Feasibility of Fluorescent Image-Guided Transoral Robotic Surgery for HPV+ Oropharynx Cancers Using Indocyanine Green

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Introduction

- 13,000 patients are diagnosed with oropharyngeal squamous cell carcinoma annually
- Transoral Robotic Surgery (TORS) is a minimally invasive approach to treat human papillomavirus (HPV) + oropharyngeal squamous cell carcinoma (OPSCCa)[1]
- 10-20% cases report positive surgical margins, as delineation of tumor margins remains a significant challenge
- Tumors are hypervascular in nature[2,3]
- Systemically delivered indocyanine green (ICG) can passively accumulate in the tumors, and demarcate tumor from normal tissue

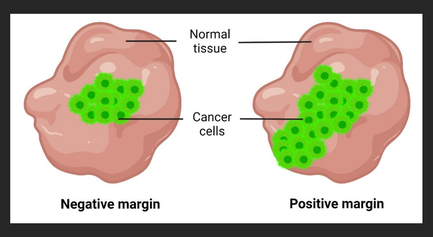


Figure 1. Transoral robotic surgery in HPV+ OPSCCa can result in positive or negative surgical margins

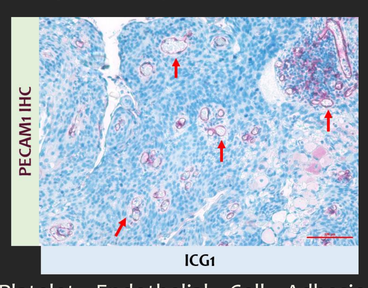


Figure 2. Platelet Endothelial Cell Adhesion Molecule 1 (PECAM1) Immunohistochemistry demonstrates highly vascular/hypervascular tumors in OPSCCa patients (red arrows)

Inclusion criteria and demographics

- Patients with a diagnosis of HPV+ OPSCCa undergoing TORS were enrolled in a prospective, observational cohort study (n=10)
- Patients enrolled for non-oropharyngeal cancer surgeries with no prior history of oropharyngeal cancer were included as controls (n=8)
- Patients were intravenously injected prior to surgery with 25 mg of ICG
- Surgery was performed as standard-of-care using the Da Vinci robot
- ICG Firefly filter used for visualization of tumors

Table 1. Demographics of patients enrolled in the study

	Patients enrolled (n=10)
Gender, n (%)	
Male	9 (90)
Female	1 (10)
Age, Avg years ± SD	58.8 ± 5.5
Race, n (%)	
White	10 (100)
Other	0 (0)
Prior history of head and neck cancer, n (%)	
Yes	0 (0)
No	10 (100)
History of smoking, n (%)	
Yes	4 (40)
No	6 (60)

IVIS-robot correlation

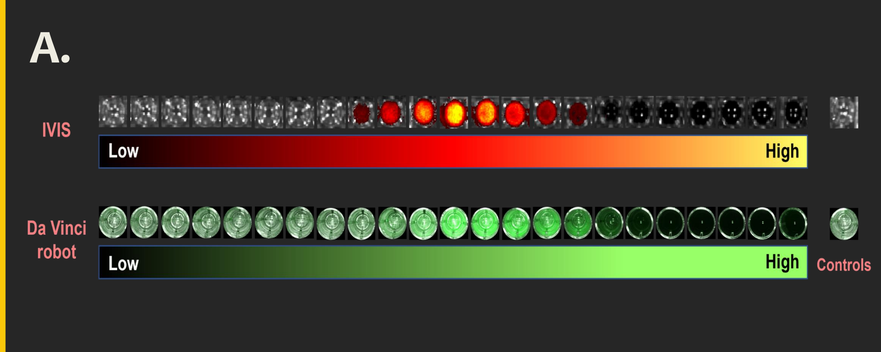


Figure 3. Visualization of ICG fluorescence. **A)** ICG is visualized using the In Vivo Imaging System (IVIS) and Da Vinci robot system **B)** Image analysis and quantification of ICG **C)** Correlation between signal from IVIS and Da Vinci robot are significant

Successful negative margins

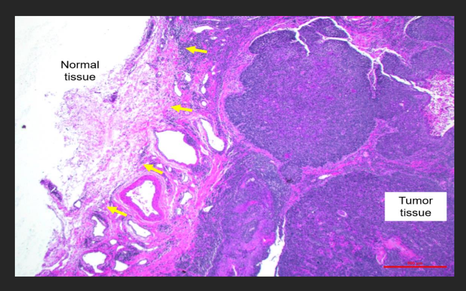


Figure 4. H&E image of tumor tissue margin. Yellow arrows represent the margin between the tumor and normal tissue.

Da Vinci robot imaging

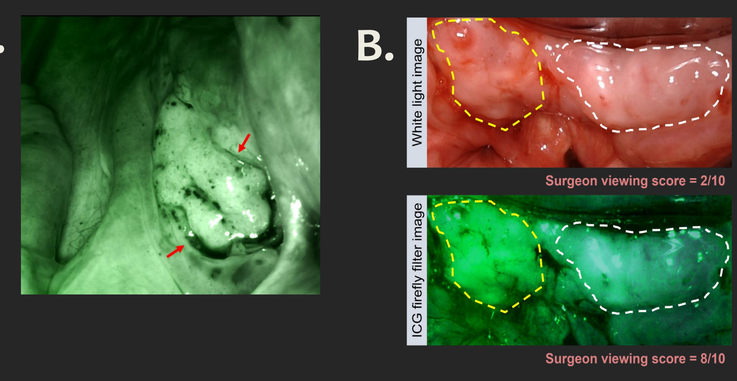


Figure 5. Visualization of tumors using Da Vinci robot. **A)** Distinct identification of primary tumor margins **B)** Visualization of tumor tissue (yellow dotted line) and normal tissue (white dotted line).

Timing of injection

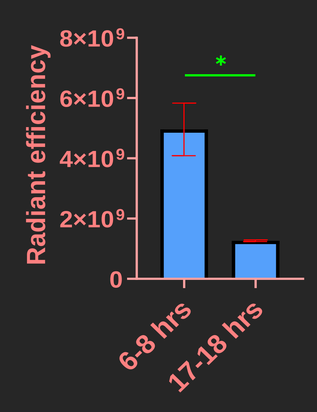


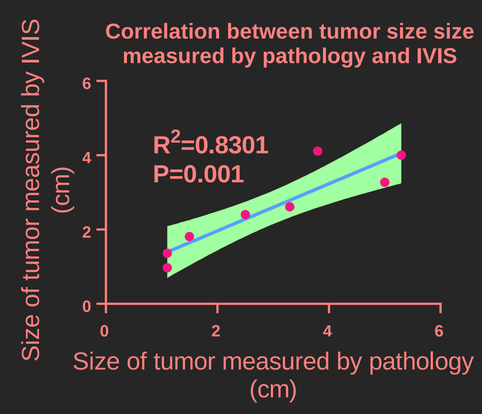
Figure 6. Preoperative injection timing affects ICG concentration in tumor tissue.

IVIS-pathology correlation

A.

		Patients with HPV+ oropharynx carcinoma		
	n=23	Condition positive	Condition negative	
IVIS imaging outcome	Test outcome positive	True positive (TP) = 8	False positive (FP) = 2	Positive predicted value =TP / (TP + FP) = **80%**
	Test outcome Negative	False negative (FN) = 0	True negative (TN) = 13	Negative predicted value =TN / (TN + FN) = **100%**
		Sensitivity =TP / (TP + FN) = **100%**	Specificity =TN / (FP + TN) = **86.7%**	
		Accuracy =TP + TN / (TP + TN +FP + FN) = **91.3%**		

B.



IVIS quantifies ICG

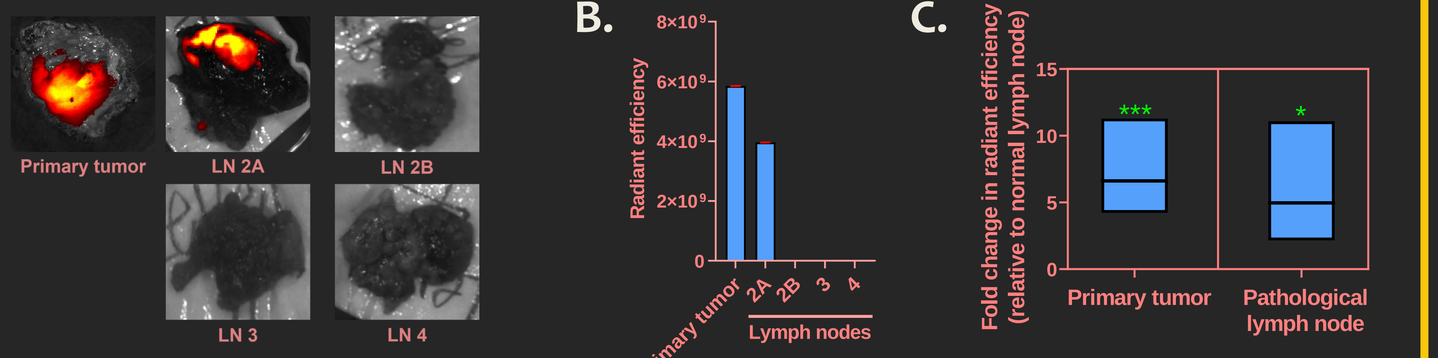


Figure 7. Visualization of tumoral tissue using IVIS. **A)** IVIS imaging detects ICG in primary tumor and lymph nodes **B)** ICG concentration quantification. **C)** 6.6- and 5-fold increase in ICG accumulation in primary tumor and pathological lymph node, respectively. Data represent mean ± SD. P *<0.05, P ***≤0.001

Figure 8. Correlation between IVIS and pathology. **A)** Diagnostic accuracy statistics predicts 91% accuracy between IVIS and pathology **B)** Correlation between IVIS and pathology as diagnostics tools for identifying primary carcinoma.

Conclusions

- Successful identification of primary tumors and margins using ICG
- Successful resection of tumoral tissue with negative surgical margins
- ICG firefly filter enables better visualization of small and deeply-embedded tumoral tissue
- Significant correlation between IVIS and Da Vinci robot for ICG signal detection
- IVIS demonstrated 91% accuracy in identifying carcinoma in tissue samples
- IVIS can be used as an adjunct diagnostic tool for identification of tumoral tissue

Future directions

- Identify underlying biochemical properties responsible for ICG accumulation
- Correlate gene expression profile with ICG accumulation
- Explore ICG accumulation patterns at margin versus center of tumor

Acknowledgment

This research was supported by the Huntsman Cancer Foundation.
We would also like to acknowledge Bio Render for Figure 1.

References

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2. Gupta AK et al Preoperative embolization of hypervascular head and neck tumors. *Australas Radiol*. Oct 2007;51(5):446-52
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