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Review

Towards real time AI-augmented fluorescence-guided surgery: Evidence and translational readiness across neurosurgical, gynaecological, and thoracic oncology

Omar Shafi [a,*], Mirkomol Mirzarakhimov [b], Siena Martin [a], Darcy Gabriel [a], Un Hou Chan [c], Saurabh Phadnis [d], Hasan Asif [e], Mauro Camacho [a]

[a] Department of Medicine, St George's Medical School, City St George's, Blackshaw Road Tooting, London, SW17 0QT, UK
[b] Department of Medicine, Brunel Medical School, Kingston Ln, Uxbridge, UB8 3PH, UK
[c] School of Biomedical Engineering & Imaging Sciences Rayne Institute, King's College London, St. Thomas' Hospital, Westminster Bridge Road, London, SE1 7EH, UK
[d] Gynaecological Oncology Service, The Royal London Hospital, Whitechapel Rd, London, E1 1FR, UK
[e] Neurosurgery Unit, St George's Hospital, Blackshaw Road Tooting, London, SW17 0QT, UK

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ABSTRACT

Fluorescence-guided surgery (FgS) is increasingly used across oncologic specialties to enhance intraoperative visualisation of tumour tissue and lymphatic drainage; however, its clinical impact remains limited by heterogeneous tracer uptake, variable signal intensity, and reliance on subjective visual interpretation, leading to inter-operator variability, uncertainty at tumour margins, residual disease, and inconsistent nodal assessment. This narrative review examines the role of artificial intelligence (AI) in addressing these limitations, synthesising evidence published between January 2000 and December 2025 across neuro-oncology, gynaecological oncology, and thoracic oncology. In neuro-oncology, early clinical and preclinical studies have directly evaluated real-time AI-enhanced interpretation of intraoperative fluorescence, including quantitative analysis of 5-aminolevulinic acid (5-ALA) and hyperspectral imaging, providing proof-of-concept evidence that AI can augment margin detection beyond subjective visual assessment. In contrast, gynaecological and thoracic oncology currently lack validated studies in which AI directly interprets intraoperative fluorescence signals, despite fluorescence imaging being clinically established in both fields; instead, AI development in these specialties has progressed primarily in adjacent domains such as radiomics, digital pathology, risk stratification, surgical planning, and intraoperative computer vision, demonstrating technical maturity but limited integration into fluorescence-guided decision-making. Overall, the available evidence supports proof-of-concept feasibility for real-time AI-enhanced fluorescence interpretation in neuro-oncology, while identifying a clear translational gap in gynaecological and thoracic oncology that warrants targeted research to integrate existing AI capabilities into intraoperative fluorescence-guided surgery.

1. Methods

1.1. Literature search strategy and scope

i. A structured literature search was conducted to identify studies published between January 2000 and December 2025 examining fluorescence-guided surgery (FgS), intraoperative imaging, and artificial intelligence (AI) within oncological surgery.
ii. Formal database searches were performed in PubMed/MEDLINE, Scopus, and the Cochrane Library, restricted to English-language publications. Search strategies were constructed as specialty-specific Boolean queries for neuro-oncology, gynaecological oncology, and thoracic oncology, supplemented by a cross-cutting AI query focused on intraoperative and real-time surgical imaging. Search terms combined concepts relating to fluorescence imaging (e.g. 5-aminolevulinic acid, indocyanine green, near-infrared fluorescence, hyperspectral imaging), surgical intervention (e.g. intraoperative guidance, resection margins, extent of resection), oncology, and artificial intelligence (e.g.

* Corresponding author.
E-mail address: m2301849@sgul.ac.uk (O. Shafi).

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deep learning, computer vision, augmented reality). Database-specific adaptations were applied where required.

iii. In addition to structured database searches, targeted supplementary searches were undertaken using Google Scholar and EMBASE, alongside backward and forward citation screening of key articles, to identify supporting or interdisciplinary studies not consistently captured by database indexing, particularly within rapidly evolving AI and intraoperative imaging literature.

1.2. Study selection and screening

i. Search results from all databases were merged and deduplicated using a structured algorithmic approach based on digital object identifiers (DOIs), normalised titles, and publication year, with retracted publications excluded prior to screening. Records were initially screened at title and abstract level.

ii. Title–abstract screening was supported by a rule-based computational pipeline for deduplication and keyword filtering, with all eligibility decisions confirmed by manual author review. Records were retained if they demonstrated relevance to oncological surgery, intraoperative or operative context, and fluorescence imaging and/or AI-based image interpretation. Studies were excluded if they were limited to non-surgical diagnostics (e.g. radiomics-only, screening or prognostic modelling), purely preclinical or in-vitro work without translational relevance, or unrelated imaging modalities.

iii. Full-text review was undertaken where indicated to confirm eligibility and relevance. In total, 13,553 records were identified across databases, with 9410 records remaining after deduplication and exclusion of retracted publications. Following screening, 40 studies identified through formal database searching were prioritised as the core evidence base, comprising outcome-critical clinical studies and highly influential translational or methodological publications. A further 66 studies, identified through supplementary searching and citation chaining, were included to provide contextual, methodological, and translational support. Study identification, screening, and inclusion are summarised using a PRISMA-style flow diagram (Fig. 1).

1.3. Eligibility criteria

i. Studies were eligible for inclusion if they met the following criteria:
   - Study design: Randomised controlled trials, prospective or retrospective cohort studies, systematic reviews, meta-analyses, narrative reviews, and selected case series where these provided relevant clinical, technical, or translational insight.
   - Population: Adult or paediatric patients undergoing oncological surgery.
   - Intervention: Use of established or investigational fluorescence tracers (e.g. 5-ALA, ICG, tumour-targeted fluorophores) and/or AI-based methods applied to intraoperative image interpretation, segmentation, or visualisation.
   - Outcomes: Clinically or technically relevant endpoints, including margin status, extent of resection, sentinel lymph node detection, morbidity, recurrence, survival metrics, or demonstrable impact on intraoperative decision-making or workflow.

1.4. Data synthesis and quality assessment

i. Given heterogeneity in study design, clinical context, fluorescence agents, and AI methodologies, findings were synthesised narratively rather than through quantitative meta-analysis. Studies were grouped thematically into: (i) clinical applications of FgS, (ii) limitations of fluorescence interpretation, and (iii) AI-based approaches to intraoperative image analysis and decision support.

ii. Methodological quality assessment was performed only for outcome-critical clinical and translational studies that directly evaluated intraoperative fluorescence-guided surgery, AI-assisted intraoperative imaging, or patient-relevant outcomes. Quality appraisal was conducted qualitatively using study-design–appropriate criteria, focusing on internal validity, risk of bias, and applicability to intraoperative decision-making rather than numerical scoring. Appraisals

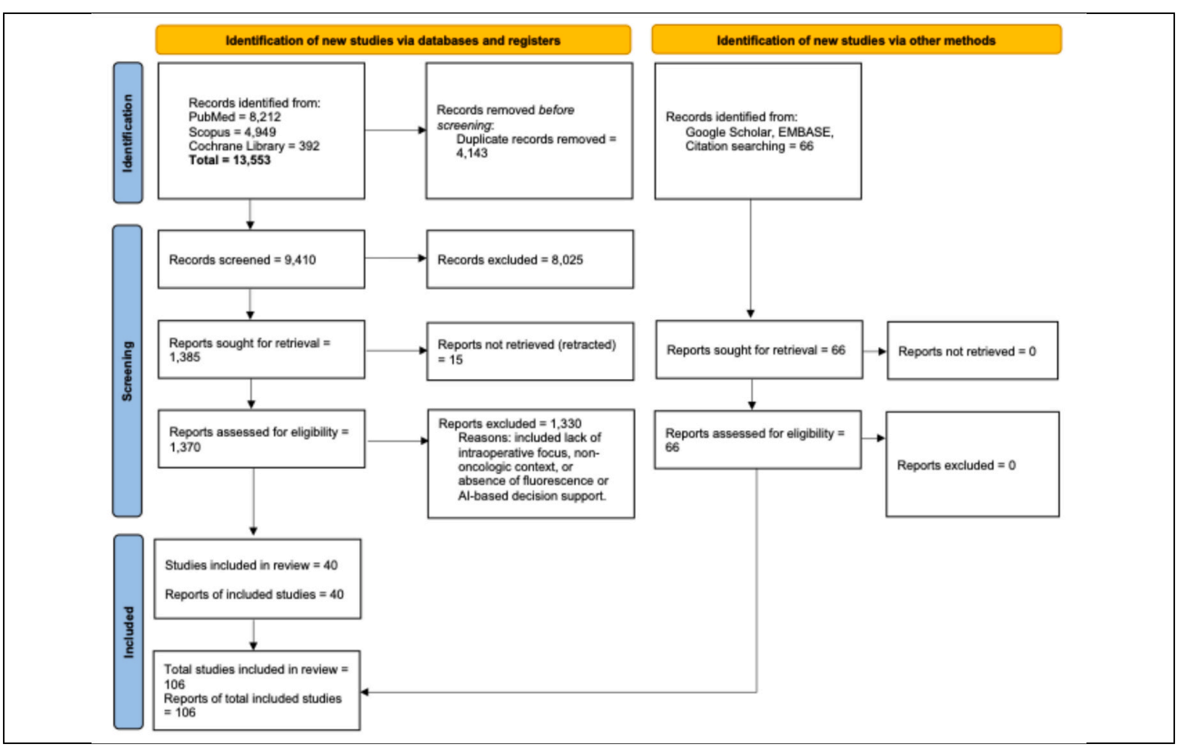

Fig. 1. PRISMA-style flow diagram of literature search, screening, and study selection.

and assessments were agreed by consensus amongst all authors. Narrative reviews, consensus statements, and purely technical feasibility studies were not subjected to formal quality appraisal. Results are summarised in Supplementary Table S1.

1.5. Ethical considerations

i. This review involved no primary data collection and did not require ethical approval. All included studies were reviewed to confirm appropriate ethical approval and informed consent where applicable.

2. Literature

Fluorescence-guided surgery (FgS) is used across multiple oncologic specialties to support intraoperative visualisation, but the role of artificial intelligence (AI) within these workflows differs substantially by domain. In neuro-oncology (NO), early clinical and preclinical studies have begun to explore direct, AI-enhanced interpretation of fluorescence signals, providing proof-of-concept evidence for quantitative intraoperative guidance. In contrast, gynaecological and thoracic oncology (GO and TO) were selected because fluorescence imaging (FI) is already clinically established in these fields, and AI capabilities are actively being developed across closely related domains such as imaging, pathology, risk stratification, and surgical planning. However, validated studies applying AI directly to intraoperative fluorescence interpretation are currently lacking. The sections that follow present NO as an evidence-informed application of AI-enhanced FgS. GO and TO are examined as specialties in which Fg workflows are already established and AI methods are developed in adjacent clinical domains, creating a clear basis for future application to direct intraoperative fluorescence interpretation.

2.1. Clinical imperative for precise tumour resection and nodal assessment

i Neuro-Oncology (NO)

Survival Impact of Maximising Resection Extent in Glioblastoma: Achieving complete tumour resection in neurosurgery is crucial in preventing disease persistence, subsequent tumour regrowth and patient mortality, this emphasises the importance of precision during surgical intervention. The extent of tumour resection significantly influences disease persistence. A study by Lacroix et al. involving 416 patients with glioblastoma multiforme (GBM) found that those who underwent gross total resection (GTR) (defined as≥98% of tumour volume removed) had a median survival of 13 months (95% CI: 11.4-14.6 months), compared to 8.8 months (95% CI: 7.4-10.2 months) for those with subtotal resection (STR), (defined as <98% removed) with a statistical significance of $p < 0.0001$. The 5-year survival rate was almost exclusively observed in the GTR group. This highlights the critical role of thorough resection in prolonging survival [1]. Further supporting these findings, a meta-analysis of 37 studies involving 41,117 patients with GBM revealed that GTR significantly reduces mortality compared to STR. For 1-year survival, the relative risk (RR) of mortality for GTR vs STR was 0.62 (95% CI: 0.56–0.69; $P < 0.001$), indicating a 38% reduction in the risk of death. The number needed to treat (NNT) was calculated as 9, suggesting one additional patient survives 1 year for every nine patients undergoing GTR instead of STR. At 2 years, GTR demonstrated a RR of 0.84 (95% CI: 0.79–0.89; $P < 0.001$), with an NNT of 17. Additionally, the likelihood of disease progression was significantly reduced with GTR. At 1 year, the RR for progression was 0.66 (95% CI: 0.43–0.99; $P < 0.001$), reflecting a 34% reduction in progression risk. These findings underscore the critical role of maximising resection extent in improving survival and delaying tumour progression in GBM patients [2]. Additional studies are summarised in Table 1.

Table 1
Studies Comparing GTR vs STR in Glioblastoma: Overall Survival (OS) Outcomes.

Author	Year	Sample Size	Median OS (GTR)	Median OS (STR)	Key Findings
Chaichana et al.	2014	259	14.4 months (70% EOR)	10.5 months (=< 70% EOR)	Minimum extent of resection (EOR) of 70% significantly associated with improved survival and delayed recurrence [3].
Ewelt et al.	2011	103	13.9 months	7 months	GTR extends survival significantly in elderly patients with glioblastoma [4]
Pichlmeier et al.	2008	243	15.2 months	9.9 months	EOR predicted longer survival across all patient subgroups. GTR demonstrated consistent survival advantages over STR [5].
Li et al.	2016	1229	15.2 months (100% resection of contrast-enhancing tumour)	9.8 months (78% to <100% EOR)	Complete resection of contrast-enhancing tumour was associated with significantly longer survival compared with incomplete resection, independent of other prognostic factors (HR 1.53, $p < 0.001$) [6].
Grabowski et al.	2014	128	<98%, Mean survival = 14 months.	>98%, Mean survival = 16 months.	The volume of residual tumour emerged as the most critical radiological factor influencing survival in this study [7].

Clinical Utility and Outcome Benefits of 5-ALA Fg Resection in Glioblastoma: FI has revolutionised neurosurgical practice, particularly in glioblastoma resection, by providing real-time visualisation of tumour tissue (See Fig. 2 for a visual example). The most widely used dye, 5-ALA, is administered orally 3–4 h before surgery. Once absorbed, it crosses the blood-brain barrier and selectively accumulates in tumour cells, to their hypermetabolic state. Tumour cells metabolise 5-ALA into the fluorescent compound protoporphyrin IX (PPIX), which emits a red-pink signal under blue-violet light, enabling visual distinction from non-fluorescent healthy brain. Intraoperative blue-light microscopy enhances tumour margin visualisation, supporting more complete resection and underpinning its guideline-recommended use in malignant glioma surgery [8].

FgS using 5-ALA has revolutionised glioblastoma resection by enhancing surgical precision and improving outcomes. A meta-analysis by Eljamel (2015) reviewed 20 studies involving 565 patients and found that FgS achieved a mean GTR rate of 75.4% (95% CI: 67.4–83.5), significantly higher than conventional methods. This increased resection extent correlated with a mean time to tumour progression of 8.1 months (95% CI: 4.7–12, $p < 0.001$), underscoring its role in delaying disease

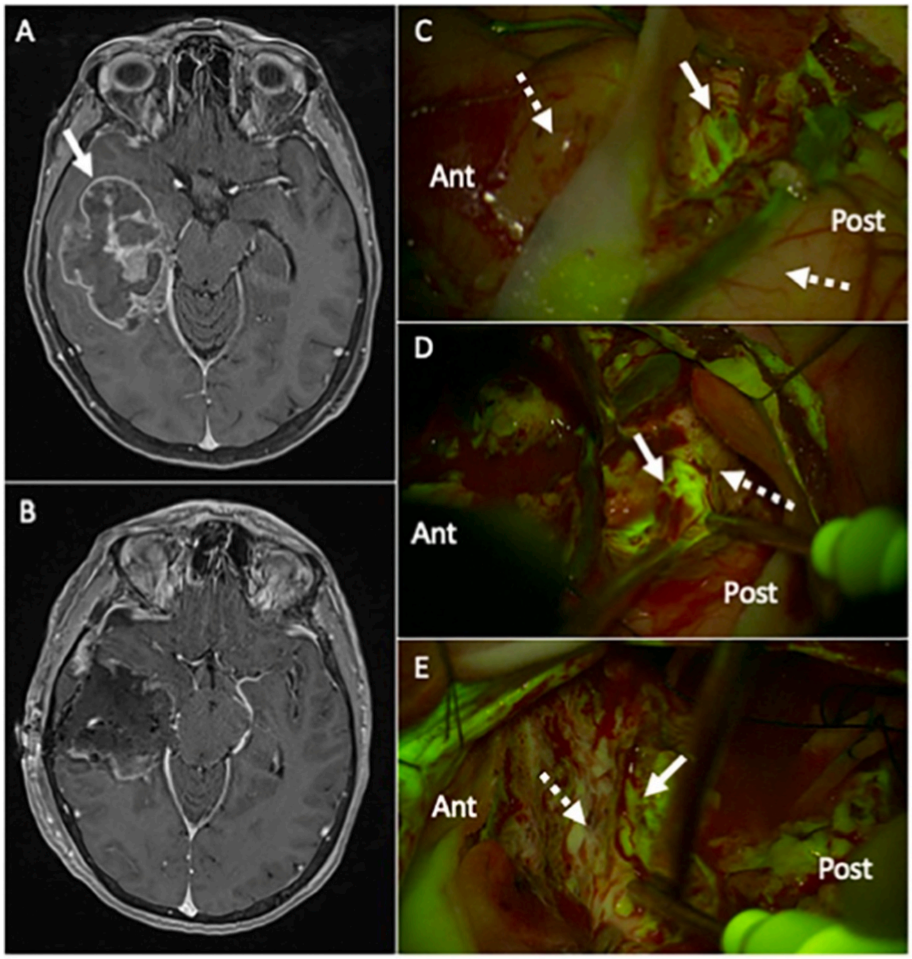

Fig. 2. Sodium fluorescein–guided glioma resection, demonstrating bright green–yellow tumour fluorescence under a Y560 filter. Although mechanistically distinct from 5-ALA–induced protoporphyrin IX fluorescence, both agents rely on qualitative visual interpretation, highlighting the subjectivity and reproducibility limits that motivate AI-assisted intraoperative fluorescence analysis [9] Licensed under the Creative Commons Attribution Licence. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

persistence. Furthermore, the study reported a 6.2-month mean OS gain (95% CI: 1–13, $p < 0.001$), suggesting a potential impact on survival. This evidence highlights the transformative potential of 5-ALA–FgS in optimising tumour resection and improving survival in glioblastoma patients [10]. Additionally, a study by Mirza et al. (2021) found that patients undergoing 5-ALA–guided resection had a median OS of 17.47 months, compared to 10.63 months in those who had surgery without 5-ALA guidance [11]. The study also noted improved postoperative performance status and a lower incidence of new neurological deficits in the 5-ALA group, validating the safety and efficacy of this technique. Collectively these findings highlight a strong association between 5-ALA-guided surgery and improved postoperative outcomes [11]. Additional studies found in Table 2.

Limitations of 5-ALA Fluorescence: One limitation of 5-ALA FI is the variability in fluorescence intensity that can occur due to metabolic heterogeneity or insufficient PPIX accumulation at tumour margins. This variability can result in weak fluorescence signals that are undetectable to the naked eye, particularly in challenging surgical fields where factors such as obscuration by blood or indistinct tumour margins further complicate visualisation [17,18]. Despite improved 5-ALA fluorescence detection, intraoperative interpretation remains surgeon-dependent and limited by heterogeneous signal, tumour biology, and blood obscuration [10,11]. Incorporating AI into this workflow could improve detection by enabling real-time analysis of fluorescence signals and supporting more accurate assessment of tumour margins. Where fluorescence is absent or equivocal, multimodal strategies, such as combining 5-ALA guidance with intraoperative MRI, may provide complementary anatomical information to support more complete resection and address limitations of FgS alone [8,11,19].

Residual Tumour Progression and the Need for More Precise Intraoperative Detection: Residual tumour progression is a critical concern in neurosurgery, particularly when treating glioblastoma and other high-grade gliomas. Tumours that are not fully resected continue to grow, leading to disease progression and ultimately diminishing patient survival. Achieving complete tumour resection is vital in reducing this risk. Studies have consistently shown that patients undergoing GTR experience significantly improved outcomes, with a decrease in tumour progression and a longer OS [1,2]. For example, Villani et al. (2022) reported that approximately 70% of glioblastoma patients experience disease progression within one year of diagnosis, highlighting the aggressive natural history of the disease and supporting the rationale for maximal tumour resection to delay recurrence [20]. However, complete resection must be balanced with the preservation of essential brain tissue, particularly in regions that control vital functions. In these cases, FI technologies, such as 5-ALA-guided surgery, have proven to be invaluable in improving the EOR. They allow surgeons to visualise tumour margins more precisely, which reduces the risk of leaving residual tumour cells behind. Nonetheless, there remains a challenge: the variability of fluorescence intensity, which may cause difficulties in identifying small or poorly fluorescing tumour cells, particularly at the

Table 2
Comparison of Progression-Free Survival (PFS), OS, and GTR Rates in FgS vs. Without.

Author	Year	Sample Size	With FI such as 5 – ALA or SF	Without FI	Key Findings
Stummer et al.	2006	322	Median PFS at 6 months - FI: 41% (95% CI: 32.8–49.2)	Median PFS at 6 months - white light: 21% (95% CI: 14.0–28.2)	FgS resulted in a 65% complete resection rate, compared to 36% with white light [12].
Schatlo et al.	2015	199	Median OS (iMRI + 5-ALA): 17.9 months	Median OS (Non-iMRI): 13.8 months	Combined use of iMRI and 5-ALA improved GTR rates and unadjusted survival outcomes; adjusted impact not significant [13].
Picart et al.	2023	147	GTR rate: 79.1%; Median PFS: 10.0 months; Median OS: 18.7 months.	GTR rate: 47.8%; Median PFS: 10.3 months; Median OS: 20.1 months.	5-ALA increased GTR rates significantly but did not improve PFS or OS compared to white-light surgery [14]
Schebesch et al.	2022	347	Median EOR 100.0%; Median PFS 8.12 months; Median OS 16.7 months	Median EOR 96.4%; Median PFS 6.94 months; Median OS 15.5 months	Fg resection significantly increased extent of resection and was associated with longer PFS and OS compared with white-light surgery in a prospective registry cohort [15].
Xiao et al.	2024	67	GTR rate: 84.4%; Median PFS: 11.2 months; Median OS: 18.2 months.	GTR rate: 60.0%; Median PFS: 7.7 months; Median OS: 14.0 months.	FgS significantly improved GTR rates (84.4% vs. 60%) and PFS (11.2 months vs. 7.7 months) compared to white-light surgery. No significant difference in OS [16].

tumour's margins [17,18]. Incorporating AI into this process can help overcome these limitations by providing real-time, data-driven insights, which could significantly improve tumour detection and precision in resection [21]. Ultimately, the precision with which tumours are resected, alongside technological advancements, plays a crucial role in reducing residual disease and improving long-term patient outcomes.

AI Innovations in Fg and Intraoperative Surgical Imaging: Nonetheless, emerging AI research in NO demonstrates clear potential to transform FgS from subjective visual assessment into quantitative, standardised intraoperative guidance. Building on this, deep-learning systems are already being applied across glioma surgery for diagnostic modelling, prognostic prediction and intraoperative support [22]. More specifically, recent hyperspectral imaging work shows that deep-learning models can correct wavelength-dependent artefacts, unmix complex fluorophore spectra, and generate quantitative PpIX maps with far greater accuracy than classical linear methods. Autoencoder-based correction achieves near-perfect correlation with ground-truth PpIX (R = 0.98–0.997) and reduces specular artefacts and margin variability, enabling more reliable quantification of low-visibility fluorescence in human biopsy data [23]. Machine-learning benchmarks on clinical hyperspectral datasets demonstrate that deep-learning methods can distinguish tumour from normal tissue with median macro-F1 scores of approximately 70%, supporting margin detection even when 5-ALA fluorescence is weak or absent [24]. Moreover, hyperspectral deep-learning methods improve tumour–brain contrast and support more objective delineation of glioma tissue across heterogeneous tumour types, extending beyond visual fluorescence alone [25]. A multiparametric MRI deep-learning model predicts intraoperative 5-ALA fluorescence in lower-grade gliomas with approximately 80% balanced accuracy, enabling preoperative identification of tumours likely to contain fluorescent anaplastic foci and supporting targeted intraoperative sampling [26].

At NHNN Queen Square, AI-assisted computer-vision analysis of intraoperative video has demonstrated reliable real-time performance; in a study of >5000 aneurysm-clipping frames, AI support increased consultant accuracy from 77% to 92%, confirming the feasibility of high-fidelity intraoperative video interpretation. Early anatomical-recognition work in endoscopic pituitary surgery also shows that AI can interpret complex skull-base anatomy, improving novice accuracy from 66% to 79% [27]. These studies highlight that adoption depends not only on accuracy but on trust, explainability and cognitive workload, reinforcing that fluorescence-AI systems must provide interpretable, workload-appropriate guidance rather than opaque overlays [27]. In parallel, the IDEAL-Robotics consensus provides a structured pathway for safe surgical-AI evaluation, emphasising staged development, comparative assessment and long-term monitoring [28]. Together, these advances indicate that the technical foundation for AI-assisted intraoperative interpretation exists, although further research is required to adapt them to FgS-tumour and ensure real-time explainability and surgeon–AI alignment.

ii Gynaecological Oncology (GO)

Importance of Lymph Node Resection in Gynaecological Cancers: Lymph node involvement is a key route for metastasis in GO, with spread to extra-peritoneal sites, including para-aortic nodes, significantly worsening prognosis and underscoring the importance of accurate nodal assessment [29,30]. Accurate nodal assessment determines FIGO stage and guides adjuvant therapy. Traditionally achieved by systematic pelvic and para-aortic lymphadenectomy, its morbidity led to adoption of the sentinel lymph node (SLN) approach, which targets the first draining nodes most likely to contain metastases [31–33]. In endometrial cancer, a large single-centre study of 1532 patients demonstrated that removing more than seven pelvic lymph nodes was associated with a 32% reduction in mortality risk (HR 0.68) and a 46% reduction in progression risk (HR 0.54) [34]. Similarly, in cervical cancer, SEER database analysis of 5522 women with stage IA2–IIA disease found that, among node-negative cases, removal of 21–30 nodes (HR 0.76) and >30 nodes (HR 0.64) improved overall survival compared to fewer than 10 nodes [35]. A SEER study of 703 node-positive vulvar cancer patients found improved survival when more than six lymph nodes were removed during inguinofemoral lymphadenectomy. Three-year overall survival was 50.6–61.1% for 7–45 nodes versus 36.1% for 1–6 nodes (HR 1.44; p = 0.013) [36]. While lymph node involvement is prognostically important, systematic lymphadenectomy is associated with substantial morbidity, including lymphoedema, lymphocyst formation, and neurovascular injury [37]. The goal is precision, maximising oncologic benefit while minimising harm by targeting likely diseased nodes through SLN mapping, advanced imaging, and emerging AI-guided approaches.

Although lymphadenectomy improves staging accuracy, its morbidity in GO has driven a shift toward less invasive, precision-based approaches. In endometrial cancer, a meta-analysis of 1922 women showed a higher risk of lymphoedema or lymphocyst formation after lymphadenectomy (RR 8.39; 95% CI 4.06–17.33) [38]. In cervical cancer, a meta-analysis of 3079 early-stage patients reported perioperative lymphatic complications in 3.48% of cases following radical hysterectomy with pelvic lymphadenectomy [39]. In vulval cancer, retrospective data highlight frequent wound complications and persistent lymphoedema after inguinofemoral dissection [40]. In ovarian cancer, the LION trial found no survival benefit from systematic pelvic and para-aortic lymphadenectomy (median OS 69.2 vs 65.5 months; HR 1.06; 95% CI 0.83–1.34; $p = 0.65$) but higher complications (repeat laparotomy 12.4% vs 6.5%; 60-day mortality 3.1% vs 0.9%) [41]. These studies highlight the trade-off between staging precision and surgical morbidity, supporting the shift toward safer alternatives (Table 3).

ICG Fluorescence Sentinel Node Mapping: Fg SLN mapping has become an important innovation across GO, offering high diagnostic accuracy with reduced morbidity compared to conventional lymphadenectomy. Traditionally, lymph node evaluation in GO relied on complete lymphadenectomy or dual-tracer methods using blue dye and technetium-99. While effective, these were logistically demanding and carried procedural risks. Indocyanine green (ICG) fluorescence offers a superior alternative, enabling real-time lymphatic visualisation with higher detection accuracy. In early-stage cervical cancer, ICG achieved significantly higher bilateral detection (93.2% vs. 77.7%, $p = 0.004$) and overall sentinel node identification (99.0% vs. 92.2%) than patent blue dye, detecting all metastatic nodes compared with only two-thirds by blue dye [46]. Furthermore, Fg SLN mapping is regarded as the "ideal" technique for detecting sentinel nodes, combining high accuracy with minimal invasiveness [47]. In endometrial cancer, ICG-based fluorescence SLN mapping achieves ~97% per-patient detection and ~96% sensitivity, including in high-grade cohorts when validated SLN algorithms are used [33]. In vulvar cancer, near-infrared fluorescence using ICG has demonstrated promising sentinel lymph node detection rates and excellent safety, comparable to current standard techniques [48]. In ovarian cancer, a prospective multicentre study demonstrated that ICG-guided SLNB is feasible, with an overall detection rate of 67.7%, increasing to 88.9% during immediate staging, and showed 100% sensitivity with no false-negative cases, supporting its potential accuracy and safety in nodal staging [49]. Early feasibility studies further indicate that ICG-based SLN mapping is technically feasible and potentially valuable for staging in ovarian cancer, though current evidence remains limited and largely exploratory [50]. However, fluorescence-based SLN mapping has limitations, with false negatives related to technique, injection approach, and low-volume disease, and accuracy remains operator-dependent, highlighting the need for improved imaging and technological support [51]. Table 4 summarises ICG detection rates, diagnostic accuracy, and practical advantages across GO, with subsequent sections expanding on the role of FI in lymph node staging.

Limitations of Current Fluorescence and Sentinal Node Techniques: Despite the proven effectiveness of fluorescence agents, current studies highlight important limitations in FgS and SNLB, many of which relate to variability in signal interpretation and reliability. Detection rates remain variable; in ovarian cancer, Uccella et al. (2019) reported an overall SLN detection rate of 67.7%, falling to 41.7% in delayed staging procedures. Separately, preclinical studies show that activatable fluorescence probes may suffer from limited specificity, with Nakamura et al. (2017) demonstrating modest specificity (61%) due to non-specific probe activation in adjacent non-malignant tissues [49,54]. High false-positive rates persist, with Tanyi et al. (2023) reporting a lesion-level false-positive rate of 32.7%, highlighting challenges in reliably distinguishing true disease from background signal. Moreover, current phase III intraoperative fluorescence trials are designed primarily to detect macroscopic disease, and reliable identification of very small lesions or micrometastases remains unproven [55]. For example,

Table 3
Summary of key studies demonstrating increased morbidity associated with systematic lymphadenectomy in GO.

Author	Year	Patient Cohort	% With Negative Nodes	Morbidity	Key Finding
Beesley VL et al. *Australian National Endometrial Cancer Study Group*	2015	1243 women with endometrial cancer, median follow-up 3–5 years	Majority stage I; nodal metastases were uncommon (>80% node-negative)	13 % developed secondary lower-limb lymphoedema	Increasing nodal yield independently predicted lymphoedema risk, rising stepwise with number of nodes removed. Absolute risk exceeded 50% only in women undergoing extensive lymphadenectomy (≥15 nodes) in the presence of additional risk factors [42].
Yost KJ et al., *Obstetrics & Gynecology*	2014	591 women with endometrial cancer (median 6.2 years follow-up) from Mayo Clinic	~90 % (majority FIGO I–II, low-grade endometrioid tumours)	47 % developed lower-limb lymphoedema overall (36.1 % hysterectomy only vs 52.3 % with lymphadenectomy; attributable risk 23 %)	Lymphadenectomy independently doubled lymphoedema risk (OR 2.04; 95% CI 1.39–2.99) and reduced quality of life [43].
Togami S et al., *Japanese Journal of Clinical Oncology*	2018	169 women with stage IA2–IIB cervical cancer undergoing pelvic lymphadenectomy	64.5 % (109/169 node-negative)	Lower-limb lymphoedema 16.6 %, pelvic lymphocele 18.9 %	Removing ≥28 nodes or performing circumflex iliac node dissection increased lymphoedema risk (OR 3.37 and 3.92). Greater dissection extent raised morbidity [44].
Rouzier R et al. *Journal of the American College of Surgeons*	2003	194 women with primary vulvar squamous cell carcinoma undergoing various extents of inguinofemoral dissection	Nodal metastases identified in 22% of dissected groins (groin-level analysis)	Chronic leg lymphoedema >6 months in 47 % after full inguinofemoral LND vs 11 % after limited medial inguinal/femoral LND. More extensive dissection and sartorius transposition significantly increased oedema ($p = 0.011$).	Extent of lymphadenectomy independently predicted lymphoedema. Morbidity increased with radicality, while survival and recurrence were unaffected. Vein-sparing, limited dissections reduced complications without loss of oncologic control [45].
Harter P et al., *LION Trial, N Engl J Med*	2019	647 women with FIGO stage IIB–IV advanced epithelial ovarian cancer and clinically normal nodes after complete macroscopic resection	Clinically node-negative at randomisation (normal nodes before and during surgery); 55.7% had occult histologic metastases in LND arm.	Higher morbidity with lymphadenectomy: repeat laparotomy 12.4% vs 6.5%, infections 25.8% vs 18.6%, 60-day mortality 3.1% vs 0.9%	Systematic pelvic and para-aortic lymphadenectomy showed no survival benefit (HR 1.06; 95% CI 0.83–1.34) but increased morbidity, confirming no advantage in node-negative advanced disease [41].

Table 4
SLN detection rates, diagnostic accuracy, and practical benefits of ICG use across GO.

Author	Cancer Type	Detection Rates	Accuracy/Key Outcomes	Advantages
Wess et al. (2024)	Cervical	93.2% (ICG), 77.7% (patent blue), 99.0% (ICG + patent blue)	No false-negative SLNs were reported in the ICG group	Higher bilateral detection rates and metastatic node identification with ICG [46].
Koual et al. (2021)	Vulvar	Detection rates across included studies ranged from 89.7 to 100%	No adverse events; equivalent to gold-standard dual labelling techniques	Safe, feasible alternative with logistical advantages compared with dual-labelling techniques [48]
Uccella et al. (2019)	Ovarian	67.7% overall, 88.9% (immediate staging), 41.7% (delayed staging)	Sensitivity and negative predictive value were 100% within this preliminary multicentre cohort, with no false-negative SLNs reported	Feasibility in ovarian cancer; potential to reduce lymphadenectomy morbidity [49].
Gelissen et al. (2019)	Endometrial and Cervical	Bilateral SLN mapping successful in younger women (mean 60.8 years) vs failure in older women (64.7 years).	Age and menopausal status independently associated with bilateral mapping success (age $p = 0.0054$; premenopausal $p = 0.042$). No association with BMI, stage, grade, histology, LVSI, tumour size, depth, or location.	SLN mapping feasible in endometrial and cervical cancer; older/postmenopausal patients have higher failure risk, informing counselling and contingency planning [52]
Laufer et al. (2024)	Cervical	Overall: 88–100%, Bilateral: 74.1–98.5%	4 mL ICG concentration of 1.25 mg/mL achieved high detection rates and minimal variability; NPV ≥97% in most high-quality included studies.	A commonly used protocol (4 mL, 1.25 mg/mL) was associated with high and consistent detection rates across studies [53]

frozen section analysis in Wess et al. (2024) had a sensitivity of just 25% for micrometastases, reinforcing the limitations of existing intraoperative assessment and the reliance on postoperative ultrastaging to prevent missed nodal disease [46]. Technical limitations of SLN fluorescence tracers, including dye extravasation during injection and variable lymphatic drainage or localisation, further degrade signal quality and visibility, compounding intraoperative uncertainty [56]. Additionally, dependence on specialised dyes, imaging platforms, and trained personnel may limit reproducibility and widespread adoption, particularly outside well-resourced surgical centres [57]. Together, these limitations underscore the need for more objective, standardised approaches to fluorescence interpretation to improve intraoperative reliability.

Micrometastatic Disease as a Persistent Limitation in Fg SLNB: Despite significant advances, Fg SLNB remains limited by residual micrometastatic disease across GO, largely due to constraints in intraoperative detection sensitivity. In endometrial and cervical malignancies, conventional histopathology frequently fails to detect low-volume nodal disease that is subsequently identified by SLN ultrastaging [58,59]. This limitation extends to ovarian cancer, where SLN ultrastaging reveals low-volume nodal disease in patients initially considered node-negative, highlighting the sensitivity gap of standard staging [60]. Moreover, micrometastatic nodal disease is associated with a markedly increased relapse risk, with 5-year disease-free survival falling from ~89% in node-negative patients to ~50% in those with micrometastases, underscoring the clinical consequences of missed low-volume disease [61]. Integrating AI with FI may improve micrometastasis detection by enabling more sensitive, pattern-based interpretation of weak or heterogeneous fluorescence signals and reducing false negatives, with further implications discussed later.

AI Applications in GO Relevant to Future Fg Workflows: Although direct AI-enhanced interpretation of intraoperative FI has not yet been established in GO, extensive progress in adjacent AI applications across imaging, pathology, and treatment planning demonstrates that AI methods are already embedded within the specialty. This existing AI activity provides a rationale for examining how similar approaches could be extended to Fg workflows. Accordingly, AI radiomics models in GO have been widely explored for diagnostic and characterisation tasks, including tumour classification, nodal risk prediction, and histological and molecular stratification. Many studies report high discriminative performance, often with AUCs around 0.90 or higher for specific tasks, providing a plausible platform from which AI methods could later be adapted to intraoperative Fg workflows, although current evidence remains heterogeneous and largely retrospective [62]. AI-enhanced screening tools have further accelerated this progress: automated colposcopy and cytology systems now reach accuracies approaching 95%, outperforming routine human interpretation and reducing variability in early detection [63]. Parallel advances in radiotherapy demonstrate similar gains, with AI-driven contouring and dose-optimisation producing clinically acceptable plans in over 90% of cases, reducing inter-observer variation and accelerating workflow efficiency [64]. Together, these developments show that GO is already an AI-active specialty. Although fluorescence-specific AI tools remain under-validated, existing algorithms, computational frameworks, and analytic pipelines developed for imaging and decision support have potential to be directly leveraged for FI, with current limitations driven primarily by data availability and validation rather than technical capability.

iii Thoracic Oncology (TO)

Surgical Outcomes and Limitations in Lung Cancer Resection: TO encompasses a broad range of surgical procedures within the thorax, such as targeting tumours of the heart, lung, mediastinum and chest wall. Lung cancer is the most prevalent form of cancer globally [65]. It is classified into two primary histological categories: small-cell lung carcinoma (SCLC) and non-small cell lung carcinoma (NSCLC). For localized NSCLC, surgical resection remains the cornerstone of curative treatment [66], with the primary objective being complete tumour removal (R0 resection). Despite this, traditional surgical oncology approaches have notable limitations, highlighting the potential for innovative advancements in this field. One population-based study by Strand et al. analysed the long-term survival outcomes of 3211 patients in Norway who underwent surgical resection for primary lung cancer (Strand et al., 2006). The study found a five-year relative survival rate of 46.4% overall, with survival varying significantly by stage: 58.4% for Stage I, 28.4% for Stage II, 15.1% for Stage IIIa, 24.1% for Stage IIIb, and 21.1% for Stage IV. Lobectomy was associated with the best outcomes, with upper lobectomy demonstrating superior survival compared to lower lobectomy ($p = 0.017$), while pneumonectomy had poorer survival rates. Prognostic factors associated with reduced survival included male sex, older age, larger tumour size, adenocarcinoma and large cell carcinoma histology, right-sided resections, non-lobectomy procedures, and involvement of resection margins. Notably, infiltration of resection margins is a key factor of poor prognosis, suggestive of opportunity for innovation in precision resection. See Fig. 3 for visual example.

Further studies have progressed to investigate survival prognosis by margins status, see Table 5. A retrospective study by El-Sherif et al. (2007) reviewed 81 patients with stage I non-small cell lung cancer (NSCLC) who underwent sublobar resection (SR). Patients were stratified according to the distance from the tumour to the resection margin: <1 cm (n = 41) versus ≥1 cm (n = 40). The study demonstrated that resection margins distance significantly affected local recurrence rates. Local recurrence occurred in 14.6% (6/41) of patients with margins <1 cm, compared with 7.5% (3/40) of patients with margins ≥1 cm ($p = 0.041$). Wedge resection was significantly more likely to result in

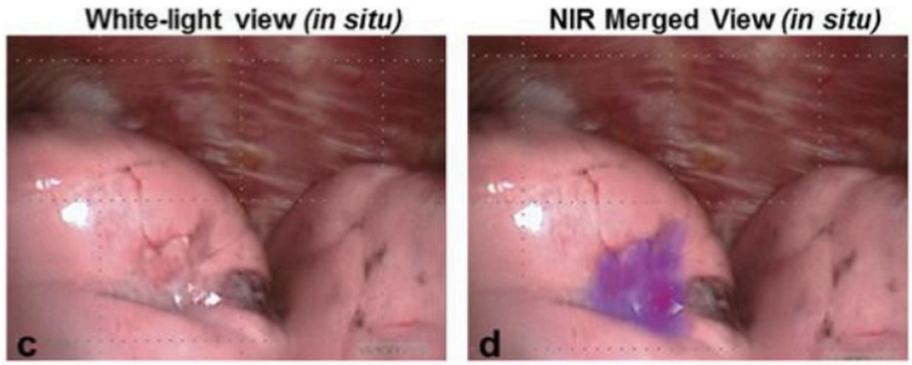

Fig. 3. Enhanced Intraoperative Tumour Visualisation Using Near-Infrared FI. Figure provides a comparison of standard white-light view (left) and near-infrared (NIR) merged view (right) in situ during lung cancer resection [67]. Licensed under the Creative Commons Attribution Licence.

Table 5
Prognostic impact of resection type and margin status on recurrence and survival in NSCLC.

Author	Year	Sample Size	Resection Type/Margins Status	Recurrence/Survival Rate	Prognosis	Key Findings
Strand et al.	2006	3211	Lobectomy (upper vs. lower), Pneumonectomy	5-year relative survival: Overall 46.4%; Stage I: 58.4%, Stage II: 28.4%, Stage IIIa: 15.1%, Stage IIIb: 24.1%, Stage IV: 21.1%	Best for lobectomy, especially upper; worst for pneumonectomy	Upper lobectomy had better survival than lower ($p = 0.017$). Pneumonectomy associated with poorer survival. Survival strongly stage dependent. Margin involvement noted as a poor prognostic factor.
El-Sherif et al.	2007	81	SR (55 wedge, 26 segmentectomy); margin <1 cm (n = 41) vs ≥ 1 cm (n = 40)	Local recurrence (by margin): 14.6% (6/41) vs 7.5% (3/40), $p = 0.041$. Local recurrence (by procedure): wedge 14.5% (8/55) vs segmentectomy 3.8% (1/26), $p = 0.002$.	Better local control with ≥1 cm margins and with segmentectomy vs wedge.	Margins <1 cm were associated with higher local recurrence. Wedge resections were more likely to have <1 cm margins (82.9% vs 52.5% for ≥1 cm group; $p = 0.003$). Segmentectomy achieved better locoregional control and was suggested as preferable when SR is used.
Wolf et al.	2017	182	Wedge resection for NSCLC ≤2 cm; Margin distances analysed (avg. 8.3 mm)	33 recurrences and 59 deaths over mean 49.6 months; margin >9 mm → best recurrent-free survival; margin >11 mm → best OS.	Larger margins associated with lower recurrence and better survival.	Increased margin distance independently predicted lower recurrence (OR 0.90) and improved OS (HR 0.94). Margins >9 mm gave longest recurrence-free survival; >11 mm gave longest OS. Supports wedge resection when adequate margins are achieved [69].
Lin et al.	2017	96,324	Stage I–IIIA NSCLC; analysis of surgical margin positivity across 809 facilities.	5-year survival significantly lower in margin-positive resections; outperforming facilities had HR 0.80–0.88 compared to others.	Margin positivity linked to worse survival; facility performance varies.	Risk-adjusted margin-positive rate is a valid surgical quality metric. Margin positivity (4.4% overall) independently associated with worse survival. High-performing institutions had significantly better 5-year survival outcomes [70].
Osarogiagbon et al.	2016	112,998	NSCLC resections; positive margins in 4.7% of cases.	5-year survival: 58.5% (complete resection) vs. 33.8% (incomplete resection); $p < 0.001$	Positive margins significantly worsen survival.	Incomplete resection independently associated with worse survival. Adjuvant chemotherapy improved survival across stages; radiotherapy worsened survival in stage I. Institutional and demographic factors linked to increased margin positivity [71].

margins <1 cm. Among patients with margins <1 cm, 82.9% (34/41) underwent wedge resection, compared with 52.5% (21/40) in the ≥1 cm margin group ($p = 0.003$). When analysed by procedure type, local recurrence occurred in 14.5% (8/55) of patients undergoing wedge resection, compared with 3.8% (1/26) following segmentectomy ($p = 0.002$). Segmentectomy was also associated with no regional recurrences, whereas regional recurrence occurred in 10.9% (6/55) of wedge resections ($p = 0.013$). The study concludes that inadequate surgical margins contribute to increased local recurrence following SR, and that segmentectomy is preferable to wedge resection when SR is indicated, due to its higher likelihood of achieving margins ≥1 cm and reducing locoregional recurrence risk [68]. Achieving adequate resection margins is limited by surgical technique and tumour location, with non-anatomical wedge resection often producing smaller margins due to reduced anatomical guidance, particularly for centrally located lesions. Although preoperative CT-guided localisation aids lesion targeting, it lacks sufficient resolution for precise intraoperative margin assessment [67]. Integrating FI and AI may support more precise resection by improving intraoperative margin assessment.

Near-Infrared Fluorescence for Tumour Detection in Lung Cancer Surgery: A recent systematic review published in Life examined near-infrared (NIR) fluorescence tumour-targeted imaging in lung cancer surgery, highlighting its potential to improve intraoperative tumour detection, identify additional lesions, and reduce tumour-positive resection margins, thereby supporting more complete (R0) resections [67]. The review also highlights the persistent challenge of incomplete resections (R1/R2), which occur in 2.8–12.7% of patients and are associated with poorer survival and higher disease persistence rates. From an initial pool of 2199 articles, 43 studies met the inclusion criteria, focusing on intraoperative or in vivo detection of lung tumours and metastases using near-infrared imaging agents. The study describes the use of fluorescent dyes including ICG and OTL38, with NIR FI using wavelengths of 650–900 nm to penetrate tissue. While the technique provides real-time, non-invasive visualisation of tumours and improves detection of small pulmonary nodules and tumour margins, interpretation remains dependent on intraoperative visual assessment [67]. A summary of key studies is presented in Table 6, highlighting different ICG delivery methods, including intravenous, CT-guided, and inhalation routes. Across studies, high detection rates and safe localisation of small pulmonary nodules were reported, alongside improved margin visualisation during lung cancer surgery.

Limitations of NIR Fluorescence in Lung Cancer Surgery: NIR FI, while a promising technology for improving tumour visualisation during lung cancer surgeries, has notable limitations that highlight the need for further advancements. Penetration depth is restricted to, making this technique less effective for detecting deeper tumours [75]. Observer variability further complicates the technology's reliability, as fluorescence signal interpretation currently lacks standardised, quantitative guidelines. Many fluorescent agents also face challenges with stability and specificity, and while more targeted agents like OTL38 show promise, they are dependent on the expression of specific molecular targets, limiting their broader applicability [75,76]. Furthermore, the cost of NIR FI systems and probes remains a significant barrier to widespread clinical adoption. These limitations underscore the critical need for advancements in this field, namely, the integration of AI to enhance signal interpretation, improve tumour-specific targeting, and standardise fluorescence quantification [77,78]. Such innovations might address current challenges, increasing precision in and the utility of NIR Fg surgeries in cancer resection.

Residual Disease and the Need for More Precise Intraoperative Margin Assessment: Residual tumour progression remains a significant challenge in lung cancer surgeries, with evidence indicating that incomplete resections (R1/R2) lead to increased recurrence rates and reduced survival. For instance, studies have shown that positive margins are associated with a nearly 50% reduction in five-year survival rates compared to complete resections (R0) [79]. This emphasises the critical need for achieving maximal resection without causing excessive damage to surrounding structures. However, even to the trained eye, the margin of resection can be difficult to assess intraoperatively, and variability between surgeons and the reliance on subjective judgment remain key limitations [68]. Imaging techniques such as CT and frozen section analysis offer valuable guidance but have known constraints, including limited resolution, false negatives, and logistical inefficiencies [67]. More recently, integrating AI with near-infrared FI has shown promise in improving real-time intraoperative margin assessment, building on established preoperative image analysis to enhance visualisation and reduce residual disease.

Extension to Cardiac Oncology: Lung cancer dominates TO due to its high incidence and mortality, so this paper focuses on thoracic oncology with emphasis on lung cancer surgery. Yet, intraoperative FI and AI also hold strong potential in cardiac oncology. Primary cardiac tumours are rare (0.001–0.3% of autopsies), but metastatic cardiac involvement is more frequent (2.3–18.3%), highlighting an underexplored opportunity for precision, AI-guided cardiac tumour resections [80–82].

AI Capability in TO Supporting **Future Research for FI:** Across TO, AI is already widely used in preoperative and diagnostic workflows. For lung cancer screening and diagnosis, deep-learning algorithms for pulmonary nodule detection on CT and radiographs have demonstrated pooled sensitivity ~93% (95% CI 85–98%) and pooled AUC ~0.90 [83]. Radiomics and AI models now support classification, lymph-node spread and staging, and molecular profiling and prognosis, improving accuracy over traditional reading and assisting multidisciplinary lung cancer decision-making pipelines [84]. In surgical and perioperative care, machine-learning tools already outperform traditional risk scores for postoperative complications and mortality after thoracic and cardiac surgery. For example, random-forest models achieve AUCs up to ~0.87 for mortality prediction, compared with ~0.70–0.74 for conventional models such as EuroSCORE or STS [85]. AI-powered 3D segmentation and anatomical reconstruction support surgical planning, while computer-vision systems in thoracic surgery demonstrate early feasibility for intraoperative guidance and phase recognition [86]. In this context, the established use of AI for image interpretation, risk modelling, and procedural planning in TO highlights a technical readiness that could support future exploration of AI-assisted near-infrared fluorescence for margin assessment and nodule localisation, even though direct AI-based interpretation of intraoperative fluorescence signals has not yet been demonstrated.

3. Limitations and barriers to AI-enhanced FgS

Despite the demonstrated clinical utility of FgS, its translation into

Table 6
FI in lung cancer surgery: Detection and margin accuracy.

Author	Year	Fluorescent Agent	Detection Rate	Accuracy	Key Findings
Neijenhuis et al.	2022	ICG, OTL38	Intraoperative detection of lung tumours and metastases across 43 studies	Tissue penetration up to 10 mm; resolution sufficient to detect small nodules	NIR FI provides real-time, non-invasive tumour visualisation, improves localisation of pulmonary nodules, and supports more complete (R0) resections. Incomplete resections (R1/R2) remain a key challenge.
Mao et al.	2017	ICG	68/76 nodules detected (89.5%); 9 additional nodules found missed by CT and white-light	Sensitivity: 88.7%; PPV: 92.6%	ICG-guided NIR imaging identified sub-centimetre nodules during thoracoscopic resection. Detected additional malignant/atypical nodules not seen by standard imaging. Demonstrated feasibility and safety [72].
Li et al.	2021	ICG (CT-guided injection)	98.4% (504/512 nodules localized)	High localisation accuracy; mean nodule size: 9.1 mm; depth: 8.9 mm	CT-guided ICG injection safely and accurately localized small pulmonary nodules (<2 cm) prior to VATS resection. Asymptomatic pneumothorax occurred in 5.9%, but no major complications. Recommended for routine use [73].
Quan et al.	2020	ICG via inhalation	Tumour margin detection in all lung specimens (n = 6); clear visualisation of tumour margin on pleural surface	Tumour margin detection efficiency: 2.9 (IQR 2.7–3.3); inhalation had 2x higher margin detection vs. IV ICG	Inhalation of low-dose ICG enabled rapid, prolonged, and highly effective intraoperative visualisation of lung tumour margins. Superior to intravenous injection in both preclinical and clinical settings. Safe and lung-specific [74].

consistent, real-time intraoperative decision support has yet to be fully realised, reflecting technical, clinical, and regulatory challenges. As discussed earlier, intraoperative FI is still largely interpreted qualitatively, with signal reliability affected by ambient lighting, tissue optical properties, blood contamination, and heterogeneous fluorophore uptake, leading to inter-operator variability and inconsistent margin visualisation [10,12,17]. While AI offers a means to mitigate these limitations through pixel-level segmentation, signal enhancement, and multimodal integration, its performance is currently constrained by the availability of large, well-annotated intraoperative datasets. Dataset curation remains challenging due to heterogeneity in imaging platforms, acquisition protocols, tumour biology, and operative environments, limiting generalisability, particularly in clinically critical scenarios characterised by weak or ambiguous fluorescence signals, such as deep-seated or eloquent tumours [16,18,87,88]. Clinical integration introduces additional challenges: AI systems must operate in real time, integrate seamlessly with existing surgical hardware, and deliver interpretable outputs that support rather than increase cognitive workload. Although multimodal fusion of FI with iMRI, CT, or ultrasound can enhance anatomical context, reliable intraoperative registration and fusion remain technically demanding in dynamic surgical fields [13,67]. Regulatory and ethical barriers further complicate deployment, as adaptive AI systems challenge existing medical device approval pathways and data-protection requirements restrict multi-institutional data sharing, underscoring the need for transparency, safety, and accountability before widespread adoption [18,88]. Nevertheless, across specialties, convolutional neural networks (CNN)-based approaches have demonstrated the ability to identify tumour tissue at the pixel level in related intraoperative imaging contexts rather than fluorescence-guided workflows, presenting outputs as quantitative spatial maps of tissue classification or margin status, with uncertainty-aware visualisation offering a mechanism to support surgeon judgement rather than replace it [21,22,89].

4. Feasibility evidence informing future of AI in FgS

Early clinical evidence suggests that AI can enhance FI across multiple surgical oncology settings, although current data remain limited to feasibility and proof-of-principle studies. In NO, Shen et al. applied deep-CNNs to ICG–based NIR-II fluorescence images in a prospective intraoperative study of 23 glioma patients, achieving an AUC of 0.945 for tumour versus non-tumour discrimination and demonstrating higher sensitivity than experienced neurosurgeons at comparable specificity, correcting over 70% of surgeon classification errors [21]. Although extent of resection and survival outcomes were not assessed, this study provides early clinical evidence that AI-assisted fluorescence analysis can improve intraoperative tumour assessment. In GO, a proof-of-principle study in 21 patients with early-stage cervical cancer showed that a CE-IVD–certified deep learning algorithm applied to hematoxylin and eosin–stained whole-slide images of fluorescence-mapped sentinel lymph nodes detected all macro- and micrometastases across 47 nodes, achieving 100% sensitivity with no false-negative results [90], demonstrating improved precision and efficiency despite the absence of direct clinical outcome measures. In Thoracic surgery, a first-in-human feasibility report evaluated an AI-assisted augmented-reality system during two robotic lower lobectomies, where deep-learning–derived 3D reconstructions from pre-operative CT were manually registered and overlaid onto the live endoscopic feed, maintaining surgeon-judged registration across operative phases with minimal blood loss and uneventful recovery workflows [91]. Although FI was not used, this study demonstrates the feasibility of real-time AI integration into intraoperative visualisation, supporting future adaptation to Fg workflows.

5. Conclusion

AI is already being actively adopted across neurosurgical, gynaecological, and thoracic oncology, with demonstrated impact in imaging, pathology, risk stratification, and intraoperative visualisation. Within FgS specifically, the degree of AI integration remains heterogeneous. NO currently provides the most direct evidence of real-time AI augmentation of intraoperative fluorescence interpretation, enabling quantitative decision support beyond subjective visual assessment. In GO and TO, Fg workflows are well established, and AI methods are mature in adjacent clinical domains; however, their direct application to real-time intraoperative fluorescence interpretation has not yet been systematically validated. Nonetheless, this divergence reflects differences in translational maturity rather than technical limitation and highlights a clear opportunity for focused research to integrate established AI methodologies into live FgS workflows. Together, the available evidence supports AI-augmented FgS as a promising and active area of translational development, with a strong rationale to call for further research aimed at bridging existing AI capabilities into Fg operative decision-making and defining their clinical value across surgical specialties.

6. Future directions and clinical translation

AI-enhanced FgS is evolving beyond proof-of-concept and now requires structured translational development to support safe clinical adoption. Progress depends on addressing key implementation challenges while leveraging emerging frameworks, particularly the need for large, diverse training datasets. Federated learning (FL) offers a practical solution by enabling decentralised model training without direct data sharing, as demonstrated by paediatric neurosurgical initiatives such as FL-PedBrain, which showed strong generalisability across 19 sites with minimal performance deviation from centrally trained models, highlighting its potential applicability to FI workflows [92–94]. Transparent evaluation and reproducibility will be essential, with reporting standards such as CONSORT-AI and SPIRIT-AI providing critical structure for AI-enabled clinical trials [95]. Effective translation will also depend on seamless workflow integration, with growing recognition that surgical AI systems must be co-designed with surgeons to ensure interpretability, trust, and compatibility with real-world operative decision-making [78]. Human-centred design and human-in-the-loop architectures can enhance situational awareness and intraoperative judgement when embedded appropriately within complex surgical environments [96]. Beyond the operating theatre, pathway-level integration, usability, and evidence generation will determine scalability, while prospective multicentre validation remains necessary given that current AI-FgS evidence is largely limited to feasibility studies [97,98]. Finally, responsible deployment will require addressing algorithmic bias, ensuring equitable patient benefit, establishing post-market surveillance, and advancing regulatory frameworks under MHRA and UKCA/CE, alongside cost-effectiveness analyses to support adoption across diverse healthcare systems [99]. In addition to MHRA and UKCA/CE pathways, AI-based medical devices intended for intraoperative decision support are regulated in the United States through established FDA routes including 510(k) clearance, De Novo classification, and Premarket Approval (PMA), depending on device risk and availability of predicate technologies. Most AI-enabled imaging and decision-support systems currently reach clinical use via the 510(k) or De Novo pathways, while higher-risk or autonomous systems may require more stringent premarket evidence, including PMA-level review. Recent regulatory analyses highlight the FDA's evolving approach to machine-learning–based software as a medical device (SaMD), with emphasis on transparency, real-world performance monitoring, and total product lifecycle governance [100].

Health-economic considerations will be central to successful clinical translation of AI-enhanced FgS. Current FgS platforms already incur additional costs related to specialised imaging systems and fluorophores, while AI integration is expected to introduce further expenditure through software development, computational infrastructure, data governance, and regulatory compliance. However, health-economic analyses from adjacent FgS technologies demonstrate that upfront implementation costs may be partially offset by downstream system-level benefits, including improved resection completeness and gains in quality-adjusted life-years (QALYs), life-years (LYs), and progression-free life-years (PFLYs) [101]. Across oncologic surgery, inadequate margin clearance is consistently associated with worse oncological outcomes and frequently necessitates additional interventions, including re-operation and adjuvant radiotherapy or chemotherapy, with substantial downstream implications for patients and healthcare systems. Large population-level analyses across common solid tumours demonstrate that positive surgical margins are associated with increased treatment intensity, higher rates of additional procedures, and poorer survival, thereby amplifying long-term care burden and health-system utilisation. Improving intraoperative margin assessment and surgical precision therefore represents an important opportunity to optimise oncologic value by reducing avoidable downstream treatments and resource use [102]. From a health-economic perspective, evaluation of intraoperative technologies, including AI-enhanced FgS, should extend beyond upfront costs to include downstream treatment burden and long-term outcomes. Incorporating economic alongside clinical endpoints is essential for value-based adoption.

CRediT authorship contribution statement

Omar Shafi: Writing – review & editing, Writing – original draft, Visualization, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Mirkomol Mirzarakhimov:** Writing – review & editing, Writing – original draft, Methodology. **Siena Martin:** Writing – review & editing, Writing – original draft. **Darcy Gabriel:** Writing – review & editing. **Un Hou Chan:** Writing – review & editing, Writing – original draft. **Saurabh Phadnis:** Writing – review & editing, Writing – original draft, Validation, Supervision, Formal analysis. **Hasan Asif:** Writing – review & editing, Writing – original draft, Supervision. **Mauro Camacho:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Methodology.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.suronc.2026.102364.

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