

Consensus Statement

Consensus conference statement on fluorescence-guided surgery (FGS) ESSO course on fluorescence-guided surgery



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ABSTRACT

Background: Fluorescence-guided surgery (FGS) has emerged as an innovative technique with promising applications in various surgical specialties. However, clinical implementation is hampered by limited availability of evidence-based reference work supporting the translation towards standard-of-care use in surgical practice. Therefore, we developed a consensus statement on current applications of FGS.

Methods: During an international FGS course, participants anonymously voted on 36 statements. Consensus was defined as agreement $\geq 70\%$ with participation grade of $\geq 80\%$. All participants of the questionnaire were stratified for user and handling experience within five domains of applicability (*lymphatics & lymph node imaging; tissue perfusion; biliary anatomy and urinary tracts; tumor imaging in colorectal, HPB, and endocrine surgery, and quantification and (tumor-) targeted imaging*). Results were pooled to determine consensus for each statement within the respective sections based on the degree of agreement.

Results: In total 43/52 (81%) course participants were eligible as voting members for consensus, comprising the expert panel ($n = 12$) and trained users ($n = 31$). Consensus was achieved in 17 out of 36 (45%) statements with highest level of agreement for application of FGS in tissue perfusion and biliary/urinary tract visualization (71% and 67%, respectively) and lowest within the tumor imaging section (0%).

Conclusions: FGS is currently established for tissue perfusion and vital structure imaging. Lymphatics & lymph node imaging in breast cancer and melanoma are evolving, and tumor tissue imaging holds promise in early-phase trials. Quantification and (tumor-)targeted imaging are advancing toward clinical validation. Additional research is needed for tumor imaging due to a lack of consensus.

1. Introduction

Near-infrared (NIR) fluorescence imaging, also referred to as

fluorescence-guided surgery (FGS), has emerged as a promising technique to improve surgical precision and decision-making by providing real-time visual enhancement of tissues of interest and essential

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anatomical structures during surgical procedures [1]. The application of FGS in surgical oncology can be divided in four domains: 1) visualization of lymph nodes and lymphatic channels [1–3]; 2) detection of primary tumors and (occult) metastatic lesions [1–3]; 3) visualization of vital structures (e.g., the biliary tree and ureters) [4,5]; and 4) assessment of tissue perfusion [4–7]. FGS uses a fluorescent contrast agent that absorbs and emits near-infrared light ($\lambda = 700$ –1300 nm), detectable by a NIR fluorescence imaging system. Fluorescent contrast agents can be categorized either as targeted or as non-targeted. The most frequently used non-targeted fluorescent contrast agent is indocyanine green (ICG) [8]. Clinical studies have focused on its use for Sentinel Lymph Node (SLN) mapping; assessment of tissue and anastomosis perfusion, and identification of hepatic tumors, and visualization of the biliary tree [9–14]. Tumor-targeted fluorescent agents are composed of a fluorophore linked to a targeting moiety (e.g., antibody, peptide, or ligand), that selectively binds to proteins or receptors overexpressed on tumor cells [15–17]. The assessment of clinical and oncological benefits of FGS has been a topic of interest in larger randomized trials, with promising results [18–24]. Tumor-targeted fluorescence imaging is a relatively new domain with an ongoing clinical validation of tumor-targeted fluorescent contrast agents. Recently, the first targeted fluorophore, OTL-38 (Pafalocianine, Cytalux®, OnTarget Laboratories, USA) for ovarian and primary lung cancer was FDA-approved [25]. Furthermore, various tumor-targeted probes are currently being evaluated in phase II and III [16,26–29].

Although the interest in NIR fluorescence-guided surgery has grown rapidly, recommendations for clinical implementation by novice-adaptors remains scarce [30]. To address this issue, a consensus statement was developed during the annual *European Society of Surgical Oncology (ESSO) Course on Fluorescence-Guided Surgery*. The statement assessed practical applications of FGS in general surgery and surgical oncology. An anonymized questionnaire was used to discuss statements relating to the main domains of applicability, stratified by individual user experience [31].

2. Methods

2.1. Course structure

The two-day course began with introductory lectures on the fundamentals and technical aspects of fluorescence imaging, including its historical context. It included five sessions covering the primary application domains. Faculty shared scientific evidence and literature, leading to plenary discussions and followed by participants anonymously completing a questionnaire. All participants engaged in practical, hands-on sessions demonstrating NIR fluorescence imaging principles with diverse commercial imaging systems.

2.2. Questionnaire

The research team prepared a structured online questionnaire, which underwent language verification by two course chairs (ALV, JSDM). The questionnaire was conducted electronically via Google Forms survey software (Google LLC., California, United States). For confidentiality, responses were kept anonymous, with access limited to the study moderators (MAvD and ODB). It comprised five sections, aligning with the course sessions, featuring a total of 36 statements. These sections were 1) *Fluorescence imaging of lymphatics & lymph nodes* [n = 13 statements]; 2) *Fluorescence imaging for tissue perfusion using ICG* [n = 7 statements]; 3) *Fluorescence imaging of the biliary anatomy and urinary tracts* [n = 6 statements]; 4) *Fluorescence imaging of tumors in Colorectal, HPB and Endocrine surgery* [n = 5 statements]; 5) *What's new and prospects: Quantification and (Tumor-)targeted imaging* [n = 5 statements]. The questionnaire provided participants with the following answer options – Agree, Neutral, or Disagree – to indicate their level of agreement with each statement.

Participants, including chairs, faculty, and course attendees, were

invited to contribute to the conference's consensus statement. Those who agreed to participate in the questionnaire also provided consent for result publication. Ethical approval was waived as the study was not under the Medical Research Involving Human Subjects Act (WMO). Participants indicated their professional roles (*Medical specialist, Resident, PhD- or Post-doc researcher*) and course roles (*Chair, Faculty, or Course participant*) and stated if they were already using FGS in their daily clinical practice. Participants were categorized into three groups: *the expert panel* (comprising course chairs and faculty), *trained users* (course participants with a minimum of 10 performed fluorescence-guided procedures within a specific area), and non-experienced individuals. Expert panel and trained users' experience within specific (sub)sections was assessed. Trained users with less than 10 performed fluorescence-guided procedures within the specified (sub)sections were excluded from voting for consensus, as well as participants who did not complete the two-day course. Non-experienced participants, without prior FGS experience, were also excluded from voting but their input was recorded for trend analysis and course improvement guidance.

2.3. Consensus agreement

To determine consensus, a minimum agreement of 70% was required for each statement, with at least 80% participation in voting per (sub) section [32]. A pooled consensus for agreement was calculated based on the proportional distribution of agreement in the *expert panel* and *trained users* voting groups, respectively. The pooled results were used to determine if consensus on agreement was reached for each statement within the (sub)sections.

3. Results

3.1. Study cohort

A total of 52 participants completed the questionnaire, categorized into three groups: an expert panel (n = 12), trained users (n = 31), and novice adaptors/non-experienced (n = 9), demographics of the course participants are presented in **Table 1**. Among the total participants, 43 individuals (81%) met the criteria to serve as voting members for the consensus agreement. The varying experience levels in NIR fluorescence imaging among participants resulted in different numbers of voting members within the expert panel and trained users group across (sub) sections. Pooled consensus was achieved in 17 out of 36 statements (45%) concerning agreement, with no consensus on disagreement for

Table 1
Demographics of course participants.

Demographics of course participants		Total group – n = 52 (%)
Professional role	Surgical Medical Specialist	34 (65%)
	Non-Surgical Medical Specialist	4 (8%)
	Resident/Researcher	14 (27%)
	PhD/Post-Doc	
Continent of practice	Asia	3 (6%)
	Europe	45 (86%)
	North-America	2 (4%)
	Oceania	1 (2%)
	South-America	1 (2%)
Nature of employment	Academic	11 (21%)
	Non-academic	41 (79%)
Experience and training in FGS-principles	Yes, Expert panel	12 (23%)
	Yes, Trained users	31 (60%)
	No, Non-experienced-users	9 (17%)
Completion of the 2-day course	Yes, Chair/Faculty	12 (23%)
	Yes, Course participant	40 (77%)
	No	0 (0%)

any of the 36 statements. A high participation level (>80%) was observed for 35 out of 36 statements (97%), except for one statement in the trained user's group, where no voting members had sufficient clinical experience in imaging endocrine tumors. For detailed consensus results, refer to Tables 2–6. The distribution of votes from the novice adaptors/non-experienced group can be found in Supplementary Tables S1–5.

3.2. Fluorescence imaging of lymphatics & lymph nodes

Pooled consensus for agreement was achieved in 6 out of 13 (46%) statements concerning fluorescence imaging of lymphatics and lymph nodes (Table 2). This consensus was observed for the efficacy of intraoperative NIR fluorescence imaging in breast (93% agreement), gastric, esophageal (88% agreement), melanoma (76% agreement), and

gynecological tumors (74% agreement). However, consensus was not reached for colorectal and neuroendocrine tumors. As for adopting intraoperative NIR fluorescence imaging of lymphatics and lymph nodes as standard-of-care, consensus was achieved solely for breast (76% agreement) and melanoma surgery (81% agreement). There was no consensus on completely replacing conventional SLN localization (e.g., radionuclide-based Tc-99) with NIR fluorescence imaging.

3.3. Tissue perfusion using ICG

Pooled consensus for agreement was achieved in 5 out of 7 (71%) statements related to ICG-based fluorescence imaging for tissue perfusion (Table 3). This consensus was observed for standard-of-care fluorescence angiography in vascular (75% agreement), reconstructive (84% agreement), and gastrointestinal surgery (83% agreement), but

Table 2

Statements on fluorescence imaging lymphatics & lymph nodes.

Statements on fluorescence imaging of lymphatics & lymph nodes	Expert panel votes distribution (%)	Trained users votes distribution (%)	Pooled Consensus reached for agreement (Yes/No)
Consensus reached (If >80% participation & >70% agreement)			
Fluorescence imaging of lymphatics & lymph nodes			
<i>Fluorescence imaging is effective for the visualization of lymphatics & (sentinel) lymph nodes in:</i>	n=12	n=16	
Colorectal cancer	33% 42% 25%	73% 20% 7%	No (58%)
Breast cancer	92% 8%	93% 7%	Yes (93%)
Endometrial, Cervical, Vulvar cancer	67% 25% 8%	80% 13% 7%	Yes (74%)
Melanoma	83% 17%	93% 7%	Yes (88%)
Gastric, Esophageal cancer	73% 27%	79% 21%	Yes (76%)
Neuroendocrine tumors	67% 25% 8%	36% 57% 7%	No (52%)
<i>Fluorescence imaging should be standard-of-care for visualization of lymphatics & (sentinel) lymph nodes in:</i>	n=12	n=16	
Colorectal cancer	25% 25% 50%	53% 40% 7%	No (39%)
Breast cancer	92% 8%	60% 40%	Yes (76%)
Endometrial, Cervical, Vulvar cancer	67% 25% 8%	40% 53% 7%	No (54%)
Melanoma	91% 9%	71% 29%	Yes (81%)
Gastric, Esophageal cancer	42% 33% 25%	64% 36%	No (53%)
Neuroendocrine tumors	17% 67% 17%	29% 64% 7%	No (23%)
<i>Fluorescence imaging should replace conventional (sentinel) lymph node localization (e.g. Tc-99)</i>	67% 17% 17%	25% 50% 25%	No (46%)

Table 2 represents the distribution of votes on statements regarding fluorescence imaging of lymphatics & lymph nodes for the expert panel and trained users. In all statements the participation level of 80% was reached. Consensus was reached when a minimum agreement of 70% was reached. Pooled consensus for agreement was calculated based on the proportional distribution of agreement in the expert panel and trained users voting groups, respectively. The pooled results were used to determine if consensus on agreement was reached for each statement within the (sub)sections.

Legend for table: Answer 'agree'; 'neutral'; 'disagree', specified distribution in % for groups

Table 3

Statements on fluorescence imaging for tissue perfusion using ICG.

Statements on fluorescence imaging for tissue perfusion using ICG	Expert panel votes distribution (%)	Trained users votes distribution (%)	Pooled Consensus reached for agreement (Yes/No)
Consensus reached (>80% participation & >70% agreement)			
Fluorescence imaging for tissue perfusion using ICG	n=12	n=18	
<i>Fluorescence imaging should be standard-of-care for perfusion assessment in vascular surgery</i>	75%  25% 	72%  22%  6% 	Yes (74%)
<i>Fluorescence imaging should be standard-of-care for perfusion assessment in reconstructive surgery</i>	100% 	67%  28%  5% 	Yes (84%)
<i>Fluorescence imaging should be standard-of-care for perfusion assessment in gastro-intestinal surgery</i>	75%  25% 	90%  5%  6% 	Yes (83%)
<i>Fluorescence imaging should be standard-of-care for perfusion assessment in endocrine surgery</i>	75%  17%  8% 	61%  33%  6% 	No (61%)
<i>Hemodynamic variables (e.g. cardiac output, blood pressure) must be considered when evaluating the fluorescence signal</i>	75%  25% 	75%  15%  10% 	Yes (75%)
<i>Quantification of the fluorescence signal using time-intensity curves improves the reproducibility for tissue perfusion assessment</i>	67%  25%  8% 	90%  10% 	Yes (79%)
<i>Hyperspectral imaging has the potential to replace perfusion assessment using ICG</i>	42%  42%  17% 	42%  53%  5% 	No (50%)

Table 3 represents the distribution of votes on statements regarding fluorescence imaging for tissue perfusion using ICG for the expert panel and trained users. In all statements the participation level of 80% was reached. Consensus was reached when a minimum agreement of 70% was reached. Pooled consensus for agreement was calculated based on the proportional distribution of agreement in the expert panel and trained users voting groups, respectively. The pooled results were used to determine if consensus on agreement was reached for each statement within the (sub)sections.

Legend for table: Answer  'agree';  'neutral';  'disagree', specified distribution in % for groups

not in endocrine surgery. There was also consensus (75% agreement) on the importance of considering hemodynamic variables (e.g., cardiac output, blood pressure) when interpreting fluorescence signals. Additionally, consensus was reached (79% agreement) on the value of using time-intensity-based signal quantification to enhance the reproducibility of tissue perfusion analysis. However, no consensus was achieved on the potential of hyperspectral imaging to replace fluorescence angiography with ICG.

3.4. Biliary and urinary tracts

Pooled consensus for agreement was achieved in 4 out of 6 (67%) statements on fluorescence imaging of the biliary and urinary tracts (Table 4). Specifically, there was consensus on effective identification of the biliary tracts (83% agreement) and earlier visualization of the critical view of safety using ICG fluorescence cholangiography (83% agreement). However, consensus was not reached on the standard-of-care use of ICG for biliary tract visualization, nor on the replacement of conventional cholangiography with fluorescence cholangiography. Furthermore, pooled consensus for agreement was obtained for NIR fluorescence visualization of the urinary tracts to reduce the risk of iatrogenic urethral injury during pelvic surgery (72% agreement). It was also agreed that renally cleared and intravenously administered dyes were preferable to retrograde urethral injection of a fluorescent dye via a urinary catheter (79% agreement).

3.5. Tumors of colorectal, hepatopancreatic biliary (HPB) and endocrine origin

None of the statements on fluorescence imaging in general oncology, surgical oncology, colorectal tumors, hepatopancreatic biliary tumors, and endocrine surgery reached a pooled consensus for agreement (Table 5). Pooled consensus was also not achieved for improving radical resection rates (R0) through fluorescence imaging, including the necessity of frozen section analysis for each fluorescent spot, irrespective of its appearance under white light. In the case of FGS for colorectal tumors, no pooled consensus was reached regarding the pivotal role of fluorescence endoscopy in ensuring adequate Watch&Wait programs for rectal and/or esophageal cancer. Likewise, the use of ICG-based fluorescence imaging as a standard-of-care during colorectal liver metastases resection did not attain consensus. Due to insufficient experienced voting members, no pooled consensus was reached regarding the role of FGS in endocrine oncological surgery.

3.6. What's new and prospects: quantification and (tumor-)targeted imaging

Pooled consensus for agreement was obtained in 2 out of 5 (40%) statements concerning "Quantification and (tumor-)targeted imaging" (Table 6). There was consensus on the importance of scientific evidence for individual fluorescent dyes to improve their indications, optimal dosing, and dosing-imaging intervals (96% agreement). Additionally, consensus was reached on integrating perfusion assessment techniques

Table 4

Statements on fluorescence imaging of the biliary anatomy and urinary tracts.

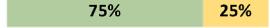
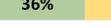
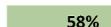
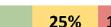
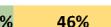
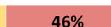
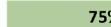
Statements on fluorescence imaging of the biliary anatomy and urinary tracts	Expert panel votes distribution (%)	Trained users votes distribution (%)	Pooled Consensus reached for agreement (Yes/No)
Consensus reached (>80% participation & >70% agreement)			
Fluorescence imaging in biliary tract using ICG	n=12	n=11	
<i>Fluorescence imaging using ICG in biliary tract identification is effective for extrahepatic biliary structures</i>	75%  25% 	91%  9% 	Yes (83%)
<i>Minimal invasive cholecystectomy with ICG fluorescence imaging leads to earlier visualization of the critical view of safety (CVS)</i>	75%  25% 	91%  9% 	Yes (83%)
<i>Fluorescence imaging using ICG should be standard-of-care for visualization of biliary tracts</i>	75%  25% 	36%  55%  9% 	No (56%)
<i>Fluorescence imaging using ICG should replace conventional cholangiography</i>	58%  25%  17% 	9%  46%  46% 	No (34%)
Fluorescence imaging of the urinary tracts	n=12	n=6	
<i>The use of fluorescence imaging decreases the risk of urinary tract damage during lower abdominal surgical procedures</i>	83%  8%  8% 	60%  40% 	Yes (72%)
<i>An IV administered and renally cleared fluorescent dye is preferred over retrograde urethral injection of a fluorescent dye via a urinary catheter</i>	75%  17%  8% 	83%  17% 	Yes (79%)

Table 4 represents the distribution of votes on statements regarding fluorescence imaging of the biliary anatomy and urinary tracts for the expert panel and trained users. In all statements the participation level of 80% was reached. Consensus was reached when a minimum agreement of 70% was reached. Pooled consensus for agreement was calculated based on the proportional distribution of agreement in the expert panel and trained users voting groups, respectively. The pooled results were used to determine if consensus on agreement was reached for each statement within the (sub)sections.

Legend for table: Answer  'agree';  'neutral';  'disagree', specified distribution in % for groups

into a multimodal imaging system to achieve an objective manner of perfusion assessment (82% agreement). However, consensus was not reached regarding the reliability of quantified absolute fluorescence intensities in perfusion assessment, the preference for smaller molecules (peptides and nanobodies) in (tumor-)targeted fluorescence imaging over antibody-based dyes, and the significance of shifting towards developing and evaluating dyes in the NIR-II spectrum.

3.7. Referencing to results from novice-adaptors

Comparing the consensus results from the voting participants to the novice adaptors gives an interesting insight. The novice-adaptors reached agreement in 16 of 36 statements ($\geq 70\%$). Overall novice-adaptors on average reached an agreement on 22 out of 36 statements.

4. Discussion

The results of this consensus paper demonstrate that the opinions of experts and trained users vary greatly by application, as well as variation within the expert panel and trained users within the degree of consensus for individual statements. The consensus reached in this conference highlights the agreement among participants on 45% (17/36) of the individual statements across five distinct sections. Notably, the sections focusing on imaging tissue perfusion and imaging vital structures exhibit strong consensus, with 71% and 68% consensus on the agreement,

respectively, indicating widespread support for further clinical implementation as standard-of-care practices. Consensus on imaging of lymphatics & lymph nodes was predominantly reached for breast cancer and melanoma, which is also supported by currently available literature [33, 34]. As for imaging of tumor tissue (0% consensus) the degree of consensus attained indicates ongoing research and exploration is required to establish and prove its clinical value, while its feasibility has already been demonstrated in phase I and II trials. Quantification methods and tumor-targeted imaging (40%) are in a transitional phase, moving from (early) clinical translation to prove their clinical value through larger prospective clinical trials.

Consensus among the participants was reached on the effective use of fluorescence imaging for visualization of lymphatics & lymph nodes in breast, gynaecological, gastric, esophageal, and melanoma tumors. Nonetheless, only in breast cancer and melanoma consensus was reached for implementation as standard-of-care in daily clinical practice. This discrepancy in acceptance could potentially be attributed to the long-standing use of Tc-99 as the gold standard among clinicians. One viable strategy could involve a transitional period during which both modalities are employed concurrently. Following the demonstration of equivalent or enhanced sensitivity and specificity, a full transition to fluorescence imaging could be considered. Recently, Bargon et al. (2022) showed with their INFLUENCE-trial that ICG-fluorescence may be used as a safe and effective alternative to 99 m Tc-nanocolloid for SLN procedures in patients with breast cancer [34]. The consensus

Table 5

Statements on fluorescence imaging of tumors in Colorectal, HPB and Endocrine surgery.

Statements on fluorescence imaging of tumors in in Colorectal, HPB and Endocrine surgery	Expert panel votes distribution (%)	Trained users votes distribution (%)	Pooled Consensus reached for agreement (Yes/No)
Consensus reached (>80% participation & >70% agreement)			
Fluorescence imaging in Surgical oncology	n=12	n=19	
<i>The use of fluorescence imaging improves the radical resection rate (R0)</i>	50% (green) 42% (yellow) 8% (red)	53% (green) 42% (yellow) 5% (red)	No (52%)
<i>Each fluorescent spot must be sent for frozen section analysis regardless of their white light appearance</i>	17% (green) 42% (yellow) 42% (red)	45% (green) 22% (yellow) 33% (red)	No (31%)
Fluorescence-guided surgery of Colorectal tumors	n=12	n=19	
<i>Fluorescence endoscopy is pivotal for adequate watch&wait programs in rectal and/or esophageal cancer</i>	25% (green) 50% (yellow) 25% (red)	44% (green) 39% (yellow) 17% (red)	No (21%)
Fluorescence-guided surgery of HPB tumors	n=12	n=11	
<i>Fluorescence imaging using ICG should be used as standard-of-care during the resection of colorectal liver metastases</i>	58% (green) 33% (yellow) 8% (red)	46% (green) 36% (yellow) 18% (red)	No (52%)
Fluorescence-guided surgery of Endocrine tumors	n=6	n=0	
<i>fluorescence-guided surgery for endocrine tumors will be indispensable to prevent morbidity and preserve QoL for patients who have a long life ahead of this</i>	33% (green) 58% (yellow) 8% (red)	No clinical experience	-

Table 5 represents the distribution of votes on statements regarding fluorescence imaging of tumors in Colorectal, HPB and Endocrine surgery for the expert panel and trained users. In all statements, except Fluorescence-guided surgery of Endocrine tumors the participation level of 80% was reached. Consensus was reached when a minimum agreement of 70% was reached. Pooled consensus for agreement was calculated based on the proportional distribution of agreement in the expert panel and trained users voting groups, respectively. The pooled results were used to determine if consensus on agreement was reached for each statement within the (sub)sections.

Legend for table: Answer ■ 'agree'; ■ 'neutral'; ■ 'disagree', specified distribution in % for groups

reached in this study is in agreement with the statement made by Dip et al. (2022), that fluorescence imaging serves as an important tool for the visualization of lymphatics & (sentinel) lymph nodes (SLNs) [30].

Multiple prospective studies have demonstrated that (ICG) fluorescence angiography in abdominal surgery is feasible and has the potential to improve surgical outcomes and reduce complication rates in various surgical procedures, which is also reflected in our consensus agreement [7,24,35–39]. Consensus was reached for standard-of-care implementation of fluorescence perfusion assessment in vascular, reconstructive, and gastro-intestinal surgery, which corresponds to the consensus conference statement by Dip et al. (2022) [30]. This evidence could be further strengthened by the upcoming results of other multi-centre randomised phase III trials (AVOID-study, NCT04712032) [40]. The consideration of hemodynamic variables in fluorescence perfusion assessment is important for result reliability. However, participant consensus varies on its necessity due to inconclusive evidence. The approach of quantifying and normalizing signals over time for clinical relevance is discussed, emphasizing time-specific intensity inflow and outflow metrics. Yet, opinions differ on their superiority over maximum fluorescence intensity for tissue perfusion assessment.

Various fluorescence perfusion parameters can be extracted,

including time-specific intensity inflow and outflow parameters, which are considered to be superior to absolute fluorescence intensity parameters (e.g., maximum fluorescence intensity) in quantifying tissue perfusion [41]. The suggested time-intensity-based approach is supported by recent literature and presented as a generic workflow, though not universally accepted among the voting members in this consensus statement. Its potential stems from offering detailed perfusion insights, but evidence for its superiority remains inconclusive due to experimental variability, technical limitations, and participant biases [42–46].

Fluorescence imaging for the real-time visualization of the biliary anatomy and urinary tracts has been proven to be feasible and effective. Therefore, it has the potential to prevent surgical complications related to surgical interventions. It is one of the main domains of FGS which for certain indications has proven its beneficial value as a readily available tool in minimally invasive surgery through larger randomized trials [19, 20]. Based on the proportion of votes indicating agreement among the expert panel (75% agreement) compared to the trained users (36% agreement), the expert panel justifies the implementation of fluorescence cholangiography as a standard-of-care for minimally invasive cholecystectomies, taking into consideration the potential benefits to patients in comparison to the associated costs and time. For urinary tract

Table 6

Statements What's new? Quantification and (Tumor-)targeted imaging.

Statements on What's new and prospects: Quantification and (tumor-)targeted imaging	Expert panel votes distribution (%)	Trained users votes distribution (%)	Pooled Consensus reached for agreement (Yes/No)
Consensus reached (>80% participation & >70% agreement)			
General fluorescence imaging	n=12	n=31	
<i>More scientific evidence is required for each individual fluorescent dye to improve and determine their indications for use, optimal dose and optimal dosing-imaging interval</i>	100%	90% 	Yes (96%)
What's new and prospects: Quantification and (Tumor-)targeted imaging	n=12	n=31	
<i>Interpretation of the quantified absolute fluorescence intensity in perfusion imaging is not reliable</i>	67%  25%	47%  20%	No (57%)
<i>The integration of perfusion assessment techniques into a multimodal imaging system is necessary to make significant progress towards objective perfusion assessment</i>	68% 	97% 	Yes (82%)
<i>Smaller molecules (e.g. peptides, nanobodies) are preferred over antibody-based dyes for tumor-targeted fluorescence imaging</i>	67% 	52%  7%	No (60%)
<i>Research should focus on development and evaluation of dyes in the NIR-II spectrum</i>	50%  8%	52%  16%	No (51%)

Table 6 represents the distribution of votes on statements regarding fluorescence imaging of tumors in Colorectal, HPB and Endocrine surgery for the expert panel and trained users. In all statements the participation level of 80% was reached. Consensus was reached when a minimum agreement of 70% was reached. Pooled consensus for agreement was calculated based on the proportional distribution of agreement in the expert panel and trained users voting groups, respectively. The pooled results were used to determine if consensus on agreement was reached for each statement within the (sub)sections.

Legend for table: Answer  'agree';  'neutral';  'disagree', specified distribution in % for groups

imaging, no FDA approved fluorescent dye which is cleared renally is currently available. ZW800-1 and IS-001, which showed promising results first clinical trials [47,48]. Consensus among experts supports the use of fluorescence visualization of the urinary tracts to reduce the risk of iatrogenic ureteral injuries during lower abdominal surgical procedures.

Fluorescence imaging for the detection and visualization of tumor tissue has attracted significant research interest in surgical oncology, mainly in the subdomains of colorectal, HPB, and endocrine surgery [49–52]. Underlined by the numerous phase II and III clinical trials currently running [Pancreatic cancer: *cRGD-ZW800-1* (NCT05518071); Breast cancer: *LUM015* (NCT04440982); Head & Neck cancer: *Cetuximab-IRDye800CW* (NCT03134846); *Panitumumab-IRDye800* (NCT04511078); Prostate cancer: *OTL-78* (EudraCT-2019-002393-31)] and phase III trials [Breast cancer: *LUM015* (NCT03686215), Colorectal cancer: *SGM-101* (NCT03659448)]. However, the evidence for improved patient and oncological benefit (e.g. radical resection rates) is still scarce, which is reflected by the degree of consensus in our statement. While none of the statements in the section on tumor-imaging reached consensus for agreement, the multitude of votes was represented by positive (agree) and neutral, instead of negative (disagree) votes. Specifically for tumor-targeted fluorescent dyes, the progress towards widespread clinical availability is relatively slow due to the time-consuming process of clinical translation and validation, and the high costs of its development and production [2,53,54]. To advance the

clinical implementation of fluorescence imaging towards standard-of-care use in daily practice, supporting evidence from large (randomized) trials evaluating the (oncological) value for individual applications is incremental and thereby simultaneously creating structured guidelines describing the optimal dose and timing of administration for individual applications, and subsequent training programs.

Prospects in the field of FGS are signal standardization and quantification, the development of target-specific dyes with advanced protein engineering and lower molecular weight to improve target efficacy and tumor penetration at an affordable price [16,55]. Furthermore, the (pre) clinical research field is recently focusing on the exploration of the NIR-II imaging window and its combination with other molecular imaging techniques, such as photoacoustic imaging and hyper-/multispectral imaging [56,57].

Consensus statements, while valuable, inherently contain a subjective element influenced by potential biases within a group of experts in a specific field. To address this inherent subjectivity, we assembled an international group of experts from various surgical specialties in academic and non-academic health care institutes, aiming to achieve a diverse and representative perspective on the field of FGS. Our research team developed the questionnaire and accompanying statements, which were subject to review and approval by the faculty of the ESSO course. Additionally, we used the panel of course participants as a control group to reflect these diverse viewpoints. Nonetheless, it is important to acknowledge the presence of a certain level of bias may persist.

Consequently, we took this potential bias into account when assessing the degree of consensus and carefully considered the results within the context of the existing body of evidence. Using this approach we aimed to give transparency and ensure that our consensus statement provides a balanced perspective, integrating the viewpoints of expert panel members and trained users in FGS. Moreover, in instances where a lack of empirical evidence was apparent for specific applications, we refrained from making strong recommendations. Instead, we made recommendations for further research in those areas, recognizing the importance of empirical data in guiding future developments and practices.

Given the known limitations consensus statements in general, this consensus statement offers a unique perspective, integrating the viewpoints of expert panel members and trained users. We based our consensus on the ESSO-course framework, covering all main application domains, including quantified fluorescence assessment and (tumor-)targeted imaging, to provide an oncological perspective on NIR fluorescence imaging applicability. The ESSO-course framework received positive feedback from participants. All of the 40 attending course participants (excluding chairs and faculty) expressed confidence in utilizing FGS for specific indications in their clinical practice. Additionally, 39 out of 40 participants (98%) felt well-prepared for a safe introduction to FGS after completing the two-day course.

In conclusion, 17 out of 36 (45%) individual statements in five sections reached consensus. The sections on imaging of tissue perfusion using ICG and imaging of vital structures have a growing body of evidence for further clinical implementation. Demonstrating effectiveness in improving patient outcomes, there is a solid basis for standard-of-care in procedure-specific indications, such as anastomotic perfusion assessment and biliary tree visualization. While some other areas have been shown to be feasible and effective (e.g. lymphatic mapping) for successful translation into clinical practice, it seems higher-quality evidence is still required to validate disease and procedure specific benefits on clinical outcomes. The availability of structured guidelines, high-quality scientific evidence and structured training programs, could help establish near-infrared fluorescence imaging as an increasingly valuable tool in the surgeon's toolkit.

Declaration of potential conflicts of interest

SG is a full-time employee of Intuitive Surgical. The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Summary declarations of interest

SG is a full-time employee of Intuitive Surgical. The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

CRediT authorship contribution statement

M.A. van Dam: Data curation, Funding acquisition, Formal analysis, Writing – review & editing, Study concepts, Study design, Data acquisition, Quality control of data and algorithms, Data analysis and interpretation, Statistical analysis, Manuscript preparation, Manuscript editing. **O.D. Bijlstra:** Data curation, Funding acquisition, Formal analysis, Writing – review & editing, Study concepts, Study design, Data acquisition, Quality control of data and algorithms, Data analysis and interpretation, Statistical analysis, Manuscript preparation, Manuscript editing. **R.A. Faber:** Data curation, Funding acquisition, Writing – review & editing, Data acquisition, Manuscript review. **M.I. Warmerdam:** Data curation, Funding acquisition, Writing – review & editing, Data acquisition, Manuscript editing, Manuscript review. **M.P. Achiam:** Writing – review & editing, Manuscript review. **L. Boni:** Writing –

review & editing, Manuscript review. **R.A. Cahill:** Writing – review & editing, Manuscript review. **M. Chand:** Writing – review & editing, Manuscript review. **M. Diana:** Writing – review & editing, Manuscript review. **S. Gioux:** Writing – review & editing, Manuscript review. **S. Kruijff:** Writing – review & editing, Manuscript review. **J.R. Van der Vorst:** Writing – review & editing, Manuscript review. **R.J. Rosenthal:** Writing – review & editing, Manuscript review. **K. Polom:** Writing – review & editing, Manuscript review. **A.L. Vahrmeijer:** Writing – review & editing, Manuscript editing, Manuscript review. **J.S.D. Mieog:** Writing – review & editing, Data curation, Formal analysis, Study design, Data analysis and interpretation, Manuscript editing, Manuscript review.

Declaration of AI and AI-assisted technologies in the writing process

During the preparation of this work the authors used ChatGPT (august version 3) in order to improve readability and language. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

Declaration of competing interest

Statement: One author has disclosed the following potential conflicts of interest: S. Gioux (SG) is a full-time employee of Intuitive Surgical. The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ejso.2023.107317>.

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