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# Photobiomodulation therapy mitigates cardiovascular aging and improves survival

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## Abstract

**Background:** Photobiomodulation (PBM) therapy, a form of low-dose light therapy, has been noted to be effective in several age-associated chronic diseases such as hypertension and atherosclerosis. Here, we examined the effects of PBM therapy on age-associated cardiovascular changes in a mouse model of accelerated cardiac aging.

**Methods:** Fourteen months old Adenylyl cyclase type VIII (AC8) overexpressing transgenic mice (n = 8) and their wild-type (WT) littermates (n = 8) were treated with daily exposure to Near-Infrared Light

(850 nm) at 25 mW/cm<sup>2</sup> for 2 min each weekday for a total dose of 1 Einstein (4.5 pJ/cm<sup>2</sup> or fluence 3 J/cm<sup>2</sup>) and compared to untreated controls over an 8-month period. PBM therapy was administered for 3.5 months (Early Treatment period), paused, due to Covid-19 restrictions for the following 3 months, and restarted again for 1.5 months. Serial echocardiography and gait analyses were performed at monthly intervals, and serum TGF-β1 levels were assessed following sacrifice.

**Results:** During the Early Treatment period PBM treatments: reduced the age-associated increases in left ventricular (LV) mass in both genotypes ( $p = 0.0003$ ), reduced the LV end-diastolic volume (EDV) in AC8 ( $p = 0.04$ ); and reduced the left atrial dimension in both genotypes ( $p = 0.02$ ). PBM treatments substantially increased the LV ejection fraction ( $p = 0.03$ ), reduced the aortic wall stiffness ( $p = 0.001$ ), and improved gait symmetry, an index of neuro-muscular coordination ( $p = 0.005$ ). The effects of PBM treatments, measured following the pause, persisted. Total TGF-β1 levels were significantly increased in circulation (serum) in AC8 following PBM treatments ( $p = 0.01$ ). We observed a striking increase in cumulative survival in PBM-treated AC8 mice (100%;  $p = 0.01$ ) compared to untreated AC8 mice (43%).

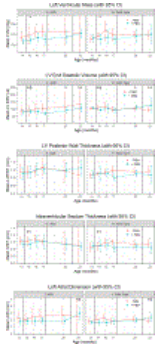
**Conclusion:** PBM treatment mitigated age-associated cardiovascular remodeling and reduced cardiac function, improved neuromuscular coordination, and increased longevity in an experimental animal model. These responses correlate with increased TGF-β1 in circulation. Future mechanistic and dose optimization studies are necessary to assess these anti-aging effects of PBM, and validation in future controlled human studies is required for effective clinical translation.

**Keywords:** AC8; TGF-β1; aging; heart; mice; photobiomodulation.

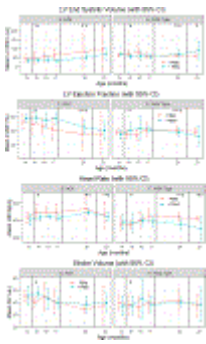
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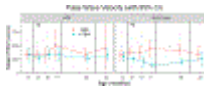
## Figures



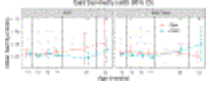
**Figure 1:** Mean Echocardiography parameters for heart...



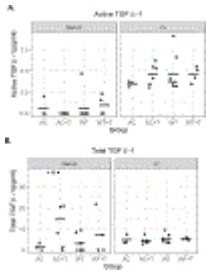
**Figure 2:** Mean Echocardiography parameters for heart...



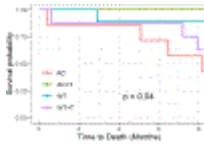
**Figure 3:** Mean parameters for Aortic wall...



**Figure 4:** Mean parameters for Gait by...



**Figure 5:** TGF-β1 levels were assessed with...



**Figure 6:** Kaplan-Meier cumulative survival curves. There...

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