats could be observed in medical schools in response to COVID-19 pandemic regarding the use of resources, assessment strategies and performance of anatomy teaching (Longhurst et al., 2020; Pather et al., 2020).

Histology and microscopic anatomy, core disciplines of anatomy, traditionally involve the practical utilization of optical microscopes in order to identify cellular and subcellular structures with the goal to understand the structure-function relationship of cell types and tissues. Histology and gross anatomy are taught separately at most universities but the order of teaching these subjects is handled differently. Simultaneously with the technological progress (Aeffner et al., 2018; Zarella et al., 2019), more and more digital tools for histology teaching have been developed over the last two decades: the use of virtual instead of optical microscopy (Helle et al., 2013; Kuo and Leo, 2019; Mione et al., 2013; Paulsen et al., 2010), interactive e-learning platforms (Khalil et al., 2013; Sander and Golas, 2013), technology-supported interactive response systems (Rinaldi et al., 2017), flipped-classroom approaches (Cheng et al., 2017) and others (Black and Smith, 2004; Kotzé and Mole, 2015; Zilverschoon et al., 2019). Some of these elements have already been integrated successfully in the curriculum within a blended-learning format (Merk et al., 2010), but only few attempts to teach a histology course in a completely digital format have been reported yet (Barbeau et al., 2013).

When implementing education from face-to-face into online settings it is important to monitor that all students make the transition to the new education environment equally well and that no subgroup is "left behind". This is particularly important, since recent observations have shown an emergency of learning inequalities in remote teaching (Czerniewicz et al., 2020). Therefore, we paid attention to particular groups of students when implementing our online-only digital histology class during the Corona pandemic: One important variable is the gender-related use of information and communication technology (ICT). When the technologies were introduced first, male students were engaged more in ICT than female students (Lockheed, 1985). The gender-moderated differences in computer literacy, however, decreased over time with a tendency to even favoring female students over the past years (Fraillon et al., 2014). The tendency is in line with the observation that female students seem to be better at communicating online and are more self-disciplined in the use of online resources (McSporran and Young, 2001). Another relevant aspect are age-related effects in an online learning environment. Students born after 1980 grew up with ICT and are referred to as "digital natives", suggesting that most of the younger students are familiar with online environments. Medicine students in Germany show considerable variance concerning age at most universities because the selection procedure facilitates a certain percentage of more mature students to study medicine. Mature students are students, who are older than the average age, often set to a cut-off point of 25 years (Tones et al., 2009). In general, mature students have had a longer time since graduating from high-school and might have acquired additional responsibilities (e. g. family, financial support etc.) compared to younger students (Imlach et al., 2017; Ngo-Ye, 2014).

The aim of our study was to accompany and assess an online-only digital histology course via the Zoom web conference tool that we implemented during the summer term 2020 as a consequence of the pandemic situation in Germany. We applied a synchronous format with theoretical introductions and interactive elements such as virtual microscopy, teamwork in breakout sessions and multiple-choice questions for two large semester cohorts of second and third-semester medical students. We report that an online-only histology course with elements of active learning is technically realizable, effective with respect to learning results and well accepted among students even for larger cohorts.

2. Material and methods

2.1. Cohort

Data have been collected from two semester cohorts of second and third semester undergraduate medical students at the Westfälische Wilhelms-University Münster in Germany during the regular pre-clinical curriculum in the summer term 2020. The second semester consisted of 192 students (63% female and 37% male students) and none of these students were repeating the course. The third semester consisted of 200 students (62% female and 38% male students). Since all repeaters were attached to the third semester, this cohort included 39 students repeating class who failed the exam in previous in-person versions. The mean student age was 21.7 years in the second semester and 23.9 years for the third semester. Another difference between the two cohorts was that the third semester students had already participated in the gross anatomy course in their previous term.

2.2. Video conferencing

The software Zoom (Zoom Video Communications, Inc.; versions 4.8 – 5.1.) is a commercial online video conferencing tool which was used as a platform to conduct our online-only digital histology course. Initially developed for video conferencing and online chat, Zoom is also used for teleconferencing, distance learning and private relations. The system requirements include a stable wired or wireless (>3G) broadband internet connection, as well as speakers, microphone and a webcam. Multiple operating systems (macOS 10.9 or later, Windows 7 or later, several Linux-based systems) and browsers (IE, Edge, Firefox, Chrome, Safari) are supported. Furthermore, Zoom can be used with tablet and mobile devices (iOS, Android, Surface PRO2, Blackberry) in addition to desktop or notebook computers. The Westfälische Wilhelms-University Münster closed a contract with Zoom, which guarantees stricter privacy protection according to the general data protection regulation ("Datenschutz-Grundverordnung") of the European Union. Potential critical functions of Zoom, for example login via a Facebook account, were deactivated in our version of the software. To join sessions, students had to register with their university ID and password. After successful registration students received an email with a hyperlink and a password to the conference session. In order to control for authorization, we matched the registered students with the official list of participants for the course before we enabled the participation. Students used the software with a desktop client, which can be downloaded for free and without a license. To host sessions lasting longer than 40 min with many participants, the lectures used commercial licenses acquired by the University of Münster. Students without the technical requirements had the opportunity to get access through a computer pool of the university. To prevent misuse, remote access to sessions were restricted to several countries in advance.

To facilitate participation, the students received an email with all course dates, which they could directly import into their digital calendars. About half an hour before the lessons started, the students could join directly through a hyperlink. If students dropped out of the session on account of technical issues, they were able to enter again with the same link. After joining, the students were first directed to a waiting room until the course started. Meanwhile the lecturers could test technical issues in the main meeting room (e.g., presentation, microphone, webcam, preparation of breakout rooms), invisible for the students in the waiting room. The lecturer in the main room usually shared the screen during the theoretical introductions that was presented in Keynote from an additionally attached iPad tablet computer which also allowed easy annotations or highlighting during the presentations via the Apple Pencil. During the theoretical introductions in the main room, the audio signal of students was muted and the private chat option was restricted to prevent distractions. However, students could chat with the additional lecturers present throughout the course to ask questions and discuss technical issues. Also, the students had the opportunity to digitally raise their hand, whereby they were unmuted by the lecturers to ask questions or comment. The students were regularly encouraged to turn on their webcams to transmit a video signal.

2.3. Online breakout rooms and working in small groups

Zoom enables the use of so-called breakout rooms, facilitating group work and interaction with lecturers. Students in the main room were regularly distributed into such smaller groups of predefined size and duration. Around 2–3 times during a three-hour course session the students were randomly assigned to breakout rooms, unmuted, and instructed to solve a certain problem in groups of 5–10 students. The instructions usually included several images of histological slides, which had to be identified, discussed and/or annotated. One of the students had to share their screen, so that all student in a breakout room could annotate the image using the “commentary” function in Zoom. Meanwhile the students could monitor the remaining time before automatically heading back to the main session. The lecturers visited the breakout sessions to answer questions, give instructions and feedback. Students in the breakout rooms had the opportunity to “call for help” out of the rooms. The duration of the breakout sessions ranged from 10–25 min, depending on the task. The students were regularly encouraged to use the commentary function in breakout rooms.

2.4. Virtual microscopy

During the main sessions, the lecturer also frequently shared the screen to perform virtual microscopy with our custom histology software “Virtuelle Mikroskopie” that we have used in the mandatory histology course since 2008/2009, albeit in a classroom setting equipped with a computer pool and students in presence. This software is based on a collection of about 200 different digitized specimens from all relevant tissues/organs. The lecturer could switch between several samples of the same histological specimen to demonstrate variability, zoom in and out and annotate cellular and subcellular structures. However, the students had no off-campus access to this virtual microscope due to technical limitations. Future versions of the digital microscopy course with off-campus access are planned for the immediate future, in particular if pandemic restriction continue to be in place.

2.5. Digital multiple-choice questions

Zoom enables to include multiple-choice questions without any additional software, which was regularly used at the beginning of a course to enable feedback on the students’ learning progress and to identify potential gaps in knowledge. The students had about one-and-a-half-minute time to choose between five options, often including the evaluation of a characteristic part of a histologic image. Lecturers had the opportunity to monitor the total response rate and the chosen answers in real time. Afterwards the correct result and the percentage of answers selected were presented back to the students and the answers were briefly reviewed.

2.6. Course materials and personnel resources

Presentation slides and histological sections shown in the course were available to the students from our university website. Few days before the course, the lecturers uploaded their teaching slides and a preliminary version of images without annotations, so the students could prepare for the course. Afterwards the full version of the presentation with pictures of the annotated specimen was uploaded as a script version. Furthermore, the students had online access to several e-books of histology with their university accounts. The suggested reading material for the individual parts of this course included references to two widely used German histology text books: Kummer, Wolfgang (2018), Lehrbuch Histologie, 5th edition, München; and Lüllmann-Rauch, Renate (2019), Taschenlehrbuch Histologie, 6th edition, Stuttgart. They were also available in multiple copies through our campus library, and in digitized versions from the publisher. Since our course is based on a synchronous format with work-sessions in smaller groups, the personnel required and the time resources allocated to the course were the same as in in the face-to-face settings. In fact, additional time and effort on behalf of the lecturers was needed for preparation and implementation of the online course, for example, to acquire the digital competencies with video conferencing software, designing virtual small-group working and selecting specimen for virtual microscopy, as well as for establishing the infrastructure.

2.7. Digital evaluation

Our faculty uses a custom-made, strictly anonymous online evaluation tool called “EVALuna”, which is hosted on remote servers and not linked to any student administration services. Another important feature is that evaluating a course is obligatory for the students before participating in the exams. In the tradition of mixed-method approach, the system provides the opportunity to use 5-point Likert scales (from 1 to 5), as well as free text questions. Students had to answer in the following questions: “I can give an evaluation to this event.”, “I participated to the course with the following frequency:”, “Rate the course on a free scale (from 1 to 100)”, “Rate the digital implementation of the course”. The following questions concerning digital learning were additionally asked of the second semester cohort: “How did you like the digital implementation of the histology course (in terms of compatibility, quality, clarity etc.)”, “How did you like the implemented digital tools (in terms of breakout rooms, questionnaire tools, commentary function etc.)”, “Did you have technical issues during the class?”, “The following elements helped me with learning: A) Virtual microscopy and annotations, B) Breakout rooms with the instructions, C) Commentary function in the breakout rooms, D) Help of the lecturers in the breakout rooms, E) Recognition tasks during the lectures.”

2.8. Digital examination

In order to pass the course, the students had to be present in more than 85% of course days, to evaluate the course and to pass a multiple-choice test (1 out of 5 answers correct or incorrect) at the end of the course. The test included 50 questions of which 30 questions contained images mostly of stained light microscopic specimen with structures that had to be recognized. Students had to answer at least 60% of questions correctly in order to pass. Students had to register for the examination online and were able to cancel registration before the examination. Most students took the digital exam on their own computers at home by logging into an exam software via vpn (virtual private network) connections. We offered several on-campus computers for students with instable WiFi connections. During the test the students had to open a Zoom session with a second device (smartphone, tablet) and were filmed from behind to prevent cheating attempts. Groups of ten students were monitored online via these Zoom sessions by one surveillance person. If the WiFi connection of the students interrupted, exam was seen as a failed attempt but this occurred only in around 0.003% of all exams at the University. Due to the novel situation during the early days of the SARS-CoV-2 pandemic, "failed attempts" had no other consequences than taking the necessity to take test again after the following semester. To become accustomed with the procedure, the students were allowed to write a "practice test" beforehand. Implementation of the exam software and surveillance was supported by the "Institut für Ausbildung und Studienangelegenheiten (IfAS)" of our faculty, an institute responsible for medical teaching affairs.

2.9. Data collection and statistical analysis

Data were collected during the lectures (attendance) and after the course through our evaluation and examination tools provided by the IfAS. We analyzed the data using Prism 7.0e (GraphPad) and Excel for Mac (Microsoft, version 16.16.25). A histogram and descriptive statistics were performed first. A D'Agostino and Pearson test was used to test for normality. Students' *t*-test was applied to parametric data. For multiple samples of nonparametric data, Kruskal–Wallis test and Dunn's multiple comparison test were performed. All the tests were performed under a significance value below $\alpha = 0.05$. Results of the statistical testing is specified by a two-tailed *p*-value.

3. Results

3.1. Concept of the fully digital histology course in Münster

Traditional histology courses often encompass theoretical introductions, and guided microscopic lab sessions plus teamwork in small groups. Following the normal curriculum at our University, students of the second semester participate in the dissection (gross anatomy) course and third semesters take the histology course. As consequence of the pandemic situation in early 2020, we postponed the dissection course and provided histology courses for the second and third semester online. Two 19-day courses were scheduled for the two cohorts, each comprising two online sessions of about three hours per week and cohort. As the adaptation to online format had to happen within a couple of weeks, the content of these courses followed our regular on-site course (Table 1).

In preparation of the histology course in digital format, we tried to consider recent evidence about distance learning (Valai et al., 2019). In order to allow live interactions between learner-instructor, as well as between students, a synchronous teaching format with focus on video conferencing was preferred. This more elaborate and personnel-intensive approach was chosen to enable implementation of active learning elements. The course materials (presentation slides, and annotated histology images) were provided online before and after each course day, respectively. The content of the theoretical introductions referred to specific chapters of two widely used histology textbooks (chapter 2.6), allowing students to prepare themselves for each session. Attention was payed to adapt the content to the learning schedule and make it coherent (Bentley et al., 2012) with the official guidelines of the IMPP (German National Institute for state examinations in Medicine, Pharmacy and Psychotherapy) (IMPP, 2014). As outlined in Table 1, the knowledge about histological tissues of the first four course days formed the basis for the subsequent topics. The first session was a repetition of basic cell biological knowledge such as organelles and subcellular compartments, while the last course day was devoted to choose topics and exercises in differential diagnostics of unknown specimen. The actual online sessions were not archived and could not be downloaded later.

Video conferences were the core element of each course day. We implemented different educational methods to create variations and increase interaction, motivation and personal engagement. Referring to the rich evidence about clickers in education (Chen et al., 2017), multiple choice questions were shown and discussed at the beginning of each course. To overcome anonymity and stimulate peer-interactions (Buchenroth-Martin et al., 2017), breakout sessions were established. One main goal was to prevent passivity of the students and promote active learning. The prototypical sequence of a three-hour course day is shown as a scheme (Fig. 1).

3.2. Regular student attendance during the digital histology course

Student attendance to lectures has been associated with higher exam performance (Sund and Bignoux, 2018) and can be seen as a valid measure for educational success. Influencing aspects of student attendance can be divided in personal factors, course-related factors and in unavoidable factors such as illness or family commitments (Lang et al., 2008). In order to successfully pass, regular participation in the histology course is mandatory at our university with an obligatory attendance rate of over 85%. However, we could observe in the past that the absenteeism rate is increasing on Fridays or on a day between a weekend and a statutory holiday, where students tend to use the "gap day" for private activities. Further, when an exam in another subject is approaching, students tend to skip histology course days. We therefore monitored attendance of students on each digital histology course day using meta-data provided by Zoom (Fig. 2a). Because of technical issues such as instable internet connections, the attendance rate fluctuated slightly, mostly at the beginning and end of breakout room settings (not shown).

We observed that the second semester students showed a median attendance rate of 97.4% or 187 participants ($SD = 2.74$, 95% $CI = 186, 189$) and the third semester students a median of 97.5% or 196 participants ($SD = 3.24$, 95% $CI = 194, 198$) (Fig. 2a). There was no obvious fluctuation of course attendance over the 19 course days, suggesting that an online format might be more robust to absenteeism compared to on site teaching. The overall difference of attendance between both semesters is due to different sizes of the semester cohorts (chapter 2.1). Regarding the permanent use of the video signal/webcam activity suggested to the students, more fluctuation was observed (Fig. 2b). Assuming non-parametrical data, Wilcoxon-test showed no significant differences for both semesters $Z(N = 19) = 26$, $p = 0.614$. The transmission of video signals from students had its maximum during the second and third course day (third semester: 41 students; second semester: 63 students) but

Table 1
Content and sequence of topics and specimen during the online histology course. The online histology class consisted of 19 course days and covered most human tissues. First four course days dealt with histological tissues in general. Course days 5-19 focused on light microscopy of organs, and mostly provided different stainings and specimen for each. In addition, transmission electron microscopy images were used.

	Day	Topic covered	Specimen discussed
	1	Introduction, short review of key aspects of cell biology (organelles, specializations)	Electron microscopic images of different cell types & tissues
Tissues	2	Histological methodology, Epithelium	Tissue processing & important stainings, jejunum, glandula submandibularis, trachea, ureter, cornea, ala of the nose, finger pad
	3	Connective tissue, cartilage and bone	Embryonic head, umbilical cord, tendon, spleen, finger pad, ovary, parotid gland, kidney, trachea, embryonic finger, ear cup, intervertebral disc, woven bone (os parietale), long (lamellar) bone,
	4	Muscle tissue, nerve tissue	Skeletal muscle, cardiac muscle, ileum, uterus, peripheral nerve,
	5	Skin, skin appendages	Finger pad, ala of the nose, scalp, axillary skin, eye lid
	6	Glands, endocrine system	Hypothalamus, Hypophysis, Thyroid gland, Adrenal gland
	7	Blood, cardiovascular system	Blood smear, Aorta, Artery, Vein, Capillary
	8	Immune system, lymphatic organs	Lymph node, tonsilla palatina, lingual tonsil, pharyngeal tonsil, spleen (rinsed, non-rinsed), thymus (juvenile, adult)
	9	Nasal cavity, olfactory organ, respiratory system	Concha nasalis, regio olfactoria, trachea, bronchia, lung
Organs	10	Mouth cavity, salivary glands of the head	Tongue (papilla vallata, papilla foliata, papilla filiformis), Glandulae (parotis, submandibularis, sublingualis), developmental of teeth (fetal head)
	11	Esophagus, stomach, small intestine	Esophagus, stomach (fundus), transition pylorus-duodenum, duodenum, jejunum, ileum
	12	Large intestine, liver, gall bladder, pancreas	Colon, appendix vermiformis, liver, gall bladder, endo-/exocrine pancreas
	13	Urinary system	Kidney (cortex, medulla), ureter, urinary bladder
	14	Male reproductive system	Testicles, epididymis, funiculus spermaticus, prostate, gl. bulbourethralis, penis,
	15	Female reproductive system 1/2	Ovary with follicles, tuba uterina, uterus, cervix uteri, vagina,
	16	Female reproductive system 2/2	Placenta, mammary gland
	17	Eye, ear	Eye (anterior, posterior), eye lid, inner ear (cochlea, vestibular organ)
	18	Central nervous system	Spinal cord, cerebellum, hippocampus isocortex
	19	Differential diagnostics and choice topics	Lymphatic organs, exocrine glands, luminal organs, teeth

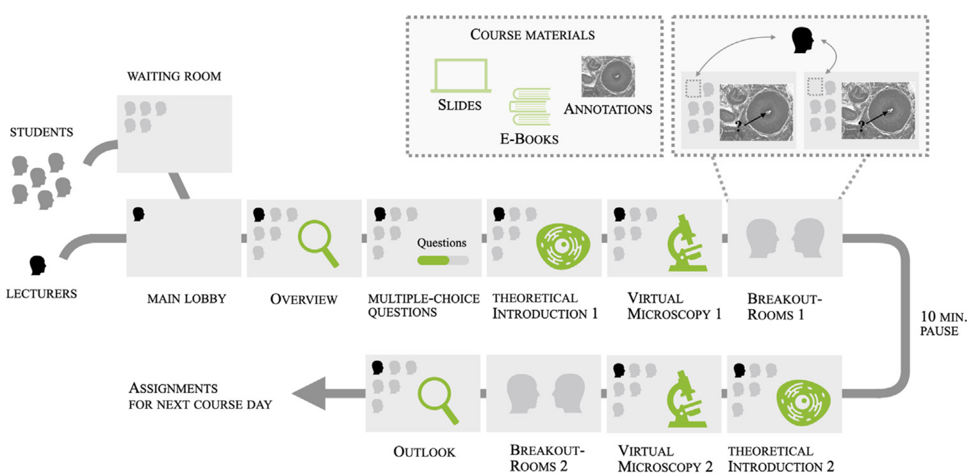

Fig. 1. Prototypical sequence of an online histology course day. After joining the main session from the waiting room, the courses usually started with an overview about the course day and two or three multiple-choice questions about the content of previous sessions. Afterwards one sequences of theoretical introduction, demonstration of the slides in the virtual microscopy with live-time annotations and an instructed breakout room session with a certain task was performed, followed by a 10-minute break. The second half of the course day started with the same sequence as described above. During the breakout rooms the lecturer had the opportunity to jump through different rooms. One lecturer with host privileges remained in the main session in order to help students with technical issues and general questions. Towards the end more virtual microscopy and breakout room sessions were planned. At the end of the course day, an outlook of the next course day was given. Students got suggested assignments related to the topic. During some course days open questions in the main lobby were allowed (not shown).

was decreasing rapidly afterwards in both cohorts despite regular reminders from lecturers to switch on the video signal. The minimum was reached on day 14 (second semester: 5 students) and on day 12 and 17 (third semester: 6 students). A “steady-state” was eventually evident, in which more or less the same students had their webcams/video signals activated during the whole course. After each request to switch on the webcams, a minor increase in webcam activity could be recognized, just to decrease again quickly during the session (not shown). Due to the sudden change to digital environment during the early days of the pandemic situation, students were not enforced during our histology course to turn on their video signal.

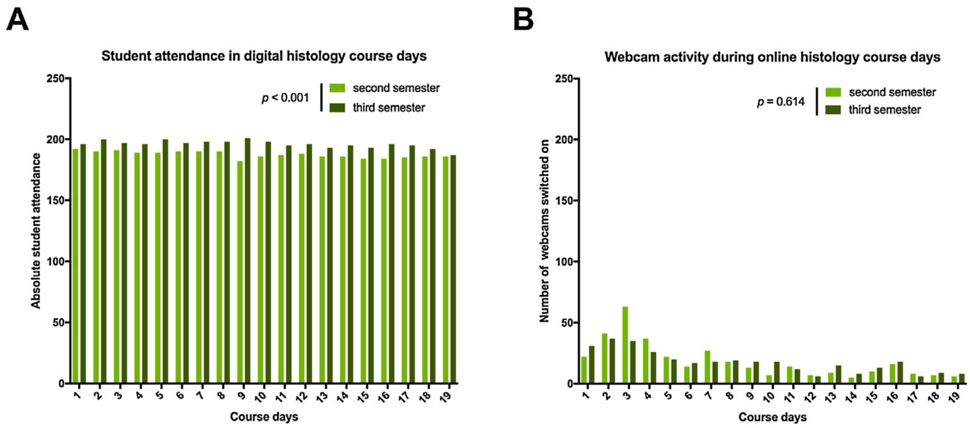

Fig. 2. Student attendance in online histology course days. A) Interleaved bars showing the absolute number of student attendance throughout the 19 course days for second semester (light green) and third semester (olive green). B) Interleaved bars showing webcam activity (number of webcams switched on during theoretical introduction 1) for second semester (light green) and third semester (olive green). (For interpretation of the references to color in the figure legend, the reader is referred to the web version of this article.)

3.3. *Test results reveal high effectiveness of the digital histology course*

In order to successfully complete the histology course, the students had to pass an online examination at the end of the course. The exam consisted of 50 multiple-choice questions, covering the entire content of the course days. We analyzed the MC tests with respect to overall results, failure rate, distribution of scores and we performed age- and gender-related correlations (Fig. 3). In the second semester cohort, 135 of 192 students registered for the exam (70%) and 132 took part in the exam (69%). In the third semester, 175 out of 201 students registered for the exam (87%) and 170 students took the exam (85%). However, when we deducted the group of repeaters in the third semester (n = 29), exam registration in the third semester was falling to 141 students (70%) and 139 who took the exam (69%). Thus, the registration and participation numbers were comparable between second and third semester when adjusted for repeaters. Registration and participation of about 70% as seen in our histology course during the first "Corona semester" appears somewhat below the values for previous years, possibly reflecting the feeling of insecurity that permeated the early period of the pandemic situation among students.

Concerning exam results, the median for the second semester was 71% correct answers (SD = 18.5%, 95% CI = 65%, 72%). For the third semester cohort including repeaters, the median was 74% correct answers (SD = 20.2%, CI = 67%, 73%). For the third semester without repeating students, the value was 76% correct answers (SD = 19.8, 95% CI = 68%, 75%). D'Agostino & Pearson normality test was significant ($K2$ = 22.06, p < 0.01) for all semesters, indicating non-parametric distribution. Consequently, we applied the Kruskal–Wallis test for non-parametrical data that showed no statistical significance (H = 3.05, p = 0.217), indicating that the third semester students, did not perform better in the histology course than the second semester in exam points reached (Fig. 3a, b). This result was surprising to us because the third semester students already participated in the gross anatomy (dissection) course before, However, in terms of failure rate the third semester with 41 failed examinations out of 170 (24.1%, min. 5/50 points, max. 29/50 points) outperforms the second semester with 38 failed examinations out of 132 (29%, min. 10/50 points, max. 29/50 points), especially when the repeating students are excluded (20%, min. 11/50 points, max. 29/50 points) (Fig. 3b).

Furthermore, the availability of data from two large cohorts allowed us to test for putative effects of students' age and gender on the exam results under the condition of an online-only histology course. We observed that age was negatively correlated with points reached in the second semester (Pearson $r(129) = -0.26$, p = 0.0023 and the third semester (Pearson $r(168) = -0.46$, p < 0.001) (Fig. 3c). However, the strength of this association is considered to be small to medium (Cohen, 1988), and was similar to histology course under non-pandemic conditions (data not shown). A Kruskal–Wallis test was then performed to test for gender-specific effects in both semesters comparing the results from male and female students, respectively. No significant differences in performance could be found in both semesters, indicating a gender-fair learning environment during the digital histology course (H = 2.59, p = 0.459) (Fig. 3d).

3.4. *Evaluation of the digital histology course shows high acceptance*

At the end of the course, students had to complete an evaluation form using the online tool "EVALuna", provided by the IfAS for all curricular teaching at our Medical Faculty. Since participation in evaluation is obligatory to take part in the exam, high response rates were reached. 96% of both the second and third semester students responded to the request. In addition, 88% of students claimed to have participated in more than 75% of all course days. For the third semester, 93% claimed having participated in more than 75% of the course. These self-assessment values seemed plausible and consistent with attendance rates reported above. On a scale between 1 ("very good") to 100 ("very bad") points, the online histology course was rated with a median of 21 points in the second semester (SD = 21.7), and a median of 22.5 points out of 100 points in the third semester (SD = 17.7), revealing high overall acceptance of the format with little difference between the two cohorts (Fig. 4a). Moreover, when we compared the results with those of previous semesters under non-pandemic conditions (M = 28 points, 95% CI = 26.2, 31.1), we found that the overall evaluation of the online histology course was at least as positive as the courses held in presence (Fig. 4a).

Finally, we had the opportunity during the evaluation to ask the second semester students questions about the specific elements of the digital histology course that could be answered on a Likert scale. These students rated the multiple-choice questions as most helpful and the breakout rooms as least helpful (Fig. 4b). The recognition tasks in the virtual microscopy, where students had to find out which organ or specimen was shown, were seen as quite helpful. Only two students in the second semester claimed having technical issues very often. The somewhat negative rating for the

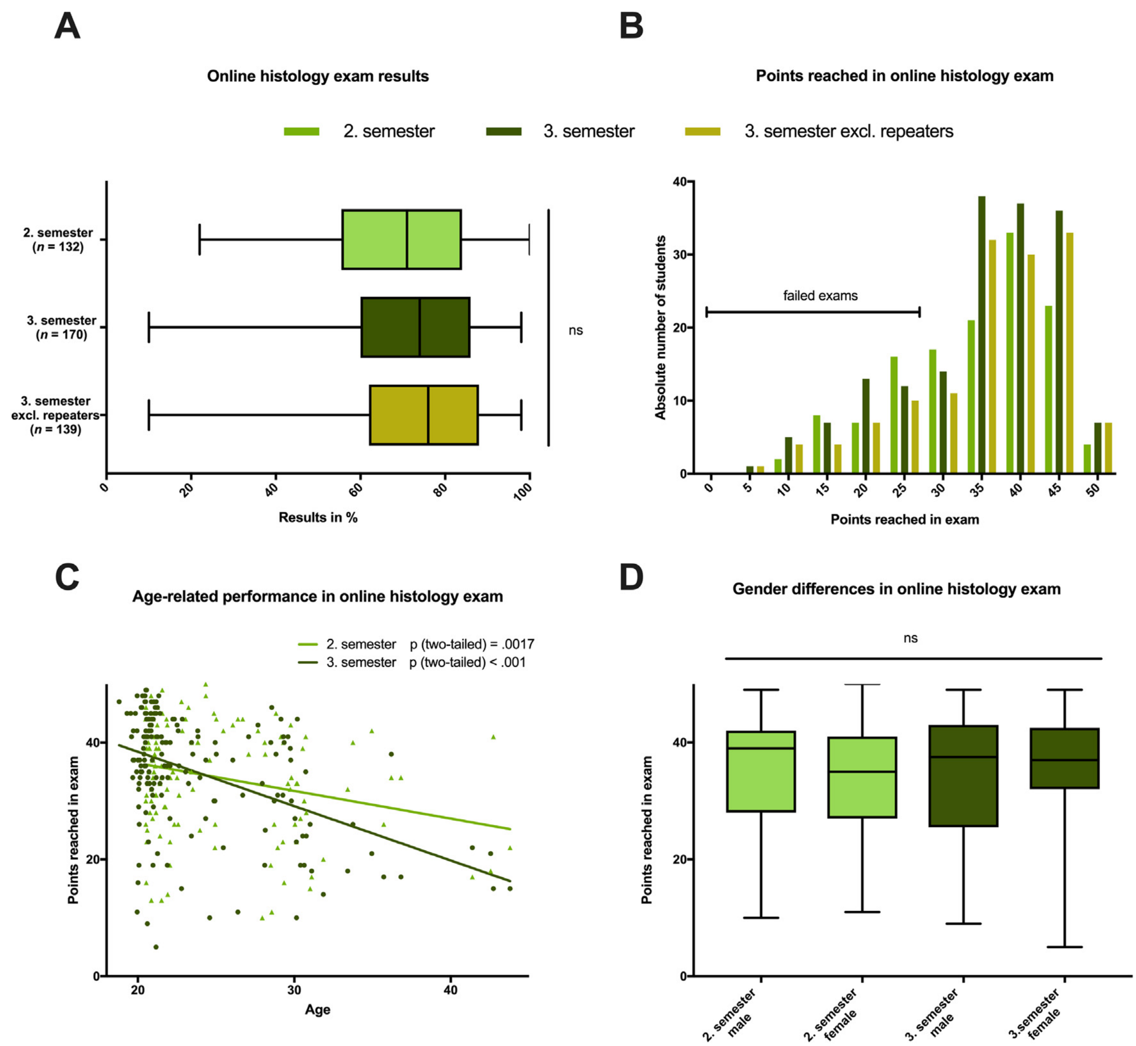

Fig. 3. Online histology exam results. A) Examination results are shown in a boxplot with median and lower 25% and upper 25% quartile, for students of the second semester ($n = 132$), third semester ($n = 170$), and of the third semester without repeating students ($n = 139$). B) Histogram showing reached points in the exam for second semester (light green), third semester (olive green) and third semester repeaters excluded (yellow bars). C) Scatterplot with correlation analysis of age and exam performance for second semester (light green) and third semester (olive green) and given p-value. Most of the students were around 20 years, but in both semesters the age shows a significantly negative correlation with the performance in the exam. D) Gender-related differences is shown in boxplots with median, lower 25% and upper 25% quartile for both, male and female performances and both semesters. (For interpretation of the references to color in the figure legend, the reader is referred to the web version of this article.)

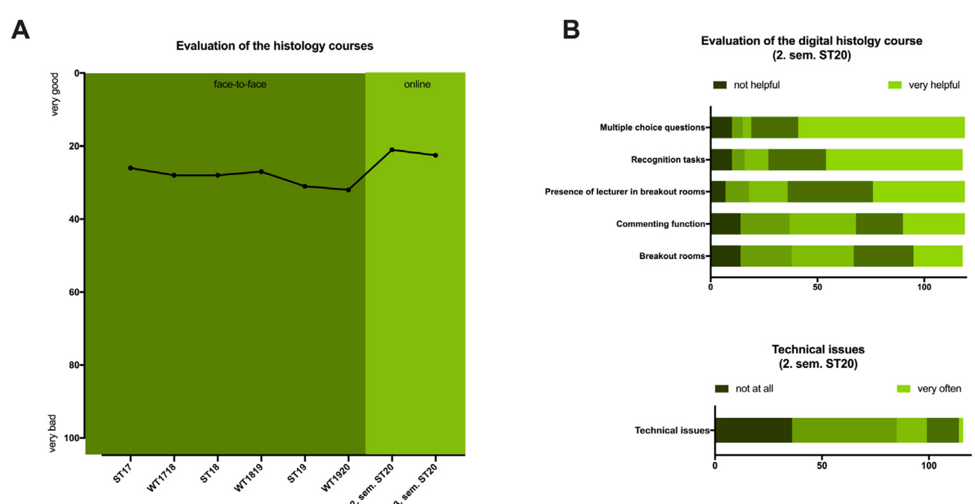

Fig. 4. Evaluation results of the online histology course. A) Diagram showing the evaluation of the histology course in the last three years. Both semesters rated the course as equally good (scale 1 "very good" to 100 "very bad"). Compared with the face-to-face histology courses, the overall rating of the digital histology course is at least as good, if not slightly better evaluated. B) Bars showing evaluation of the online histology course of the second semester. ST, summer term; WT, winter term; sem., semester.

breakout room sessions on the Likert scale were surprising because in the free-text answers, which are a voluntary part of the evaluation, many students reported positive aspects of these breakout rooms. They emphasized that the breakout rooms provided “more variety” and “it increased the interactivity”. In contrast, the length of the breakout rooms with 15−20 min was frequently considered as “too long”. As for the size of the breakout rooms, the students prefer “small groups of three to four students”. Some students also requested “additional pauses”, “more exercises” and “more repetitions” and claimed to have “problems setting the right focus in learning”.

4. Discussion

Digitalization in medicine has long been recognized as an important topic in general but the medical education field has been lagging behind in this development. The COVID-19 pandemic acted as an accelerator for the development of online teaching formats that involve students actively. Already before the appearance of SARS-CoV-2, anatomical education has changed considerably over the last decades throughout the world (Cheng et al., 2020). There has been a tendency in medical schools to progressively substitute computerized learning for traditional teaching methods (Hopkins et al., 2011), not the least because it is considered a possible, though regrettable, remedy for continuous shortage of qualified anatomy educators (Wilson et al., 2020). Interestingly, anatomists, often portrayed as conservative, have been pioneers in computer-based educational innovations (Grosser et al., 2020; Oertel et al., 2020; Schober et al., 2013; Trelease, 2016).

The use of online virtual microscopy tools is already a common add-on or even mandatory part of their courses in many anatomical institutions (Paulsen et al., 2010). Even though many universities around the world have been using blended-learning formats in histology for many years, the conceptualization and implementation of online-only courses into the curriculum have not been systematically evaluated yet. It is crucial in the educational process to determine the outcomes of teaching and guidance. It is particularly important because the current discussion clearly emphasizes learning inequality during the COVID-19 pandemic (Czerniewicz et al., 2020). Therefore, a closer look at the digital transformation and its nuances helps us not just to give feedback to the faculty, but to understand where exactly putative problems and challenges of our students are in order to develop more effective and fair curricula. As many others organizations, our institute introduced virtual microscopy back in the years 2008/2009 to support undergraduate teaching of histology. Experiences gained during these years and development of our software “Virtuelle Mikroskopie” facilitated the transition into an online.only format. Positive experiences with video conferencing tools during the pandemic have been recently reported (Srinivasan, 2020), as well as positive results of newly developed e-learning tools in histological education (Drees et al., 2020).

However, first trials with an online histology course were already reported by Schoenfeld-Tacher and McConnell in 2001, who compared the students’ performance and interaction in the online histology course with those in a traditional face-to-face setting (Schoenfeld-Tacher and McConnell, 2001). Their results revealed that the online students outperformed the on-site students in a pre-post-test, and furthermore showed more frequent interactions amongst students and between students and instructors. The limitation of this study derives from the number of participants, which was quite low with only $n = 11$ students attending the online-course. Several years later, in 2013, Barbeau et al. investigated the effects of an online-only digital histology course in a virtual classroom with synchronous and asynchronous lectures, which they offered during the summer term 2011 (Barbeau et al., 2013). No significant differences between the students’ performance and course ratings in online class was found when compared to face-to-face classes and mixed classes, teaching face-to-face and online simultaneously. However, the validity of this study is limited due to the low evaluation rate of only 36% in the online class and 6.3% in the mixed group.

In this study we presented and evaluated our mostly positive experiences with a synchronous online histology class for two semester cohorts at a Germany university. For the assessment, we used a mixed-method approach, in which quantitative data (student attendance, results of the examinations, quantitative evaluation of the course) and qualitative data (free-text evaluation) were included in order to evaluate the new course format.

4.1. Digital histology course is technically realizable

Using the Zoom platform, it was possible to provide a synchronous online-only histology class for more than 200 students with pre-existing software solutions (Fig. 4b). The system showed stable running behavior, and the only technical problem appeared after a software update of Zoom, which affected the number of breakout rooms that could be used in parallel. Complains were related to the company via the University IT department and, though no feedback was received, the problem disappeared after a couple of weeks.

Although only few of our students reported technical problems, they are frustrating for those who did. Struggling with technical issues can reduce student’s engagement, increase drop-out rates and significantly influence the learning experience. Our experience shows that even though the technical preparation of the teaching platform was accurate, unpredicted complications such as compatibility problems or software updates can occur and interrupt the learning session. This is likely to happen in larger semester cohorts in particular. Based on our experience, we recommend to have at least one coworker with digital proficiencies available during the course, who is just monitoring the proceedings, the chat function and the waiting room for students with technical issues, always ready to intervene in the background without disturbing or interrupting the course itself. This coworker should be introduced to the students in the first lecture as a contact person for technical issues. Yet we recommend to prepare a plan-b, especially when using digital learning methods such as breakout rooms.

4.2. Digital histology course is well accepted among students

While recent observations of online teaching have shown that digital learning is realizable (Cuschieri and Calleja Agius, 2020; Srinivasan, 2020), we wanted to know if it is also accepted by our students. The digital transformation of a standard histology course described above was well accepted among our students of two different semesters. Satisfaction with e-learning environments is a significant aspect in the evaluation of general learning environments (Virtanen et al., 2016). This is reflected by high and stable attendance rates in synchronous learning sessions (Fig. 2a) and the positive course evaluations (Fig. 4a). It should be noted that though the course was mandatory, the students could miss up to 4 days without failing regular attendance. Interestingly, fluctuations in the students’ attendance, which we regularly observe in face-to-face courses, where students tend to be more absent towards the end of the course, did not occur. One reason may be higher comfort and time-saving aspects of the remote access opportunity. However, since most of the students switched off their webcams during the classes, it is not verified, whether they were actually participating actively in the class or if they were just present or logged in during the teaching period. Regarding the decreasing rates of webcam activity during the course (Fig. 2b), we conclude that it is uncomfortable for the students to switch on their webcams during the whole session, as they may feel observed by others or do not want others "invade" their privacy. Although the reasons to prefer anonymity were not entirely clear, limited equipment or inferior WiFi connections were frequently cited. Another explanation might be that the students have the tendency to "lay back" in online settings or were confronted with cognitive overload (Ambrose, 2020). Since more webcams were switched on during the breakout sessions, in which more attendance with a video signal could be observed (not quantitated), the technical issues are surely not the only reason for the observed reluctance to share the video signal. However, the strong tendency to hide behind a black screen led our faculty to the decision to make attendance with active video signal generally mandatory in the current winter term 2020/2021. Nevertheless, based on the written evaluations, examination results and our experiences in the breakout rooms, we had the impression that most students actively participated in the course.

4.3. Nuances of digital histology learning

Students declared multiple-choice-questions and virtual microscopy with recognition tasks as most helpful for them in preparation of the exam (Fig. 4b). This result is indicating the student's preference of more active learning elements, which has repeatedly been shown to improve examination performance when compared to passive learning in medical education (Graffam, 2007; Kooloos et al., 2020). The finding is also in line with the acceptance and effectiveness of virtual microscopy (Aeffner et al., 2018; Barbeau et al., 2013; Gatumu et al., 2014; Hamilton et al., 2012; Kuo and Leo, 2019; Lee et al., 2018; Paulsen et al., 2010; Schmidt et al., 2011), which can be adopted excellently into distance learning of histology. Moreover, students' request for more "mini quizzes" seems omnipresent (Srinivasan, 2020). In contrast, the use of breakout rooms was somehow controversial among students (Fig. 4b). Our data suggest that the breakout room sessions were not rejected per se, but the framework should be changed: The students mostly prefer smaller breakout rooms with up to four students each and with shorter durations of less than 20 min. However, many students evaluated breakout room sessions as a good opportunity to ask questions and overcome the anonymity of digital learning environments. Evidence from the research about computer-supported cooperative learning can be embedded to further improve collaboration quality in breakout sessions in the future (Radkowitsch et al., 2020).

4.3.1. Prior participation in the dissection course is no predictor of success in online histology

Another observation of this study is that our third semester students, who – in contrast to the second semester – successfully completed the dissection course and gross anatomy prior to the histology course, did not perform significantly better in the histology exams with respect to their scores (Fig. 3a). This is a surprising result; however, the failure rate was 10% lower in this group. We predicted that an extensive engagement with gross anatomy had spillover effects on histology performance based on greater familiarity with anatomical terminology, understanding function of organs and transfer of knowledge. It could also be a manifestation of the phenomenon that students "learn only as much as is necessary to pass", which could explain the same overall performance, but lower failure rate in the third semester. This result has limitations: An important confounder for this observation is that the students in the third semester had a different schedule parallel to our course, including seminars in biochemistry and physiology. This schedule likely represents a higher work-load, and thus, the third semester might not have had the same amount of time to prepare for the exam. Another important limitation of this study is that about one third of students in both semesters attended the course but did not participate in the exam. This phenomenon of procrastination increased over the last years but was, similarly observed in face-to-face settings, too. The reasons for the drop-outs are not clear, however there might be different reasons: Some students may have decided to skip the course right away in order to repeat it in the next semester with better preparation. Others could have been overloaded with the material or may have had private issues or that they struggled with the online environment. These results should be considered when restructuring the curriculum in the future.

4.3.2. The struggle of repeating students

Repeating students usually tend to perform worse than those studying in the reference cohort that includes all students with the minimally required number of semesters at each milestone. This experience was partly reflected in our results (Fig. 3). To identify the so called "at-risk" students, some universities started to develop predictive models based on machine learning methods and student activity data (Wolff et al., 2013). An association between gender, ethnicity and majors with repeating anatomy examination have been proposed in face-to-face environments (Schutte, 2016). Students who participate less active in face-to-face settings seem to participate less in online environments as well (Holland et al., 2016). Along this line, online courses have been suggested to be less effective for weaker students (Jaggars and Bailey, 2010). Reduced attendance and interaction were suggested to be one important reason for this phenomenon (Stuckey-Mickell and Stuckey-Danner, 2007). Furthermore, when offered both face-to-face lectures and online resources, it has been shown that repeating students tend to overlook the online material (Holland et al., 2016).

4.3.3. Online histology course is gender-neutral

Demographic aspects, such as gender-specific effects have been shown to play a role in online environments. There is evidence that female and male students differ in their interaction with technology (e.g. caused by increased use of interactive elements) (Cuadrado-García et al., 2010) and that female students perform better in e-learning environments (Fraillon et al., 2014). Psychological constructs, such as test anxiety has been shown to be crucial for female students' performance in online environments, whereas self-efficacy for learning and performance was more important for male students (Yukselturk and Bulut, 2009). Even though the literature is favoring female students as more successful in online academic achievement, our data do not suggest gender-related effects on performance for undergraduate medical students (Fig. 3d). This observation can be explained by a cohort-specific effect. Notwithstanding the conceptualization of the course with numerous collaborative elements with random assignments of the students into the breakout rooms may have additionally contributed to it. Auxiliary of human-human or human-machine interactions through guidance in online learning environments could be further achieved by predefined collaboration scripts (Fischer et al., 2013), a reasonable opportunity especially for undergraduate students. However, relevant endpoints – other than examination performance – were not measured in this study and cannot be ruled out.

4.3.4. Mature students perform worse in online histology course

Concerning age and exam performance, a significantly negative correlation has been found in both semesters (Fig. 3c). Since the oldest student in this study is around 40 years old, it seems unlikely that this effect is caused by a lack of computer literacy or access to ICT. So, do age have a direct effect on academic output? Considering numerous factors, it has been shown that age itself not be associated with academic performance (Imlach et al., 2017). Many other variables, such as intrinsic factors (e. g. motivation, personality)- and extrinsic factors (e. g. learning environment) were shown to be better predictors of academic success (Laidra et al., 2007). The question remains, why mature students of both semester cohorts in our study performed worse than younger students. An explanation could be that mature students traditionally exhibit different characteristics concerning socio-economic status, motivation and other social and psychological variables (Schuetze and Slowey, 2000). Often, the double burden of having a job outside of university leads to less learning time. Mature students in Germany mostly completed an apprenticeship in the medical field, which helped them entering into medical school and where they continue working during medical school. Yet in our experience, they appear more courageous in the interactions, contributing tremendous amount of input into the collaboration groups and younger students often benefit from the clinical-practical knowledge of mature students. The question remains, whether the worse academic performance of mature students in online histology might be explained by effects other than the digital learning environment itself or is apparent in the same way also in face-to-face environments.

4.4. Challenges and limitations of online (histology) teaching

The challenges of an online histology course are related to the limitations of online teaching in general. Therefore, two relevant aspects have to be discussed when evaluating our online histology course.

4.4.1. Dealing with the passivity-problem

Our data support the frequently made observation that some students in online environments have the tendency to turn into passive observers rather than active participants. Although it is not entirely clear whether these students may learn the content to the same extent as in face-to-face settings, it remains questionable that they are able to actively apply their knowledge to new questions which is one of the main educational objectives of histology lab courses. We highly recommend synchronous lectures and interactive elements such as breakout-sessions in order to give individual feedback and instructions. Teachers should be aware of this passivity-problem in distance learning and actively counteract not only during the lectures but also with offerings inside and outside the virtual classroom. This however requires huge personnel resources and is at least as much cost-intensive as on-site teaching. One should definitely not come to the misconception, that technology is replacing the lecturers or the effort that is necessary for the preparation of a good lecture. The usage of technology strongly depends on the specific context of medical education, the individuals and circumstances and is subject to continuous development and change.

4.4.2. Lack of social interactions

In the times of COVID-19, the lack of social interactions and networks is negatively associated with mental health status (Elmer et al., 2020), which is critical for first semester students or younger undergraduate students without a stable social network. Showing less online activity, less interactions and subsequent physical and social isolation, the pandemic might hit weaker students and repeating students even more severely. From a constructivist perspective the lack of social-interactions and the opportunity to attend co-constructional processes may pose a hindrance, which is especially plausible for asynchronous learning environments with video lectures only (Langfield et al., 2018). We experienced that frequent and instructed group work in breakout sessions have the potential to increase online interactions and – at least partially – overcome this issue in a short-term. Mandatory attendance and enforced webcam activity might further integrate all students into the learning environment. In addition, remedial programs in medical education, which have been proposed to support study skills (e. g. time management and self-regulation skills etc.) of at-risk students (Kalet et al., 2017; McGinn et al., 2020) need to be relocated into an online format to provide further support.

5. Limitations of the study

The main limitation of our study derives from its study design without a bona fide control group. Especially when looking at fairness of the learning environment, our observational design does not allow an extended comparison of online versus on-site histology teaching because no otherwise identical cohort was taught face-to-face. Furthermore, no data about the quality of the student-student or student-lecturer interaction have been acquired. Another limitation derives from the fact that around one third of the students who participated in the online histology lectures did not register for the examination due to procrastination, indicating a survivorship bias of the data. Also, further research is required to determine whether competence, gained through the use of virtual microscopy in an online course, is transferable into face-to-face environments.

6. Conclusion

The anatomical sciences education is facing a rapid transition into an online learning environment during COVID-19 pandemic. This study surveyed the implementation of an online-only histology course with active learning components and reports the experiences with two large semester cohorts. Results show that such an implementation of a synchronous learning environment is technically feasible based on video conferencing software and virtual microscopy resource. We observed that an online-only histology course is effective for learning and well-accepted among students. Our experiences support the positive potential of digital, remote learning at least for parts of the anatomical curriculum during the COVID-19 pandemic, and, possibly, in the time after the pandemic situation. However, successful online courses in our experience require at least as much resources and personnel as face-to-face settings.

Ethical statement

Hereby, I Dogus Darici consciously assure that for the manuscript Implementation of a fully digital histology course in the anatomical teaching curriculum during COVID-19 pandemic the following is fulfilled:

1) This material is the authors' own original work, which has not been previously published elsewhere.

2) The paper is not currently being considered for publication elsewhere.

3) The paper reflects the authors' own research and analysis in a truthful and complete manner.

4) The paper properly credits the meaningful contributions of co-authors and co-researchers.

5) The results are appropriately placed in the context of prior and existing research.

6) All sources used are properly disclosed (correct citation). Literally copying of text must be indicated as such by using quotation marks and giving proper reference.

7) All authors have been personally and actively involved in substantial work leading to the paper, and will take public responsibility for its content.

The violation of the Ethical Statement rules may result in severe consequences.

I agree with the above statements and declare that this submission follows the policies as outlined in the Guide for Authors and in the Ethical Statement.

Declaration of interest

The authors of this manuscript have no competing interests to declare.

Submission declaration

The authors declare that the work described has not been published previously.

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CRediT authorship contribution statement

D. Darici: Conceptualization, Data analysis, Statistical analysis, Writing and Visualization; **C. Reissner:** Conceptualization; **J. Brockhaus:** Conceptualization; **M. Missler:** Conceptualization, Writing and Visualization, Supervision.

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