

UCLA Radiology

NEWSLETTER OF THE DEPARTMENT OF RADIOLOGICAL SCIENCES

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The Fight Against COVID-19



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Chair's Message



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A common observation is crises often accelerate trends already underway. “The most difficult social problem in the matter of Black health...was to understand why so few White Americans were bothered by it. The poor Black lives were spent in the most unhealthy parts of the city and in the worst houses, with minimal medical attention.” This could easily be a current quote, but it was written by sociologist, W.E.B. DuBois in 1899. Unfortunately, this remains relevant today and COVID has unfortunately accelerated health care inequities in our minority populations, especially Black communities. There are, however, some hopeful signs the pandemic is beginning to hasten steps to address these inequities.

UCLA Radiology has taken steps under its control to help resolve some health care disparities. They include bringing UCLA Radiology expertise in diagnostic imaging, interventional radiology, and operations management directly to the Martin Luther King, Jr. Community Hospital (MLK), which serves a predominantly Black community. Our faculty, technologists, nurses, nurse practitioners and administrators run MLK's Department of Radiology. This team delivers inpatient care of the highest quality, something UCLA Radiology takes pride in. Building on this track record, we are grateful for a future opportunity to incorporate our IR fellows into our MLK care team. They will provide superior care to our MLK patients while enriching their diverse clinical experience.

UCLA Radiology recently took another step to address inequities in care that predate the pandemic but have been exacerbated by the COVID crisis. Supported by a \$2.7 million grant, the “Mammosphere Project” led by Drs. Ashley Prosper, Hannah Milch, Cheryce Fischer, and William Hsu, will broaden our contribution to reducing disparities faced by people of color (POC) especially in the more recently identified underserved medical environment of outpatient care. We will bolster preventive outpatient care by leveraging radiology's role in breast cancer and lung cancer screening. Historically, participation in these screening programs in underserved minority communities has been low for various social, cultural and personal reasons. Less access to outpatient care has been exacerbated for POC in Los Angeles during this pandemic. Rising to meet the urgency driven by COVID, the Mammosphere Project has developed an innovative strategy to communicate through social and personal networks to increase participation in proven screening programs and to specifically narrow gaps in the diagnosis and treatment of both breast and lung cancer.

One of Mammosphere's key innovations is using “influencer models” born of the social media age to improve health care. Another innovation is to boost poor adherence to lung cancer screening (LCS) guidelines by linking that care with better-established mammography screening in an effort to overcome socioeconomic, cultural and psychological barriers, especially among African-Americans, who have historically been diagnosed with lung cancer at higher stages and who have experienced lower five-year survival than Non-Hispanic Whites. They, however, have been shown to derive comparably greater mortality reductions with earlier lung cancer detection through LCS. This novel linking draws on varied resources: health care advocates, patient navigators, social networks, even transportation for more convenient access.

This project begins at an encouraging time in cancer screening as some structural racial barriers are beginning to fall. This March, the USPSTF lowered the age and smoking history cutoffs for low-dose LCS, effectively doubling screening eligibility among African Americans and women. There is clear urgency not only to rectify historical inequities, but also counter COVID's effect on screening rates.

While the COVID crisis has brought tragedy across our nation, especially to minority communities, the innovation and tireless efforts of UCLA Radiology faculty offer a small ray of light and hope in reversing health care inequities. UCLA Radiology's presence has had significant beneficial impact on the care of MLK patients and this pioneering engagement continues to grow substantially in its goal of reducing health care disparities by providing tangible, clinical benefits to our predominately Black underserved communities. We recognize the importance and urgency of these actions and we will be unrelenting in our efforts to build equity in health care. 

New Project to Increase Lung Cancer Screening Adherence

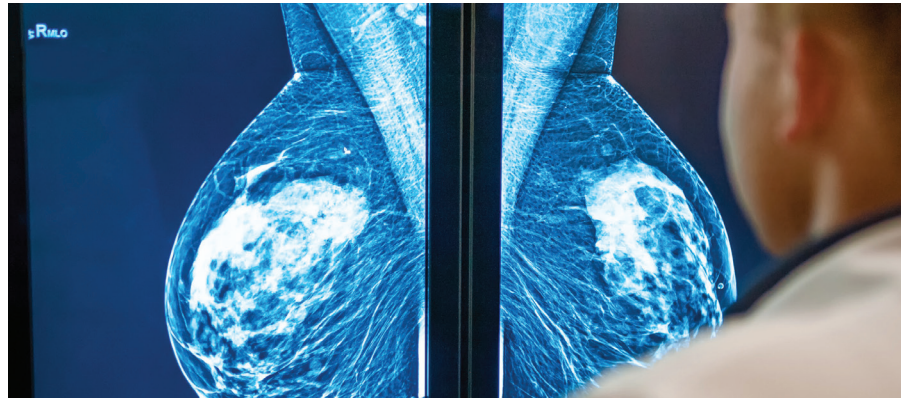


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Despite the fact that both breast cancer screening with mammography and lung cancer screening with low dose computed tomography (LDCT) scanning can lead to early cancer detection and significant reductions in mortality — ranging from 20 to 40 percent in those who meet screening criteria — mammography is well utilized by patients (76 to 81 percent), while adherence to lung cancer screening guidelines is woefully low (5 to 12 percent).



Several factors contribute to this, including smoking stigma, lack of familiarity with recommendations and the complexity of qualification criteria. African American/Black current and former smokers derive the greatest mortality benefits from regular LDCT screening for lung cancer, yet underserved populations generally receive fewer medical screening services and suffer worse outcomes from cancer and other diseases.

Employing education and networking to improve compliance

A group of UCLA radiologists and informaticists — led by Ashley Prosper, MD, Hannah Milch, MD, William Hsu, PhD, and Cheryce Fischer, MD — have been granted \$2.7 million over three years to carry out research aimed at increasing guidelines-based utilization of LDCT lung cancer screening. The team intends to leverage the high adherence to breast cancer screening guidelines to improve adherence to lung cancer screening guidelines. The new study — the Mammosphere Project — will recruit women who receive regular mammograms and assess their eligibility for lung cancer screening and other image-based screening services. In addition, women recruited to participate in the study will be provided with tools to serve as health advocates for people around them (including family and friends) who are less likely to participate in screening due to fear, stigma, lack of knowledge and other factors. The researchers hypothesize that eligible women undergoing breast cancer screening will be more likely to participate in lung cancer screening and can utilize their influence over family and friends in their social networks to increase overall screening adherence in their communities.

Recognizing the significance of psychological barriers to cancer screening, the team aims to measure participants' levels of fear, fatalism and concern for future consequences, tracking their changes over time. The project will uniquely track referrals by women within their social networks and provide educational materials via a patient portal and a patient navigator who can connect patients with available screening resources. To improve convenience, efforts will be made to schedule multiple screening imaging exams at one time. The research will provide a patient-centered, personalized report of cancer risk at the completion of the initial visit based on personal and family history using current risk models to inform screening recommendations.

The researchers will track differential health outcomes and adherence to screening between the study group and a non-participant age-matched control group after three years; the effectiveness of the referral/influence model; and changes in levels of anxiety, fear, stigma and other psychological factors that may be associated with reduced screening adherence.

Hannah Milch, MD, assistant clinical professor of radiology at UCLA, already completed a pilot study in which over 800 women seen for breast cancer screening at UCLA were surveyed to determine their eligibility for lung cancer screening, their awareness of lung cancer screening and their adherence to lung cancer screening guidelines. As reported in our Autumn 2020 newsletter, she found that the majority (63 percent) of the women eligible for lung cancer screening had never heard of lung cancer screening with LDCT. “There is an opportunity here to inform and offer lung cancer screening services to these eligible women who



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have already shown an interest in cancer screening by receiving routine mammograms. These women may also be in position to influence family and friends who may also be eligible for screening,” explains Dr. Milch.

Lung cancer screening and health disparities

Dr. Milch is collaborating in the new research with Ashley Prosper, MD, assistant professor of radiology at UCLA, to build on the earlier survey and attempt to increase awareness of lung cancer screening with LDCT and adherence to screening guidelines, especially in historically underserved populations. One way the study aims to reach patients from across a range of socioeconomic and cultural backgrounds will be to recruit women receiving screening mammograms through local safety net primary care clinics.

The grant includes funding for screening exams and blood work required for risk assessment. Recognizing potential transportation barriers to screening adherence, the study will work to provide transportation to participants in need.

In a subanalysis of National Lung Screening Trial (NLST) data by race, African Americans reported higher rates of characteristics associated with poorer lung cancer outcomes, including being current smokers (though with lower overall cigarette consumption) and having higher rates of comorbidities. In spite of this, African Americans undergoing lung cancer screening with LDCT experienced the greatest reduction in lung cancer mortality of any racial or ethnic group, in addition to a greater reduction in all-cause mortality than white participants. Yet in reports from clinical screening programs, African Americans who meet the eligibility criteria for lung cancer screening are less likely to receive lung cancer screening and to have longer times to follow-up than white patients. In addition, studies showed the USPSTF’s original lung screening criteria to be insufficiently inclusive, with African American/Black smokers developing lung cancer at younger ages and with smoking histories below the original 30 pack-year cutoff.

“I am greatly encouraged by the revised USPSTF lung screening criteria released earlier this month. By decreasing the required age to 50 and lowering the smoking history to 20 pack-years, we anticipate the number of individuals eligible for lung screening with low dose CT to double, with a notable increase in eligibility for African American/Black smokers who have been shown to develop lung cancer before reaching eligibility under the old guidelines,” says Dr. Prosper. “The timing of this project — receiving funding to improve screening services at a time when lung screening eligibility is expanding — is ideal.”

The effect of the COVID-19 pandemic

Patients eligible for lung cancer screening have smoking histories and comorbidities that put them at increased risk of infection and of severe complications of COVID-19. In late April of 2020, the Radiological Society of North America COVID-19 Task Force suggested postponing nonurgent outpatient imaging, including lung cancer screening.

One study from the University of Cincinnati found that after screenings at their hospital resumed, the percentage of patients with lung nodules suspicious for malignancy had increased significantly (from 8 percent to 29 percent), and referrals for intervention by thoracic surgery or interventional pulmonology among tumor board patients had also notably increased (from 21.2 percent to 44 percent).

Of particular concern is the role that COVID-19 could play in exacerbating existing inequities in lung cancer screening. “It is entirely possible that the COVID-19 pandemic could make disparities in screening worse, given underserved communities have clearly been hit harder in many ways by this pandemic. Proactive strategies are needed to address the possible worsening of health care disparities in cancer screening,” explains Dr. Milch.

The disruption of lung cancer screening caused by COVID-19 may further hamper efforts to improve compliance with screening guidelines as health advocates struggle to increase utilization of a screening exam that is underrecognized by those whom it could benefit most.

Image-based screening

Image-based screening plays an increasingly important role in preventive care and early detection medicine, having grown immensely over the past 50 years; it is the recommended screening for many major diseases, including both breast and lung cancer. NLST provided the first evidence of a significant lung cancer mortality benefit from LDCT in older moderate smokers. Beyond lung cancer early detection, LDCT provides a critical window into disease detection and risk stratification for cardiovascular and pulmonary diseases.

Funds for the new study come from a \$200 million settlement paid by Wyeth Inc. to resolve claims that it misled women about the cancer risks associated with its hormone replacement therapy products. UCLA is one of six institutions in California to share in settlement money donated to medical research after the plaintiff group and lawyers had claimed their shares. 

COVID's Effect on Screening Mammography and Breast Cancer Detection

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In April of 2020, the Centers for Disease Control and Prevention (CDC) and the Centers for Medicare and Medicaid Services both published guidelines recommending that non-urgent procedures, including routine cancer screening, be postponed to prevent healthy patients from being exposed to the SARS-CoV-2 virus at medical facilities. UCLA Health halted almost all screening mammography for about six weeks in the Spring of 2020, as did a majority of other health centers across the country.

UCLA's suspension of mammography applied only to screening mammograms, not to diagnostic mammograms. "It's important to note that we never told symptomatic women not to come to the doctor when they had a concern. We did, however, triage these exams and help patients and providers decide when it may be safe to postpone coming in," states Hannah Milch, MD, assistant clinical professor of radiology.

"At UCLA, we typically perform about 150 screening mammograms a day," continues Dr. Milch. "It's a really big part of what we do in breast radiology." She points out that because of the COVID-19 pandemic, "millions of women across the country and thousands of women at UCLA were not getting this important breast cancer screening test that has been shown to save lives."

The pandemic's effect on women's breast health is likely to extend well beyond the delay caused by the disruption to screening mammography services. Some women cancelled or failed to schedule screening appointments due to their reluctance to visit health care facilities during the pandemic. Other factors affecting breast cancer screening include loss of jobs and health care benefits, childcare issues and the economic and psychological effects of the pandemic, all of which may linger for some individuals long after the public health crisis has abated.

Not surprisingly, new breast cancer diagnoses were down amid the pandemic-driven decrease in screening mammography. At UCLA, a 29 percent decrease in all newly diagnosed breast cancers and a 58 percent decrease in screen-detected breast cancers were observed from March to August 2020 compared to the same time period in 2019 (see table below). Early-detection

	2019		2020		P Value
	Count	Percent of Total	Count	Percent of Total	
Total Malignancies	218	—	155	—	0.018*
Screen-detected Malignancies	125	57.34%	53	34.19%	0.001*
Diagnostic-detected Malignancies	93	42.66%	102	65.81%	0.496

*Significant p-values (p<0.05)


Number of total malignancies, screen-detected malignancies, and diagnostic-detected malignancies diagnosed from 3/15/2019-8/15/2019 and 3/15/2020-8/15/2020. Screen-detected malignancies were diagnosed as a result of a finding on a screening mammogram. Diagnostic-detected malignancies were diagnosed as a result of clinical concern (e.g. breast lump). *Authors: Claire Lis, MD; Lucy Chow, MD; Hannah Milch, MD; Stephanie Lee-Felker, MD; Anne Hoyt, MD*

orthodoxy suggests that this decrease in new diagnoses would lead to higher breast cancer mortality down the road. One published study suggests a potential increase of 33,890 deaths in the U.S. from all cancers due to COVID-19's effect on cancer care.

But the actual effect of delayed or cancelled breast cancer screenings remains unknown. Mammography screening guidelines have evolved over time, but determining optimal utilization is inherently problematic given the tradeoffs between the benefits of early detection and the costs of unnecessary testing and medical care — costs that include the increased anxiety and sometimes morbidity that patients are subject to in addition to the financial costs.

The COVID-19 pandemic may present an opportunity to learn more about the costs and benefits of screening mammography. It is the type of natural experiment that can be especially valuable to researchers in areas where manipulating care for purposes of experimentation would be ethically untenable.

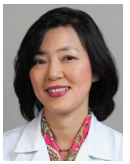
"We are going to be looking at the size and stage of breast cancers detected after COVID — are they bigger because women waited longer between screenings," explains Dr. Milch. Even if that proves to be the case, Dr. Milch points out that the delay in detection may not affect outcomes for most women. "The treatment for breast cancer is so good now that with the exception of some highly aggressive subtypes, the difference in treating a one-centimeter tumor and a two-centimeter tumor may not justify such frequent screening for all eligible women. A more risk-stratified approach to screening mammography is already an active area of research."

Dr. Milch stresses that more study is needed both to understand the long-term consequences of reduced breast cancer screening during the COVID-19 pandemic and to determine if this can inform screening mammography guidelines. Nationwide breast cancer outcomes during the pandemic are currently under investigation by the Breast Cancer Surveillance Consortium. "While more study is needed to determine the impact of these delayed and missed screenings, the COVID pandemic may ultimately provide insights that have important implications for future routine breast care and cancer screening," explains Dr. Milch. 

COVID's Role in Neurological Disease Remains Uncertain

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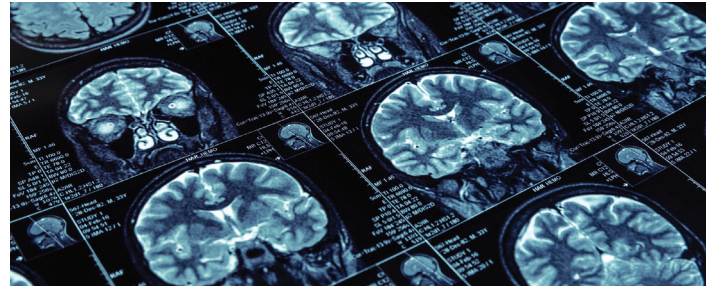
While the SARS-CoV-2 virus is known to primarily attack the lungs, there have been many reports of neurological manifestations, including encephalitis due to infection and occlusive and hemorrhagic stroke. Neurological complications of COVID-19 appear to correlate with the severity of the underlying COVID infection, with even younger patients suffering severe cases that produce neurological symptoms.

Published accounts from the Spring 2020 surge of COVID patients in New York suggested that in addition to neurological symptoms of headache, dizziness, myalgia, seizures, weakness and alterations of consciousness, COVID patients were suffering ischemic stroke (0.4 to 2.7 percent), intracranial hemorrhage (0.2 to 0.9 percent) and encephalopathy (0.04 to 0.2 percent) at higher rates than other patients.

Noriko Salamon, MD, PhD, professor of radiology and neuroradiology at the David Geffen School of Medicine at UCLA cautions, "I don't think we have enough evidence yet to reach conclusions about COVID's role in neurological conditions seen in some patients." She points out that severely ill COVID patients are often both immunocompromised and hypoxic. The presumed complications and sequelae of COVID may be less dependent on direct action of the SARS-CoV-2 virus and more a consequence of the poor health status of severely ill COVID patients. "Nothing can be identified at this point as typical about neurological disease in COVID patients," states Dr. Salamon. "COVID patients may exhibit some neurological symptoms because of the hypoxic environment created by COVID's well-documented effect on pulmonary function."


While pointing out that many of the most seriously ill patients cannot undergo imaging for their neurological symptoms because their hypoxia is not adequately managed, Dr. Salamon says that the majority of COVID patients seen at UCLA who display neurological symptoms indicative of stroke are in fact negative for stroke on MRI. "Probably less than 30 percent of these patients have abnormal brain scans," she says. "The majority of these cases have an unremarkable MRI, and the things that we do see on MRI are often likely to be conditions that predate the patient's COVID infection." Dr. Salamon adds that neurological symptoms in ICU patients where MRI fails to reveal abnormalities in the brain are not atypical for patients who are very ill with non-COVID conditions.

Despite her caution in attributing neurological conditions directly to COVID, Dr. Salamon points to recent UCLA research published in the journal *Stroke* that supports the idea that endothelial cells lining blood vessels in the brain are susceptible to the SARS-CoV-2 virus. Using vascular imaging — including cell wall molecular analysis, the team of researchers determined that in COVID patients, expression of the ACE2 (angiotensin-converting enzyme 2) receptor increased with vessel size and flow rate. If this is related to viral preferential attachment to vessel walls, it could help account for the atypical areas of vessel occlusion noted in some COVID patients.



While typical locations for atherosclerosis are bifurcation points where turbulent blood flow is associated with stenosis, vessel occlusion in COVID patients is often seen in more distal, high-flow areas.

As for COVID patients diagnosed with encephalitis due to neurological infection, Dr. Salamon warns against assuming that the SARS-CoV-2 virus is the infecting agent. COVID patients are immunosuppressed and are susceptible to any number of viral, bacterial and fungal infections. "While it is difficult to say that COVID is the direct cause of a neurological infection, it's very easy to say that COVID creates a state of immunosuppression that can lead to these infections," explains Dr. Salamon. In her experience, imaging studies of COVID patients who have neurological infections show the same distribution of the infection as do imaging studies for other viral diseases, such as Japanese encephalitis, West Nile virus, Epstein-Barr and herpes encephalitis. Dr. Salamon states, "The overlapping veno-occlusive, hypercoagulable status of COVID patients gives infection a good environment in which to thrive."

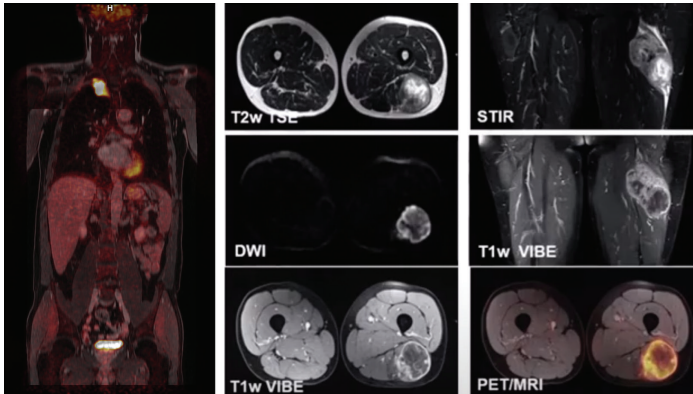
Starting with the first reports of COVID's neurological manifestations that came out of the early surge in New York, Dr. Salamon and her colleagues at UCLA have been especially vigilant for neurological disease among the COVID patients that they evaluate. "Early experience with COVID patients and preliminary analysis led to a popular notion that COVID causes stroke in young people and COVID causes infections — as if COVID is a bug that can initiate certain types of infections or certain types of stroke," explains Dr. Salamon. "I don't have this impression from seeing COVID patients at UCLA." She feels that there isn't currently sufficient evidence to conclude that the SARS-CoV-2 virus causes either infection or cerebrovascular disease directly. But because COVID causes some patients to become devastatingly ill, it can create an environment in which neurological disease can flourish. Neuroradiologists will continue to play an important role in helping to care for these seriously ill patients and are often crucial to their management and recovery from SARS-CoV-2 infection. 

Recognizing the Advantages of PET/MR

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The first PET/MR scanner is expected to be installed at UCLA in late May or early June of 2021. There are only around 250 dedicated PET/MR systems operational worldwide, with around 50 located in the US (compared to over 2,000 sites using PET and PET/CT systems in the US). PET/MR is a hybrid imaging device that is still mostly limited to large academic centers.



Courtesy Prof. Ken Herrmann (Essen, Germany)

Whole-body coronal 18F-FDG PET/MR in a patient with NSCLC (left). Regional multiparametric MR sequences and fused 18F-FDG PET/MR in a patient with soft tissue sarcoma of the left upper leg (right).

Similar to PET/CT, PET/MR images mostly encompass the whole body from head to mid-thigh or foot. Unlike the sequential acquisition of a PET/CT scanner, MR and PET images are acquired simultaneously in the Siemens Biograph mMR.

Standard whole body MR sequences for anatomic correlation can be complemented with dedicated regional MR protocols benefiting from the improved MR soft tissue contrast, the information gathered from multiparametric MR sequences, or for example, the use of hepatobiliary contrast agents. Simultaneously, molecular PET information is acquired using radiotracers such as the pan-cancer tracer 18F-FDG for detection of increased glucose metabolism, 68Ga-DOTA-TOC for imaging of somatostatin receptor positive neuroendocrine tumors, or the newly FDA approved radiotracer 68Ga-PSMA-11, which has become a game changer for patients with prostate cancer.


According to a survey of 39 international sites, clinical PET/MR operation had a strong focus on oncology (88 percent), neurology (9 percent), and cardiology (3 percent).

Within oncologic applications, PET/MR can be used as a pan-cancer imaging device similar to PET/CT. However, the costs, workflow considerations and the strengths and limitations of PET/MR do not suggest using it as a replacement for PET/CT. Rather it should be used to specifically improve clinical care and diagnosis in selected patients, such as those with head and neck cancer, prostate cancer, and brain tumors.

Obvious strengths of PET/MR include the improved soft tissue contrast derived from MR images and the information gained from diffusion weighted and dynamic contrast enhanced imaging. Moreover, the improved convenience for patients scheduled for

both imaging procedures creates value. Radiation dose, although a topic of controversy, is significantly lower using PET/MR in comparison to PET/CT. This has particularly been studied in pediatric cancer patients. This advantage is offset by the more frequent requirement of sedation for adult and pediatric PET/MR studies. Less obvious strengths of PET/MR are an improved PET count statistic since the PET acquisition can be prolonged for the time of the MR acquisition per bed position, and better motion correction in comparison to PET/CT.

PET/MR operations address clinical problems and research questions (47 percent and 45 percent, respectively). Potential research applications are limitless and explore topics as diverse as prognostic and predictive biomarkers derived from PET and multiparametric MR that have great potential to improve assessments of treatment response and outcome predictions.

PET/MRI operation is a team effort. Protocols are still in development and indications are evolving. The partnership between radiology and nuclear medicine at UCLA is an excellent starting point to establish PET/MR as a highly relevant imaging modality at UCLA. 

UCLA SMART Health Looking to Data and Technology for Transformative Change

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The UCLA Center for Systematic, Measurable, Actionable, Resilient, and Technology-driven (SMART) Health is a campus-wide collaborative that looks to the integrated transformation of health care through emergent data and technologies. Led by Alex Bui, PhD, the center brings together diverse UCLA experts to shape how digital and data-driven health care technologies will help to manage risk, reliability, resilience, uncertainty and precision in future biomedical research and clinical care.

The goals of the center are to enable team science around digital health care technologies, support interdisciplinary education and training, and catalyze partnerships with industry and NGOs. smarthealth.ucla.edu/

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UCLA Health's hospitals in Westwood and Santa Monica placed #1 in California and #4 in the nation in the 2020-2021 U.S. News & World Report survey.

Our locations

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