

Artificial Intelligence and Imaging in Melanoma Care: An Update

Research is confirming that artificial intelligence and machine learning algorithms may revolutionize the speed of melanoma diagnosis.

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An early melanoma diagnosis is more likely to have a positive outcome than one diagnosed later. That's a fact, but patients often delay having skin lesions checked for a variety of reasons, including long wait times to see a dermatologist—if they can even find one close by. In many cases, a primary care doctor is the first clinician to evaluate a skin lesion and make a melanoma diagnosis—a task that even experienced clinicians find challenging. But help is on the way. Research is confirming that artificial intelligence (AI) and machine learning algorithms can detect melanoma with remarkable accuracy and may revolutionize the speed of diagnosis. New imaging technologies are also being studied that can help inform and guide diagnosis and treatment decisions. A session at MRA's 2023 Scientific Retreat, led by Dr. Maria Wei, of the University of California San Francisco, focused on the potential of both technologies to improve outcomes for patients as well as workloads for physicians.

Artificial Intelligence Can Boost Screening Accuracy

Disparities in melanoma care and outcomes exist, and are associated with race, place of residence, provider type, as well as insurance status. New and faster methods of melanoma detection can be especially helpful for groups of patients who have difficulty accessing care, said Dr. Wei. Problems getting to healthcare providers and insurance status can determine where and when a person seeks care. Rural areas have fewer dermatologists than urban areas, so primary care providers are often the most likely clinicians to first evaluate a skin lesion in rural communities, said Dr. Wei. Providers in rural areas also perform more skin biopsies than those in urban areas and could benefit from additional diagnostic tools, she said.

To address some of the barriers to access, the American Academy of Dermatology now recommends the expanded use of teledermatology. "This is really quite a change from before the [COVID-19] pandemic when teledermatology was not widely used," said Dr. Wei. "Since the pandemic, teledermatology has not just been accepted, but embraced." Patients are now having video visits and sending images to their primary care physicians. Dr. Wei and her team are looking at how teledermatology can be combined with AI to detect melanoma at the earliest possible stage in collaboration with Veteran's Administration (VA) hospitals around the country, who often

treat a diverse patient population.

Dr. Albert Chiou of Stanford University agreed that teledermatology has helped patients get expert opinions about lesions, but added that it often can place additional burden on limited healthcare resources. For example, for the first time at his institution, the number of virtual encounters with patients submitting photos in the past year equaled the volume of traditional in-person visits. Dr. Chiou and his team are working to develop an AI-assisted triage tool to help with diagnosis of melanoma.

The team is also working to overcome biases that have emerged with existing AI models that may make these systems less robust in detecting melanoma in realistic clinical scenarios, particularly among skin of color. Overcoming these biases is very important if AI algorithms are to improve—and not exacerbate—existing health disparities among racial and ethnic minorities as it relates to melanoma early detection.

Dr. Chiou's analysis showed that including diverse data sets, including images of melanoma among diverse skin tones and less common forms of melanoma, can improve the diagnostic performance of these algorithms. His team has also collected data from 811 patients who provided photos of skin lesions. Using these data and elements from a previous AI algorithm, the team developed a new classifier algorithm for melanoma lesions. To further train the classifier, they added more than 20,000 additional images from previous patients. They are currently evaluating the performance of their classifier, which they named the MRA-Stanford-Cleveland Clinic (MRA-SC) dataset, using benchmark datasets to assess its ability to identify malignant tumors and malignant melanocytic lesions. The team will use the algorithm to assess its potential to help triage lesions in the primary care setting.

New Imaging Technologies May Help with Diagnosing Melanoma and Predicting Responses to Immunotherapy

Dr. Jesse Wilson of Colorado State University, an engineer, is studying laser-based imaging techniques that do not require a biopsy to help diagnose melanoma. He described his team's efforts to see whether a software plugin with existing clinical instrumentation could generate images that look like conventional biopsy sections. He also discussed the use of "image2image neural networks," which are machine learning techniques used to help clinicians visualize and identify melanoma-specific features in dermoscopy photographs. This tool may help researchers understand how artifacts in current datasets confuse neural networks. It may also lead to the generation of more accurate melanoma datasets that can then be used to develop better computer vision algorithms, in addition to direct clinical applications. "We would like to see if this could be a useful tool for primary care settings for a physician to prioritize referrals to a specialist, and to help inform their decision to biopsy," said Dr. Wilson. He plans to submit a grant application to the National Institutes of Health in June to continue this work.

Once a physician has accurately diagnosed melanoma, the next challenge is determining whether a recommended treatment will work for the patient. "Immunotherapy is expensive, so it will be

helpful to identify patients who will actually respond,” said Dr. Pratip Bhattacharya, of the MD Anderson Cancer Center. Dr. Bhattacharya, a physicist, said that his team is developing an imaging tool to predict responses to immunotherapy by actually viewing metabolic processes as they unfold in live tissue. “We are essentially trying to do real-time imaging of immunotherapy resistance,” he said.

Solving the mystery of resistance began with an idea that the build-up of acid in the space surrounding cells in the tumor microenvironment was one of the key causes of resistance. The team then looked at options for imaging that microenvironment. They found that “hyperpolarized” (HP) magnetic resonance spectroscopy could provide a 10,000-fold better imaging signal than conventional magnetic resonance imaging (MRIs). “The downside is that there is a very small window of time, a couple of minutes, to get real-time metabolic imaging,” said Dr. Bhattacharya. The challenge now is to see whether the team can use what they see to develop a biomarker for immunotherapy resistance. They are also studying a melanoma mouse model to determine whether changing the pH sensitivity in the tumor microenvironment before and after starting immunotherapy, could improve responses to checkpoint immunotherapy in melanomas expected to be treatment resistant.

Dr. Michael Postow of the Memorial Sloan Kettering Cancer Center is also studying immune responses to therapy by exploring PET (positron emission tomography) imaging of CD8+ T cells (cytotoxic T lymphocytes), white blood cells that can recognize and destroy cancer cells. The number of CD8+ T cells in the tumor microenvironment has been shown to correlate with treatment outcomes. But obtaining biopsies to count CD8+ T cells is not easy, and it usually does not reflect the entirety of the tumor, said Dr. Postow. To overcome this challenge, his team is using PET scanning with a radioisotope (called a radioisotope PET tracer) that can detect CD8+ T cells. The researchers are also using another imaging technique called autoradiography which is used to measure the presence of radioactivity in different tissues. In these studies, autoradiography on tumor tissue that has been removed from patients after receiving the radioisotope PET tracer is being used to confirm that the tracer is in the tumor microenvironment and is associated with CD8+ T cells.

A phase 2 clinical trial is underway to see whether CD8+ T cell PET imaging will correlate with major pathologic responses (defined as a tumor that completely disappears or reduces to less than 10% of the original tumor size) after one dose of neoadjuvant therapy (nivolumab + ipilimumab delivered before surgery) in patients with resectable stage 3 and 4 melanoma.

Dr. Postow presented very early results from five of the seven patients accrued in the study so far. One dose of the neoadjuvant therapy appeared to result in some type of pathologic response with low toxicity in several of the patients. The researchers were able to visualize melanoma tumors using CD8+ T cell PET imaging and confirmed that the radioactive PET tracer was in the resected tumors using autoradiography. “The long-term goal is to see whether this approach can inform mechanisms of response and resistance of new immunotherapies in development,” said Dr. Postow. This novel imaging technique can potentially be used as an on-treatment biomarker which can help guide treatment decision making and determine pathologic response to treatment.

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