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肺磨玻璃结节亚肺叶切除术中的动态切缘策略

——基于术前影像亚型与多模态术中技术

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摘 要

目的：探讨针对以磨玻璃结节(GGO)为特征的早期肺癌，在亚肺叶切除术中实施个体化“动态切缘”(Dynamic Margin)策略的理论基础与实践路径。方法：综述GGO的影像–病理学特征，剖析当前国际切缘指南的共识与分歧，并总结术中导航与切缘评估技术的最新进展。结果：传统“一刀切”的切缘标准无法适应GGO亚型(纯磨玻璃结节[pGGO]与混合性磨玻璃结节[mGGO])的生物学异质性。基于实性成分占比(consolidation tumor ratio, CTR)的精准风险分层可明确不同亚型GGO的侵袭潜能与复发风险，国际指南对切缘距离的推荐存在显著差异，而三维重建、支气管镜定位、吲哚菁绿(ICG)荧光导航等术中技术及冰冻病理、分子成像等切缘验证手段，为个体化切缘决策提供了技术支撑。讨论：“动态切缘”策略通过术前影像分层制定初始计划，术中整合实时导航与多维度验证技术动态调整切除范围，可在确保肿瘤根治性的同时，最大限度地保留肺功能。结论：“动态切缘”整合了多学科前沿技术，有望优化早期GGO型肺癌的手术决策，实现肿瘤控制与功能保存的最佳平衡。

关键词

肺磨玻璃结节，亚肺叶切除术，切缘距离，动态切缘，术中导航，CTR分层，个体化手术

Dynamic Margin Strategy in Sub-Lobar Resection for Lung Ground-Glass Nodules

—Based on Preoperative Imaging Subtypes and Multimodal Intraoperative Techniques

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Abstract

Objective: To explore the theoretical basis and practical pathway of implementing an individualized "dynamic margin" strategy during sublobar resection for early-stage lung cancer characterized by ground-glass nodules (GGO). Methods: We reviewed the imaging-pathological characteristics of GGO, analyzed the consensus and discrepancies in current international margin guidelines, and summarized the latest advances in intraoperative navigation and margin assessment technologies. Results: The traditional "one-size-fits-all" margin standard is not adaptable to the biological heterogeneity of GGO subtypes (pure ground-glass nodules [pGGO] and mixed ground-glass nodules [mGGO]). Precision risk stratification based on the consolidation tumor ratio (CTR) can clarify the invasive potential and recurrence risk of different GGO subtypes. There are significant differences in margin distance recommendations among international guidelines, while intraoperative technologies such as three-dimensional reconstruction, bronchoscopic localization, and indocyanine green (ICG) fluorescence navigation, as well as margin verification methods including frozen section pathology and molecular imaging, provide technical support for individualized margin decision-making. Discussion: The "dynamic margin" strategy formulates an initial plan through preoperative imaging stratification, dynamically adjusts the resection range by integrating real-time navigation and multi-dimensional verification technologies during surgery, and can maximize lung function preservation while ensuring oncological radicality. Conclusion: The "dynamic margin" strategy, integrating cutting-edge multidisciplinary technologies, is expected to optimize surgical decision-making for early-stage GGO-type lung cancer, achieving the best balance between tumor control and functional preservation.

Keywords

Lung Ground-Glass Nodule, Sub-Lobar Resection, Margin Distance, Dynamic Margin, Intraoperative Navigation, CTR Stratification, Individualized Surgery

1. 引言

低剂量螺旋 CT (LDCT)筛查的普及与影像技术的进步显著提高了肺磨玻璃结节(ground-glass opacity, GGO)的检出率，其中直径 ≤ 2 cm 的 GGO 构成早期肺癌的主体[1]。这一趋势推动亚肺叶切除术(包括肺段/楔形切除)从肺功能受限患者的替代方案，逐步成为特定早期肺癌(尤其是 GGO 为主型病变)的首选术式[2]。关键 III 期研究(如 JCOG0802 [3]和 CALGB 140503 [4])证实：对于直径 ≤ 2 cm 的周围型非小细胞肺癌(NSCLC)，亚肺叶切除术的生存结局非劣于肺叶切除术，奠定了其在外科治疗中的重要地位。

然而，亚肺叶切除术的成功高度依赖手术切缘的充分性。传统切缘距离标准("≥2 cm 或≥肿瘤直径")[5] [6]在应对具有独特生物学行为的 GGO 亚型时面临严峻挑战。根据高分辨率 CT 表现，GGO 可分为纯磨玻璃结节(pure ground-glass opacity, pGGO, CTR = 0)与混合性磨玻璃结节(mixed ground-glass opacity, mGGO, CTR > 0)，二者在病理基础及侵袭潜能上存在本质差异[7] [8]。pGGO 多表现为惰性生长[7] [9] [10]，而 mGGO 的实性成分占比与侵袭潜能呈显著正相关，且影像学边界常无法准确反映真实侵袭范围[11] [12]。这种“一刀切”的固定切缘标准导致临床实践中的“双重困境”：对 pGGO 过度切除造成肺功能浪费，对高侵袭性 mGGO 则可能因切缘不足增加局部复发风险。

当前关于 GGO 亚肺叶切除术切缘距离标准的循证指南与临床实践存在显著分歧，凸显了该领域研究的核心缺口：首先，现有综述未系统整合 pGGO/mGGO 及其 CTR 分层与切距、复发风险的关系。其次，术中导航技术价值未充分挖掘，冰冻切片、切缘细胞学检查、术中分子成像等可实时量化切缘，但其对个体化切缘决策的贡献尚未被系统评述。

为弥合上述缺口，本综述首次提出“动态切缘”策略：该策略强调在术前基于精准的影像学亚型分层(pGGO/mGGO + CTR 分级)初步制定个体化切缘计划；在术中，利用实时导航技术可视化边界，结合术中冰冻、分子细胞学验证即时调整切除范围。本综述的核心目标在于弥合多学科研究孤岛，为优化早期肺癌亚肺叶切除术的切缘决策提供坚实的理论基础与实践指导，最终实现肿瘤根治与肺功能保留的最佳平衡，推动早期肺癌外科治疗迈向精准化与个体化新时代。

2. GGO 的影像学－病理学基础与 STAS 切缘挑战

2.1. GGO 亚型的影像－病理关联与生物学特性

pGGO 在影像学上表现为均匀的磨砂玻璃样阴影，不掩盖肺血管或支气管结构，其病理本质以前驱病变或低度恶性潜能肿瘤为主。前瞻性研究[9] [13]表明，对于最大直径 ≤ 2 cm 的 pGGO，亚肺叶切除术后的 10 年总生存率可达 98.5%，局部复发率低于 1%，反映出其惰性的生物学行为。但是一项纳入 24 项研究的 Meta 分析显示[7]，pGGO 术后病理中约 60%为原位腺癌(adenocarcinoma *in situ*, AIS)或微浸润腺癌(minimally invasive adenocarcinoma, MIA)，浸润性腺癌(invasive adenocarcinoma, IAC)占比高达 27%，且其中半数并非贴壁为主型。这一发现对当前指南[14]将纯 GGO 一概归类为贴壁为主型病变并归入临床 0 期的做法提出了挑战。

相比之下，mGGO 则呈现显著异质性。CTR 大小与肿瘤的预后显著相关，亚肺叶切除的复发风险随 CTR 的增加持续升高[15]，当 CTR > 0.5 时，复发率增幅最为显著，故临床实践中常以 CTR = 0.5 为界，将 GGO 分为磨玻璃为主型(CTR < 0.5)和实性为主型(CTR > 0.5)。病理学研究显示，mGGO 的磨玻璃区域可存在贴壁样、腺泡样乃至微乳头样成分(发生率为 11.9%)，而其内部实性区域中微乳头/实体型等高侵袭成分占比可达 28.5%，并与气腔播散(spread through air spaces, STAS)密切相关[12]。由于这种结构异质性，mGGO 的影像学边界常难以准确反映实际侵袭范围：影像所测实性成分直径多小于病理侵袭灶，导致近半数患者出现临床 T 分期低估。

2.2. STAS：GGO 亚肺叶切除术中的切缘决策挑战

气腔播散(STAS)作为肺腺癌的一种侵袭性模式，是亚肺叶切除术后局部复发的重要危险因素，对切缘决策构成核心挑战。其挑战性源于两方面：其一，STAS 多见于实性成分占比高(CTR > 0.5)的病变，这些脱离主瘤的细胞导致影像学边界无法反映真实侵袭范围[12] [16]；其二，现有证据表明，对于肿瘤直径 ≤ 2 cm 的 STAS 阳性患者，亚肺叶切除术后的无进展生存期显著劣于肺叶切除术[17]。更严峻的是，术中冰冻切片对 STAS 的检出灵敏度有限(约 56.4%) [18]，即使术中对切缘宽度评估满意(如切缘/肿瘤直径比 > 1)，仍无法排除 STAS 微转移灶残留所带来的复发风险[19]。凸显了现有技术下针对 STAS 肺腺癌确保切缘安全的巨大困难。这种 STAS 相关的切缘风险差异，进一步支持了根据 GGO 亚型及 CTR 分层制定个体化切缘策略的必要性。

3. 当前切缘距离标准：指南共识与争议

3.1. 当前指南的分歧

目前国际权威指南对亚肺叶切除术中切缘距离标准的建议仍存在明显差异，尤其在针对磨玻璃结节(GGO)不同亚型的处理策略上(表 1)。

NCCN 指南(2024 v4)推荐亚肺叶切除术适用于≤2 cm 的外周型非小细胞肺癌(non-small cell lung cancer, NSCLC)，要求手术切距需“≥2 cm 或≥肿瘤直径”，但未区分 GGOs 的 CTR 差异[20]。

欧洲胸外科医师学会(ESTS) 2023 指南[21]推荐：对于位于肺外周 1/3 区域的 pGGO，推荐施行楔形切除术；对于位于肺中央区域的 pGGO，则推荐行肺段切除术。对于 mGGO，一律推荐肺段切除术联合淋巴结清扫。无论采用何种切除方式，微创手术应作为首选术式。为保障肿瘤完整切除，该指南要求术中切距需满足以下任一条件：距离 ≥ 1 cm 或切距/肿瘤直径比(margin to tumor diameter ratio, M/T) ≥ 1。

中华医学会肺癌临床诊疗指南(2024 版) [22]推荐：对于临床分期为 cT1a~bN0 期、含有 GGO 成分且位于肺外周的 NSCLC，应优先考虑亚肺叶切除术，其中肺段切除术应作为首选术式。对于同样处于 cT1a~bN0 期但肺功能储备不足或合并其他严重并发症等不宜行肺叶切除的高危患者，推荐行楔形切除术，肺段切除术可作为次选方案。同时指南强调，无论采取何种亚肺叶切除方式(肺段切除或楔形切除)，均需确保肺实质切缘距离 ≥ 2 cm 或≥肿瘤直径。

中国专家共识(2024) [23]在亚肺叶切除术的切缘处理上提出了更精细化的手术选择方式标准——基于 CTR 和位置进行推荐：① pGGO：外周 1/3 区推荐楔形切除术；中/外 1/3 区或肺段内推荐肺段/复合肺段/联合亚段切除。② mGGO：CTR < 0.25 且外周 1/3 区推荐楔形切除术；0.25 ≤ CTR < 0.5 推荐肺段切除术；CTR ≥ 0.5 推荐肺叶或肺段切除术(选择肺段切除时须确保术中淋巴结评估阴性)；楔形切除特殊要求：在满足基本切缘距离原则“>2 cm 或>肿瘤最大径”基础上，肉眼肿瘤切缘距离需>5 mm；若术中评估不足 5 mm，必须通过冰冻切片病理检查证实切缘阴性。若评估不足，需中转肺段或肺叶切除术。

多项研究进一步支持个体化切缘策略。El-Sherif 等[24]发现，切缘 < 1 cm 时局部复发率显著升高(19% vs 8%, P = 0.003)，建议至少≥1 cm。Mohiuddin 等[25]支持对≤2 cm 结节采用 1.5~2.0 cm 切缘，超过 1.5 cm 未见额外获益(P = 0.033)。Sawabata 等[26]提出 M/T 比值 ≥ 1 与更好生存相关。Moon 等[27]强调，对于含 GGO 的肺腺癌，切缘/浸润成分比值 > 1 可显著改善预后。

Table 1. Comparison of international guidelines for margin distance standards in GGO sub-lobar resection
表 1. 国际指南对 GGO 亚肺叶切除切距标准的对比

指南/共识	pGGO (CTR = 0)	mGGO-CTR ≤ 0.25	mGGO-0.25 < CTR ≤ 0.5	mGGO-CTR > 0.5
NCCN 2024	≥2 cm 或≥肿瘤直径	≥2 cm 或≥肿瘤直径	≥2 cm 或≥肿瘤直径	≥2 cm 或≥肿瘤直径
ESTS2 023	切缘 ≥ 1 cm 或≥肿瘤直径	切缘 ≥ 1 cm 或≥肿瘤直径	切缘 ≥ 1 cm 或≥肿瘤直径	切缘 ≥ 1 cm 或≥肿瘤直径
中国肺癌临床指南 2024	≥2 cm 或≥肿瘤直径	≥2 cm 或≥肿瘤直径	≥2 cm 或≥肿瘤直径	≥2 cm 或≥肿瘤直径
中国共识 2024	≥0.5 cm (楔形切除)	楔形 + ≥0.5 cm	段切 + ≥2 cm 或≥肿瘤直径	肺叶或肺段切除 (≥2 cm 或≥肿瘤直径)

3.2. 核心争议焦点剖析

3.2.1. pGGO 的切缘距离安全性争议

NCCN 与中国指南仍推荐 pGGO 切缘应“≥2 cm 或≥肿瘤直径”。但新证据显示该标准可能过于严

格。JCOG0804 研究表明[28]，pGGO 中不存在高级别亚型或 STAS，对于 CTR ≤ 0.25 的外周 pGGO，楔形切除(切距 ≥ 5 mm)的 5 年 OS (overall survival)与 RFS (recurrence-free survival)分别达 99.4%和 99.7%，10 年 OS 与 RFS 也均超过 98.5%。Li 等[10]报道即使 pGGO 术后诊断为 IAC，10 年 RFS 仍为 100%。Kim 等[29]支持≥5 mm 切缘距离是无复发生存的显著预后因素，且浸润性成分对预后无额外影响(HR = 8.21, p = 0.063)。这些结果提示，当前“≥2 cm”标准对 pGGO 可能过于严格，需根据其低侵袭生物学行为制定更合理的切缘范围。

3.2.2. mGGO 的 CTR 分层切缘距离争议

对于“影像学非浸润性”肺癌(≤2 cm, CTR ≤ 0.25)，有研究[28]验证，针对该类型周围型肺腺癌，亚肺叶切除术(主要为楔形切除术，并将楔形切除的安全切缘距离阈值设定为≥5 mm)的 5 年 RFS 达 99.7% (90%置信区间[CI]：98.3%~99.9%)，5 年 OS 为 99.4% (95% CI: 97.5%~99.8%)，充分证实该术式的肿瘤学有效性。对具有一定浸润特征的 mGGO (如肿瘤 ≤ 3 cm 且 CTR ≤ 0.5)，JCOG1211 [30]显示肺段切除 5 年 RFS 达 98.0%；Ma 等[31]在排除 AIS/MIA 后发现，肺段切除术与肺叶切除术的 5 年 OS 和 RFS 无统计学差异。Zhang 等[32]报道对于≤2 cm 且 0.25 < CTR ≤ 0.5 患者，楔形切除与肺段切除 5 年 RFS 无统计学差异(97.87% vs 97.73%, P = 0.987)，但对 2~3 cm 且 CTR ≤ 0.5 者，楔形切除 RFS 显著较低(90.61% vs 100%, P = 0.043)，提示肺段切除对较大或实性成分较高的 mGGO 具有局部控制优势。值得注意的是，长期随访显示即便 AIS/MIA 患者，第二原发肺癌发生率在 10 年时可达 5.6%~7.7% [33] [34]，中位发生时间约 87~97 个月。因此首次手术中最大限度保留肺实质(如精准楔形切除)对预留二次手术机会具有重要意义。

对更具侵袭性的 mGGO (≤2 cm, CTR > 0.5)，JCOG0802/WJOG4607L [3]证实肺段切除相比肺叶切除具有更高 5 年 OS (94.3% vs 91.1%)，且复发后接受根治性治疗的比例更高(93% vs 80%)，确立了肺段切除在此类患者中的地位。尽管 Hattori 等[35]认为 CTR > 0.5 后无需再细分，但 Xi 等[36]发现 CTR > 0.75 时微乳头/实体成分比例和淋巴结转移率显著升高；Jing 等[37]也认为 CTR > 0.75 是 IA 期肺腺癌预后不良的独立危险因素。因此，切距达标在此类患者中的关键作用不容忽视。多变量分析[38]提示影像学实性结节、切缘 < 肿瘤直径、男性性别是局部–区域复发(locoregional recurrence, LRR)的危险因素。一项回顾性研究[39]指出，对亚实性结节(≤3 cm, GGO ≥ 10%)，切缘 ≤ 0.5 cm 和 CTR 对 RFS 有潜在影响，并提出 M/T > 1.0 可能是更可靠的局部复发预测指标。

为更精准筛选适合亚肺叶切除的侵袭性 GGO 患者，一项包括 19 个中心的前瞻性 III 期试验[40]正在进行，其以“总直径 < 3 cm 且实性成分 < 2 cm”为入组标准(取代传统 CTR)，以 5 年 RFS 和 OS 为主要终点，验证肺段切除的非劣效性。该设计基于上海胸科医院研究[41]，认为实性成分的绝对大小(而非总大小或 CTR)是预测组织学亚型和预后的更优指标，因此提出实性成分 ≤ 2 cm 或为更合理的手术筛选阈值。

综上，尽管 CTR 分层为 mGGO 手术策略制定提供了重要依据，但并非唯一因素。当前证据表明：1) 切缘应随浸润程度(体现为 CTR 或实性成分大小)动态调整；2) 实性成分绝对大小可能在预后判断中较 CTR 比例更为关键；3) 第二原发肺癌风险凸显首次手术中肺保护的重要性。因此，“动态切缘”不仅依赖于个体化影像–病理特征设定切缘，更需借助术中实时导航与快速病理技术实现精确切除与切缘确认，从而在肿瘤控制与功能保留之间达到最优平衡。

4. 术中技术创新：从经验决策到实时导航

亚肺叶切除术的成功高度依赖术中精确的定位与切缘的实时判断。近年来，术中导航、术中冰冻、术中分子细胞学技术的发展显著提升了手术精度，使得“动态切缘”有了更丰富的决策思路。

4.1. 术中定位技术革新

4.1.1. 三维重建

三维重建通过软件提取术前 CT 数据，将肺动脉、肺静脉、支气管的二维图像转化为血管树与支气管树的三维影像，精准识别个体化解剖结构、肺段划分及目标肺段毗邻关系。该技术对术前定位、手术规划、术前模拟及术中导航具有重要价值[42]，尤其是虚拟定义的段间平面及切除边缘可进行充分的手术模拟，为制定个体化手术方案提供参考依据。研究表明，人体肺血管解剖变异的发生率超过 30% [43]，三维重建对这些解剖变异的检出率高达 85% [44]，术前充分识别这些解剖变异能够使外科医生优化手术入路，大幅缩短手术时长、减少术中出血量并提高手术成功率[45]。在评估切缘方面，一项对比研究显示，在手术规划中使用三维成像的患者(n = 36)实现了 100%的满意手术边缘率。而在仅用二维 CT 的对照组(n = 32)中，有 4 例患者(4/32)因边缘不足需追加楔形切除——差异具有统计学意义，这凸显了三维重建的优势[46]。但三维重建的准确模拟需要术前高质量的 CT 数据，部分肺血管及支气管变异无法准确模拟，且三维重建时肺部处于膨胀状态且位于正常解剖位置，而术中单肺通气后患肺萎陷并受多方牵拉，可能偏离正常解剖位置，从而影响术中解剖结构的正确识别[47]。

4.1.2. 支气管镜辅助定位

支气管镜辅助定位技术是在术前通过导航支气管镜精确引导至目标病灶附近，置入标记物定位目标病灶及判断切除范围。置入的标记物有弹簧圈[48]、染色剂[49] [50]、射频识别标记[51]等。而导航支气管镜分为虚拟导航支气管镜(virtual bronchoscopy navigation, VBN)与电磁导航支气管镜(electromagnetic navigation bronchoscopy, ENB)。经 VBN 辅助定位技术又称虚拟辅助肺图(virtual-assisted lung mapping, VAL-MAP)技术，通过导航支气管将染色剂(通常是 ICG 或亚甲蓝)注射到目标段支气管附近的支气管黏膜下或穿透支气管壁到脏层胸膜下，再通过计算机重建技术绘制清晰的肺结节位置和安全切缘范围的肺部图像。前瞻性多中心研究[52]显示出 98.0%的成功切除率及 87.7%的充足切距。有研究表明[53]，VAL-MAP 技术辅助的亚肺叶切除术的长期疗效令人满意。而 ENB 需将患者置于磁场中，使用传感探头实时定位支气管镜头方位，随时调整探头位置，从而引导支气管镜到达目标病灶进行定位[54]。有研究经 ENB 置入射频识别标记物(RFID)，可精准定位深部肺内结节，通过识别射频信号强度来确定最佳切除线，获得了足够的切缘[55]。一项荟萃分析[56]显示，ENB 标记成功率达 96%，VBN 标记成功率为 94%。现行 ENB/VBN 技术主要依赖术前 CT 影像，而术中肺容积改变、肺不张及呼吸运动导致的结节位移会影响病灶空间位置关系(被称为“CT-身体差异”) [57]。有研究[58]表明，锥形束 CT (Cone-Beam CT, CBCT)可作为术中三维影像的实时导航技术，能实时监控支气管镜导航过程从而提升定位的精确性，但 CBCT 需要在特定的杂交手术室内进行。支气管镜辅助定位的适应症尚不明确，但对于无法手指触诊的结节，Suzuki 等[59]主张对直径 < 10 mm、深度 > 5 mm 的结节进行术前标记，Tamura 等[60]则提出直径 < 15 mm 且深度 > 10 mm 的结节术中探查较为困难，因此更适合支气管镜辅助定位。

与经皮肺穿刺定位相比，支气管镜能更安全到达深部、肺尖及膈肌附近等穿刺禁区，并且避免了穿刺引起的气胸、咯血、胸膜反应、空气栓塞等并发症。但也有研究表示支气管镜辅助定位在右上肺尖段定位时近一半患者失败[61]。该方法的缺点在于需要一位熟悉气管镜的医师协助手术或术者需熟练掌握支气管镜的使用，同时该定位方法操作复杂、价格高昂、需要特殊设备等。

4.1.3. ICG 荧光导航

吲哚菁绿(indocyanine green, ICG)荧光导航手术显著提升了手术精准度。ICG 作为近红外荧光染料，结合人血清白蛋白后可增强荧光强度。术中应用近红外荧光成像(near-infrared fluorescence imaging, NIRF)技

术，有效增强术者对肺段边界及肿瘤切缘的视觉辨识能力。ICG 给药途径主要包括静脉注射与支气管灌注：前者操作便捷但显影时间短(约 30~180 秒)，且在肺气肿或肺纤维化病例中边界可能模糊；后者通过直接灌注可实现持续显影，需经支气管镜导航辅助定位[62]。多项研究证实 ICG-NIRF 应用于胸腔镜肺段切除术安全可行，能快速显影段间平面并缩短手术时间[63]-[65]。该技术通过实时可视化肺段结构确保精确切除，降低切缘阳性风险，并能识别需补充切除的亚理想切缘。Wada 等[50]的研究显示，ICG 引导肺段切除术的切缘阳性率显著低于标准胸腔镜技术。ICG-NIRF 的应用原理依赖于靶肺段循环的中断，据此分为靶段动脉阻断后注射 ICG 与靶段静脉阻断后注射 ICG 两种策略。研究表明，两种 ICG-NIRF 方法形成的分界线均与改良膨胀–萎陷平面高度吻合，并且节省了等待时间[66] [67]。近期 Zhao 等[68]尝试术中临时阻断靶段动/静脉后注射 ICG 实施楔形切除术，术后切缘距离为(16.5 ± 3.9) mm，所有切缘均为阴性，但其长期疗效仍需进一步随访验证。雾化吸入 ICG 的显影范围也可获得阴性切缘，同时降低了气管支气管损伤风险，但安全性需更多研究确证[69]。ICG 的缺点在于偶尔会遇到过敏反应，对碘过敏的患者不能使用 ICG。严重 COPD、肺气肿或碳末沉积患者段间平面识别率可能降低[70]，此时需术者与术前三维重建对比确认段间平面是否吻合。且近红外荧光穿透深度有限，对于深部结节可能难以获得适当的切距[71]。值得注意的是，随着外科医师经验的积累，ICG-NIRF 成像所提供的附加临床增益效应可能趋于减弱[72]。

技术名称	优点	缺点	适应场景
三维重建	精准识别解剖结构，指导手术规划与术前模拟；缩短手术时长，减少术中出血	依赖高质量 CT 数据；部分解剖变异无法准确重建；存在“CT-身体差异”	所有亚肺叶切除病例，尤其适用于肺段解剖复杂者，是术中辅助定位的基础
支气管镜辅助定位	标记成功率高，安全性高，深部结节定位优势	需熟练掌握支气管镜技术；设备昂贵，操作复杂；缺乏统一适应症标准	直径 ＜15 mm、深度 ＞10 mm 的不可触及结节；深部/肺尖/膈肌附近结节
ICG 荧光导航	多种给药途径，可缩短手术时间及实时显影段间平面。	深部结节显影差；特定患者(如严重肺气肿、肺纤维化、碳末沉积)段间平面识别率低；过敏反应；	肺段切除术中段间平面识别；外周结节切缘可视化

尽管如此，虽然这些方法确实有助于识别肿瘤位置及设计切除范围，但它们无助于保证手术切缘的状态，因此，仍需要以下技术实时判断切缘是否阳性或切距是否足够。

4.2. 术中切缘的实时判断

4.2.1. 术中冰冻(Frozen Section Pathology, FSP)

准确评估切缘对确保肿瘤根治至关重要。尽管荟萃分析[73]显示FSP与最终病理的总体一致率达88%，且在定位技术及术中导航辅助的亚肺叶切除术中，切缘阳性率总体较低，但一旦发生，其对患者的复发和生存影响显著。通常若 FSP 提示切缘阳性，外科医生会进一步切除以获取阴性切缘。JCOG0802 中要求对所有亚肺叶切除术进行 FSP 评估，CALGB140503 中 84%的患者使用了 FSP 评估切缘状态。在 CALGB140503 试验中行亚肺叶切除术的总体切缘阳性率为 12/281 (4.27%)，FSP 正确识别了 12 名阳性切缘患者中的 10 名(83.3%)。同样，Ortiz 等[74]的研究发现，在 642 例计划行亚肺叶切除的患者中，术中冰冻识别了最终诊断切缘阳性 8 例患者中的 7 例(87.7%)。提示了术中冰冻在诊断术中切缘的重要性。值得注意的是，若 FSP 提示“至少微浸润性腺癌”，且肿瘤直径 ＞15 mm、CT 值 ＞−450 HU，则高度提示为具有较高复发风险的浸润性腺癌，此类患者行亚肺叶切除可能不足[75]。此外，一项大规模前瞻性研究[18]认为，FSP 虽具有高特异性和中等一致性，但对 STAS 检测敏感性不足。所以，FSP 并非完美，评估切缘存在一定的限制，如取样误差、将恶性肿瘤误认为淋巴细胞或腺体、将原位疾病误认为化生等[76]，

因此仍需开发更优的检测方法。

4.2.2. 术中切缘细胞学检查

术中切缘细胞学检查被认为是评估切缘状态的有效手段[77]。Miyoshi 等人[78]回顾性研究了 289 例术中缝合钉仓灌洗细胞学检查阴性病灶中仅 7 例(2%)出现了切缘复发的情况，且其中 6 例的显微切距 < 1 cm。因此，尽管术中实施缝合钉仓灌洗细胞学检查可有效评估手术切缘的细胞学状态，但对于显微切距 < 1 cm 的病变，即使细胞学结果为阴性仍需密切监测，可能还需长期随访。Kurihara 等人[79]进一步开发了基于交流电场(AC)混合的快速钉仓灌洗免疫细胞化学检测，可在 20 分钟内完成切缘评估，且较传统 HE 染色更敏感。该研究中尽管所有病例冰冻切片均诊断切缘阴性，但快速 ICC 诊断为切缘阳性的 4 例患者中有 2 例出现局部/切缘复发，因此该技术有望成为肺亚肺叶切除术后快速判定切缘恶性状态的临床工具。但相关高质量研究较少，仍需更多的研究以提高证据质量。

4.2.3. 术中分子成像

术中分子成像(intraoperative molecular imaging, IMI)是结节定位和切缘评估的前沿技术。其通过靶向荧光探针与肿瘤特异性生物标志物(如叶酸受体 α、CEA、组织蛋白酶等)结合，实时显示肿瘤边界及微转移灶。若切缘有荧光信号，则提示可能有癌细胞残留。一项纳入 92 名患者的多中心 II 期临床试验表明，叶酸受体靶向造影剂 OTL38 能定位 12%术者未能发现的病灶，并检出 9%被误判为阴性的阳性切缘，约 26%的患者从中获益。该研究认为 IMI 仅对距离表面小于 2 厘米的外周结节敏感，对于需要肺段或肺叶切除的较深结节无效[80]。目前相关 III 期临床试验(NCT04241315)正在进行。其他靶向成像剂如 EGFR 抗体帕尼单抗(Panitumumab) [81]和组织蛋白酶靶向显影剂 VGT-309 [82]也在探索中。新型 pH 激活型纳米探针安全性良好，但当前证据不支持其常规应用[83]。

4.2.4. 术中标本成像

术中标本成像技术也取得了进展。研究首次提出在术中将切除标本经支气管充气后行 CT 扫描，同步测量肿瘤最大径与切缘长度。结果显示，CT 测量的肿瘤最大径与大体标本测量值高度吻合($r = 0.971$, $P < 0.0001$)，表明对于隐匿性肺内病变，术中充气 CT 技术能可靠确认病灶存在并精准评估切缘长度，其测量值较传统病理测量更能反映活体状态下的真实解剖关系[84]。值得注意的是，加拿大研究发现术中 CT 测量的切缘距离较术后病理切缘平均缩短 10.6%，提示外科医生需意识到这种差异，尤其对于亚实性和位置较深的[85]。

5. 讨论

本综述系统剖析了早期肺癌亚肺叶切除术中 GGO 病变切缘标准的核心争议与前沿进展，首次提出并论证了“动态切缘(dynamic margin)”策略的科学依据与临床实施路径。该策略的核心在于突破传统“一刀切”的静态标准，构建一个基于术前精准分层、术中实时导航与验证的个体化切缘决策体系。

首先，本文综述表明：pGGO 具有惰性生物学行为，≥5 mm 切缘即可满足根治需求；mGGO 的复发风险随 CTR 升高而增加，CTR > 0.5 时需更严格的切缘标准(≥2 cm 或≥肿瘤直径)。国际指南对切缘的推荐仍存在显著差异：NCCN 与中国指南坚持“≥2 cm 或≥肿瘤直径”，ESTS 将阈值降至≥1 cm 或 M/T ≥ 1，而中国专家共识则首次基于 CTR 分层提出差异化要求。与此同时，术中技术如三维重建、支气管镜辅助定位、ICG 荧光导航以及术中冰冻、细胞学与分子成像等，为切缘的实时评估与调整提供了关键支撑，实现了从“经验性切缘”向“精准化切缘”的转变。在此基础上，本综述进一步提出“动态切缘”策略的实践路径，主要包括以下两个方面：

一是术前基于高分辨率 CT 明确 GGO 亚型(pGGO/mGGO)及实性成分占比(CTR)，制定初始切缘计划——pGGO 及 CTR < 0.25 的 mGGO 采用楔形切除 + ≥5 mm 切缘即可满足根治需求；0.25~0.5 CTR 的 mGGO 需根据肿瘤直径选择楔形或肺段切除(切距 ≥ 肿瘤直径)；CTR > 0.5 的 mGGO 推荐肺段切除(切距 ≥ 2 cm 或≥肿瘤直径)，CTR > 0.75 者慎选亚肺叶切除。值得注意的是，近年来有研究表明，实性成分的绝对大小可能较 CTR 更能准确预测组织学亚型与预后[41]。因此，未来在制定分层策略时，应考虑建立“CTR + 实性成分大小”的双重评估标准，以进一步提高风险分层的科学性及手术指征的精准性。

二是术中依托多模态技术动态调整：术前三维重建规划解剖路径，不可触及结节采用支气管镜辅助定位(ENB/VBN)或 ICG 荧光导航，切缘评估以冰冻病理为基础，必要时联合细胞学或分子成像验证，术中标本成像辅助精准测量切距。需要特别指出的是，术中冰冻病理对 STAS 的检测敏感性有限，因此在 FSP 结果阴性但临床高度怀疑 STAS 存在(如 CTR > 0.5、影像学实性成分明显)的情况下，外科医生应采取预防性补偿策略，即在满足基本切缘标准的基础上适当扩大切除范围甚至必要时转为肺叶切除，而非完全依赖冰冻病理结果，以降低因微转移灶残留导致的局部复发风险。

该策略的核心价值在于实现“根治性”与“功能性”的平衡：通过术前分层避免 pGGO 过度切除(切缘从 2 cm 缩减至 0.5 cm)，同时降低高 CTR mGGO 的切缘残留风险；术中导航技术解决了隐匿性结节定位难题，实时验证手段提升了切缘判断的准确性，尤其为多原发癌高危患者预留了二次手术空间。

本文的局限性主要体现为：其一，核心分层指标 CTR 的阈值缺乏多中心大样本头对头验证，且未明确实性成分绝对大小与 CTR 的决策优先级，分层精准性有待提升；其二，术中分子成像等关键技术循证等级不足，特殊基础疾病患者的技术适配方案缺失；其三，支撑证据多源于东亚人群，多发 GGO、老年衰弱等特殊患者覆盖不足，普适性受限；其四，依赖高端设备导致临床可及性低，缺乏标准化操作流程与质量控制体系；其五，未充分评估长期肺功能、生活质量及卫生经济学效益，术者主观判断等混杂因素控制欠缺。

6. 结论

“动态切缘”策略通过整合 GGO 亚型及 CTR 的术前精准分层，结合三维重建、荧光导航、术中冰冻等多模态技术，实现了亚肺叶切除切缘决策的个体化与精准化。该策略可在确保肿瘤根治的同时，最大限度保留肺实质功能，尤其适配早期 GGO 型肺癌的生物学异质性，为临床实践提供了可操作的技术路径，推动早期肺癌外科治疗向“精准化 - 个体化”方向发展。

参考文献

[1] Adams, S.J., Stone, E., Baldwin, D.R., Vliegenthart, R., Lee, P. and Fintelmann, F.J. (2023) Lung Cancer Screening. *The Lancet*, **401**, 390-408. https://doi.org/10.1016/s0140-6736(22)01694-4

[2] Seguin-Givelet, A., Lafouasse, C., Gossot, D., *et al*. (2025) Sublobar Resection in Early-Stage NSCLC: Towards a New Therapeutic Standard? *Bulletin du Cancer*, **112**, 3s24-3s30.

[3] Saji, H., Okada, M., Tsuboi, M., Nakajima, R., Suzuki, K., Aokage, K., *et al*. (2022) Segmentectomy versus Lobectomy in Small-Sized Peripheral Non-Small-Cell Lung Cancer (JCOG0802/WJOG4607L): A Multicentre, Open-Label, Phase 3, Randomised, Controlled, Non-Inferiority Trial. *The Lancet*, **399**, 1607-1617. https://doi.org/10.1016/s0140-6736(21)02333-3

[4] Altorki, N., Wang, X., Damman, B., Mentlick, J., Landreneau, R., Wigle, D., *et al*. (2024) Lobectomy, Segmentectomy, or Wedge Resection for Peripheral Clinical T1aN0 Non-Small Cell Lung Cancer: A Post Hoc Analysis of CALGB 140503 (Alliance). *The Journal of Thoracic and Cardiovascular Surgery*, **167**, 338-347.e1. https://doi.org/10.1016/j.jtcvs.2023.07.008

[5] Kim, D.H., Na, K.J., Park, I.K., Kang, C.H., Kim, Y.T. and Park, S. (2021) Long-Term Outcomes in Stage I Lung Cancer after Segmentectomy with a Close Resection Margin. *Journal of Chest Surgery*, **54**, 361-368. https://doi.org/10.5090/jcs.21.045

[6] Schuchert, M.J., Pettiford, B.L., Keeley, S., D'Amato, T.A., Kilic, A., Close, J., *et al*. (2007) Anatomic Segmentectomy in the Treatment of Stage I Non-Small Cell Lung Cancer. *The Annals of Thoracic Surgery*, **84**, 926-933. https://doi.org/10.1016/j.athoracsur.2007.05.007

[7] Woo, W., Kang, D., Cha, Y.J., Kipkorir, V., Song, S.H., Moon, D.H., *et al*. (2024) Histopathologic Fate of Resected Pulmonary Pure Ground Glass Nodule: A Systematic Review and Meta-Analysis. *Journal of Thoracic Disease*, **16**, 924-934. https://doi.org/10.21037/jtd-23-1089

[8] Zhai, W.Y., Wong, W.S., Duan, F.F., Liang, D.C., Gong, L., Dai, S.Q., *et al*. (2022) Distinct Prognostic Factors of Ground Glass Opacity and Pure-Solid Lesion in Pathological Stage I Invasive Lung Adenocarcinoma. *World Journal of Oncology*, **13**, 259-271. https://doi.org/10.14740/wjon1499

[9] Kato, H., Shiono, S., Suzuki, H., Uramoto, H., Abe, J., Maeda, S., *et al*. (2024) A Prospective 10-Year Follow-Up Study after Sublobar Resection for Ground-Glass Opacity-Dominant Lung Cancer. *Scientific Reports*, **14**, Article No. 21243. https://doi.org/10.1038/s41598-024-72248-8

[10] Li, D., Deng, C., Wang, S., Li, Y., Zhang, Y. and Chen, H. (2023) Ten-Year Follow-Up Results of Pure Ground-Glass Opacity-Featured Lung Adenocarcinomas after Surgery. *The Annals of Thoracic Surgery*, **116**, 230-237. https://doi.org/10.1016/j.athoracsur.2023.01.014

[11] Ye, T., Shen, X., Wang, S., Wu, H., Wang, Y., Hu, H., *et al*. (2025) Study of the Radiologic and Pathologic Correlations for Subsolid Lung Adenocarcinoma with the Application of Whole-Mount Sections (ECTOP1011). *Translational Lung Cancer Research*, **14**, 341-352. https://doi.org/10.21037/tlcr-2024-1063

[12] Yin, Q., Wang, H., Cui, H., Wang, W., Yang, G., Qie, P., *et al*. (2020) Meta-Analysis of Association between CT-Based Features and Tumor Spread through Air Spaces in Lung Adenocarcinoma. *Journal of Cardiothoracic Surgery*, **15**, Article No. 243. https://doi.org/10.1186/s13019-020-01287-9

[13] Yoshino, I., Moriya, Y., Suzuki, K., Wakabayashi, M., Saji, H., Aokage, K., *et al*. (2023) Long-Term Outcome of Patients with Peripheral Ground-Glass Opacity-Dominant Lung Cancer after Sublobar Resections. *The Journal of Thoracic and Cardiovascular Surgery*, **166**, 1222-1231.e1. https://doi.org/10.1016/j.jtcvs.2023.01.019

[14] Travis, W.D., Brambilla, E., Noguchi, M., Nicholson, A.G., Geisinger, K., Yatabe, Y., *et al*. (2011) International Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society: International Multidisciplinary Classification of Lung Adenocarcinoma: Executive Summary. *Proceedings of the American Thoracic Society*, **8**, 381-385. https://doi.org/10.1513/pats.201107-042st

[15] Yun, J.K., Kim, J.Y., Ahn, Y., Kim, M.Y., Lee, G.D., Choi, S., *et al*. (2024) Predicting Recurrence after Sublobar Resection in Patients with Lung Adenocarcinoma Using Preoperative Chest CT Scans. *Radiology*, **313**, e233244. https://doi.org/10.1148/radiol.233244

[16] Suh, J.W., Jeong, Y.H., Cho, A., Kim, D.J., Chung, K.Y., Shim, H.S., *et al*. (2020) Stepwise Flowchart for Decision Making on Sublobar Resection through the Estimation of Spread through Air Space in Early Stage Lung Cancer. *Lung Cancer*, **142**, 28-33. https://doi.org/10.1016/j.lungcan.2020.02.001

[17] Mantovani, S., Pernazza, A., Bassi, M., Amore, D., Vannucci, J., Poggi, C., *et al*. (2022) Prognostic Impact of Spread through Air Spaces in Lung Adenocarcinoma. *Interactive CardioVascular and Thoracic Surgery*, **34**, 1011-1015. https://doi.org/10.1093/icvts/ivab289

[18] Cao, H., Zheng, Q., Deng, C., Fu, Z., Shen, X., Jin, Y., *et al*. (2024) Prediction of Spread through Air Spaces by Intraoperative Frozen Section for Patients with CT1N0M0 Invasive Lung Adenocarcinoma: A Multicenter Observational Study (ECTOP-1016). *Annals of Surgery*, **281**, 187-192. https://doi.org/10.1097/sla.0000000000006525

[19] Eguchi, T., Kameda, K., Lu, S., Bott, M.J., Tan, K.S., Montecalvo, J., *et al*. (2019) Lobectomy Is Associated with Better Outcomes than Sublobar Resection in Spread through Air Spaces (STAS)-Positive T1 Lung Adenocarcinoma: A Propensity Score-Matched Analysis. *Journal of Thoracic Oncology*, **14**, 87-98. https://doi.org/10.1016/j.jtho.2018.09.005

[20] Riely, G.J., Wood, D.E., Ettinger, D.S., Aisner, D.L., Akerley, W., Bauman, J.R., *et al*. (2024) Non-Small Cell Lung Cancer, Version 4.2024: NCCN Clinical Practice Guidelines in Oncology. *Journal of the National Comprehensive Cancer Network*, **22**, 249-274. https://doi.org/10.6004/jnccn.2204.0023

[21] Cardillo, G., Petersen, R.H., Ricciardi, S., Patel, A., Lodhia, J.V., Gooseman, M.R., *et al*. (2023) European Guidelines for the Surgical Management of Pure Ground-Glass Opacities and Part-Solid Nodules: Task Force of the European Association of Cardio-Thoracic Surgery and the European Society of Thoracic Surgeons. *European Journal of Cardio-Thoracic Surgery*, **64**, ezad222. https://doi.org/10.1093/ejcts/ezad222

[22] Baohui, H. and Jie, W. (2024) Chinese Medical Association Guideline for Clinical Diagnosis and Treatment of Lung Cancer (2024 Edition). *Chinese Journal of Oncology*, **46**, 805-843.

[23] Deruo, L. (2024) Expert Consensus on the Surgical Approach for Lung Cancer with Ground-Glass Nodules ≤ 2 cm Based on High-Resolution CT (2024 Edition). *Chinese Journal of Thoracic and Cardiovascular Surgery*, **40**, 385-391.

[24] El-Sherif, A., Fernando, H.C., Santos, R., Pettiford, B., Luketich, J.D., Close, J.M., *et al*. (2007) Margin and Local Recurrence

after Sublobar Resection of Non-Small Cell Lung Cancer. *Annals of Surgical Oncology*, **14**, 2400-2405. https://doi.org/10.1245/s10434-007-9421-9

[25] Mohiuddin, K., Haneuse, S., Sofer, T., Gill, R., Jaklitsch, M.T., Colson, Y.L., *et al*. (2014) Relationship between Margin Distance and Local Recurrence among Patients Undergoing Wedge Resection for Small (≤2 cm) Non-Small Cell Lung Cancer. *The Journal of Thoracic and Cardiovascular Surgery*, **147**, 1169-1177. https://doi.org/10.1016/j.jtcvs.2013.11.056

[26] Sawabata, N., Maeda, H., Matsumura, A., Ohta, M. and Okumura, M. (2012) Clinical Implications of the Margin Cytology Findings and Margin/Tumor Size Ratio in Patients Who Underwent Pulmonary Excision for Peripheral Non-Small Cell Lung Cancer. *Surgery Today*, **42**, 238-244. https://doi.org/10.1007/s00595-011-0031-6

[27] Moon, Y., Park, J.K. and Lee, K.Y. (2020) The Effect of Resection Margin Distance and Invasive Component Size on Recurrence after Sublobar Resection in Patients with Small (≤2 cm) Lung Adenocarcinoma. *World Journal of Surgery*, **44**, 990-997. https://doi.org/10.1007/s00268-019-05276-5

[28] Suzuki, K., Watanabe, S., Wakabayashi, M., Saji, H., Aokage, K., Moriya, Y., *et al*. (2022) A Single-Arm Study of Sublobar Resection for Ground-Glass Opacity Dominant Peripheral Lung Cancer. *The Journal of Thoracic and Cardiovascular Surgery*, **163**, 289-301.e2. https://doi.org/10.1016/j.jtcvs.2020.09.146

[29] Kim, J.Y., Lee, G.D., Choi, S., Kim, H.R., Kim, Y., Kim, D.K., *et al*. (2025) Revisiting Margin Adequacy in Sublobar Resection for Pure Ground-Glass Opacity Adenocarcinomas. *Lung Cancer*, **205**, Article ID: 108595. https://doi.org/10.1016/j.lungcan.2025.108595

[30] Aokage, K., Suzuki, K., Saji, H., Wakabayashi, M., Kataoka, T., Sekino, Y., *et al*. (2023) Segmentectomy for Ground-Glass-Dominant Lung Cancer with a Tumour Diameter of 3 cm or Less Including Ground-Glass Opacity (JCOG1211): A Multicentre, Single-Arm, Confirmatory, Phase 3 Trial. *The Lancet Respiratory Medicine*, **11**, 540-549. https://doi.org/10.1016/s2213-2600(23)00041-3

[31] Ma, Z., Zhang, Y., Han, H., Wang, S., Li, Y. and Chen, H. (2024) Segmentectomy versus Lobectomy for Ground-Glass Opacity Dominant CT1N0 Invasive Lung Adenocarcinoma. *Translational Lung Cancer Research*, **13**, 1201-1209. https://doi.org/10.21037/tlcr-24-191

[32] Zhang, C., Pan, Y., Li, H., Zhang, Y., Li, B., Zhang, Y., *et al*. (2024) Extent of Surgical Resection for Radiologically Subsolid T1N0 Invasive Lung Adenocarcinoma: When Is a Wedge Resection Acceptable? *The Journal of Thoracic and Cardiovascular Surgery*, **167**, 797-809.e2. https://doi.org/10.1016/j.jtcvs.2023.06.010

[33] Yotsukura, M., Asamura, H., Motoi, N., Kashima, J., Yoshida, Y., Nakagawa, K., *et al*. (2021) Long-Term Prognosis of Patients with Resected Adenocarcinoma *in Situ* and Minimally Invasive Adenocarcinoma of the Lung. *Journal of Thoracic Oncology*, **16**, 1312-1320. https://doi.org/10.1016/j.jtho.2021.04.007

[34] Li, D., Deng, C., Wang, S., Li, Y., Zhang, Y. and Chen, H. (2022) Ten-year Follow-Up of Lung Cancer Patients with Resected Adenocarcinoma *in Situ* or Minimally Invasive Adenocarcinoma: Wedge Resection Is Curative. *The Journal of Thoracic and Cardiovascular Surgery*, **164**, 1614-1622.e1. https://doi.org/10.1016/j.jtcvs.2022.06.017

[35] Hattori, A., Matsunaga, T., Takamochi, K., Oh, S. and Suzuki, K. (2016) Neither Maximum Tumor Size nor Solid Component Size Is Prognostic in Part-Solid Lung Cancer: Impact of Tumor Size Should Be Applied Exclusively to Solid Lung Cancer. *The Annals of Thoracic Surgery*, **102**, 407-415. https://doi.org/10.1016/j.athoracsur.2016.02.074

[36] Xi, J., Yin, J., Liang, J., Zhan, C., Jiang, W., Lin, Z., *et al*. (2021) Prognostic Impact of Radiological Consolidation Tumor Ratio in Clinical Stage IA Pulmonary Ground Glass Opacities. *Frontiers in Oncology*, **11**, Article 616149. https://doi.org/10.3389/fonc.2021.616149

[37] Jing, W., Liu, M., Li, W., Li, D., Wu, Y. and Lv, F. (2024) Prognostic Implication of Consolidation-to-Tumor Ratio in Early Lung Adenocarcinoma: A Retrospective Cross-Sectional Study. *Quantitative Imaging in Medicine and Surgery*, **14**, 3366-3380. https://doi.org/10.21037/qims-23-1438

[38] Nakagawa, K., Watanabe, S., Wakabayashi, M., Yotsukura, M., Mimae, T., Hattori, A., *et al*. (2025) Risk Factors for Locoregional Relapse after Segmentectomy: Supplementary Analysis of the JCOG0802/WJOG4607L Trial. *Journal of Thoracic Oncology*, **20**, 157-166. https://doi.org/10.1016/j.jtho.2024.10.002

[39] Kamtam, D.N., Berry, M.F., Lui, N.S., Satoyoshi, M., Elliott, I.A., Liou, D.Z., *et al*. (2024) What Is an Adequate Margin during Sublobar Resection of ≤3 cm N0 Subsolid Lung Adenocarcinomas? *The Annals of Thoracic Surgery*, **118**, 801-809. https://doi.org/10.1016/j.athoracsur.2024.04.018

[40] Li, H., Wang, Y., Chen, Y., Zhong, C. and Fang, W. (2023) Ground Glass Opacity Resection Extent Assessment Trial (GREAT): A Study Protocol of Multi-Institutional, Prospective, Open-Label, Randomized Phase III Trial of Minimally Invasive Segmentectomy versus Lobectomy for Ground Glass Opacity (GGO)-Containing Early-Stage Invasive Lung Adenocarcinoma. *Frontiers in Oncology*, **13**, Article 1052796. https://doi.org/10.3389/fonc.2023.1052796

[41] Lin, B., Wang, R., Chen, L., Gu, Z., Ji, C. and Fang, W. (2021) Should Resection Extent Be Decided by Total Lesion Size or Solid Component Size in Ground Glass Opacity-Containing Lung Adenocarcinomas? *Translational Lung Cancer Research*, **10**, 2487-2499. https://doi.org/10.21037/tlcr-21-132

[42] Heuts, S., Sardari Nia, P. and Maessen, J.G. (2016) Preoperative Planning of Thoracic Surgery with Use of Three-Dimensional Reconstruction, Rapid Prototyping, Simulation and Virtual Navigation. *Journal of Visualized Surgery*, **2**, Article 77. https://doi.org/10.21037/jovs.2016.03.10

[43] Oza, H. and Doshi, B. (2023) Morphological and Morphometric Study of Pulmonary Vein Anatomy in Relation to Cardiac Invasive and Electrophysiological Procedures. *Anatomy & Cell Biology*, **56**, 428-434. https://doi.org/10.5115/acb.23.141

[44] Chen, X., Dai, C., Peng, M., Wang, D., Sui, X., Duan, L., *et al*. (2025) Artificial Intelligence Driven 3D Reconstruction for Enhanced Lung Surgery Planning. *Nature Communications*, **16**, Article No. 4086. https://doi.org/10.1038/s41467-025-59200-8

[45] Wang, B., Guo, Y., Tang, J. and Yu, F. (2019) Three-Dimensional Custom-Made Carbon-Fiber Prosthesis for Sternal Reconstruction after Sarcoma Resection. *Thoracic Cancer*, **10**, 1500-1502. Https://doi.org/10.1111/1759-7714.13084

[46] Xue, L., Fan, H., Shi, W., Ge, D., Zhang, Y., Wang, Q., *et al*. (2018) Preoperative 3-Dimensional Computed Tomography Lung Simulation before Video-Assisted Thoracoscopic Anatomic Segmentectomy for Ground Glass Opacity in Lung. *Journal of Thoracic Disease*, **10**, 6598-6598. https://doi.org/10.21037/jtd.2018.10.126

[47] Wu, Z., Huang, Z., Qin, Y. and Jiao, W. (2022) Progress in Three-Dimensional Computed Tomography Reconstruction in Anatomic Pulmonary Segmentectomy. *Thoracic Cancer*, **13**, 1881-1887. https://doi.org/10.1111/1759-7714.14443

[48] Toba, H., Kondo, K., Miyoshi, T., Kajiura, K., Yoshida, M., Kawakami, Y., *et al*. (2013) Fluoroscopy-Assisted Thoracoscopic Resection after Computed Tomography-Guided Bronchoscopic Metallic Coil Marking for Small Peripheral Pulmonary Lesions. *European Journal of Cardio-Thoracic Surgery*, **44**, e126-e132. https://doi.org/10.1093/ejcts/ezt220

[49] Jeong, J.H., Park, H., Choi, C., Oh, J.H., Lee, G.D., Kim, D.K., *et al*. (20212) Preoperative Electromagnetic Navigation Bronchoscopy-Guided One-Stage Multiple-Dye Localization for Resection of Subsolid Nodules: A Single-Center Pilot Study. *Thoracic Cancer*, **13**, 466-473. https://doi.org/10.1111/1759-7714.14283

[50] Wada, H., Yamamoto, T., Morimoto, J., Sakairi, Y., Suzuki, H., Nakajima, T., *et al*. (2020) Near-Infrared-Guided Pulmonary Segmentectomy after Endobronchial Indocyanine Green Injection. *The Annals of Thoracic Surgery*, **109**, 396-403. https://doi.org/10.1016/j.athoracsur.2019.08.083

[51] Yutaka, Y., Sato, T., Tanaka, S., Miyahara, S., Yoshizawa, A., Morita, S., *et al*. (2022) Feasibility Study of a Novel Wireless Localization Technique Using Radiofrequency Identification Markers for Small and Deeply Located Lung Lesions. *JTCVS Techniques*, **12**, 185-195. https://doi.org/10.1016/j.xjtc.2021.11.019

[52] Sato, M., Kobayashi, M., Kojima, F., Tanaka, F., Yanagiya, M., Kosaka, S., *et al*. (2018) Effect of Virtual-Assisted Lung Mapping in Acquisition of Surgical Margins in Sublobar Lung Resection. *The Journal of Thoracic and Cardiovascular Surgery*, **156**, 1691-1701.e5. https://doi.org/10.1016/j.jtcvs.2018.05.122

[53] Yamaguchi, H., Sato, M., Yamamoto, K., Ueda, K., Date, H., Chen-Yoshikawa, T., *et al*. (2022) Virtual-Assisted Lung Mapping in Sublobar Resection of Small Pulmonary Nodules, Long-Term Results. *European Journal of Cardio-Thoracic Surgery*, **61**, 761-768. https://doi.org/10.1093/ejcts/ezab421

[54] Wang, Y. and Chen, E. (2024) Advances in the Localization of Pulmonary Nodules: A Comprehensive Review. *Journal of Cardiothoracic Surgery*, **19**, Article No. 396. https://doi.org/10.1186/s13019-024-02911-8

[55] Yutaka, Y., Nishikawa, S., Tanaka, S., Ohsumi, A., Nakajima, D., Menju, T., *et al*. (2024) Extended Segmentectomy for Intersegmental Lesions with Intraoperative Surgical Margin Assessment by Radiofrequency Identification Markers. *JTCVS Techniques*, **28**, 141-150. https://doi.org/10.1016/j.xjtc.2024.08.027

[56] Yanagiya, M., Kawahara, T., Ueda, K., Yoshida, D., Yamaguchi, H. and Sato, M. (2020) A Meta-Analysis of Preoperative Bronchoscopic Marking for Pulmonary Nodules. *European Journal of Cardio-Thoracic Surgery*, **58**, 40-50. https://doi.org/10.1093/ejcts/ezaa050

[57] Zhang, J., Chen, E., Xu, S., Xu, L., Hu, H., Dong, L., *et al*. (2024) Virtual Bronchoscopic Navigation with Intraoperative Cone-Beam CT for the Diagnosis of Peripheral Pulmonary Nodules. *BMC Pulmonary Medicine*, **24**, Article No. 146. https://doi.org/10.1186/s12890-024-02930-0

[58] Yutaka, Y., Sato, T., Hidaka, Y., Kato, T., Kayawake, H., Tanaka, S., *et al*. (2022) Electromagnetic Navigation Bronchoscopy-Guided Radiofrequency Identification Marking in Wedge Resection for Fluoroscopically Invisible Small Lung Lesions. *European Journal of Cardio-Thoracic Surgery*, **63**, ezad006. https://doi.org/10.1093/ejcts/ezad006

[59] Suzuki, K., Nagai, K., Yoshida, J., Ohmatsu, H., Takahashi, K., Nishimura, M., *et al*. (1999) Video-Assisted Thoracoscopic Surgery for Small Indeterminate Pulmonary Nodules: Indications for Preoperative Marking. *Chest*, **115**, 563-568. https://doi.org/10.1378/chest.115.2.563

[60] Tamura, M., Oda, M., Fujimori, H., Shimizu, Y., Matsumoto, I. and Watanabe, G. (2010) New Indication for Preoperative Marking of Small Peripheral Pulmonary Nodules in Thoracoscopic Surgery. *Interactive CardioVascular and Thoracic Surgery*, **11**, 590-593. https://doi.org/10.1510/icvts.2010.241018

[61] Huang, Y., Jin, L.Y., Fei, W., Ni, Y.Y., Chen, Y.J., Xu, H.C., *et al*. (2025) The Application of Virtual Navigation Bronchoscopy Assisted Localization in Thoracoscopic Sublobectomy and Its Impact on Perioperative Outcomes. *Chinese*

Journal of Thoracic and Cardiovascular Surgery, **41**, 212-219.

[62] Sekine, Y., Koh, E. and Hoshino, H. (2021) The Efficacy of Transbronchial Indocyanine Green Instillation for Fluorescent-Guided Wedge Resection. *Interactive CardioVascular and Thoracic Surgery*, **33**, 51-59. https://doi.org/10.1093/icvts/ivab054

[63] Bae, S.Y., Yun, T., Park, J.H., Na, B., Na, K.J., Park, S., *et al*. (2024) Comparative Study of Indocyanine Green Intravenous Injection and the Inflation-Deflation Method for Assessing Resection Margins in Segmentectomy for Lung Cancer: A Single-Center Retrospective Study. *Journal of Chest Surgery*, **57**, 450-457. https://doi.org/10.5090/jcs.24.008

[64] Sun, Y., Zhang, Q., Wang, Z., Shao, F. and Yang, R. (2021) Feasibility Investigation of Near-Infrared Fluorescence Imaging with Intravenous Indocyanine Green Method in Uniport Video-Assisted Thoracoscopic Anatomical Segmentectomy for Identifying the Intersegmental Boundary Line. *Thoracic Cancer*, **12**, 1407-1414. https://doi.org/10.1111/1759-7714.13923

[65] Huang, J., Chen, Q., Hong, S. and Hong, J. (2024) Comparison of ICG-Guided Near-Infrared Fluorescence Imaging and Modified Inflation-Deflation Method in Identifying the Intersegmental Plane during Lung Segmentectomy of Infants. *Journal of Pediatric Surgery*, **59**, 1708-1713. https://doi.org/10.1016/j.jpedsurg.2024.03.061

[66] Sun, Y., Zhang, Q., Wang, Z., Shao, F. and Yang, R. (2019) Is the Near-Infrared Fluorescence Imaging with Intravenous Indocyanine Green Method for Identifying the Intersegmental Plane Concordant with the Modified Inflation-Deflation Method in Lung Segmentectomy? *Thoracic Cancer*, **10**, 2013-2021. https://doi.org/10.1111/1759-7714.13192

[67] Sun, Y., Zhuang, Y., Wang, Z., Jiao, S., Yao, M., Zhang, Q., *et al*. (2024) Indocyanine Green Fluorescence Identification of the Intersegmental Plane by the Target Segmental Vein-First Single-Blocking during Thoracoscopic Segmentectomy. *BMC Surgery*, **24**, Article No. 299. https://doi.org/10.1186/s12893-024-02582-1

[68] Zhao, Y., You, B. and Li, H. (2025) Evaluation of the Short-Term Efficacy of Fluorescence Thoracoscopy-Assisted Temporary Occlusion of Pulmonary Arteries and Veins in Sublobar Resection for Early-Stage Non-Small Cell Lung Cancer. *Chinese Journal of Gastrointestinal Surgery*, **63**, 124-129.

[69] Xu, H., Wu, X., Zhao, S., Wang, Z., Jiang, G., Li, Y., *et al*. (2025) Indocyanine Green Nebulization Visualizes the Pulmonary Bronchus during Video-Assisted Thoracoscopic Surgery. *Journal of Cardiothoracic Surgery*, **20**, Article No. 113. https://doi.org/10.1186/s13019-024-03130-x

[70] Iizuka, S., Kuroda, H., Yoshimura, K., Dejima, H., Seto, K., Naomi, A., *et al*. (2016) Predictors of Indocyanine Green Visualization during Fluorescence Imaging for Segmental Plane Formation in Thoracoscopic Anatomical Segmentectomy. *Journal of Thoracic Disease*, **8**, 985-991. https://doi.org/10.21037/jtd.2016.03.59

[71] Sun, Y., Zhang, Q., Wang, Z. and Shao, F. (2023) Real-Time Image-Guided Indocyanine Green Fluorescence Dual-Visualization Technique to Measure the Intraoperative Resection Margin during Thoracoscopic Segmentectomy. *Asia-Pacific Journal of Clinical Oncology*, **19**, e39-e44. https://doi.org/10.1111/ajco.13771

[72] Patel, Y.S., Farrokhyar, F., Simunovic, M. and Hanna, W.C. (2025) Near-Infrared Fluorescence-Guided Segmentectomy: Added Benefit of Indocyanine Green Dye Diminishes with Surgeon Experience. *Surgical Innovation*, **32**, 211-221. https://doi.org/10.1177/15533506251315979

[73] Li, F., Yang, L., Zhao, Y., Yuan, L., Wang, S. and Mao, Y. (2019) Intraoperative Frozen Section for Identifying the Invasion Status of Lung Adenocarcinoma: A Systematic Review and Meta-Analysis. *International Journal of Surgery*, **72**, 175-184. https://doi.org/10.1016/j.ijsu.2019.10.047

[74] Ortiz, B.A., Engrav, S.K., Roden, A.C., Boland, J.M., Aubry, M., Abdallah, F.A., *et al*. (2025) Impact of Frozen Section Pathology Examination of Surgical Margins in Sublobar Pulmonary Resections for Clinical Stage IA Non-Small Cell Lung Cancer. *The Annals of Thoracic Surgery*, **120**, 1044-1051. https://doi.org/10.1016/j.athoracsur.2025.04.005

[75] Liao, Y., Li, Z., Song, L., Xue, Y., Chen, X. and Feng, G. (2024) Development and Validation of a Model for Predicting Upstage in Minimally Invasive Lung Adenocarcinoma in Chinese People. *World Journal of Surgical Oncology*, **22**, Article No. 135. https://doi.org/10.1186/s12957-024-03414-5

[76] Nagano, M. and Sato, M. (2023) Impact of Surgical Margin after Sublobar Resection of Lung Cancer: A Narrative Review. *Journal of Thoracic Disease*, **15**, 5750-5759. https://doi.org/10.21037/jtd-23-711

[77] Higashiyama, M., Kodama, K., Takami, K., *et al*. (2002) Intraoperative Lavage Cytologic Analysis of Surgical Margins as a Predictor of Local Recurrence in Pulmonary Metastasectomy. *Archives of Surgery*, **137**, 469-474. https://doi.org/10.1001/archsurg.137.4.469

[78] Miyoshi, T., Yoshida, J., Aokage, K., Tane, K., Ishii, G. and Tsuboi, M. (2019) Stapling Cartridge Lavage Cytology in Limited Resection for Pulmonary Malignant Tumors: Assessment of Cytological Status of the Surgical Margin. *Heliyon*, **5**, e01240. https://doi.org/10.1016/j.heliyon.2019.e01240

[79] Kurihara, N., Imai, K., Takashima, S., Nanjo, H., Hiroshima, Y., Ito, S., *et al*. (2022) Stapler-Lavage Cytology Using a New Rapid Immunocytochemistry for Evaluating Surgical Margin Status after Pulmonary Sublobar Resection. *General Thoracic and Cardiovascular Surgery*, **70**, 359-365. https://doi.org/10.1007/s11748-021-01733-y

[80] Gangadharan, S., Sarkaria, I.N., Rice, D., Murthy, S., Braun, J., Kucharczuk, J., *et al*. (2021) Multiinstitutional Phase 2 Clinical Trial of Intraoperative Molecular Imaging of Lung Cancer. *The Annals of Thoracic Surgery*, **112**, 1150-1159. https://doi.org/10.1016/j.athoracsur.2020.09.037

[81] Bhattacharyya, S., Patel, N.L., Wei, L., Riffle, L.A., Kalen, J.D., Hill, G.C., *et al*. (2014) Synthesis and Biological Evaluation of Panitumumab-IRDye800 Conjugate as a Fluorescence Imaging Probe for EGFR-Expressing Cancers. *MedChemComm*, **5**, 1337-1346. https://doi.org/10.1039/c4md00116h

[82] Bou-Samra, P., Kennedy, G.T., Chang, A., Guo, E., Azari, F.S., Din, A., *et al*. (2025) Phase 2 Clinical Trial of VGT-309 for Intraoperative Molecular Imaging during Pulmonary Resection. *The Annals of Thoracic Surgery*, **119**, 625-633. https://doi.org/10.1016/j.athoracsur.2024.05.019

[83] Kennedy, G.T., Azari, F.S., Chang, A., Bou-Samra, P., Desphande, C., Predina, J., *et al*. (2024) A Phase 2 Multicenter Clinical Trial of Intraoperative Molecular Imaging of Lung Cancer with a pH-Activatable Nanoprobe. *Molecular Imaging and Biology*, **26**, 585-592. https://doi.org/10.1007/s11307-024-01933-x

[84] Kamimura, G., Ueda, K., Suzuki, S., Maeda, K., Hakamada, H. and Sato, M. (2022) Intraoperative Computed Tomography of a Resected Lung Inflated with Air to Verify Safety Surgical Margin. *Quantitative Imaging in Medicine and Surgery*, **12**, 1281-1289. https://doi.org/10.21037/qims-21-562

[85] Kitazawa, S., Bernards, N., Gregor, A., Sata, Y., Hiraishi, Y., Ogawa, H., *et al*. (2024) Feasibility of Computed Tomography-Derived Surgical Margin Assessment in an *ex Vivo* Sublobar Lung Resection Model. *Interdisciplinary CardioVascular and Thoracic Surgery*, **40**, ivae211. https://doi.org/10.1093/icvts/ivae211