Morning Meeting

Presenter：FMR3 陳冠翰
Supervisor：洪偉誠醫師

2025/08/13

Patient profile

- ID：
- Name：吳O雪
- Gender：Female
- Age：59-year-old
- Past history:

  Hypertension/ Diabetes mellitus/ Hyperlipidemia

  Breast cancer s/p OP + C/T, decades ago

Chief complaint

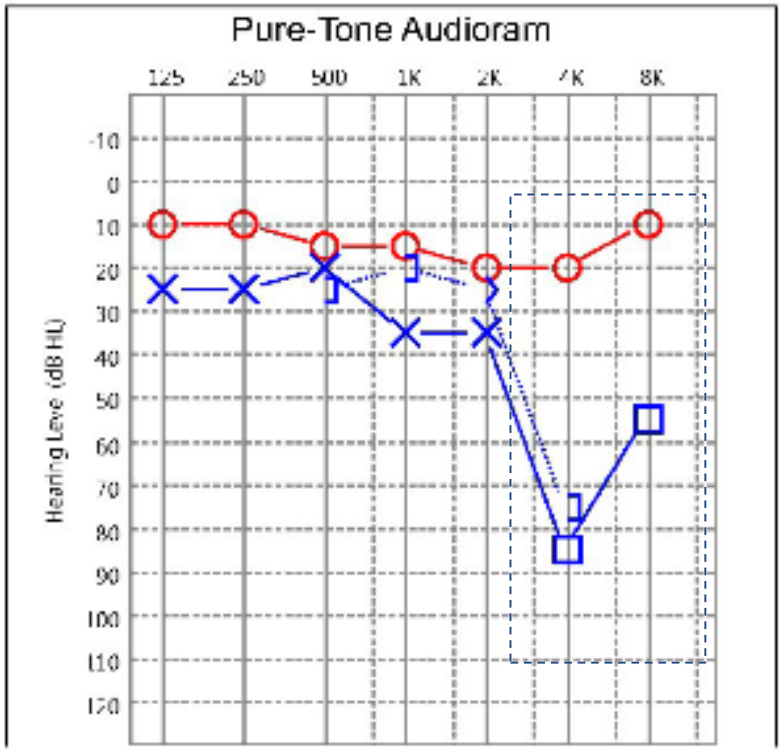
Progressive left hearing loss for more than one year.

Present Illness

2025
06/04

- Hearing loss, left for a year
- **Tinnitus(+, Left),** Aural fullness(-), vertigo(-)
  Noise exposure(-)
- Pure Tone Audiometry:

Pure-Tone Audioram

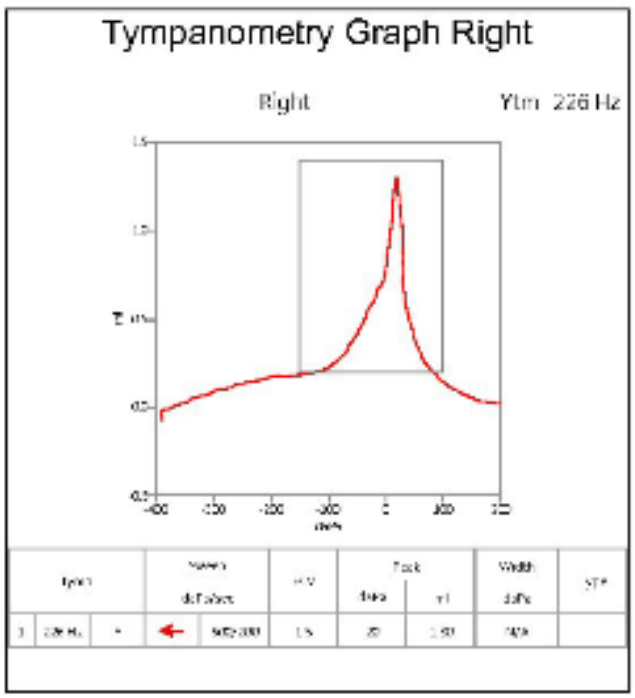


AC PTA 18 dB BC PTA SII 97 %

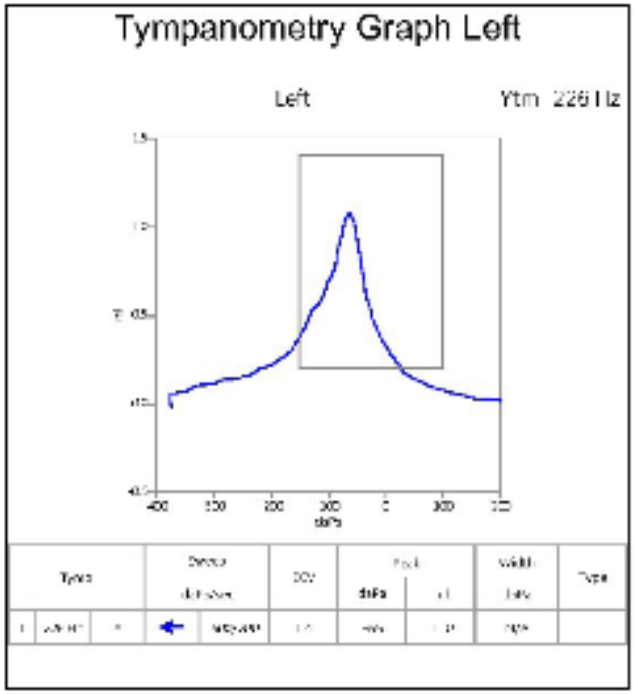
AC PTA 44 dB BC PTA 36 dB SII 50 %

Speech Test				
Ear	Test Type	Aided	%	dB HL
R	SRT			20
L	SRT			40

Tympanometry Graph Right



Tympanometry Graph Left



Present Illness

2025 06/04

- Hearing loss, left for a year
- **Tinnitus(+, Left),** Aural fullness(-), vertigo(-)
  Noise exposure(-)
- Pure Tone Audiometry:
  Left sensorineural hearing loss
  → Plan: arrange Auditory Brainstem Response

Present Illness

2025 06/04

- Hearing loss, left for a year
- **Tinnitus(+, Left),** Aural fullness(-), vertigo(-)
  Noise exposure(-)
- Pure Tone Audiometry:
  Left sensorineural hearing loss
  → Plan: arrange Auditory Brainstem Response

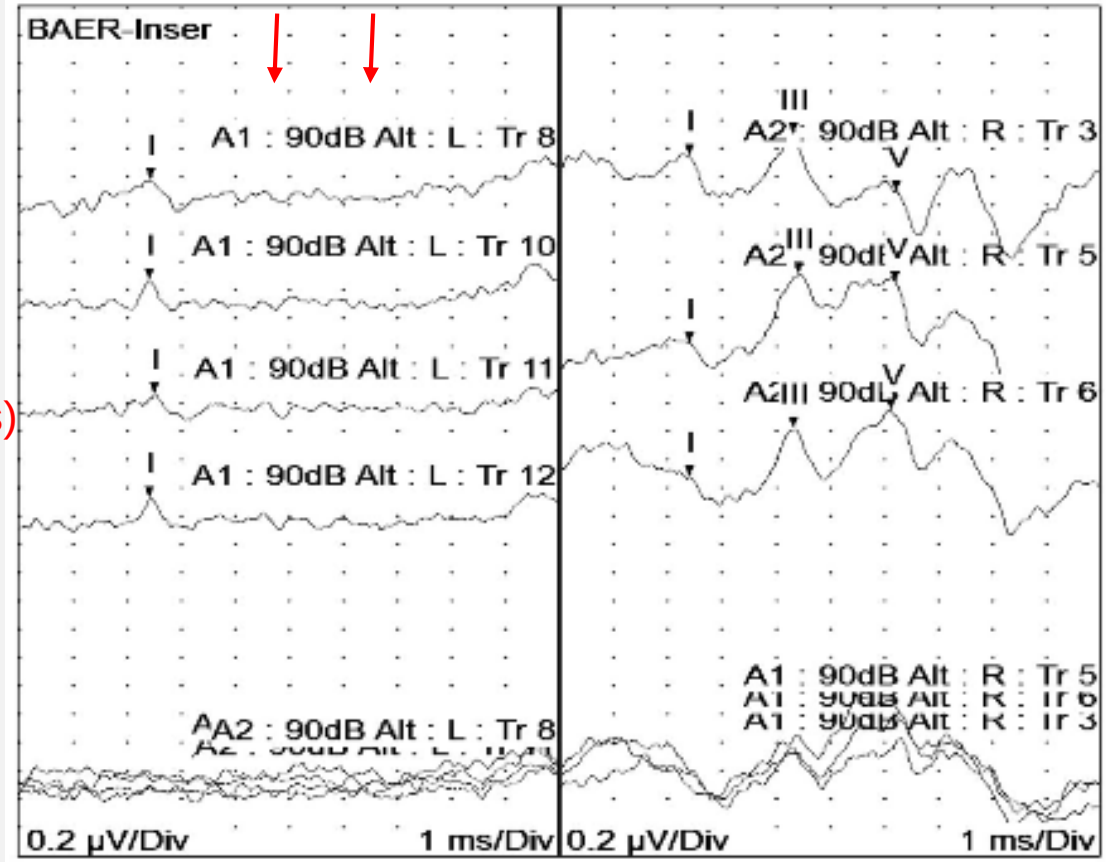
2025 06/11

- Auditory Brainstem Response(ABR)

Trace	I (ms)	III (ms)	V (ms)	I-V (ms)	I-III (ms)	III-V (ms)
*A2 : 90dB Alt : R : Tr 3	1.41	3.31	5.22	3.81	1.90	1.91
*A2 : 90dB Alt : R : Tr 5	1.42	3.42	5.20	3.78	2.00	1.78
*A2 : 90dB Alt : R : Tr 6	1.41	3.31	5.13	3.72	1.90	1.82
*A1 : 90dB Alt : L : Tr 8	1.44	8.98	8.98	7.54	7.54	0.00
*A1 : 90dB Alt : L : Tr 10	1.42	8.98	8.98	7.56	7.56	0.00
*A1 : 90dB Alt : L : Tr 11	1.52	8.98	8.98	7.46	7.46	0.00
*A1 : 90dB Alt : L : Tr 12	1.42	8.98	8.98	7.56	7.56	0.00

*Data was acquired using Inserts, 1.00 millisecond(s) has been subtracted from cursor values.

Left
Wave III/V(Loss)



Present Illness

2025 06/04

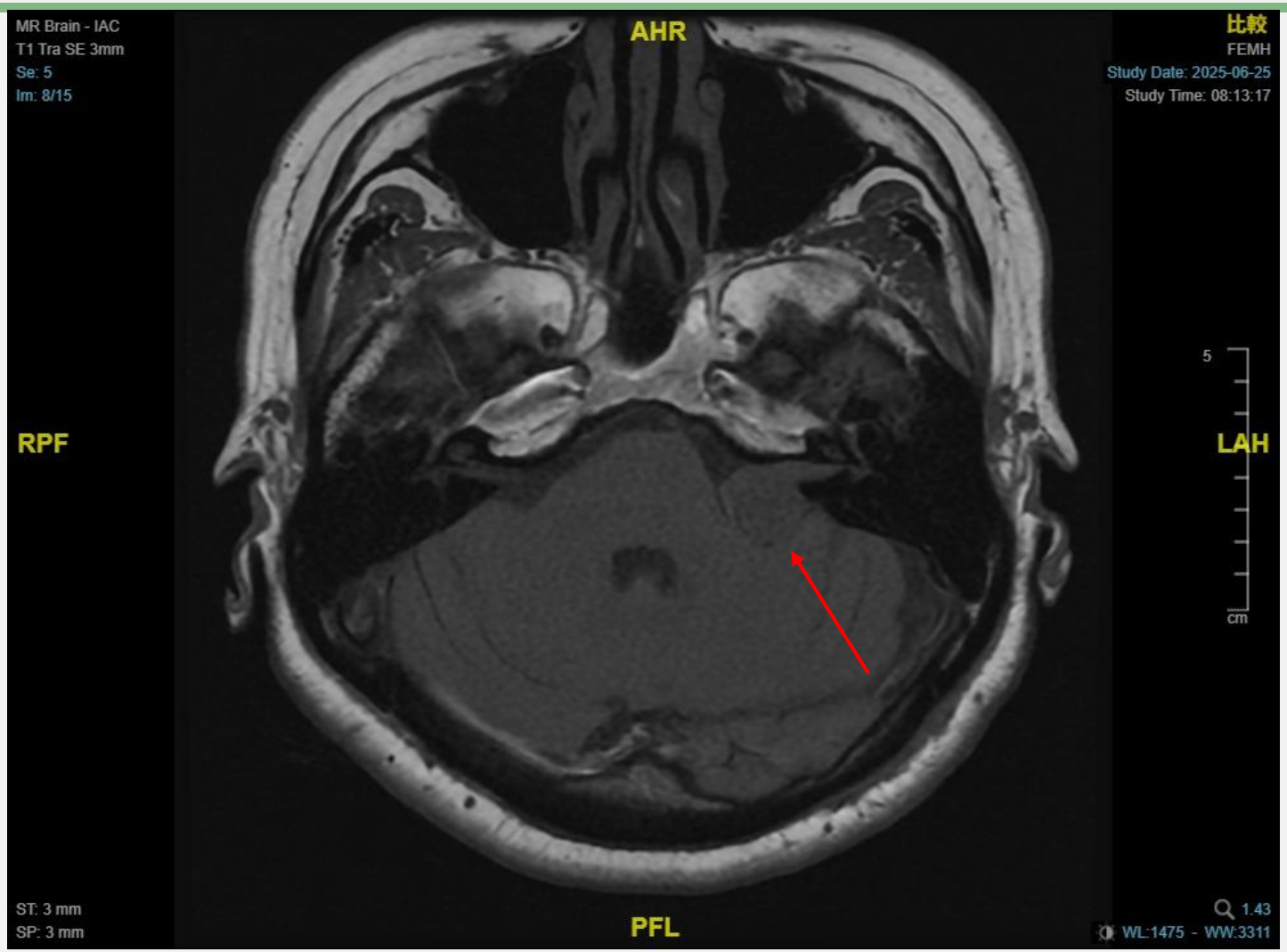
- Hearing loss, left for a year
- **Tinnitus(+, Left),** Aural fullness(-), vertigo(-)
  Noise exposure(-)
- Pure Tone Audiometry:
  Left sensorineural hearing loss
  → Plan: arrange Auditory Brainstem Response

2025 06/11

- Auditory Brainstem Response(ABR)
  Loss of Wave III & V
  Suspect lesion in central auditory pathway,
  beyond the cochlea
  (Retrocochlear lesions, Brainstem pathology)

  Plan: arrange IAC MRI

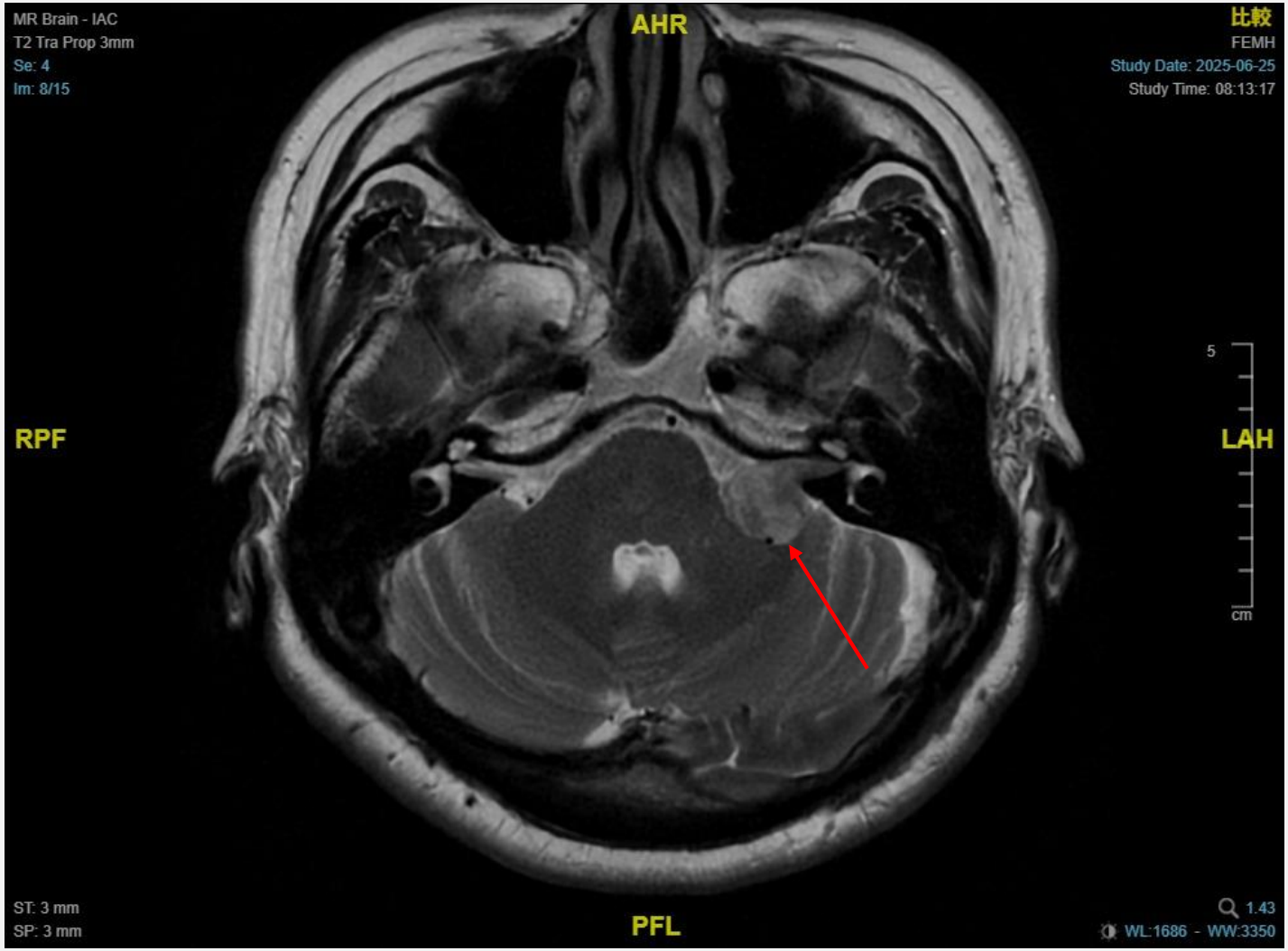
IAC MRI(2025/06/25)



Ice-cream-on-cone shape

T1: Iso-Intenseisointenseisointense

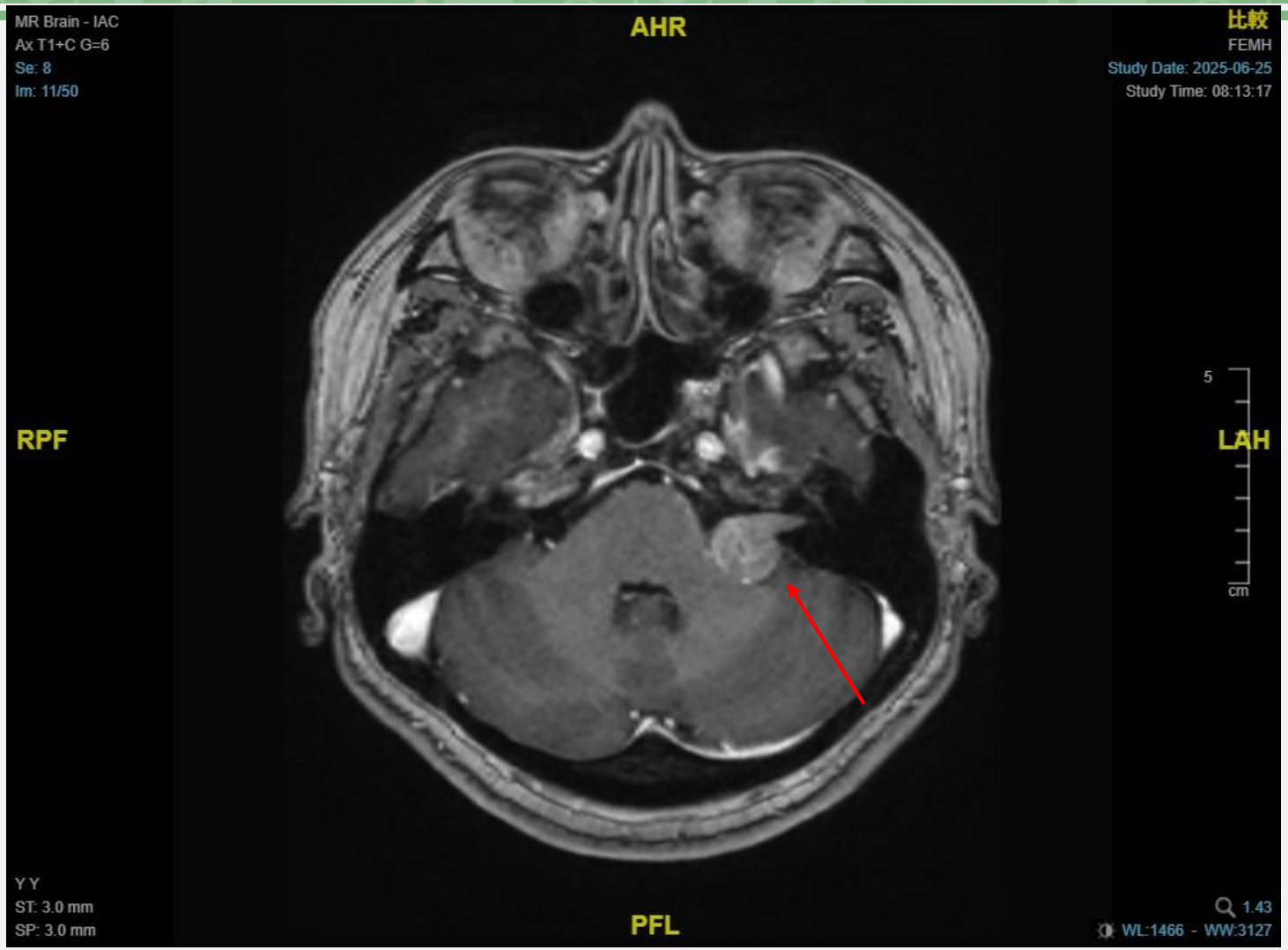
IAC MRI(2025/06/25)



Ice-cream-on-cone shape

T2: High-Intensesointenseisointense

IAC MRI(2025/06/25)



Ice-cream-on-cone shape, Size: 2.09x1.55 cm
T1 with contrast: Heterogenous enhancement

Present Illness

2025 07/09

- IAC MRI(6/25):
  An ice-cream-on-cone shape mass located in left cerebellopontine angle. (2.09x1.55 cm)
  Favors Vestibular schwannoma

- Plan: refer to Radiation oncologist

Present Illness

2025 07/09

- IAC MRI(6/25):
  An ice-cream-on-cone shape mass located in left cerebellopontine angle. (2.09x1.55 cm)
  Favors Vestibular schwannoma

- Plan: refer to Radiation oncologist

2025 07/10

- Radiation oncologist:
  Stereotactic Radiosurgery(SRS)
  - 1200 cGy in one daily fraction

Final diagnosis

- **Left vestibular schwannoma, 2.09x1.55 cm**

Plan:

Scheduling Stereotactic Radiosurgery(SRS)

Discussion
Vestibular schwannoma

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EUROPEAN ASSOCIATION OF NEURO-ONCOLOGY

Introduction

- **Epidemiology**
  - Incidence: 3~5/100000 persons-years

  - Median age of diagnosis: 50 years old
  - **Unilateral**: 90% (Right = Left)
    Bilateral: **NF2 gene** – NF2-related schwannomatosis (NF2)
  - Male = Female

Introduction

- **Histopathology**
  - Vestibular schwannomas arise from perineural elements of the Schwann cell
  - Superior = Inferior branches of the vestibular nerve >> Cochlear nerve(Rare)
  - Malignant degeneration is extremely rare

Introduction

- **Clinical presentation**
  - **Cochlear nerve**:
    Symptomatic cochlear nerve involvement occurred in 95 percent of patients
    Hearing loss(95%), **Tinnitus**(63%)
  - **Vestibular nerve:** 61%
    Unsteadiness, Vertigo
  - Trigeminal nerve/ Facial nerve: rare
  - Mass effect to posterior fossa structures:
    Ataxia, dysarthria, dysphagia, aspiration, and hoarseness
    Death

Introduction

- **Diagnosis**
  - Physical examination:
    Hearing tests, Neurologic examination of other cranial nerve
  - Audiometry, PTA:
    Asymmetric sensorineural hearing loss
    More prominent in the higher frequencies
  - Auditory brainstem response, **ABR**:
    → Most accurate screening modality prior to MRI
    → Abnormalities in 90~95% of patients with tumors >1 cm.
  - Imaging:
    Contrast-enhanced MRI >>High-resolution CT

Cerebellopontine angle masses(MRI)

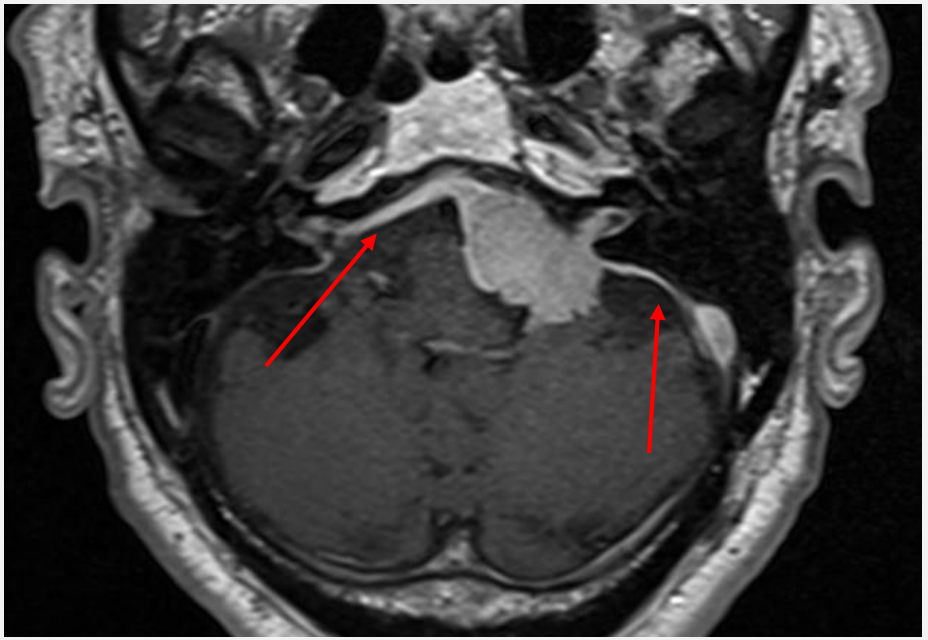
- **Enhancing mass**
  - **Vestibular schwannoma: most common(~80%)**
  - **Meningioma: 2nd most common (~10%) >> others**
- **High T1 signal mass**
  - Hemorrhagic vestibular schwannoma
  - Cerebellopontine angle lipoma
  - Neurenteric cyst
- **CSF density mass**
  - **Epidermoid cyst: 3rd most common (~5%)**
  - Arachnoid cyst
- **Other masses**

Cerebellopontine angle masses(MRI)

- **Enhancing mass**
  - **Vestibular schwannoma: most common(~80%)**
    - Typically centered on the IAC, more rounded
    - **"Trumpeted Internal Auditory Canal" Sign**
    - Microhemorrhages
  - **Meningioma: second most common (~10%)**
    - Broad-based, arising from the dura
    - Often with a "**Dural tail**" sign
    - Calcification

Cerebellopontine angle masses(MRI)

Vestibular schwannoma
Rounded
Trumpeted Internal Auditory Canal Sign



Cerebellopontine angle meningioma
Broad-based
Dural tail sign

Introduction

- **Management**
  - **Watchful waiting**
    Observation are to monitor tumor growth and hearing function
  - **Radiation therapy**
    Stereotactic radiosurgery (SRS)
    ->Multiple convergent beams, High single dose of radiation
    Stereotactic radiotherapy (SRT)
    ->Multiple convergent beams, series of treatment sections
  - **Surgery**
    Total or near-total resection

Koos grade

The Koos grading system[69]

Koos Grade		Tumor Description
I		Small intracanalicular tumor
II	<2 cm	Small tumor with protrusion into the cerebellopontine angle; no contact with the brainstem
III	<3 cm	Tumor occupying the cerebellopontine cistern with no brainstem displacement
IV	>3 cm	Large tumor with brainstem and cranial nerve displacement

Introduction

- **Management**
  - **Small tumors (Koos grade I and II), asymptomatic**
    Observation with series of MRI

    Evidence class III, recommendation level C
  - **Small tumors (Koos grade I and II)**
    Partial hearing loss or vestibular symptoms
    Shared decision-making
    Treatment timing: no consensus
    Treatment modality: SRS/SRT >> Surgery
  - **Small tumors (Koos grade I and II), Complete hearing loss**
    Shared decision-making
    Goal: Preservation of nearby cranial nerve function
    Treatment modality: SRS/SRT >> Surgery

Introduction

- **Management**
  - **Koos grade III tumors**
    Shared decision-making
    Surgery or SRS/SRT
    (Tumor size, cranial nerve function, patient age and comorbidities, fitness for surgery, and patient preferences)

  - **Koos grade IV tumors**
    Goal: Decompression of the brainstem and cranial nerves
    Surgery
    - Complete resection or
    - Near-total resection followed by SRS/SRT

Evidence class III, recommendation level B

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JAMA | Original Investigation

Upfront Radiosurgery vs a Wait-and-Scan Approach for Small- or Medium-Sized Vestibular Schwannoma
The V-REX Randomized Clinical Trial

Dhanushan Dhayalan, MD; Øystein Vesterli Tveiten, MD, PhD; Monica Finnkirk, RN; Anette Storstein, MD, PhD; Karl Ove Hufthammer, MSc, PhD; Frederik Kragerud Goplen, MD, PhD; Morten Lund-Johansen, MD, PhD; for the V-REX Trial investigators

JAMA. 2023;330(5):421-431. doi:10.1001/jama.2023.12222

V-REX trial

JAMA

- **Introduction**
  - For treating small- to medium-sized vestibular schwannoma **Upfront radiosurgery** or **Waiting to treat** until tumor growth
  - **Objective**
    To determine whether upfront radiosurgery provides **superior tumor volume reduction** to a wait-and-scan approach for small- to medium-sized vestibular schwannoma

JAMA. 2023;330(5):421-431. doi:10.1001/jama.2023.12222

V-REX trial

JAMA

- **Methods**
  - Investigator-initiated, randomized, investigator-blinded, Randomized Clinical Trial(1:1)
  - Norwegian National Unit for Vestibular Schwannoma, Haukeland University Hospital
  - Time: 2014/10/28~2017/10/03 (Follow~2021/10/20)

JAMA. 2023;330(5):421-431. doi:10.1001/jama.2023.12222

V-REX trial

JAMA

- **Methods**
  - Patients:
    - **18-70 years old**
    - **Newly diagnosed (<6 months)**
    - **Unilateral vestibular schwannoma**
    - **Maximal tumor diameter of less than 2 cm**
    (Measured on Magnetic Resonance Imaging)
  - Exclusion criteria
    - **Severe comorbidity**
    - **Type 2 neurofibromatosis(Patient, 1st degree relative)**

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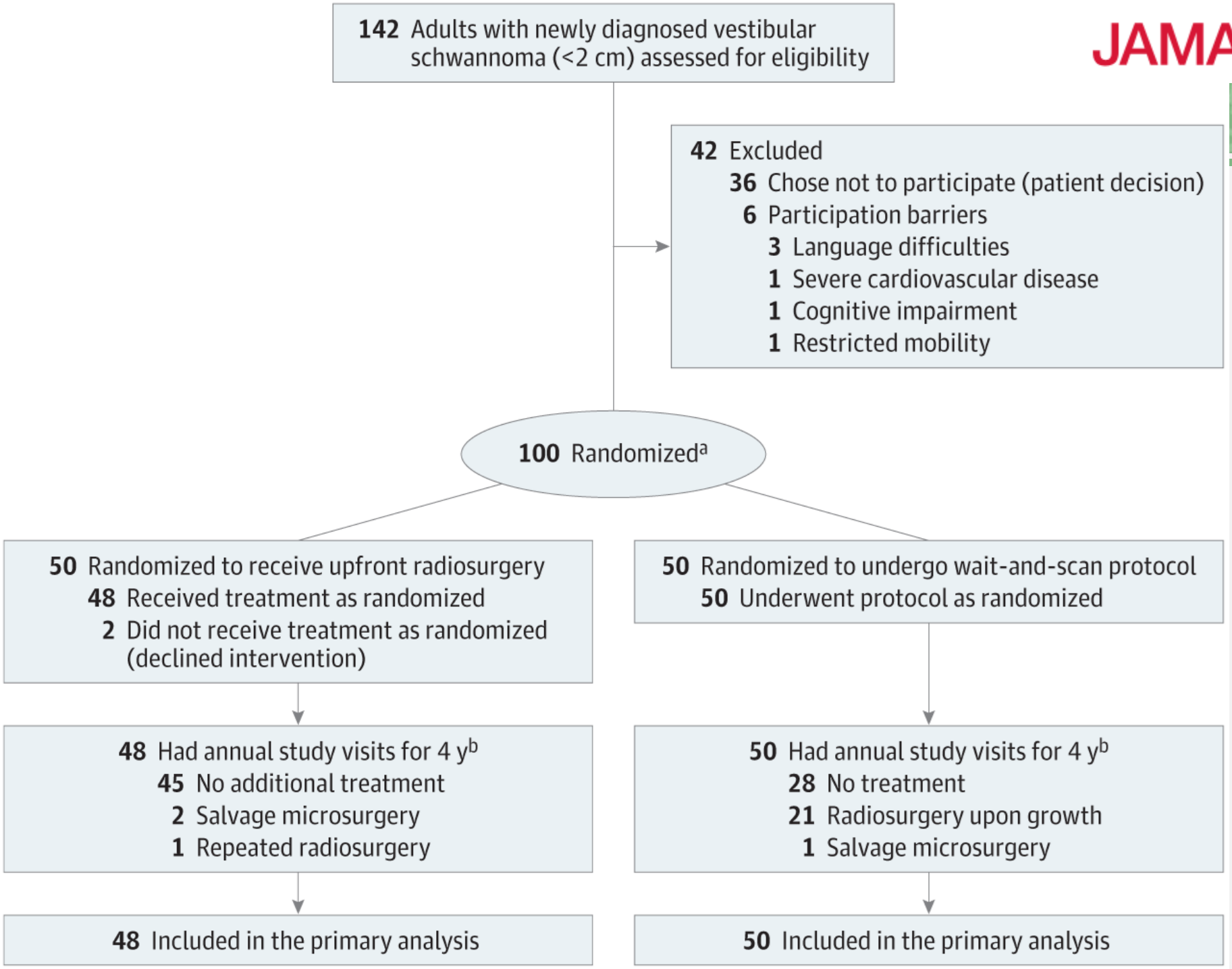
142 Adults with newly diagnosed vestibular schwannoma (<2 cm) assessed for eligibility
42 Excluded
36 Chose not to participate (patient decision)
6 Participation barriers
3 Language difficulties
1 Severe cardiovascular disease
1 Cognitive impairment
1 Restricted mobility
100 Randomized[a]
50 Randomized to receive upfront radiosurgery
48 Received treatment as randomized
2 Did not receive treatment as randomized (declined intervention)
50 Randomized to undergo wait-and-scan protocol
50 Underwent protocol as randomized
48 Had annual study visits for 4 y[b]
45 No additional treatment
2 Salvage microsurgery
1 Repeated radiosurgery
50 Had annual study visits for 4 y[b]
28 No treatment
21 Radiosurgery upon growth
1 Salvage microsurgery
48 Included in the primary analysis
50 Included in the primary analysis

V-REX trial

JAMA

- **Intervention**
  - Radiosurgery:
    - **12 Gy to the tumor margin**
    - **Limit the falloff dose to the brainstem and the modiolus of the cochlea**

    - **MRI: Baseline & every year**
  - Outcomes:
    Primary: ratio between tumor volume at the trial end at 4 years and baseline (V4:V0)

    Secondary:
    Symptoms / Cranial nerve examinations/ Hearing outcomes
    Video nystagmography/ 8 PANQOL score

JAMA. 2023;330(5):421-431. doi:10.1001/jama.2023.12222

Table 1. Baseline Characteristics of Patients in the V-REX Trial[a]

Characteristic	Upfront radiosurgery (n = 48)	Wait and scan (n = 50)
Age, mean (SD), y	54 (12)	54 (10)
Sex, No. (%)		
Female	22 (46)	19 (38)
Male	26 (54)	31 (62)
Radiological characteristics, No. (%)		
Left-sided tumor	19 (40)	19 (38)
Intracanalicular tumor	18 (38)	16 (32)
Tumor volume		
Mean (SD), mm^3	765 (799)	514 (588)
Median (IQR), mm^3	362 (206-942)	328 (190-566)
Patient-reported symptoms, No. (%)[b]		
Hearing loss	45 (94)	42 (84)
Tinnitus	36 (75)	43 (86)
Dizziness	27 (56)	26 (52)
Balance problems	27 (56)	19 (38)
Fatigue	29 (60)	24 (48)
Headache	21 (44)	25 (50)
Facial pain	3 (6)	5 (10)
Changes in taste	4 (8)	2 (4)

Clinical findings		
Asymmetric facial sensation, No. (%)	6 (13)	3 (6)
Absent corneal reflex, No./total (%)	1/44 (2)	1/48 (2)
House-Brackmann Score, No. (%)[c]		
I	48 (100)	49 (98)
II	0	1 (2)
III-VI	0	0
Audiometry		
Pure-tone average, mean (SD), dB[d]	45 (24)	38 (20)
Word recognition score, mean (SD), %[e]	72 (39)	84 (27)
AAO-HNS classification, No./total (%)[f]		
A	32/47 (68)	39/48 (81)
B	2/47 (4)	2/48 (4)
C	2/47 (4)	1/48 (2)
D	11/47 (23)	6/48 (12)
Dynamic posturography[g]		
Composite equilibrium score, mean (SD)	65 (14)	68 (16)
Unsteady on posturography[h]	26 (54)	22 (44)
Video nystagmography[i]		
Caloric asymmetry, mean (SD), %	50 (35)	41 (29)
Canal paresis on tumor side	23 (49)	26 (54)

PANQOL, mean (SD)[j]		
Total score	71 (18)	73 (17)
Anxiety	74 (23)	78 (24)
Facial dysfunction	89 (14)	88 (18)
General health	65 (20)	65 (19)
Balance	75 (26)	75 (28)
Hearing loss	58 (23)	59 (26)
Energy	66 (24)	68 (23)
Pain	67 (35)	73 (31)

V-REX trial

- **Results**
  - Primary outcome

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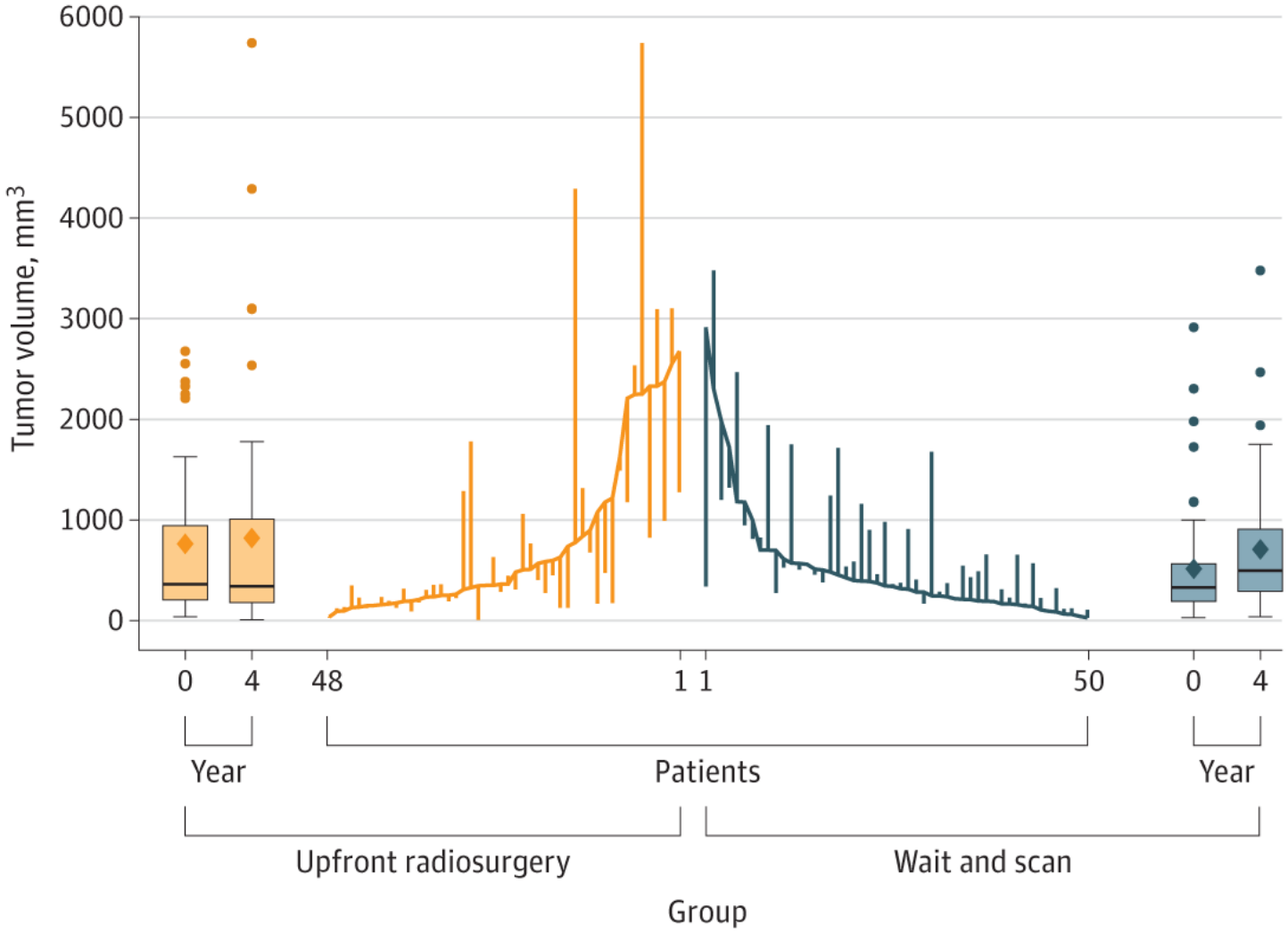

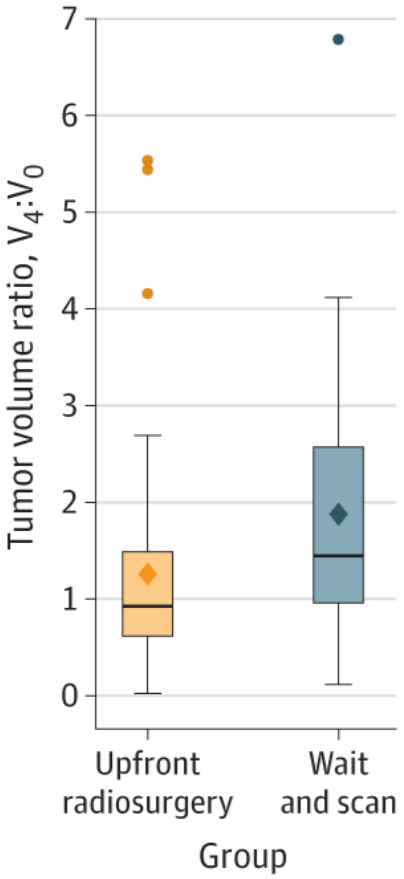

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V-REX trial

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- **Results**
  - Primary outcome
    The ratio of tumor volume at 4 years relative to baseline (V4:V0)(Geometric means)

    Upfront radiosurgery : Wait-and-scan = 0.87 : 1.51

    The wait-and-scan approach to upfront radiosurgery ratio of geometric means **was 1.73 (95% CI, 1.23-2.44; P = .002)**

  - Secondary Outcomes:

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Difference OR

Secondary outcome[d]				
Patient-reported symptoms, %[e]				
Hearing loss	45 (94)	43 (86)	8 (−5 to 21)	2.44 (0.60 to 9.05)
Tinnitus	40 (83)	40 (80)	3 (−12 to 19)	1.25 (0.48 to 3.62)
Dizziness	21 (44)	22 (44)	0 (−19 to 19)	0.99 (0.45 to 2.28)
Balance problems	29 (60)	21 (42)	18 (−1 to 36)	2.11 (0.92 to 4.63)
Fatigue	31 (65)	24 (48)	17 (−3 to 34)	1.98 (0.86 to 4.39)
Headache	15 (31)	8 (16)	15 (−2 o 31)	2.39 (0.94 to 6.38)
Facial pain	2 (4)	5 (10)	−6 (−18 to 5)	0.39 (0.08 to 2.01)
Changes in taste	11 (23)	5 (10)	13 (−2 to 28)	2.68 (0.90 to 7.36)
Clinical examinations				
Absent corneal reflex	5 (10)	6/49 (12)	−2 (−15 to 12)	0.83 (0.26 to 3.19)
Asymmetric facial sensation	6 (12)	0/49 (0)	12 (3 to 25)	Not calculable
House-Brackman Score progression[f]	8/47 (17)	6/48 (12)	5 (−10 to 19)	1.44 (0.48 to 4.74)
Audiometry[g]				
Pure-tone average, mean (SD), dB	60 (24)	61 (27)	−2 (−8 to 5)	
Word recognition score, mean (SD), %	42 (38)	47 (40)	−6 (−19 to 7)	
Serviceable hearing	16 (33)	20 (40)	−7 (−25 to 12)	0.75 (0.33 to 1.65)

PANQOL, mean (SD)[j]				
No.	47	48		
Total score	68 (18)	71 (17)	−2 (−7 to 3)	
Anxiety	80 (21)	78 (22)	1 (−6 to 9)	
Facial dysfunction	81 (21)	85 (17)	−4 (−12 to 3)	
General health	59 (22)	58 (24)	1 (−7 to 8)	
Balance	71 (25)	75 (22)	−3 (−10 to 3)	
Hearing loss	57 (24)	56 (23)	1 (−6 to 8)	
Energy	61 (24)	68 (21)	−7 (−14 to 0)	
Pain	69 (35)	75 (31)	−7 (−18 to 4)	
Dynamic posturography[h]				
Composite equilibrium score, mean (SD)	68 (19) (n = 43)	72 (15) (n = 42)	−4 (−10 to 2)	
Unsteady on posturography, No./total (%)	15/43 (35)	11/42 (26)	9 (−11 to 27)	1.51 (0.62 to 3.95)
Video nystagmography[i]				
No.	44	43		
Caloric asymmetry, mean (SD), %	48 (35)	48 (30)	0 (−12 to 12)	
Canal paresis on tumor side, No./total (%)	28/44 (64)	33/43 (77)	−13 (−31 to 6)	0.53 (0.22 to 1.28)

V-REX trial

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- **Results**
  - Primary outcome
    The ratio of tumor volume at 4 years relative to baseline (V4:V0)(Geometric means)

    Upfront radiosurgery : Wait-and-scan = 0.87 : 1.51

    The wait-and-scan approach to upfront radiosurgery ratio of geometric means **was 1.73 (95% CI, 1.23-2.44; P = .002)**

  - Secondary Outcomes
    Reduced facial sensation on clinical examination:
    Upfront radiosurgery : Wait-and-scan = 6: 0 (Baseline - 6: 3)

    Others: no significant difference

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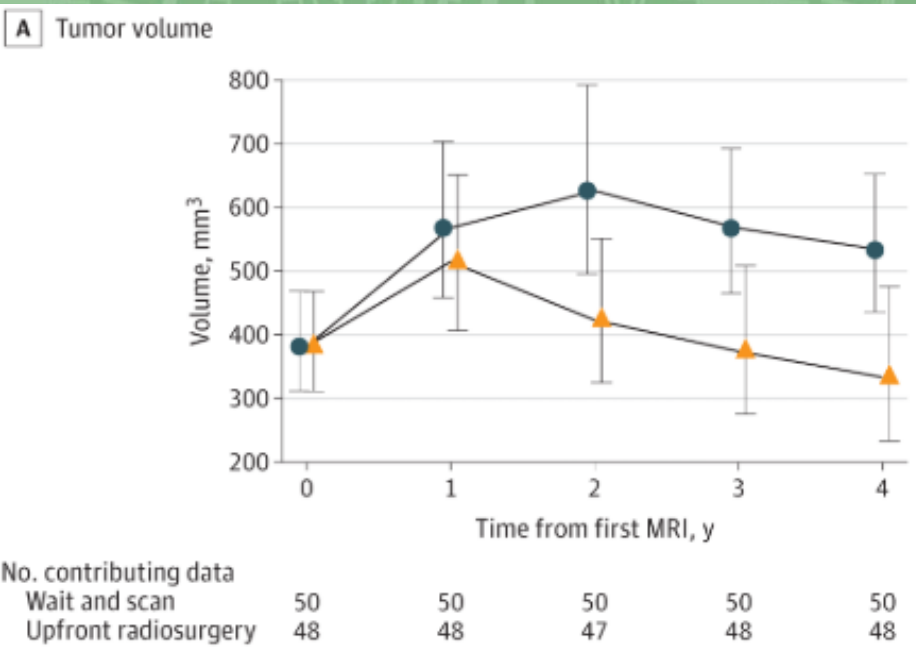
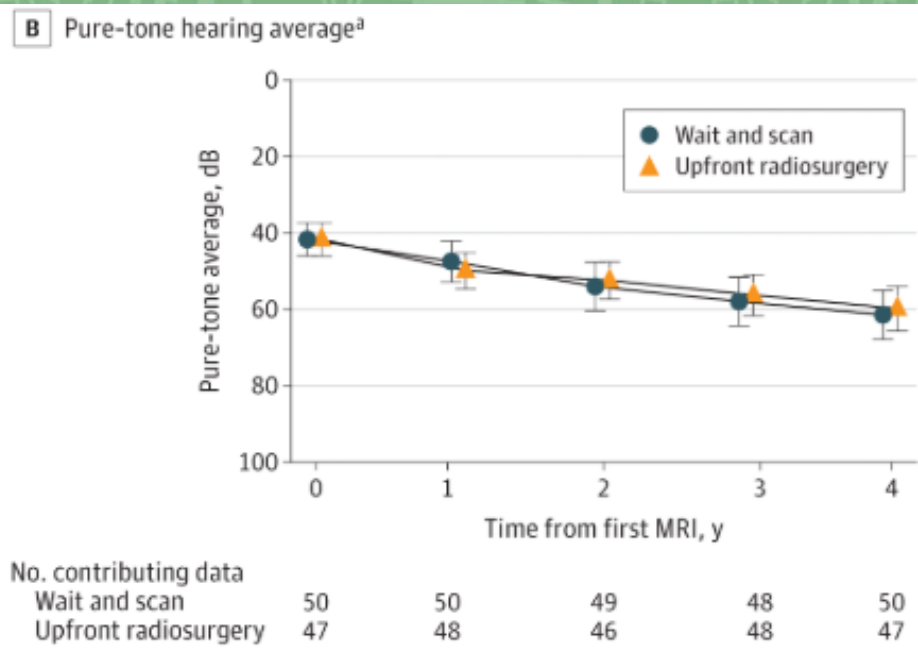
V-REX trial





- **Mean pure-tone average**
  - ➢ Declined in both groups during the study period
  - ➢ Upfront radiosurgery @ Year 4: 60 dB
  - ➢ Wait-and-scan @ Year 4: 61 dB

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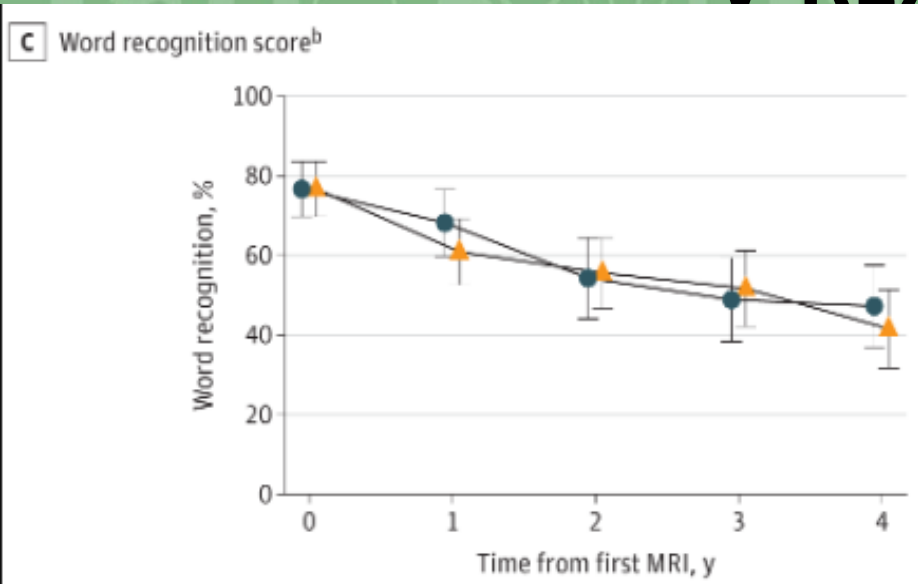
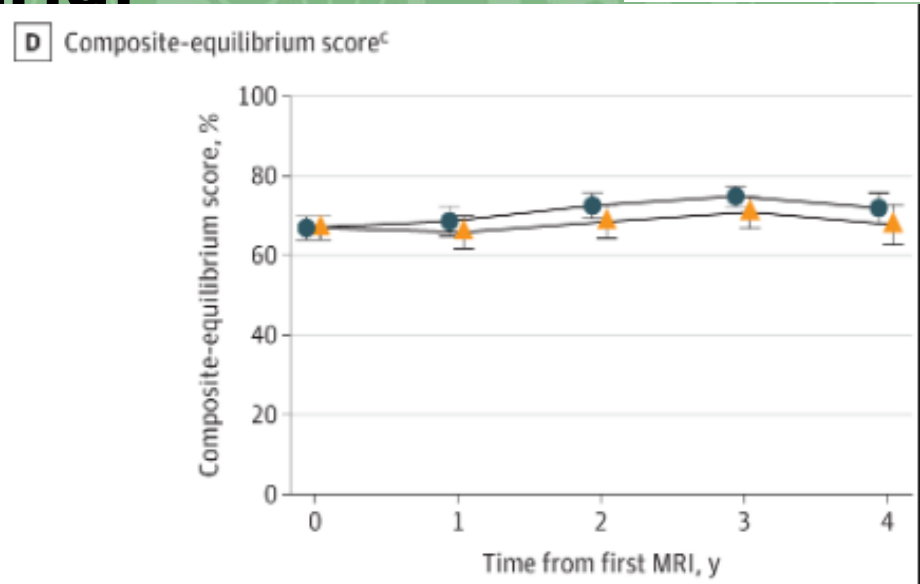
V-REX trial





- **Mean word recognition score**
  - ➢ Declined in both groups during the study period
  - ➢ Upfront radiosurgery @ Year 4: 42 %
  - ➢ Wait-and-scan @ Year 4: 47 %

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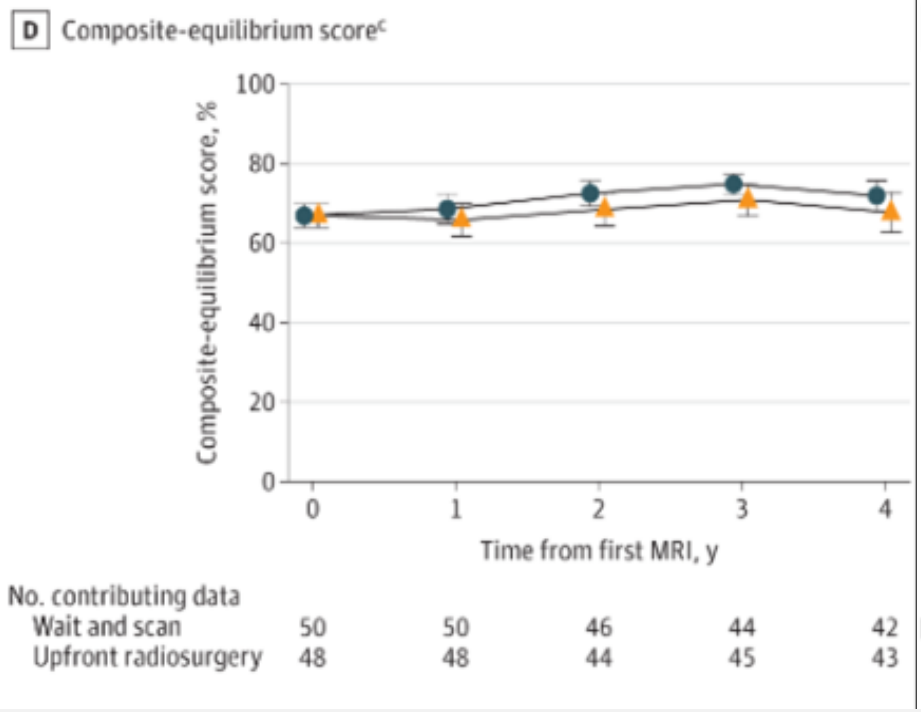
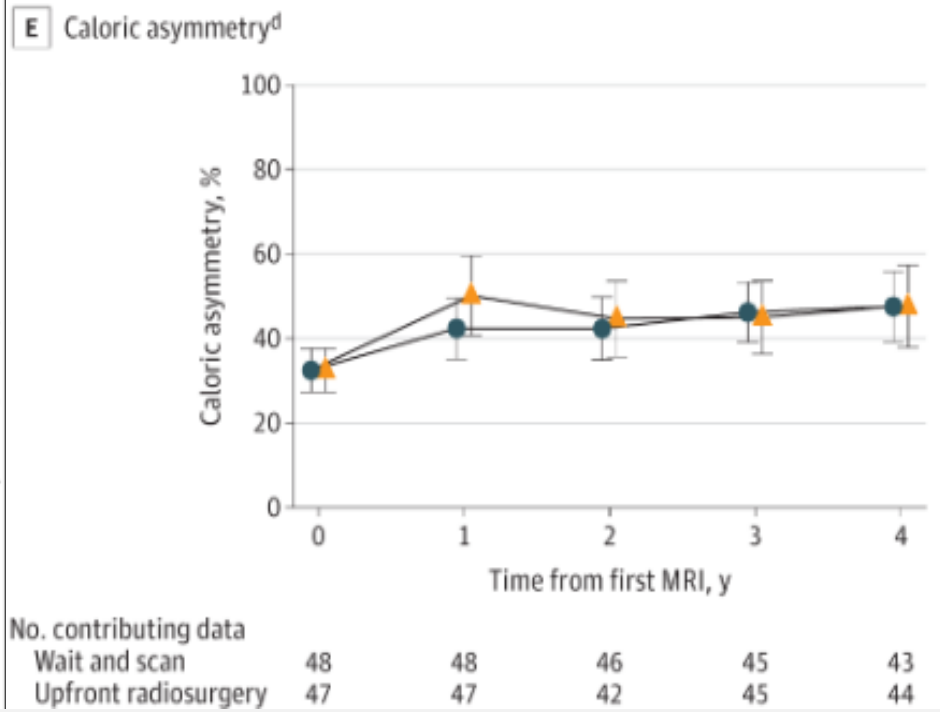
V-REX trial

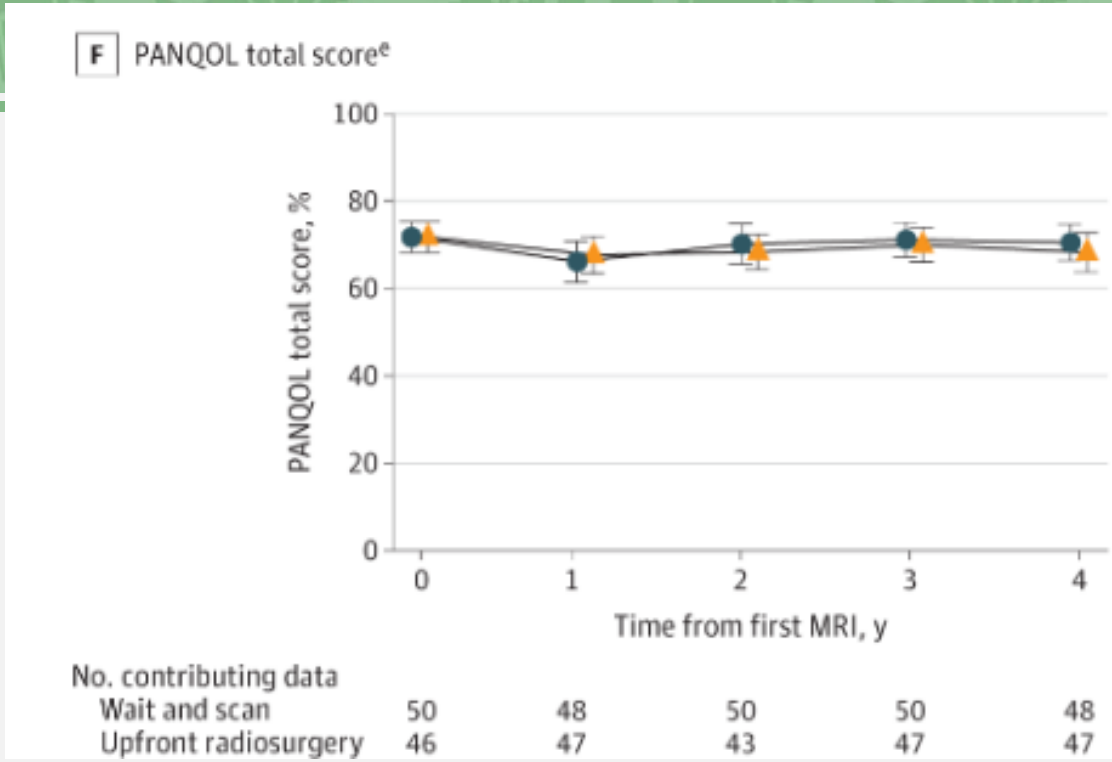




- **Vestibular function**
  - ➢ Composite-equilibrium score: increase
  - ➢ Caloric asymmetry: increase

JAMA. 2023;330(5):421-431. doi:10.1001/jama.2023.12222

V-REX trial



- **PANQOL total score**
  - ➢ Neither of the groups demonstrated significant change
  - ➢ Upfront radiosurgery @ Year 4: 68 point
  - ➢ Wait-and-scan @ Year 4: 71 point

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V-REX trial

JAMA

- **Results**
  - ➢ Safety Outcomes
    No deaths or radiation-associated complications
    - Hydrocephalus
    - Brainstem necrosis
    - Radiation-induced tumors
    - Malignant transformation

  - ➢ The risk of salvage microsurgery : Low
    - Upfront radiosurgery: Wait-and-scan group = 4% : 2%

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V-REX trial

JAMA

- **Discussion**
  - **No randomized clinical trials** have compared the efficacy of upfront radiosurgery with a wait-and-scan approach
    - Two prospective nonrandomized, non-blinded studies:
    Upfront radiosurgery → smaller tumor size
  - In this randomized clinical trial
    Initial treatment approach of Upfront radiosurgery resulted in significantly greater tumor volume reduction at 4 years than the initial wait-and-scan approach
  - Both groups demonstrated similar progressive, unilateral hearing loss.

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V-REX trial

JAMA

- **Discussion**
  - The results of this trial reinforce radiosurgery as an effective treatment modality regarding tumor growth
  - ←→However, in recent decades, vestibular schwannoma management has evolved to prioritize functional outcomes over a radiographic cure
  - **Cranial nerve function, particular hearing**
    Two systematic reviews:
    60% hearing preservation during the first 2 to 5 years following radiosurgery among patients with serviceable hearing = Patients treated with observation alone.

Systematic review of hearing preservation after radiotherapy for vestibular schwannoma. Otol Neurotol. 2018;39(3):273-283
Hearing preservation after stereotactic radiosurgery for vestibular schwannoma: a systematic review. J Clin Neurosci. 2009;16(6):742-747.

V-REX trial

JAMA

- **Discussion**
  - Widespread access to brain MRI
    -->Increased detection of small vestibular schwannomas associated with mild symptoms
    -->Raising concerns about potential overtreatment.

  - In this trial, **56%** of the patients in the **wait-and-scan** group remained untreated after 4 years because there was no evidence of tumor growth
    -->These finding **support** an initial wait-and-scan approach from a health economic perspective

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V-REX trial

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- **Limitation**
  - Tumor volume was selected as the primary outcome
    → Not a reliable surrogate for clinically impactful treatment
  - Included patients whose tumors had a maximum cerebellopontine angle diameter of 2 cm
    → Findings may not be valid for larger tumors
  - Yearly follow-up visits
    → May have overlooked acute transient adverse events
  - **10-year follow-up of the trial is planned in the 2024-2027**
    → No conclusions can be drawn about outcomes beyond the 4-year trial period at this time

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V-REX trial

JAMA

- **Conclusion**
  - Among patients with newly diagnosed small- and medium-sized vestibular schwannoma, upfront radiosurgery demonstrated a significantly **greater tumor volume reduction** at 4 years compared with a wait-and-scan approach
  - Further investigation of long-term clinical outcomes is needed

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Back to our patient

- A 59-year-old woman present with left hearing loss
- PTA: Left SNHR, ABR: Loss of Wave III & V
  →Suspect lesion beyond the cochlea
- MRI:
  An ice-cream-on-cone shape mass located in left cerebellopontine angle. (2.09x1.55 cm)
- Left Vestibular schwannoma, KOOs grade III
- Plan: Stereotactic Radiosurgery(SRS)
  → Tumor volume(V) ; Hearing function(?)

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Reference

- https://jamanetwork.com/journals/jama/fullarticle/2807745#google_vignette
- https://academic.oup.com/neuro-oncology/article/22/1/31/5555902
- https://www.uptodate.com/contents/vestibular-schwannoma-acoustic-neuroma

Thanks for attention