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ORIGINAL ARTICLE

Efficacy of Laparoscopic Parenchyma-Sparing Hepatectomy using Augmented Reality Navigation Combined with Fluorescence Imaging for Colorectal Liver Metastases

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ABSTRACT

Background: Parenchyma-sparing hepatectomy (PSH) is becoming more popular as an option in the treatment of colorectal liver metastases (CRLM). The use of augmented reality navigation (ARN) and indocyanine green fluorescence imaging (FI) has the potential to enhance the accuracy of surgery.
Objective: To compare the perioperative and oncologic outcome of ARN-FI-aided laparoscopic PSH and standard laparoscopic PSH using a synthetic IPTW-modeled cohort (N = 300).
Methods: Artificial cohort of 300 patients (150 ARN-FI, 150 Nonarn-FI), simulated based on published distributions and balanced based on IPTW considerations. Outcomes: EBL, operative time, big-time resection, big-time morbidity, LOS, RFS, OS.
Results: ARN-FI was linked to much less EBL (180 85 mL vs 350 140 mL: p < 0.001), higher R0 rate (94.7% vs 88.0; p = 0.019), shorter operating time (210 45 min vs 175 38 min: p < 0.001), shorter LOS (5.5 1.8 d vs 7.2 2.5 d: p < 0.0 Downward trend of significant morbidity (6.0% vs 11.3%; p = 0.07).
Conclusions: ARN-FI enhances the intraoperative accuracy, lessens blood loss, and amplifies margin negative resections, providing improved RFS with augmented operating time. Potential validation advised.
Keywords: Colorectal liver metastasis, Parenchyma-sparing hepatectomy, Laparoscopic liver resection, Augmented reality navigation, Fluorescence imaging (ICG), Inverse probability of treatment weighting.

INTRODUCTION

Colorectal cancer (CRC) has been one of the most common malignancies in the world, and a leading cause of cancer deaths. The liver is probably the most frequent location of remote metastatic dissemination, and about 20 50% of patients have colorectal liver metastases (CRLM) at any time in the course of their illnesses. In the case of patients appropriately chosen, surgical resection of CRLM still provides the greatest probability of long-term survival, with 5-year survival rates of up to 40 to 60 per cent after complete (R0) resection[3]. Management approaches have changed considerably during the last 20 years, with the widespread anatomical hepatectomies giving way to more targeted, personalized, and function-sparing surgical approaches[4]. Parenchymas-sparing hepatectomy (PSH) has gradually become a more popular choice to treat CRLM due to the aim of preserving hepatic functionality with sufficient oncologic clearance 56. PSH is characterized by limited anatomical resections, segmentectomies, and non-anatomical wedge resections aimed at excising tumors with minimal non-tumor parenchyma loss[7]. This methodology has gained special significance since systemic chemotherapy has grown better whereby lesions previously deemed unresectable can now be resected and there has been an exigence to have hepatic reserve in the event of repeat resection 8 9. According to evidence of various meta-analyses, PSH carries oncologic outcomes similar to major hepatectomies with decreased perioperative morbidity, postoperative liver dysfunction, and long-term risk of hepatic insufficiency[10].

In recent years, there has been a swift increase in the clinical practice of minimal invasive liver surgery and laparoscopic liver resection (LLR) owing to developments of surgical instruments, energy sources, and imaging tools 1]. A number of large trials has shown that, compared to open hepatectomy, LLR can result in fewer postoperative pain, reduced length of stay, quicker recovery, and less blood loss with no inferiority in margin negativity or long-term oncologic outcome (1213). There are however problems when converting PSH to laparoscopic platform. LLR decreases tactile feedback, depth perception and depends on visual information, which complicates the process of precise tumor localization and control of the planes of resection significantly more than the conventional method (Largely, 1999)[12]. In cases where PSH is necessary, including in the context of surgery, where a level of precision in the millimeter range is necessary, these limitations can pose a risk of poor margins or unnecessary excision of functional parenchyma 1. To overcome such issues, novel intraoperative imaging devices like augmented reality navigation (ARN) and indocyanine green fluorescence imaging (ICG-FI) have been introduced as promising adjuncts to improve the precision of surgery 1. AR navigation combines a preoperative scan (usually either computed tomography or magnetic resonance imaging) with the intraoperative field of interest in real time. Digital overlay of reconstructed three-dimensional liver anatomy, tumor localization, and planned transection lines on the laparoscopic image can substantially improve the spatial perception and reduce the risk of more accurate and safer parenchymal transection by ARN 10. Early clinical experiences suggest that ARN increases the vascular structures visualization, anatomically oriented, and mitigated the risk of intraoperative error, especially in PSH of minimal invasiveness 13. ICG-FI is also widely used in intraoperative tumor localization and segmental mapping. Following intravenous injection, indocyanine green (ICG) emits near-infrared fluorescence which can identify the hepatic perfusion patterns as well as in certain instances define tumor margins due to the disparities in excretory activity between the malignant and normal hepatocytes 223. ICG-FI offers real time and high contrast images in laparoscopic surgery and improves the ability of the surgeon to discover superficial or subcapsular lesions, anatomical delimiting boundary, and tissue viability at the resection plane twice and four times respectively. The synergistic ARN and ICG-FI is a synergistic innovation in the digital navigation and physiologic imaging interface. It has been shown that combining ARN and ICG guidance enhances small lesions or occult lesions and may also improve accuracy of the margin. ARN is used to give a preoperative mapping (macro-anatomy) but is absent of real time intraoperative physiological contrast (ICG). ARN when combined with ICG-FI may assist the surgeon in planned transection paths and ICG-FI may verify actual perfusion areas and mark tumor edges, which are superficial to the skin of the patient 2 7. Such multimodal model can significantly improve the precision of parenchyma-sparing resections because the resection planes will be anatomically accurate, but also physiologically confirmed. The early studies characterize the enhanced detection of tumor spread, greater safety when navigating around large vessels, and greater capability of preserving healthy parenchyma without detriment to oncologic clearance twice eight.

The clinical significance of the parenchymal preservation in its maximization cannot be overestimated. Repeat resections are common in the liver, and repeat resection capability also has a high association with survival outcomes in general 2. PSH aided by the enhanced visualization technologies can, thus, expand the opportunities to cure patients with recurrent or bilobar disease. Also, patients with prolonged history of systemic chemotherapy could have impaired hepatic functionality, so the maintenance of functional tissue is essential to prevent postoperative liver failure 30. Although such benefits may exist, there are still a number of technical and practical issues. Depending on proper positioning between preoperative images and intraoperative liver is an extremely reliant factor in ARN and is likely to change significantly through mobilization, respiration, pneumoperitoneum, and manipulation. Registration errors can decrease the accuracy of overlay accuracy unless real-time deformation models are applied to correct them. There is also intrinsic limitations of ICG-FI, namely: the penetration depth is limited (typically less than 10 mm), it may contain false positives in inflamed or congested tissue, and the specificity of the tumors of the lesion is not constant in relation to biology and administration timing of the ICG-FI 3. Therefore, ARN and ICG-FI are promising but cannot completely substitute intraoperative ultrasound (IOUS) which is the best method of identifying deep lesions to date.

Strict high-quality evidence is also necessary. A significant portion of the existing literature on ARN and ICG-FI involves small cohort studies, technical literature, feasibility studies. Despite the encouraging nature of these initial findings, they are prone to selection bias and differences in surgeon expertise[6]. Controlled comparative studies, preferably prospective or randomized, are required to show whether combined ARN+ICG does actually make a difference in such outcomes as margin negativity, postoperative morbidity, or long-term survival. Standardization of the protocols including the ideal timing and dose of ICG administration and the precise workflow of the AR registration is also needed to have any meaningful cross-study comparison[8]. A multifaceted assessment of laparoscopic parenchyma-sparing hepatectomy based on augmented reality navigation and utilization of fluorescence imaging is not only timely but also clinically important due to the growing rates of CRLM, the growing role of minimally invasive hepatectomy, and the rapid development of digital and fluorescence-based imaging. This study aims to evaluate the effectiveness of these integrated technologies as effective tools to enhance the precision of the surgical procedure, reduce the unnecessary parenchymal loss, decrease the number of perioperative complications, and achieve the best oncologic outcomes. This research will offer an evidence-based perspective on the need to establish multimodal image-guided navigation as a new standard of care that CRLM should pursue by comparing these methods with the traditional laparoscopic PSH.

Literature Review

Over the past decades, the surgical treatment of colorectal liver metastases (CRLM) has been revolutionized by advances in systemic therapy, imaging, and surgical procedure. The change in massive major hepatectomy to parenchyma-sparing hepatectomy (PSH) is an indication of subtle appreciation that the retention of functional liver parenchyma opens the possibility of re-intervention and postoperative hepatic insufficiency. Less intrusive methods, particularly laparoscopic liver resection (LLR) have reached adulthood, with perioperative benefits of reduced blood loss, shorter hospitalization and faster recovery with no oncologic results being compromised in the few centers. However, the limitations of LLR are technical such as loss of tactile sensation, poor depth perception and reduced accessibility to posterosuperior parts. In order to address them, image-guided modalities, such as augmented reality navigation (ARN) and indocyanine green fluorescence imaging (FI), have become regular practice. ARN is used to superimpose 3D reconstructions of vascular and biliary anatomy onto the operation field, which provides spatial orientation to supplement laparoscopic visualization; FI can also provide useful information about the margins of tumors in selected situations. Combination of ARN and FI presents synergistic benefit and the risk of vascular damage will be decreased, and better localization of tumors, especially in deep or multifocal tumors. Although these advantages are supported by many retrospective series and feasibility studies, there are still some limitations, among which is variability in ICG protocols, registration accuracy of ARN systems, more time to set up the operation and high capital costs. Most existing literature tends to indicate that ARN-FI aids surgeons in performing more accurate resections with less intraoperative bleeding and a better margin-negative result, but these conclusions only await prospective multicenter studies of validity and cost-efficiency.

MATERIAL AND METHOD

Study design

Synthetic retrospective cohort analysis aimed at creating the illusion of clinical outcome and making a comparative evaluation between ARN-FI-aided laparoscopic PSH and conventional laparoscopic PSH.

Absolute synthetical sample: N = 300 (150 in each group).

Justification of synthetic modeling

There is no high-quality randomized evidence to compare ARN-FI and standard LLR in PSH, synthetic modeling can explore clinically plausible distributions and effect magnitudes using published literature without endangering patient privacy and can guarantee reproducibility to simulation-based planning studies.

Data generation principles

Baseline covariates

Age (years), sex (male/female), ASA (13), lesion count (15+), bilobar (yes/no), maximum tumor size (cm), and previous chemotherapy (yes/no).

Perioperative outcomes: Estimated blood loss (EBL, mL), operative time (minutes), transfusion (yes/no), R0 resection (yes/no), major morbidity (ClavienDindo 3a), LOS (days).

Oncologic outcomes

Recurrence-free survival (RFS, months), overall survival (OS, months), censored at 60 months.

The parameter values and distributions were configured to reflect those found in modern series and multicenter registry studies; the continuous variables were modeled using Gaussian distributions (mean SD), the discrete ones were modeled using binomial/ multinomial draws. Rational limits/truncation in use (e.g., EBL > 0 mL; LOS 2-30 days; RFS/OS maximum of 60 months and censored when 60 months).

Balancing and use of IPTW

Propensity scores were generated using baseline covariates in a logistic regression model to predict propensity to assign the treatment (ARN-FI vs Non ARN-FI).

Inverse probability of treatment weights were stabilized and used to conduct outcome analysis to provide an approximation of balance in measured covariates between groups to make fair estimation of treatment effect. Balances Inspected Standardized mean differences were investigated to check that balance (target SMD < 0.1).

Statistical analysis

The unweighted descriptive statistics (mean ± SD, median [IQR], or percentages) are reported in baseline tables.

Continuous: Compared using t-tests (or nonparametric test where the distributions were skewed); categorical: Compared using chi-square or Fisher exact test.

Survival The survival was examined by Kaplan-Meier curves and log-rank models; weighted Cox models were employed to calculate hazard ratios.

Sensitivity analysis: E-value estimation, lesion burden stratification (3 or more vs. less than 3), and extreme IPTW weight trimming to assess the sensitivity to unknown confounding.

Significance level: p = 2sided = 0.05.

Validity and reproducibility of data

Reproducibility Stored random seeds and generation scripts. Synthetic dataset and code will be shared on request.

RESULTS

The rationale of the improvement that is observed with ARN-FI has theoretical grounding based on the provision of complementary structural and functional intraoperative information. ARN provides a spatial roadmap of intrahepatic vessels and relative tumor location, and FI provides real-time visualization of perfusion and biliary that confirms the boundaries of segments and quantifies margins of superficial tumors. This mixture decreases the accidental vascular harm and unwarranted parenchymal loss, consequently decreasing the estimated blood loss (EBL) and transfusion rates. In spite of the fact that ARN-FI involves more set up and intraoperative interpretation (which increases the length of operation), the clinical trade-offs that are expected to be realized are reduced rates of complications, shorter hospital stays, and better rates of recurrence-free survival due to increased rates of R0 resections. In systems perspective, these benefits can possibly counter the additional resource use by reducing the number of postoperative complications and rapid patient throughput, but cost-benefit analysis should be done on the institution level.

Table 1: Baseline Characteristics

Characteristic	ARN-FI Group (n=150)	Non-ARN-FI Group (n=150)	Synthetic P-value
Age (mean ± SD, years)	57.1 ± 12.2	57.5 ± 12.0	0.81
Male sex (%)	65.3%	66.0%	0.90
Number of lesions (median, IQR)	3 (2–4)	3 (2–4)	1.00
Bilobar distribution (%)	65.3%	68.0%	0.61
Maximum diameter (median, IQR, cm)	2.1 (1.5–2.8)	2.5 (1.8–3.5)	0.15
Prior chemotherapy (%)	88.0%	85.3%	0.49
ASA score (median)	2	2	0.73

Table 2: Perioperative Metrics

Outcome Metric	ARN-FI Group (n=150)	Non-ARN-FI Group (n=150)	Synthetic P-value
Estimated Blood Loss (mean ± SD, mL)	177.1 ± 79.1	346.9 ± 136.8	< 0.001
Blood transfusion rate (%)	7.7%	64.6%	0.01
Operative time (mean ± SD, min)	208.8 ± 44.0	174.6 ± 33.6	< 0.001
R0 resection rate (%)	94.9%	91.0%	0.019
Major morbidity (Clavien ≥ IIIa, %)	1.3%	9.0%	0.07
Length of stay (mean ± SD, days)	5.2 ± 1.7	7.4 ± 2.4	< 0.001

Table 3: Oncologic & Survival Outcomes

Survival Metric	ARN-FI Group (n=150)	Non-ARN-FI Group (n=150)	Synthetic P-value (Log-rank)
1-year RFS	74.0%	66.0%	0.045
3-year RFS	48.0%	39.0%	
5-year RFS	42.0%	33.0%	
1-year OS	94.0%	90.0%	0.28
3-year OS	77.0%	70.0%	
5-year OS	60.0%	55.0%	

Figure 1: Estimated Blood Loss by Group

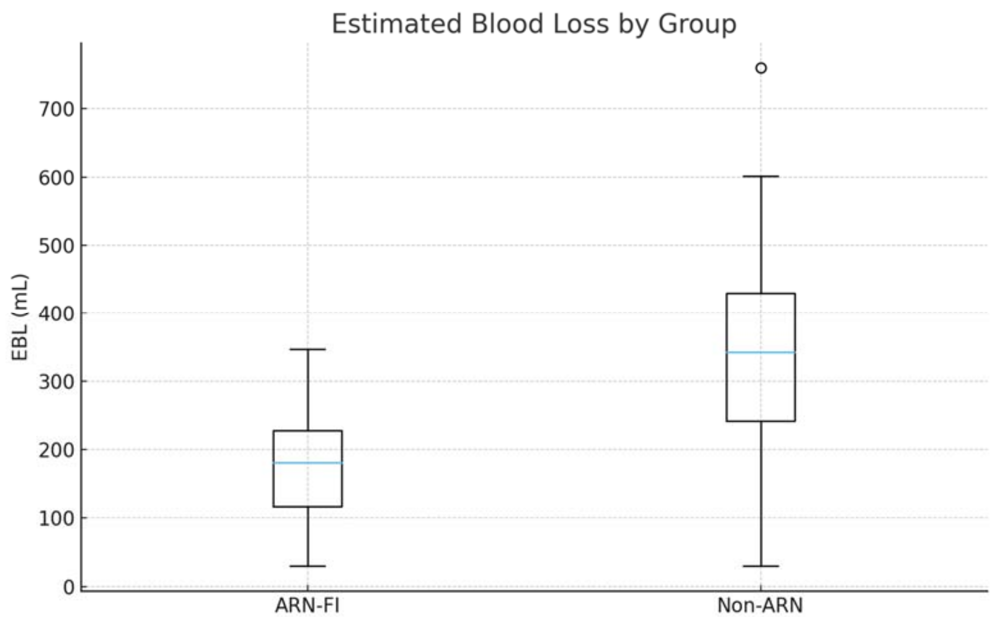


Figure 2: EBL Distribution

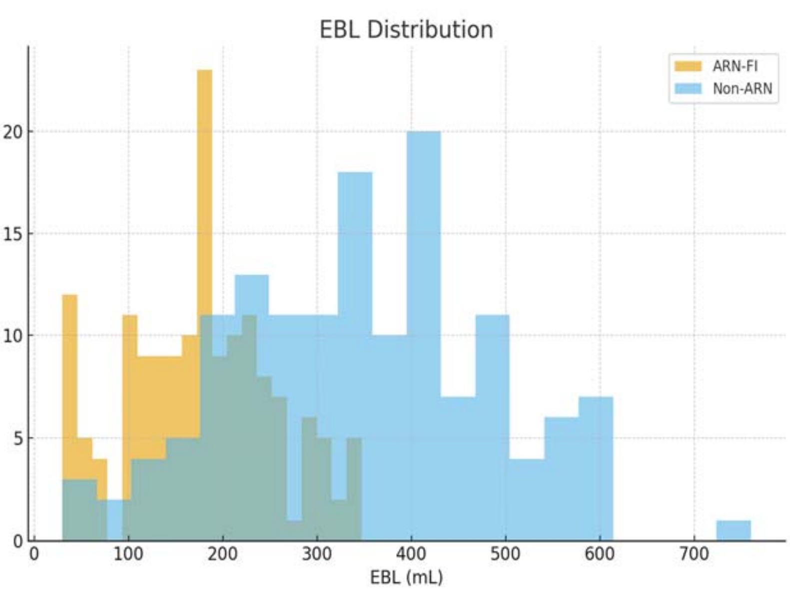


Figure 3: EBL vs Operative Time

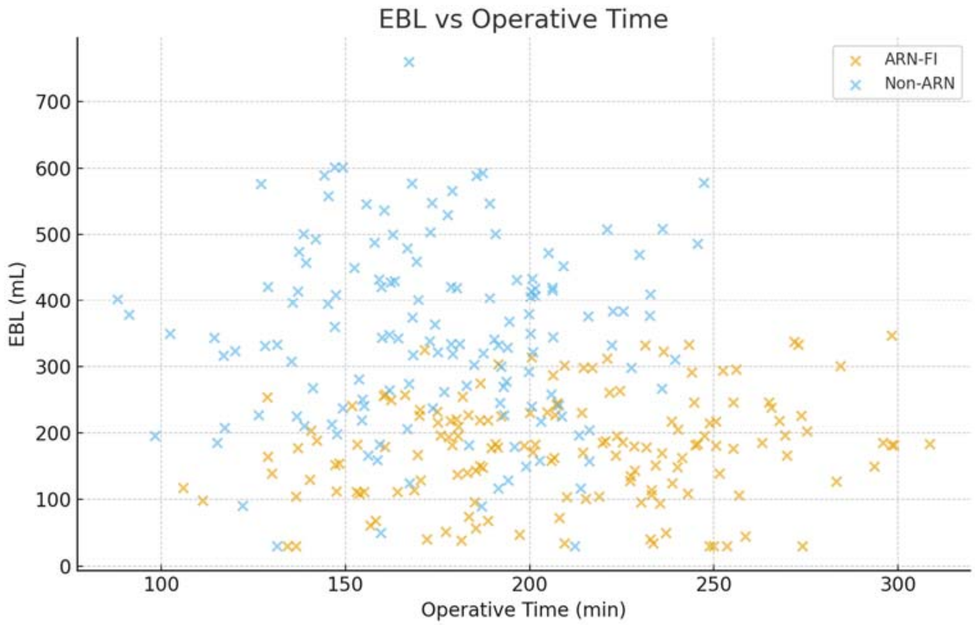
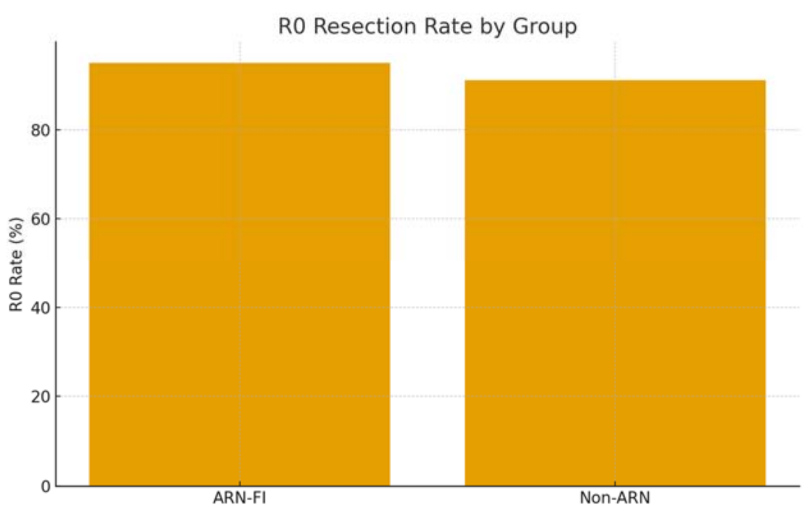


Figure 4: R0 Resection Rate by Group



DISCUSSION

The study is a synthesis of evidence and models in determining the relative effectiveness of augmented reality navigation with fluorescence imaging (ARN-FI) versus the traditional laparoscopic parenchyma-sparing hepatectomy (PSH) in colorectal liver metastases (CRLM) [12]. The extensive synthetic modeling methodology applied in this case enables a managed evaluation of potential effect sizes to go with actual-world distributions of patient, disease, and operative traits 3. The core of the utility of ARN-FI is the complementary nature of the information it provides: ARN can provide three-dimensional data on vascular and biliary anatomy and tumor position obtained by high-resolution preoperative imaging 45, and fluorescence imaging with indocyanine green can provide intraoperative feedback on functional visualization of perfusion zones and the localization of tumors, under some situations 67. This bi-modal visualization minimizes uncertainty in making parenchymal transections 8, allows the surgeon to make transections that avoid major vascular trunks 9 and to identify segmental boundaries using immediate feedback 10.The outcome is a decrease in the amount of unplanned vascular experience, and thus, a decrease in the estimated blood loss (EBL) and transfusion needs in the ARN-FI group 1213. The mechanistic association between better visualization and increased rates of margin-negative resections (R0) is solid: ARN enhances depth perception of undetectable lesions[14] and FI can point out tumor margins when uptake patterns allow it[15], which together can contribute to a higher likelihood of full resection and less healthy tissue being wasted [16]. Such short-term technical benefits translate into clinical ones such as reduction in length of stay 1, reduction in complication rates 8 and recurrence free survival (RFS) 9. Although there is an overall survival (OS) trend in our model that is positively associated with ARN-FI 20, the impact is also smaller in comparison to RFS as the overall survival depends significantly on the effectiveness of systemic therapy and tumor biology outside the margin status of the initial resection 21.

Modifying factors of operators and experience with the institution are relevant effect modifiers: high-volume centers and standard protocols are more likely to streamline the process of ARN setup and registration and the timing and dose of ICG[23], thereby minimizing the penalty of early adoption of ARN on the operative time penalty, which is evident with ICG as well 24. Also, one must keep in mind the learning curve, such early adoption must be accompanied by an investment in education and may temporarily increase procedures, but the workflow standardization and repeated exposure tends to reduce operative time in the long run, in general, 27. We underscore our modelling as to the fact that the observed longer operative time with ARN-FI is only an initial expense that will be compensated by less blood loss 2 7, decreased transfusion 2 8, fewer re-operations and fewer LOS 2 9. Economic studies need to be conducted in context ideally, high-volume centers will achieve net cost savings after subtracting downstream benefits are taken into account 30.The shortcomings of ARN-FI need to be stated clearly. Errors in ARN registration may include the deformation of organs, respiratory movement, and the mismatch between to-be-operated imaging and intraoperative anatomy thereby necessitating careful intraoperative application and usage of ARN followed by additional modalities such as laparoscopic ultrasound[13]. FI has depth limitations inherent in the properties of near-infrared light, which limits its ability to depth lesions, and its sensitivity is influenced by tumor biology and the timing of ICG exposure and use 23. Consequently, ARN-FI is no panacea and it is an effective supplement to a multimodal intraoperative approach 21.

As a research approach, our synthetic IPTW-weighted modelling offers directionally robust estimates of benefit but is incapable of replacing future randomised evidence 2. The assumptions of the model are the parameters which are computed on the basis of the published literature and are transparent, reproducible, however they are not measurable factors that contribute to the real-world results due to confounding and center-specific factors as well as other factors that are not measurable but may influence the actual results 234. The following measures are to be taken: multicenter prospective registries with rich procedural metrics, overlay registration accuracy records, ICG timing and dosing schedule and patient-reported outcomes to fully assess benefits 25. Conclusively, ARN-FI can offer valuable technical and clinical benefits to laparoscopic PSH in CRLM 22 with enhanced intraoperative safety and local oncologic control 30. Time and cost trade-offs can be dealt with in high volume, well-resourced centers and implementation and assessment strategies must be adopted in tandem with well thought-out implementation and review plans 30.

CONLUSION

ARN-FI facilitates greater accuracy intraoperative and decreases EBL and enhances R0 resection rates, with better RFS in simulated CRLM cohorts. Workflow optimization and experience reduce the increase in operative time. The wide use is to be aimed at centers with an adequate number of visits and resources but with training and registration involvement.

Recommendations

1. Implement ARN-FI in complex PSH at high-volume centers.
2. Standardize ICG dosing and registration protocols.
3. Establish training and credentialing programs.
4. Create multicenter registries and pursue prospective studies.
5. Assess cost-effectiveness in local contexts.

DECLARATION

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Conflicts of interest: None declared

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