A Dose-Escalation Trial Evaluating Indocyanine Green Fluorescence Imaging for Rotator Cuff Vascularity During Arthroscopy

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INTRODUCTION:

Tendon vascularity is a critical factor in rotator cuff healing, yet methods for assessing perfusion are lacking. Indocyanine green (ICG) fluorescence imaging has demonstrated promise in other surgical disciplines but has not been standardized in shoulder arthroscopy. This Phase I dose-escalation trial aimed to evaluate the safety, optimal dosing, and clinical utility of ICG fluorescence imaging for real-time visualization of rotator cuff perfusion using a fluorescence-enabled arthroscope.

METHODS:

Patients undergoing arthroscopic rotator cuff repair were prospectively enrolled and received one of four intravenous ICG doses: 7.5mg, 12.5mg, 25mg, or 50mg. Intraoperative fluorescence imaging was performed using the Stryker Advanced Imaging Modality (AIM) arthroscopy system. Surgeons assessed fluorescence visibility, clinical relevance, and clinical actionability using standardized Likert scales. For comparative analysis, patients were stratified into two groups: low-dose (≤25 mg) and high-dose (50 mg). Fisher's Exact Test and Mann-Whitney U tests analyzed inter-group differences. Significance was set at $p \leq 0.05$.

Fluorescence Quantification

In cases where surgeons "agreed" or "strongly agreed" that fluorescence was visible (n=9), intraoperative video stills were analyzed using FIJI (ImageJ, version 1.53; NIH). Images were converted to 8-bit grayscale (0–255) and fluorescence intensity was quantified within regions of interest (ROIs). Cumulative fluorescent area (pixels^2) and weighted mean grayscale intensity were calculated. Where applicable, background ROIs were used to calculate signal-to-background ratio (SBR).

RESULTS:

Patient Demographics:

The cohort had a mean age of 57.3 years, 52% were male, and the mean BMI was 30.1. Most were ASA Class 2 (81%) with Goutallier Grade 0 fatty infiltration (71%). Supraspinatus tears were present in 95% of cases while 33% of cases involved both the supraspinatus and infraspinatus. One revision surgery occurred, unrelated to the study.

Low vs. High Dose Analysis:

The high-dose group demonstrated a higher rate of surgeon-reported fluorescence visibility, with 55.6% of cases rated as "Strongly Agree" that fluorescence was observed ($p = 0.322$). In contrast, only 16.7% in the low-dose group were rated as "Strongly Agree." Regarding clinical significance and actionability, 75.0% of low-dose cases were rated "Strongly Disagree" for clinical significance ($p = 0.416$) and 91.7% for clinical actionability ($p = 0.273$). In the high-dose group 44.4% "Strongly Disagreed" with clinical significance and 55.6% with actionability. Although these differences did not reach statistical significance, fewer high-dose cases were judged as clinically insignificant or inactionable. Notably, across both groups, no surgeon rated the fluorescence as "Strongly Agree" for influencing intraoperative decision-making.

Fluorescence Quantification:

All selected cases demonstrated quantifiable fluorescence. The weighted mean grayscale intensity across ROIs was 61.3 (range, 21.4–162.0) on an 8-bit scale. While the fluorescence signal was detectable in all cases analyzed, signal variability was high, and the clinical utility remained limited.

DISCUSSION AND CONCLUSION:

ICG fluorescence imaging was feasible during arthroscopic rotator cuff repair. While higher doses trended toward improved visualization of the rotator cuff vascular bed, the fluorescence signal was not deemed clinically significant or actionable at any dose level. Notably, trends toward dose-dependent differences in fluorescence intensity and surgeon-reported visibility suggest a potential relationship that did not reach significance in this limited cohort.

Figure 1: Intraoperative Subscapular Green (ICG) Fluorescence Imaging of the Rotator Cuff Footprint

Figure 2: Fluorescence Observed Stratified by Low vs. High ICG Dose

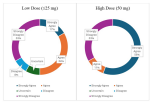

Figure 3: Clinically Significant Fluorescence Stratified by Low vs. High ICG Dose

Figure 4: Clinically Actionable Fluorescence Stratified by Low vs. High ICG Dose

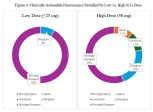

Table 1: Patient Cohort Demographics

N	Total	21
	7.5mg	2
	12.5mg	5
	25mg	5
	50mg	9
Age		57.33 ± 11.37
Sex	Male	11/21 (52.38%)
	Female	10/21 (47.62%)
BMI (kg/m²)		30.05 ± 5.18
ASA	Classification 1	2/21 (9.52%)
	Classification 2	17/21 (80.95%)
	Classification 3	2/21 (9.52%)
ASES		54.41 ± 25.10
Pronis		60.01 ± 18.95
VAS		44.78 ± 29.33
Goutraillet	Grade 0	15/21 (71.43%)
	Grade 1	6/21 (28.57%)
Rotator Cuff Tear	Supraspinatus	20/21 (95.24%)
	Infraspinatus	8/21 (38.1%)
	Multi-Tendon Tear	7/21 (33.33%)
Follow-up (Years)		3.35 ± 1.16

Table 2: Fluorescence Imaging Outcomes Stratified by ICG Dose

Result		Overall (N = 21)	7.5mg (N = 2)	12.5mg (N = 5)	25mg (N = 5)	50mg (N = 9)
Fluorescence Observed	Strongly Agree	2/21 (9.53%)	0	0	1 (20%)	1/9 (11.11%)
	Agree	12/21 (57.14%)	0	1 (50%)	4 (80%)	7/9 (77.78%)
	Uncertain	1/21 (4.76%)	0	1/5 (20%)	0	0
	Disagree	1/21 (4.76%)	1/2 (50%)	0	0	0
	Strongly Disagree	4/21 (19.05%)	1/2 (50%)	1 (20%)	0	2/9 (22.22%)
Clinical Significance of Fluorescence	Strongly Agree	0	0	0	0	0
	Agree	2/21 (9.52%)	0	1/5 (20%)	0	1/9 (11.11%)
	Uncertain	0/21 (0.00%)	0	0	0	0/9 (0.00%)
	Disagree	2/21 (9.53%)	0	0	2/5 (40%)	2/9 (22.22%)
	Strongly Disagree	17/21 (81.05%)	2/2 (100%)	4/5 (80%)	3/5 (60%)	6/9 (66.66%)
Fluorescence is Clinically Actionable	Strongly Agree	0	0	0	0	0
	Agree	2/21 (9.76%)	0	0	0	1/9 (11.11%)
	Uncertain	1/21 (4.76%)	0	0	0	1/9 (11.11%)
	Disagree	2/21 (9.53%)	0	0	0	2/9 (22.22%)
	Strongly Disagree	15/21 (71.43%)	2/2 (100%)	4/5 (80%)	5/5 (100%)	5/9 (55.56%)

Table 3: Fluorescence Imaging Outcomes Stratified by ICG Dose

Result		Low Dose (N = 12)	High Dose (N = 9)
Fluorescence Observed	Strongly Agree	2/12 (16.67%)	1/9 (11.11%)
	Agree	8/12 (66.67%)	7/9 (77.78%)
	Uncertain	1/12 (8.33%)	0
	Disagree	0/12 (0.00%)	0
	Strongly Disagree	4/12 (33.33%)	2/9 (22.22%)
Clinical Significance of Fluorescence	Strongly Agree	0	0
	Agree	1/12 (8.33%)	1/9 (11.11%)
	Uncertain	0	0/9 (0.00%)
	Disagree	2/12 (16.67%)	2/9 (22.22%)
	Strongly Disagree	9/12 (75%)	6/9 (66.66%)
Fluorescence is Clinically Actionable	Strongly Agree	0	0
	Agree	0	1/9 (11.11%)
	Uncertain	1	0/9 (0.00%)
	Disagree	2/12 (16.67%)	2/9 (22.22%)
	Strongly Disagree	11/12 (91.67%)	5/9 (55.56%)