



## GROUND GLASS OPACIFICATION

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**Ground-glass opacification/opacity (GGO)** is a descriptive term referring to an area of increased attenuation in the lung on computed tomography (CT) with preserved bronchial and vascular markings. It is a non-specific sign with a wide aetiology including infection, chronic interstitial disease and acute alveolar disease.

### Pathology

#### Aetiology

Ground-glass opacities have a broad aetiology:

- Normal expiration
- Partial filling of air spaces
- Partial collapse of alveoli
- Interstitial thickening
- Inflammation
- Oedema
- Fibrosis
- Proliferation of neoplasm

### Morphological forms

- Focal Ground-Glass Opacification
- Diffuse Ground-Glass Opacification
- Isolated Diffuse Ground-Glass Opacification<sup>[5]</sup>

### Differential diagnosis

Broadly speaking, the differential for ground-glass opacification can be split into<sup>[5]</sup>:

- Infectious processes (usually opportunistic)
- Chronic interstitial diseases
- Acute alveolar diseases
- Other causes.

### Opportunistic infections

- Pneumocystis pneumonia (PCP/PJP)
- Cytomegalovirus Pneumonia (CMV)
- Herpes Simplex Virus Pneumonia (HSV)
- Respiratory Syncytial Virus  
Bronchiolitis (RSV): type of infectious Bronchiolitis
- Other infectious causes.

### Chronic interstitial diseases

- Eosinophilic Pneumonias: GGO can be seen in many of the eosinophilic pneumonias but is most commonly seen in.<sup>[2]</sup>

- Simple Pulmonary Eosinophilia (SPE): nodules with a GGO halo.
- Idiopathic Hypereosinophilic Syndrome (IHS): nodules with a GGO halo.
- Acute Eosinophilic Pneumonia (AEP): bilateral patchy areas of GGO with interlobular septal thickening.
- Eosinophilic drug reactions: peripheral airspace consolidation and GGO.
- Idiopathic Interstitial Pneumonias<sup>[3]</sup>
- Non-Specific Interstitial Pneumonia: GGO with linear or reticular markings, micro nodules, consolidation, and micro cystic honeycombing.
- Usual Interstitial Pneumonia (UIP): focal GGO with macrocystic honeycombing, reticular opacities, traction bronchiectasis, and architectural distortion.
- Cryptogenic Organising Pneumonia (COP): formerly Bronchiolitis obliterans with organising pneumonia (BOOP); GGO with airspace consolidation and mild bronchial dilatation.
- Exudative phase of acute interstitial pneumonia (AIP): diffuse lung consolidation with GGO.
- Respiratory Bronchiolitis-associated interstitial lung disease (RB-ILD): patchy GGO centrilobular nodules and bronchial wall thickening
- Desquamative Interstitial Pneumonia (DIP): GGO with linear or reticular opacities
- Lymphoid Interstitial Pneumonia (LIP): GGO often in association with perivascular cystic lesions, septal thickening, and centrilobular nodules
- Sarcoidosis (pulmonary manifestations of sarcoidosis).

### Acute alveolar disease

- Alveolar Oedema or pulmonary oedema
- Cardiogenic Pulmonary Oedema
- Adult Respiratory Distress Syndrome (ARDS)
- Other causes of non-cardiogenic pulmonary oedema

- Hypersensitivity Pneumonitis: especially acute and subacute forms

#### Other causes

- Neoplastic processes with a lepidic proliferation pattern
  - Atypical adenomatous hyperplasia
  - Localised adenocarcinoma
  - Adenocarcinoma In Situ Or Minimally Invasive (formerly bronchioalveolar cell carcinoma)
- Drug toxicity

#### Rare causes

- Focal Interstitial Fibrosis: a non-neoplastic entity with a nodular ground-glass opacity that does not change over a long period of time; may be mistaken for a neoplastic process
- Aspergillosis: a nodule with surrounding ground-glass opacity (CT halo sign) is rare except in severely immunocompromised patients
- Thoracic Endometriosis
- Traumatic lung injury (pulmonary contusion)
- Poisoning, e.g. acute/subacute phase of paraquat poisoning
- Pulmonary Cryptococcus Infection: solitary or multiple pulmonary nodules with or without peripheral GGO
- Granulomatosis With Polyangiitis
- Henoch-Schönlein purpura.

Pulmonary nodules are small, generally spherical abnormalities, commonly noted incidentally on chest radiography or CT scan. Ground glass opacification are a subset of pulmonary nodules or masses with non-uniformity and less density than solid nodules. GGO are usually described as either pure ground glass or part solid nodules. Management of GGO focuses on identifying those ground glass opacities that are or will become cancerous. Serial CT imaging is the preferred modality for this purpose. Overtime most cancerous GGO's will enlarge, develop solid components or both. Serial CT scanning can identify these changes and thus GGO malignancies at an early, curable stage. The most common cancer manifesting with GGO on CT is adenocarcinoma in situ, also known as minimally invasive adenocarcinoma, formerly known as bronchioalveolar carcinoma. Multiple tumor types can also co-exist or develop inside complex GGO, with solid or sub-solid components. The natural history of cancerous GGO such as adenocarcinoma in situ is typically more indolent course with a lower risk of invasion, compared to solid lung cancers. As with management of solid nodules, the goal is identify and cure (usually through resection) all dangerous cancers, and to avoid resection in benign tumors. With GGO, the risks of observation with serial imaging are usually lower, but the observation epochs significantly longer in order to achieve these goals. Infection must also be considered as a possible aetiology for GGO/ sub solid nodules, more with solid nodules.

#### Recommended management of GGO/ Sub solid nodules

Recommendations suggest GGO's be categorized into less than or equal to 5mm and greater than 5mm with measurements not to include tenths of mm.

#### Pure GGO Pulmonary Nodules

Nodules <5 mm diameter

- ➔ No routine follow up is suggested for pure GGO's less than or equal to 5 mm
- ➔ For suspicious pure GGO's less than or equal 5 mm a CT scan can be obtained at 2 and 4 years
- ➔ Suspicious morphology
- ➔ High risk patient due to co-morbidities
- ➔ Malignant transformation <1%

Nodules >5 mm diameter

A CT scan between 6 & 12 months should be obtained to confirm persistence and then a CT scan every 2 years until the 5 year mark. At that time, the physician and patient can stop following the nodule, assuming benignity and stability.

#### Part Solid (Sub-solid) Pulmonary nodules

GGO cannot truly be defined as part solid until after the nodule is larger than 6 mm diameter.

<5 mm sub solid nodules

- ➔ No routine follow up is recommended for part solid GGO's less than 6 mm
- ➔ As with pure GGOs a suspicious nodule can be followed with a 2 and 4 year CT scan.

>5mm Sub solid Nodules

Part solid GGO > 5mm should have a CT scan between 3 and 6 months to confirm persistence. If the overall nodule size is unchanged and the solid component remains less than 6 mm an annual CT scan should be performed for 5 years at which time the physician can stop following the nodule assuming stability. Part solid nodules have a much higher risk of malignancy, however part solid GGO with a solid component less than 6 mm typically represent either adenocarcinoma in situ or minimally invasive adenocarcinoma with low risk of malignant transformation.

Persistence of part solid nodule is confirmed with a 3-6 months follow up, as many GGO and part solid GGO represent infectious or inflammatory aetiologies and have a reasonable chance at resolution on relatively short term follow up imaging.

For part solid nodules with particularly suspicious morphology, a growing solid component, or a solid component larger than 8 mm a PET/ CT biopsy or resection is recommended.

A solid component larger than 5 mm co-relates with a substantial likelihood of local invasion. The larger the

solid component, the greater the risk of local invasion and metastasis.

#### **Multiple sub solid nodules or GGO**

The category of multiple sub solid nodules represent a special category as they often represent infectious or inflammatory process.

#### **Multiple sub solid nodules <5mm diameter**

In patients with multiple sub solid nodules smaller than 6 mm, an initial follow up scan is recommended at 3-6 months, with the consideration of follow up at approximately 2 and 4 years to confirm stability depending on clinical setting.

#### **Multiple sub solid nodules >5mm diameter**

In patients with multiple sub solid nodules with at least one nodule that is 6mm or larger, management decisions should be based on the most suspicious nodule. If the persistence is confirmed on CT scan after 3-6 months, then subsequent CT scans should follow the recommendations from the category of the most suspicious nodule. If multiple nodules are 6 mm or larger than the one that is determined to be most suspicious should guide timing of future scans. The current guidelines put more emphasis on the physician patient relationship, allowing more flexibility in management styles pending patient preferences.

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