

FREEDOM

Stereotactic radiosurgery for refractory cancer pain

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Ausaf A. Bari MD PhD FAANS

Associate Professor and Vice Chair

Director, Functional Neurosurgery Program

UCLA Department of Neurosurgery

Disclosures

NIH UH3 NS113661

Deep Brain Stimulation of the Subgenual Cingulate Cortex for the Treatment of Medically Refractory Chronic Low Back Pain

Principle Investigator

NIH 1UG1EY032039

Visuomotor Prosthetic for Paralysis

Co-PI

NIH UH3 NS107673

Responsive Neurostimulation for Post-traumatic Stress Disorder

Co-Investigator

NIH #1K01DA060327 (JR)

Speaker and Consultant for Medtronic

Speaker and Consultant for RebrAln

Advisory Board: Nervonik

Speaker: BrainLab

Speaker and Advisory Board: Insightec

Fellowship Funding: Boston Scientific, Medtronic, Abbott

FREEDOM study funding: BrainLab



Burden of Cancer Pain

66.4%

Pain in advanced, metastatic
or terminal cancer

**Different pain mechanisms often
coexist**

Somatic

Bone and soft-tissue involvement

Visceral

Thoracic, abdominal or pelvic disease

Neuropathic

Nerve or plexus involvement

van den Beuken-van Everdingen et al. J Pain Symptom Manage. 2016;51:1070–1090.e9. Lovo et al. Cureus. 2022;e25430



Refractory Cancer Pain

Up to 30%

of terminally ill cancer patients
with intense pain may be
refractory to opioid treatment

Limits of opioid escalation

Gastrointestinal symptoms, sedation
and respiratory depression

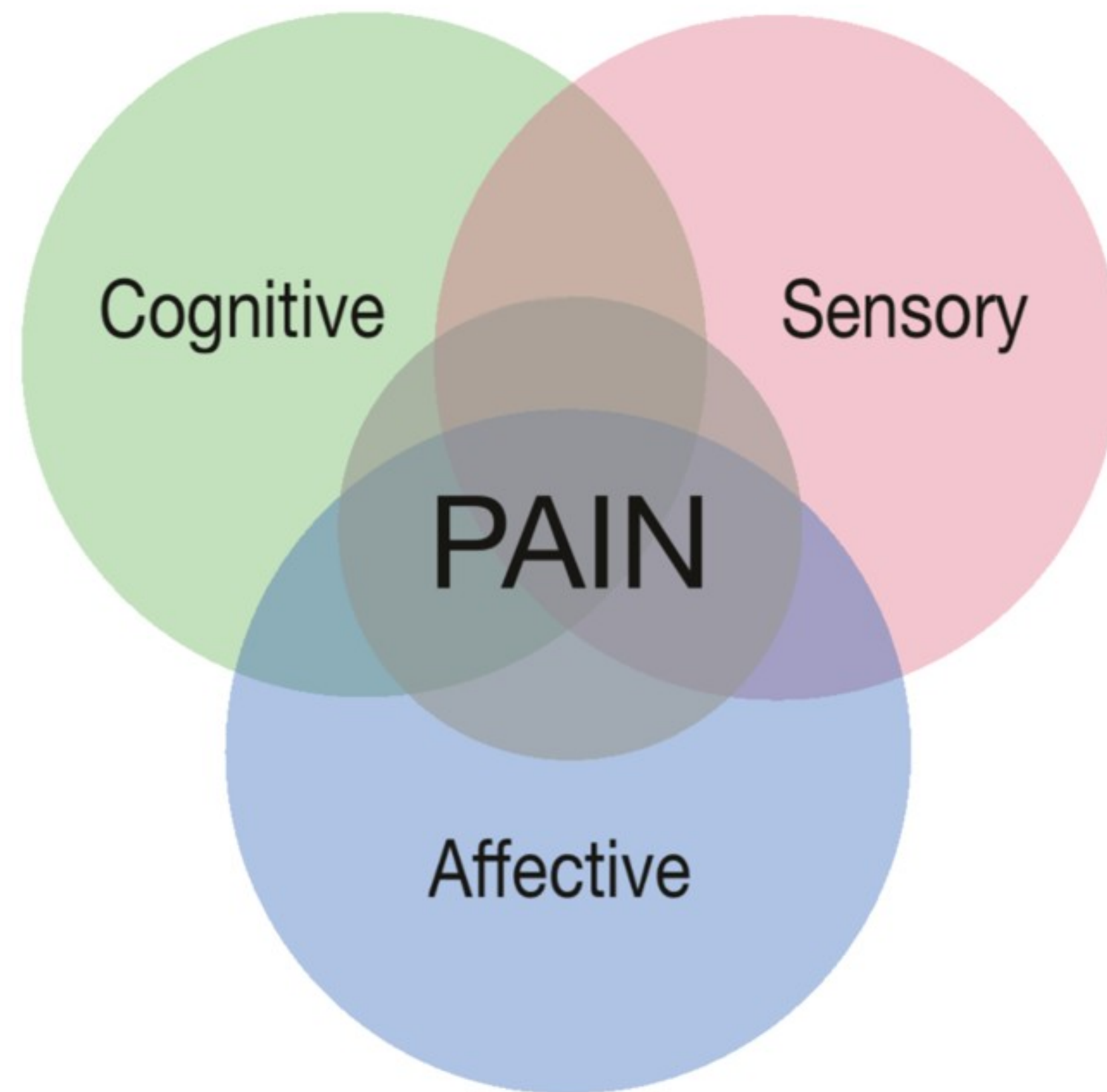
Few effective alternatives

Diffuse, mixed pain may persist
despite local and interventional care

Lovo et al. Cureus. 2022;14:e25430. Estimate applies to terminally ill patients with intense pain.



Nociception and Pain



Nociception

Neural encoding of a noxious stimulus

Sensory-discriminative

Where is it? How intense is it?

Affective-motivational

How unpleasant is it?

How much suffering does it cause?

Cognition adds attention, expectation and meaning

SRS Hypophysectomy for Cancer Pain

Pituitary / gland–stalk irradiation: small, selected cancer cohorts

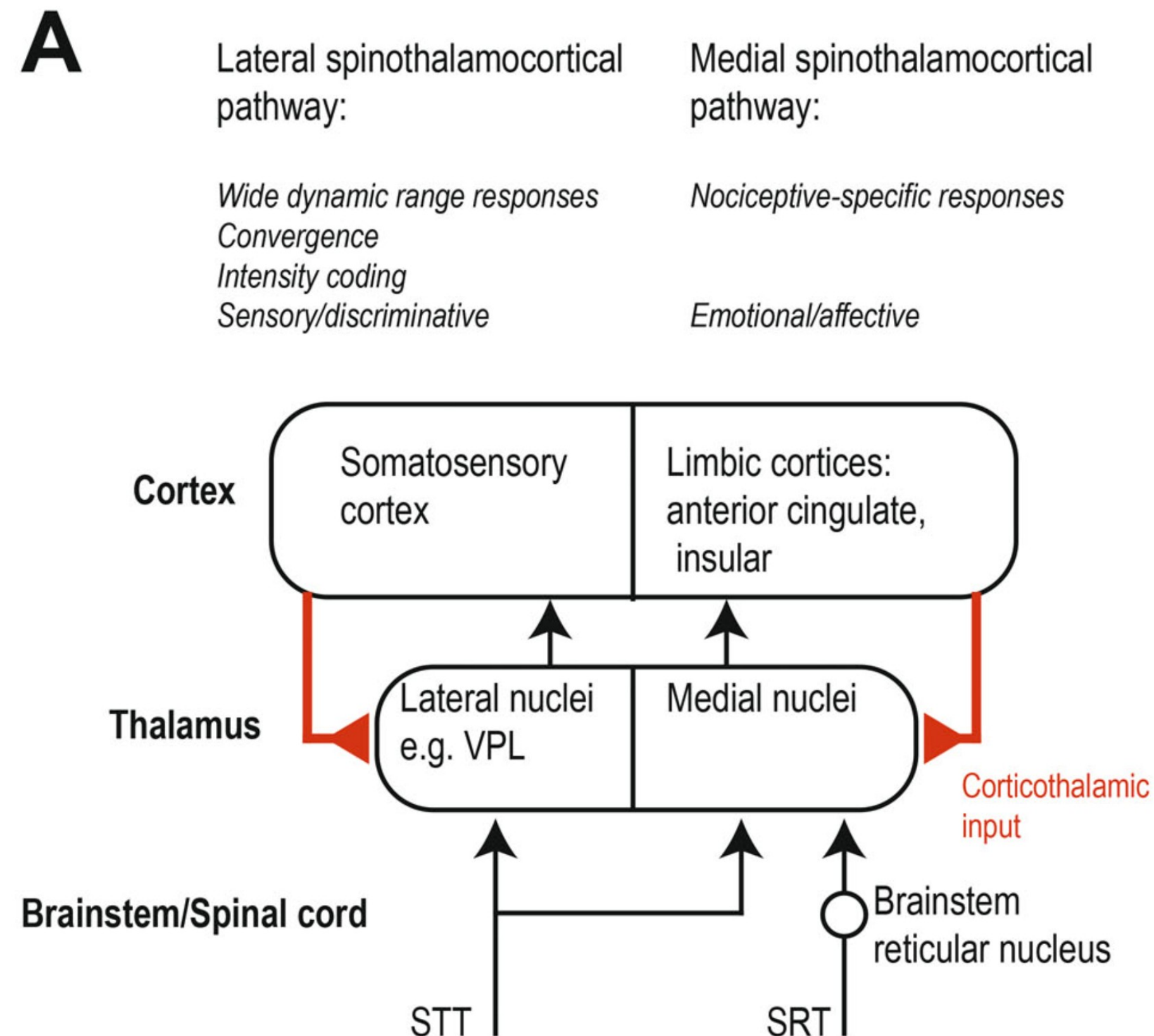
Study	Patients / dose	Reported analgesia	Durability / safety
Hayashi 2002	9 patients Dmax 160 Gy	9/9 pain resolution Within several days	Relief until death Follow-up 1–24 months
Kwon 2004	7 patients Dmax 150–160 Gy	7/7 significant relief Within several days	2 recurrences 1 transient DI / hypopituitarism
Lovo 2019	11 treated, 10 evaluable Dmax 150 Gy	8/10 initial responders Within 2–5 days	3/10 died without substantial pain 5/10 had substantial pain at end of life

- Rapid analgesia is plausible. Durability varies, and endocrine risk remains relevant.
- Typical response within days.
- Mechanism unknown but may involve changes in oxytocin.

Hayashi et al. J Neurosurg. 2002;97:433–437. Kwon et al. JKNS. 2004;36:286–290. Lovo et al. Cureus. 2019;e4811

CM/Pf and Pain Processing

Centromedian–parafascicular complex



Noxious stimulus salience

Medial thalamic circuits help regulate which pain signals gain attention

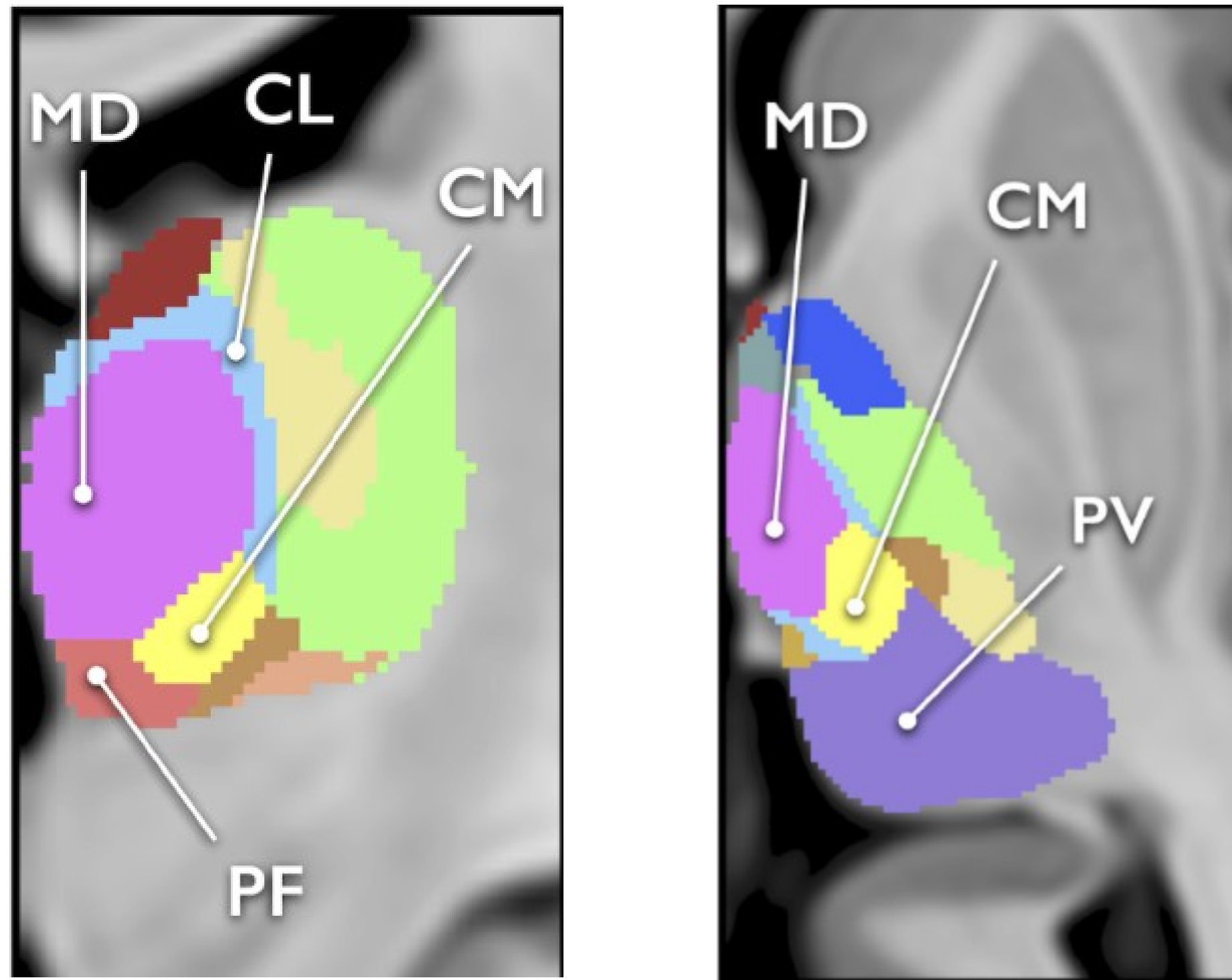
Affective pain processing

Connections with limbic networks provide a rationale for modulating the experience of pain

Diagram: Groh, Mease & Krieger. e-Neuroforum. 2017. doi:10.1515/nf-2017-A019

CM/Pf and Pain Processing

Centromedian–parafascicular complex



Kraus/Morel Atlas superimposed on MNI

Noxious stimulus salience

Medial thalamic circuits help regulate which pain signals gain attention

Affective pain processing

Connections with limbic networks provide a rationale for modulating the experience of pain

CM/Pf SRS for Cancer Pain

Cancer cohorts reviewed by Lovo and colleagues

Study	Patients / dose	Pain response	Durability / safety
Leksell 1972	25 with malignant pain 200–250 Gy	6 virtually pain-free 4 moderate, 9 slight 6 without relief	6 pain-free for >1 year 2 delayed hemianesthesia
Steiner 1980	52 treated; 50 classified 140–250 Gy	8 good, 18 moderate 24 without significant relief	Variable benefit Sensory / oculomotor effects
Lovo 2019	1 cancer-related case Contralateral CM/Pf 140 Gy	Anesthesia dolorosa after maxillary sinus carcinoma Relief within 48 hours	Died 31 days after SRS without pain

Historical doses and response definitions differ; the cancer evidence remains limited

Lovo 2022, Table 1 and Discussion; Leksell 1972; Steiner 1980; Lovo 2019. Steiner reports outcomes for 50 of 52 treated.

Broader CM/Pf Pain Literature

Mixed and predominantly non-cancer pain cohorts

Study	Cohort / dose	Reported benefit	Clinical limits
Young 1995	20 with diverse pain disorders 140–180 Gy	About two thirds had good or excellent relief	Follow-up 1–22 months 1 fatal radiation necrosis after bilateral treatment
Urgosik 2018	30 with non-cancer pain Unilateral CM/Pf, 145–150 Gy	13/30 had >50% pain relief Median onset: 3 months	4 responders later relapsed No neurological deficits
Lovo 2019	14 treated, 10 evaluable Contralateral CM/Pf, 140 Gy	7/10 initial >50% relief 5/10 at final follow-up	Only one cancer-related case Benefit could be brief

Analgesia is possible, but onset, durability and safety vary across techniques

Young et al. Stereotact Funct Neurosurg. 1995;64(suppl 1):172–181. Urgosik & Liscak. J Neurosurg. 2018. Lovo et al. 2019;e6421

Triple-Target SRS: Three Initial Cases

Neurohypophysis plus bilateral CM/Pf, Dmax 90 Gy per site

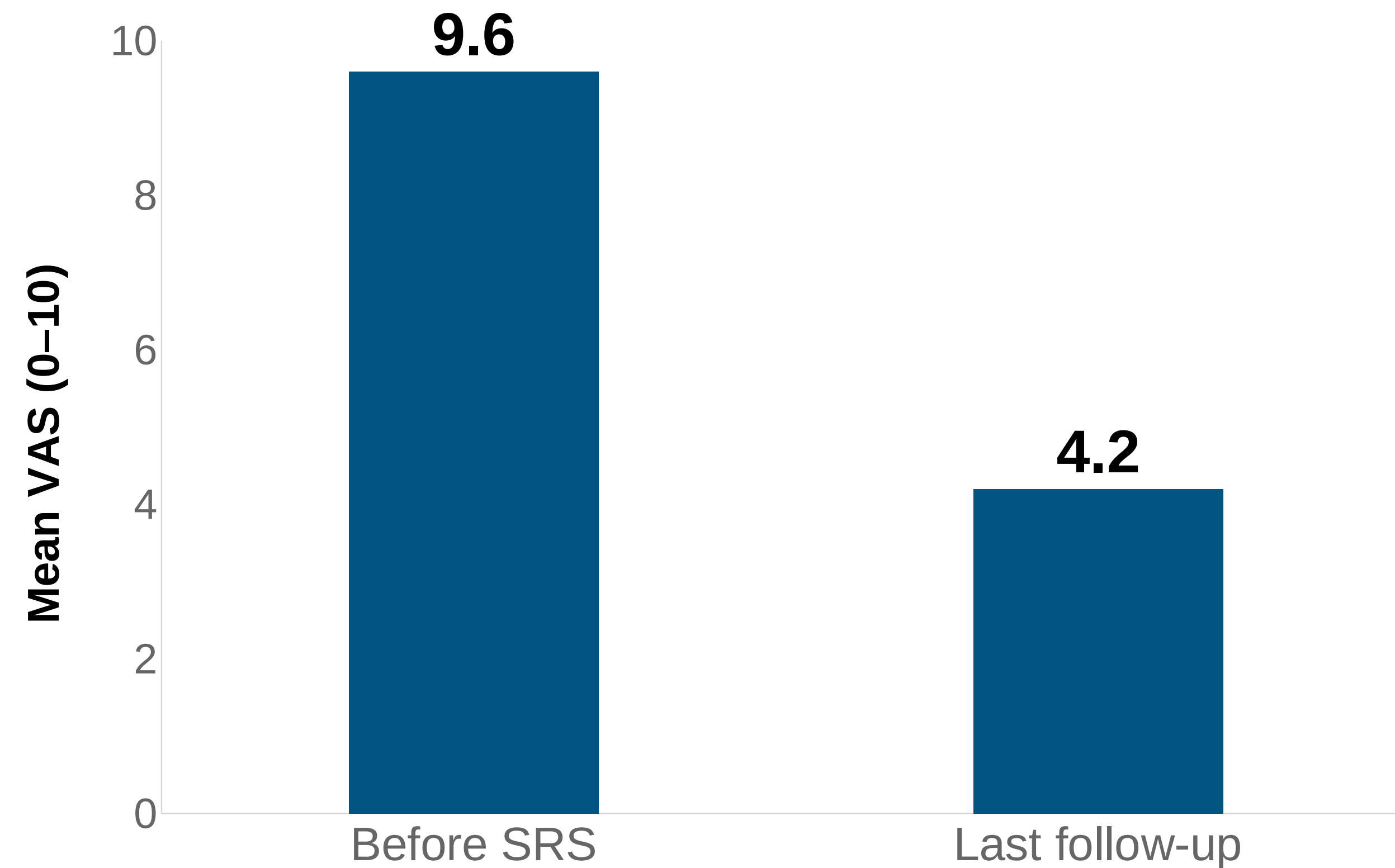
Rationale: mixed pain may persist after pituitary SRS alone;
thalamic benefit can be inconsistent or short-lived

Case	VAS before SRS	VAS at 72 h	VAS at death	Time to death
1	10	5	3	21 days
2	10	6	4	29 days
3	10	5	6	30 days

Pain improved but persisted. All three patients had only weeks of follow-up.

Lovo et al. Cureus. 2022;14:e25430. VAS = visual analogue scale, 0–10

Triple-Target SRS: Expanded Series



8 patients

Includes the original 3 cases

5 of 8

reduced opioid requirements

Uncontrolled series

Follow-up: 21–107 days

Del Cid et al. Br J Pain. 2025;19:396–403. Final assessment occurred at different times for different patients



The FREEDOM Trial

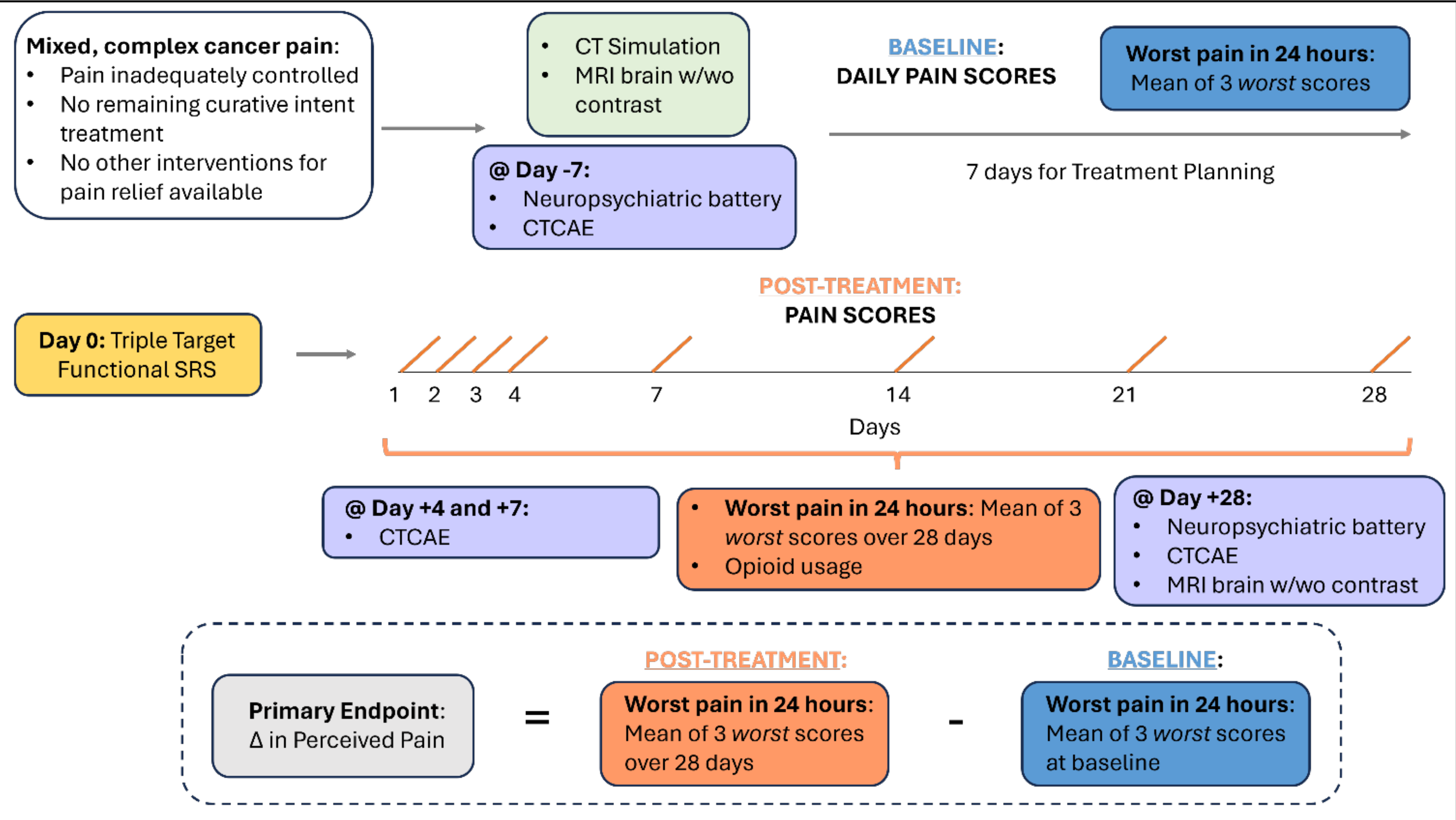
Functional Radiosurgery for Easing or Eliminating Debilitating Oncologic Morbidity

- UCLA single-center, prospective, single-arm study
- Up to 24 enrolled patients
- Single-session SRS to bilateral CM/Pf and the neurohypophysis
- The quality of life (QOL) assessment will be conducted with the Brainlab Visiontree electronic patient reported outcome (ePRO) platform.
- Planned in Brainlab Elements Cranial SRS w/ Cones

Study funding: Brainlab

FREEDOM Trial Overview

UCLA prospective study: up to 24 patients



What FREEDOM Adds

Independent prospective validation

UCLA cohort: 19 evaluable patients, up to 24 enrolled

Prespecified pain endpoint

Three baseline scores versus the three worst post-treatment scores

Repeated BPI assessments through day 28

Opioid use, suffering and function

Morphine-equivalent dosing, pain anxiety, mood, sleep and daily function

Prospective safety monitoring

First 10 patients: inpatient observation through at least day 4

FREEDOM protocol, June 2025. Single-arm, unblinded study. BPI = Brief Pain Inventory



FREEDOM Eligibility

Inclusion

Adults ≥ 18 years

Mixed, complex cancer pain
BPI worst pain $> 8/10$ despite optimized
opioids

No suitable further pain procedure
or the patient declines it

Consent and ability to complete
study procedures

Exclusion

Intracranial malignancy or prior brain RT

Prior craniotomy, DBS, LITT or
interfering intracranial hardware

Unable to tolerate imaging or lie flat

Pregnancy, breastfeeding or unwilling
to use birth control during participation

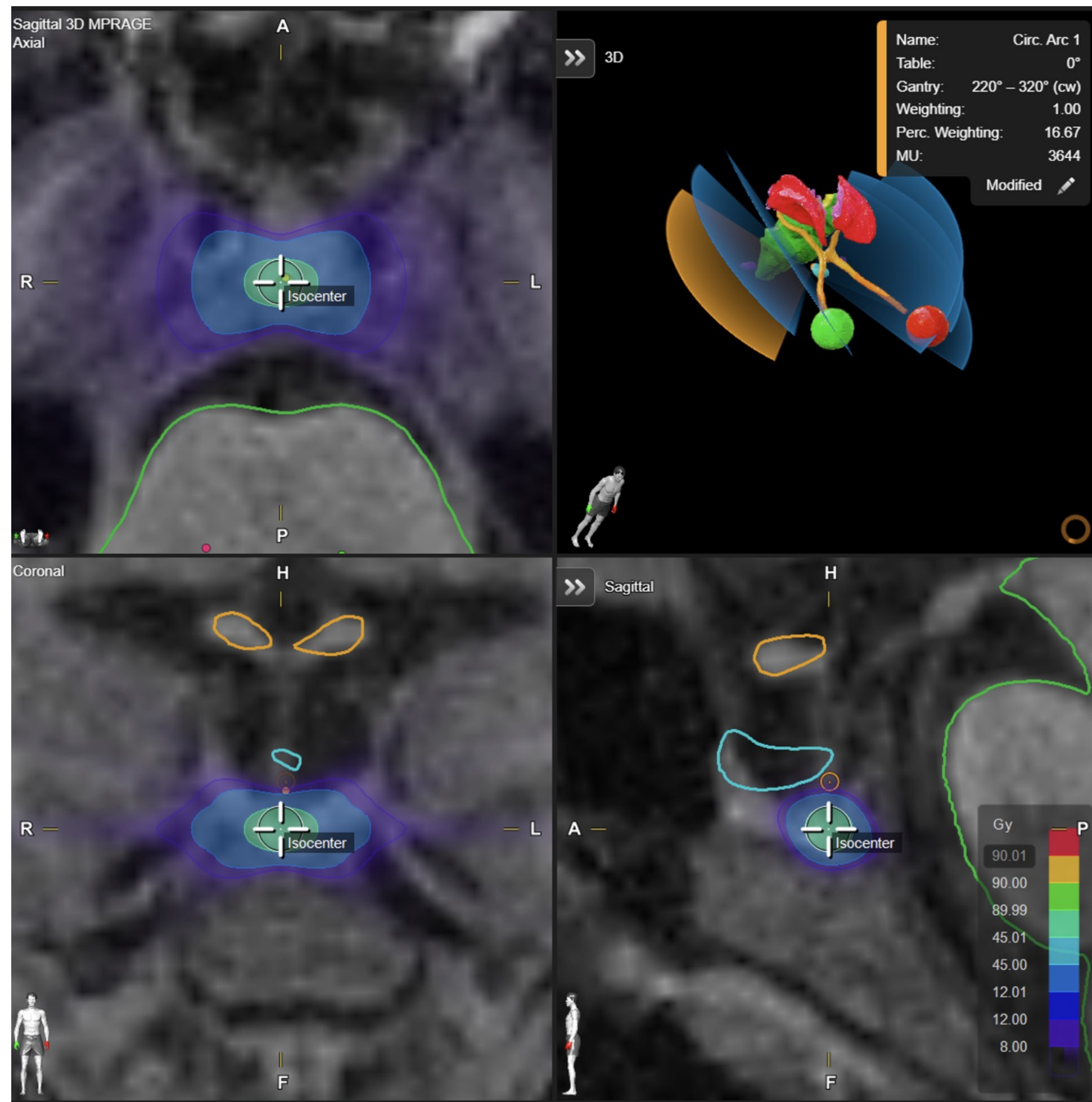
Other safety or compliance concerns

FREEDOM protocol, patient selection. DBS = deep brain stimulation. LITT = laser interstitial thermal therapy

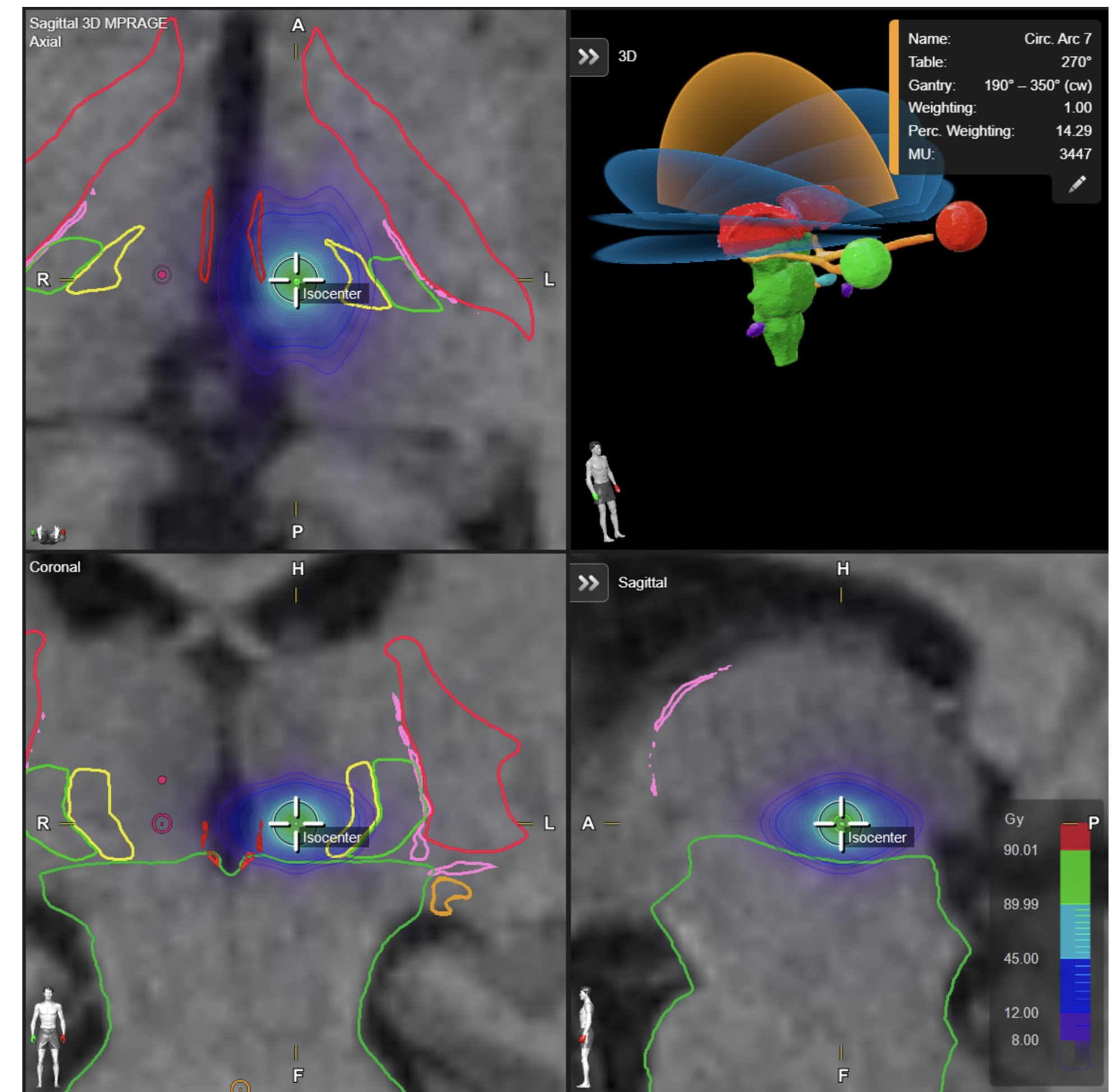
FREEDOM SRS Targeting Strategy

Bilateral CM/Pf and neurohypophysis: Dmax 90 Gy per site in one session

Neurohypophysis



Bilateral CM/Pf



Summary

- Cancer pain often combines somatic, visceral and neuropathic mechanisms and can remain severe despite optimized treatment.
- SRS to the bilateral CM/Pf and neurohypophysis has shown early analgesic benefit in small series, but its durability and safety remain uncertain.
- FREEDOM will prospectively evaluate pain relief, opioid use and safety in 19 evaluable patients at UCLA.

Questions?

