Measuring the Efficacy of Percutaneous Cryoneurolysis in the Management of Patients With Plateaued or Refractory Shoulder Spasticity

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DISCLOSURES

Paul Winston has received educational and research grants and acted on advisory boards and as a consultant for Pacira BioSciences, Inc.; AbbVie; Merz Therapeutics; and Ipsen. All of the relevant financial relationships listed have been mitigated.

Mahdis Hashemi has no relevant financial relationships with ineligible companies to disclose and no non-financial conflicts of interest relevant to this activity.

Eve Boissonnault has received educational grants from AbbVie and received honoraria, acted on advisory boards, and acted as a consultant for Pacira BioSciences, Inc.; AbbVie; Merz Therapeutics; and Ipsen. All of the relevant financial relationships listed have been mitigated.

Daniel Vincent has acted as a consultant for Pacira BioSciences, Inc. and received funding per session from Island Health. All of the relevant financial relationships listed have been mitigated.

Fraser MacRae has no relevant financial relationships with ineligible companies to disclose and no non-financial conflicts of interest relevant to this activity.

Jia Song, **Meng-Hsuan Sung**, and **Sandy Shi** are employees of Pacira BioSciences, Inc. and **Jia Song** and **Sandy Shi** own stock in the company. All of the relevant financial relationships listed have been mitigated.

Introduction

Conventional treatments for spasticity are costly and have limited duration for some patients[1,2]

In the United States, the use of botulinum toxin to control shoulder girdle spasticity is off-label

There is a need for novel treatment options to improve patient outcomes

The muscles most commonly targeted for management of shoulder spasticity include the pectoralis major and minor, subscapularis, and latissimus dorsi[3,4]

The suprascapular nerve provides ~70% of sensory input to the shoulder[3]

Percutaneous cryoneurolysis is a minimally invasive technique that has been used to reduce pain associated with knee osteoarthritis,[5] total knee arthroplasty surgery,[6] and neuralgia[7]

A previous case series suggested that cryoneurolysis may be a promising treatment for spasticity, but additional data are needed[8]

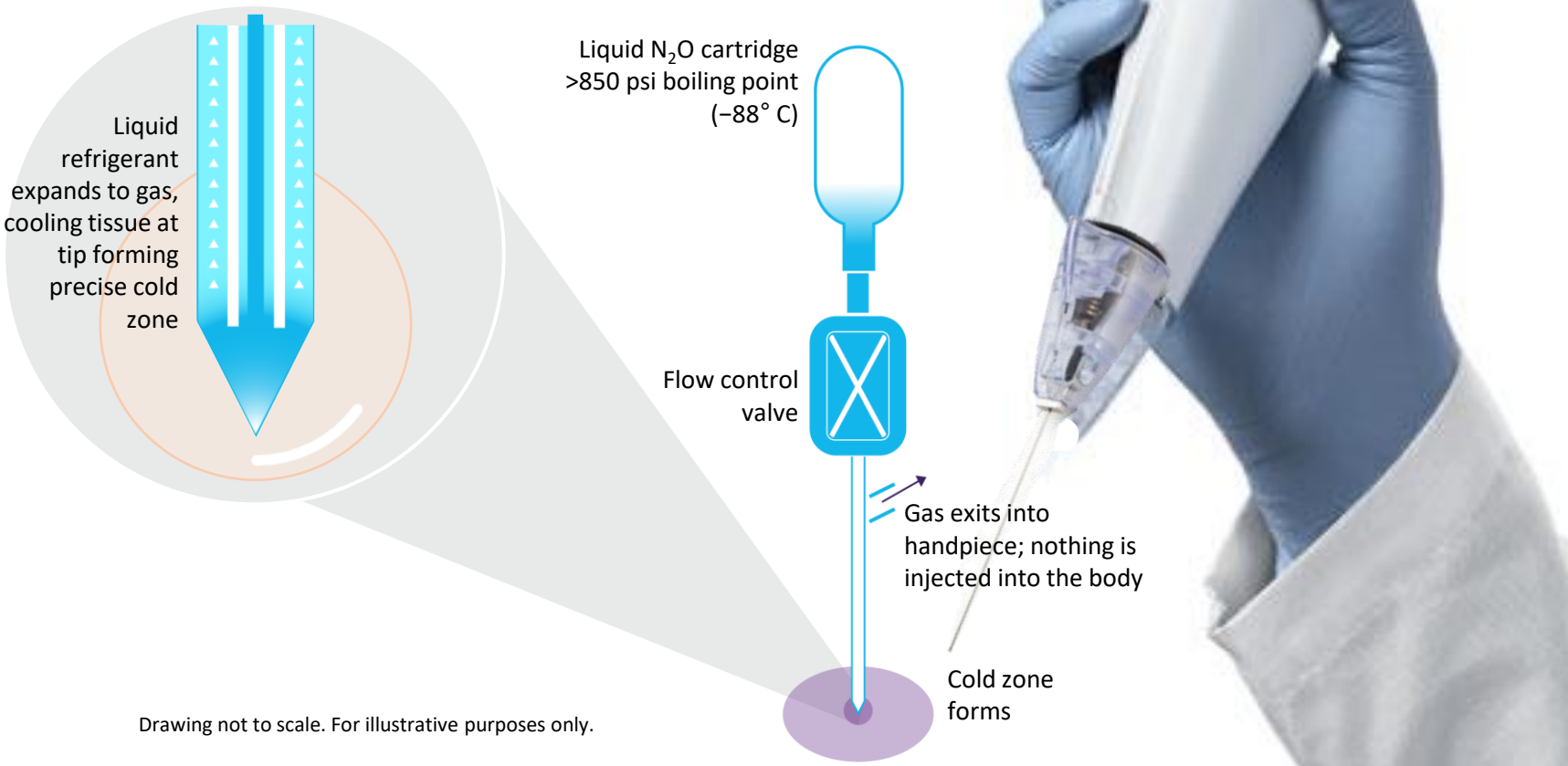
Objective: to evaluate the outcomes of cryoneurolysis in patients with spastic shoulder who had plateaued in prior treatments, including botulinum toxin therapy

1. Orsnes GB et al. *Acta Neurol Scand*. 2000;101(4):244-248; 2. Ward A et al. *J Rehabil Med*. 2005;37(4):252-257; 3. Fitterer JW et al. *Front Neurol*. 2021;12:668370; 4. Simpson DM et al. *PM R*. 2017;9(2):136-148; 5. Radnovich R et al. *Osteoarthritis Cartilage*. 2017;25(8):1247-1256; 6. Urban JA et al. *Arthroplast Today*. 2021;10:87-92; 7. Kim CH et al. *Pain Physician*. 2015;3:E363-E368; 8. Winston P et al. *Arch Rehabil Res Clin Transl*. 2019;1(3-4):100030.

Methods: Cryoneurolysis Procedure

- This repeated-measures pilot study (NCT04670783) included participants who underwent cryoneurolysis to the lateral and/or medial pectoral nerves
  - In some cases, neurolysis was applied to the suprascapular nerve to manage pain

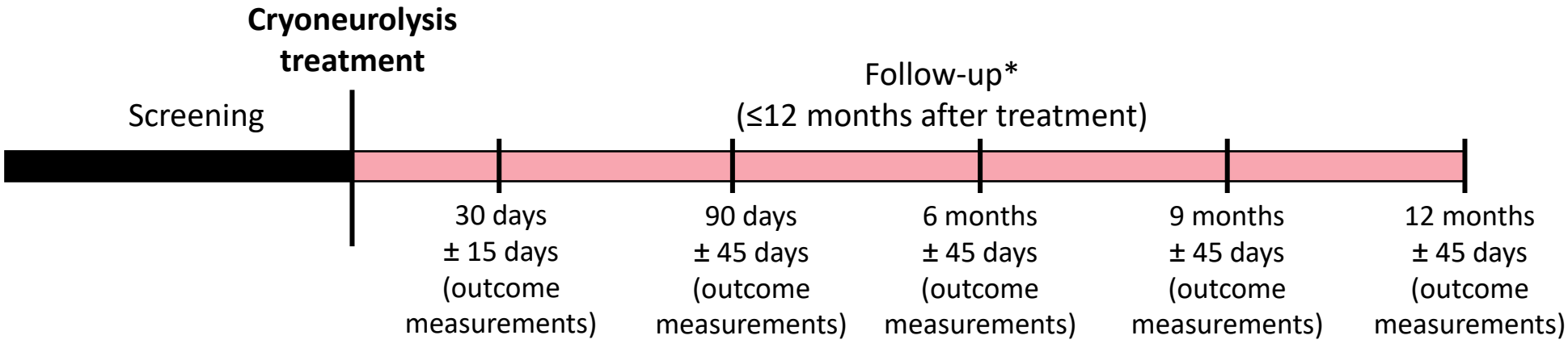
- Probe cooled to between −60°C and −88°C near the targeted nerve[1-3]
  - Cooling causes secondary axonotmesis and Wallerian degeneration, allowing for axonal regrowth[4]
- Effects can be prolonged for several months in some cases[5]



Drawing not to scale. For illustrative purposes only.

1. Rubenstein J et al. *Am J Phys Med Rehabil*. 2021;100(5):e65; 2. Winston P et al. *Arch Rehabil Res Clin Transl*. 2019;1(3-4):100030; 3. Shaffer JP et al. *Orthop J Sports Med*. 2022;10(5):23259671221096095; 4. Guirguis M et al. Cryotherapy. In: Deer TR et al, eds. *Deer's Treatment of Pain*. Springer Cham; 2019:283-289; 5. Radnovich R et al. *Osteoarthritis Cartilage*. 2017;25(8):1247-1256.

Methods: Study Design and Outcomes



Outcome	Measure†
Mean active ROM	ROM during abduction, external rotation, and flexion
MAS score	Muscle tone during abduction, external rotation, and flexion
V1	Maximal passive stretch during abduction, external rotation, and flexion
GAS	Patient satisfaction

GAS, goal attainment scale; MAS, modified Ashworth scale; ROM, range of motion; V1, maximal passive stretch.
*All participants have a least 6 months of follow-up. †Each was measured at 30 days, 90 days, 6 months, 9 months, and 12 months.

Methods: Eligibility Criteria

Inclusion criteria	Exclusion criteria
• Adults with upper extremity spasticity causing functional impairment, who have plateaued in outcomes, in which the clinical examination suggested further interventions can be trialed	• Being unable to attend the treatment schedule
• Upon clinical examination, V1 measures on upper extremity demonstrated that further range may be possible (versus management of contracture)	• Underwent prior neurolytic procedure to the nerve such as phenol or cryoneurolysis in the past 2 years
• Reducible spasticity (versus contracture) in a diagnostic nerve block to determine whether cryoneurolysis would be beneficial	
• Participants were offered a cryoneurolytic procedure and consented to undergo the procedure	

V1, maximal passive stretch.

Results: Baseline Characteristics

47 participants underwent cryoneurolysis of the shoulder

At baseline, participants **had reduced median active ROM and high median scores on MAS** during abduction, external rotation, and flexion, **suggesting severe spasticity with possible musculotendinous contracture**

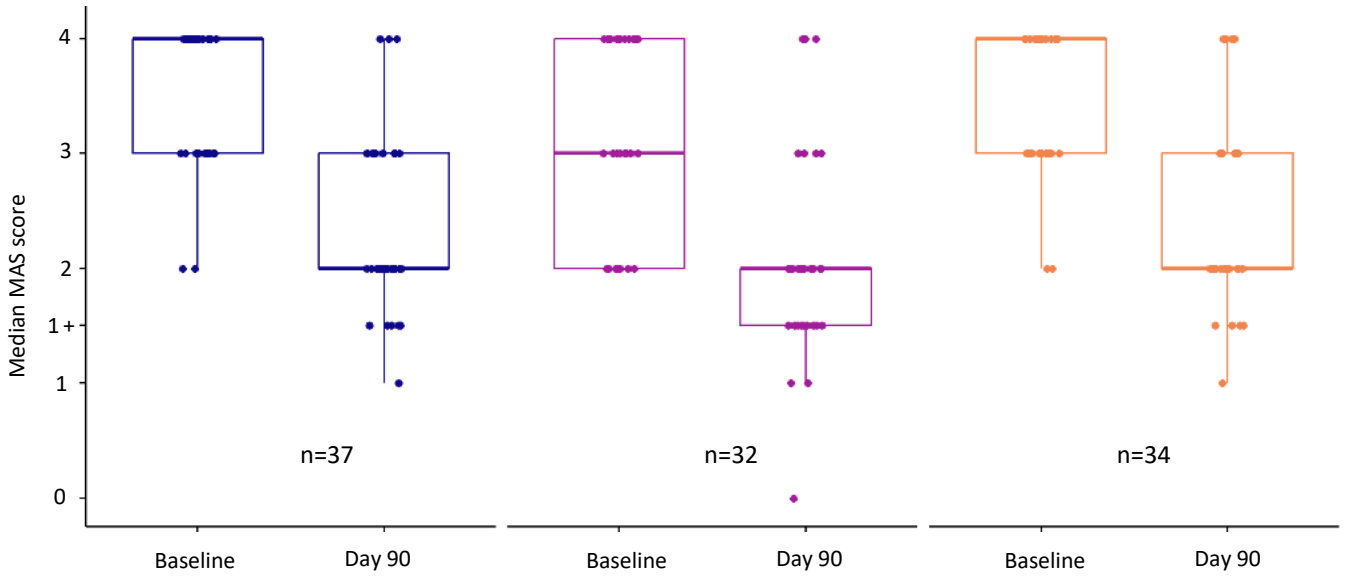
Outcome	Baseline (n=47)
Median active ROM (IQR)	
Abduction	60.0 (50.0, 70.0)
External rotation	20.0 (−11.2, 26.3)
Flexion	57.5 (40.0, 68.8)
Median MAS score (IQR)	
Abduction	4.0 (3.0, 4.0)
External rotation	3.0 (2.0, 4.0)
Flexion	4.0 (3.0, 4.0)
V1 (IQR)	
Abduction	95.0° (85.0°, 105.0°)
External rotation	30.0° (15.0°, 40.0°)
Flexion	95.0° (86.2°, 105.0°)

IQR, interquartile range; MAS, modified Ashworth scale; ROM, range of motion; V1, maximal passive stretch.

Results: 90-Day Changes From Baseline

- 40 patients completed the 90-day follow-up at the time of this analysis
- **Significant improvements were observed in MAS** scores for abduction, external rotation, and flexion (*P*<0.001)

MAS scores at baseline and 90 days



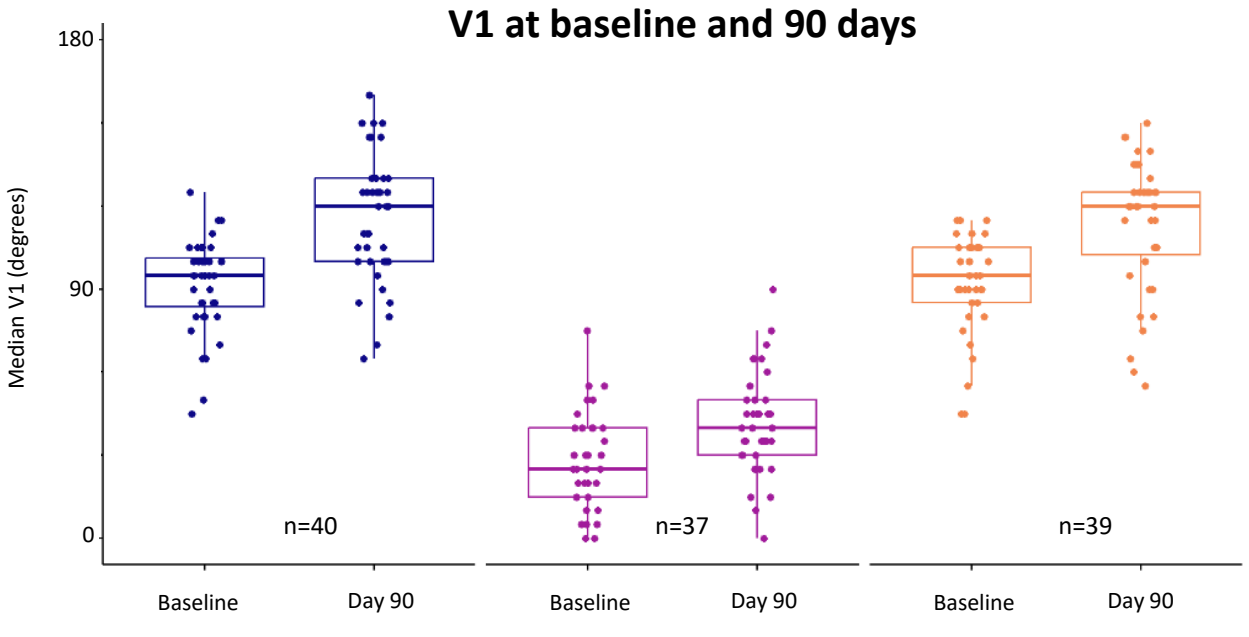
Outcome	90-day change (n=40)	*P* value
Median MAS scores (IQR)		
Abduction	−1.0 (−2.0, −1.0)	<0.001
External rotation	−1.0 (−2.0, −0.5)	<0.001
Flexion	−1.0 (−1.9, −1.0)	<0.001

Abduction
External rotation
Flexion

IQR, interquartile range; MAS, modified Ashworth scale.

Results: 90-Day Changes From Baseline (cont)

- **Significant improvements were observed in V1** for abduction, external rotation, and flexion (*P*<0.0001)*
  - These changes resulted in a 3-dimensional change in ROM
- There was a numerical **increase in mean improvement per patient in GAS scores at 90 days** (10.5 points)



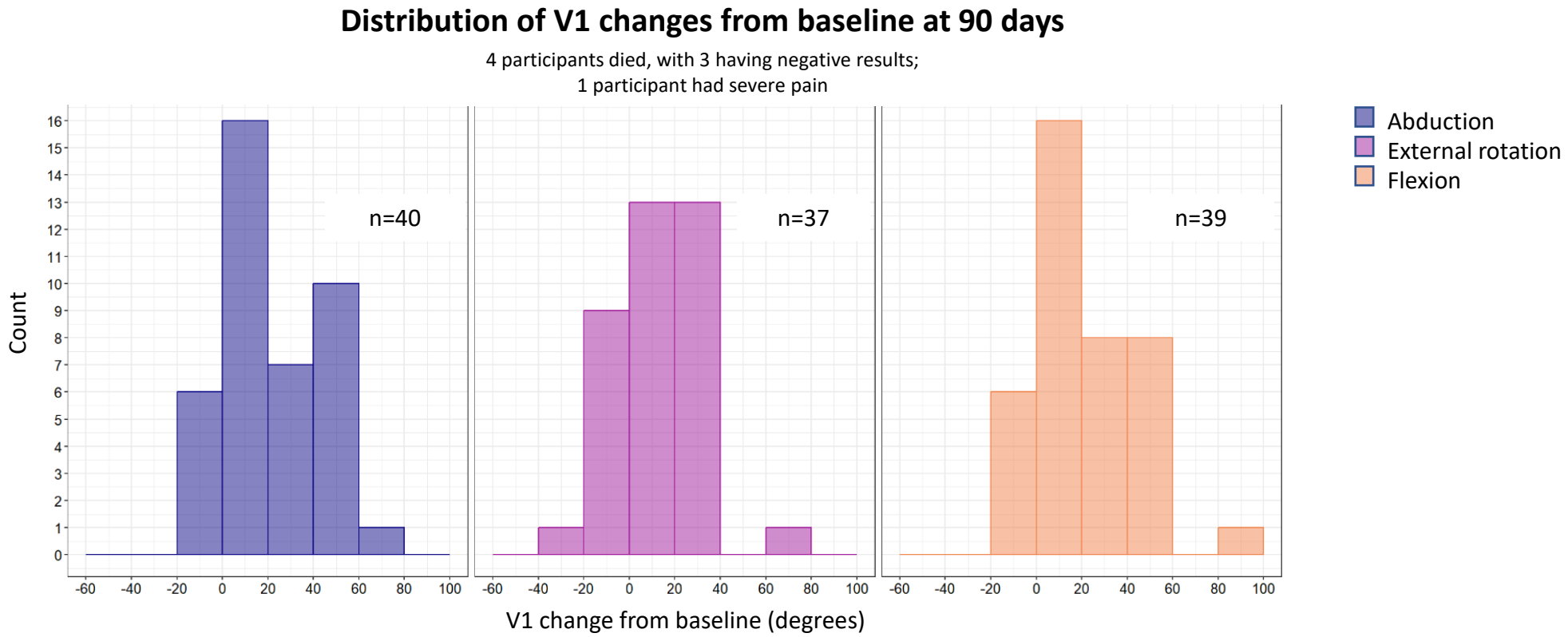
Outcome	90-day change (n=40)	*P* value
V1 (IQR)		
Abduction	20.0° (8.8°, 45.0°)	<0.001
External rotation	15.0° (0.0°, 35.0°)	<0.001
Flexion	20.0° (10.0°, 37.5°)	<0.001

*Wilcox P value is reported.

GAS, goal attainment scale; IQR, interquartile range; ROM, range of motion; V1, maximal passive stretch.

Results: 90-Day Changes From Baseline (cont)

- **44%, 38%, and 44% of participants experienced >20° improvements** in V1 abduction, external rotation, and flexion scores at 90 days, respectively



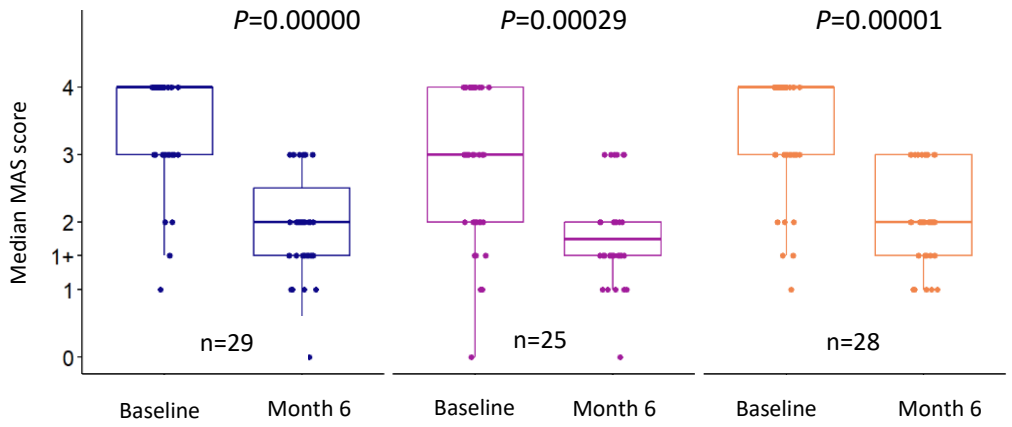
V1, maximal passive stretch.

Results: 180-Day Changes From Baseline

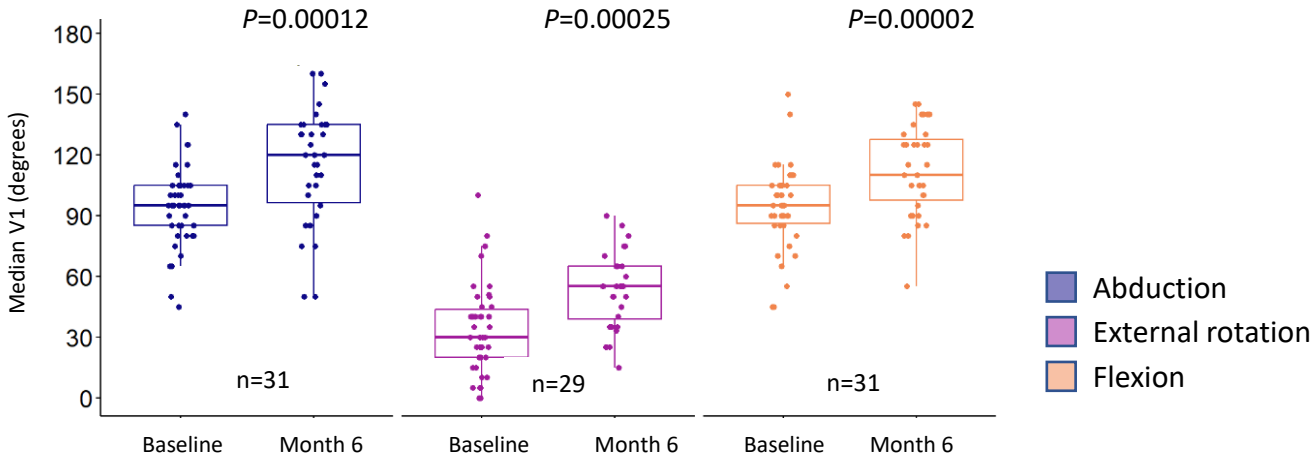
- **Improvements in MAS scores and V1*** were **sustained** at the **6-month follow-up** (*P*≤0.0003)
- There was a numerical **increase in mean improvement per patient in GAS scores** at 180 days (13.8 points)

Outcome	Median MAS scores (IQR)	Median V1 (IQR)
Abduction	−1.00 (−2.00, −1.00)	20.00° (2.50°, 37.50°)
External rotation	−1.00 (−1.50, −0.50)	15.00° (3.00°, 30.00°)
Flexion	−1.00 (−1.50, −0.88)	15.00° (5.00°, 35.00°)

MAS scores at baseline and 180 days



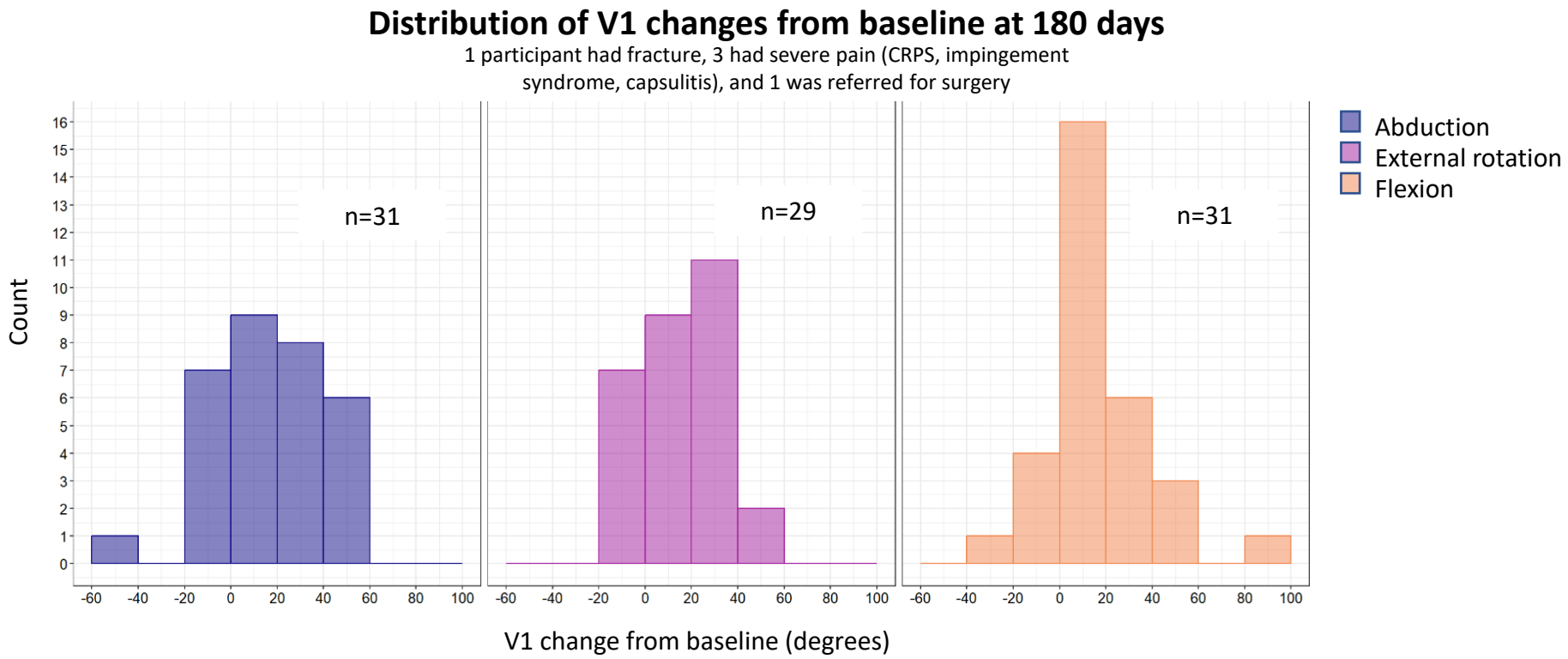
V1 at baseline and 180 days



*Wilcox *P* value is reported.
IQR, interquartile range; MAS, modified Ashworth scale; V1, maximal passive stretch.

Results: 180-Day Changes From Baseline (cont)

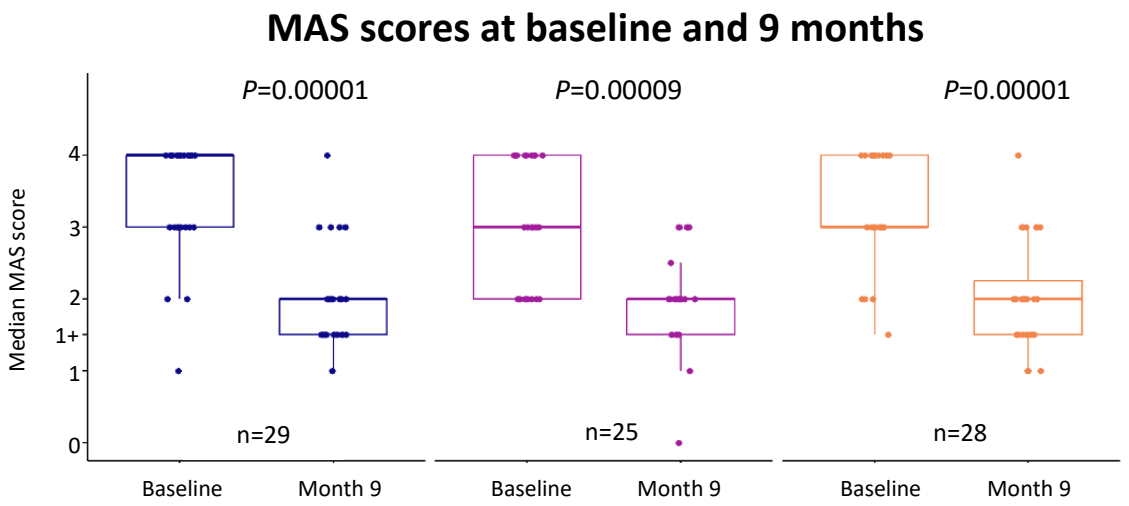
- **45%, 45%, and 32% of participants experienced >20° improvements** in V1 abduction, external rotation, and flexion scores at 6 months, respectively
  - 1 participant had a humerus fracture resulting in low abduction values (−60°)

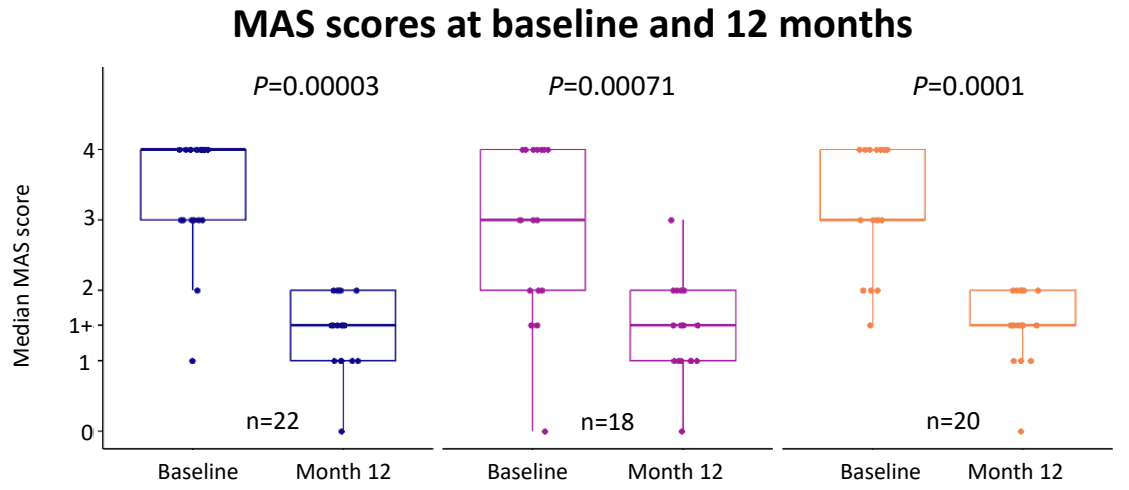


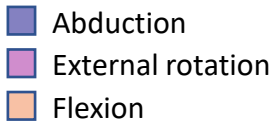
CRPS, complex regional pain syndrome; V1, maximal passive stretch.

Results: Changes From Baseline to 9 and 12 Months

- Participants with follow-up data at 9 months and 12 months had **sustained significant improvements in MAS** scores at 9 ($P \leq 0.00009$) and 12 months ($P \leq 0.00071$)
- **Significant sustained improvements were also observed in V1** at 9 ($P \leq 0.00028$) and 12 months ($P \leq 0.0013$) across abduction, external rotation, and flexion measures*







*Wilcox *P* value is reported.
MAS, modified Ashworth scale; V1, massive passive stretch.

Conclusions

1. Participants in the study had **markedly reduced flexion**, as well as abduction and external rotation, associated with increased tone, which classically indicated clinical **presence of severe spasticity**

2. Percutaneous cryoneurolysis of the medial and lateral pectoral nerves and/or suprascapular nerve was associated with **improvements in shoulder ROM, spastic tone, and clinically meaningful[1] improvements in GAS scores at 90 and 180 days[1]**

3. Improvements in shoulder ROM and spastic tone were maintained at later time points; longer follow-up is ongoing to confirm sustainability of improvements

GAS, goal attainment scale; ROM, range of motion.

1. López de Munain L et al. *Eur Neurol*. 2019;82(1-3):1-8.

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