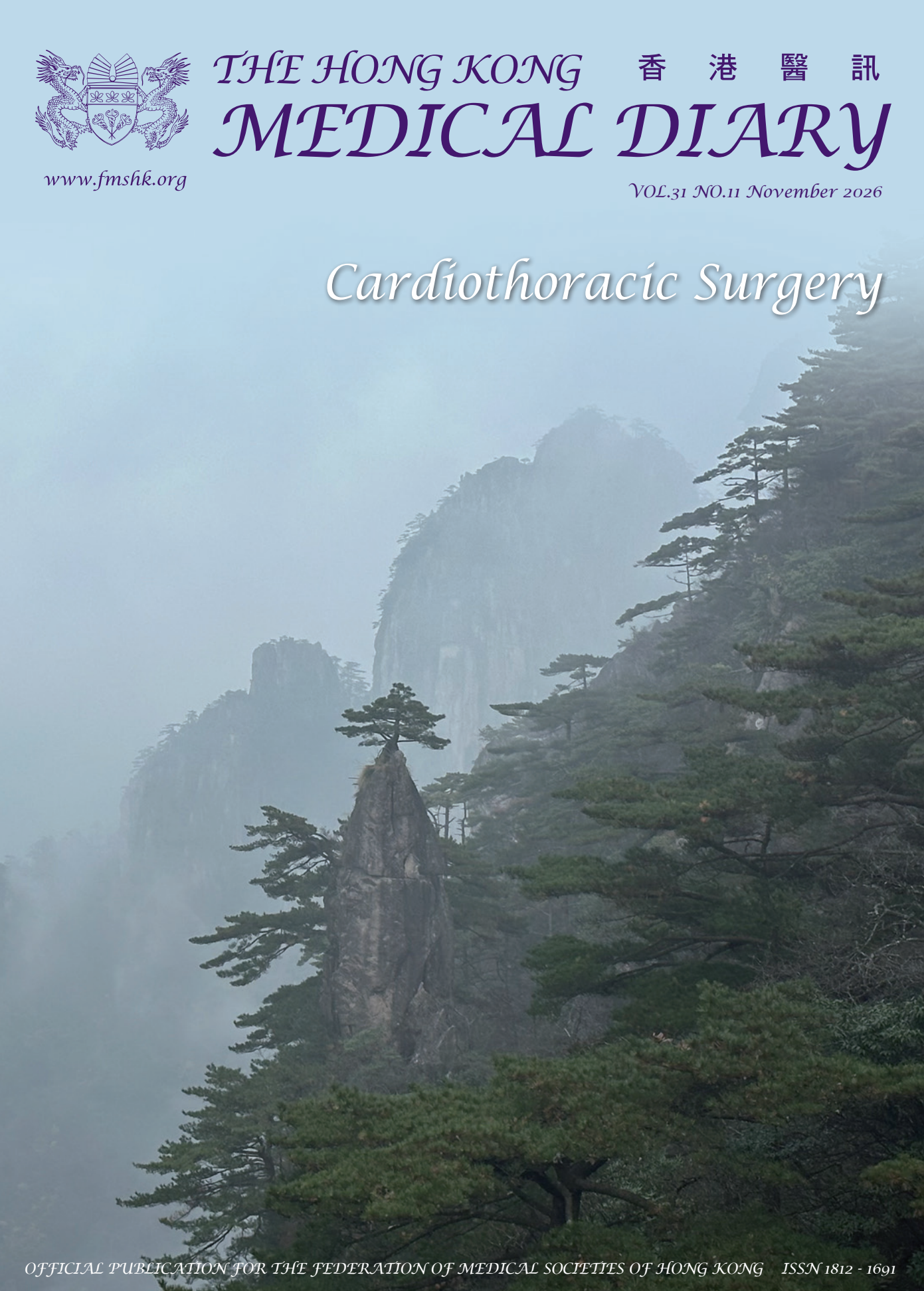
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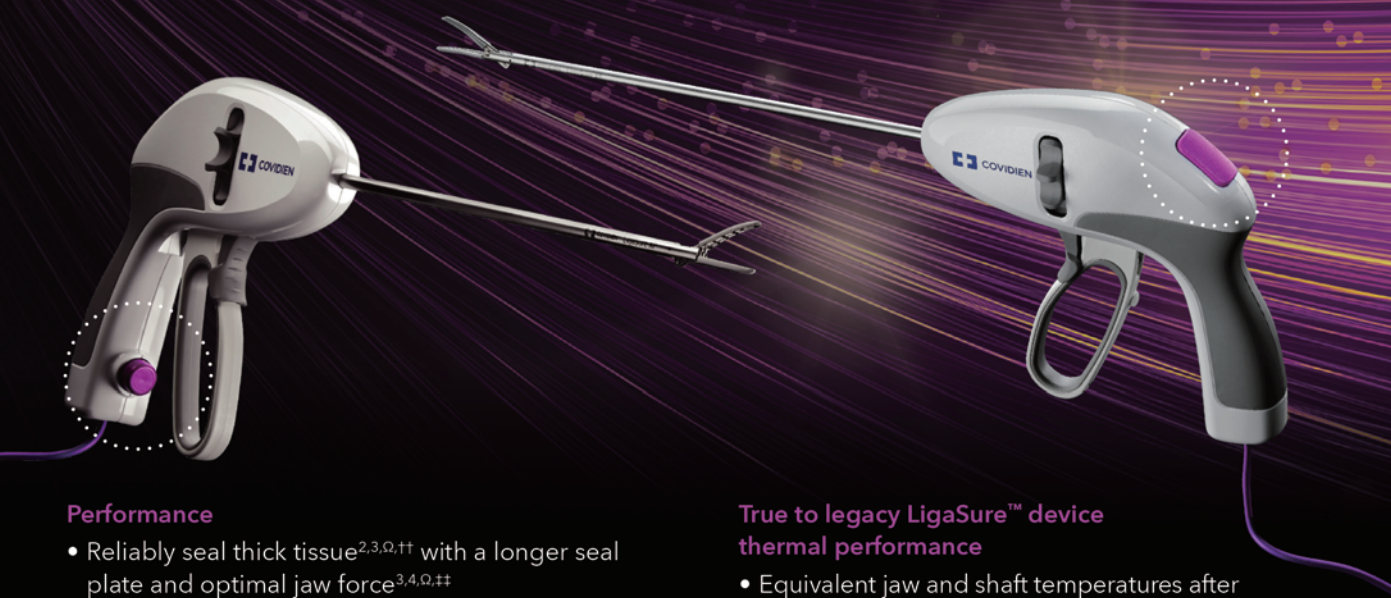
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The Cover Shot



This is a picture taken when I travelled in Huangshan. It is called Mengbi Shenghua (夢筆生花), meaning dream brush flowering rock basically a slender stone pillar looking like a giant brush with a pine tree growing from its tip like an ink flower. Viewing from a distance, it is everybody's imagination. To a poet, this is the stroke of a celestial hand. To a tired traveller, it might be nothing more than an odd rock. For a geologist, he might see the effect of wind and water over millions of years. The granite pinnacle and its withering pine remained unchanged; what shifts is people's perception influenced by their mood, memory and knowledge. Therefore, we don't see things as they are; we see them as we are.



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Editorial

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Issue Editors





Dr Clement Shui-wah CHIU Dr Vincent Wing-shun NG

The first description of ground-glass opacity (GGO) on a computed tomography (CT) scan is generally attributed to Gamsu and colleagues in 1989, who identified it as a 'hazy increased CT density' on high-resolution CT(HRCT). At that time, this finding was thought to be an indicator of inflammatory process.

In 1996, the Fleischner Society formally proposed the concept of the pulmonary ground-glass nodule. In the following decades, more evidence showed that GGO may represent the pre-invasive stage of pulmonary adenocarcinoma. Some GGOs will eventually develop into invasive adenocarcinoma. With the wide availability of CT scans in health check and screening programme for lung cancer, GGO is a common finding. Doctors are often asked for the opinion and management of the GGO, which is an incidental finding on CT scan during a health check-up. Most GGOs are due to inflammatory process and will resolve spontaneously after a few months. Some GGOs, especially those with a solid component and other malignant features, are of great concern in the management.

In general, a follow-up CT 3 - 6 months after the initial detection of GGO is necessary to confirm the persistence of the GGO. For GGO-dominated adenocarcinomas, they are rather indolent and remain stable for a number of years before becoming invasive adenocarcinomas. Regular CT surveillance is recommended to monitor GGOs and avoid overtreatment of an indolent lesion. The interval of surveillance CT varies from three to twelve months interval depending on how suspicious the GGO is. The duration of CT surveillance is difficult to define. About 13 % - 16 % of GGOs will grow after five years of stability on CT. Therefore, CT surveillance will still be advisable after five years. Indications for further investigation, tissue diagnosis and surgical resection are when there is evidence of growth of GGO or appearance of a solid component in the GGO.

For surgical management of GGO-dominated adenocarcinomas, limited resection (wedge or segmentectomy) has been shown non-inferiority in the long-term results when compared with the standard lobectomy for non-small cell lung cancer. In summary, it is important to recognise that GGO is a common finding in HRCT. It needs regular CT surveillance. Biopsy and surgical intervention would be indicated for those high risk GGO or when there is evidence of growth of GGO and appearance of a solid component inside the GGO during CT surveillance. Limited resection with lung conservation has played an important role in the management of GGO-dominated adenocarcinomas.

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Energy Ablation for Ground-Glass Lung Lesions: A Comprehensive Review

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This article has been selected by the Editorial Board of the Hong Kong Medical Diary for participants in the CME programme of the Medical Council of Hong Kong (MCHK) to complete the following self-assessment questions in order to be awarded 1 CME credit under the programme upon returning the completed answer sheet to the Federation Secretariat on or before 30 November 2026.

INTRODUCTION

The widespread adoption of low-dose computed tomography (LDCT) for lung cancer screening has led to a marked increase in the detection of ground-glass lesions (GGLs), comprising both pure ground-glass nodules and part-solid lesions. These lesions pose a diagnostic and management challenge: while many are indolent or represent pre-invasive adenocarcinoma in situ or minimally invasive adenocarcinoma, a significant proportion will progress to invasive lung cancer over time. Surgical resection remains the standard of care for suitable candidates, offering definitive histology and excellent survival. However, a substantial number of patients are unfit for surgery due to advanced age, impaired cardiopulmonary reserve, or significant comorbidities. Moreover, the indolent behaviour of many GGLs and the multifocal nature of some adenocarcinomas demand parenchyma-sparing, repeatable therapeutic options.

Energy ablation has emerged as a valuable, minimally invasive alternative for treating lung malignancies in non-surgical candidates. International guidelines, including the 2021 Expert Consensus on Thermal Ablation of Pulmonary Subsolid Nodules and the CIRSE Standards of Practice, endorse image-guided ablation as a feasible and safe curative-intent strategy for early-stage non-small cell lung cancer (NSCLC) and GGLs in selected patients[1,2]. This review provides an overview of the available energy modalities and delivery platforms, with a particular focus on CT-guided radiofrequency ablation (RFA) and cryoablation.

MEANS OF ENERGY-ABLATION DELIVERY

Precise targeting of GGLs is the cornerstone of successful ablation. Two principal image-guidance strategies are currently employed: CT-guided percutaneous ablation and bronchoscopic navigation-guided ablation.

CT-Guided Ablation

CT guidance is the most established and widely used technique for energy ablation of lung lesions. The procedure is performed in an interventional CT suite, often under conscious sedation or general anaesthesia. High-resolution CT provides real-time or near-real-time visualisation of the lesion, the applicator, and the developing ablation zone. For GGLs, which frequently have ill-defined margins on scans, planning CT with thin slices is crucial. The operator must assess the optimal skin entry point, needle trajectory to avoid fissures, bullae, large vessels and bronchi, and determine the number and configuration of applicators required to achieve a sufficient ablative margin. Sequential scans during probe placement and ablation allow immediate detection of complications such as pneumothorax or haemorrhage. The versatility of CT guidance permits treatment of lesions in all lung zones, although proximity to the mediastinum, hilum, or diaphragm increases technical difficulty and risk[13,14,15]. CT-guided ablation has been the platform for the vast majority of published outcomes, including the large single-centre series by Vogl and colleagues.

Bronchoscopic Navigation-Guided Ablation

Ablation via the transbronchial route is an evolving alternative that seeks to reduce the pleural complications inherent to percutaneous puncture. Using navigation bronchoscopic approach, a flexible catheter is steered through the airways to the target bronchus. A microwave or RFA probe is then advanced either directly into the lesion or, if the nodule lies outside the airway, through a transparenchymal access tract created with a needle and balloon-dilatation technique (bronchoscopic transparenchymal nodule access, BTPNA). This approach avoids pleural violation and may therefore have a lower pneumothorax rate, while also enabling simultaneous diagnostic biopsy. At present, bronchoscopic ablation remains complementary to CT guidance, with the latter remaining the standard for definitive treatment[10,11].

Energy Sources

RadioFrequency Ablation (RFA)

RFA relies on an alternating electric current (375 - 500 kHz) delivered through an electrode directly into the tissue, causing ionic agitation, frictional heating,

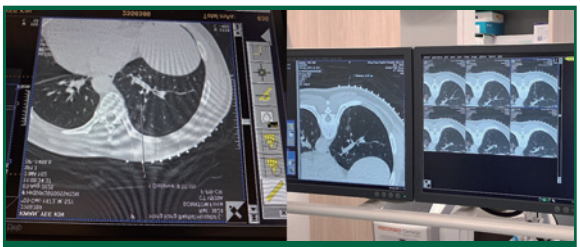
and coagulative necrosis (Fig. 1 & 2). In the lung, the high intrinsic impedance of aerated parenchyma limits current flow, so modern systems employ internally cooled or multi-tined expandable electrodes to enlarge the ablation zone (Fig. 3 & 4). RFA has been extensively studied for lung tumours, with the landmark RAPTURE trial demonstrated RFA asa safe and feasible means of treatment[9].

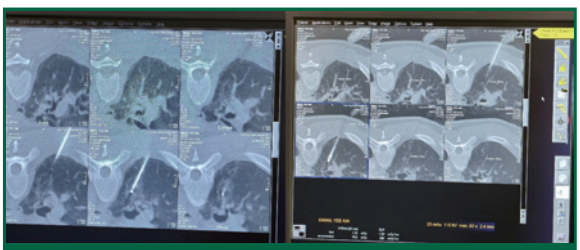


Fig. 1: RFA probe (Clinical photo from personal collection)



Fig. 2: RFA generator (Clinical photo from personal collection)


Fig. 3: GGO lesion (Clinical photo from personal collection)


Fig. 4: GGO lesion undergoing RFA (Clinical photo from personal collection)

In the context of GGLs, studies have specifically evaluated CT-guided RFA. Kodama et al. treated 33 pure GGLs (mean size 14 mm) and achieved a local control rate of 100 % at a median follow-up of 42 months with no local progression[8]. These data underscore that GGLs, with their low cellular density and absence of a robust stromal reaction, may be particularly susceptible to thermal injury, even with moderate temperature rises. However, RFA has notable limitations. The "heat-sink" effect from adjacent vessels, particularly in solid components, may lead to incomplete ablation at the tumour periphery. In addition, the impedance rise during ablation in desiccated lung can prematurely terminate energy delivery, potentially leaving the target volume undertreated. The Frankfurt group, led by Prof Vogl, has contributed extensively to understanding the determinants of RFA success. In a study of 134 NSCLC patients, Vogl et al. identified tumour size, location near a large vessel, and the use of a clustered electrode as independent predictors of local tumour control. Their earlier long-term analysis of RFA for lung metastases demonstrated a 5-year overall survival of 39 %, reinforcing the role of RFA in oligometastatic disease[3].

Cryoablation

Cryoablation destroys tissue through cycles of rapid freezing and slow thawing using argon gas, exploiting the Joule-Thomson effect. The extreme cold (-140 °C to - 160 °C) causes direct cellular injury from intracellular ice crystal formation, osmotic dehydration, and delayed microvascular thrombosis. A distinct advantage of cryoablation is the visibility of the "ice ball" as a well-demarcated low-attenuation area on CT, allowing precise intra-procedural monitoring of the ablation margin (Fig. 5 to 8). Furthermore, the collagenous architecture of the lung is preserved, which may reduce the risk of bronchopleural fistula and post-ablation cavitation. The procedure is also considerably less painful, and is often performed under local anaesthesia or monitored anaesthetic control[12].

Cryoablation has been successfully applied to GGLs. The excellent conspicuity of the ice ball on CT is especially advantageous for treating lesions with a predominant ground-glass component, where the soft-tissue window may fail to delineate the target border. The Frankfurt experience with cryoablation, published by Vogl and colleagues, included 30 patients with pulmonary metastases treated percutaneously; the technique yielded a primary technique efficacy of 93.3 % at three months with a low rate of major complications. In a larger cohort, Vogl demonstrated that cryoablation of metastatic lung nodules could achieve sustained local tumour control comparable to RFA, while causing less post-procedural pain and allowing treatment of centrally located lesions with appropriate precautions[6].

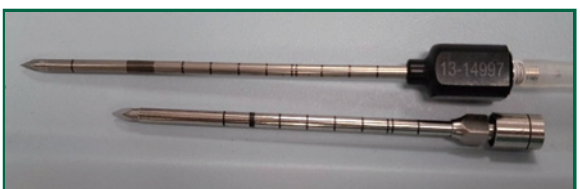


Fig. 5: Cryo probe (Clinical photo from personal collection)



Fig. 6: Testing for ice-ball forming (Clinical photo from personal collection)

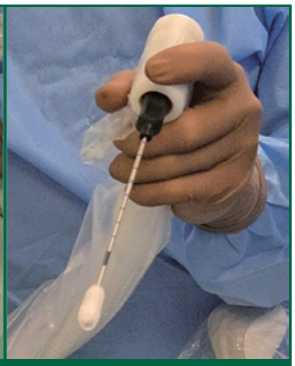


Fig. 7: Ice-ball formation (Clinical photo from personal collection)

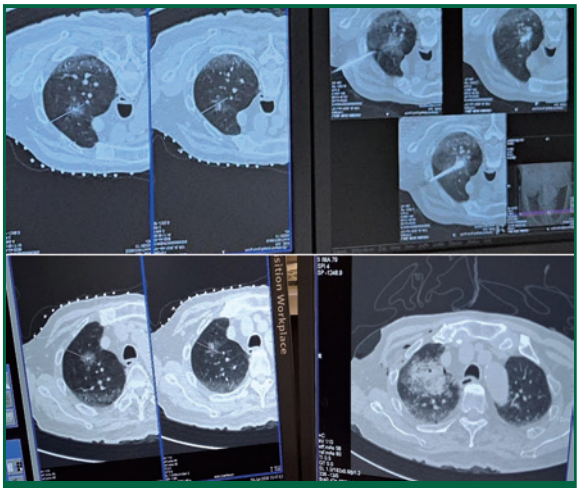


Fig. 8: GGO lesions undergoing CryoAblation (Clinical photo from personal collection)

Microwave Ablation (MWA)

MWA uses electromagnetic waves (typically 915 MHz or 2.45 GHz) to induce rapid oscillation of water molecules, generating homogeneous high temperatures up to 150 °C. Compared with RFA, microwave energy propagates effectively through aerated, charred, or desiccated tissue without impedance limitations, resulting in larger and more predictable ablation zones in shorter times[13,14]. MWA is also less susceptible to the heat-sink effect. The Frankfurt group has pioneered clinical MWA research: Vogl et al. reported a single-centre experience with 108 patients harbouring malignant lung tumours; technique efficacy was achieved in 89 % of lesions with a median ablation time of 10 minutes, and a low 5 % pneumothorax rate requiring drainage. MWA can be delivered via multiple antennas for confluent ablation of larger GGLs or ground-glass lesions with a solid component > 5 mm, where the tumour biology may demand wider margins[4,5,7].

Other Modalities

Laser interstitial thermal therapy (LITT) and irreversible electroporation (IRE) have been explored in the lung but remain investigational. IRE, a non-thermal technique, disrupts cell membranes through high-voltage electric pulses while sparing the extracellular matrix, but it requires general anaesthesia, cardiac synchronisation, and multiple needle placements, making it less practical for routine GGL ablation.

CT-GUIDED RFA AND CRYOABLATION IN FOCUS

Given the biologic fragility and favourable prognosis of GGLs, the ideal ablation modality should offer predictable, controllable tissue destruction with an exemplary safety profile. CT-guided RFA and cryoablation currently satisfy these requirements most convincingly, and a growing body of evidence supports their use as first-line local therapies in inoperable patients.

Comparative Efficacy in GGLs

Direct randomised comparisons between RFA and cryoablation for GGLs do not exist. However, retrospective and prospective observational data suggest both achieve similar high local control rates exceeding 90 % at 2 - 3 years for nodules ≤ 2 cm[12]. Certain recent multicentre propensity-matched analysis (although not restricted to GGLs), cryoablation was associated with a lower rate of local tumour progression compared with RFA for stage I NSCLC, potentially due to the superior intra-procedural visualisation of the ice ball enabling more precise margin assessment. For GGLs specifically, where the target is often subtle on CT, this real-time feedback provides a major clinical advantage.

Complication Profile

Both modalities share the generic risks of percutaneous lung puncture: pneumothorax, pleural effusion, haemoptysis, and infection. The pneumothorax rate after CT-guided RFA for GGLs ranges from 15 - 35 %, with 5 - 10 % requiring chest tube drainage. Cryoablation carries a marginally higher risk of pneumothorax in some series because of the larger-calibre probes, though the prolonged tissue adherence during freezing may limit air leak. Conversely, post-ablation syndrome (fever, malaise) and pleural pain are substantially more common with RFA, often necessitating opioid analgesia, whereas cryoablation is typically well tolerated. Life-threatening haemorrhage or bronchopleural fistula is rare (< 1 %) with either technique when cases are selected appropriately.

Patient Selection and Technical Considerations

Multidisciplinary tumour board evaluation is mandatory. Patients with biopsy-proven or highly suspicious persistent GGLs, who are medically inoperable or decline surgery, are ideal candidates. A pre-procedural CT with intravenous contrast and a recent pulmonary function test are essential. RFA is best suited for pure or part-solid GGLs ≤ 3 cm that are not immediately adjacent to major vessels or the heart, where heat-sink could compromise the ablation margin. Cryoablation, with its ability to monitor the ice ball, is favoured for lesions

abutting the pleura, chest wall, or fissures, as well as for centrally located GGLs when a thorough risk-benefit analysis is performed. Multiple ipsilateral GGLs can be treated in one session, although the risk of pneumothorax increases with each puncture. The Frankfurt group's extensive data, including Vogl's analyses of local control factors, emphasise that a sufficient ablative margin is the single most critical determinant of long-term success, irrespective of energy modality.

FUTURE DIRECTIONS

Advances in image fusion, cone-beam CT, and robotic needle guidance are poised to further refine percutaneous ablation accuracy. On the bronchoscopic front, the integration of real-time tip-tracked needles and advanced navigation with thermal ablation catheters may enable a "no-puncture" outpatient ablation procedure for peripheral GGLs. Combining ablation with systemic immunotherapy is another exciting area, as local tumour destruction may release neoantigens and prime an abscopal anti-tumour immune response, a concept being tested in ongoing clinical trials for both RFA and cryoablation.

CONCLUSION

Energy ablation is a cornerstone of the modern multidisciplinary management of ground-glass lung lesions in patients who are not surgical candidates. CT-guided RFA and cryoablation, supported by robust long-term data and expert consensus, offer excellent local tumour control with acceptable morbidity. The choice of modality should be individualised based on lesion characteristics, location, and patient tolerance. The pioneering work of Prof Vogl and the Frankfurt group has been instrumental in establishing the safety and efficacy profiles of RFA, MWA, and cryoablation in the lung. As technology evolves - towards bronchoscopic delivery and immunomodulatory combinations - energy ablation is set to become an even more integral part of curative-intent therapy for early-stage lung cancer and its precursors.

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Programme Details & Admission Requirement

Application Deadline
28-2-2027 (FT) , 30-4-2027(PT)

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MCHK CME Programme Self-assessment Questions

Please read the article entitled "Energy Ablation for Ground-Glass Lung Lesions: A Comprehensive Review" by Dr Vincent Wing-shun NG and complete the following self-assessment questions. Participants in the MCHK CME Programme will be awarded CME credit under the Programme for returning completed answer sheets via fax (2865 0345) or answer link: https://forms.gle/iRB5mPhNPQYRuwBj9 or by mail to the Federation Secretariat on or before 30 November 2026. Answers to questions will be provided in the next issue of The Hong Kong Medical Diary. (Address: Duke of Windsor Social Service Bldg., 4/Fl., 15 Hennessy Rd., Wan Chai. Enquiry: 2527 8898)

Questions 1 - 10: Please answer T (true) or F (false)

1. **The 2021 Expert Consensus on Thermal Ablation of Pulmonary Subsolid Nodules and CIRSE Standards of Practice endorse image-guided ablation as a curative-intent strategy for early-stage NSCLC and GGLs.**
2. **Radiofrequency ablation (RFA) delivers energy at frequencies typically between 375-500 kHz, causing tissue destruction through ionic agitation and frictional heating.**
3. **Lung Albation, as a treatment option for local control of lung cancer, can totally replace surgery.**
4. **Cryoablation is generally associated with more post-procedural pain than RFA, often requiring opioid analgesia.**
5. **Microwave ablation (MWA) is more susceptible to the heat-sink effect and impedance limitations compared to RFA, making it less predictable for treating GGLs adjacent to blood vessels.**
6. **Bronchoscopic navigation-guided ablation avoids pleural violation and may therefore have a lower pneumothorax rate compared to CT-guided percutaneous ablation.**
7. **One distinct advantage of cryoablation over RFA is that the "ice ball" appears as a well-demarcated area on CT, allowing precise intra-procedural monitoring.**
8. **Irreversible electroporation (IRE) is a thermal technique that is widely used for routine GGL ablation due to its simplicity and minimal equipment requirements.**
9. **For GGLs abutting the pleura, chest wall, or fissures, cryoablation is favoured over RFA because of its ability to monitor the ice ball and the preservation of collagenous architecture.**
10. **Lung Ablation can serve as a palliative-intent treatment option for lung tumours with symptoms e.g. haemoptysis.**

ANSWER SHEET FOR NOVEMBER 2026

Please return the completed answer sheet to the Federation Secretariat on or before 30 November 2026 for documentation. 1 CME point will be awarded for answering the MCHK CME programme (for non-specialists) self-assessment questions.

Energy Ablation for Ground-Glass Lung Lesions: A Comprehensive Review

Dr Vincent Wing-shun NG

MBBS (HK), FRCSEd, FCSHK, FHKAM (Surgery)
Specialist in Cardiothoracic Surgery

Answer Link

1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 ☐

Name (block letters):_____ HKMA No.: _____ CDSHK No.: _____

HKID No.: __ __ - __ __ __ __ X X (X) HKDU No.: _____ HKAM No.: _____

Contact Tel No.:_____ MCHK No. / DCHK No.: _____(must fill in)

Answers to October 2026 Issue

Small Wounds for Small Patients: the Expanding Role of Paediatric Interventional Radiology

1. T 2. F 3. F 4. T 5. T 6. T 7. F 8. F 9. T 10. F

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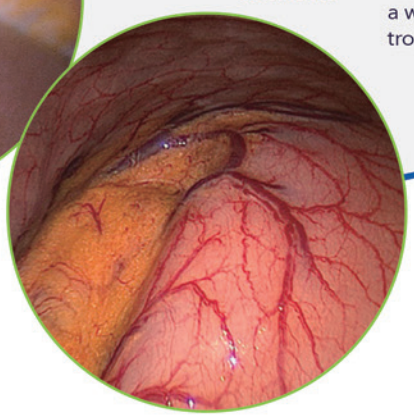
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1. Based on internal test report #RE00383135 Rev B, Clearify™ Cleaning Efficacy Engineering Study, p. 9, February 24th, 2022
2. Based on internal test report #RE00022323. Clearify™ Plug Design Qualification, September 2015.

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Surgical Management of Ground-Glass Nodules of the Lung: Indications and Lobectomy versus Limited Resection



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INTRODUCTION

Pulmonary nodules are common findings in the computerised tomography (CT) scanning of the thorax. The nodules can be classified into solid and subsolid nodules[1,2]. Subsolid nodules are also known as ground glass nodules or opacities (GGN or GGO). Widespread adoption of low dose high resolution computed tomography (HRCT) for lung cancer screening programme[1,2] and incidental health check ups has dramatically increased the detection rate of pulmonary GGO, which ranged from 1.5 to 11 % depending on the specific screened population. Based on their internal composition, GGOs are subclassified into pure GGOs (pGGOs), which contain no solid component, and mixed GGOs (mGGOs), also known as part solid nodules which harbour both ground glass and solid elements. Consolidation to tumour ratio (CTR) (Fig. 1) is also used to reflect the proportion of solid component in a ground-glass lesion. CTR is 1 in solid nodule and 0 in pGGO. For accurate characterisation and measurement of small pulmonary nodules using lung window images, contiguous thin section (< 1.5 mm, typically 1mm) CT should be used. In general, GGO, especially mGGO is more likely to be malignant when compared to an incidentally detected solid nodule[3].

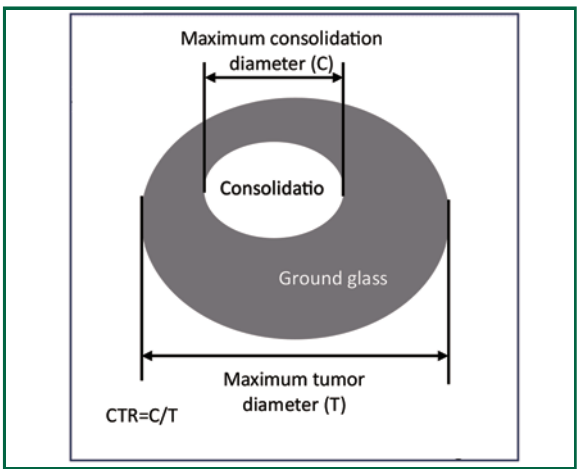


Fig. 1: Consolidation to tumour ratio (CTR) is also used to reflect the proportion of solid component in a ground-glass lesion (Excerpted from https://www.jtcvs.org/article/S0022-5223%2812%2901595-4/fulltext)

The pathological spectrum of GGOs is remarkably diverse. They may represent benign inflammatory processes, focal fibrosis, or intrapulmonary lymph nodes, but they also constitute the entire pre invasive and early invasive stages of lung adenocarcinoma, from atypical adenomatous hyperplasia (AAH) and adenocarcinoma in situ (AIS) to minimally invasive adenocarcinoma (MIA) and frankly invasive lepidic predominant adenocarcinoma (LPA). Radiologically, the ground-glass component usually corresponds to non-invasive or pre-invasive AAH and MIA histology, while the solid part corresponds to invasive histology[13,14,15]. Importantly, AIS and MIA are widely regarded as the "surgical cure window" for lung adenocarcinoma, with near 100 % disease free survival following complete resection.

Lung cancers that present as radiographic GGOs represent a subtype with distinct biological behaviour and outcomes. The natural history of most GGOs is indolent; studies have shown GGOs which persist for several years follow an indolent course. Kobayashi and colleagues[48] showed the average period of growth for subsolid nodules is 3 - 4 years. Most growing nodules exhibit growth within three years. However, among pGGOs that remain stable for 10 years, about 13 % eventually will grow, indicating that some pGGOs can grow even following a long period of stability[6]. Therefore, CT surveillance in GGOs may extend up to 10 years or beyond as some GGOs will become invasive adenocarcinoma after years of radiological stability. In addition, for GGOs, there is no evidence of significant differences in long term survival between surveillance and surgery. This underscores the cardinal clinical dilemma: when and how to intervene. It is important in balancing the imperative of not missing a curable cancer against the risk of overtreating an indolent lesion.

WHEN AND HOW TO INTERVENE

Surgical management of GGOs should base on two important questions: indications for surgery (what patients and which nodules warrant resection) and the choice of surgical procedure: lobectomy versus limited resection (sublobar resection), which includes wedge resection or segmentectomy. For decades, lobectomy with systematic lymph node dissection has been the gold standard for early stage non small cell lung cancer (NSCLC), based on the landmark Lung Cancer Study Group trial LCSG 821[72] that showed superior local control and survival for lobectomy over limited resection for early T1N0 lung cancers. However, that trial was conducted in the era of conventional CT and predominantly solid nodules. The biological behaviour of GGO dominant adenocarcinomas is distinctly more

indolent, and recent large scale randomised controlled trials - notably JCOG0802[73] and CALGB 140503[74] both have demonstrated that limited resection can be oncologically non inferior to lobectomy in selected patients with small sized peripheral NSCLC. The 2023 American Association for Thoracic Surgery (AATS) Expert Consensus on management of subsolid lung nodules reflects updated insights based on the latest literature, focusing on the correlation between radiologic findings and pathological classifications, individualised surveillance and surgical strategies[141].

INDICATIONS FOR SURGERY IN GGO

Determining the appropriate timing and threshold for surgical resection of GGOs is a nuanced process that integrates nodule morphology, size, growth kinetics, patient characteristics, and multidisciplinary consensus. Unlike solid tumours, where size and PET avidity strongly guide clinical management, GGOs demand a more conservative and dynamic approach.

Morphology of the GGO in CT scan

Certain features were associated with higher invasive risk[59]:
1. Larger size > 10.5 mm
2. Larger solid component (> 6 mm)
3. Features of lobulated or spiculated margin
4. Architectural distortion
5. Presence of air bronchogram
6. Adjacent pleural retraction
7. Abnormal pulmonary artery or vein transversing inside GGO
8. Atypical pulmonary cyst with growing wall thickness and nodularity
9. Multiloculated cyst with increased wall thickness, loculation, nodularity and consolidation.

Nodule Size and Density

Pure GGOs (pGGOs) generally carry a very low risk of invasive malignancy. For pGGOs < 5 mm, the likelihood of malignancy is negligible, and annual CT follow up is universally recommended. For pGGOs ≥ 5 mm, guidelines advocate periodic surveillance with CT every 6 - 12 months, depending on stability. Surgical resection is typically reserved for pGGOs that demonstrate interval growth, an increase in mean diameter (average of longest and shortest diameter) ≥ 1.5 mm[9,14] or the new appearance of a solid component, as these are highly suggestive of transition to a more aggressive state. For GGOs > 10 - 15 mm that remain persistent in surveillance CT may also be considered for biopsy or resection.

Mixed GGOs or part-solid nodules demand greater clinical concern. The indications for surgical resection include part solid nodules ≥ 8 mm with morphological features of lobulated and spiculated margin persisting at follow up CT or part solid nodules with a solid component > 6 mm at follow up[141]. A part solid nodule with a solid component > 8 mm is also considered a strong indication for further diagnostic work up, which may include PET CT, non surgical biopsy, or direct surgical excision.

GROWTH KINETICS AND VOLUME DOUBLING TIME

Serial CT surveillance is indispensable for GGO management. Increase in size ≥ 1.5 mm in mean diameter or a clear increase in solid proportion on follow up CT is an unequivocal trigger for surgery[94,141]. Some institutions also employ volumetric analysis and 3D reconstruction to quantify growth more precisely. Long-Kanker Screening Onderzoek (NELSON trial[36,37,38], nodules with relative growth of more than 25 % in volume and a volume doubling time (VDT) of less than 400 days were defined as positive. Importantly, the decision to operate should not be based on a single time point scan; rather, it should follow at least one confirmatory scan after an initial suspicious finding to exclude transient inflammatory changes. .

The Curative Time Window

When surgery is considered for GGOs with growth, resection should be suggested within the "curative time window", which is defined as AIS and MIA stages in pathology (radiologically likely represented by pure GGOs < 3 cm and mGGOs with a solid component < 6 mm) because these patients can achieve a 100 % survival rate and can be really cured.

Patient Related Factors

Surgical candidacy is not determined solely by nodule characteristics. The patient's age, performance status, pulmonary reserve, other comorbidities, and personal preferences must be carefully weighed. For elderly patients or those with limited cardiopulmonary reserve, a strategy of active surveillance may be entirely appropriate, even for mGGOs with low risk features, as competing risks of mortality from other causes may outweigh the benefit of immediate resection. Conversely, young, fit patients with a growing mGGO are ideal candidates for timely surgery.

THE ROLE OF MULTIDISCIPLINARY TEAM (MDT) EVALUATION

Given the complexity of GGO interpretation, no single specialty should decide on surgical indication independently. A MDT comprising thoracic surgeons, radiologists, pathologists, and medical oncologists provides the most balanced assessment. The AATS expert Consensus[141]: current guidelines uniformly endorse MDT decision making as the standard of care for GGO management.

Surgical Treatment

Lobectomy versus Limited Resection (Sublobar Resection)

Once the decision to operate is made, the surgeon faces a fundamental choice: to perform a standard lobectomy or opt for a more parenchyma sparing limited resection, which includes wedge resection (non anatomical) or anatomical segmentectomy(anatomical). This choice

has profound implications for oncological radicality, perioperative morbidity, long term pulmonary function, and quality of life. The historical dominance of lobectomy has been challenged by modern evidence, but the debate is far from settled, and the optimal approach must be individualised.

The LCSG 821 trial in 1995[72] randomly assigned patients with clinical T1N0 (≤ 3 cm) non-small cell lung cancer (NSCLC) to lobectomy or limited resection (mostly wedge)[72]. It found that limited resection was associated with a tripled local recurrence rate (17 % vs 6 %) and a 30 % increase in overall death for patients who underwent limited resections. In Western nations, lobectomy became the undisputed standard of care for resectable NSCLC.

Two practice changing randomised controlled trials have reevaluated the role of limited resection in small sized peripheral NSCLC – precisely the population of most GGO related lesions. JCOG0802 (published in The Lancet, 2022[73]) was a multicentre, non inferiority trial that randomised 1,106 patients with clinical stage IA NSCLC (tumour diameter ≤ 2 cm, CTR > 0.5) to lobectomy versus segmentectomy. At a median follow up of 7.3 years, the 5 year overall survival was 94.3 % in the segmentectomy group versus 91.1 % in the lobectomy group, not only demonstrating non inferiority but actually suggesting a survival benefit for segmentectomy. The 5-year relapse free survival was also comparable.

Interestingly, locoregional recurrence appeared to increase after segmentectomy compared to lobectomy (10.5 % versus 5.4 %), yet the lower rate of overall survival in the lobectomy group could have been attributed to a higher number of patients who died from a second cancer. Another surprising finding from the trial included the relatively modest improvement in FEV1 after segmentectomy compared to lobectomy - a 3.5 % difference when measured one year after surgery. Regarding postoperative outcomes, the participating institutions achieved a mortality rate of 0 % in both surgical arms.

CALGB 140503 (published in The New England Journal of Medicine, 2023[74]) enrolled 697 patients with clinical T1aN0 (≤ 2 cm) peripheral NSCLC, including both solid and part solid nodules, and compared lobectomy with sublobar resection (mainly segmentectomy, with wedge allowed for non anatomically resectable lesions). At a median follow up of seven years, the 5 year disease free survival was 63.6 % for sublobar resection versus 64.1 % for lobectomy, confirming non inferiority (HR = 1.01; 90 % CI, 0.83 1.24). Overall survival also showed no significant difference (80.3 % vs. 78.9 %; HR = 0.95; 95 % CI, 0.72 1.26). The investigators did not observe any substantial difference between treatment groups regarding the incidence of locoregional or distant disease recurrence. A 6-month postoperative evaluation of pulmonary function showed a between group difference of two percentage points in median percentage of predicted FEV1 in favour of the sublobar resection group. It should be noted that more than half of the patients in the sublobar arm underwent wedge resections rather than anatomical segmentectomies.

These two trials collectively provide robust level 1 evidence that for peripheral NSCLC ≤ 2 cm - which includes the vast majority of operable GGOs with a solid component - sublobar resection, particularly anatomical segmentectomy, is an acceptable alternative to lobectomy, with comparable survival, lower perioperative morbidity, and better functional preservation, albeit at the cost of a modestly increased local recurrence rate.

ONCOLOGICAL OUTCOMES: LOCAL RECURRENCE, DISTANT METASTASIS, AND SURVIVAL

The central trade off is between local control and overall survival. Both JCOG0802 and CALGB 140503 consistently showed that limited resection increases the risk of local recurrence (by about 5 - 8 percentage points). However, because most local recurrences after sublobar resection occur at the margin or in the same lobe and are amenable to salvage therapy (re resection, radiotherapy, or ablative techniques), overall survival remains unaffected. Moreover, GGO dominant tumours have a lower propensity for lymphatic and haematogenous spread; the risk of occult nodal metastasis is exceedingly low for pGGO and even for mGGO with a CTR ≤ 0.5. This biological indolence explains why a less radical resection does not compromise survival. Studies have shown that thoracoscopic anatomic segmentectomy for the treatment of pulmonary GGOs is able to achieve similar short term and long term outcomes to those of lobectomy.

Distant metastasis rates are similar between the two procedures, suggesting that systemic control is governed by tumour biology rather than the extent of local excision. Importantly, both trials included patients with solid nodules; for pure GGNs or minimally invasive tumours, the local recurrence advantage of lobectomy is likely even smaller, and the functional benefit of segmentectomy becomes more compelling.

Pulmonary Function and Quality of Life

Preservation of lung parenchyma is a major argument in favour of limited resection. Although the functional difference at 6 - 12 months is modest (an average 2 - 3 % advantage in FEV1), it may be clinically meaningful for patients with pre existing COPD or poor pulmonary reserve. For patients with multiple primary GGOs (a common scenario), repeated limited resections can preserve enough lung function to avoid respiratory disability Quality of life assessments from both trials indicate a slight but consistent benefit in physical functioning and symptom scores favouring sublobar resection.

Perioperative Morbidity and Mortality

Sublobar resection is generally associated with shorter operative time, less blood loss, reduced chest tube duration, and shorter hospital stay compared to lobectomy. Compared to segmentectomy, wedge resection has a significantly lower rate of complications (3.8 % vs 7.7 %, P = 0.008) and a shorter operating time (65 min vs 114 min). For elderly or frail patients, the reduced morbidity of limited resection can be a decisive factor.

Nodal Assessment and Surgical Margins

A crucial warning is that wedge resection (non anatomical) is not equivalent to segmentectomy. Wedge resection does not allow systematic lymph node sampling, and the margin distance may be inadequate. Both JCOG0802 and CALGB 140503 predominantly used segmentectomy (about 80 - 85 % of sublobar cases), with wedge reserved for very small peripheral, very lesions. The National Comprehensive Cancer Network (NCCN) (107) guidelines recommend that for peripheral T1abN0 GGO-dominant tumours, segmentectomy and wedge resection should be strongly considered. Shared decision making with MDT and incorporating the patient's understanding of the indolent nature of most GGOs and the potential morbidity of surgery, is essential. When sublobar resection is performed, anatomical segmentectomy with adequate lymph node evaluation was the preferred procedure (at least sampling of hilar and mediastinal stations) and a surgical margin > 5 mm cm to minimise local recurrence.

Recent studies[73,74,82,84] demonstrated that wedge resection could yield comparable results for patients with GGO dominant NSCLC ≤ 2 cm and CTR between 0.25 and 0.5. For patients with peripheral GGO dominant lung cancer < 2 cm and CTR < 0.5, sublobar resection achieves excellent outcomes, with wedge resection is first choice. Five year recurrence free survival following wedge resection was 96.89 % for patients with GGO ≤ 2 cm (CTR ≤ 0.5[81,82]. For deeply located GGNs, segmentectomy if technically feasible, should be the choice, whereas wedge would compromise margins and is discouraged.

Given the evidence, the choice between lobectomy and segmentectomy should be individualised. For nonperipheral GGOs > 2 cm and < 3 cm segmentectomy is increasingly preferred because of adequate margin, and local recurrence after segmentectomy is very low. For mGGOs > 3 cm with a large solid component (CTR > 0.5), lobectomy still offers superior local control for patients with adequate pulmonary reserve: however, in patients with borderline FEV1 or DLCO, segmentectomy is the clear choice to avoid postoperative respiratory failure. Multiple GGOs: for patients with synchronous or metachronous bilateral GGOs, segmentectomies or wedge resections (for peripheral lesions) are preferred to preserve maximum parenchyma for future interventions.

The AATS expert consensus provides specific recommendations that reflect updated insights on subsolid nodule management. In practice, many academic centres now adopt a risk stratified approach: low risk GGOs (pGGO, or mGGO with CTR ≤ 0.25) are often treated with wedge or segmentectomy; intermediate risk lesions (CTR 0.25 - 0.5) may still receive segmentectomy; and high risk lesions (CTR > 0.5 or size > 2 cm) are managed with lobectomy, unless function is compromised. The decision should always be discussed with the patient, explaining the trade off between a slightly higher local recurrence risk and better preservation of lung function.

CONCLUSION

The surgical management of pulmonary ground glass nodules has evolved from a standard lobectomy approach to a nuanced, patient and nodule tailored strategy. Indications for surgery have become more conservative, emphasising growth and solid component evolution, and relying heavily on multidisciplinary collaboration to avoid overtreatment of indolent lesions. The AATS expert consensus provides evidence based guidance for thoracic surgeons and other medical professionals who care for patients with subsolid nodules.

The pivotal JCOG0802[73], and CALGB 140503 trials[74] have firmly established that sublobar resection is non inferior to lobectomy in overall survival for small sized (≤ 2 cm) peripheral NSCLC, including the majority of clinically relevant GGOs, with the advantages of better pulmonary function preservation and lower morbidity, albeit with a slightly higher local recurrence rate. Segmentectomy should be cautiously performed for patients with radiologically solid dominant non lepidic invasive adenocarcinoma, especially for those with high grade patterns.

The future direction lies in further refining patient selection. Molecular biomarkers, radiomics, and artificial intelligence based growth prediction models may soon enable even more precise differentiation between indolent and aggressive GGOs, potentially allowing some patients to avoid surgery altogether. For those who do proceed, minimally invasive limited resection will likely become the dominant procedure for the vast majority of GGOs, with lobectomy reserved for larger or more solid lesions. Importantly, high quality surgical technique - ensuring negative margins and adequate nodal assessment - is the cornerstone of successful limited resection. Ultimately, the goal is not simply to remove the nodule, but to cure the patient while preserving the best possible quality of life, a principle that now guides the modern surgical management of ground glass nodules of the lung.

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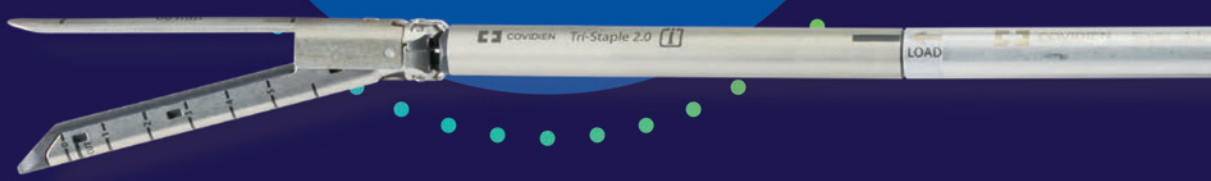
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Managing Pulmonary Nodules: Balancing Early Detection and Overdiagnosis -Pulmonologist Perspective



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ABSTRACT

Lung cancer remains the leading cause of cancer mortality in Hong Kong. Unlike Western populations, where smoking predominates as the primary risk factor, up to 40 - 50 % of lung cancers in East Asian patients occur in never-smokers and frequently present as subsolid nodules (pure ground-glass opacities [GGOs] or GGOs with solid components). Incidental pulmonary nodules are detected in up to 30 % of chest CT examinations. Driver oncogene alterations are more prevalent in Asian populations, and genetic factors are increasingly implicated alongside environmental exposures. Nevertheless, over 70 % of screen-detected lesions manifest as indolent GGOs, suggesting that many may never progress to clinically significant disease[1–2].

The central challenge lies in aligning expanding low-dose CT (LDCT) practice with emerging evidence to maximise benefit while minimising overdiagnosis and its associated harms - namely, the detection of cancers that would not become clinically apparent or cause death during a patient's lifetime if left undiscovered. In 2023, the Hong Kong Centre for Health Protection (CHP) and the Cancer Expert Working Group did not recommend routine or mass population LDCT screening for asymptomatic individuals, including those at average risk. Even for high-risk groups (heavy smokers), the CHP cited insufficient local data to fully assess benefits versus harms, advising that high-risk individuals consult their primary care physicians to weigh the risks of false positives and potential follow-up investigations before making an informed and individualised decision[3]. A prospective multicentre study in never-smokers (aged 55 - 75 years) with risk factors (family history, environmental exposures, chronic lung disease, etc.) demonstrated a high invasive lung cancer detection rate with a favourable stage shift (many stage 0/I). Family history emerged as a strong risk factor (1.6-fold increase; higher with multiple relatives or maternal side), supporting the feasibility of LDCT in high-risk never-smokers, with cancer detection rates competitive with smoker-focused trials[4].

PREVALENCE OF PULMONARY NODULES ON LDCT AND SIZE CRITERIA FOR POSITIVE FINDINGS

In the National Lung Screening Trial (NLST), approximately 24 % of LDCT scans were positive (nodules ≥ 4 mm or other suspicious findings) across screening rounds[5]. In a Korean study, prevalence was as high as 55.8 %, reflecting higher rates of subsolid nodules[6]. Other large trials align with Fleischner Society and Lung-RADS adaptations, commonly using ≥ 5 - 6 mm mean diameter as thresholds for action[7].

RISK STRATIFICATION AND PRETEST PROBABILITY OF MALIGNANCY

Pretest probability assessment integrates clinical and radiological factors to guide management. The Brock model, recommended by the British Thoracic Society, calculates the probability of malignancy based on the following parameters:

- Patient factors: Age, sex (female sex confers higher risk), family history of lung cancer, and emphysema.
- Nodule factors: Size, type (higher risk: part-solid > solid > pure ground-glass), upper lobe location, spiculation, and nodule count (fewer nodules increase risk for the dominant nodule).

Probability thresholds are categorised as: < 5 % low risk (surveillance), 5 - 65 % intermediate risk (further imaging/biopsy subject to joint decision), and > 65 % high risk (more aggressive evaluation)[8].

LDCT Monitoring Intervals per Current Guidelines

The Fleischner Society 2017 guidelines (updated for 2025 applications) for incidental nodules emphasise size (mean diameter) and risk stratification for solid nodules (< 6 mm, 6 - 8 mm, > 8 mm), pure ground-glass (< 6 mm, ≥ 6 mm), and part-solid nodules[9]. Lung-RADS (v2022) for screening uses categories 1 - 4 with shorter intervals for suspicious findings, including pulmonary cysts, nodule characteristics and location, and interval growth[10].

Radiological Findings Warranting Early Histological Proof

Not all nodules require immediate biopsy; most small, stable lesions warrant surveillance. Early histological confirmation (via CT-guided transthoracic needle biopsy, bronchoscopy, or surgery) is indicated when features suggest high malignancy risk or progression:[11]

- **Size**: Solid nodules > 8 mm or part-solid with solid component ≥ 6 - 8 mm.
- **Growth**: Documented increase, particularly new or enlarging solid components in subsolid nodules.
- **Morphology**: Spiculated or irregular margins, lobulation, pleural retraction, or thick/irregular cavitation.
- **Attenuation and location**: Upper lobe predominance; persistent or enlarging subsolid nodules.
- **PET/CT avidity**: FDG uptake in nodules > 8 - 10 mm supports malignancy, though sensitivity is limited for small or ground-glass lesions.
- **Additional features**: Associated lymphadenopathy, multiple suspicious nodules without dominant benign features, or high pretest probability (> 65 % by Brock).

Interventional Approaches to Pulmonary Nodules

Interventional options are broadly divided into CT-guided transthoracic needle biopsy (CT-TTNB) and bronchoscopic approaches.

CT-Guided Transthoracic Needle Biopsy

CT-TTNB offers a high diagnostic yield, approximately 90 %, as it is performed under real-time imaging guidance. However, it carries a notable risk of pneumothorax (20 - 25 %), with chest tube insertion required in 5 - 15 % of cases[12–13]. It cannot be combined with mediastinal staging and is generally of lower procedural cost than bronchoscopic biopsy in the absence of pneumothorax or other complications. This approach is most suitable when bronchoscopic approaches are contraindicated or likely to fail (e.g. very peripheral lesions without airway access), and is preferred for peripheral lesions in patients with good lung function who can tolerate potential pneumothorax. It is performed under local anaesthesia, though some patients may find the procedure uncomfortable.

Bronchoscopic Biopsy

Contemporary bronchoscopic biopsy incorporates various modalities, including peripheral radial endobronchial ultrasound (diagnostic yield 65 - 73%) with or without guided sheath,[14] virtual (see Fig. 1) or electromagnetic navigation bronchoscopy (ENB) (diagnostic yield ~ 70 %),[15] and robotic-assisted bronchoscopy (diagnostic yield ~ 80 %),[16] with escalating costs. Diagnostic yield is highly dependent on the presence of a positive bronchus sign, with lower yield for lesions in the upper lobes and dependence on operator expertise. The risk of pneumothorax is generally low (< 5 %)[15]. Bronchoscopic biopsy is most suitable for nodules with a positive bronchus sign and when safety is a priority (e.g. in patients with emphysema or poor lung reserve who cannot tolerate pneumothorax). It is preferred when mediastinal staging is also needed during the same procedure.

EBUS-TBNA for Mediastinal Staging

In patients with positive or equivocal mediastinal/hilar lymph nodes on PET scan, convex probe endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is the first-line tool, as it provides a high diagnostic yield (93 - 97 %) under real-time guidance. It carries a very low complication risk (< 1 %) and allows molecular testing, including next-generation sequencing, while enabling mediastinal staging that has largely replaced mediastinoscopy[17].

Upfront Surgical Resection

Upfront surgical resection under video-assisted thoracic surgery (VATS) may be considered without preoperative biopsy when there is a high pretest probability of malignancy > 65 % based on validated models,[18] in a surgically fit patient, when biopsy risk is high or yield likely low, and after shared decision-making and multidisciplinary discussion. Surgical approaches are discussed elsewhere in this issue.

CASE PRESENTATION

A 59-year-old man, a non-smoker with a family history of lung cancer, underwent a health check-up LDCT of the thorax, which revealed an incidental 1.1 cm lung nodule with a slightly irregular border at the right lung base (Fig. 2). No internal calcification or cavitation was observed; the radiology report suggested that neoplasm could not be excluded. No enlarged hilar or mediastinal lymph nodes were discerned. Bronchoscopy with bronchoalveolar lavage (BAL) was performed; cytology was negative for malignancy but demonstrated inflammatory cells. Microbiology grew methicillin-susceptible Staphylococcus aureus (MSSA); fungal and mycobacterial cultures were negative. A course of antibiotics according to susceptibility was administered. Reassessment CT demonstrated complete resolution of the nodule (Fig. 3).

DISCUSSION

This case illustrates the diagnostic challenges encountered when managing a solitary lung lesion in a patient with a family history of lung cancer. The lesion's proximity to the diaphragm rendered CT-guided needle biopsy potentially risky, while bronchoscopic biopsy might not reach the lesion for histological confirmation. Bronchoscopy, however, provided microbiological evaluation and guided appropriate antibiotic therapy before empirical surgical resection was considered. For suspicious pulmonary nodules, referral to a pulmonologist or adoption of a multidisciplinary approach may prevent futile surgery, even when both the lesion and the patient appear surgically suitable.

CONCLUSIONS

Pulmonary nodules are common incidental or screening-detected findings on chest CT, posing diagnostic challenges that require balancing early malignancy detection with avoidance of unnecessary interventions. In Asian populations, the epidemiology

differs notably from Western cohorts, with a higher proportion of lung cancers occurring in never-smokers (particularly women) and a greater prevalence of subsolid nodules, often linked to adenocarcinoma spectrum lesions. Current guidelines emphasise LDCT surveillance intervals, radiological features warranting prompt histological evaluation, and validated pretest probability models such as the Brock model. Tailored approaches incorporating regional epidemiological data and patient-specific risk factors are essential for Asian contexts to optimise outcomes while minimising overdiagnosis and its associated harms.

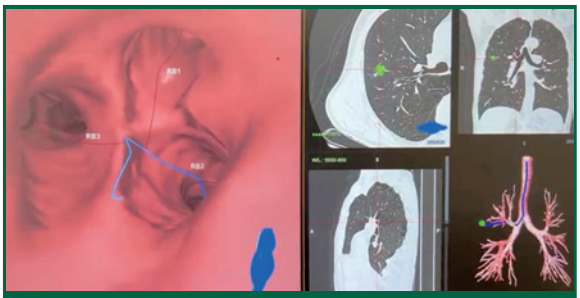


Fig. 1: Vitural Bronchoscopy guided bronchoscopic biopsy (Personal collection)

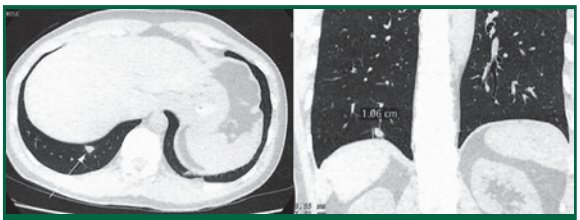


Fig. 2: It showed a 1.1 cm lung nodule at the right lung base, close to diaphragm (Personal collection)

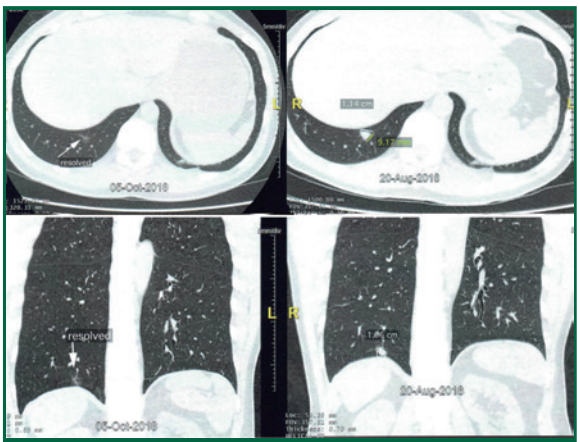


Fig. 3: It showed the resolved lung nodule before (right side) and after (left side) bronchoscopy and a course of antibiotics (Personal collection)

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Radiological Features of Ground-Glass Nodules of the Lung and the Role of CT-Guided Biopsy

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INTRODUCTION

Lung cancer remains a leading cause of cancer-related morbidity and mortality worldwide[5]. It was the commonest cancer in Hong Kong, accounting for 16.1 % of new cancer cases in 2023[11]. The prognosis is strongly stage-dependent, with early-stage disease detected as ground-glass opacity (GGO) carrying a 5-year survival rate approaching 100 %[3]. The increasing utilisation of low-dose CT (LDCT) for lung cancer screening, coupled with advances in CT technology, has dramatically increased the detection rate of pulmonary nodules, particularly those with ground-glass attenuation[2,5].

A ground-glass nodule (GGN) is defined as a circumscribed area of increased pulmonary attenuation that does not completely obscure the underlying bronchial and vascular structures, typically measuring ≤ 30 mm in diameter[2]. They are commonly detected as incidental findings and in screening programmes, creating a growing clinical need for reliable risk stratification. Although many GGNs are benign or transient, persistent GGNs are frequently associated with lesions along the lung adenocarcinoma spectrum, representing a continuum from preinvasive lesions - atypical adenomatous hyperplasia (AAH) and adenocarcinoma in situ (AIS) - to minimally invasive adenocarcinoma (MIA) and frankly invasive adenocarcinoma (IAC)[2,5,8].

Because imaging appearances overlap substantially among these entities, the optimal management of GGNs remains a subject of intense clinical interest. While CT-guided percutaneous biopsy is a well-established technique for diagnosing pulmonary nodules, its application to GGNs presents unique challenges and requires careful consideration of the radiological features that influence both the decision to biopsy and the technical success of the procedure[5,6,9]. This manuscript aims to review the current understanding of the radiological features of GGNs and to define the evolving role of CT-guided biopsy in their diagnostic pathway.

Radiological Features of Ground-Glass Nodules

The accurate characterisation of GGNs on CT is fundamental to determining the risk of malignancy and guiding further management. A combination of morphological and quantitative features should be assessed systematically[5,9].

Classification and Terminology

Standardised terminology is essential for clear communication and consistent management. Based on the Fleischner Society guidelines, nodules are classified by attenuation[2,8] (Fig. 1):

- Pure Ground Glass Nodule (pGGN): A nodule with ground-glass attenuation throughout, without any solid component.

- Part-Solid Nodule (PSN): A nodule containing both ground-glass and solid soft-tissue attenuation components.

- Solid Nodule: A nodule with completely soft-tissue attenuation, obscuring underlying structures.

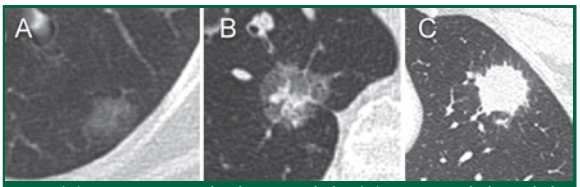


Fig. 1(A): Pure Ground Glass Nodule; (B): Part-Solid Nodule; (C): Solid Nodule
(Excerpted from https://www.researchgate.net/figure/Classification-of-lung-nodule-density-A-Ground-glass-nodule-B-Part-solid-nodule-C_fig1_317012515)

This distinction is clinically important because the solid component correlates more strongly with invasive histology and a higher risk of malignancy. In practice, the size and persistence of the solid portion are often more informative than the total nodule diameter alone[12].

Technically, accurate detection and characterisation require thin-section CT images (≤ 1 mm slice thickness), acquired at full inspiration, using a sharp reconstruction algorithm[2,8].

CT Morphological Characteristics

Nodule Size

Nodule size is a critical parameter in assessing malignancy risk and guiding follow-up. The Fleischner Society (Fig. 2) recommends that for a solitary pGGN > 6 mm, follow-up CT should be performed at 6 - 12 months to confirm persistence, and then every two years for five years. For a solitary PSN > 6 mm, initial follow-up at 3

- 6 months is recommended, and then annually for five years if unchanged and solid component < 6 mm[5,9].

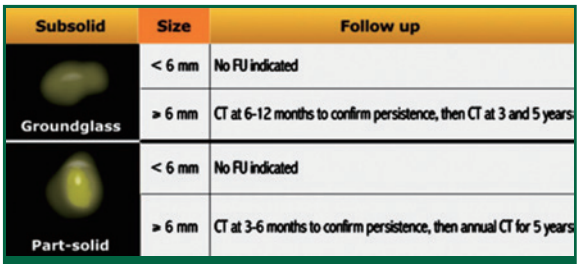


Fig. 2: Fleischner Society (2017) recommendation for solitary subsolid nodule follow up (From Radiology Assistant)

The size cut-off for distinguishing invasive from preinvasive lesions has been a focus of research. A diameter of ≥ 10 mm is often cited as a threshold associated with increased likelihood of invasiveness[5,9]. However, size alone is an inadequate predictor, and other features must be considered[5,9].

Margin and Interface

The characteristics of the nodule border (Fig. 3) provide valuable diagnostic information:

- Lobulation: An irregular, scalloped contour of the nodule margin. This is a well-recognised sign of malignancy and is an independent predictor of invasiveness[5,7,9].
- Spiculation: Fine linear strands extending from the nodule margin into the surrounding lung parenchyma. The presence of spiculation is a strong indicator of malignancy[5,7].
- Ill-Defined Boundary: A margin that is not sharp and distinct[7].

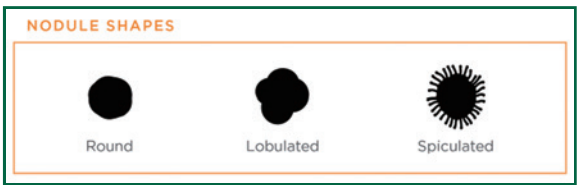


Fig. 3: Nodule border (Personal collection)

In general, clear and smooth margins are more commonly associated with benign or preinvasive lesions, while irregular, spiculated, or lobulated margins raise suspicion for invasion[2,5].

Internal Features

Several internal characteristics of GGNs are associated with malignancy and invasiveness:

- Vacuole Sign (Fig. 4) : A small, air-containing lucency within the nodule[4].

- **Cystic formation (Fig. 5)** : Lung cancer associated with cystic airspaces (LCCAs) was first defined by Farooqi et al. as "lung cancers that abut or are in the wall of cystic airspaces identified at CT, regardless of the pathology findings and irrespective of the presence of emphysema elsewhere in the lung"[14].

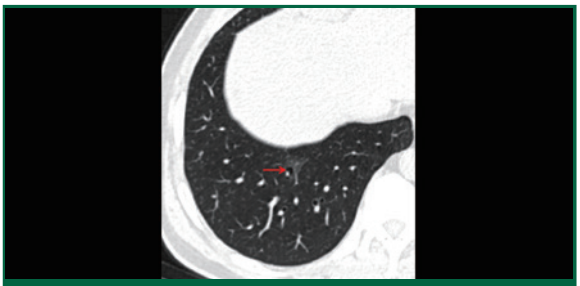


Fig. 4: Vacuole sign. A small, air-containing lucency within the nodule[4]. (Excerpted from "Bubble-like lucency in pulmonary ground glass nodules on computed tomography: a specific pattern of air-containing space for diagnosing neoplastic lesions." Cancer Imaging 2024 Apr 2;24:47. doi: 10.1186/s40644-024-00694-8)

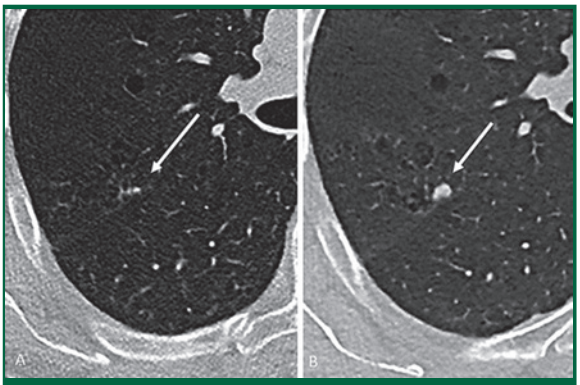


Fig. 5: Small area of increased density in the right superior lobe, adjacent to cystic emphysematous area (a) that increased in size and density after one year (b) and was proven to be an adenocarcinoma (Excerpted from "Lung Cancers Associated with Cystic Airspaces" Cancers 2025, 17(2), 307; https://doi.org/10.3390/cancers17020307.)

- Air Bronchogram (Fig. 6) : The presence of air-filled bronchi within the nodule. This can be seen in both benign and malignant lesions, but persistent air bronchograms within a GGN are often associated with adenocarcinoma[5,9].



Fig. 6: The air bronchogram sign in GGN (IAC) on a multiplanar reformation image, which is manifested as branching air density connecting with the proximal bronchus. GGN: ground glass nodule. IAC: invasive adenocarcinoma (Excerpted from https://www.researchgate.net/figure/The-air-bronchogram-sign-in-GGN-IAC-on-multiplanar-reformation-image-which-is_fig3_379517005)

- Solid Component (Fig. 7) : In PSNs, the size and proportion of the solid component are crucial. The consolidation-to-tumour ratio (CTR) is a key metric, where a higher CTR is associated with more invasive disease[1,5]. A persistent PSN with a solid component > 6 mm is considered highly suspicious for malignancy[5,9].

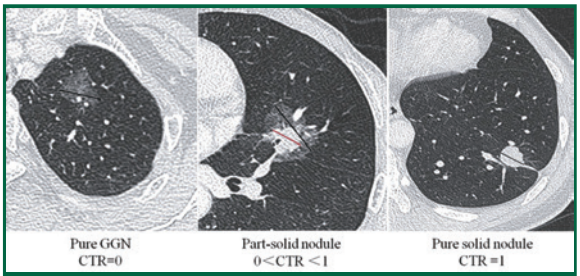


Fig. 7: Radiological measurements for consolidation-to-tumour ratio (CTR), the solid component size (red line), and tumour size (black line) (Excerpted from "Lung Adenocarcinomas Manifesting as Radiological Part-Solid Nodules Define a Special Clinical Subtype" TRANSLATIONAL ONCOLOGY Volume 14, Issue 4P617-627 April 2019)

- Vessel-Related Signs: Abnormalities in the pulmonary vessels associated with the nodule, such as vessel convergence, dilatation, or distortion, are known as tumour vascular signs and suggest neoplastic infiltration[5,9].

Ancillary Signs

- Pleural Tagging (Fig. 8)

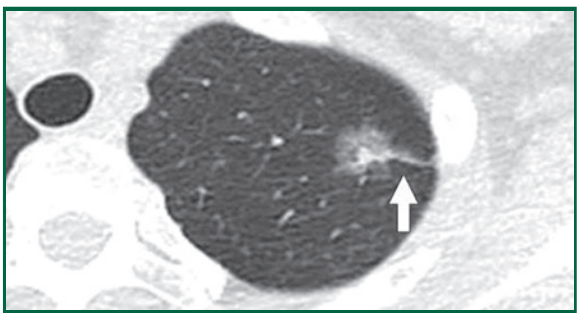


Fig. 8: Adenocarcinoma with pleural tag (arrow) in a 49-year-old woman (Excerpted from "Pleural Tags on CT Scans to Predict Visceral Pleural Invasion of Non-Small Cell Lung Cancer That Does Not Abut the Pleura" Radiology Volume 279, Number 2 https://doi.org/10.1148/radiol.2015151120)

- Pleural/Fissural Retraction (Fig. 9) : This sign, where the visceral pleura is pulled towards the nodule, is a classic feature of malignancy due to tumour desmoplasia and fibrosis[5,7,9].

- Location: An upper lobe distribution has been linked to a higher risk of malignant tumours, with the right upper lobe having the highest incidence of lung cancer[5].

A narrative review published in 2024 emphasised that multiple imaging features should be combined rather than interpreted in isolation, because no single sign is definitive[13].

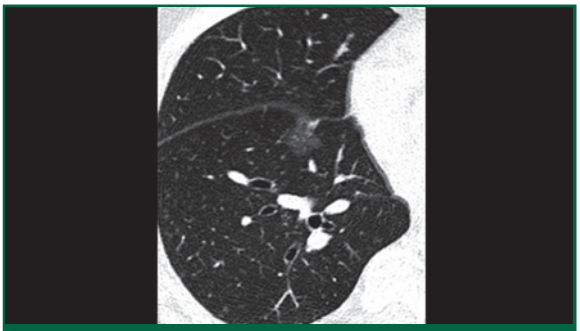


Fig. 9: Ground glass density in right lower lobe causing fissural retraction (Excerpted from "Imaging diagnostics of pulmonary ground-glass nodules: a narrative review with current status and future directions". 2024 Jul 18;14(8):6123–6146. doi: 10.21037/qims-24-674)

LUNG-RADS VS FLEISCHNER SOCIETY GUIDELINES

Choosing between Lung-RADS and the Fleischner Society Guidelines is not a matter of clinical preference or personal choice; rather, it depends entirely on how and why the CT scan was performed. Both systems provide standardised recommendations for managing pulmonary nodules, but they are tailored to completely different patient populations and clinical settings[18].

Follow Lung-RADS if the scan is a low-dose CT (LDCT) specifically performed for lung cancer screening in an asymptomatic, high-risk individual (e.g. qualifying long-term smokers).

Follow Fleischner Society Guidelines if the nodule was found incidentally on a CT scan ordered for another reason.

Exceptions will be the following:

- Known Malignancy: If a patient has an active primary cancer elsewhere, nodules are evaluated for potential metastasis based on oncologic protocols, not Fleischner or Lung-RADS.
- Immunocompromised Patients: Nodules in immunocompromised individuals are treated primarily as potential active infections and require immediate clinical evaluation.
- Age Limits: Fleischner guidelines explicitly do not apply to patients under 35 years of age.
- Symptomatic Patients: If a nodule is accompanied by acute symptoms of infection (such as fever, severe cough, or active inflammation), infectious workup takes priority.

CONVENTIONAL-DOSE (STANDARD) VS LOW-DOSE (LDCT) VS ULTRA-LOW-DOSE (ULDCT) CHEST CT

Choosing between these chest CTs come down to balancing diagnostic detail against radiation exposure. The fundamental rule in radiology is ALARA (As Low As Reasonably Achievable): use the lowest radiation dose that provides sufficient image quality to answer the specific clinical question.

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VAXNEUVANCE helps protect pediatrics against ST3-associated IPD[1]

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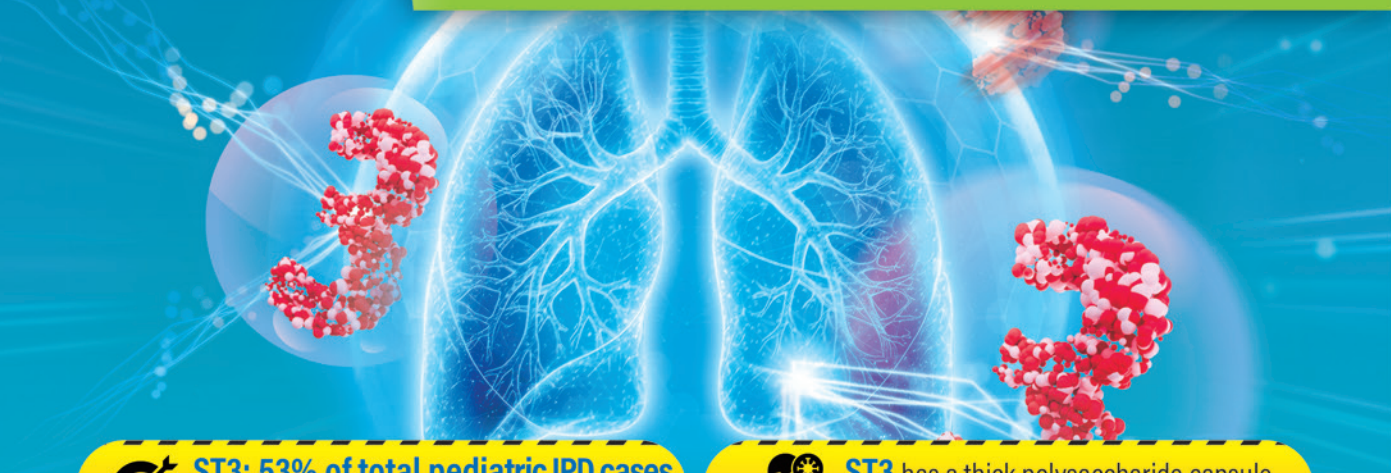
Infants

According to a phase 3, randomized, double-blind study (n=1720)

PCV15 was non-inferior to PCV13 for all 15 shared serotypes based on IgG response rates at PD 3 and demonstrated superior immunogenicity against ST3[2]

73% **higher immunogenicity against ST3 vs PCV13**[1,2]
GMC ratio (PCV15/PCV13): 1.73 (95% CI 1.61-1.87) P<0.001

>92% of participants experienced at least one AE. The most common AEs were those solicited in the trial, with the 3 most frequently reported AEs being irritability, somnolence, and injection-site pain[2]



ST3: 53% of total pediatric IPD cases in Hong Kong in 2025[3,*]

ST3 has a thick polysaccharide capsule, **making it highly virulent**[4]

ST3: ~40% of AMR serotypes based on epidemiological analyses of medical records in pediatric patients (n=37661)[5] (AMR narrows treatment options, making treatment more challenging![6])

*According to data from CHP

Study design (Lupinacci R, et al. 2023): This study was a phase 3, randomized, active comparator-controlled, double-blind study to evaluate the safety, tolerability, and immunogenicity of a 4-dose regimen of Vaxneuvance in healthy infants (protocol V114-029). It was conducted from June 2019 to May 2021. The study enrolled 1720 participants randomized in a 1:1 ratio to receive a 4-dose vaccination regimen of Vaxneuvance (n=858) or PCV13 (n=856). Primary immunogenicity objectives were to compare Vaxneuvance to PCV13 for non-inferiority for all serotypes using anti-PnPs serotype-specific IgG response rates (proportion of participants meeting the serotype-specific IgG threshold value of ≥ 0.35 lg/ml) at 30 days PD3 and IgG geometric mean concentrations (GMCs) at 30 days PD3 and 30 days PD4. Serotypes 22F and 33F were compared to the lowest response rate or IgG GMC for any of the 13 shared serotypes among recipients of PCV13, excluding serotype 3. For IgG GMCs, the lower bound of the 2-sided 95 % CI for the Vaxneuvance/ PCV13 GMC ratios needed to be > 0.5 to meet non-inferiority criteria. Secondary objectives were to compare Vaxneuvance to PCV13 for superiority for IgG against serotypes 3, 22F, and 33F using anti-PnPs serotype-specific IgG response rates at 30 days PD3 and IgG GMCs at 30 days PD3 and 30 days PD4. For IgG response rates and IgG GMCs to serotypes 22F and 33F, the lower bound of the 2-sided 95 % CI for the between-group differences needed to be > 10 percentage points and > 2.0, respectively, to meet superiority criteria. For shared serotype 3, superiority based on IgG response rates and IgG GMCs was demonstrated if the lower bound of the 2-sided 95 % CI for the between-group differences needed to be > 10 percentage points and > 1.2, respectively.[2]

Study design (Lau JCH, et al. 2023): Data were retrieved from the population-wide CDARS, for hospitalisation episodes with IPD, invasive infections, and OM from 2012-2019 for patients aged <18 years. Diagnosis were defined by International Classification of Diseases, 9th Revision, Clinical Modification, 40503 episodes were identified from 37661 patients. Collected data include patient demographics, diagnoses, and microbiological culture and laboratory test results — including antimicrobial sensitivity and serotyping. Descriptive statistics were tabulated by each hospitalisation episode for (1) antimicrobial susceptibility(Sensitive/Intermediate/Resistance); and (2) serotype of the the isolate.[5]

Abbreviations: AEs=adverse events; AMR=antimicrobial resistance; CDARS=clinical data analysis and reporting system; CHP=Centre for Health Protection; CI=confidence interval; GMC=geometric mean concentration; IgG=immunoglobin G; IPD=invasive pneumococcal disease; GMT=geometric mean titer; OM=otitis media; PCV13=13-valent pneumococcal conjugate vaccine; PCV15=15-valent pneumococcal conjugate vaccine; PD=post-dose; PnPs=pneumococcal polysaccharide; ST3=serotype 3

References: 1. VAXNEUVANCE product circular, MSD. **2.** Lupinacci R, et al. A phase 3, multicenter, randomized, double-blind, active-comparator-controlled study to evaluate the safety, tolerability, and immunogenicity of a 4-dose regimen of V114, a 15-valent pneumococcal conjugate vaccine, in healthy infants (PNEU-PED). Vaccine. 2023;41(53):1142-1152. **3.** Centre for Health Protection, Communicable Disease Watch, Report on IPD. **4.** Hammerschmidt S, et al. Illustration of Pneumococcal Polysaccharide Capsule during Adherence and Invasion of Epithelial Cells. Infect Immun. 2005;73(8):4653–4667. **5.** Lau JCH, et al. PVI0695 - Antimicrobial resistance in paediatric patients with pneumococcal infection in Hong Kong - epidemiology analysis of medical records 2012-2019' (ID 620) [Poster 0310] - E-poster viewing: AS08.b Bacterial pneumonia (ID 167). ESPID 2023. **6.** Subramanian R, et al. Persistence of Pneumococcal Serotype 3 in Adult Pneumococcal Disease in Hong Kong. Vaccines (Basel). 2021;9(7):756.

VAXNEUVANCE Selected Safety Information Indications: •Vaxneuvance is indicated for active immunisation for the prevention of invasive disease, pneumonia and acute otitis media caused by Streptococcus pneumoniae in infants, children and adolescents from 6 weeks to less than 18 years of age. •Vaxneuvance is indicated for active immunisation for the prevention of invasive disease and pneumonia caused by Streptococcus pneumoniae in individuals 18 years of age and older. •The use of Vaxneuvance should be in accordance with official recommendations. **Dosing:** Vaccination with Vaxneuvance is recommended for selected individuals as follows: Individuals 18 years of age and older •1 dose (0.5 mL). •The need for revaccination with a subsequent dose of Vaxneuvance has not been established. Paediatric population •The safety and efficacy of Vaxneuvance in children and adolescents less than 18 years of age please consult the full prescribing information. Special populations •One dose of Vaxneuvance may be given to individuals who have one or more underlying conditions predisposing them to an increased risk of pneumococcal disease (e.g., adults living with human immunodeficiency virus (HIV) or immunocompetent adults 18 to 49 years of age with risk factors for pneumococcal disease). **Contraindications:** Hypersensitivity to the active substances, to any of the excipients, or to any diphtheria toxoid-containing vaccine. **Precautions:** •In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded. •Vaxneuvance must not be administered intravascularly. •As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of a rare anaphylactic event following the administration of the vaccine. •Vaccination should be postponed in individuals suffering from acute severe febrile illness or acute infection. The presence of a minor infection and/or low-grade fever should not delay vaccination. •As with other intramuscular injections, the vaccine should be given with caution to individuals receiving anticoagulant therapy, or to those with thrombocytopenia or any coagulation disorder such as haemophilia. Bleeding or bruising may occur following an intramuscular administration in these individuals. •The potential risk of apnoea and the need for respiratory monitoring for 48-72 hours should be considered when administering the primary immunisation series to very premature infants (born ≤ 28 weeks of gestation) and particularly for those with a previous history of respiratory immaturity. As the benefit of vaccination is high in this group of infants, vaccination generally should not be withheld or delayed. •Immunocompromised individuals, whether due to the use of immuno-suppressive therapy, a genetic defect, HIV infection, or other causes, may have reduced antibody response to active immunisation. Safety and immunogenicity data for Vaxneuvance are available for individuals living with HIV infection. Safety and immunogenicity data for Vaxneuvance are not available for individuals in other specific immunocompromised groups (e.g., haematopoietic stem cell transplant) and vaccination should be considered on an individual basis. •As with any vaccine, vaccination with Vaxneuvance may not protect all vaccine recipients. Vaxneuvance will only protect against Streptococcus pneumoniae serotypes included in the vaccine. •This medicinal product contains less than 1 mmol sodium (23 milligrams) per dose, i.e. essentially 'sodium-free'. **Adverse events:** The most frequently reported adverse reactions following vaccination with Vaxneuvance were solicited. The most frequent adverse reactions were pyrexia, injection-site pain, fatigue, myalgia, headache, injection-site swelling, injection-site erythema and arthralgia. The majority of solicited adverse reactions were mild (based on intensity or size) and of short duration (≤ 3 days); severe reactions (defined as being extremely distressed or unable to do usual activities or size > 7.6 cm) occurred in (4.5% of children and adolescents; severe reactions (defined as an event that prevents normal daily activity or size > 10 cm) occurred in <1.5% of adults across the clinical program. •Older adults reported fewer adverse reactions than younger adults. •For detailed side effects, please consult the full prescribing information. **Drug interactions:** •Different injectable vaccines should always be administered at different injection sites. •Immunosuppressive therapies may reduce the immune responses to vaccines. Infants and children aged 6 weeks to less than 2 years •Vaxneuvance can be given concomitantly with any of the following vaccine antigens, either as monovalent or combination vaccines: diphtheria, tetanus, pertussis, poliomyelitis (serotypes 1, 2 and 3), hepatitis A, hepatitis B, Haemophilus influenzae type b, measles, mumps, rubella, varicella and rotavirus vaccine. Children and adolescents 2 to less than 18 years of age •There are no data on the concomitant administration of Vaxneuvance with other vaccines. Data from a post-marketing clinical study evaluating the impact of prophylactic use of antipyretics (ibuprofen and paracetamol) on the immune response to other pneumococcal vaccines suggest that administration of antipyretics concomitantly or within the same day of vaccination may reduce the immune response after the infant series. Responses to the booster dose administered at 12 months were unaffected. The clinical significance of this observation is unknown. Adults •Vaxneuvance can be administered concomitantly with seasonal quadrivalent influenza vaccine (split virion, inactivated). There are no data on the concomitant administration of Vaxneuvance with other vaccines. **Pregnancy** •There is limited experience with the use of Vaxneuvance in pregnant women. •Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryo/foetal development, parturition or post-natal development. •Administration of Vaxneuvance in pregnancy should only be considered when the potential benefits outweigh any potential risks for the mother and the foetus. **Breast-feeding** •It is unknown whether Vaxneuvance is excreted in human milk. **Fertility** •No human data on the effect of Vaxneuvance on fertility are available. Animal studies in female rats do not indicate harmful effects.

Before prescribing, please consult the full prescribing information.

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HK-PVC-00325 Jun/2026

CAPVAXIVE®
Pneumococcal 21-valent
Conjugate Vaccine

CAPVAXIVE (PCV21) :

A *NEW* pneumococcal vaccine aligned with evolving serotypes in IPD prevention[1-3]



Distinctively covers top 3 serotypes (3, 15A, 23A) in adults aged ≥65 years in 2025[2,3,†]

22 serotypes coverage[2,#]

- According to a phase 3 trial in adults (n=717), PCV21 demonstrated **comparable immunogenicity against ST3** compared with PCV15[4]
- **Established safety profile:** Most adverse events were mild-to-moderate injection-site pain, and fatigue, typically resolving within 3 days. The proportion of participants with solicited injection-site and systemic AEs were generally similar between vaccine groups within each cohort. Serious adverse events were experienced by 1.8% of all participants, including 1.2% of those who received PCV21, 3.4% of those who received PCV15, and 3.5% of those who received PPSV23. No deaths occurred during the study[4]

†The top 3 serotypes (3, 15A and 23A) causing IPD in adults aged ≥65 years in 2025 in Hong Kong[2]
#PCV21 is approved for the prevention of invasive disease caused by 22 *Streptococcus pneumoniae* serotypes in adults[3]

Study design (Scott P. et al. 2024): This was a phase 3, double-blind (cohorts 1 and 2), open-label (cohort 3), multicenter, active comparator, parallel assignment study. A total of 717 adults (vaccine-experienced adults ≥50 years of age) were enrolled to receive a single dose of pneumococcal vaccine as follows: cohort 1 (n = 350) previously received PPSV23 and were randomized 2:1 to receive PCV21 or PCV15, respectively; cohort 2 (n = 281) previously received PCV13 and were randomized 2:1 to receive PCV21 or PPSV23, respectively; cohort 3 (n = 106) previously received PPSV23 + PCV13, PCV13 + PPSV23, PCV15 + PPSV23, or PCV15 and all received open-label PCV21. Immunogenicity was evaluated 30 days postvaccination using opsonophagocytic activity geometric mean titers and immunoglobulin G geometric mean concentrations for all PCV21 serotypes. The primary immunogenicity objective was to evaluate the serotype-specific opsonophagocytic activity (OPA) geometric mean titers (GMTs) at 30 days postvaccination for all V116 serotypes. Secondary objectives were to evaluate the serotype-specific IgG geometric mean concentrations (GMCs), as well as the geometric mean fold rise (GMFR) and proportion of participants with a ≥4-fold rise in serotype-specific antibodies from baseline (day 1) to 30 days postvaccination for all V116 serotypes. Safety was evaluated as the proportion of participants with adverse events.[4]

Abbreviations: AEs=adverse events; CHP=Centre for Health Protection; CI=confidence interval; GMCs=geometric mean concentrations; GMT=geometric mean titre; IPD=Invasive Pneumococcal Disease; OPA=opsonophagocytic activity; PCV15=15-valent pneumococcal conjugate vaccine; PCV21=21-valent pneumococcal conjugate vaccine; ST3=serotype 3

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CAPVAXIVE Selected Safety Information

Indications: • CAPVAXIVE is indicated for active immunisation for the prevention of invasive disease and pneumonia caused by *Streptococcus pneumoniae* in individuals 18 years of age and older. • The use of CAPVAXIVE should be in accordance with official recommendations. **Dosing:** Vaccination with CAPVAXIVE is recommended for selected individuals as follows: Individuals 18 years of age and older •1 dose (0.5 mL). • The need for revaccination with a subsequent dose of CAPVAXIVE has not been established. Paediatric population • The safety and efficacy of CAPVAXIVE in children younger than 18 years of age have not been established. No data are available. **Contraindications:** Hypersensitivity to the active substances including diphtheria toxoid, or to any of the excipients. **Precautions:** • In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded. • As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of a rare anaphylactic event following the administration of the vaccine. • Vaccination should be postponed in individuals suffering from acute severe febrile illness or acute infection. The presence of a minor infection and/or low-grade fever should not delay vaccination. • As with other intramuscular injections, the vaccine should be given with caution in individuals receiving anticoagulant therapy or those with thrombocytopenia or any coagulation disorder (such as haemophilia) because bleeding or bruising may occur following an intramuscular administration in these individuals. • Anxiety-related reactions, including vasovagal reactions (syncope), hyperventilation or stress-related reactions may occur in association with vaccination as a response to the needle injection. Stress-related reactions are temporary and resolve on their own. It is important that precautions are in place to avoid injury from fainting. • Safety and immunogenicity data on CAPVAXIVE are not available for individuals in immunocompromised groups. Vaccination should be considered on an individual basis. Based on experience with pneumococcal vaccines, immunocompromised individuals, including those receiving immunosuppressive therapy, may have a reduced immune response to CAPVAXIVE. • As with any vaccine, vaccination with CAPVAXIVE may not protect all vaccine recipients. This vaccine will only protect against *Streptococcus pneumoniae* serotypes included in the vaccine and to the cross-reactive serotype 15B. • This medicinal product contains less than 1 mmol sodium (23 mg) per dose, that is to say, essentially 'sodium-free'. • This medicinal product contains 0.5 mg of polysorbate 20 in each dose. Polysorbates may cause allergic reactions. **Adverse events:** The most frequently reported adverse reactions following vaccination with CAPVAXIVE in individuals 18 years of age and older were solicited. Overall, the most frequently reported adverse reactions were injection-site pain, fatigue, headache, and myalgia. The majority of local and systemic adverse reactions for individuals who received CAPVAXIVE were mild or moderate (based on intensity or size) and of short duration (≤ 3 days); severe reactions (defined as an event that prevents normal daily activity or size > 10 cm) occurred in ≤ 1.0% of adults. • For detailed side effects, please consult the full prescribing information. **Drug interactions:** • Different injectable vaccines should always be administered at different injection sites. • CAPVAXIVE can be administered concomitantly with quadrivalent influenza vaccine (split virion, inactivated). There are no data on the concomitant administration of CAPVAXIVE with vaccines other than influenza vaccines. **Pregnancy:** • There are no data on the use of CAPVAXIVE in pregnant women. • Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryo/foetal development, parturition or post-natal development. • Administration of CAPVAXIVE in pregnancy should only be considered when the potential benefits outweigh any potential risks for the mother and the foetus. **Breast-feeding:** • It is unknown whether CAPVAXIVE is excreted in human milk. **Fertility:** • No human data on the effect of CAPVAXIVE on fertility are available. Animal studies in female rats do not indicate harmful effects.
Before prescribing, please consult the full prescribing information.

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HK-PCN-00003 Aug/2026

Conventional-Dose (Standard) Chest CT
- Radiation Dose: 5-7 mSv (equivalent to about 2 - 3 years of background radiation).
- When to Choose: Diagnostic evaluations requiring high soft-tissue detail, contrast enhancement, or assessment of deep mediastinal structures.

Low-Dose Chest CT (LDCT)
- Radiation Dose: 1-1.5 mSv (up to 80 % reduction compared to standard CT).
- When to Choose: Routine screening or ongoing surveillance of non-acute lung parenchyma abnormalities without IV contrast.

Ultra-Low-Dose Chest CT (ULDCT)
- Radiation Dose: < 0.2 - 0.5 mSv (comparable to 1 to 3 standard chest X-rays).
- When to Choose: Rapid lung parenchymal checks using advanced iterative reconstruction techniques where minimal radiation is essential, particularly for young or frequently imaged patients.

THE ROLE OF CT-GUIDED BIOPSY IN GGN MANAGEMENT

Although malignant lesions are a major concern, not all GGNs represent cancer. Benign causes include focal inflammation, organising pneumonia, atypical infection, haemorrhage, focal fibrosis, and other nonspecific inflammatory processes.

The overlap between benign and malignant imaging appearances means that radiologic suspicion alone cannot always establish a diagnosis. This is particularly true for small pure GGNs, which may remain stable for long periods yet still harbour adenocarcinoma-spectrum pathology. For that reason, a combination of surveillance and tissue sampling is often required in selected cases.

CT-guided percutaneous needle biopsy is a reliable procedure for diagnosing malignant pulmonary nodules, with a reported sensitivity of approximately 90 % for lung cancer diagnosis[5,9]. However, its application to GGNs, particularly pGGNs, presents specific challenges that must be carefully considered.

Indications and Patient Selection

The decision to proceed with a CT-guided biopsy is based on a risk-benefit analysis, integrating patient factors, nodule characteristics, and surgical candidacy[10].

Indications for CT-Guided Biopsy in GGNs[10]:
- A persistent GGN that demonstrates growth in size or increase in attenuation (development or enlargement of a solid component) on follow-up CT.
- A GGN with highly suspicious morphological features suggestive of invasive disease (e.g. large size, spiculation, pleural retraction).
- In patients who are not ideal surgical candidates, a tissue diagnosis can guide the use of alternative therapies.
- When the patient prefers to have a definitive diagnosis before proceeding with surgical resection.

Technical Considerations and Challenges

Biopsying GGNs is technically more demanding than biopsying solid nodules due to their subtle nature and often small size.

- Low Yield for pGGNs: pGGNs, by definition, have no solid component. The target is a faint area of increased attenuation, making accurate needle placement difficult and increasing the risk of a non-diagnostic or false-negative result. In my department, the smallest pGGN that is amenable to diagnostic CT-guided biopsy is 3 mm.
- Pneumothorax: The overall incidence of pneumothorax during CT-guided lung biopsy ranges from 15 % to 40 %. While many cases are minor and resolve on their own, roughly 3 % to 15 % of patients require a chest tube[15].
- Haemoptysis and pulmonary haemorrhage: mild haemoptysis occurred in 13 %[17].
- Systemic Air Embolism: Exceedingly rare (0.02 % - 0.21 %) but potentially fatal complication of CT-guided lung biopsy. It occurs when atmospheric air enters a pulmonary vein, causing bubbles to travel to the brain or coronary arteries, which can lead to ischaemic stroke or cardiac arrest[16].
- Targeting in PSNs: For PSNs, targeting the solid component significantly increases the diagnostic yield. This highlights the importance of identifying the solid portion on CT for procedure planning[5].

Alternative Approaches for Difficult GGNs

Given the limitations of percutaneous biopsy for some GGNs, alternative approaches are often employed.

- CT-Guided Localisation and VATS Resection: For small, peripheral GGNs that are difficult to biopsy or localise surgically, a combined approach is effective. Preoperative CT-guided placement of markers (e.g. Kopan's hookwire, methylene blue or indocyanine green) can localise the nodule, allowing for a subsequent targeted video-assisted thoracoscopic surgery (VATS) wedge resection.
- Surgical Resection as Diagnosis: In many cases, particularly for pGGNs with suspicious features or growth, the recommended course is diagnostic surgical resection (usually via VATS) without a preceding biopsy, as it provides both a definitive diagnosis and treatment in a single procedure[3].

HIGHLIGHTS OF CT GUIDED BIOPSY OF GGN

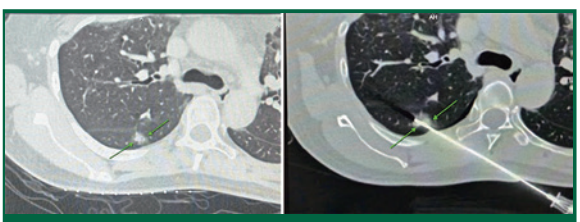


Fig. 10: Adenocarcinoma (Clinical photos from personal collection)

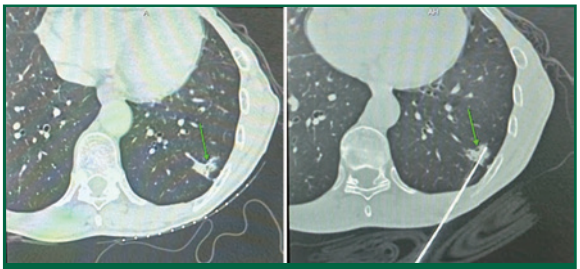


Fig. 11: Organising pneumonia (Clinical photos from personal collection)

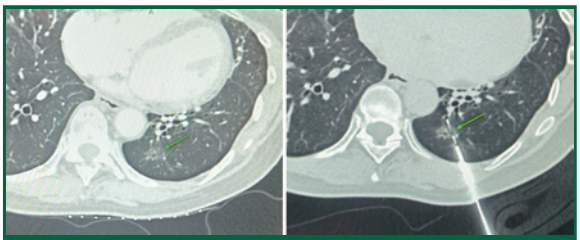


Fig. 12: Adenocarcinoma (Clinical photos from personal collection)

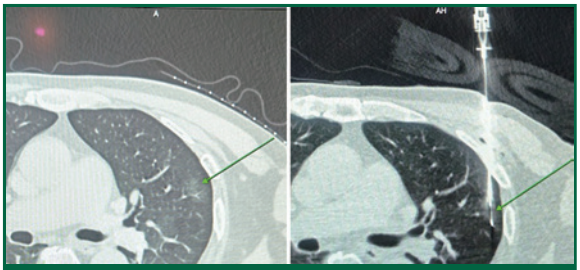


Fig. 13: Atypical adenomatous hyperplasia (at least) (Clinical photos from personal collection)

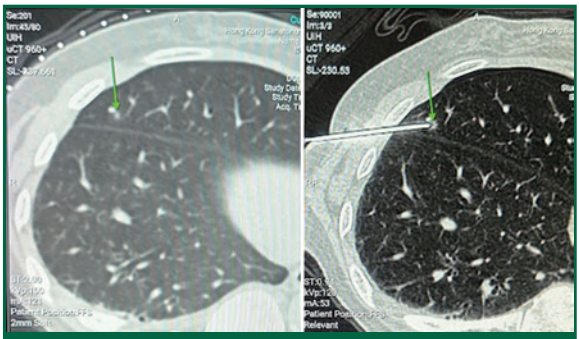


Fig. 14: Non-specific fibrosis, chronic inflammation (Clinical photos from personal collection)

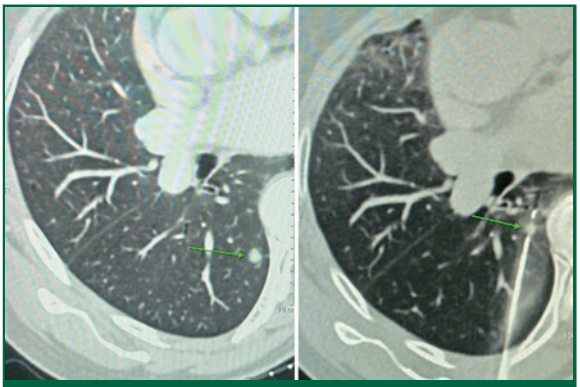


Fig. 15: Adenocarcinoma (Clinical photos from personal collection)

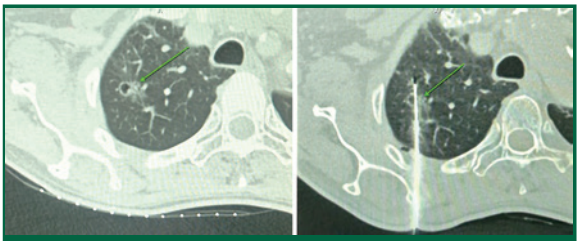


Fig. 16: Adenocarcinoma (Clinical photos from personal collection)

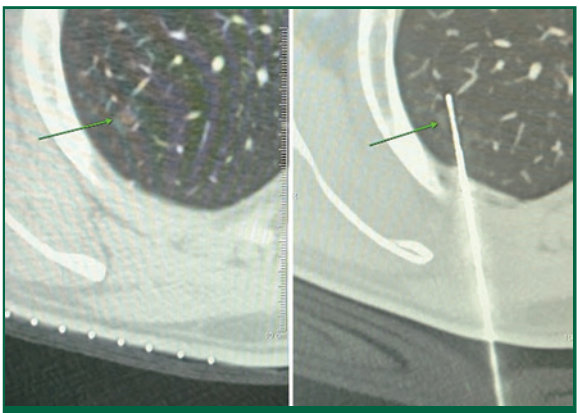


Fig. 17: Adenocarcinoma (Clinical photos from personal collection)

CONCLUSION

Pulmonary GGNs are common CT findings with a wide differential diagnosis and variable malignant potential. Thin-section CT features such as nodule size, margin characteristics, internal structure (particularly the presence of solid components), and ancillary signs like pleural retraction help stratify risk, but imaging findings alone are often insufficient for definitive diagnosis. CT-guided biopsy has a meaningful role in selected suspicious lesions and demonstrates good diagnostic performance, although pneumothorax and sampling limitations must be considered. An integrated approach combining CT morphology, lesion behaviour over time, and targeted tissue sampling offers the best pathway for individualised management.

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Dermatology Quiz

Dermatology Quiz

Dr Lai-yin CHONG

MBBS(HK), FRCP, FHKCP, FHKAM(Med)

Specialist in Dermatology & Venereology



Dr Lai-yin CHONG



Fig. 1: Extensive pustules of different sizes over the back



Fig. 2: Some pustules emerged into larger "lake" of pus over the thigh

This middle-aged woman presented with acute onset of generalised painful pustular lesions over her trunk and limbs for several days. She had fever, chills, fatigue, myalgia and arthralgia. Her past health was good, except before the onset of these lesions, she had "dermatitis" and had been treated with a short course of oral prednisolone. There was no other drug history. Family history was insignificant. On examination, she looked quite ill, together with extensive pustular lesions over a tender erythematous base (Fig. 1 and 2).

Questions

1. What are your diagnosis and differential diagnoses?
2. What is the present dilemma about this disease entity?
3. How do you manage this patient?

(See P. 32 for answers)

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Reference: 1.Haecker, F. M., & Sesia, S. (2016). Vacuum bell therapy. Annals of cardiothoracic surgery, 5(5), 440. 2.Velayos, M., Alonso, M., Delgado-Miguel, C., Estefanía-Fernández, K., Muñoz-Serrano, A. J., Santamaría, M. V. L., ... & De La Torre, C. A. (2022). Percutaneous cryoanalgesia: a new strategy for pain management in pectus excavatum surgery. European Journal of Pediatric Surgery, 32(01), 073-079. 3.Martínez-Ferro, M. M., Fraire, M. C., & Bernard, M. S. (2008, August). Dynamic compression system for the correction of pectus carinatum. In Seminars in pediatric surgery (Vol. 17, No. 3, pp. 194-200). WB Saunders. 4.Weijing, L., Ximin, F., Jianying, S., Mengyun, Z., Xuehua, F., Yawei, X., & Liqiong, H. (2021). Cardiac shock wave therapy ameliorates myocardial ischemia in patients with chronic refractory angina pectoris: a randomized trial. Frontiers in Cardiovascular Medicine, 8, 664433.

Date / Time	Function	Enquiry / Remarks
2 MON 2:00 PM	**HKMA CME Portal (Online)** **HKMA-KWC CME Online Lecture Series on Common Medical Conditions for GP in 2026** **Topic: Mycobacterium Other Than Tuberculosis (MOTT) in Sputum and Radiological Abnormalities on Chest X-ray (CXR)** Organisers: The Hong Kong Medical Association and Kowloon West Cluster of HA Speaker: Dr Daniel Chi-yuen YIP	HKMA CME Dept. Tel: 2527 8452 1 CME Point
3 TUE 2:00 PM	**In-person / HKMA CME Portal (Online)** **HKMA-HKSH CME Programme 2026** **Topic: Syncope in Children and Adolescents: Red Flags You Should Not Ignore** Organisers: The Hong Kong Medical Association and Hong Kong Sanatorium & Hospital Speaker: Doctor who is specialist in Paediatric Cardiology Venue: The HKMA Wanchai Premises, 5/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	HKMA CME Dept. Tel: 2527 8452 1 CME Point
7:00 PM	**Certificate Course on Foundations of Conflict Competence in Healthcare (Video Lectures)** Organisers: The Federation of Medical Societies of Hong Kong & Hong Kong Society for Healthcare Mediation Speaker: Dr Ludwig TSOI	Tel: 2821 3512
4 WED 7:00 PM	**Certificate Course on Rehabilitation 2026 - Bridging Technology, Specialty Care and Practice (Video Lectures)** Organisers: The Federation of Medical Societies of Hong Kong, & Hong Kong Association of Rehabilitation Medicine Speakers: Dr Siu-piu LAM & Ms Sally POON	Tel: 2821 3512
5 THU 2:00 PM	**In-person / HKMA CME Portal (Online)** **The HKMA CME Hybrid Lecture** **Topic: From Early Screening to Advanced Management: Integrating Modern Tools into Daily BPH Practice** Organiser: The Hong Kong Medical Association Speaker: Dr Terence Chun-ting LAI Venue: HKMA Central Clubhouse, 2/F, Chinese Club Building, 21-22 Connaught Road Central, Central	HKMA CME Dept. Tel: 2527 8452 1 CME Point
7 SAT 2:00 PM	**In-person / HKMA CME Portal (Online)** **The HKMA Medico-Legal Conference 2026** **Topics: 1) Proposed Medical Registration (Amendment) Bill 2026; Impact on the Medical Profession** **2) Overview of the Mandatory Reporting of Child Abuse Ordinance** **3) Recent Cases for Social Media for Promotion** **4) Hot Medico-Legal Issues in Hong Kong – Learning from the MPS Case Files** Organiser: The Hong Kong Medical Association Speakers: Mr David KAN, Ms Sally WONG, Ms Sandy CHO and Dr Sara JAMIESON Venue: HKMA Central Clubhouse, 2/F, Chinese Club Building, 21-22 Connaught Road Central, Central	HKMA CME Dept. Tel: 2527 8452 2.5 CME Points
9 MON 2:00 PM	**HKMA CME Portal (Online)** **The HKMA CME Online Lecture** **Topic: Oxidative Stress and The Aging Brain: Understanding NAC, Cognitive Health, and The Changing Landscape of Dementia Care** Organiser: The Hong Kong Medical Association Speaker: Dr Kwok-keung WONG	HKMA CME Dept. Tel: 2527 8452 1 CME Point
10 TUE 2:00 PM	**In-person** **The HKMA CME Lecture in Physical Attendance Mode** **Topic: Topic on Diabetes Management** Organiser: The Hong Kong Medical Association Speaker: To-be-confirmed Venue: Crystal Ballroom A&B, 2/F, The Cityview, 23 Waterloo Road, Kowloon	HKMA CME Dept. Tel: 2527 8452 1 CME Point
7:00 PM	**Certificate Course on Foundations of Conflict Competence in Healthcare (Video Lectures)** Organisers: The Federation of Medical Societies of Hong Kong & Hong Kong Society for Healthcare Mediation Speaker: Dr Abraham WAI	Tel: 2821 3512
11 WED 7:30 AM	**The Hong Kong Neurosurgical Society Monthly Academic Meeting - To be confirmed** Organiser: Hong Kong Neurosurgical Society Speaker(s): Dr Berkley Chun-Hin CHEUNG Chairman: Dr Samuel Siu-kei LAM Venue: Seminar Room, G/F, Block A, Queen Elizabeth Hospital; or via Zoom meeting	CME Accreditation College: 1.5 points College of Surgeons of Hong Kong Dr Jason Chow Tel: 2595 6456 Fax. No.: 2965 4061
7:00 PM	**Certificate Course on Rehabilitation 2026 - Bridging Technology, Specialty Care and Practice (Video Lectures)** Organisers: The Federation of Medical Societies of Hong Kong, & Hong Kong Association of Rehabilitation Medicine Speakers: Dr Chung-wai LAU & Mr Oswald KANG	Tel: 2821 3512
12 THU 2:00 PM	**HKMA CME Portal (Online)** **The HKMA CME Online Lecture** **Topic: Faecal Calprotectin in Clinical Practice: From Differential Diagnosis to Emerging Microbial Biomarkers in IBD** Organiser: The Hong Kong Medical Association Speaker: Professor Jakob BEGUN	HKMA CME Dept. Tel: 2527 8452 1 CME Point
13 FRI 2:00 PM	**HKMA CME Portal (Online)** **The HKMA Adult Immunisation Campaign 2026 CME Online Lecture** **Topic: Topic on HPV Vaccination** Organiser: The Hong Kong Medical Association Speaker: Dr Tin-yau WONG	HKMA CME Dept. Tel: 2527 8452 1 CME Point
16 MON 2:00 PM	**HKMA CME Portal (Online)** **The HKMA CME Online Lecture** **Topic: From Gut to Hair: A Synbiotic Approach to Hair Loss Management** Organiser: The Hong Kong Medical Association Speaker: Dr Evelyn Lee-kung YEO	HKMA CME Dept. Tel: 2527 8452 1 CME Point
17 TUE 7:00 PM	**Certificate Course on Foundations of Conflict Competence in Healthcare (Video Lectures)** Organisers: The Federation of Medical Societies of Hong Kong & Hong Kong Society for Healthcare Mediation Speaker: Dr Kah-lin CHOO	Tel: 2821 3512
18 WED 2:00 PM	**In-person / HKMA CME Portal (Online)** **The HKMA Adult Immunisation Campaign 2026 CME Hybrid Lecture** **Topic: Topic on Pneumococcal Vaccination** Organiser: The Hong Kong Medical Association Speaker: To-be-confirmed Venue: Crystal Ballroom A&B, 2/F, The Cityview, 23 Waterloo Road, Kowloon	HKMA CME Dept. Tel: 2527 8452 1 CME Point
19 THU 2:00 PM	**In-person / HKMA CME Portal (Online)** **The HKMA CME Hybrid Lecture** **Topic: Individualized Treatment of Asthma Patients in Private Clinic Setting** Organiser: The Hong Kong Medical Association Speaker: Dr King-ying WONG Venue: The HKMA Central Clubhouse, 2/F, Chinese Club Building, 21-22 Connaught Road Central, Central	HKMA CME Dept. Tel: 2527 8452 1 CME Point

Date / Time	Function	Enquiry / Remarks
20 FRI 2:00 PM	**HKMA CME Portal (Online)** **The HKMA Adult Immunisation Campaign 2026 CME Online Lecture** **Topic: Topic on Herpez Zoster Vaccination** Organiser: The Hong Kong Medical Association Speaker: To-be-confirmed	HKMA CME Dept. Tel: 2527 8452 1 CME Point
23 MON 2:00 PM	**HKMA CME Portal (Online)** **The HKMA CME Online Lecture** **Topic: From Clinical Symptoms to Actionable Insights: Clinical Application of GI Panel and Faecal Calprotectin Test** Organiser: The Hong Kong Medical Association Speaker: Dr Patrick Kai-fung TSANG	HKMA CME Dept. Tel: 2527 8452 1 CME Point
24 TUE 7:00 PM	**Certificate Course on Foundations of Conflict Competence in Healthcare (Video Lectures)** Organisers: The Federation of Medical Societies of Hong Kong & Hong Kong Society for Healthcare Mediation Speaker: Dr Robert LAW	Tel: 2821 3512
25 WED 2:00 PM	**HKMA CME Portal (Online)** **The HKMA CME Online Lecture** **Topic: From Guidelines to Practice: How Can We Navigate the Expanding Diabetes Toolbox?** Organiser: The Hong Kong Medical Association Speaker: Dr Rose Zhaowei TING	HKMA CME Dept. Tel: 2527 8452 1 CME Point
26 THU 2:00 PM	**In-person / HKMA CME Portal (Online)** **The HKMA CME Hybrid Lecture** **Topic: Optimising Dyspepsia Management in Primary Care: Rational Combination Therapies and the Clinical Value of Digestive Enzymes** Organiser: The Hong Kong Medical Association Speaker: Dr Fook-hong NG Venue: The HKMA Central Clubhouse, 2/F, Chinese Club Building, 21-22 Connaught Road Central, Central	HKMA CME Dept. Tel: 2527 8452 1 CME Point

FMSHK Meetings

26 THU 7:00 PM	**FMSHK Executive Committee Meeting** Organiser: The Federation of Medical Societies of Hong Kong Venue: Council Chamber, 4/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	Ms Mabel TSANG Tel: 2527 8898
7:30 PM	**FMSHK Council Meeting** Organiser: The Federation of Medical Societies of Hong Kong Venue: Council Chamber, 4/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	Ms Mabel TSANG Tel: 2527 8898
8:00 PM	**FMSHK Annual General Meeting** Organiser: The Federation of Medical Societies of Hong Kong Venue: Council Chamber, 4/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	Ms Mabel TSANG Tel: 2527 8898
8:30 PM	**FMSHK Foundation Meeting** Organiser: The Federation of Medical Societies of Hong Kong Venue: Council Chamber, 4/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	Ms Mabel TSANG Tel: 2527 8898

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18 Nov 2026	Roles of Occupational Therapy for Patients Undera Care of Chinese Medicine	Mr. Carl YIP Occupational Therapist I The Chinese Medicine Hospital of Hong Kong
25 Nov 2026	Occupational Life-Style Redesign for People with Chronic Illness	Mr. KF LEUNG Occupational Therapist Chairman of The Greater Bay Area Occupational Therapy Alliance
2 Dec 2026	The Mystery of Chronic Pain	Dr. Mary CHU Occupational Therapist Private Practice
9 Dec 2026	Roles of Occupational Therapists in Driving Readiness for Elder Drivers	Mr. Jonathan CHOW Senior Occupational Therapist Hospital Authority Driver Trained Occupational Therapist
16 Dec 2026	Neuropsychological Mechanisms and Occupational Therapy Strategies for Cognitive Fatigue	Dr. Emily SIN Occupational Therapist Assistant Professor Hong Kong Shue Yan University
23 Dec 2026	Executive Functioning Training for People with ADHD – From Childhood to Young Adults	Ms. Magdalene POON Senior Occupational Therapist Convener of Child & Adolescent Services Specialty Group HKOTA

Date : 18, 25 Nov and 2, 9, 16, 23 Dec 2026 (Wed)
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Answers to Dermatology Quiz

Answers:

1. Generalised pustular psoriasis (GPP) should be the preliminary diagnosis. The most important differential diagnosis is acute generalised exanthematous pustulosis (AGEP), others include sepsis, subcorneal pustular dermatosis, eosinophilic folliculitis, etc.

   Generalised pustular psoriasis (GPP) is an uncommon, severe, autoinflammatory skin disease characterised by acute onset of extensive outbreaks of sterile pustules over erythematous and tender bases. Flares can be triggered by systemic infections, sudden withdrawal of systemic corticosteroids, certain drugs (paradoxical reaction in TNF-inhibitor, terbinafine), stress, or pregnancy (historically called impetigo herpetiformis).

   Acute generalised exanthematous pustulosis (AGEP) (also known as drug-induced toxic pustuloderma) is mostly due to drugs (> 90 %), mostly aminopenicillins or macrolides. In children, occasionally it can be triggered by infections ,such as Epstein-Barr virus, Cytomegalovirus, Human Herpesvirus or Enterovirus.

   When compared with GPP, AGEP usually occur more rapidly, usually within two days of exposure to a definite history of drug culprit. It has no history of psoriasis, initial predominance in intertriginous folds, tiny pinhead size of pustules, shorter duration of pustules and fever, rapid resolution after drug cessation and rarely has arthralgia.

2. There is still a dilemma on whether GPP is true psoriasis, or they are two distinct diseases but with an association. It is now known that GPP is tied with IL-36 receptor antagonist deficiency due to single gene mutation (IL36RN). IL36 signalling pathway is central to the pathogenesis, leading to overproduction of IL8 and other CXCL chemokines, and thus marked neutrophil infiltrates. While in psoriasis vulgaris, it is polygenetic, with IL17 T-lymphocytes and IL23/IL17 pathway as the central axis of pathogenesis and with minimal neutrophil infiltrates.

3. GPP is a dermatological emergency requiring prompt medical evaluation. During severe flares, patient frequently requires hospitalisation to manage fluid balance, prevent infection, and stabilise vital signs. Traditional systemic therapies include retinoids, cyclosporine, methotrexate, or even systemic steroid may be needed in severe flare. Modern biologic treatment like Spesolimab (anti-IL36 inhibitor) has been formally approved to rapidly target the primary inflammatory pathway.

   GPP often runs an unpredictable relapsing cycle of acute flares and partial remissions. Smoking should be quit as it may increase the risk of developing pustular psoriasis. It is a potential life-threatening disease. In patients with compromised cardiorespiratory function, they may die of cardiac failure, respiratory infection, or complications of treatments.

Dr Lai-yin CHONG
MBBS(HK), FRCP, FHKCP, FHKAM(Med)
Specialist in Dermatology & Venereology

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2. Based on internal report #R0064457 rev A, Verification report LigaSure™ renal bench burst pressure evaluation of the Valleylab™ FT10. May 3, 2015.

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