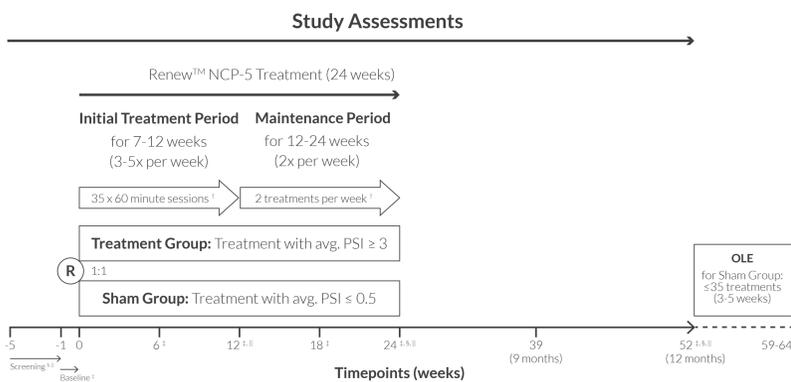


## Background

Vascular dementia and Alzheimer's disease (AD) share an association with hemodynamic risk factors. Exercise can improve cerebral blood flow (CBF), which is associated with a decrease in cognitive decline. However, patients with AD or mild cognitive impairment (MCI) may have limited exercise capacity due to age-related physical restrictions. Renew™ NCP-5 is an FDA-cleared, external counterpulsation (ECP) device which improves coronary and peripheral vascular hemodynamics by sequential compression and decompression of vascular beds in synchrony with the cardiac cycle (Figure 1), and is currently used to treat patients with chronic stable angina. ECP may provide the same hemodynamic benefit for cerebral perfusion and cognitive function.

## Methods

- **Classification:** Pivotal
- **Design:** Single-blind
- **Randomization:** 1:1 ECP Treatment: Sham Therapy  
*Sham therapy will crossover to open label at completion of follow-up period.*
- **Total Sites:** 16 (13 USA, 1 Singapore, 1 Ireland, 1 UK)
- **Total Patients:** 100-250
- **Primary Endpoint:** Avg. change in vADAS-cog at weeks 12, 18, and 24 from baseline
- **Exploratory Endpoints:** Imaging measures of hippocampal volume and cerebral blood flow
- **Study Enrollment:** November 2018–January 2020 (expected)



## Results

We hypothesise that Renew™ NCP-5 therapy will lead to effective treatment or delay of cognitive impairment in study participants.

## Learning Objectives

- Evaluate the efficacy and safety of Renew™ NCP-5 external counterpulsation as a therapeutic option for patients with MCI due to Alzheimer's disease or mild dementia of Alzheimer's type.
- Establish an understanding of the potential role of external counterpulsation with Renew™ NCP-5 in addressing hemodynamic risk factors associated with cognitive decline.
- Test whether treatment with Renew™ NCP-5 can delay or reduce cognitive impairment in patients with MCI due to AD or mild dementia of the Alzheimer's type.

## Conclusion

This pivotal study aims to evaluate the efficacy and safety of Renew™ NCP-5 as a therapeutic option for patients with MCI due to AD or MD of Alzheimer's type.

## Treatment of Mild Cognitive Impairment due to Alzheimer's Disease or Mild Dementia of the Alzheimer's Type: Design and Rationale of the Randomized Pivotal Study of Renew™ NCP5

Patrick M. Moriarty, Lauryn K. Gorby, Eric Ecklund-Johnson, William Brooks, Rebecca Lepping, David H. Salat, Jonathan Helfgott, Jeffrey M. Burns

# Renew™ NCP-5 External Counterpulsation for the Treatment of Alzheimer's Disease and Mild Cognitive Impairment: Pivotal trial design and rationale



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## Tables & Figures

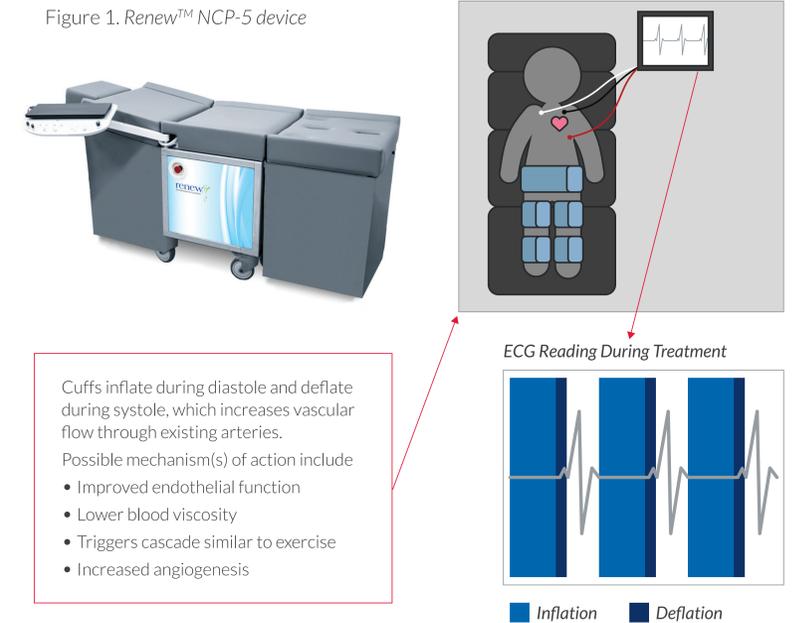


Table 1. Key Inclusion and Exclusion Criteria

Key Inclusion Criteria
55–85 years of age
Able to provide consent or have legally authorized representative/caregiver who can provide consent
Have a clinical diagnosis consistent with 2011 NIA-AA "core clinical criteria" guidelines for: (i) The diagnosis of dementia due to Alzheimer's disease or (ii) The diagnosis of mild cognitive impairment due to Alzheimer's disease
Stable medications for past 30 days and plan to remain on stable medications for treatment of chronic conditions
Subject should have a caregiver, study partner, or companion who may conduct the assessment over the phone if they don't accompany the participant
Must have the potential to improve by $\geq 2$ points in the vADAS-Cog

Key Exclusion Criteria
Unwilling or unable to participate in study procedures
Weight $> 297$ lbs or $> 135$ kg
Major confounding neurodegenerative or psychiatric disorder unrelated to this study
Active or history of cerebral hemorrhage
Evidence of any of the following of the 2011 NIA-AA guidelines on the diagnosis of dementia due to Alzheimer's disease:
• Substantial concomitant cerebrovascular disease
• Core features of dementia with Lewy bodies other than dementia itself
• Prominent features of behavioral variant frontotemporal dementia
• Prominent features of semantic variant primary progressive aphasia or nonfluent/agrammatic variant primary progressive aphasia
• Evidence for another concurrent, active neurological disease, non-neurological medical comorbidity, or use of medication that could have a substantial effect on cognition
In the opinion of the investigator, any current clinically-significant systemic illness or medical condition that is likely to result in deterioration of the subject's condition, affect the subject's safety during the study, or be incompatible with performance of the study procedures
Current use of medications that in the investigator's judgement are incompatible with the study goals
Presence of any of the contraindications for using the Renew™ NCP-5 device
Unwilling or unable to maintain stable exercise regimen throughout the trial