The VERIFY STUDY

Validation of Early Prognostic Data for Recovery
Outcome after Stroke for Future, Higher Yield Trials

Newsletter May 2023 Issue 17

Team, we are getting there!! We are over 10% of our enrollment goal, and have some important site activations on the way to get us at a steady state for enrollment success! Thanks so much everyone 🙂

- Pooja Khatri, MD, MSc

New enrollments since last newsletter

- Duke University, +2
  - PI- **Dr. Feng,** PSC- **Tato Sokhadze**
- Emory, +1
  - PI- **Dr. Borich**, PSC- **Susan Murphy**
- University of Michigan, +1
  - PI- **Dr. Krishnan**, PSC- **Shannen Bolde**
- University of Utah, +2
  - PI- **Dr. Richards,** PSC- **Megan Gardner**
- University of Alabama, +2
  - PI- **Dr. Gropen**, PSC- **Tammy Davis**
- Massachusetts General Hospital, +1
  - PI- **Dr. Lin**, PSC- **Julie DiCarlo**
- UPMC, +1
  - PI- **Dr. Wittenberg,** PSC- **Jason Weimer**
- UVA, +1
  - PI- **Dr. Aldridge** PSC- **Miah Perch**
- U of Wisconsin, +1
  - PI- **Dr. Ahmed,** PSC- **Sima Sayyahmelli**

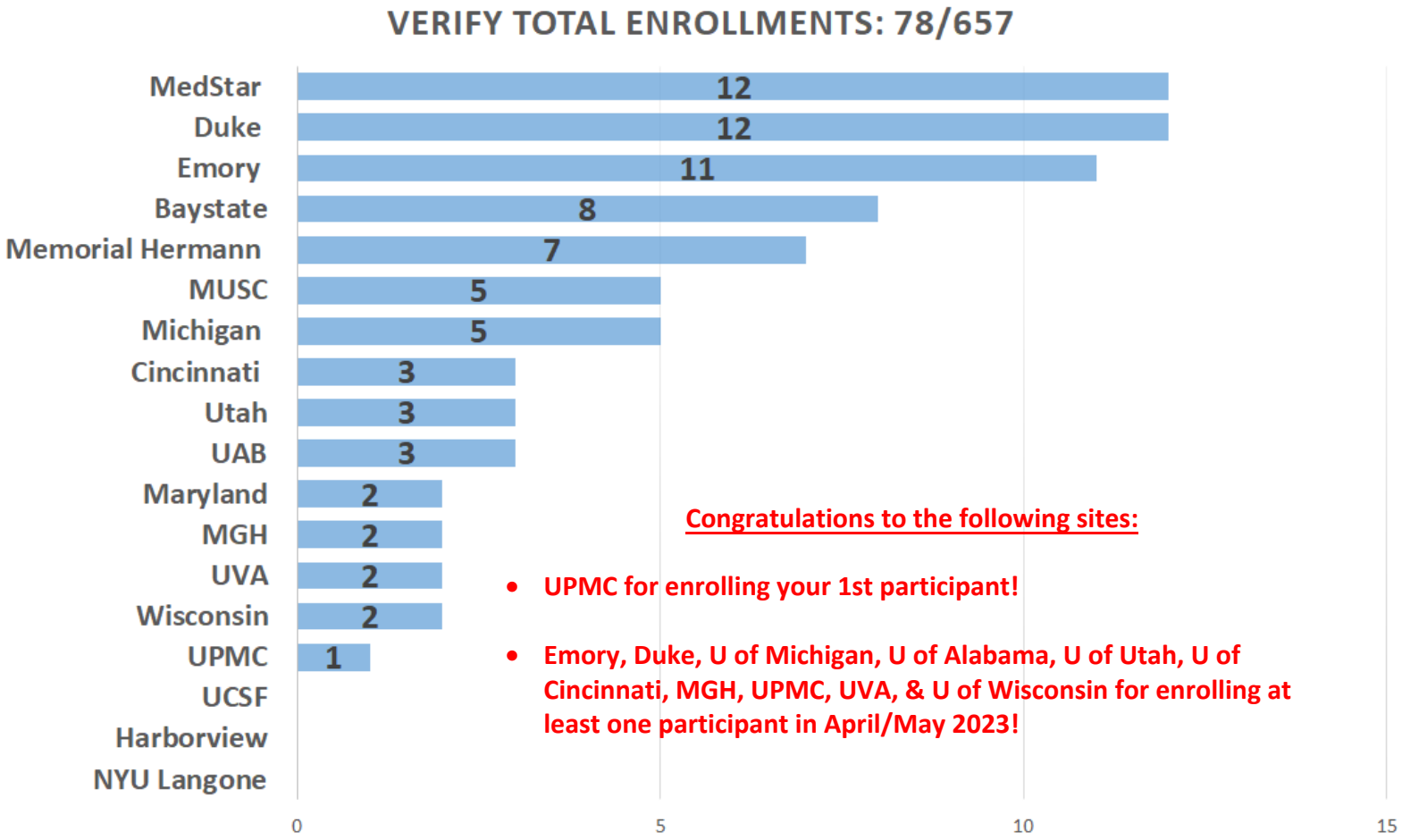
Payment Schedule Updates

- Sites will receive an extra $500 for consenting or performing TMS procedure on weekend (Sat/Sun) or holiday
  - While the study MRI may be more difficult to obtain during the weekend/holidays, remember to also initiate discussion on scheduling it with your MRI tech during the weekend or on Monday morning.
  - Study MRI is obtained within the study timeframe (72-168 hrs)

****The updated payment schedule is available via the same payment schedule link in your site's CTA.****

- Patient Payment: The study team has decided to keep payment schedule as is ($150 provided to participants during the last study visit).
  - The last study visit is the most time consuming and requires a dedicated visit.
  - The last study visit contains our primary endpoint data (FM/ARAT).
  - The cIRB had no issues with approving payment schedule.

Enrollment Graphs

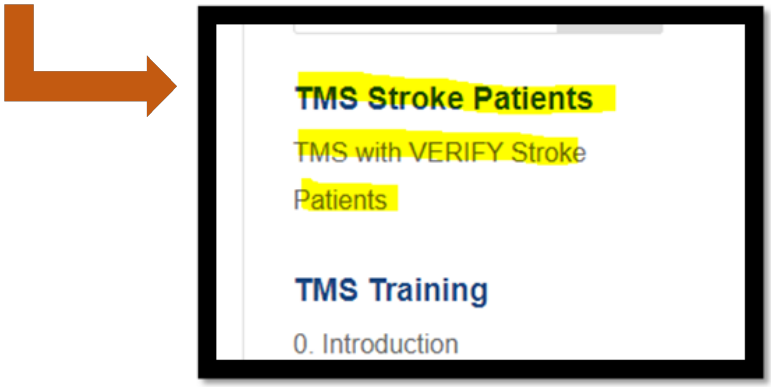


Congratulations to the following sites:

- **UPMC for enrolling your 1st participant!**
- **Emory, Duke, U of Michigan, U of Alabama, U of Utah, U of Cincinnati, MGH, UPMC, UVA, & U of Wisconsin for enrolling at least one participant in April/May 2023!**

TMS Reminders

- Information for TMS with stroke patients is listed under a separate header on the TMS training website: https://verifytraining.blogs.auckland.ac.nz/



- If you can't determine MEP status you should try to reschedule a re-test if it still falls within the 72 – 168 hour post-stroke window.

****Any VERIFY patients without a usable MEP status determination will have to be excluded from the study primary analysis.****

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- In addition, An absence of MEPs in BOTH the ECR and FDI at 100% MSO during bilateral facilitation and with systematic coil positioning attempted is NEEDED to call a stroke patient MEP-.

- If electrical noise appears during bilateral facilitation it is likely the patient is causing electrical noise issues by pulling on the electrodes and/or cables.
    - This will often show up as a prolonged stimulus artifact.
    - Changing the patient's posture while facilitating to prevent this happening should eliminate the noise.

Tips for TMS Tolerability

- Be mindful with choice of words:
  - When using 100% MSO stimulation, preferable word choice includes:
    - **"This is the highest intensity we're going to use"**
    - **"We won't be going any higher than this"**

- Try to avoid using the following word choices as these word choices could elicit anxiety from the stroke patients.
    - **"We're at 100% intensity"**
    - **"We're at the highest intensity possible."**

- Offer the patient earplugs
  - A source of discomfort from TMS can be the sound of the TMS click.
  - Earplugs can help decrease this discomfort.

- The TMS assistant can do the following:
  - Check on the patient
  - Offer encouraging words
  - See if the patient needs a break

- Tell the patient how many stimulations are left
  - This can help them be more willing to finish the session.
    - For example, if you are at 100% MSO with bilateral facilitation you might say "you've done a great job so far, we're so close to the end so is it okay if we do 8 more stimulations while you squeeze both hands? Then we'll be all done."

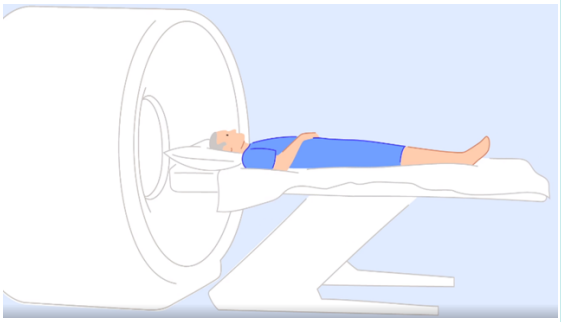
- The above tips can be found at the TMS training website under "TMS with Stroke Patients" tab:
  - https://verifytraining.blogs.auckland.ac.nz/tms-stroke-patients/

MRI Reminders: Phantom Scans

- Phantom scan(s) of study-specific 3D-T1 sequence collected at study start-up for site activation.

- Phantom scan(s) are collected every 6 months (2 times per year) to ensure quality certification of MRI protocol over time.
  - This will help to prevent unusable MRI data

- Phantom scan(s) are needed after any scanner hardware upgrades and/or software changes before scanning any new patient.
  - Please notify the imaging team of any upcoming MRI upgrade if known in advance.



- Email reminders will be sent out at every 5, 6, and 7-month window interval for upcoming phantom scans set to expire
  - If phantom scan not obtained after 7-month window, then activated site **will be placed on enrollment hold** until phantom is obtained.

Behavioral Assessment Recertification Reminders

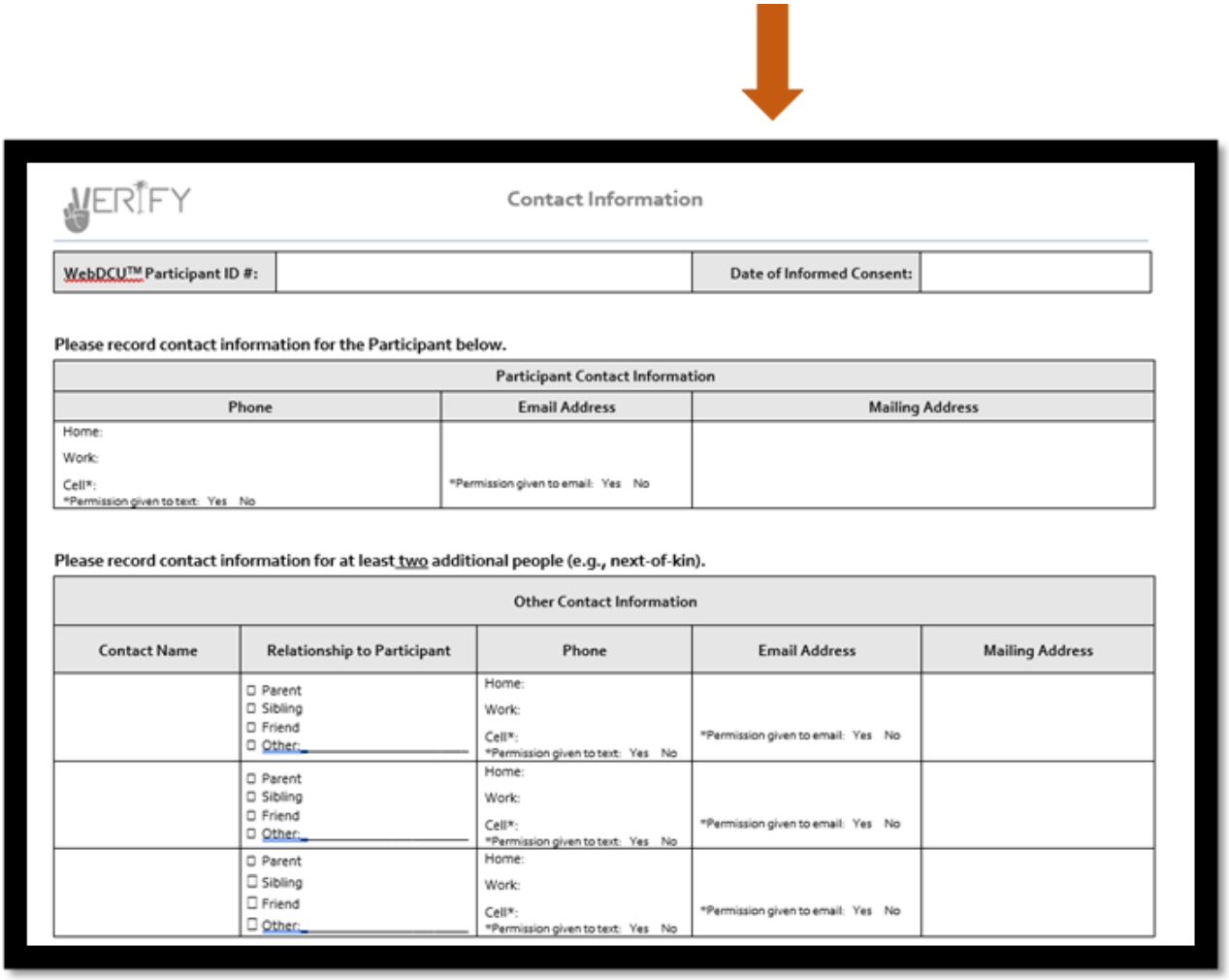
- Below table shows when you need to be recertified on each behavioral assessment.
- Table is also located in MOP & Virtual Training Protocol slides
  - Both are accessible in Toolbox tab of WebDCU.
- FM & ARAT require recertification **every 6 months.**
- The Cramer Lab will send reminder emails at 1 month AND 1 week prior to your training expiring. This will serve as a reminder to complete your recertification.
- It is the sites responsibility to ensure no assessment is performed by study personnel with expired training.

Platform	Assessment Name	Recertification	Link to training
Bluecloud	Upper Extremity Fugl-Meyer Scale	Every 6 months	https://secure.bluecloud.net/verify-study
	Action Research Arm Test	Every 6 months	
	Rankin Focused Assessment	Every 2 years	
MoCA Website	Montreal Cognitive Assessment	Every 2 years	https://www.mocatest.org/get-certified
TMS Website	SAFE Score Training	Every 1 year	https://verifytraining.blogs.auckland.ac.nz/
	TMS Safety Checklist Training	Only 1 time	
DCU Campus	Modified Rankin Scale	Every 2 years	https://dcu.musc.edu/campus/
	NIH Stroke Scale	Every 2 years	
	Behavioral Assessments Training Certification: • Motor Activity Log-14 (amount of use) • 10- Meter Walk Test • EQ-5D (EuroQol-5D) • Geriatric Depression Scale-15Q • NeuroQOL-Anxiety-8Q • Star Cancellation Test • Pain Visual Analog Scale	Every 1 year	
TMS Website (TMS Training-Only for TMS Operators)	Online TMS training modules & practical TMS training with healthy volunteers. (Note: After successful completion of online TMS training, TMS operators will receive a "green light" email confirming they can proceed with the practical TMS training).	Only 1 time	https://verifytraining.blogs.auckland.ac.nz/
	Recertification Quiz for TMSOs	Every 1 year	

Tips for Day 90 (Visit 6)

- At time of consent, confirm that participant is willing to come back for in-person Day 90 visit.
    - Day 90 visit can also be completed at the participant's home. The study will reimburse gas mileage for site staff (up to $40)
    - If pt is unable or unwilling to return for in-person Day 90 visit, then do **NOT** consent the participant.

- Ensure the **contact information form** is fully completed before the participant is discharged from the hospital.
    - This way, sites will have the information needed to recontact and provide reminders to the participant regarding Day 30 and Day 90 visits.
    - The contact information form is available in the Toolbox tab of WebDCU.



VERIFY

Contact Information

WebDCU™ Participant ID #:		Date of Informed Consent:	

Please record contact information for the Participant below.

Participant Contact Information		
Phone	**Email Address**	**Mailing Address**
Home: Work: Cell*: *Permission given to text: Yes No	*Permission given to email: Yes No	

Please record contact information for at least two additional people (e.g., next-of-kin).

Other Contact Information				
Contact Name	**Relationship to Participant**	**Phone**	**Email Address**	**Mailing Address**
	☐ Parent ☐ Sibling ☐ Friend ☐ Other:_____	Home: Work: Cell*: *Permission given to text: Yes No	*Permission given to email: Yes No	
	☐ Parent ☐ Sibling ☐ Friend ☐ Other:_____	Home: Work: Cell*: *Permission given to text: Yes No	*Permission given to email: Yes No	
	☐ Parent ☐ Sibling ☐ Friend ☐ Other:_____	Home: Work: Cell*: *Permission given to text: Yes No	*Permission given to email: Yes No	

- Before the participant is discharged from the hospital, sites can also look to see whether a standard of care (SOC) clinic visit can be scheduled in the same timeframe as Day 90. If so, you can discuss with participant and hopefully schedule it before they are discharged.
    - Can plan to complete Day 90 before or after SOC visit to help reduce burden on participant.

Subject Lost to follow-up

- Sites should attempt to contact the subject 3 different times by phone.
    - These times/dates should be documented in the electronic medical record or subject binder.

- If the subject is unable to be contacted by phone to schedule/complete day 30 or 90 visit, then the site should send a letter to the subject.
    - The **subject lost to follow-up letter** template has been cIRB approved and is available in the toolbox tab of WebDCU.

VERIFY

Follow Up Letter

(Date)

(Subject Name)

(Subject Address)

Dear (Subject Name),

This letter is being sent to you as a participant in the VERIFY study. According to our records, you were scheduled for a study visit on (enter date). Our attempts to reach you by telephone at [Insert telephone number(s)] on three separate occasions have been unsuccessful. Please contact us at [Insert telephone number(s) (and site contact name and title)] so that your study visit can be rescheduled either in-person or remotely.

If you have decided to discontinue your study participation, please notify us of your decision so that we can update our records [and conduct any final study procedures]. Your prompt attention is appreciated.

Sincerely,

[Insert PI name]

(PI Signature)

Science Corner

Optimal Intensity and Duration of Walking Rehabilitation in Patients With Chronic Stroke
A Randomized Clinical Trial

Pierce Boyne, PT, DPT, PhD, NCS; Sandra A. Billinger, PT, PhD; Darcy S. Reisman, PT, PhD; Oluwole O. Awosika, MD, MS; Sofia Buckley; Jamiah Burson, BS; Daniel Carl, PhD; Matthew DeLange, PT, DPT; Sarah Doren, PT, DPT; Melinda Earnest, PT, DPT, ATC; Myron Gerson, MD; Madison Henry, PT, DPT; Alli Horning, BS; Jane C. Khoury, PhD; Brett M. Kissela, MD, MS; Abigail Laughlin, BS; Kiersten McCartney, PT, DPT; Thomas McQuaid, BS; Allison Miller, PT, DPT, PhD, NCS; Alexandra Moores, MS; Jacqueline A. Palmer, PT, DPT, PhD; Heidi Sucharew, PhD; Elizabeth D. Thompson, PT, PhD, NCS; ErinWagner, MS; JaimieWard, MS; Emily PattonWasik, PT, DPT; Alicen A. Whitaker, PT, DPT; HenryWright, PT, DPT; Kari Dunning, PT, PhD

IMPORTANCE: For walking rehabilitation after stroke, training intensity and duration are critical dosing parameters that lack optimization.

OBJECTIVE: To assess the optimal training intensity (vigorous vs moderate) and minimum training duration (4, 8, or 12 weeks) needed to maximize immediate improvement in walking capacity in patients with chronic stroke.

DESIGN, SETTING, AND PARTICIPANTS: This multicenter randomized clinical trial using an intent-to-treat analysis was conducted from January 2019 to April 2022 at rehabilitation and exercise research laboratories. Survivors of a single stroke who were aged 40 to 80 years and had persistent walking limitations 6 months or more after the stroke were enrolled.

INTERVENTIONS: Participants were randomized 1:1 to high-intensity interval training (HIIT) or moderate-intensity aerobic training (MAT), each involving 45 minutes of walking practice 3 times per week for 12 weeks. The HIIT protocol used repeated 30-second bursts of walking at maximum safe speed, alternated with 30- to 60-second rest periods, targeting a mean aerobic intensity above 60%of the heart rate reserve (HRR). The MAT protocol used continuous walking with speed adjusted to maintain an initial target of 40% of the HRR, progressing up to 60% of the HRR as tolerated.

MAIN OUTCOMES AND MEASURES: The main outcome was 6-minute walk test distance. Outcomes were assessed by blinded raters after 4, 8, and 12 weeks of training.

RESULTS: Of 55 participants (mean [SD] age, 63 [10] years; 36 male [65.5%]), 27 were randomized to HIIT and 28 to MAT. The mean (SD) time since stroke was 2.5 (1.3) years, and mean (SD) 6-minute walk test distance at baseline was 239 (132) m. Participants attended 1675 of 1980 planned treatment visits (84.6%) and 197 of 220 planned testing visits (89.5%). No serious adverse events related to study procedures occurred. Groups had similar 6-minute walk test distance changes after 4 weeks (HIIT, 27m[95%CI, 6-48 m]; MAT, 12m[95%CI, −9 to 33 m]; mean difference, 15m[95%CI, −13 to 42 m]; P = .28), but HIIT elicited greater gains after 8 weeks (58m[95%CI, 39-76m] vs 29m[95%CI, 9-48 m]; mean difference, 29m [95%CI, 5-54 m]; P = .02) and 12 weeks (71m[95%CI, 49-94m] vs 27m[95%CI, 3-50 m]; mean difference, 44m[95%CI, 14-74 m]; P = .005) of training; HIIT also showed greater improvements than MAT on some secondary measures of gait speed and fatigue.

CONCLUSIONS AND RELEVANCE: These findings show proof of concept that vigorous training intensity is a critical dosing parameter for walking rehabilitation. In patients with chronic stroke, vigorous walking exercise produced significant and meaningful gains in walking capacity with only 4 weeks of training, but at least 12 weeks were needed to maximize immediate gains.

JAMA Neurology

Webinars

- PI/CRC webinars occur on the 3rd Monday of each month, 4pm-5pm EDT. **Next PI/CRC webinar is on 05.15.2023.**
  - https://ucincinnati.zoom.us/j/96525424408 Meeting ID: 965 2542 4408
- CRC webinars occur on the 4th Tuesday of each month, 12pm-1pm EDT. **Next CRC webinar is on 05.23.2023**
  - https://ucincinnati.zoom.us/j/93360687517 Meeting ID: 933 6068 7517

Study Contact Information

CIRB- Regulatory contacts:

Betsy Casillo betsy.casillo@advarra.com 513.619.1679
Kalli Beasley beasleki@ucmail.uc.edu

CTA contact:

Aimee Nance nanceae@ucmail.uc.edu 513.558.6566
Sasha Simms simmssc@ucmail.uc.edu 513.558.3924

All other study questions:

Lisa Mundo mundokl@ucmail.uc.edu

Race to Activation Tracker

Site Name	CTA Executed	CIRB Approved	DOA Approved	Investigator agreement form's uploaded	TMS Shipping Address entered	TMS Machine obtained	At least 1 TMSO online training Completed	Greenlighted to start TMS HV Training	Uploaded TMS HV data to RedCAP	TMS HV Training Completed for at least 1 TMSO	TMS Technique Check	MRI Phantom Approved	All WebDCU Documents uploaded	Site Activation Meeting Completed	Site Activated
Harborview Medical Center															
Ronald Reagan UCLA Medical Center															
Montefiore Medical Center															
University of Texas Southwestern Medical Center															
San Francisco General Hospital															
Houston Methodist Hospital															
Mount Sinai Hospital															
OSU Wexner Medical Center															
Lahey Hospital & Medical Center															
Pennsylvania Hospital															
Prisma Health Richland Hospital															
Penn State Hershey Medical Center							0								
University of Iowa Hospitals & Clinics															
Froedtert & Medical College of Wisconsin															
University of Rochester Strong Memorial Hospital							0								
Corewell Heath Butterworth Hospital							0								