American College of Radiology ACR Appropriateness Criteria® Diffuse Lung Disease

Variant: 1 Suspected diffuse lung disease. Initial Imaging.

Procedure	Appropriateness Category	Relative Radiation Level
Radiography chest	Usually Appropriate	€
CT chest without IV contrast	Usually Appropriate	⊗ ⊗
CT chest with IV contrast	May Be Appropriate	⊗ ⊗
MRI chest without and with IV contrast	Usually Not Appropriate	0
MRI chest without IV contrast	Usually Not Appropriate	0
CT chest without and with IV contrast	Usually Not Appropriate	⊗ ⊗
FDG-PET/CT skull base to mid-thigh	Usually Not Appropriate	***

<u>Variant: 2</u> Confirmed diffuse lung disease. Suspected acute exacerbation or acute deterioration. Initial Imaging.

Procedure	Appropriateness Category	Relative Radiation Level
Radiography chest	Usually Appropriate	€
CT chest without IV contrast	Usually Appropriate	∵
CT chest with IV contrast	May Be Appropriate	∵
MRI chest without and with IV contrast	Usually Not Appropriate	0
MRI chest without IV contrast	Usually Not Appropriate	0
CT chest without and with IV contrast	Usually Not Appropriate	∵ ∵
FDG-PET/CT skull base to mid-thigh	Usually Not Appropriate	⊗⊗⊗

<u>Variant: 3</u> Confirmed diffuse lung disease without acute clinical deterioration. Routine follow-up imaging clinically indicated.

Procedure	Appropriateness Category	Relative Radiation Level
CT chest without IV contrast	Usually Appropriate	���
Radiography chest	May Be Appropriate (Disagreement)	€
CT chest with IV contrast	May Be Appropriate	���
MRI chest without and with IV contrast	Usually Not Appropriate	0
MRI chest without IV contrast	Usually Not Appropriate	0
CT chest without and with IV contrast	Usually Not Appropriate	€€
FDG-PET/CT skull base to mid-thigh	Usually Not Appropriate	⊗⊗⊗

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Summary of Literature Review

Introduction/Background

Diffuse lung diseases (DLD) may also be referred to as diffuse parenchymal lung diseases or interstitial lung diseases. These terms represent a diverse array of disorders affecting the lung parenchyma that are grouped together due to similar clinical, radiographic, or pathologic mechanisms [1,2]. The term "interstitial" is misleading in many cases as a majority of these pathologies demonstrate involvement of the alveola, airways, or both, in addition to the pulmonary interstitium. The potential causes of DLD are broad and include multiple idiopathic diseases, connective tissue diseases, vasculitides, granulomatous diseases, inhalational exposures, genetic conditions, and drug reactions with several hundred established clinical syndromes and pathologies currently identified [1,2]. Imaging of these diseases can be complicated by overlap of imaging patterns with other disease processes, such as infection or malignancy, which are outside the scope of this discussion. See the ACR Appropriateness Criteria® topics on "Acute Respiratory Illness in Immunocompetent Patients" [3], "Acute Respiratory Illness in Immunocompromised Patients" [4], and "Noninvasive Clinical Staging of Primary Lung Cancer" [5] for further imaging guidance.

Clinical suspicion of DLD is frequently seen in patients with chronic dyspnea (see the ACR Appropriateness Criteria® topic on "Chronic Dyspnea-Noncardiovascular Origin" [6]), nonproductive cough, established inhalational exposures (see the ACR Appropriateness Criteria® topic on "Occupational Lung Diseases" [7]), or a diagnosis of another systemic disease that is known to be associated with lung involvement, such as connective tissue disease or vasculitis. Treatment and prognosis of DLD is highly varied and depends greatly on the underlying cause of lung injury as well as any associated conditions. Imaging and other biomarker testing play a critical role in diagnosis and follow-up of many of these diseases, although multidisciplinary discussion involving pulmonologists, radiologists, pathologists, and other clinical specialists is the current standard for diagnosis of several DLDs [2,8-10].

Some of the DLDs, such as idiopathic pulmonary fibrosis, demonstrate episodes of acute exacerbation or acute deterioration as a result of the intrinsic DLD itself. These episodes typically manifest with a 1 to 2 month prodrome of worsening dyspnea or cough and progressive lung disease [11-16]. The development of acute exacerbations is not rare and has significant impact on mortality [17]. Clinically, these episodes frequently overlap with other causes of respiratory illness, such as infection, pulmonary embolism, heart failure, or malignancy. These other causes of acute clinical decline are outside the scope of this work and are best addressed in other ACR Appropriateness Criteria documents.

Special Imaging Considerations

CT imaging for DLDs requires special consideration. CT protocols should be tailored to meet individual needs based on the clinically suspected DLDs. Specifically, utilizing a high-resolution CT (HRCT) protocol (see the <u>ACR-STR Practice Parameter for the Performance of High-Resolution Computed Tomography (HRCT) of the Lungs in Adults [18])</u> that uses thin-section images of the lung parenchyma is essential, and adjunct sequences including expiratory images and prone images are frequently of benefit in evaluating these conditions [19-22]. Additionally, volumetric CT data acquisition can facilitate multiplanar thin-section reconstructions, which aids evaluation of DLD distribution [23-26]. In this document, statements regarding the appropriateness of

noncontrast CT include the use of such HRCT sequences based on the suspected diffuse lung disease and clinical questions.

Initial Imaging Definition

Initial imaging is defined as imaging at the beginning of the care episode for the medical condition defined by the variant. More than one procedure can be considered usually appropriate in the initial imaging evaluation when:

• There are procedures that are equivalent alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care)

OR

• There are complementary procedures (ie, more than one procedure is ordered as a set or simultaneously wherein each procedure provides unique clinical information to effectively manage the patient's care).

Discussion of Procedures by Variant

Variant 1: Suspected diffuse lung disease. Initial Imaging.

Variant 1: Suspected diffuse lung disease. Initial Imaging. A. CT Chest

CT findings and patterns in DLD are often sufficient to permit either a limited differential or confident single diagnosis and play a role in multiple clinical diagnosis algorithms [9,10,27]. Imaging pattern characterization on HRCT is especially important in the diagnosis of usual interstitial pneumonia [9,27-31]. Incorporation of HRCT interpretation into multidisciplinary discussions of DLD result in improved diagnostic accuracy and confidence [2,10,32-37]. In cases in which tissue confirmation is required, the location of imaging abnormalities on CT may help guide appropriate biopsy sites [9,27]. Numerous studies support the increased sensitivity and specificity of CT over chest radiography for lung parenchymal changes related to DLD [38-51]. Adequate correlation has been reported between CT disease extent and severity of symptoms and physiologic testing for several DLDs [44,52-57]. The presence and extent of HRCT imaging features of DLD may also serve as important prognostic variables [58-76]. Multiple quantitative imaging techniques evaluating diagnosis and prognosis are based on CT imaging [68,77-83]. There is no relevant literature to support the use of CT with intravenous (IV) contrast for initial imaging of DLD; however, IV contrast may be of use in evaluation of alternative diagnoses with overlapping clinical features or conditions that also involve the pleura, mediastinum, and pulmonary vessels (see the ACR Appropriateness Criteria® topics on "Acute Respiratory Illness in Immunocompetent Patients" [3], "Chronic Dyspnea-Noncardiovascular Origin" [6], "Noninvasive Clinical Staging of Primary Lung Cancer" [5], and "Suspected Pulmonary Embolism" [84]).

Variant 1: Suspected diffuse lung disease. Initial Imaging. B. FDG-PET/CT Skull Base to Mid-Thigh

There is limited research supporting the use of fluorine-18-2-fluoro-2-deoxy-D-glucose (FDG)-PET/CT in some DLDs, which does not currently support the use of FDG-PET/CT for initial imaging. FDG-PET/CT may have a secondary role for evaluation of some DLDs because of increased FDG activity that correlates with disease severity and prognosis. A majority of relevant studies focus on

sarcoidosis and a minority on fibrotic DLD, including idiopathic pulmonary fibrosis [85-105].

Variant 1: Suspected diffuse lung disease. Initial Imaging. C. MRI Chest

There is limited research supporting the use of MRI in DLDs, which does not currently support the use of MRI for initial imaging. Small studies have shown adequate concordance of MRI findings with CT in established cases of DLD utilizing a variety of specialized MRI sequences. Some MRI sequences in the setting of DLD may provide additional functional information, such as tissue characterization, gas transfer efficiency, and lung elasticity [106-118].

Variant 1: Suspected diffuse lung disease. Initial Imaging. D. Radiography Chest

A normal chest radiograph in the setting of suspected DLD does not exclude the possibility of clinically important DLD [119]. Multiple studies demonstrate the increased sensitivity and specificity of CT over radiographs for evaluation of DLD [38-47,49-51,120,121]. Chest radiography serves the primary function of evaluating for alternative diagnoses, such as infection or cardiogenic edema (see the ACR Appropriateness Criteria® topics on "Acute Respiratory Illness in Immunocompetent Patients" [3], "Acute Respiratory Illness in Immunocompromised Patients" [4], "Chronic Dyspnea-Noncardiovascular Origin" [6], and "Rib Fractures" [122]). Obtaining a baseline chest radiograph at time of initial diagnosis of DLD may assist with diagnosis of these other conditions via radiograph on follow-up.

Variant 2: Confirmed diffuse lung disease. Suspected acute exacerbation or acute deterioration. Initial Imaging.

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A. CT Chest

CT can confirm the presence of airspace abnormalities consistent with acute exacerbation or acute deterioration of DLD [11-16,123,124]. Additionally, CT may help exclude alternative causes for worsening clinical symptoms, such as pneumothorax, infection, or malignancy. For suspected cases of acute exacerbation of idiopathic pulmonary fibrosis, development of new airspace disease on CT is a required diagnostic feature [14]. Additionally, the distribution and extent of findings on CT in the setting of acute exacerbation of idiopathic pulmonary fibrosis has demonstrated prognostic value [12]. There is no relevant literature to support the use of CT with IV contrast for imaging of suspected acute exacerbation or acute deterioration of confirmed DLD, although IV contrast may help in the evaluation for alternative diagnoses with overlapping clinical features (see the ACR Appropriateness Criteria® topics on "Acute Respiratory Illness in Immunocompetent Patients" [3] and "Suspected Pulmonary Embolism" [84]).

Variant 2: Confirmed diffuse lung disease. Suspected acute exacerbation or acute deterioration. Initial Imaging.

B. FDG-PET/CT Skull Base to Mid-Thigh

There is limited research supporting the use of FDG-PET/CT in some DLDs, which does not currently support FDG-PET/CT for imaging of acute exacerbation or acute deterioration of DLD.

Variant 2: Confirmed diffuse lung disease. Suspected acute exacerbation or acute deterioration. Initial Imaging.

C. MRI Chest

There is limited research supporting the use of MRI in some DLDs, none of which currently supports the use of MRI for imaging of acute exacerbation or acute deterioration of DLD.

Variant 2: Confirmed diffuse lung disease. Suspected acute exacerbation or acute deterioration. Initial Imaging.

D. Radiography Chest

There is no research supporting the use of chest radiography for imaging of acute exacerbation or acute deterioration in DLD. Numerous studies demonstrate the increased sensitivity and specificity of CT over radiographs for evaluation of DLD [38-47,49-51,120,121]. In this setting, chest radiography serves the primary function of evaluating for alternative diagnoses, such as pneumothorax, infection, or cardiogenic edema (see the ACR Appropriateness Criteria® topic on "Acute Respiratory Illness in Immunocompetent Patients" [3]).

Variant 3: Confirmed diffuse lung disease without acute clinical deterioration. Routine follow-up imaging clinically indicated.

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A. CT Chest

There are no data to support routine follow-up or surveillance imaging of confirmed DLD. However, a variety of clinical scenarios may warrant such repeat imaging. Longitudinal data available from multiple serial CT examinations can provide improvements in diagnostic accuracy, evaluation of disease reversibility, stability, or progression, and an estimation of prognosis for a number of pathologies [8,10,69,70,125-152]. Several DLDs demonstrate temporal evolution of their imaging findings on HRCT, which allows for a more specific diagnosis on follow-up imaging than on initial imaging [9,27,59-64,67,68,72,73,76,142,145,147,150,153,154]. Numerous studies support the increased sensitivity and specificity of CT over chest radiography for lung parenchymal changes related to DLD [38-51]. There is no research to support the use of CT with IV contrast for follow-up imaging of DLD; however, IV contrast may be of use in evaluation of alternative diagnosis with overlapping clinical features or conditions that also involve the pleura, mediastinum, and pulmonary vessels (see the ACR Appropriateness Criteria topics on "Chronic Dyspnea-Noncardiovascular Origin" [6], "Noninvasive Clinical Staging of Primary Lung Cancer" [5], and "Suspected Pulmonary Embolism" [84]).

Variant 3: Confirmed diffuse lung disease without acute clinical deterioration. Routine follow-up imaging clinically indicated.

B. FDG-PET/CT Skull Base to Mid-Thigh

There is limited research supporting the use of FDG-PET/CT in DLDs. In sarcoidosis, FDG-PET/CT can be used as a marker of disease extent and severity, and it can assist in follow-up and monitoring of treatment response [86,87,89,92,93,95,96,98-100]. Research supporting the use of FDG-PET/CT is more limited in other DLDs but has been evaluated in some studies of lung fibrosis [90,91,102].

Variant 3: Confirmed diffuse lung disease without acute clinical deterioration. Routine follow-up imaging clinically indicated.

C. MRI Chest

There is limited research supporting the use of MRI in DLD, none of which currently supports the use of MRI for follow-up imaging. Small studies have shown adequate concordance of MRI findings with CT in established cases of DLD utilizing a variety of specialized MRI sequences. Some

MRI sequences in the setting of DLD may provide additional functional information, such as tissue characterization, gas transfer efficiency, and lung elasticity. [106-118].

Variant 3: Confirmed diffuse lung disease without acute clinical deterioration. Routine follow-up imaging clinically indicated.

D. Radiography Chest

There is no research supporting the use of chest radiography over CT for follow-up imaging of confirmed DLD without acute clinical deterioration. Multiple studies demonstrate the increased sensitivity and specificity of CT over radiographs for evaluation of DLD [38-47,49-51,120,121].

Summary of Highlights

- **Variant 1**: Radiography chest or CT chest without IV contrast is usually appropriate as the initial imaging of patients with suspected DLD. These procedures are equivalent alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care).
- **Variant 2**: Radiography chest or CT chest without IV contrast is usually appropriate as the initial imaging of patients with suspected acute exacerbation or acute deterioration of confirmed DLD. These procedures are equivalent alternatives (ie, only one procedure will be ordered to provide the clinical information to effectively manage the patient's care).
- **Variant 3**: CT chest without IV contrast is usually appropriate as the routine follow-up for patients with confirmed DLD without acute clinical deterioration. The panel did not agree on radiography chest for this clinical scenario. There is insufficient medical literature to conclude whether or not these patients would benefit from radiography chest. This procedure is controversial in this patient population but may be appropriate.

Supporting Documents

The evidence table, literature search, and appendix for this topic are available at https://acsearch.acr.org/list. The appendix includes the strength of evidence assessment and the final rating round tabulations for each recommendation.

For additional information on the Appropriateness Criteria methodology and other supporting documents, please go to the ACR website at https://www.acr.org/Clinical-Resources/Clinical-Tools-and-Reference/Appropriateness-Criteria.

Appropriateness Category Names and Definitions

Appropriateness Category Name	Appropriateness Rating	Appropriateness Category Definition
Usually Appropriate	7, 8, or 9	The imaging procedure or treatment is indicated in the specified clinical scenarios at a favorable riskbenefit ratio for patients.
May Be Appropriate	4, 5, or 6	The imaging procedure or treatment may be indicated in the specified clinical scenarios as an alternative to imaging procedures or treatments with a more favorable risk-benefit ratio, or the risk-benefit ratio for patients is equivocal.

May Be Appropriate (Disagreement)	5	The individual ratings are too dispersed from the panel median. The different label provides transparency regarding the panel's recommendation. "May be appropriate" is the rating category and a rating of 5 is assigned.
Usually Not Appropriate	1, 2, or 3	The imaging procedure or treatment is unlikely to be indicated in the specified clinical scenarios, or the risk-benefit ratio for patients is likely to be unfavorable.

Relative Radiation Level Information

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, because of both organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared with those specified for adults (see Table below). Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria Radiation Dose Assessment Introduction document.

Relative Radiation Level Designations

Relative Radiation Level*	Adult Effective Dose Estimate Range	Pediatric Effective Dose Estimate Range	
0	0 mSv	0 mSv	
	<0.1 mSv	<0.03 mSv	
	0.1-1 mSv	0.03-0.3 mSv	
	1-10 mSv	0.3-3 mSv	
	10-30 mSv	3-10 mSv	
	30-100 mSv	10-30 mSv	

^{*}RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (e.g., region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as "Varies."

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The ACR Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the FDA have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

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