

Targeting Nociceptive and Cholinergic Nerves in Irradiated Oropharyngeal Cancer Model Reveals Novel Mechanism for Dysphagia

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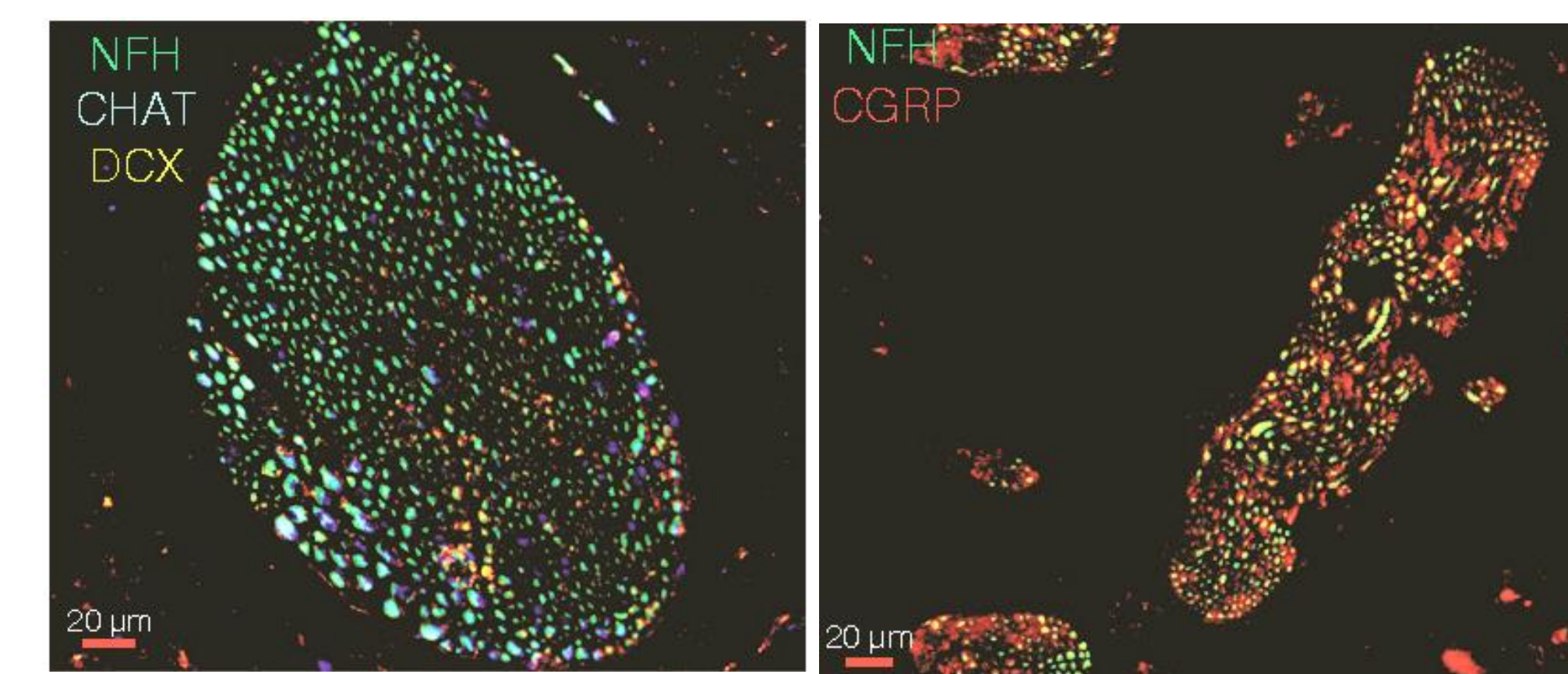
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Background

- Oropharyngeal squamous cell carcinoma (OPSCC) is one of the most common types of head and neck cancer
- Treatment for OPSCC includes surgery, radiation therapy, chemotherapy, or a combination of therapies
- Despite advances in treatment, dysphagia (difficulty swallowing) is still a major burden for patients with OPSCC

In our previous study, we showed that enrichment of cholinergic (CHAT) and nociceptive (CGRP) neurons is associated with dysphagia in OPSCC patients. However, the direct role of CHAT and CGRP neurons in dysphagia in the murine OPSCC tumor model has never been investigated.

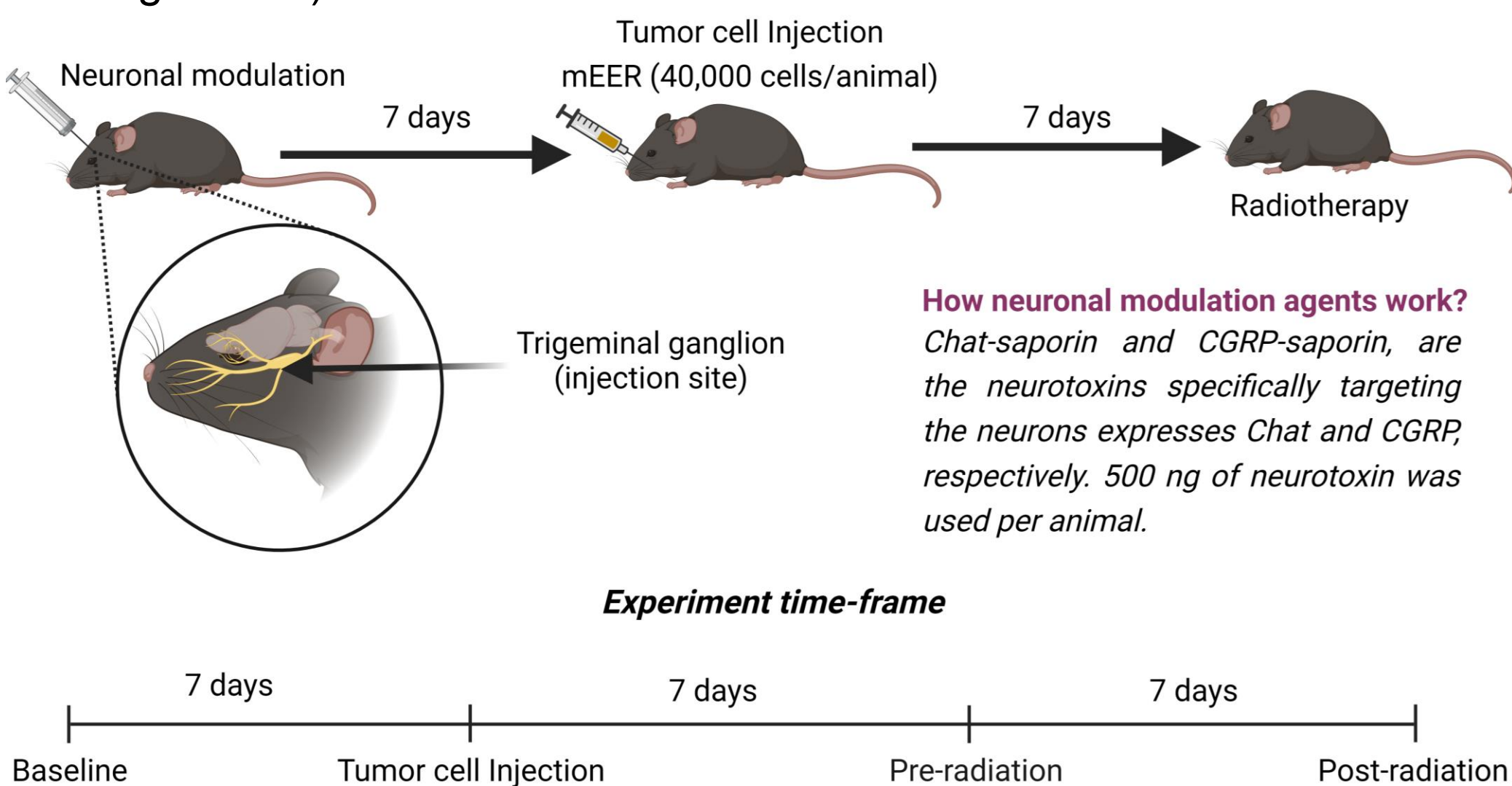


Hypothesis

In the present study, we hypothesized that modulation of cholinergic (CHAT+) and nociceptive (CGRP+) neurons might correlate with improved swallowing functions.

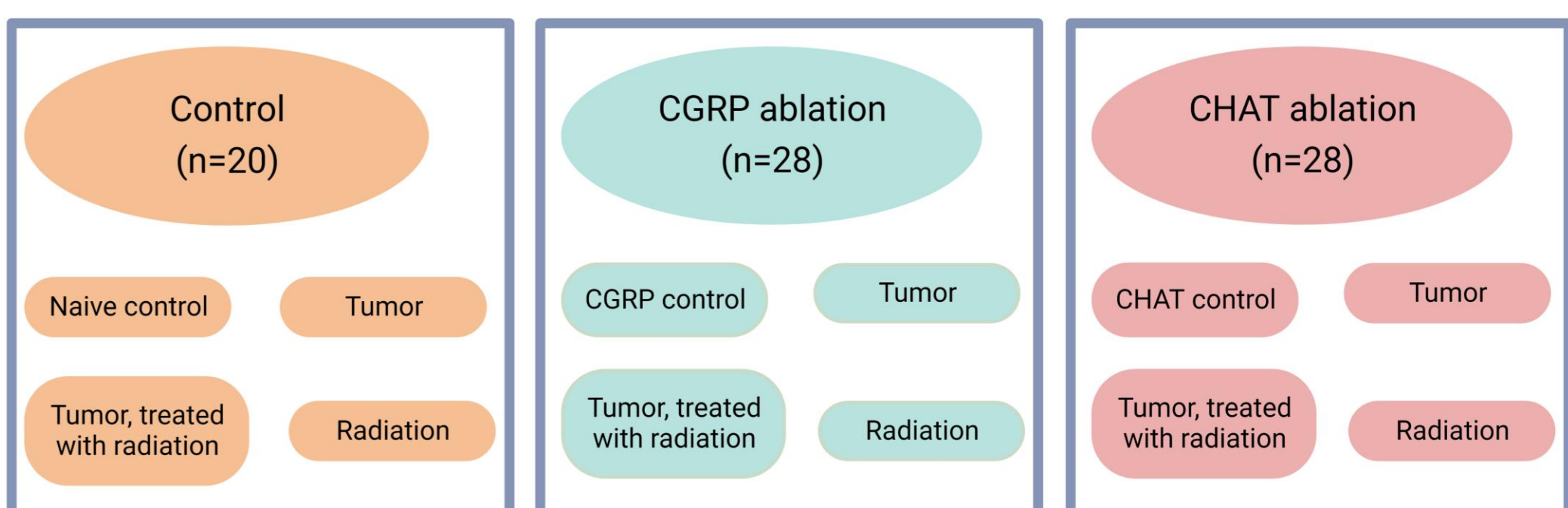
Materials and Methods

- Neuronal modulation: saporin SAP^{CGRP/CHAT} conjugated antibody
- Injection of OPSCC tumor cells into the tonsillar fossa
- Radiation treatment: 24 Gy in 3 consecutive doses (8 Gy per day)
- Behavioral analysis: using Lickometer (10-minute test per animal)
- Data analysis: JMP pro15 (p -value of <0.05 considered statistically significant)

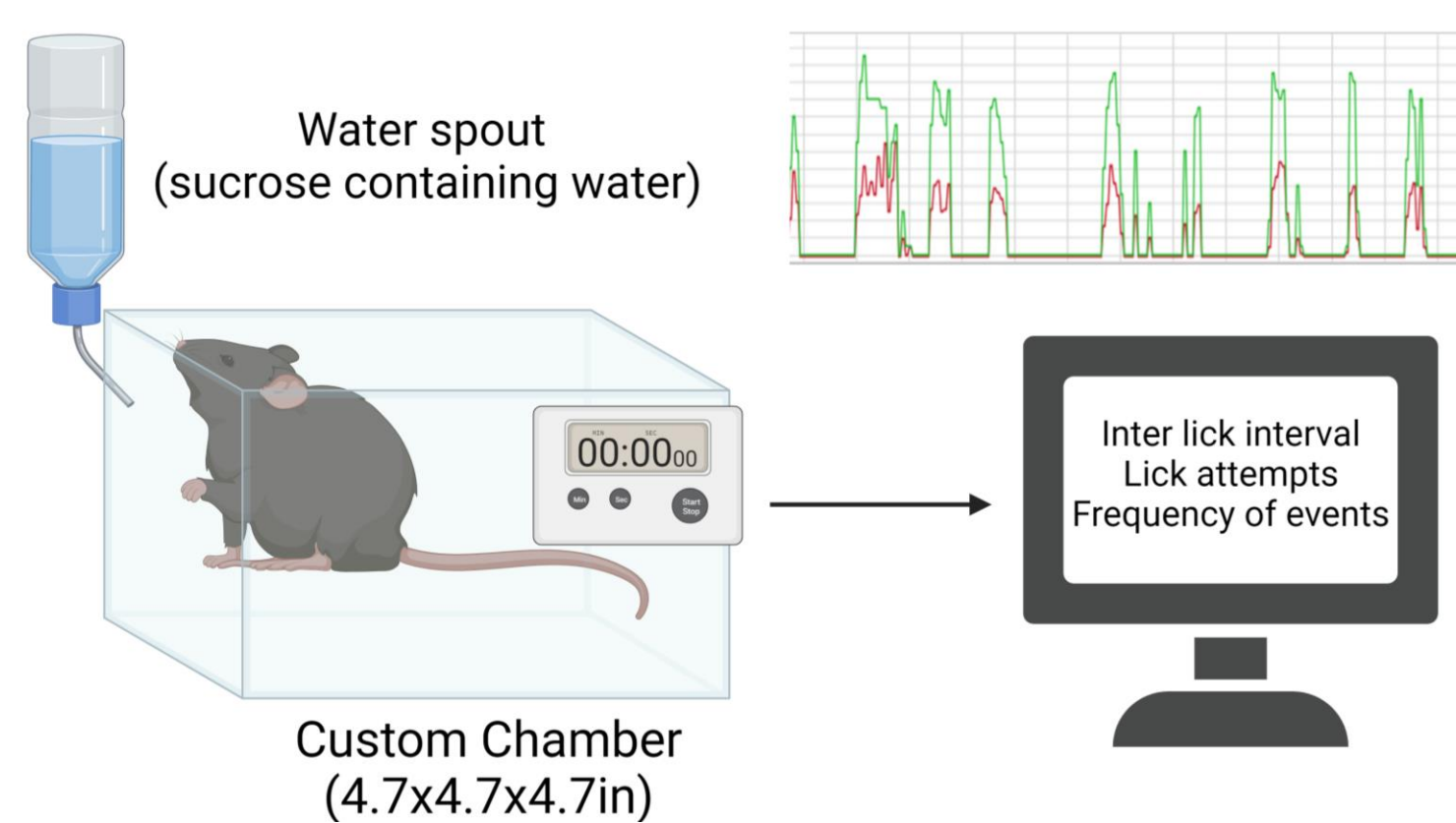


Experimental group allocation

Three experimental groups were formed, and animals were randomly assigned. The age ranged from 4-6 weeks and the c57BL/6J strain was used. The ratio of males to females was 50:50.



Behavioral assessment using Lickometer



Parameters used for data analysis

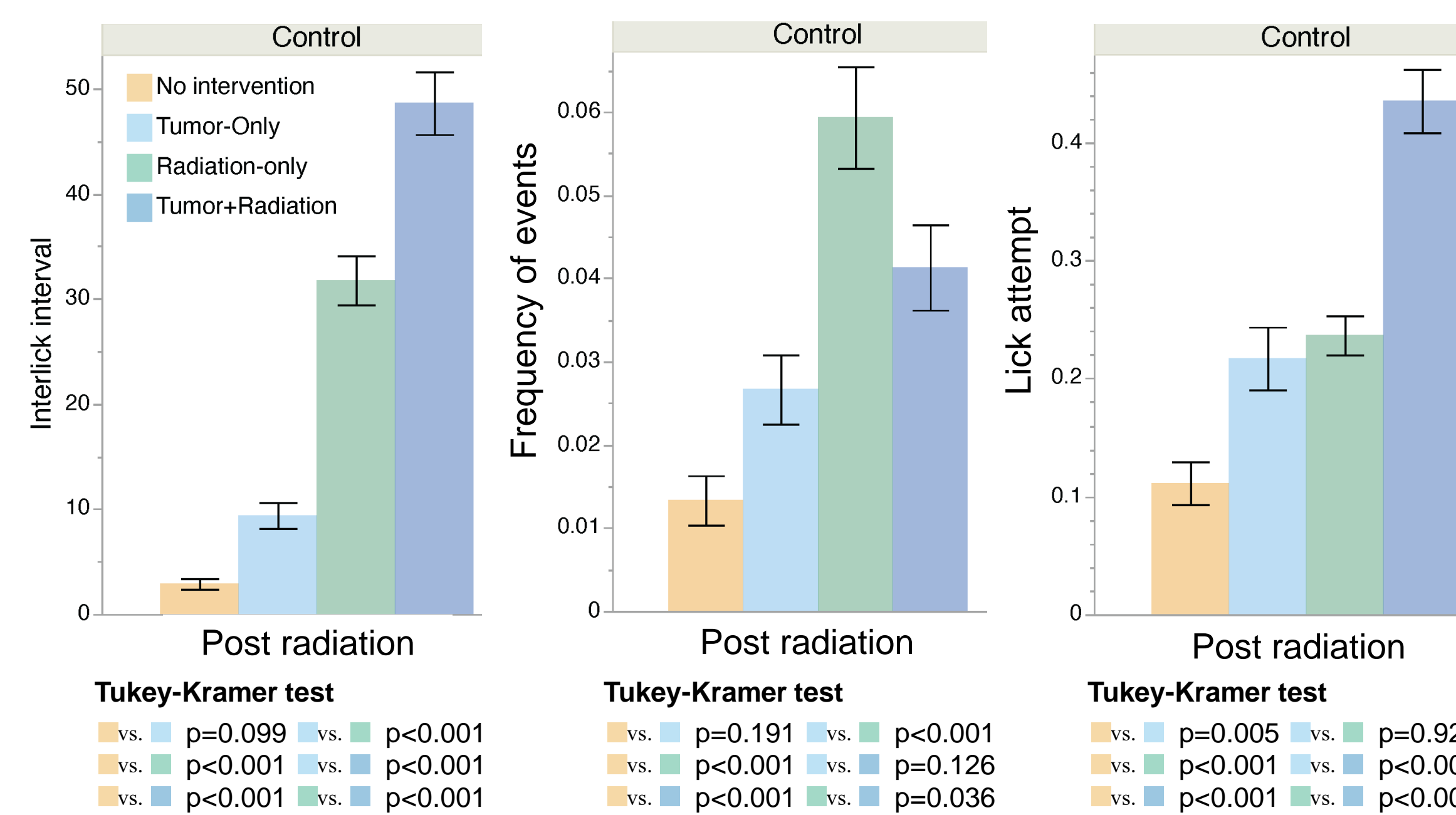
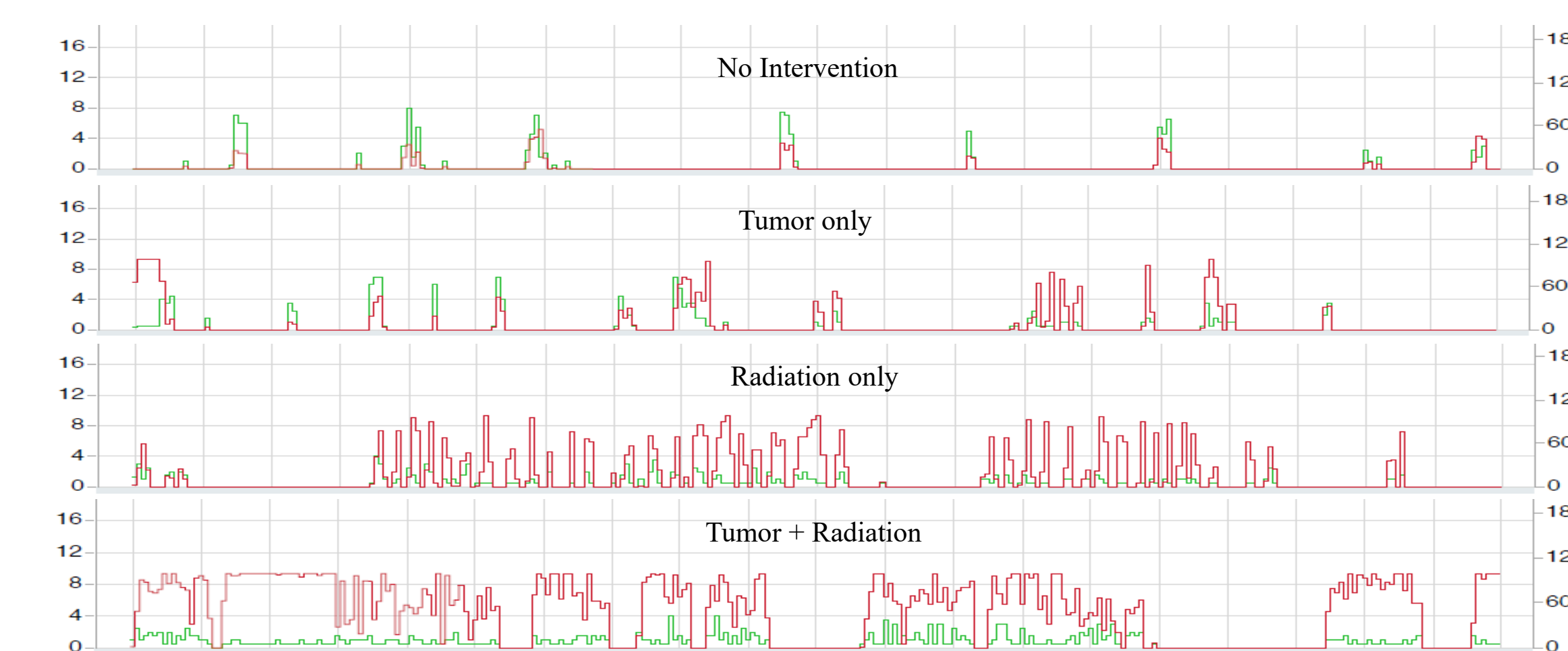
Inter lick interval (ILI): a higher ILI represent poor swallow outcomes

Frequency of events: a lower frequency of events represents good swallow outcomes

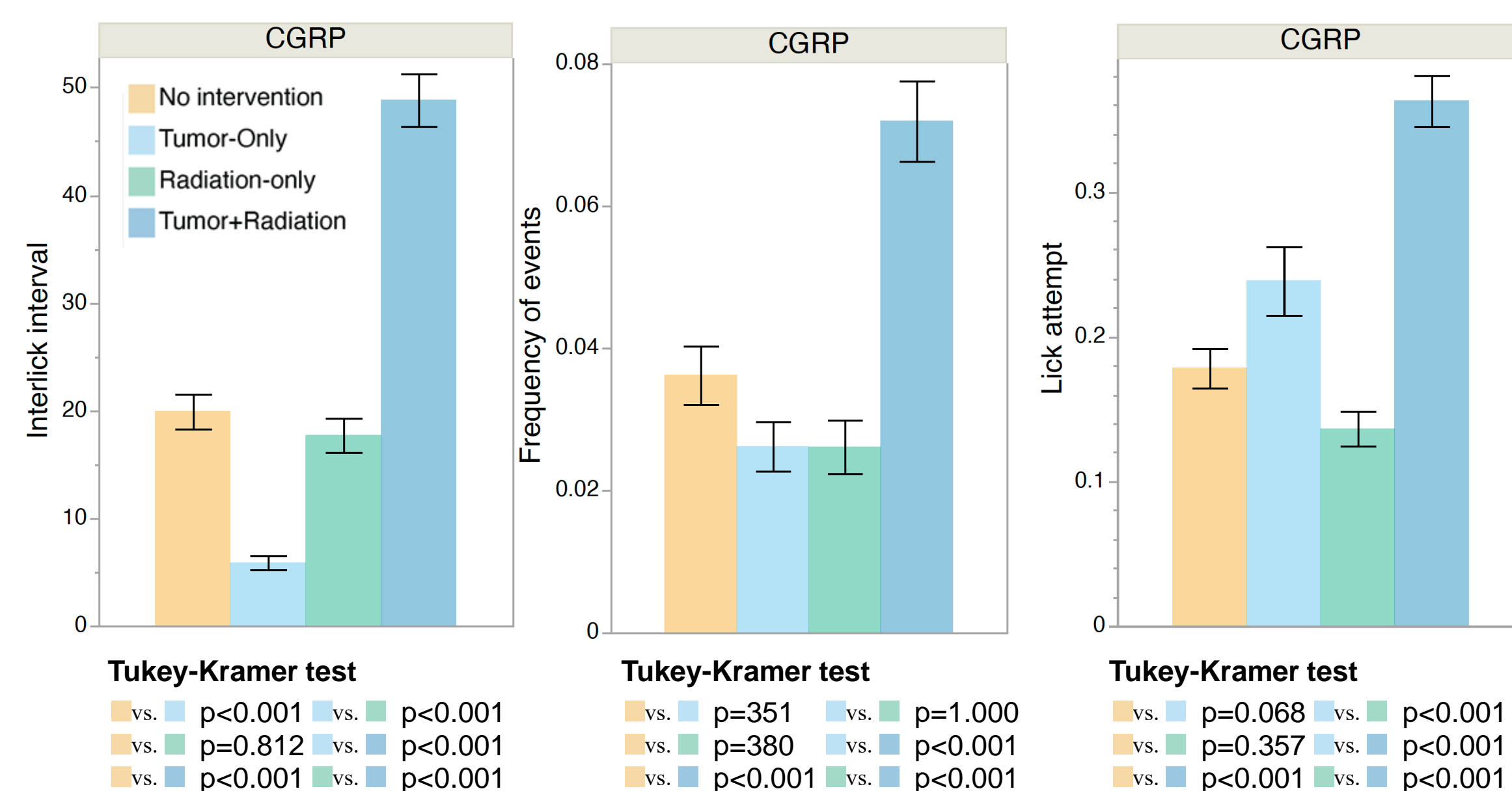
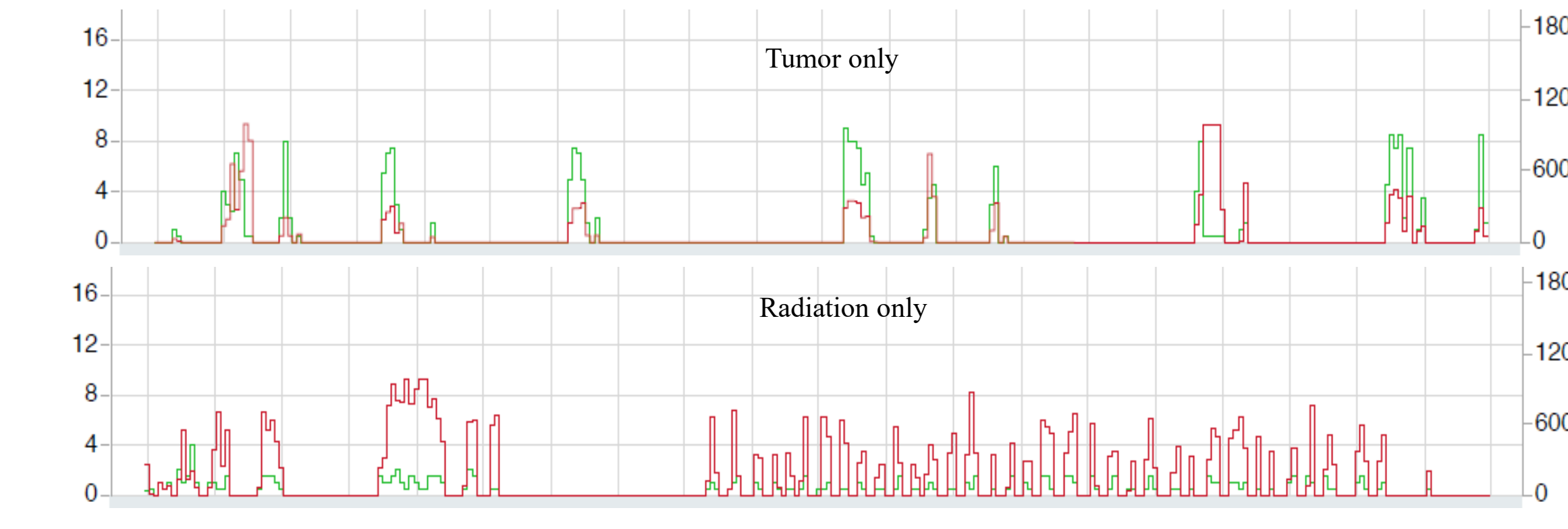
Lick attempt: a higher lick attempt represents poor swallow outcomes

Results

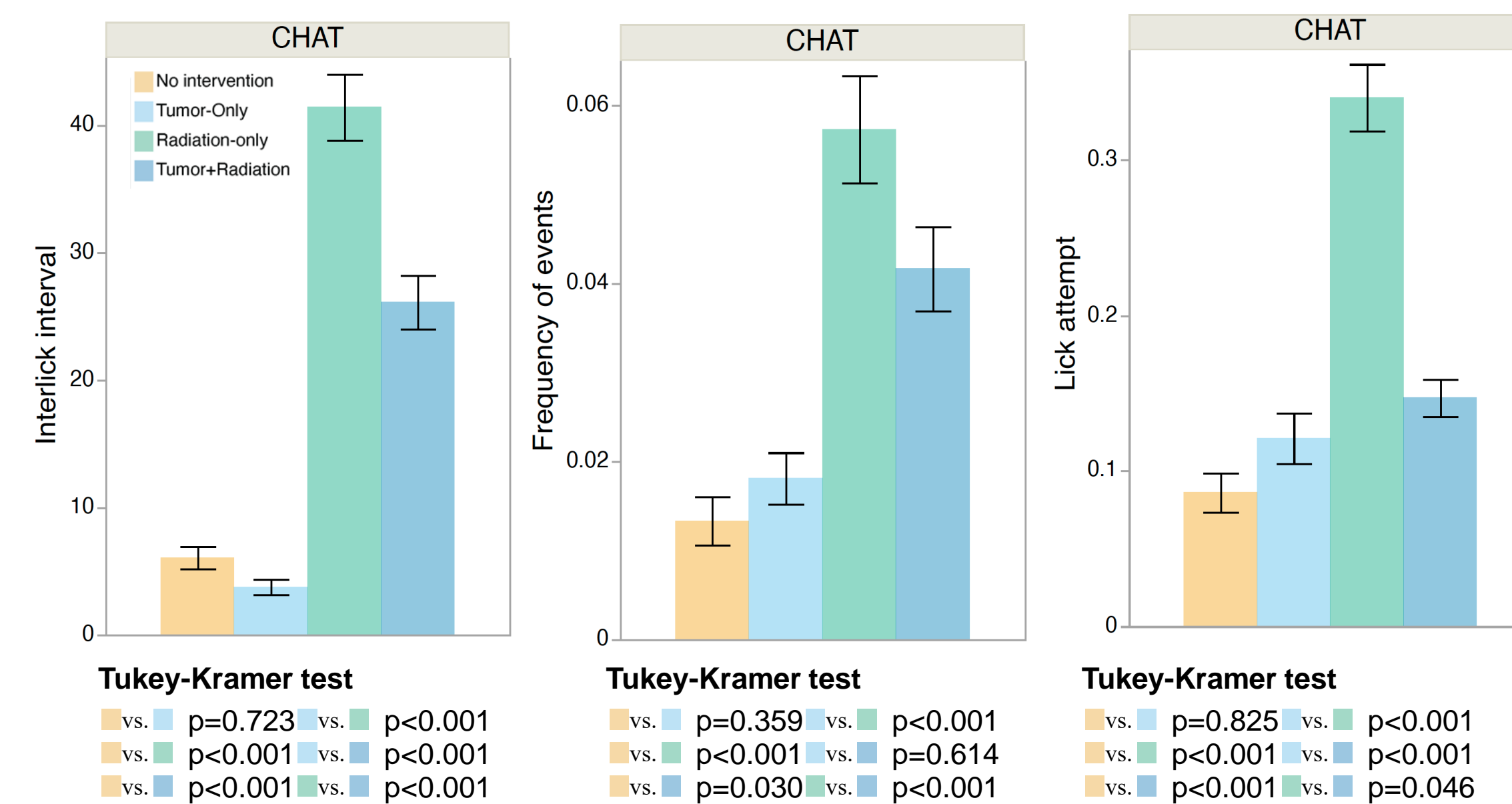
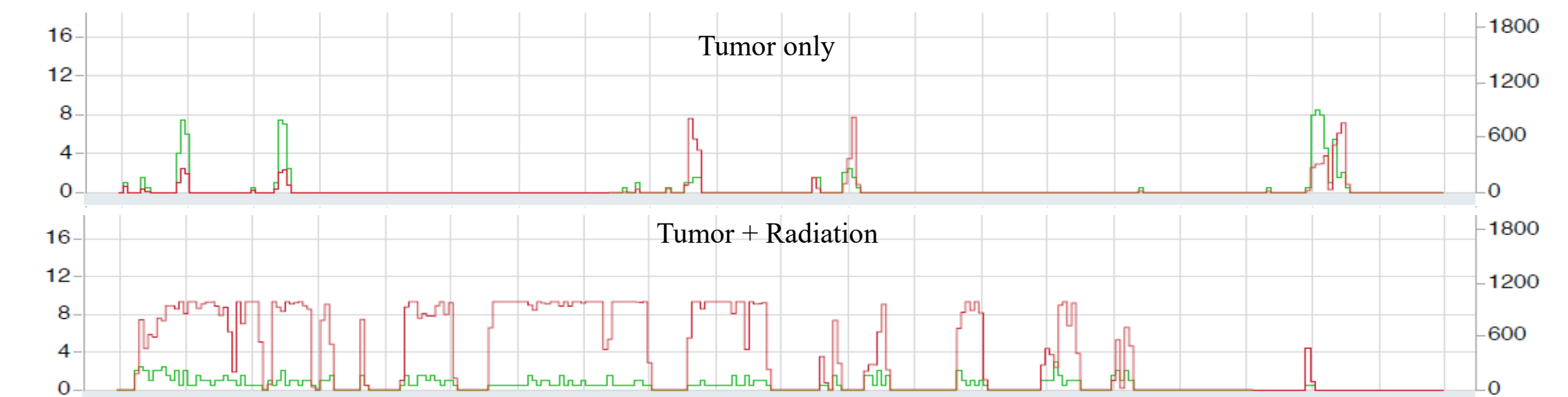
Swallowing function, no neuromodulation



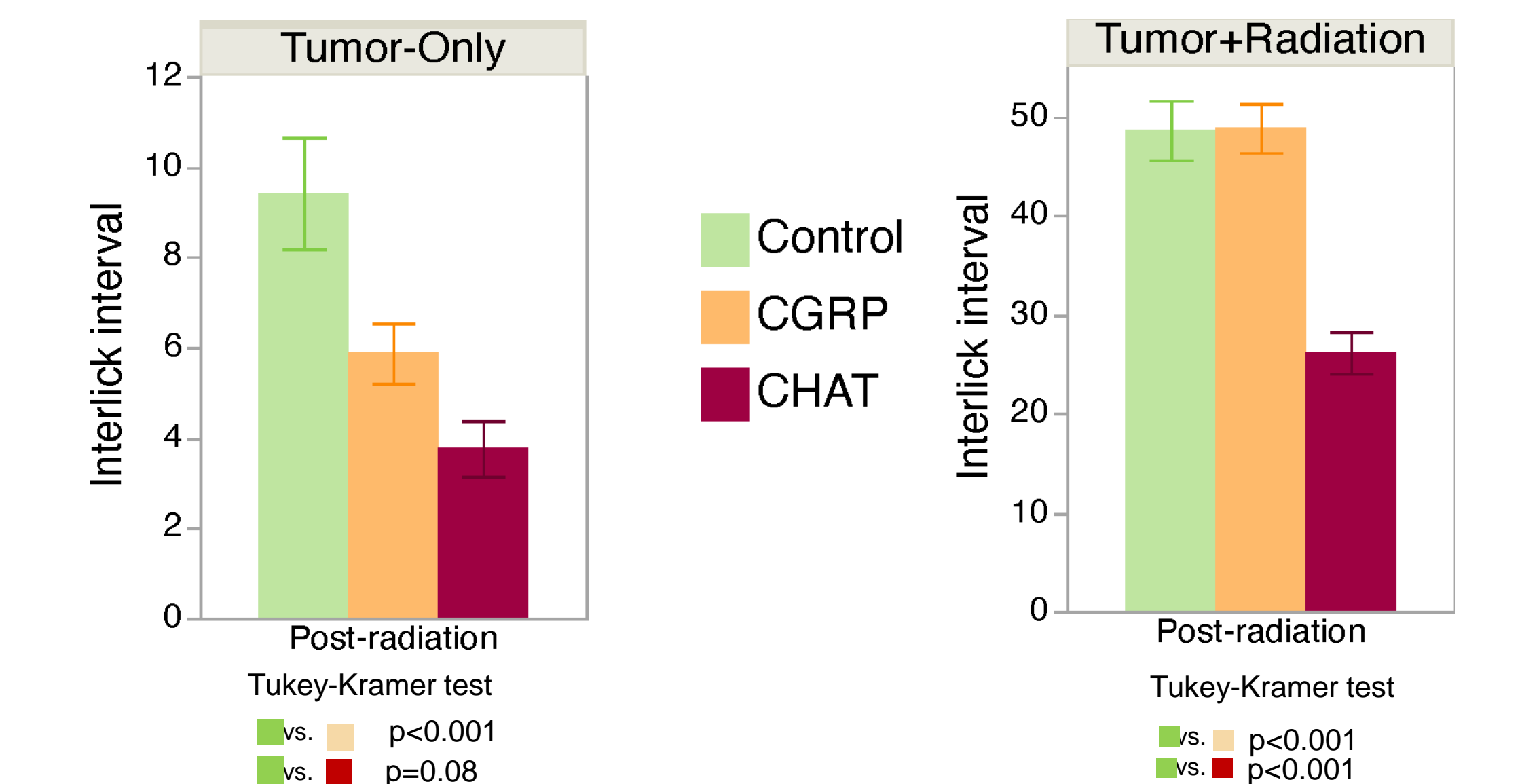
CGRP ablation



CHAT ablation



Post-radiation swallowing function improves following CHAT ablation



Concluding Remarks

- This study establishes a novel murine OPSCC model that merits further investigation to explore the role of nerves in dysphagia
- Cholinergic (CHAT) and nociceptive neurons (CGRP) play an important role in swallowing outcomes
- The enrichment of CHAT and CGRP in OPSCC TME could potentially lead to long-term (post-treatment) swallowing impairment
- Targeting CHAT and CGRP could be a novel strategy for OPSCC patients with dysphagia

Acknowledgement

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Reference

Amit *et al.* Loss of *p53* drives neuron reprogramming in head and neck cancer. Nature. 2020; 449-454.



Please watch
Lickometer video

