# The Impact of Serial Remote Ischemic Conditioning on Dynamic Cerebral Autoregulation in Healthy Adults

**The First Hospital of Jilin University**

**NCT 04899362**

**April 10th, 2021**

## Background

Remote ischemic conditioning (RIC) refers to an intervention that offers remote tissues and organs a resistance capacity to ischemia/reperfusion injury through small doses of reversible episodes of ischemia and reperfusion that activate neurogenic pathways, humoral factors, and the immune system. Recent studies have demonstrated that RIC could increase cerebral perfusion, promote hematoma resolution, facilitate recovery of nerve function, and improve the clinical prognosis of patients with cerebrovascular diseases. However, the mechanism is not fully elucidated. Our previous study found that dynamic cerebral autoregulation (dCA), an important indicator of cerebrovascular function which related to the prognosis of cerebrovascular disease, was improved after once round of RIC; however, the exact effect of serial RIC on dCA was unclear. Additionally, the dCA alteration period after serial RIC remains unknown. Solving these problems will help us to formulate detailed strategies for the safe and effective application of RIC in patients with cerebrovascular disease.

Hence, the objective of this study was to observe the exact impact of serial RIC on dCA. This included determining when dCA was increased during serial RIC and the duration of the effect of serial RIC.

## Eligibility Criteria

**Inclusion Criteria:**

- age from 18 to 50, both genders
- willing to participate in follow-up visits

Exclusion Criteria:

- current or having a history of chronic physical diseases or mental diseases
- suffering from infectious diseases in late one month
- pregnant and lactating women
- smoking or drinking
- inability to cooperate sufficiently to complete the dCA examination

## Arms and Interventions

**Experimental:** RIC group

RIC was induced by 4 cycles of extremities ischemia (5-minute blood-pressure cuff inflation to 200 mm Hg, followed by 5-minute cuff deflation).All subjects will take 14 RIC intervention, blood collection and 10 dCA measurements.

**Device:** BB-RIC-D1/LAPUL Medical Devices Co, Ltd, China

The RIC consisted of 4 cycles of extremities ischemia (5-minute blood pressure cuff inflation to 200 mm Hg, followed by 5-minute cuff deflation). The tourniquets were applied to one side upper arm. This intervention was undertaken twice a day for 7 days.

**Procedure/Surgery:** Intravenous blood collection

Nurses will collect intravenous blood 3ml four times (at baseline and the first, seventh and eighth day of the study). The blood samples will be stored for laboratory test.The blood samples only use for the trial.

**Device:** dCA measurement

Serial measurements of dCA were performed at 10 days, baseline, 1st, 2ed, 4th, 7th, 8th, 10th, 14th, 21th and 35th of the study.The continuous ABP was measured non-invasively using a servo-controlled plethysmograph (Finometer Pro, the Netherlands) at the middle finger. Two 2 MHz transcranial Doppler probe was used to measure continuous cerebral blood flow velocity (CBFV) simultaneously in the bilateral middle cerebral arteries at a depth of 45-60 mm Endtidal CO2 was monitored using a capnograph (MultiDop X2, DWL, Sipplingen, Germany). The probes were placed over temporal windows and fixed with a customized head frame. CBFV and continuous arterial blood pressure were recorded simultaneously from each subject in the supine position for 10 minutes. All data were recorded for further assessment and analysis.

## Outcome Measures

**Primary Outcome Measure:**

Dynamic Cerebral Autoregulation Parameter: Phase Difference(PD) in Degree [Time Frame: 36 days]

Low PD at a low frequency band indicates impairment of autoregulation, as it suggests that cerebral blood flow velocity follows the changes in arterial blood pressure with a short delay.

**Secondary Outcome Measures:**

Dynamic Cerebral Autoregulation Parameter: Gain in cm/s/mmHg [Time Frame: 36 days]

High gain at the same frequency band is also considered an indicator of compromised autoregulation for passively transferring the amplitude of arterial blood pressure to cerebral blood flow velocity.

## Statistical Analysis Plan

The data were analyzed using the Statistical Program for Social Sciences version 26.0 (SPSS; IBM, West Grove, PA). The distribution of data was assessed using a one-sample Kolmogorov–Smirnov test. Normally distributed continuous variables are shown as mean±standard deviation, and non-normally distributed data are presented as the median and interquartile range. Repeated measurement analysis of variance was used to test the differences in the observed dCA values on different days. Two general linear models were used for the repeated measurements. To observe when dCA was increased during serial RIC, dCA parameters at baseline, d1, d2, d4, and d7 were included. To assess the duration of the effect of serial RIC, baseline, d7, d8, d10, d14, d21, and d35 were included. To compare the difference between the baseline and other days, a paired t-test was used. The changes in blood biomarker levels were analyzed by Friedman test. Baseline, d1 and d7, and baseline, d7 and d8 were compared respectively. A two-tailed p-value $< 0.05$ was considered statistically significant.