While scientists recently confirmed the crucial role contact-tracing apps play in containing the COVID-19 pandemic, politicians are exploring which app architecture offers better privacy protection. However, there is no doubt that in Western countries such an entirely voluntary app can only be successful if the population at large supports it.

**How a contact-tracing app should work**

The basic principle of such an app is the exchange of individual identification numbers when people meet, a specific minimum distance is not maintained and a defined period of time is exceeded. The question whether the use of a contact-tracing app on a system level, to enable data exchange between their smartphones. The user which, in turn, generates a set of lockdown measures – now being slowly lifted alongside lowering infection rates. To prevent the infection rates from surging again, many governments are looking into coronavirus contact-tracing apps that could help to disrupt infection chains early on. The study ‘Investigation of a COVID-19 outbreak in Germany resulting from a single travel-associated primary case: a case series’, recently published in The Lancet, confirms that such an app is a crucial tool to contain the pandemic.

**Centralised versus decentralised data storage**

This is a controversial issue. In Germany, the government did not adopt an about-face and finally settled on a decentralised data storage architecture after it initially favoured a centralised approach. The same might happen in the UK. In the centralised storage approach, the server traces with whom an infected person was in contact; in the decentralised approach this task is performed by the individual smartphones.

**Country comparisons**

*Country:* Switzerland and *App:* COVID-19 tracking app was introduced voluntary.

*Country:* Germany, *App:* Corona-WarnApp. So far, the app has been downloaded 14 million times. The decision by the German government to abandon their initially favoured PEPP-PT solution was a response to severe criticism by data protection advocates. According to the government, it fully complies with European and German privacy laws. Only epidemiologically relevant contacts in the past three weeks should be stored on the users’ smartphones in anonymised form. Movement profile will not be stored and the use of the app is voluntary.

*Country:* Italy, *App:* green code are allowed to use public transport and enter shopping centres.

*Country:* UK, *App:* if a person tests positive for SARS-CoV-2 the data will be transmitted to a server. All recent contacts will be identified via Bluetooth and alerted. According to Bending Spoons, the app, which was launched 8 June, complies with European privacy laws. The company grant the Italian government rights of use and future updates are free of charge.

*Country:* other information, such as recent travel data, information regarding the social environment and health records. After having processed this data the app issues a colour code to the respective user granting (green) or denying access (red) to certain locations. A yellow respectively red code means one week and respectively two weeks self-isolation. Only those with a green code are allowed to use public transport and enter shopping centres.

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*Country:* UK-wide. However, there is a discussion as to what will happen with the data post-pandemic. Matthew Gould, CEO of NHSX – the digital innovation arm of the English National Health Service (NHS) – explained that the NHS will use the data only with the data owner’s consent and will be stored a maximum of 28 days. In the meantime, however, technical and ethical concerns were raised within the government and a second app with a decentralised architecture is being developed just in case the first app turns out to be not supportable. So far the NHS has not committed to a timeline on when the app will be launched.
Corona control in Taiwan

Despite its proximity to China, Taiwan contained COVID-19 successfully, without a lockdown or movement restriction measures introduced elsewhere. With few new cases reported, life almost returned to normal. Behind the scenes, however, efforts have continued to maintain that positive situation. The medical directors of Taipei Medical University Hospital (TMUH), a 7,278-bed facility in the Taiwanese capital, have explained how the coronavirus affects clinical workflows.

When in doubt, isolate

The hospital aims to beat the infection risk with strict prevention measures, Dr Chen explained. Any patient who presents with fever or respiratory stress symptoms is considered a potential Covid-19 patient. This policy, according to the superintendent, is key to Taiwan’s success in beating the virus. And indeed, the island has recorded very low case numbers and COVID fatality rate compared to its neighbours.

As far as diagnosis is concerned, TMUH uses RT-PCR tests (reverse transcription polymerase chain reaction), said Dr Lo-Yuan Chen, infection expert at the hospital. ‘This technique offers high specificity and is thus well suited to distinguish COVID-19 infections from other pathologies with similar symptoms.’

When PCR test results are unclear, a CT scan is indicated. CT furthermore is used for follow-up.

Patients with suspected infection are moved to a dedicated ward with the availability of quarantine beds.

A strictly enforced strategy and diligence pay off

To minimise infection risk, TMUH management designed an elaborate system of infection prevention and control. ‘We prepare to prevent the virus from spreading throughout the hospital,’ infection expert Dr Chen added. ‘Fortunately, the infection rate in Taiwan is very low,’ said Dr Po-Li Wei, deputy superintendent. ‘This is to a large extent, due to our government taking containment measures very early.’ After the SARS epidemic in 2003, the Taiwanese government established the National Health Command Centre (NHCC), a central institution which has also led the efforts during the current pandemic. To avoid bottlenecks, the NHCC inter alia coordinates the production of lab staff, radiologists and nurses.

TMUH was the first hospital in Taiwan to have a trust which the German public trust,’ which the German public trust,’ said TMUH head of medical affairs, operations and facility management Dr Vincent Chian.

A United strategy counters COVID-19 spread

Public acceptance of electronic health on the rise

Modernising health: Focus on updating healthcare through digital offers and services

EUROPEAN HOSPITAL
Vol 29 Issue 2/20
Healthcare via digitisation

Video consultations are rising

Report: Sonja Buske

There are many reasons why for some patients a visit to the doctor’s office is difficult or well-nigh impossible – limited mobility after surgery, old age, or a handicap. For others, particularly in rural areas, the doctor is often far away and/or difficult to reach due to poor public transport. In times of corona, another important issue emerged: infection protection. In such cases, video consultation can become a vital safety net.

More video consultation since COVID-19

The Centre for Telematics and Telemedicine (Zentrum für Telematik und Telemedizin – ZTG), co-funded by the German state of North Rhine-Westphalia, helps physicians and healthcare institutions with video consultations, from general information to selecting a suitable, certified system and to help with technological and organisational issues. The future belongs to video consultation,’ confirms ZTG managing director Rainer Beckers. Before corona, online consultations were hardly ever used, even though they’ve been a billable service for years. Since Covid-19, that has changed significantly.

Daily, ZTG is receiving inquiries from all over Germany – and ZTG team members are happy to help. As of 20 May 2020, the ZTG team members are happy to help. As of 20 May 2020, the

conferring in a patient/doctor video consultation

National Association of Statutory Health Insurance Physicians (Kassenärztliche Bundesvereinigung – KBV) listed 31 certified providers of online healthcare consultation systems in Germany. Since March, the company provided its system free of charge during the corona pandemic to office-based physicians, hospitals, midwives and social service institutions.

In 2016/17, an international standard for combined video and audio broadcasts via browser was adopted, i.e. audio and video conferences can now be held without additional software. Before this standard was implemented, patients were allowed to call the doctor but not send personal data by mail, or make a video call. State-of-the-art encryption technologies comply with very high security standards, which ensure privacy protection,’ Beckers points out.

A simple procedure

The procedure is very simple: doctor and patient agree a date and time for an online consultation. The patient receives a code to initiate the video call via desktop, tablet or even smartphone. A dedicated software package is not necessary. The patient is directed to a virtual waiting room and ‘called in’ by the doctor.

Abusing the system is virtually impossible, since the participants see each other and in most cases know each other. Patients who visit the doctor for the first time must identify themselves with an electronic health card.

Obviously, a video consultation has its limits. When a physical exam is needed, e.g. to differentiate bronchitis from pneumonia, the patient has no choice but to visit the doctor’s office. While online consultation is possible, online auscultation is still not possible, ‘It is the doctor’s responsibility to make this decision,’ Beckers explains. ‘For many other diseases and problems, such as evaluation of wounds or eczema, or follow-up exams after surgery, video consultation is perfectly well-suited. Transferring documents or X-ray images is no problem either.’

A look into the future

Indeed, auscultation per video call, Beckers says, is not as utopian as it might sound: ‘The home environment has to become a mobile diagnostic centre. That means that the video consultation has to be complemented by tele-monitoring.’

Smart blood pressure measuring devices or mobile ultrasound systems will enable the physician to collect the patient’s vital data. ‘It’s a matter of the type of equipment the patient has at home,’ says Beckers and adds confidently that ‘the future belongs to video consultation combined with tele-monitoring.’

Technology is only one aspect of modernisation – there’s also ‘digital values and digital humanism’

Professor Jörg Debatin, who is Chairman of the Health Innovation Hub at the Federal Ministry of Health, summed up that digitisation should be perceived to be going well beyond purely technological innovations.

Digitisation of healthcare requires acceptance, as well as digital values and digital humanism.

It also requires comprehensive training in the use of anonymised data and transparency with regards to the values on which the algorithms are based. By the time we achieve this, several updates will have been carried out already. (CWM)

www.healthcare-in-europe.com
Rapid response test kits—
the race is fierce

To develop and manufacture COVID-19 test kits in massive quantities was not part of their 2020 business plans. Yet, as the epidemic evolved into a global pandemic, the urgent need for diagnostic and antibody SARS-CoV-2 test kits triggered an unprecedented scramble among medical manufacturers.

Linda Carter PhD, is an information scientist at the American Chemical Society CAS division.

Clinical testing and quantified benefits of rapid COVID-19 diagnostic tests

On 1st April, EDCD, in a technical report, warned that even for compliant CE-marked rapid diagnostic tests, performance may vary in the routine testing laboratory compared with a manufacturer's performance study done for CE-marking purposes. EDCD cautioned: ‘rapid tests may be less accurate and less sensitive than laboratory-performed diagnostic tests’ and that clinical validation of the diagnostic performance of rapid tests for COVID-19 in real life should be carried out by comparing them with standard RT-PCR laboratory tests.

Example: In the UK, in one rapid round-up laboratory testing device, the SAMBA II, a compact, portable machine developed by Cambridge Uni spin-off Diagnostics for the Real World, after swabs with samples are loaded, the device searches for tiny traces of virus genetic code.

Addenbrooke’s Hospital of the Cambridge University Hospitals NHS Foundation Trust, was the first to use the device in a clinical setting. The results of a clinical study of 149 symptomatic individuals showed that SAMBA II had a 96.9% sensitivity and a 99.1% specificity, compared to the standard RT-PCR lab tests.

A subsequent hospital-based implementation study included an analysis of 992 tests of 913 symptomatic individuals over a 10-day period. Professor Ravi Gupta and researchers at the Cambridge Institute of Therapeutic Immunology and Infectious Diseases, reported in medRxiv that the tests were used mainly for emergency department patients, as well as those in the acute admission ward, presurgical patients, and the elderly being discharged to nursing homes.

The median time to a result was 3.6 hours compared to over 2 hours for the standard lab RT-PCR test. The average time that patients had to spend in a COVID-19 ‘holding ward’ before discharge or progress with treatment dropped from 58.5 hours to 50 hours. Use of single-occupancy isolation rooms also decreased, from 50.8% to 21.2%. The research team advised that the switch by Addenbrooke’s to rapid testing kept more surgical bays open for uninfected patients and prevented 11 ward closures for these patients in the 10 days after hospital-wide implementation.

Rapid result COVID-19 antibody tests

Companies responded in droves to develop rapid response antibody detection tests. Roche, for example, worked 24/7 in late March and April to develop one. In early May, the company announced that its new Eleys Anti-SARS-CoV-2 antibody, approved for EUA use by the FDA and with CE-IVD marking, started shipping worldwide.

Beckman Coulter expects to ramp up production capacity to high double-digit millions per month. The serology test has a 99.81% specificity and 100% sensitivity in detecting antibodies in blood samples taken 14 days after a PCR-confirmed coronavirus infection, according to results of nearly 5,300 samples. When processed on Roche’s Cobas e analysers, results come in 18 minutes, with a test throughput of up to 300 tests/hour. Siemens Healthcare rapidly developed a molecular PCR Fast-Track Diagnostics SARS-CoV-2 assay test kit to identify antibodies. This molecular test analyses nasal/throat swabs, detects antibodies believed to neutralise the COVID-19 virus, specifically targeting antibodies that attach to a spike protein on the surface of the virus (* CE Mark received April; FDA EUA approval May).

Rapid results take up to 10 minutes when used with Siemens high throughput immunoassay analysers, which can deliver up to 440 tests/hour, and in 18 minutes with other Siemens analysers that test up to 240 samples/hour. Tests conducted on over 1,850 samples demonstrated a 100% sensitivity and 99.8% specificity.

Siemens is ramping up production to a capacity exceeding 50 million tests per month, starting in June.

Beckman Coulter expects to report the availability of its Access SARS-CoV-2 IgG serology test in June, and plans to produce 50 million tests per month. Hospitals using the company’s highest performance immunoassay analysers will process up to 200 results per analyser per hour. Abbott, Cellex, Chembio Diagnostics, and Ortho Clinical Diagnostics have also developed tests.

Potential and perils in home test kits

Home testing kits for initial risk assessment of diabetes, high cholesterol, and colon cancer offer a more affordable and convenient option than on-site diagnostic laboratory testing. Inexpensive, patient-administered COVID-19 testing kits to diagnose coronavirus, or identify the presence of antibodies, could significantly expand population testing.

Need for hundreds of millions of such kits results in academic researchers and companies scrambling to develop them. RUCDR Infinite Biologics, part of the Rutgers University Human Genetics Institute of New Jersey, developed the first saliva self-collec- tion test to receive a FDA EUA. Everlywell also received an EUA for a self-collection test that utilises nasal swabs to collect a sample. With both, samples go to a lab for processing.

These tests are not without risk. In early April, The Guardian reported that 17.5 million coronaviruses antibody detection home test kits purchased by the British govern- ment had a low sensitivity and specificity level, according to an unnamed testing expert. The New York Times reported that home kits purchased from two Chinese compa- nies, Hangzhou Alltest Biotech and Wondfo Biotech, had been found ‘insufficiently accurate by an Oxford University Laboratory’. The test kits are not sold in the UK.

Dr Carter warns that users of home COVID-19 test kits could buy a collect a sample, or not place a sample properly in its collection medium, or return the sample late, or the manufacturer has not ensured test results will be reliable under a wide variety of conditions, or the processing agency can process samples accurately.

Research continues to develop robust, easy to use, inexpensive tests. With her team, Marit Nilsen-Hamilton PhD, a professor of biochemistry, biophysics, and molecular biology at Iowa State University, is aiming to develop a smartphone size viral testing platform, to iden- tify a DNA aptamer, a nucleic acid that behaves like antibodies in the immune system, which could recog- nise the viral cause of COVID-19, for diagnosis and antibody recognition.

Professor Ravi Gupta is a researcher at the Cambridge Institute of Therapeutic Immunology and Infectious Diseases.
Introducing ATEM Mini
The compact television studio that lets you create training videos and live streams!

Blackmagic Design is a leader in video for the medical industry, and now you can create your own streaming videos with ATEM Mini. Simply connect up to 4 HDMI cameras, computers or even technical equipment. Then push the buttons on the panel to switch video sources just like a professional broadcaster! You can even add titles, picture in picture overlays and mix audio! Then live stream to Zoom, Skype or YouTube!

Create Training and Educational Videos
ATEM Mini's includes everything you need. All the buttons are positioned on the front panel so it's very easy to learn. There are 4 HDMI video inputs for connecting cameras and computers, plus a USB output that looks like a webcam so you can connect to Zoom or Skype. ATEM Software Control for Mac and PC is also included, which allows access to more advanced "broadcast" features!

Use Professional Video Effects
ATEM Mini is really a professional broadcast switcher used by television stations. This means it has professional effects such as a DVE for picture in picture effects commonly used for commentators over a computer slide show. There are titles for presenter names, wipe effects for transitioning between sources and a green screen keyer for replacing backgrounds with graphics!

Live Stream Training and Conferences
The ATEM Mini Pro model has a built in hardware streaming engine for live streaming via its ethernet connection. This means you can live stream to YouTube, Facebook and Twitch in much better quality and with perfectly smooth motion. You can even connect a hard disk or flash storage to the USB connection and record your stream for upload later!

Monitor all Video Inputs!
With so many cameras, computers and effects, things can get busy fast! The ATEM Mini Pro model features a "multiview" that lets you see all cameras, titles and program, plus streaming and recording status all on a single TV or monitor. There are even tally indicators to show when a camera is on air! Only ATEM Mini Pro is a true professional television studio in a small compact design!

ATEM Mini .......... 289€*
ATEM Mini Pro ....... 569€*
ATEM Software Control .......... Free

*Recommended retail price excludes VAT and shipping and delivery costs. Prices subject to change.
ATEM Mini for use in training, conferencing and learning purposes only.
COVID-19: Lifespan and disinfection — the reality

Surface disinfection has proved an effective method to control COVID-19 infection, as virologists from the Ruhr University Bochum (RUB) have shown. However, an effective disinfection strategy against Coronavirus must be considered, as the virus can survive for several days on different material types including copper, carton, steel and plastic surfaces.

Whether or not a disinfectant is effective against a certain type of virus depends, among other reasons, on the structure of the virus, Steinmann explains: ‘Coronavirus is covered by a lipid membrane which stores proteins. This makes it susceptible to alcohol-based disinfectants because they destroy the membrane and inactivate the virus.’

If this membrane is missing, as, for instance, is the case with norovirus, other agents need to be used for disinfection.

The use of UV radiation has proved effective against such non-enveloped types of virus because it attacks the nucleic acids (RNA) of the virus. In concrete terms, this means that agents classed as having a limited virucidal effect are perfectly adequate for the inactivation of Coronavirus SARS-CoV-2. However, as more resistant agents, such as the aforementioned norovirus, are also present in a clinical environment, the use of more potent agents (classed as ‘virucidal’ or limited virucidal plus) may also be of benefit.

Effective disinfection should be carried out on all surfaces which have potential contact with the virus: work surfaces and surfaces close to patients, beds, and medical equipment. Current studies on SARS-CoV-2 confirm the presence of the virus – or at least its RNA – in many locations in a room where an infected patient had been accommodated: the edges of the bed, light switches, door handles, but also toilets, noses and pillows. ‘This shows that the virus is spread almost everywhere in the room via contact with hands as well as through the smallest droplets,’ Steinmann says. ‘However, thorough cleaning and disinfection can reliably deactivate the virus.’

Laboratory lifespan of SARS-CoV-2 gives indications

One of the central issues which researchers worldwide are examining concerns the lifespan of the new coronavirus on surfaces. Whilst initial calculations are mainly based on experience with the related virus types SARS-CoV and MERS-CoV, newer studies provide reliable figures on COVID-19 pathogen SARS-CoV-2. ‘One study, published in the New England Journal of Medicine, is of particular interest,’ says Steinmann. ‘US researchers examined for how long the virus survived on different materials, including copper, carton, steel and plastic surfaces. The results showed that in some cases, the virus is still present and active after several days. Everyday items such as banknotes, handlechefs and masks were tested in another study published in the Lancet Microbe: ‘The virus was still present in the inside of masks after 7 days,’ says the virologist and adds: ‘Although these measurements were taken under laboratory conditions, they give us a pretty good idea of how long the virus can remain stable in everyday conditions.’

What role does temperature play?

Currently, researchers at the RUB under junior Professor Dr Stephanie Pfaender are examining the effect of changes in room temperature on the lifespan of the virus. Scientists compared the surface stability of the virus at room temperatures of 4°C and 30°C. They found that the virus remains infectious on surfaces for roughly the same length of time in both hot and cold conditions. ‘The assumption had been that higher temperatures would lead to a lower transmission rate of SARS-CoV-2 in summer,’ says Pfaender. ‘However, it appears that the stability of the virus on surfaces is not impacted by changes in temperature.’ A potentially lower rate of infection in summer could be due to other factors such as UV radiation and humidity though, says the virologist.

Less is more in private households

Steinmann emphasises that there should be different criteria for private households as opposed to hospitals: ‘In everyday life, normal hand washing — combined with social distancing and following the correct etiquette when coughing — is usually completely sufficient. Disinfection is only required once there has actually been contact with an infected person.’ Steinmann explains, in terms of the explosive demand for disinfectants amongst private individuals as follows: ‘In many cases, this will have been impacted by a psychological effect: If you have a disinfector at home, it makes you feel safe just in case. The actual use is then not actually that important.’

If private households reach for the ‘strong stuff’, i.e. a disinfectant — they may not be doing themselves a favour, warns the expert: ‘These agents are aggressive and can attack the skin if used regularly. Without comprehensive care, this can easily result in skin injuries.’

A new study from the USA highlights how low temperature sterilisation can jeopardise effective cleansing of medical tools and lead to transmission of dangerous bacteria to patients. Steam sterilisation was shown to be the most effective and robust sterilisation technology.

A new study from the USA highlights how low temperature sterilisation can jeopardise effective cleansing of medical tools and lead to transmission of dangerous bacteria to patients. Steam sterilisation was shown to be the most effective and robust sterilisation technology.

An unexpected finding in their experiments to compare the microbicidal activity of FDA-cleared sterilisation technologies was that steam sterilisation in the presence of salt and serum — simulating inadequate cleaning of instruments prior to sterilisation — the equipment was then sterilised with VHP, ethylene oxide (EO), hydrogen peroxide gas plasma (HPGP), or steam.

This study evaluates the “robustness” of sterilisation technology that is used by hospitals throughout the United States, Rutala pointed out. “Robustness is defined as the ability to withstand and overcome adverse conditions or rigorous testing.”

He emphasised that the intention was not to compare the factors that affect sterilisation, such as temperature, duration of cycle, concentration of gas/vapour, but to simply determine whether a sterilisation technology has the same robustness or “margin of safety”.

Through their methodology, defined, we found some sterilisation technologies were more robust than others, he added.

Steam, EO and HPGP sterilisation techniques were capable of inactivating the test organisms on steam-

Confirmed: Steam sterilisation is the best method for sterilising medical devices.
Steam sterilisation is gold standard

Study puts cleansing methods to the test

Robotic instruments

'We are a medium-size German company specialising in ultrasonic equipment for cleaning, including pre-cleaning of medical instruments from different medical fields,' explained Florian Knuth, Sales Director for the Medical Division of the firm Bandelin, during an interview with Ralf Matejkwoski, of European Hospital.

Miracle of technology

We have various examinations and test reports which show that pre-cleaning in the Trison 4000 is successsfully carried out almost without needing any additional manual steps. The device was launched in 2017. More than 60 systems are currently in use in validated procedures across Europe, and user feedback is always positive. They especially value the intuitive handling, excellent cleaning results and the considerable relief in stressful working conditions.'

Could you give us a view into the future?

Robot-assisted surgery will continue to increase. There will be more providers of robotic systems, along with completely new technologies, new instruments and new procedures which will continue to alleviate and improve the treatment of patients. The Trison will be ready for the cleaning of new robotic instruments in the future. Bandelin always has an eye on new developments to ensure we can continue to meet this demand with innovative ultrasound equipment and to contribute to resource-saving cleaning of medical instruments.'

Florian Knuth studied economics in Berlin and is currently Sales Director of the Medical Division of Bandelin. He is responsible for consulting and sales of all medical ultrasonic baths used in CSSDs and medical practices. With almost ten years professional experience in the medical field, he is an expert in instrument reprocessing and decontamination applications. His knowledge and the constant exchange with the users help him understand the users’ needs and requirements in their daily work.

No more frequent cleaning

The facts illustrate that steam sterilisation is the most effective and robust sterilisation technology and has the largest margin of safety and is the least affected by protein, salt and lubricants; said Dr Rutala. ‘VHP has a significantly narrower margin of safety in killing vegetative bacteria and spores in the presence of a salt and serum challenge.’

The findings have implications within healthcare settings.

Contamination of surgical instruments does occur, but is observed and rarely reaches the patient

Dr Rutala said: ‘Surgical instruments that enter sterile tissue should be sterile because microbial contamination could result in disease transmission.

Despite careful surgical instrument reprocessing, surgeons and other healthcare personnel describe cases in which surgical instruments have been contaminated with organic material (e.g. blood). While most of these cases are observed before the instrument reaches the patient, in some cases the contaminated instrument does indeed contaminate the sterile field or, rarely, the patient. Researchers say data from this study will help clinicians in infection prevention to assess the patients infection risk when a contaminated instrument is unintentionally brought into the operating room, or used on a patient.

The study reinforces the need for meticulous cleaning and reliable and validated cleaning monitoring methods that are predictive of an infection risk,’ Rutala concluded.

Specially: powerful, essential and valued cleansing systems

Less steel carriers with a failure rate of 0% for steam, and 1.9% and 1.9% for EO and HPGP, but the failure rate for VHP was 76.8%.

The results illustrate that steam sterilisation is the most effective and robust sterilisation technology and has the largest margin of safety and is the least affected by protein, salt and lubricants,’ said Dr Rutala. ‘VHP has a significantly narrower margin of safety in killing vegetative bacteria and spores in the presence of a salt and serum challenge.’

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Economic aspects and COVID-19

The academic teaching Karlsruhe Hospital, at the University of Freiburg, is the largest hospital providing tertiary care in the Middle Upper Rhine Valley. Every year, 63,000 in-patients and 180,000 out-patients are treated in the 1,500-bed facility with 50 departments and 50 out-patient clinics. It is estimated that in Karlsruhe hospitals this size has a central lab. EH correspondent Walter Decker spoke with Dr Horst Mayer, managing senior physician of the Department of Clinical Diagnostics, about the lab and particularly automation, introduced there over recent years. The effects on the lab of COVID-19 were also explored.

Currently, the hospital has 39 full-time employees and 12 full-time support staff – mainly students. The trauma and emergency department admits about 35,000 adult patients per annum. Each day, we process on average 4,000 samples, of which approximately 1,500 are serum, 500 are coagulation and 800 are blood tests,’ explained Mayer, speaking of the lab’s involvement. ‘The remainder are coagulation tests, and 800 are blood samples. Thus, more than 4,000 samples are processed by the lab daily. Peak times are between 7-9 am. In that window, we receive 800 samples, the rest spread more or less evenly over the day.’

EH: A hospital lab usually processes more pathology samples than non-hospital labs. Is this the case in Karlsruhe?

Mayer: Indeed. Here about 50 percent of the individual samples are pathology samples; in a non-hospital lab group this would be about five percent.

Over recent years, hospital length of stay has been shrinking, while patient throughput has increased significantly. Thus also increasing the number of samples arriving in the lab and thus encouraging lab automation. Does that mean there is less time for analytics?

Definitely. We started automation more than ten years ago with a Siemens Flexlab. This automated lab system generated major benefits, because it could be operated even with a small team. It ran 24/7 and made a marked improvement because length of stay decreased and throughput increased. The new lab system, which has been installed since, offers even shorter turn-around times as well as significant quality improvements. In fact, at this point we are not running to capacity.’

Not all areas present themselves for the same degree of automation; take mass spectrometry, special microvirologer serology or pathology. What is the situation in Karlsruhe? Where did you start automation and where could the most significant effects be realised?

Obviously, there are limits to what is feasible. In terms of technology we could link a Sciex 6500 mass spectrometer to the lab system. However, I don’t consider this particularly useful at this point. Assays, which are currently performed by ELSA on MT, is that microtiter plate basis, but which can be done in an immunosay analyser linked to the system, are all transferred.

If you rank clinical disciplines by degree of automation, where would you place clinical chemistry?

We started to do old-school clinical chemistry, around the clock – tumour markers, hormones and infection markers. Currently I still consider conventional clinical chemistry relevant. Going forward, however, I think this will change over the next 10 to 15 years. Current resource-intensive methods will be replaced by molecular biology analyses, in particular their miniaturisation will be influential. In a nutshell: traditional clinical chemistry in its current form will have become obsolete.’

How did your staff structure change over recent years due to automation? Did you have to or were you able to switch staff? Did you ease the burden in labour?

Goldstein’s team is conducting the 3-D printing work for all of Northwell Health, which is a 25-hospital health-care provider in New York state, the epicentre of the crisis in the USA. ‘We have eight Formlabs’ 3-D printers with the capacity to print about 4,000 swabs a day. By the end of May, the lab had printed over 90,000 swabs which were distributed among Northwell Health hospitals and outpatient facilities,’ Goldstein said.

‘In our efforts to bring nasopharyngeal swabs into production in record time, we helped supply the Northwell Health system with a critical diagnostic tool needed to combat this disease. In a time of crisis, it is ingenuity and innovation that helped keep everyone motivated to help our community as best we can.’

Formlabs is manufacturing the nasopharyngeal swabs in its 200 3-D printer manufacturing facility in Ohio, and has the capacity to produce up to 100,000 swabs a day when printing capabilities are fully ramped up. ‘We are pricing the swabs to cover their production cost and the investment we made to ramp up production,’ said Hollander. ‘We do not intend to produce these swabs long term.’

The USF 3-D Imaging Lab holds a provision patent for the swab with the USF 3-D printer manufactured by Northwell Health. USF made a decision to share the files with any hospital that has a Formlabs printer through April 2021, Decker explained.

The science behind 3-D printed nasal swabs

Medical device approved 3-D printers are producing clinically safe and effective nasopharyngeal swabs for COVID-19 testing.

Report: Cynthia E. Keen

A nasal swab may seem rudimentary, but it is critical to tracking COVID-19 and diagnostic test kits and components – nasal swabs, collection vials, and chemical reagents – have been in short supply worldwide, especially in March. Ironically, nasopharyngeal swabs are predominantly manufactured in northern Italy and China, two countries first impacted by coronavirus.

Concerned by diminishing supplies and near impossibility to restock, the dean of the University South Florida (USF) Morsani College of Medicine, wondered if the radiology department’s 3-D Clinical Application Division could produce swabs.

3-D Clinical Applications director and imaging scientist Summer Decker PhD, with Jonathan Ford PhD, biomedic engineer and fellow medical printing expert model, create virtual analyses for simulations of injury mechanics and blood flow, for example, as well as generating anatomical models of organs and regions of the body.

In two decades of research they produced trailblazing work and numerous publications. Worldwide, their lab, located at USF Health and Tampa General Hospital, is one in about two dozen renowned for this expertise.

Immediately investigating the idea, they started to develop nasopharyngeal swab prototypes that would use materials cleared by the US FDA as patient-safe. They received one representative standard-of-care nasopharyngeal swab on the same day before creating a new design for a 3-D printer.

‘On the surface, creating a nasopharyngeal swab doesn’t seem so complicated that a design, Decker observed. ‘But it’s more complicated than it looks. We knew we couldn’t replicate components of the traditional swab, such as the flocking on the tip that collects the sample. We needed a device that could be printed as one unit, collect a sufficient mucosal and epithelial sample for viral testing, and be safe and comfortable during the collection process. Additionally, the material could not interfere with the actual testing machines.’

Decker and Ford sought ideas and advice from colleagues. They also invited 3-D medical printing expert Todd Goldstein PhD, director of Northwell Health and 3-D Design and Innovation Center, in Manhasset, NY. The final design team included the 3-D medical printing experts, infectious disease physicians, otolaryngologists, a virologist, and a pulmonary radiologist who suggested rounded nose on the top of the swab to maximize surface area to collect a sample.

Ultimately, 12 designs were investigated and prototypes printed. The prototypes were given to the design team physicians for feedback and consensus. Hospital residents and the design team tested the prototypes on themselves to identify the most comfortable designs.

The final design was a standard-length swab with a tip that has a smooth cap on the top to protect the tissue as it goes through the nasal passage. Nubs or ridges in a staggered pattern around the sides collect the sample as it goes into the nose.

An expert virologist performed robust bench lab testing to verify that the swab design would grasp enough sample and meet viral load detection requirements. The length of time the swab could hold a sample was measured. The swab also underwent rigorous compatibility testing for the collection media and the virus testing machines.

The team contacted Formlabs, a digital fabrication company and licensed medical device manufacturer based in Somerville, MA, which manufactures professional 3-D printers. The company worked with USF to optimise the design and production of the prototype swabs.

Swab sticks have an insulating sleeve - 7.8 cm from the tip, which allows the stick to be broken to the correct length so that the viral sample can be capped before transportation to a laboratory for testing, explained Stephan Hollander, Formlabs’ managing director EMEA. The most difficult part of designing these swabs to 3-D print was ensuring the material was strong enough to be used in a patient’s nose without fear of it breaking, and weak enough that it can be easily snapped and put in a vial.

USF and Northwell rapidly conducted a 120-person trial comparing the performance of the 3-D printed swab with a traditional one. The 3-D printed swabs performed as hoped, but to make sure, the clinical trial expanded to include 35 hospitals nationwide.

Goldstein’s team is conducting the 3-D printing work for all of Northwell Health, which is a 25-hospital health-care provider in New York state, the epicentre of the crisis in the USA. ‘We have eight Formlabs’ 3-D printers with the capacity to print about 4,000 swabs a day. By the end of May, the lab had printed over 90,000 swabs which were distributed among Northwell Health hospitals and outpatient facilities,’ Goldstein said.

‘In our efforts to bring nasopharyngeal swabs into production in record time, we helped supply the Northwell Health system with a critical diagnostic tool needed to combat this disease. In a time of crisis, it is ingenuity and innovation that helped keep everyone motivated to help our community as best we can.’

Formlabs is manufacturing the nasopharyngeal swabs in its 200 3-D printer manufacturing facility in Ohio, and has the capacity to produce up to 100,000 swabs a day when printing capabilities are fully ramped up. ‘We are pricing the swabs to cover their production cost and the investment we made to ramp up production,’ said Hollander.

‘We do not intend to produce these swabs long term.’

The USF 3-D Imaging Lab holds a provision patent for the swabs with the USF 3-D printer manufactured by Northwell Health. USF made a decision to share the files with any hospital that has a Formlabs printer through April 2021, Decker explained.

-readable
When we installed the first automated lab system in 2009, we were lucky because the four employees who became redundant retired – we did not have to replace them. Over the course of time we reduced the team in the core lab and transferred some team members to special diagnostics, haematology, coagulation or areas such as serology or toxicology.

A hospital lab always reflects the foci and departments of an institution as a whole. In your case, paediatric and adult oncology are major departments. How does this affect your lab?

'We see a significant demand by the oncology departments and this plays a major role in the lab. We were able to transfer several of the clinical chemistry staff mentioned above to oncology. In haematology, we have a Sysmex system with digital morphology followed by flow cytometry. Among the areas that are not part of the central lab are molecular biology, where PCRs for oncology and pathology are performed.'

Talking about PCR: how does COVID-19 affect your lab?

'Not so much. We do have a full Cobas 6800 system. The main issue, however, is the fact that we don’t have enough tests. Currently, we use Corona antibody tests.'

Do you only test your own patients and staff or do you also receive samples from outside to process?

'We receive very few external samples from office-based physicians. Our problem is the fact that non-hospital labs receive priority for tests. We only receive about 1,000 test units per week for molecular biology. Technically, we would have the capacities for many more tests. Personally, we were not tested, since the lab is considered a closed-off zone. The situation is obviously very different for our patients and the care staff.'

COVID-19 shows that medical plastic products save lives

Where would we be today without plastic?
An increasingly dynamic cardiovascular presence

In the world of laboratory diagnostics, 'Abbott' is a household name. Few people however are aware of the fact that the company, headquartered in Illinois, USA, is also leading in cardiovascular and diagnostic therapies. A number of innovations in cardiac and vascular diagnostics and therapy might soon put Abbott in the limelight. Dr Angela Germer, Regional Director DACH, and Volker Keller, Head of Marketing DACH, Vascular at Abbott, updated Daniela Zimmermann on the company's most recent developments and the plans for the future.

Abbott's German cardiovascular business, in particular, has recently faced the coronavirus pandemic in Wuhan. Whilst the Structural Heart team focuses on the treatment of structural heart disease (SHD), the Vascular team's expertise lies in diagnosis and treatment of cardiovascular conditions with systems to assess vascular physiology, guide wires, and drug-coating, as well as non-diagnostic balloons and stents.

OCT and FFR to avoid unnecessary stents

Today, some patients receive stents without proven ischemia, on suspicion so to speak. Usually, two techniques are used to assess ischemia: either fractional flow reserve (FFR) or resting full-cycle ratio (FFR). A specially designed pressure wire looks for drops in pressure caused by a stenosis. If the pressure drop significantly, the oxygen supply to the heart is impeded, says Dr Angela Germer.

Abbott uses a two-pronged approach to ensure that stents are only implanted when and where clinically needed and to improve patient outcomes firstly, the guidewire. PressureWire® X uses wireless data transmission, thus facilitating ischemia assessment by FFR; secondly, the Abbott-developed imaging solution OCT (optical coherence tomography) which allows precise measurement of vessels. ‘With this approach, we aim to optimise percutaneous coronary interventions, PCI for short, and to increase the likelihood that the right stent is placed at the right location,’ Dr Angela Germer explains.

OCT delivers high-resolution images of vessels which modern technologies, such as virtual reality (VR). In cooperation with several hospitals, the company recorded catheter-based procedures, such as FFR and OCT, and turned them into 3-D simulations to be used with VR headsets. ‘Thus, interventions can be practised virtually, which increases patient safety during the actual procedure,’ Volker Keller points out. Abbott and the international cardiologist working group (AGIK) jointly organise workshops at trade fairs and congresses, and in hospitals, to provide in-depth training for clinical staff.

The pressure wire is also used to diagnose microvascular heart disease which, in Germany alone, affects 175,000 people. Dr Germer says, ‘This condition is rather frequent among cardiac patients, but difficult to diagnose. Many patients present several times without the cardiologist being able to detect the root cause. Our PressureWire X, combined with a dedicated software solution, can help detect minute deposits in the vessels and thus identify the disease.’

The highly specialised Abbott stent portfolio covers the many requirements the tiny support structures have to fulfil in the different anatomies. Stents for the femoral artery, for example, must be able to withstand enormous biomechanical forces, such as torsion. ‘The nitinol wires in our Supera stent are not laser-cut but woven,’ Germer explains. ‘This unique technology makes Supera much sturdier than conventional stents, whilst maintaining its flexibility.’

Closure system accelerates patient mobility

Perclose ProGlide, the tried and tested closure system that deploys stents after endovascular procedures with a femoral puncture larger than 5 F without the use of collagen, is now also indicated for the femoral vein. ‘A stent is placed right at the vessel wall and the edges are joined again initiating primary healing. The closure can be tested right after the intervention. Unlike conventional sutures, Perclose ProGlide allows the patient to get up and move around quickly,’ explains Dr Germer. Thus, hospital length of stay is reduced and accompanying procedures, such as a bladder catheter, can be avoided. Another advantage: If re-access is necessary, which is, in fact, the case with several conditions, the very same site can be used, even right after the initial procedure.

Today, patients benefit hugely from implantable cardiac support systems, such as LVAD (left ventricular assist device). Abbott is currently developing the next-generation of such a device: FILVAS, fully implantable left ventricular assist system. It has no external components, such as batteries or charging ports, which patients have to carry around regularly as well.’ Keller explains, ‘but FILVAS does this by induction via an implanted coil. Since energy supply does not require opening the abdomen, patients can bathe, swim, enjoy the sauna – these are activities that are almost, or even entirely, impossible with IAD. Not to mention the fact that in conventional systems the external energy supply opening is a potential door for infections to enter the body.’

AI algorithm calculates infarction risk

Abbott not only uses diagnostic and treatment devices to improve cardiac patient care but also designs solutions based on artificial intelligence (AI). A recently developed AI-based algorithm to assess infarction risk is about to be used in clinical settings. The Abbott R&D team benefited from the in-house lab medical expertise: ‘Our algorithm correlates troponin values with other patient data, such as age, gender or prior disease,’ Keller points out. ‘This allows a detailed assessment of individual infarction risk.’ Prior to the commercial launch of the algorithm, clinical tests need to be concluded but, so far, the studies have yielded very promising results (Circulation: https://doi.org/10.1161/CIRCULATIONAHA.119.014980).

With these ambitious projects in the wings, Abbott is well positioned to expand its reputation beyond the lab and have a strong impact in cardiovascular medicine.

When classic ventilation therapy fails in COVID-19 cases

‘As the coronavirus spreads and infections with COVID-19 further increase throughout Europe, Extracorporeal Membrane Oxygenation (ECMO) therapy turns out to be a necessary option for patients with severe courses,’ Xenios AG reports. The company is now responding even further to the challenges presented by the pandemic in the first instance with the CE mark and FDA clearance (approved by the USA’s FDA through Finessmed Medical Care North America earlier in 2020). The system is available in more than 50 markets worldwide.

Extracorporeal therapy use rises

‘Today, patients benefit hugely from implantable cardiac support systems, such as LVAD (left ventricular assist device).’

For critically ill COVID-19 patients with acute lung failure and refractory hypoxemia, despite use of all standard therapy related measures, our treatment often remains the last therapeutic option and, in the best case, is a lifesaver for these patients,’ adds Dr Jiuguo Bihain, Chief Medical Officer of Xenios.

Bypassing lung function, the system clears the patient’s blood of carbon dioxide outside the body and enriches it with oxygen, giving lungs time to heal. ‘Because of the increase of critically ill COVID-19 patients, more physicians will opt for ECMO therapy.’

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The virtual medical assistant and digital patient twin

Siri and Alexa are leading the way virtual assistants meet many daily needs. Soon, similarly programmed software and a ‘digital patient twin’ will be launched into the medical world – both IT applications based on Artificial Intelligence (AI).

The virtual medical assistant and digital patient twin are two key aspects of a research project 'Models for Personalised Medicine'. Scientists at the Innovation Centre for Computer Assisted Surgery (ICCAS) in the Medical Faculty at Leipzig University aim to use these tools to improve the treatment of cancer patients.

The project has received funding of around €5.1 million from the Federal Ministry of Education and Research and is being implemented with the help of companies in the Free State of Saxony, in eastern Germany.

Different technologies have been designed with various pilot applications: 'The objective is to support the medical treatment of cancer patients with the help of IT, explains Professor Thomas Neumuth, who heads the project at ICCAS, and is also the Deputy Director of the centre. Targets include, for instance, patients with head/neck tumours. IT support starts with the tumour board, i.e. interdisciplinary discussion between surgeons, radiologists, radiotherapists or pathologists: 'Experts from different medical disciplines discuss the medical condition of the respective patient,' Neumuth explains.

'It's a type of briefing where all information relevant to the decision-making process is evaluated. The experts discuss treatment options based on this information and make a joint decision,' he explains.

In the future, the virtual assistant is to be present at these discussions as well. 'This means we won't lose any information,' he points out. However, among programming challenges will be the different volumes of sound and different positions of those who are talking in the room, which must be detected and accounted for.

Unclear pronunciation or strong accents should also not impact on word recognition. 'In contrast to conventional software, language recognition used in the context of medicine must be programmed for the specialist terminology and must also adhere to the strictest guidelines on confidentiality,' Neumuth observes.

The Leipzig-based scientists have another vision: the so-called digital twin. This is an organised collection of all information about a patient and their anamnesis: radiological images, information on underlying medical conditions and previous surgery as well as molecular-genetic data. 'This is much more complex than the electronic patient file which we already have,' Neumuth observes.

The data in the patient file has not yet been linked in a meaningful way, so comprehensive, patient-specific analyses supported by AI is not yet possible. However, the digital twin now ‘paves the way for the step from the analogue into the digital world,’ he believes.

This also includes storing treatment steps, playing through options, and updating information, explains the project manager. This objectivises medical work, makes information accessible to all experts in the team in equal measure and facilitates improved prediction of the effectiveness of treatment.

During diagnosis and therapy, the information of the data twin is compared to digital models of the clinical picture, which are optimised with the relevant studies and latest scientific findings. The computer should then support doctors with personal recommendations for cancer patients. The final decision on treatment will obviously continue to be made jointly by patients and doctors, Neumuth points out.

It is also envisaged that a patient data explorer will link patient data from radiological images and medical reports via web technology, and that it will integrate molecular-genetic tumour information into the decision-making process, or calculate patient-specific therapy profiles for surgery and radio or chemotherapy.

Different types of information contained in the digital twin should be directly linked and analysed by AI, Neumuth adds.

Many developments and tests are still needed to ensure that this and other technologies in the field of personalised cancer medicine can be directly integrated into clinical routine: ‘This will take three to five years,’ he estimates.

The objective is to create a scientific and methodological basis for personalised cancer treatment assisted by AI. In the ideal case, this means that a patient will receive personalised treatment based on the latest scientific findings, which takes into account the patient's personal situation and specific needs, with everything being transparent and explained in an understandable way.

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Report: Katrin Scheufler

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The coronavirus pandemic – an international tragedy – created unprecedented upheaval and challenges within health systems, economies, and society. In hospitals, new ways of working had to evolve. Social distancing led to virtual consultations and teleradiology has found an added dimension, with its success, practicality, and effectiveness likely to see more widespread future use. Mark Nichols asked three radiologists about their experiences of teleradiology during the epidemic, and what the future holds.

Evidence collected during the SARS-CoV-2 pandemic by a team from the University of Tennessee, USA, clearly showed changing patterns in the use of teleradiology. Dr Mohammed Quraishi, Assistant Professor of Radiology, Section Chief of Body Imaging and Informatics Director at the University of Tennessee Medical Center, believes the term “teleradiology” needs disambiguation. Often it brings to mind a radiologist far removed, geographically, perhaps, in a different country, reading for multiple hospitals with limited rapport with any specific hospital, he said. ‘I would term this “external teleradiology”, because the radiologist is external to the local group. It’s important to differentiate this from “internal teleradiology” where a radiologist is employed by the practice, reads remotely.

In the USA, practices during the pandemic increased internal teleradiology, and significantly decreased external teleradiology. The reason seems twofold: Quraishi said: ‘First, removing radiologists from the hospital makes sense when trying to mitigate the risk of contracting SARS-CoV-2 and, second, the increase in internal teleradiology – as opposed to external teleradiology – was almost certainly due to the drastic decrease in case volume.’ Internal teleradiology does not display the same time shifts during the pandemic were transferred to internal teleradiology – bringing off-site reading into the daily fold to help decrease radiologist exposure to potential SARS-CoV-2 infection, and allowing radiologists to work at home.

The increased use of internal teleradiology was seen throughout the USA – particularly in the northeast, where the pandemic had prevalence. To gauge changing teleradiology use, the group queried 290 locations, representing a geographically diverse cross section of institutions. They found an overall jump in the use of teleradiology. Around 56% of respondents said they saw enough benefit from the experience that they plan to continue similar workflows post-COVID.

Specifically, 64.8% reported decreased stress levels and 96% found improved or no change in turnaround times, a position Quraishi echoed from his personal experience. ‘I found internal teleradiology less stressful, with an overall increase in productivity,’ he said. ‘Radiologists also reported less interruptions at home allowing them to focus on interpreting studies.’

He believes the pandemic will see a change of emphasis in the use of teleradiology, with practices re-evaluating teleradiology with new business models, services and work flows, such as second opinion reads or even practices sending out studies for subspecialty interpretations.

**Teleradiology to fight burnout problems**

Given increased evidence of radiologist burnout and demands for better work-life balance, teleradiology might offer a solution. According to our survey, the majority of groups plan to incorporate internal teleradiology into the post-pandemic workflow. I predict internal teleradiology will rise across the country and, as groups get comfortable with that, there will likely be spill over into external teleradiology.

Dr Mohammed I Quraishi, Assistant Professor of Radiology, Section Chief of Body Imaging and Informatics Director at the University of Tennessee, USA, clear-
We need a global view of COVID-19

There are major complications from COVID-19 – ARDS, pulmonary embolism and neurological – that imaging can help detect, manage and/or follow up in the long term, radiologists from France and the UK explained during a recent ESR Connect session.

Report: Mélisande Rouger

ARDS – Acute respiratory distress syndrome (ARDS) is the most dreaded complication and the number one morbidity in COVID-19 patients. The incidence was up to 50% of patients in initial reports. In Strasbourg University Hospital, at epidemic peak, there was an 8% rate of admission to ICU directly after ED admission because of ARDS, according to Mickaël Ohana, a local professor of radiology who specialises in non-invasive cardiovascular and chest imaging.

ARDS diagnosis is not based solely on imaging, but, in line with Berlin criteria, is based on acute hypoxaemia plus bilateral radiographic opacities, through chest X-ray or chest CT. ‘The problem is not diagnosis – it is prediction and follow-up,’ Ohana said.

Prediction – Few papers have tried to score the risk of ARDS from an initial chest CT of a COVID-19 patient, based on either quantitative or visual reading. But these types of semi-quantitative scores are not highly reproducible, not standardised and not time-consuming.

‘I would advise simply using the ESR/ESTI visual scale, which is based on the extension of the lesions over the lung parenchyma, and then classifying in five different levels. This is a very simple visual quantification, which can be done readily for any patient. We found that, in about the first 200 patients, if you have less than 25% lung involvement, the risk of going to ICU or dying is about 18%. If you have more than 25%, the risk is much higher,’ Ohana said.

The risk of fibrosis is also a central concern in these patients. Clinicians know from other types of ARDS – not related to COVID-19 – that 50-75% of patients after ARDS are at risk of fibrosis, with varying severity, whether with radiological lesions or clinical lesions.

‘If you have fibrosis on imaging, and even if it is subclinical, it is a risk marker for mortality.’

The question that remains is regarding the risk of fibrosis in COVID-19 survivors, after ARDS. We currently do not know this risk, because we have not had enough time after the initial ICU stay, he explained.

There are different potential evolutions, from ground-glass opacities to crazy paving to consolidation. The questions radiologists must ask themselves are: How can they screen these patients to see which are leading to recovery and which are leading to fibrosis? And when should they follow up with these patients?

‘Based on experience with other types of ARDS, we think that less than three months is probably too early for follow-up CT for patients leaving the ICU. And when doing the follow-up scan, we try to optimise the acquisition protocol so as not to have over-radiation,’ he concluded.

Pulmonary embolism – An early paper, from Italy, on pulmonary embolism and COVID-19 questioned whether there was a random association between the two. Clinicians now know from a wealth of evidence that it is not random, and there is a strong association between pulmonary embolism, indeed all thrombotic phenomena, and COVID-19, according to Anand Devaraj, a professor of thoracic imaging at Imperial College London’s National Heart and Lung Institute. ‘A number of publications have shown that the rate of pulmonary embolism in patients undergoing CTPA admitted with COVID-19 is around 30%,’ he said. ‘There is also evidence to suggest that this is not just a question of pulmonary embolism, but of hypercoagulability in COVID-19 pneumonia.’

‘The parameters that suggest this phenomenon include, for example, very high D-dimer levels in patients with COVID-19.’

‘The pulmonary emboli that we see in Covid-19 pneumonia are often segmental or subsegmental. But a significant minority of patients also have quite severe clot burden, more proximally. Some patients also have very elevated right heart pressures and right heart dysfunction.’

The precise treatment and prevention of pulmonary embolism in these patients is a complex decision for clinicians based on a number of factors, taking into account hypercoagulability and the risks of haemorrhage. But there are reports of thrombolysis being effective in patients with large clot burdens and very high D-dimers, according to Devaraj. ‘In terms of parenchymal signs, there have been a number of reports describing the observation of dilated subsegmental vessels in patients with COVID-19 – known as vascular thickening, or vascular congestion – seen in up to 89% of these dilated subsegmental vessels are peripheral and branching, mimicking tree-in-bud nodularity, but very much centred on the vessel. The aetiology of these opacities is uncertain, but they could reflect thrombotic microangiopathy,’ Devaraj noted.

‘Some recent autopsy data has also pointed towards thrombi within the peripheral vasculature being present as a common phenomenon. The thrombotic hypercoagulable state that radiologists see on imaging in COVID-19 is not just pulmonary embolism; there are also reports of...’

Continued on page 14
Ultrasound could become the prime modality in emergency settings for tracking disease progression in Covid-19 patients, Mark Nicholas reports.

While chest CT has held a key diagnostic role in the recognition and categorizing of mild, moderate or severe disease in COVID-19 patients, many experts see the value of ultrasound becoming more apparent as the more efficient modality increased, with available, the value of ultrasound approaches share similar test characteristics with CT.

Ultrasound fellowship director for the Department of Emergency Medicine and the Director of Point-of-Care Ultrasound Education for Yale School of Medicine, said the key seasons ultrasound has emerged as a first liner in emergency settings to diagnose COVID-19 is largely due to the avoidance of exposure and transmission of virus particles; dissection; and preservation of PPE. ‘Emergency personnel are often the first to see, examine, and talk to a patient,’ she said. As we need to see the patient anyway, it makes sense if we perform as complete an evaluation as possible to avoid others needing to come into contact with that patient. This includes obtaining swabs, lab work and imaging. If the emergency provider can perform diagnostic imaging at the same time as evaluating the patient, then this prevents others from coming into close contact with the patient.’

Cleaning and disinfection
A second critical area is cleaning and disinfection, particularly where CT suites are fixed spaces that would be shared by COVID and non-COVID patients. ‘Many hospitals do not have enough machines, or the infrastructure to create cohorted radiology spaces. So, a CT performed on a Covid-positive patient would shut down that machine for up to an hour, so that it, and the surrounding space, can be cleaned. Contrast that with a portable ultrasound machine which can be cleaned and disinfected in a matter of minutes, with a dwell time of only 2.5 minutes between cleaning and use on the next patient.’

Liu said ultrasound offers advantages over CT, and other modalities, in the coronavirus context and points to preliminary literature in the Covid-19 context, as well as previous imaging literature on Acute Respiratory Distress Syndrome (ARDS), suggesting that lung ultrasound may help rule out COVID infection cases: both a normal and abnormal lung ultrasound may provide key clinical insights; lung ultrasound may help rule out other pulmonary diseases; cardiac ultrasound could detect heart problems caused, or exacerbated, by COVID-19; ultrasound may benefit critically ill patients needing peripheral or central venous access; POCUS can reduce the number of healthcare workers exposed while supplying immediate diagnostic information.

With all the advantages of isolation from others, speed of operation and cleaning, Liu concluded POCUS to be overall ‘the most expedient modality’. Portable chest X-ray, she added, does not have test characteristics that match CT, and findings on both CT and lung ultrasound can be seen before they appear on X-ray, though she acknowledged that all imaging has limitations.

Five reasons for diagnostic ultrasound
The 10-strong expert panel’s discussion report highlighted five reasons why diagnostic ultrasound should be considered for imaging in suspected COVID-19 infection cases: both a normal and abnormal lung ultrasound may provide key clinical insights; lung ultrasound may help rule out other pulmonary diseases; cardiac ultrasound could detect heart problems caused, or exacerbated, by COVID-19; ultrasound may benefit critically ill patients needing peripheral or central venous access; POCUS can reduce the number of healthcare workers exposed while supplying immediate diagnostic information.

Neurological complications – COVID-19 can also be responsible for neurological complications, according to Myrtum Edjafari-Goujon, a neuroradiologist at Hôpital Raymond-Poincaré, Paris-Saclay University. ‘There are two pathophysiological mechanisms suggest to explain these complications. The first is using the spread from mechanoreceptors in the lung via a synapse-connected route to the medullary cardiorespiratory centre; the second is entering the brain primarily via the olfactory bulbs,’ she said.

This second hypothesis has been validated on other types of SARS-CoV virus and was published more than ten years ago. The hypothesis is sustained by clinical symptoms such as anosmia, which is present in more than 80% of patients with mild-to-moderate forms of COVID-19. ‘Anosmia is a very specific symptom of COVID-19, especially when reported without nasal obstruction or rhinorrhea. It is also sustained by imaging publications showing reduced T2 signals of olfactory bulbs,’ she explained.

One of the first articles on brain lesions, from March 2020, described acute haemorrhagic necrotising encephalopathy, a well-known post-viral complication, especially of the influenza A virus, in which radiologists see T2/FLAIR hyperintensity within bilateral thalami and temporal lobes, evidence of haemorrhage and enhancing lesions on post-gadolinium sequences.

Cytokine storms – ‘Acute haemorrhagic necrotising encephalopathy has therefore been related to intra-cranial cytokine storms. This is interesting because cytokine storm syndromes have been recently reported in COVID-19 patients and may play a role in the development of those types of encephalopathy,’ Edjafari-Goujon noted.

Another example of the polyphism of the different secondary diseases related to COVID-19 is the aspect of the cytotoxic lesion of the corpus callosum (CLOC) in a COVID-19-positive patient. ‘There is a presence of an oedemic region of the splenium of the corpus callosum with increased T2/FLAIR signal, high DWI diffusion with restricted ADC values and reduced T1 signal on post-gadolinium injection. CLOC lesions are known to be secondary to an underlying evolving correlate and the corpus callosum is very sensitive to markedly increased levels of cytokines. Both acute haemorrhagic necrotising encephalopathy and CLOC therefore suggest specific complications related to maladaptive cytokine profile,’ she explained.

Different retrospective studies have been published reporting the prevalence of neurological complications. One from Strasbourg and another from Wuhan show that neurological manifestations may occur in 40-70% of hospitalised COVID-19 patients. In terms of neurological signs, agitation was very frequent; and in terms of brain MRI, leptomeningeal enhancements, perfusion abnormalities and cerebral ischaemic stroke have been noticed. ‘Most frequently, when a lumbar puncture was done, the RT-PCR for SARS-CoV-2 in CSF was negative. Meanwhile, new reports of rare complications are emerging, such as Guillain-Barré syndrome, Myelitis, Miller-Fisher syndrome and encephalitis,’ she added.

Besides, a study published in the New England Journal of Medicine showed an association between COVID-19 and increased incidence of migratory and prothrombotic disease, with emergent large vessel occlusion among younger patients. ‘In France, there is a 21% decrease of mechanical thrombectomy during the quarantine. But this could be questioned too, because of the significant increase in care delays,’ she said.

Anosmia and other abnormalities of the olfactory bulbs are usually linked to mild-to-moderate symptoms, often isolated, without other neurological defects and most often without any other abnormalities on MRI. Apart from anosmia, there are more severe complications, such as maladaptive cytokine profile, leptomeningitis and encephalitis, and hypoxia and thromboembolic lesions. In the second phase of the disease, inflammatory lesions can appear and radiologists have to watch for these very carefully. ‘There is a need for a global view on the disease,’ Edjafari-Goujon concluded, ‘and an epidemiological follow-up, and it is important for the physiopathological hypothesis to be validated on post-mortem studies.’
Out of adversity comes opportunity

Orders for mobile X-ray solutions made by OR Technology, in Germany, have multiplied several times since the Coronavirus COVID-19 global epidemic began, with orders from Vietnam, Luxembourg, Portugal, South Africa, Ghana and Trinidad & Tobago and many other countries. ‘With this Xray system, the challenge of the pandemic can be mastered better,’ confirmed Managing Director Bernd Oehm. In a few seconds, excellent pulmonary images of a suspected COVID-19 patient can be obtained. Our lightweight complete solution Amadeo M-DR mini, for example, is suitable for outdoor use as well as bedside imaging in hospitals or nursing homes.

This advanced all-in-one system includes all necessary components, such as X-ray detector, X-ray generator and image processing station. The user is supported by a practical X-ray assistant. The Amadeo M-DR mini enables wireless digital X-rays of the entire body trunk; the manufacturer adds.

The X-ray solution is brought directly to the patient, preventing long waiting times in crowded hospitals. The unit can be set up and ready for use in less than two minutes. Transport and operation can be carried out by one person. The integrated diagnostic software ensures a worldwide and fast exchange of information via cloud or e-mail. This saves a lot of time and transport costs, OR Technology points out. In the case of a temporary power interruption, the device can still be used to take X-ray images.

The compact X-ray unit is simple and easy to move; OR adds. ‘Folded up, it’s easy to transport and even fits into a station wagon. Steps and uneven terrain are no obstacle. The wheels allow easy 360-degree rotation even when folded, which makes it much easier to handle in confined spaces such as elevators.

Details: info@or-technology.com

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Prioritising equipment hygiene

The pandemic has put extra pressure on radiology services and radiographers are particularly at risk of catching and spreading the disease. Strict cleaning and disinfection protocols must be followed, according to Pablo Valdés Solis, President of the Spanish Society of Radiology (SERAM), who recently published new guidelines on how to protect staff and patients.

‘If you have sleeves, you should cover the equipment and especially the console area, to facilitate posterior disinfection and minimise damage risk to the equipment,’ Valdés pointed out. The equipment can be washed directly with soap and water or specific cleansers. Powerful cleansers, organic disinfectants, alcohol and disinfectant should never be used as they may damage the surface.

Disinfection is another key step of the cleaning routine, especially during the pandemic. The aim is to diminish the microorganism load, assuming that some will remain in non-threatening levels. Disinfection can be classified into three levels. The so-called low level is the elimination of bacteria, fungus and some viruses by applying the product in the examination room and on the equipment surface for less than ten minutes.

Intermediate-level disinfection consists of eliminating TB bacillus and most of the existing bacteria, viruses and fungus. High-level disinfection is the complete elimination of germs – except bacterial spores – and is traditionally used to decontaminate medical devices, such as endoscopes, anaesthetic material and other medical devices that have been in touch with a patient’s mucosa.

Sterilisation will eliminate all microorganisms, including bacterial spores, from any surface in critical material like endocavity probes, surgical material and non-reusable interventional material.

The coronavirus is covered by a lipid layer and is therefore vulnerable to soap and traditional disinfectants. For most medical equipment used in daily routine, low to intermediate disinfection is enough.
The anatamicopathologist faces a crisis. Public and private labs suffer increased caseloads, whilst pathologist numbers diminish for various reasons, including greater cancer prevalence associated with aging populations as well as improved cancer screening programs. Precision medicine typically involves more genetic testing and extensive use of immunohistochemistry to classify cancer and assess prognostic and predictive biomarkers.

In clinical practice, a notable number of pathologists are nearing retirement, yet today’s diagnostic pathology training of young doctors is limited.

Alternative: the optical microscope

Recently, digitisation and digital pathology have become widely accepted due to advances in technology and regulations. In essence, in digital pathology a scanner produces a digital copy of the traditional glass slide, to be stored in a local or cloud-based server and viewed anywhere with a computer and internet connection. Current scanners provide high fidelity digital images thanks to high magnification (40X). Additionally, high throughput scanners, with a capacity of up to a thousand slides, are capable of fast, reliable operation with little human intervention, making possible supervised overnight operation and samples ready for review by pathologists and trainees in early morning.

Licensed but a slow uptake

In 2017, the USA’s Food and Drug Administration (FDA) warranted the first license for the use of digital pathology for primary diagnosis in that country. Permission for in vitro diagnosis came sooner in Europe. Despite this, adoption of digital pathology has been slow for several possible reasons. A commonly mentioned barrier is pathologist concerns, such as digital images inferiority, or a slowdown in the sign-out process by COVID-19. Multiple users can access digital images, regardless of location, enabling second opinions and consultations. Shipping and storing glass slides on site is obviated.

Digital rather than analogue archives are more manageable; prior cases are available quicker for comparative review.

Early users report overall efficiency includes shorter reading times during diagnostic sign-out sessions, improved overall lab efficiency in the range of 20%, or more, after complete digital diagnosis, compared with analogue workflow.

In addition, the improved intra-laboratory logistics (the technician time required to sort the hundreds of slides prepared every day in the typical lab, distributing them to the responsible pathologist, collating them for tumour boards, and the added ease to manage consultations, etc.) may add to the savings and lower the financial barriers for adoption in the general adoption of digital pathology – because the development and training of AI algorithms requires vast amounts of carefully annotated digital data. Additionally, once algorithms have been developed, they can only be applied in clinical routine use in labs that have had previous clinical data. The time required for data digitisation, analysis, and results dissemination may not be replaced, early digital pathology adoptions report that, to greater efficiency, a reduced pool of pathologists can also absorb increasing caseloads. The differences in full-time equivalents (FTEs) of pathologists’ time to produce the same case load, when compared those on the microscope, versus that same group of pathologists with better efficiency after digital transformation, show that the personnel savings from fewer FTEs needed are sufficient to amortise the initial investment after 2-3 years. Additionally, these FTE savings, over five years – the typical life of a digital pathology system – do result in an additional lab profit over the fourth and fifth year, before additional expenditure is needed to renovate obsolete elements in the system. Therefore, the investment made efficiency gains that translate into a repayment of the initial amount around the second year and additional monetary gains for a further 2-3 years.

Can I work remotely?

A pillar of digital pathology is reliance on the creation of a digital twin of the glass slide, in a file accessed by anyone with the appropriate credentials from anywhere with an internet connection and a PC. The images are typically stored in a server, usually integrated within the main hospital infrastructure. From here, the digital slides can be accessed remotely via a virtual private network (VPN), that creates a secure access to the hospital IT system.

Digital pathology – luxury or necessity?

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Infrared spectroscopy as a diagnostic tool

New techniques of infrared-based technology are showing strong potential for cost-effective tissue analysis, Mark Nicholls reports.

Peter Gardner, Professor of Analytical and Biomedical Spectroscopy at the University of Manchester, outlined how hyperspectral imaging coupled with sophisticated computer algorithms can identify and grade cancerous tissue, as well as offer an indication of prognosis. The technique, Gardner said, speaking at the 6th Digital Pathology Conference last December, lends itself to automation and would be particularly useful to screen large numbers of biopsy samples for common cancers, such as prostate cancer.

Posing the question ‘Infrared spectral pathology – an academic exercise or a new diagnostic tool?’, he explained that infrared micro-spectroscopy uses an array detector with the image of the sample focused onto an array of MCT (Mercury Cadmium Telluride) detectors, so that spectra from each point on the sample can be obtained simultaneously.

‘All tissue contains molecules that vibrate, particularly if you shine infrared light through them,’ explained Gardner. The infrared light is absorbed and if we measure that, we obtain an absorption spectrum. Because we have thousands of pixels in our image, we have thousands of spectra and this makes our data.’

Reducing error rates

Focusing on prostate cancer, the team liaised with pathologists over the technique with feedback suggesting that pre-screening with infrared micro-spectroscopy would help focus on the most important cases and that automated pre or post screening of biopsy samples could reduce error rates.

‘However, Gardner stressed, ‘If looking at tissue with infrared spectroscopy, we cannot pin down individual proteins – this is not mass spectrometry – but we can get a spectroscopic fingerprint that might be indicative of something in the tissue.’

The question is, is the fingerprint different enough to say something about that tissue? We can get spectral evidence of that tissue and the in vivo has shown that reasonable results for a two-band criterion have been obtained directly from tissue component on a given histology slide. With 2.5 million spectra processed and classified in less than sixty seconds with no staining needed, or de-waxing of the sample, a drawback is the requirement for infrared transparent substrates for pristine results.

Despite this, the research team has shown that reasonable results and diagnostic information could be obtained using standard glass slides just from the region at great detail and with excellent reproducibility,’ he added, ‘we can thereby gain additional information from pathology review in an automated fashion that would otherwise be very laborious to obtain.’

Indeed, initial data showed that tissue composition analysis with DNN (deep neural networks) allows analytical robustness, automatization and standardisation and provides high reproducibility at single cell resolution.

DNA-based tumour purity estimates are more accurate than visual view or deconvolution from genome-wide omic platforms which, he said, tend to under-as well as over-estimate tumour purity respectively. Therefore, digital pathology review using DNN could be used to inform downstream molecular analyses better and investigate tissue-based metrics as potential biomarkers in clinical trials.

The door to simple, cheap, reliable bio-stratification

The question is, is the fingerprint different enough to say something about that tissue? We can get spectral evidence of that tissue and the image has evidence of the peaks in that tissue – we can see the protein peak, for example.’

The professor acknowledged that the resulting limited correlation of standard pathology assessment with DNA and RNA yield from clinical samples. As the ability to detect somatic variants in cancer samples drives personalised therapy, better tissue classification strategies could help to improve clinical diagnostic workflows.

‘An area of development is tissue segmentation by supervised machine learning for the estimation of tumour cell percentage by digital pathology,’ he said. This approach allows correlation between different levels of information and provides accurate area information for each tissue component on a given histology slide.

Excellent reproducibility

‘It allows us to look at the cell-level composition of histology slides in great detail and with excellent reproducibility,’ he added, ‘we can thereby gain additional information from pathology review in an automated fashion that would otherwise be very laborious to obtain.’

Moreover, the researchers showed that ‘reasonably good’ classifications of stroma and epithelium could be obtained directly from heavily H&E stained tissue.

Gardner, who believes the technology
Digitising pathology – one step further

Viktor Koelzer is Assistant Professor at the Institute of Pathology and Molecular Pathology at University Hospital Zurich and Honorary Senior Clinical Researcher at the University of Oxford. He is passionate about technology in application to daily diagnostic practice and research, in particular improving patient care through the implementation of high-quality, science-driven computational image analysis approaches with a focus on gastrointestinal disease and tumour immunology.

biological understanding of CRC potentially leading to better clinical stratification and treatment decisions, such as performing a surgical resection or giving adjuvant chemotherapy.

In conclusion Professor Koelzer said that Computational models can predict transcriptional subtype of CRC from standard histology sections. 1mCMS makes sequencing information interpretable through association of morphology, molecular features and outcome data and classifies samples previously unclassifiable by RNA expression profiling. It also gives a novel insight into tumour heterogeneity, is highly prognostic, and classifies endoscopic biopies and resection specimens of CRC enabling patient stratification in diverse clinical settings.

Koelzer sees a promising outlook with a better integrative approach for molecular and digital pathology. ‘Molecular classifiers can be recognised and called from H&E images, opening the door to simple, cheap and reliable biological stratification within routine workflows and existing retrospective cohorts.’

For more than 30 years, Barco has invested significantly in research and development specifically to improving workflow and clinical outcomes for healthcare professionals. Barco researchers work closely with clinicians to obtain a deep understanding of the clinical challenges and workflow realities so that they can incorporate this knowledge while developing innovative ideas for tomorrow’s healthcare products.

Toward this goal, Barco has developed display systems and technologies designed to empower clinicians to work more efficiently and diagnose more accurately to meet the demand of a growing workload in an era of unprecedented healthcare service delivery.

Digital pathology is sweeping the world over time and can be quickly transported over computer networks to bring the best people and the best images together to improve patient care. Countries vary in their uptake of this new technology, and in the United States, the FDA has cleared digital products only for a select subset of HIC applications.

Cédric Marchessoux, research engineer at Barco, explains: ‘A lot of challenges need to be addressed before digital pathology can hit the market. First of all, the images are huge, requiring very high resolution imaging devices. Moreover, analysing pathology images is a complex practice and exchanging samples or slides between labs is difficult, which prevents effective collaboration.

What people love about Barco pathology displays:
- Fast viewing, panning and zooming in on digital slides with the powerful Barco display controllers
- Intervention-free colour calibration and record-keeping with Medical QAWeb
- See more details on your slides with a variety of large, bright Barco display models
- Designed for medical use: cleanable and compliant with international medical safety and emission standards (CE, UL, etc.)

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We help medical professionals enable better health outcomes and work more efficiently in an increasingly complex healthcare enterprise.

ENABLING BRIGHT OUTCOMES
Fast detection of virus antibodies

Researchers at Hokkaido University have succeeded in detecting anti-avian influenza virus antibody in blood serum within 20 minutes, using a portable analyser they have developed to conduct rapid on-site bio tests.

If a suitable reagent is developed, a new portable analyser could be used to detect antibodies against SARS-CoV-2, the causative virus of COVID-19. Avian influenza is a poultry disease caused by influenza A virus infection. Rapid initial response for a suspected infection and continuous surveillance are essential to mitigate the damage from highly pathogenic, transmittable pathogens such as avian influenza viruses.

The group, including Keine Nishiyama, a PhD student at Hokkaido University’s Graduate School of Chemical Science and Engineering, and Professor Manabu Tokeshi of the university’s Faculty of Engineering, conducted this study to develop a new method and analyser capable of rapid, facile and selective detection of antibodies. The method is based on conventional fluorescence polarization immunoassay (FPIA) but applies a different measurement mechanism to make the analyser much smaller and portable. The analyser weighs only 5.5 kilograms.

Simultaneous examination of multiple samples

The combined use of liquid crystal molecules, an image sensor and the microfluidic device makes it possible to simultaneously examine multiple samples and reduces the volume of each sample required. Liquid crystal molecules are capable of controlling the polarisation direction of fluorescent light, while the microfluidic device has a number of microchannels as a measurement vessel. The group also developed a reagent to detect anti-H5 avian influenza virus antibody, a fluorescein-labelled protein that binds only with the antibody. The reagent was made by reproducing hemagglutinin (HA) protein fragments, which are expressed on the surface of H5 avian influenza virus, through gene recombination and by labelling fluorescent molecules to the fragments.

To make the measurement, serum collected from birds was mixed with the reagent and left for 15 minutes. The mixture was injected into the microfluidic device and measured with the portable fluorescence polarization analyser. Molecular movements of the reagent bound with the antibody will be smaller in the liquid, producing a different degree of polarisation from the reagent not bound with the antibody. The system can detect anti-H5 avian influenza virus antibody with only two microlitres of serum sample and within 20 minutes. ‘Our analyser could be used to conduct other bio tests,’ Tokeshi said, ‘if suitable reagents are developed.’