

## Impact of COVID-19 on Clinical Care and Research in Cancer Imaging: Where We Are Now

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## Key Points

- Most institutions have resumed cancer screening appointments but are working through the backlogs of postponed appointments from earlier in 2020.
- Social distancing, work-at-home policies, and altered cancer imaging workflows may continue into 2022.
- The pandemic has substantially negatively impacted cancer imaging research and funding opportunities; reassessments will likely be needed to evaluate productivity and academic progress.

"We might be tired of COVID-19. But it is not tired of us."

Tedros Adhanom Ghebreyesus, Chief of the World Health Organization, on September 11, 2020

"Vaccines do not equal zero COVID."

Michael Ryan, WHO emergencies Director on December 5, 2020

## Introduction

In April 2020, we published an editorial about the impact of COVID-19 on the cancer imaging community (1). As a painful reminder, governments in the United States and many other countries enforced stay-at-home orders and lockdowns of varying severity during the first wave of infections. Hospitals filled, sometimes beyond capacity, with persons infected with SARS-CoV-2. To reduce potential exposures to health care workers and patients, institutions typically postponed elective cancer screening studies. Facilities frequently delayed surgical procedures and follow up for oncology patients and switched to virtual visits. Oncologists tried to switch patients from intravenous to oral medications to prevent on-site infusions of drugs, saving limited personal protective equipment (PPE) and reducing interpersonal contacts for potentially immunocompromised patients. Institutions markedly reduced or even suspended research activities except for those directly related to COVID-19, shifting researchers to remote work. Restrictions interrupted ongoing experiments in the lab, and suspended clinical studies suffered unrecoverable losses of data from longitudinal cancer imaging studies analyzing disease progression and response to therapy (2). In addition, Spring of 2020 initiated a still ongoing cancellation of in-person scientific meetings with researchers, clinicians, and meeting organizers

forced to adopt virtual formats. To understand and communicate the scope of COVID-19 on cancer imaging at that time, we collected and summarized policies in place at institutions throughout the world. Our panel of experts also provided informed opinions about longer-term consequences of COVID-19 on patient care and research in cancer imaging.

Given the immense interest in the first editorial, we decided to revisit the impact of COVID-19 on cancer imaging. Although we and others heard predictions about subsequent waves of infection, few people anticipated the dramatic increases observed in the fall. We write this article in December of 2020, a time with highest numbers of new COVID-19 infections and fatalities in the United States since the pandemic started. New, more infectious mutants of SARS-CoV-2 also emerged, contributing to surging infections. Our update article on COVID-19 and cancer imaging comes in the setting of a world still struggling to manage a devastating pandemic.

### ***Where Society is Now***

The listed quotes from officials with the World Health Organization (WHO) point to ongoing challenges the world must face and overcome. “We might be tired of COVID-19. But it is not tired of us.” This quote speaks to the emotional toll of the pandemic and disruptions to essentially all aspects of life. Many institutions established web resources and support interventions to help people cope with changes in mood caused by COVID-19. Despite mounting frustrations, the need for social distancing, limited sizes of gatherings, and masks will continue since SARS-CoV-2 clearly remains a threat. Dr. Anthony Fauci, Director of the US National Institute for Allergy and Infectious Disease, projects the United States will not return to normalcy until 2022. A recent study suggests particular concern for the virus in immunocompromised cancer patients who may continue shedding SARS-CoV-2 for at least 2 months after infection (3).

“Vaccines do not equal zero COVID.” The WHO issued this statement just days before the United Kingdom began vaccinating high-risk persons, likely signaling the roll out massive vaccination campaigns across the world. While results from clinical trials show approximately 95% reductions in overall COVID-19 infections and far fewer severe infections, performance of these vaccines in real-world settings remains unknown (4,5). Even 95% protection will not completely stop all transmission, particularly given the high prevalence of disease. Persons at highest risk, including the elderly and those with underlying health problems that include at least some cancers, often respond less well to vaccines. A critical question remains unanswered: Do vaccines reduce or eliminate the spread of infection? Side effects of vaccination, reported to be more severe than current vaccines for influenza A or other infectious diseases, also present a possible barrier to widespread vaccination. Because of the requirement for two doses per person

for the frontrunner vaccines, large numbers of persons, and logistics required for storage and transport of some formulations, experts project that vaccination will continue through the summer. So, COVID-19 will not go away quietly or quickly.

With this background and the re-institution of some lockdown procedures in some countries, we again asked experts in cancer imaging for their perspectives on the current status of clinical medicine and research in cancer imaging during COVID-19. We did not gather information through a formal survey but compiled answers and opinions from experts who responded to our questions. We also do not identify specific responders or their affiliations. We frame the discussion in the context of comments by Dr. Ned Sharpless, Director of the US National Cancer Institute, who estimated that delays in diagnosis and treatment of cancer caused by COVID-19 will increase deaths from cancer by 1% for breast and colon cancer through 2030 (6). The Institute for Cancer Research in the UK estimated that COVID-19 will delay advances in cancer research by 18 months due to factors including disruptions in collaborations and shortages of resources. While true in essentially all aspects of life, COVID-19 will continue to hinder cancer imaging for years beyond the end of public masks and social distancing.

**What guidelines have institutions put in place to adapt for local COVID-19 outbreaks? Are responses to COVID-19 in the winter of 2020 different than in the spring of 2020, during the “first wave” of illness?**

In mid-March, 2020 most shutdowns and stay-at-home orders occurred around the world. During that period, there was an intense focus on suppressing COVID-19 above all other priorities, whereas, as one of our respondents stated, the general mood in late 2020 was to, “keep calm and carry on”. To balance safety versus access for clinical work and research, institutions enacted a variety of phased reopening protocols. The responses we received for institutional guidelines and practices fell into four general categories: (a) new cleaning and social practices, (b) alteration of workflows, (c) modification to patient appointments, and (d) guidelines for research settings.

***Cleaning and Social Practices***

Hospitals and other health care facilities developed multiple strategies to mitigate risk while avoiding pronounced reductions of clinical services that occurred in the spring. Reopening strategies included proscribed traffic flow patterns to minimize intersections of people; limited numbers of persons permitted in elevators and waiting areas; and designated areas marked as

COVID-19 protected or at risk. Imaging rooms and other shared areas scheduled gaps between patients for extra cleaning. At least one center shifted all elective cancer surgeries to a separate, “COVID-free” hospital. After experiencing outbreaks of COVID-19 from personnel dining together inside, institutions assigned clinical staff to staggered lunch periods and created socially-distanced dining areas.

Hospitals stockpiled PPE during the summer to avoid past shortages. PPE requirements varied among centers with some sites requiring eye protection and a surgical mask for personnel performing procedures, while others mandated full PPE with gown and N95 mask. Earlier in the pandemic, shortages of PPE resulted in forced reuse of certain equipment, most commonly N95 masks. Institutions re-emphasized frequent handwashing and procedures to safely don and doff PPE, and hand sanitizer stations sprung up in all areas of hospitals.

### ***Alteration of Workflows***

Work and meeting places shifted into an online environment in people’s homes. Most departments will continue to conduct virtual meetings at least through early 2021. To promote social distancing in reading areas, institutions rapidly expanded home workstations for diagnostic radiologists and remote read-out sessions for residents. For both research and clinical personnel, travel bans, or restrictions remain in place to limit both expenses and risks of exposure to COVID-19.

While some centers reinstated in-person teaching activities and onsite reading of studies, home workstations likely will remain even after COVID-19 because of the popularity of this work arrangement. Telework arrangements extended to administrative staff, many of whom continue to work remotely with only intermittent days onsite. When possible, clinical appointments for follow-up care also shifted to virtual visits.

### ***Modification to Patient Appointments***

With respect to patient appointments, many institutions postponed non-urgent screening exams during the early months of the pandemic. Many of these closures and postponements lasted for several weeks, delaying thousands of appointments. Postponed appointments included those for lung, breast, and colorectal cancer screenings. Among most institutions, reopening plans happened gradually over a 2-4 month period after initial lockdowns. To compensate for the months of delayed appointments, radiologists revised CT and MRI protocols with shortened scan times to help increase throughput.

Phased re-openings included resumption of postponed elective imaging studies and procedures. Typically, patients with newly diagnosed cancer, those actively undergoing treatment, and those experiencing acute symptoms received priority. Institutions began digging into the massive backlog of postponed studies, usually in chronologic order of the originally scheduled appointment. Imaging departments generally completely or almost completely recovered to pre-pandemic levels, although hospitals continue to restrict numbers of visitors for inpatients and accompanying visitors for clinic and imaging appointments.

Building access protocols commonly included self-reported or onsite temperature checks, screening questionnaires for symptoms of COVID-19, mandatory face coverings in public places, and limited access points to buildings. For outpatients, institutions frequently pre-screened them for symptoms of COVID-19 in advance of appointments to prevent potentially infected people from arriving onsite. Additionally, some clinics streamlined patient check-in and consent by use of QR codes for scanning and electronic forms. Some facilities implemented tracking systems linking building access to completion of safety modules or screening questions. Policies for asymptomatic polymerase chain reaction testing for COVID-19 varied across sites. For personnel, respondents noted requirements ranging from weekly testing for all personnel, testing recommended or encouraged, or no testing. Prior to elective surgeries, many centers required a negative test for COVID-19 and even self-isolation for patients.

### ***Guidelines for Research Settings***

Universities also implemented phased re-opening plans for research. While permitting onsite experimental work, institutions encouraged or even required computational work to be performed offsite. Wet labs operated under reduced occupancy limits and even implemented morning and evening shifts of personnel to maintain social distancing. Reported limits ranged from 30-80% with occupancy progressively increasing since shutdowns in Spring. Some local outbreaks have resulted in occupancy limits as low as 25% during the Winter. During the second and third waves of COVID-19, institutions paused progression of re-opening plans, but no respondent noted a reversal of wet lab occupancy or capacity. Clinical research in cancer imaging suffered to a greater extent. Institutions typically suspended most clinical trials with new imaging methods for up to 5 months unless studies provided direct benefits to participants. Interruptions in clinical studies extended for longer periods of time than laboratory work. Even when clinical studies reopened, institutions often excluded participants in high-risk groups, such as persons older than age 65 or with compromised immune systems. These high-risk groups include many persons with cancer. Re-opening plans generally progressed to allowing participants in some

high-risk groups, although some institutions reverted to more stringent policies for clinical studies during the third wave of infection. Particularly for studies using a series of imaging studies over time to monitor disease status and response to therapy, frequent changes in inclusion and exclusion criteria resulted in irrecoverable losses of data, numerous institutional review board deviations, and poor accrual.

### **Have institutions recaptured the number of cancer screening studies that were performed prior to the pandemic?**

All respondents noted at least partial recovery in cancer screening after shutting down in early 2020. Many patients continue to fear hospitals, and others lost health insurance due to unemployment. Both factors create obstacles that will hinder efforts to resume cancer screening and other non-emergent imaging examinations. Health care organizations and governments have started public messaging campaigns to encourage re-entry into cancer screening to prevent missed diagnoses. Resumption of cancer screening rebounded more quickly in suburban locations, which typically have more physical space for social distancing of patients. In larger urban settings, physical space in screening centers may be smaller, and persons rely more heavily on public transportation to arrive at appointments, of which both impede social distancing. Return to cancer screening continues to lag notably for under-served populations and persons living in rural settings, prompting active outreach efforts by health care facilities.

In some institutions, demand for screening now exceeds normal capacity. While due in part to expected increases in volume during Breast Cancer Awareness month in October, the large demand reflects the large backlog of screening studies. To increase capacity, facilities increased hours of operation to evenings and weekends. Sites also continue to explore creative approaches to increase numbers of patients in waiting rooms to maintain social distancing without spending money for renovations. Increasing services has strained staffing models, particularly at institutions with hiring freezes. Despite these efforts, some centers have up to 2 month delays for appointments for cancer screening studies.

Interruption of cancer screening already has had detrimental effects on patients. A presentation at the virtual 2020 San Antonio Breast Cancer Symposium compared breast cancers diagnosed during March-April 2019 and 2020 (7). During the pandemic period in 2020, patients more commonly presented with symptomatic, more advanced tumors. New diagnoses decreased by 65%, suggesting a large number of persons with undiagnosed breast cancer. On the positive

side, time to surgery decreased by a week due to greater availability of surgical suites after cancellation of elective surgeries.

### **Are faculty still working from home? What are some of the long-term plans for working at home?**

In general, most respondents reported that their institution had at least some staff still working from home in late 2020. The ability of institutions to have certain personnel work from home also served as a backup in the case that onsite personnel became ill. The quick transition to working at home at the beginning of the pandemic created an urgent need for at-home reading stations for radiologists. Obtaining home work stations for breast imagers was particularly problematic because of the need for expensive, high-resolution monitors, as well as required physicist surveys prior to use. Working at home has allowed more flexible arrangements with respect to taking care of children or elderly parents. While these arrangements make it easier to care for family members, working in the same space as children, pets, and others can still be challenging. Additionally, with the shift to at-home schooling and closures of childcare facilities, primary caregivers have had to balance childcare and clinical duties while at home. Nonetheless, many institutions have allowed staggered shifts to help with work-life balance. Respondents anticipate that some staff will continue to work at home through at the least the beginning of 2021.

### **How have institutions handled the financial constraints from closures and reduction in patient visits during 2020?**

In general, from the responses we received, many institutions are still in the planning phases of recouping financial losses from the year. National funding in European countries helped lessen the impact from the closures in the earlier part of 2020. In the US, institutions handled financial constraints by implementing salary cuts for leadership positions, not providing salary raises in 2020, reducing or freezing new hires, and in some places, furloughing workers. In the later part of 2020, many individuals that had been furloughed were brought back to their positions. Some expenses were accrued because of the altered workflows that resulted from the shutdowns including paying staff for extra work hours, hiring additional staff to keep up with backlogs, as well as renting mobile CT and MRI units. There are some areas where institutions managed to save money this year, including unused travel, party, and graduation budgets.

### **What are some of the policies that have been put in place for trainees in clinical and research settings?**



Classes and trainings generally still occur through online meeting platforms for graduate students, post-doctoral fellows, as well as medical and radiology trainees. Interviews for new trainees shifted to online platforms as well. Staggered work hours and social distancing in clinical and laboratory settings make it difficult for students to work with senior staff for training purposes. There are some concerns that students may drop out of their programs due to the pause and slow down of research during most of 2020. As for practicing trainees, some institutions implemented opt-in options for training in person. There are still capacity caps (ie 25% or 50%) at some institutions, and these capacities may be adapted based on local outbreaks. Some institutions are ramping their capacity back up, and this will likely continue once COVID-19 case counts begin to decline.

**How has clinical and/or bench work been impacted during 2020? What are some plans being put forward to continue progressing new research studies?**

COVID-19 continues to exact a mounting toll on cancer imaging research. For clinical research studies with funding linked to accrual, pauses in trials and drops in enrollment resulted in lost revenues needed to support research coordinators and imaging technologists. Donations plummeted to cancer research organizations, such as Cancer Research UK and the American Cancer Society, resulting in canceled grant programs. Government agencies diverted funds to COVID-19 research, heightening already intense competition for grants in other areas. Sustained interruptions in clinical studies blocked progress on funded research, limiting the ability to complete objectives of the grant and renew it for further research. Respondents also noted challenges with personnel. Administrative staff working offsite reduces support for research activities. Researchers have had to adjust expectations and goals for their programs. We hope that institutions and funding agencies also will reset metrics for productivity and academic promotions.

Despite the damage to cancer imaging research, the pandemic produced some benefits. During initial shutdowns in the spring, some investigators experienced unexpected “free time” to complete unfinished manuscripts and even resurrect data from some projects. Computational research, particularly in artificial intelligence, radiomics, as well as cost-effectiveness research, also flourished for some investigators because of extra time available for readers and better IT support. Many scientists shifted their studies toward COVID-19 and infectious disease to meet the demands of the pandemic and open new sources of funding. Cancer imaging research, and science in general, moved toward improved data sharing policies, which will help overcome shortfalls of new data in many sites during 2020.

## **What long-term changes are envisioned to arise in clinical cancer imaging or imaging research as a result of COVID-19?**

The first wave of COVID-19 infections caused institutions to severely restrict or stop laboratory and clinical research for several months. As infections subsided during the summer, institutions allowed at least partial resummptions of research. Clinical studies generally, but not universally, resumed enrollment. Resumption of clinical studies did not occur universally. The second and, to a greater extent, third waves of infections in the fall of 2020 paused or even reversed re-opening of research activities. Many institutions re-instated restrictions on clinical studies without direct benefits to participants. Onsite laboratory research continued as permitted within limits of new stay-at-home orders imposed by local governments, and most institutions urged or required researchers performing computational work to stay at home. These restrictions on research activities may not end until 2022.

Researchers generally shared concerns that the spike in infections would lead to another abrupt shut down in research activities. Uncertainties about the ability to continue research operations produced several downstream effects. Investigators limited or delayed breeding new research animals or starting new animal studies for fear of losing time and resources in the event of pauses or shut downs in research. Demand for PPE and disruptions in supply chains created ongoing shortages of basic research supplies, and many core research facilities operated with reduced staffing and throughput. Researchers continue to experience delays in starting new clinical imaging studies in cancer, including new immunotherapy protocols. For many respondents, COVID-19 offered no new research opportunities and markedly detracted from existing projects. Delays in scientific progress in cancer imaging will be incredibly difficult, if not impossible, to recover.

## **Has COVID-19 opened any new opportunities for the cancer imaging community?**

Despite the immense negatives of COVID-19 on cancer imaging, multiple respondents identified some positive changes. We as a community took a crash course in videoconferencing and work-at-home technologies. Teleworking reduced or eliminated commuting to onsite offices and parking congestion. Unnecessary in-person meetings ended altogether or converted to videoconferencing. Institutions rapidly upgraded IT systems to improve data management and transfer, facilitating sharing of large data sets such as images. The ability to share data among sites in ways not envisioned previously will advance research collaborations and potentially mitigate anticipated losses in funding. Renewed emphasis on studying the immune system and

ways to image immune responses offers new opportunities for interdisciplinary research in cancer immunotherapy. Applications of artificial intelligence to diagnosing COVID-19 by imaging hopefully will translate to better screening and diagnostic imaging studies for cancer. Many institutions also benefited from new funding related to research on COVID-19.

Of course, national and international scientific conferences also shifted to videoconferencing due to cancellation of in-person events. Even when in-person conferences resume, events likely will continue to expand their virtual content for both on-demand and live sessions. While increasing access to many participants, virtual conferences of all scales create challenges for networking and forming new collaborations. Loss of interpersonal interactions with resulting feelings of isolation remain an underlying concern of longer-term transitions to telework and videoconferences.

### **Concluding Remarks**

In the early months of 2020, institutions rushed to implement new practices to reduce COVID-19 exposure and keep health care personnel and patients as safe as possible. These initiatives remain in place as intuitions have adapted to this new normal. When we wrote our first editorial back in April, there were a lot of unknown factors with respect to how the pandemic would unfold. However, throughout 2020, the cancer imaging community, as well as other medical professions and societies, came together to learn, adapt, and implement new practices.

As we enter into the new year, there are a few stories that should be given attention to cast a better picture for the future. In December 2020, the Association of American Medical Colleges reported that the number of medical school applications increased by 18% compared to 2019, in what is being called the “Fauci effect”. In the midst of this pandemic, there has been inspiration felt by many prospective medical and research students to bring about the next generation of patient care. In addition, on December 11, 2020, the Food and Drug Administration officially approved emergency use of the first COVID-19 vaccine (4), and the first vaccine was administered in New York on December 14. A second emergency use authorization followed on December 18 for another vaccine. These approvals mark a pivotal point toward ending this pandemic.

As we stated in our first editorial, the actions taken during this pandemic have highlighted the collaborative efforts by clinicians and researchers alike. As we enter 2021, clinics will continue

to adapt to this pandemic to bring about the best patient care and will be innovative in determining ways to overcome the challenges faced in all aspects of cancer imaging during the last year.

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