



Hypoglossal Palsy in the Pathogenesis of Late-Radiation Associated Dysphagia

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Importance

- Late radiation associated dysphagia (late-RAD) can develop or persist years after treatment resulting in progressive functional impairment, often refractory to standard therapies
- 48%-83% of patients with late-RAD present with clinical signs of lower cranial neuropathies, most commonly hypoglossal (XII) palsy
- Hallmark clinical signs of hypoglossal palsy include lingual atrophy, deviation, and fasciculation
- It is unknown whether subclinical lingual denervation may be detectable using electromyography (EMG) prior to clinical presentation of XII palsy in survivors with late-RAD

Objectives

- Determine prevalence of lingual denervation, using needle EMG in patients with late-RAD
- Compare EMG results with EMG-blinded clinical assessment of lingual cranial nerve (CN) XII function

Design

Secondary analysis of prospective clinical trial data (NCT03612531, MANTLE trial)

Setting

Single institution, comprehensive cancer center

Participants

- Thirty disease-free, adult head and neck cancer (HNC) survivors ≥2 years post curative-intent radiotherapy for HNC enrolled for screening for the MANTLE trial
- Grade ≥2 fibrosis (per CTCAE v4.0)
- Grade ≥2 dysphagia (per videofluoroscopy DIGEST)
- Thirteen of the 30 patients participated in optional bilateral genioglossus EMG (added to study procedures in year 2 of the trial)
- Optional EMG was not conducted if platelets <50,000

	All patients (n = 30)	EMG subset (n=13)
Median Age (SD) (range)	66 (7) (53-78)	68 (5) (58-77)
Median Days post-RT (SD) (range)	4201 (2497) (878-9828)	3952 (1920) (1030-6945)
Mean Months post (SD) (range)	137 (82) (28-322)	129 (63.24) (33-228)
Sex		
Male	24	11
Female	6	2
HNC site		
Oral Cavity	3	1
Oropharynx	20	10
Hypopharynx	1	1
Nasopharynx	3	1
Supraglottic	1	0
Thyroid	1	0
Multiple Primaries	1	0
T-classification		
0	0	0
1	6	2
2	9	4
3	8	4
4	5	2
Unknown	2	1
Therapeutic Combo		
CRT	11	5
RT	4	2
Induction + RT/CRT	10	5
Surgery + PORT/POCRT	5	1
Surgery		
Neck only	2	5
Primary only	4	1
Primary + neck	7	1
Adjuvant surgery	2	0
None	15	6
Median RT dose (range)	70 Gy	70 Gy
Median RT dose – one course (range)	70 Gy (30-72)	70 Gy (66-72)
ORN		
No	22	9
Yes	8	4

Table 1. Patient demographics

Methods & Results

- Presence of hypoglossal denervation by clinical assessment. Clinical CN XII palsy classified as not present, suspected, or present per criteria in Table 2.
- Optional intramuscular electromyography (EMG) of the genioglossus pre- MANTLE intervention. Denervation potentials were graded on a 0-4 scale by a neurologist (Table 3)

CN XII palsy prevalence (n=30) **clinical signs: 70%**
(95% CI: 32-86%)

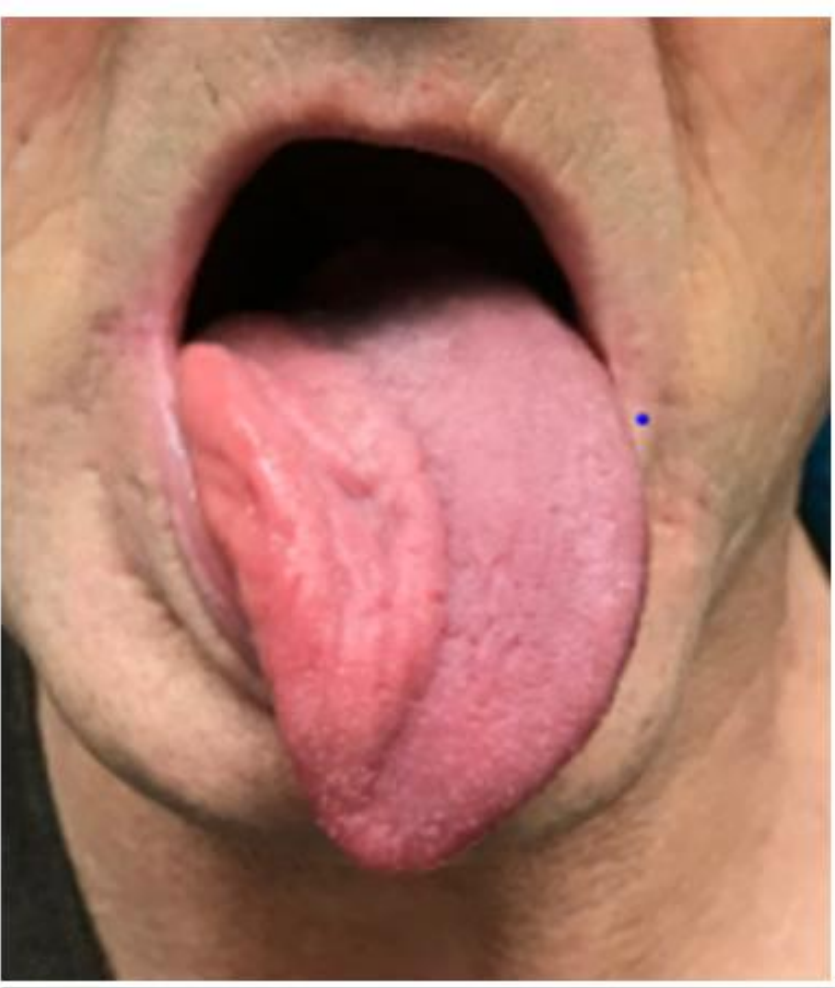


Fig. 1 Clinical Presentation of Lingual Protrusion

Clinical CNXII Palsy Classification	Atrophy	Deviation	Fasciculation
Not present	-	-	-
Suspected (Single criterion)	-/+	-/+	-/+
Present (2 or more criteria)	-/+	-/+	-/+

Table 2. Clinical cranial nerve (CN) XII examination classified as XII palsy not present, suspected, or present based on combinations of clinical features

Hypoglossal Palsy in patients with EMG	Clinically Suspected or Not Present	Clinically Present (≥2 criteria)
EMG (denervation = 0)	0/13	0/13
EMG (denervation ≥ 1)	5/13	8/13

Table 4. Clinical and EMG Presence of Hypoglossal Palsy (n=13)

CN XII palsy prevalence (n=13) **EMG: 100%**



Fig. 2 Intramuscular electromyography (EMG)

Denervation Potentials	
0	None
1	Persistent, single trains of potentials in at least 2 areas
2	Moderate number of potentials in 3 or more areas
3	Many potentials in all areas
4	Full interference pattern of potentials

Table 3. Electromyography denervation potentials grading scale

Results Continued

- Seventy percent of patients (21/30; 95% CI: 51%-85%) presented with clinical evidence (2 or more criteria) of hypoglossal denervation at baseline MANTLE evaluation
- Among the 13 who underwent EMG, all patients (13/13; 95% CI: 75%- 100%) had hypoglossal denervation potentials evident on electrophysiologic testing
- Only 8 of these 13 (62%; 95% CI: 32- 86%) demonstrated evidence of 2 or more criteria for hypoglossal denervation on clinical examination.

Conclusions & Relevance

- Lingual denervation was detected in all patients with late-RAD who underwent exploratory EMG testing, among whom almost 40 % had no clear clinical evidence of CN XII palsy. These hypothesis-generating findings suggest that subclinical denervation, specifically hypoglossal palsy, may be a contributor to functional deterioration in late-RAD, evident on EMG assessment prior to clinical presentation.
- Early detection and proactive interventions for subclinical lingual denervation may have the potential to change the trajectory of progressive functional loss common in late-RAD, with implications to related functional communication, swallowing, and quality of life.

References

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