FRI in critical care: challenges and opportunities

Functional Respiratory Imaging (FRI) did not have a place in critical care before the COVID-19 pandemic, but as healthcare systems were overloaded with an unprecedented number of patients, new technologies and solutions became more desirable. Dr. Daniel Salerno, a pulmonologist specialized in critical care at Temple University, highlights that as new FRI data become available, this technology could play a more significant role in critical care of respiratory patients, both with COVID-19 infections and beyond.

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Though most patients with COVID-19 exhibit mild symptoms, approximately 5% become critically ill and need intensive care treatment [1]. At the peak of the pandemic, hospitals across the globe were overwhelmed, with ICUs swamped by the influx of patients, requiring critical care management to accommodate the surge rapidly and dramatically. Among the ICU-admitted patients, 50–85% of them developed hypoxemia or respiratory exhaustion [2]. Timely and effective respiratory support strategies and effective patient care were therefore paramount. Functional Respiratory Imaging (FRI) has emerged as a unique computational workflow in which functional data complement respiratory images [3]. Among other novel tools, FRI holds the potential to provide new insights in critical care settings [4].

IMPACT OF THE PANDEMIC ON CRITICAL CARE

At the beginning of 2020, when the number of COVID-19 cases started to increase, pulmonary centers like the one in Temple University Hospital started to prepare for the worst. They implemented logistic adjustments, such as making more ICU beds available to ensure they could take care of the number of

patients who were going to arrive. Clinical researchers also shifted their interests, with some taking a new direction to study the phenotypes associated with this new disease and its complications. Regarding CT scans, Salerno says, "Our center is unique because we did an initial CT scan for all of our patients with COVID-19, whereas many other places in the USA or other parts of the world didn't take this approach. It allowed us to access a lot of data for our COVID-19 admissions." This policy also resulted in a large data resource for future retrospective studies.

Notably, even while managing the hefty COVID-19 volumes in Philadelphia, Temple's medical team has achieved survival rates better than the national and regional averages. The death rate for patients with COVID at Temple was 15% lower than other hospitals in Pennsylvania and 28% lower than the national average [6].

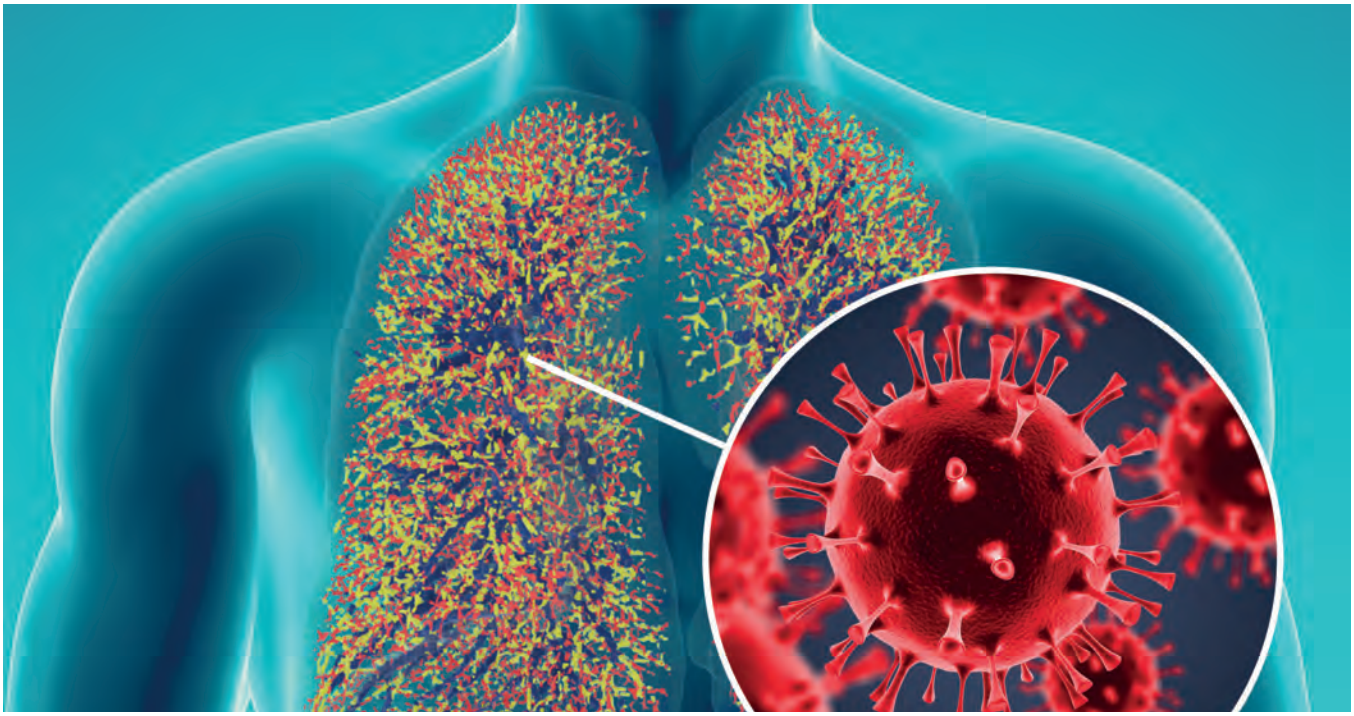
USING FRI TO ASSESS LUNG ABNORMALITIES AFTER COVID-19

Having access to this data resource has allowed Salerno and colleagues to perform retrospective studies. One such study hypothesized that CT scan parameters from the time of infection could predict abnormal lung function after COVID-19 infection [7]. The team used FRI to analyze the volume of pulmonary blood vessels in patients with COVID-19 who were hospitalized due to COVID-19-related pneumonia.

The study found that patients who had pulmonary vascular abnormalities at the time of hospitalization with COVID-19, especially in the medium and large vessels, were at higher risk of having abnormally low diffusion capacity of carbon monoxide (DLCO, a measure of lung function) even three months after discharge. "Using technologies like FRI allows you to see more than what radiologists could see and to have a quantitative approach, which allows you to do more objective determinations," says Salerno.

Recent studies from Salerno and others aim to identify the long-term effects of COVID-19 (called *long COVID*), which is the manifestation of symptoms that continue for weeks to months beyond the initial illness [8]. Salerno shared the relevance of FRI, "We can and should use FRI and other imaging approaches to do new studies regarding the chronic and long-term effects of COVID-19, especially given the amount of data that we gathered during the pandemic. There is a group in the United Kingdom that is also using imaging approaches to gather more information about people who have had COVID-19, and what they argue is that there are many parameters that can guide treatment and that are difficult or impossible to see with a plain image, but it becomes apparent when you use more sophisticated technologies. This could eventually help in discovering treatments. I think this shows the potential of the field, creating ample opportunities to execute novel research."

According to Salerno, the application of FRI is not limited to COVID-19 infections: it can also inform the treatment of other lung diseases, for example, in acute respiratory distress syndrome (ARDS). ARDS is a life-threatening ailment where the lungs are unable to provide enough oxygen to the body's vital organs [9]. "In ARDS, there are issues with blood perfusion that are difficult to evaluate in a regular CT scan. Analyses like FRI could help explain why oxygenation is more difficult in some of the individuals with ARDS."



TECHNICAL CHALLENGES OF USING FUNCTIONAL RESPIRATORY IMAGING IN CRITICAL CARE

Prior to the COVID-19 pandemic, FRI had never been used to manage critically ill patients; even now, its application to this area of medicine has only been in retrospective studies. This might be partly because many procedures that are routine in other settings are not frequently performed in critical care patients due to technical or logistic challenges. Transporting critically ill patients out of ICU alone could increase the risk of adverse events [5]. "If you want to move a patient who is in the ICU, cables can come out, mechanical ventilation settings can be changed, and that can have dramatic consequences," says Salerno. "Therefore, experienced clinicians tend to be reluctant to order CT scans to critically ill patients, unless they have a clear idea of how the information gathered from that intervention will change patient management."

The FRI technique starts with two CT scans, the first taken after deep inspiration and the second taken after normal expiration. Salerno explains, "If you have a patient who is not moving, things like holding a breath are much more difficult than what you would encounter in the non-critical care or outpatient care settings."

Salerno adds, "We are yet to employ FRI in critical care; however, this doesn't mean that there is no place for FRI in critical care. I work in a large pulmonary center with advanced critical care units with extensive lung-transplant populations that require this sophisticated tool." Salerno further illuminates the potential of FRI, "There are still cases where we could take CT scans of critically ill patients and then have additional information: the FRI analysis can be useful." He expects that as more FRI data become available, the technology will play a bigger role in critical care.

THE FUTURE OF FRI IN CRITICAL CARE

The COVID-19 pandemic has brought big changes to healthcare systems. Critical care management in particular went through some adjustments, explains Salerno. "The pandemic has changed our approach to critical care. We are taking a more aggressive approach in doing interventions on our patients now than we were doing before COVID-19." This opens the door for technologies like FRI to play a more prominent role in guiding the management of critical care patients with lung diseases. More data are needed that could better inform management and ease clinical decision-making.

Salerno describes a possible scenario, "Let us assume that we know that ARDS patients can present different phenotypes based on blood markers, categorized as hyper- or hypo-inflammatory in nature. The recommended therapeutic interventions for each state might be different. If clinicians could use FRI to recognize the different phenotypes, one can argue patients with ARDS in the ICU would need a CT scan. This is the same that we did with patients with COVID-19." In this case, the benefits of performing the scan would outweigh the risks of taking the patient out of the ICU.

Weighing the prospects of FRI in the critical care setting, Salerno concludes, "In the end, it will depend on how much research we do and how much we can prove that doing this type of image analysis can impact what we find in patients and how we treat them. If new parameters become available, it makes sense to think that FRI might become a routine procedure in critical care for pulmonary patients."

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