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EDITORIAL

To everything there is a season: taxonomy of approaches to the performance of lung scintigraphy in the era of COVID-19

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The world has been profoundly affected by the COVID-19 pandemic; stability is the exception rather than the rule. This is certainly true with respect to provision of medical care. In order to minimize exposure of others to possibly infectious material, procedures with potential to spread patient secretions were limited or proscribed in individuals with suspected or proven COVID-19 infection [1]. In the nuclear medicine arena, ventilation scintigraphy was identified as an "at-risk" procedure [2, 3] due to the potential of secretions to contaminate the exam room atmosphere [4–9].

It is striking to note the number and variety of strategies proposed in the nuclear medicine literature for evaluating pulmonary embolism during the COVID-19 pandemic, indicating determination on the part of nuclear medicine physicians to remain clinically relevant without compromising the safety of staff and patients. It is fascinating to note how many authors coopted preexisting lung scan strategies that had been previously proposed and generally sidelined in the past [10–15], adopting them as novel solutions to the unusual COVID-19 situation (Table 1). A likely contribution to the wide variety of different approaches is the variation in clinical situations prevalent when and where each method was proposed. As the viral infection waxed and waned across geographical regions, as stocks of supplies were periodically diminished and replenished, and as knowledge was accumulated and refined, it not surprising that the assumptions that inform these different methods would vary, resulting in a spectrum of different responses. Decisions taken to protect patients and staff at a particular locus in time and space were made to the best of each practitioner's ability, appropriate to that milieu but not necessarily applicable to other places or times under different prevailing conditions. Personally, the experience of working in a hospital in New York City in March and April 2020 was akin to that of working in a battlefield. There was a lack of definitive scientific information regarding the spread and pathogenicity of the virus (not fully resolved to date) [16], there were shortages of personal protective equipment (PPE) [17] and PCR testing materials [18], and the prevalence of virus was astronomical.

Upon review, the range of options proffered in the nuclear medicine literature regarding performance of lung scintigraphy during the COVID-19 surge can be grouped to yield 4 conceptually similar approaches which span the full gamut of response, listed below. Several published opinions straddle more than one approach or lack sufficient detail to allow definitive categorization. We have tried to offer examples which clearly illustrate each strategy; the illustrations furnished are not exhaustive.

Business as usual—perform ventilation and perfusion scintigraphy as usual, but with adequate PPE

There was an initial voice that advocated maintaining standard protocols for pulmonary embolism, with adequate COVID-19 screening of the patients and/or PPE precautions for the staff [19, 20]. One of the points that were raised to support this approach is that the population of patients referred for lung scintigraphy during the COVID-19 pandemic are often those very patients who are unable to undergo computed tomography pulmonary angiography (CTPA) due to allergy or

Dedicated to Dr. Shalom Buchbinder and all the valiant health care professionals who succumbed to COVID-19.

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Table 1 Prior models of scintigraphy for the diagnosis of thromboembolic disease that do not utilize ventilation scintigraphy

Authors	Year	Population	Modality	Comments
Miniati et al. [10, 11]	1996, 2008	General	Perfusion planar	Scan combined with pretest clinical probability
Sostman et al. [12]	2008	General	Perfusion planar	As above
Bajc et al. [14]	2013	General	Perfusion SPECT	As above
Sheen et al. [13]	2018	Pregnancy	Perfusion planar	Perfusion used as an initial screening test
Lu et al. [15]	2014	Oncology	Perfusion SPECT-CT	Concurrent CT used to evaluate airspace disease

azotemia. Appropriateness of this strategy therefore harkens back to the risk benefit calculus considering various factors including the pretest probability of infection, availability of sufficient protections available in the imaging suite (such as PPE and high air flow rooms), risk of anticoagulation, and availability of alternate means of diagnosis. Whether the stratagem of "business as usual" would have been defensible during the intense surge witnessed in our institution in New York is doubtful in my mind. As prevalence of disease decreases, more is understood regarding transmission of virus, and adequate protections are in place, I am confident that we will gravitate towards the lodestar of our well-calibrated pre-pandemic diagnostic protocols.

See you later—we cannot help

In diametric opposition to the prior method is that of "see you later". This method seeks to avoid lung scintigraphy during the high-risk period altogether, and refers patients to other imaging modalities, such as CTPA or Doppler sonography of the legs [21–23]. The assumption underlying this strategy is that ventilation scintigraphy cannot be safely performed, and perfusion scintigraphy without ventilation scintigraphy is insufficiently specific to be of value. The downside is that there are some patients in whom CTPA cannot be performed and alternative tests may be insufficiently sensitive to make the diagnosis of thromboembolic disease. A further concern is economic—referrals spurned may be referrals permanently lost, in spite of hard-earned evidence regarding the intrinsic value of lung scintigraphy vis-à-vis other modalities. In my mind, it is clear that under extreme conditions, where safety cannot be maintained, this strategy would be justifiable but only as an emergency short-term measure and not as an ongoing approach.

Business, but not as usual—perfusion without ventilation

The proponents of this approach believe that when requested, perfusion scintigraphy without ventilation scintigraphy can be performed in such a manner as to be a definitive study. Admittedly, perfusion scintigraphy without corresponding ventilation scintigraphy has a low specificity [24]. In preCOVID times, the approach of performing perfusion scintigraphy coupled with an assessment of pretest probability has been investigated by the PISAPED investigators [10, 11] and others [12, 14]. A major limitation of applying this method to the current situation is that we do not understand the clinical risk factors that lead to thromboembolic disease with the novel COVID-19 disease, that is, we do not have a good yardstick of pretest probability.

Another approach to improving the specificity of perfusion scintigraphy has been to combine it with SPECT-CT imaging. Here, the appearance of the lungs on CT can offer important information regarding underlying lung disease that could otherwise cause nonembolic defects on perfusion scintigraphy [25, 26]. This method is based on prior work by researchers at Memorial Sloan-Kettering Cancer Center in New York City [15] who resurrected this idea as a potential approach to the evaluation of thromboembolic disease during the COVID-19 surge [26]. The pretest probability of disease will factor heavily in the predictive value of a positive examination as the diagnostic procedure still lacks optimal specificity.

Let us see what we get but no promises—perfusion as a screening test

Somewhere between the "See you later" and "Business, not as usual" approaches, is use of stand-alone perfusion scintigraphy as a screening tool. This in fact has been our approach at the Montefiore Medical Center [27], modeled on a similar stratagem in effect at our institution for studying pregnant patients [13], and has been adopted by others as well [28]. In our application of this concept, we first confirm that each patient does not have significant parenchymal densities that would be expected to cause perfusion defects—such patients are referred directly for CTPA or leg Doppler ultrasonography. The assumption of this strategy is that the majority of the remaining patients undergoing perfusion scintigraphy will in fact have no segmental perfusion defects, and only a minority of patients will require

further testing for a definitive diagnosis. Further testing can consist of CTPA, Doppler ultrasound of the legs, or even completion ventilation-perfusion scanning when needed; indeed, one can perform the initial screening perfusion study with a relatively low level of activity, to allow immediate performance of a ventilation study if required with a larger dosage of inhaled radiopharmaceutical. This method would also be of value in a clinical setting with constrained resources; use of perfusion scintigraphy could reduce the referral load on CTPA many-fold. It also avoids administration of intravenous contrast to patients with COVID-19 where renal impairment can be an issue [29]. We have retrospectively reviewed behavior of our COVID-19 algorithm over 60 days of the surge and confirmed that in 80% of both COVID-19 infected and noninfected patients, no segmental defects were identified. An interesting variation of this concept was suggested by Lu and Macapinlac [30] who initially performed a perfusion-only planar screening examination. If segmental planar defects were in fact demonstrated, SPECT-CT imaging was performed, effectively transitioning into the Memorial Sloan-Kettering method of diagnosis described earlier [26].

In summary, a number of different responses have been proposed regarding performing lung scintigraphy for the evaluation of thromboembolic disease during the COVID-19 pandemic, and these can be conceptually organized into 4 groups. Some of the responses hold up best as temporary measures, meant to bridge a transient situation, while others seem compatible with a longer-term response. It is likely that at least some of the variation amongst published methods is due to disparity in the particular clinical and environmental circumstances extant at the time of their adoption. As such, these approaches should be periodically reviewed and revised based on changes in situational factors. The survey of approaches we have enumerated above will be of help in clarifying available stratagems. A final aspect which cannot be evaluated by the literature published to date is how these approaches will mesh with patient flow algorithms which are directed by the clinicians, that is whether the clinical team will be on the same page as the nuclear medicine physicians, or whether a well-reasoned protocol which seeks to minimize performing the ventilation examination by the nuclear medicine physicians will simply be regarded as inability or refusal to provide the service, with resultant short and long term consequences. It certainly seems appropriate to make all protocol changes in consultation with the clinical stakeholders.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Informed consent Not applicable.

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