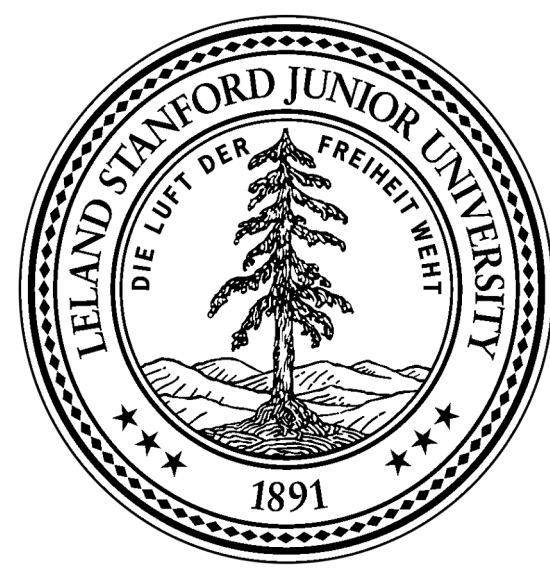




Intraoperative Sentinel Margin Identification using Fluorescent Molecular Imaging



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Introduction

Complete tumor resection with negative margins improves prognosis in head and neck cancer. Inadequate margins are associated with locoregional recurrence, additional therapies and revision surgeries. Despite this, close or positive margins (< 5 mm) are found in 15 – 30% of all head and neck cancer patients. Thus, there is a need for intraoperative margin assessment. **We conducted a clinical trial to assess the value of fluorescence guided surgery in six patients who were infused with panitumumab-IRDye800, an imaging agent that targets the epidermal growth factor receptor (EGFR), for intraoperative specimen mapping to identify the closest surgical margin.**

Patient characteristics

A schematic overview of the trial is given in Figure 1. Patients were included in a phase 1 clinical trial (NCT03733210) to evaluate the use of dual modality Panitumumab-IRDye800 and 89Zr-Pan in head and neck cancer patients to identify metastatic lymph nodes. We used the tissue collected to analyze fluorescent margin assessment for 6 of these patients. Basic patient characteristics are listed in Table 1.

Pt	Age	Sex	Tumor Location	Stage	Resection
1	68	F	left mandibular alveolar ridge-retromolar trigone SCC	T4a	L Composite resection
2	62	F	Right Base of Tongue	T1	Composite resection and marginal mandibulectomy
3	63	F	Tongue Base	T4a	Near total glossectomy
4	79	M	R Tongue	T3	R Hemiglossectomy
5	64	M	L Posterior Lateral Tongue	T2	L Partial Glossectomy
6	63	M	R Tonsillar Fossa	T3	Composite resection of oropharynx and mandible

Table 1: Patient Characteristics

Clinical Trial Overview

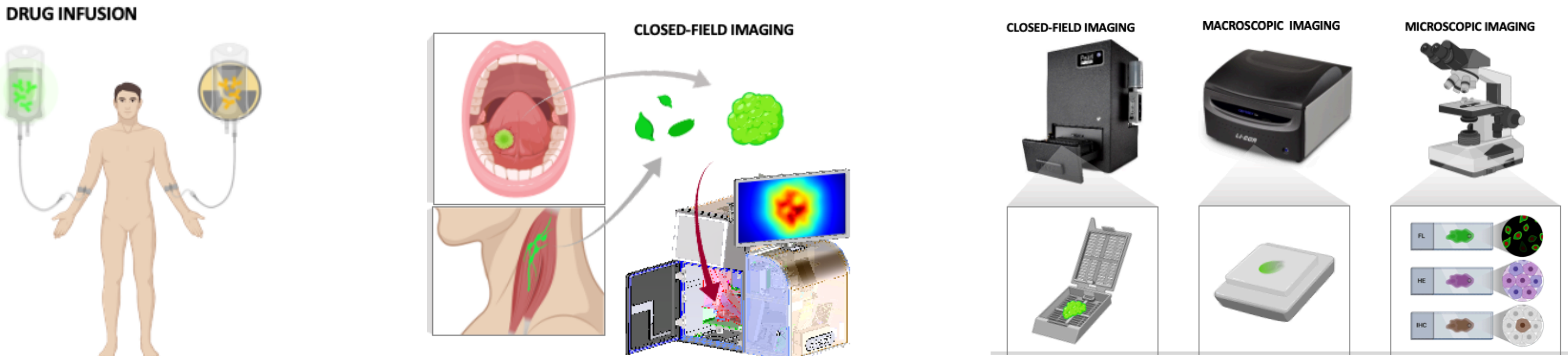


Figure 1: Schematic overview of the phase I clinical trial. Patients are infused with Panitumumab-IRDye800 and 89Zr-Pan 1-5 days prior to surgery. On the day of surgery ex vivo fluorescence imaging of the tumor is performed. The specimen is then sent for histo-pathology for routine evaluation and identification of close margins. Gold standard histo-pathology margin findings are then correlated to ex vivo fluorescence findings.

Margin Assessment

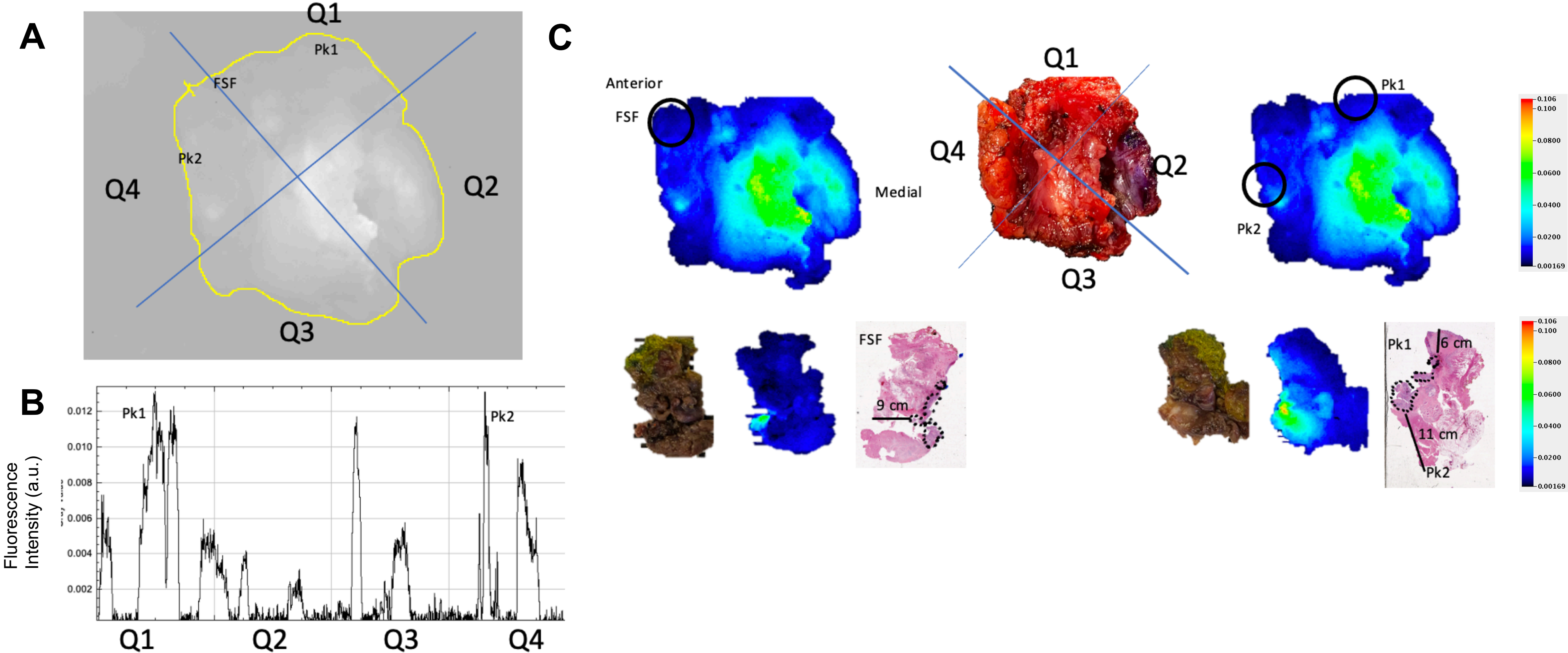


Figure 2: Margin assessment in a representative patient with a right sided base of tongue squamous cell carcinoma. A) ex vivo lesion examining the mucosal surface of the resection. The specimen is divided into four quadrants labeled Q1-Q4. Fluorescent sentinel margin analysis in this patient is demonstrated by a mask manually fitted around the periphery of the specimen (yellow outline) within 1mm of the resection edge. The Surgeon's predicted location of the sentinel margin is recorded as FSF. **B)** Graph showing the raw fluorescence intensity of each point along the mask in an 8-bit grayscale format enabling isolation of the area of highest fluorescence on the periphery (noted as Pk1 and Pk2). **C)** Sampled tissue from these locations underwent closed-field fluorescent imaging and subsequent H&E staining to evaluate the margin distance before comparison to results at final pathology.

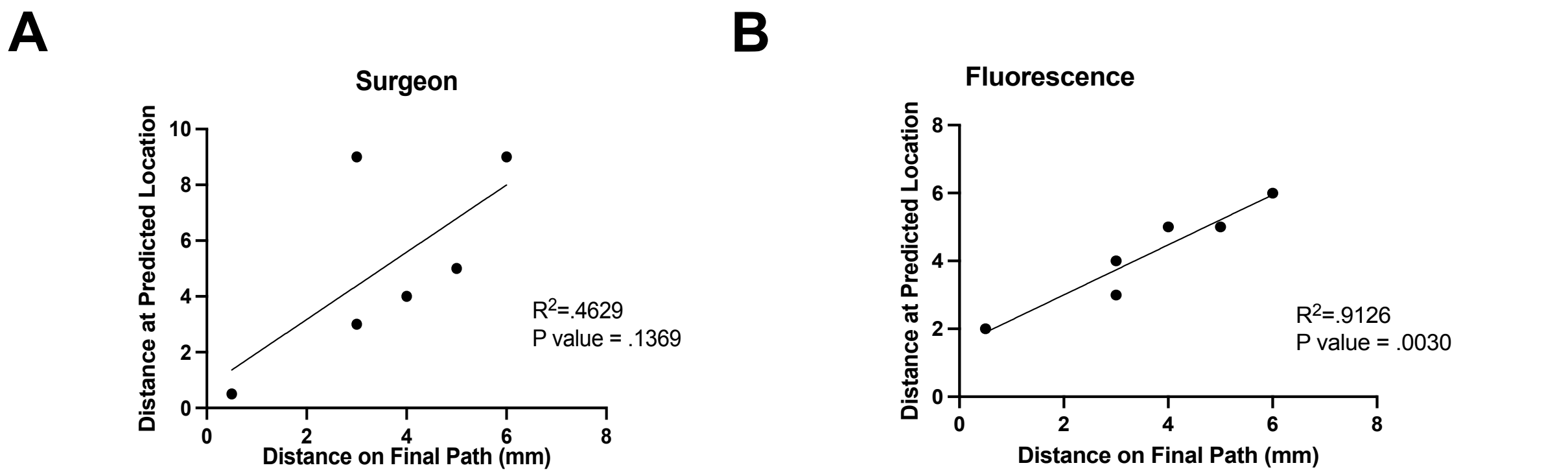


Figure 3: Correlation between distance at predicted sentinel margin by A) surgeon and B) fluorescence and distance on final pathology

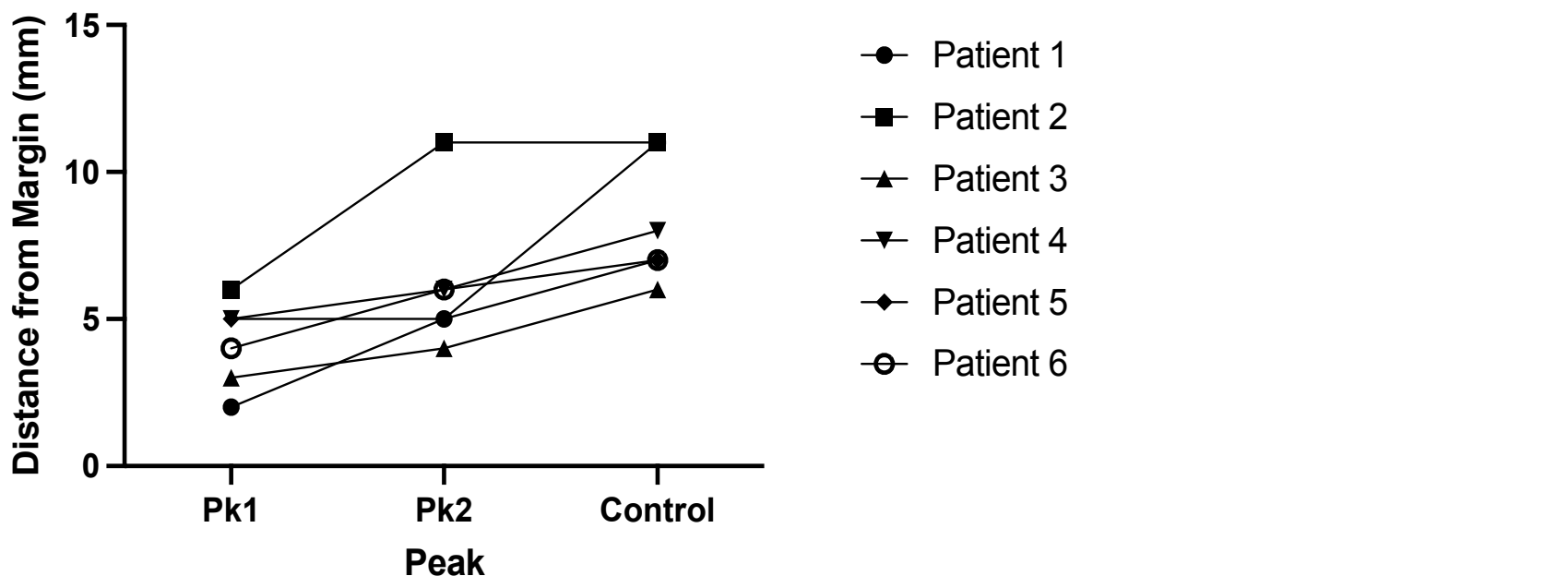


Figure 4: Graph showing margin distance trends from fluorescent peaks (Pk1 and Pk2) to control region (area of low fluorescent intensity) per patient.

Conclusion

Preliminary results from our study show that fluorescent imaging can help identify close margins. This suggests that fluorescent, intraoperative margin assessment may be superior to surgeon palpation/visualization alone, and faster than waiting on results from pathology. To demonstrate this, the close margins identified by fluorescent image analysis needs further investigation done in real time in the operating room.

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References

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