LIGHTSITE I: A Double-Masked, Randomized, Sham-Controlled Study with Photobiomodulation in Dry Age-Related Macular Degeneration Subjects

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Background

Age-related macular degeneration (AMD) is the leading contributor to vision loss and blindness in the developed world. There are no current treatments for the dry form except lifestyle modification and anti-oxidant vitamins. There is a growing body of evidence to support Photobiomodulation (PBM) in the 500-1000 nm spectrum, as a novel treatment for dry AMD. The purpose of the LIGHTSITE I study is to assess the functional and anatomical benefits of PBM using the LT-300 in a randomized, sham-controlled pilot study. We report on the interim analysis of measures of ETDRS best corrected visual acuity (BCVA) and Contrast Sensitivity (CS) as well as changes in retinal drusen volume and thickness and Quality of Life (QOL).

Methods

The LIGHTSITE I study enrolled 30 dry AMD subjects. Subjects were randomized (1:1) and received either PBM or sham treatment over 3-4 weeks with a second series 6 months from baseline (BL). Data are presented from the interim analysis out to 3 months following the initial series of PBM treatment. LT-300 uses a multi-wavelength treatment comprised of 590 nm, 670 nm and 850 nm applied to the subjects eyes for a total of 4-5 minutes per treatment per eye.

Statistical Analysis

The Sponsor and Investigators remain masked to individual treatment assignments and only group data is provided. Change from baseline is the preferred outcome metric and a linear mixed effects model by ranks was used for the statistical analysis. Some data was unavailable at the 2 or 3 month timepoints so group mean data may not reflect equal numbers at each visit. Data were compared to a previous study (TORPA II) that investigated PBM in subjects with dry AMD (*Merry et al., Acta Ophthalmologica, 2016).*

Table 1. Patient comparison between TORPA II and LIGHTSITE I studies.

	TORPA II	LIGHTSITE I
Patients (n)	24	30
Gender [female, male]	15, 9	18, 12
Total # eyes	42	46
Mean Age [range]	78 [66-95]	76 [52-90]
VA Letter Score	86	71.86 (Sham) 74 (PBM)

Results

Dry AMD AREDs Category Comparison

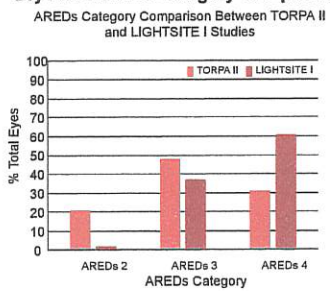


Figure 1. The AREDs classification for dry AMD subjects were compared between the TORPA II and LIGHTSITE I studies. Compared to TORPA II, LIGHTSITE I enrolled higher numbers of AREDs 4 subjects indicating more advanced stages of dry AMD.

Visual Acuity

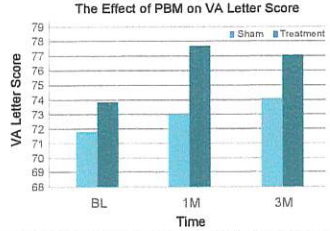


Figure 2. Subjects showed an increase in VA letter score out to 3 months following PBM from BL, ($p < 0.05$ paired t-test). A positive trend in VA change from BL in the PBM group versus the sham treatment group was seen, (Linear mixed effects model using ranks, $p = 0.079$).

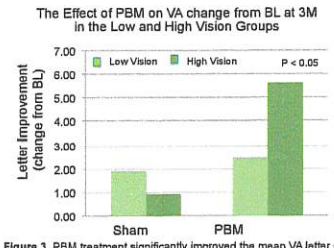


Figure 3. PBM treatment significantly improved the mean VA letter score in high vision (HV) subjects compared to sham at the 3M timepoint. Subjects were divided into either high or low vision groups depending on whether their BL vision was above or below the mean BL VA score (~74) for each treatment group, (Linear mixed effects model using ranks, $p<0.05$). No significant VA letter score benefit was seen in the LV patients.

Contrast Sensitivity

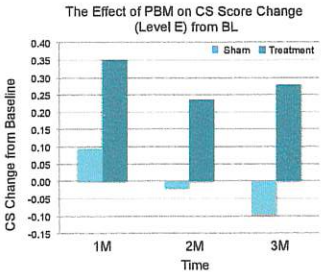


Figure 4. There was a statistically significant effect of PBM treatment on the CS score change of Level E (18 CPD) of analysis compared to BL, (Linear mixed effects model using ranks, $p<0.05$).

Visual Function Questionnaire-25

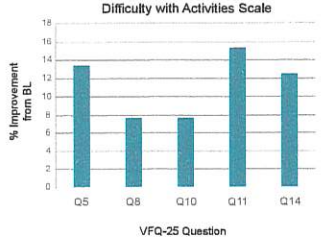


Figure 5. VFQ-25 overall composite score showed a statistically significant improvement with PBM ($p = 0.003$). Subjects showed a statistically significant improvement on Q8 and Q10 and 10-15% NS improvement in Q5, Q11 and Q14. Paired t-test, $p < 0.05$.

VFQ-25 questions [Difficulty with Daily Activity]

Q5: *How much difficulty do you have reading ordinary print in newspapers?*
Q8: *How much difficulty do you have reading street signs or the names of stores?*
Q10: *Because of your eyesight, how much difficulty do you have noticing objects off to the side while you are walking along?*
Q11: *Because of your eyesight, how much difficulty do you have seeing how people react to things you say?*
Q14: *Because of your eyesight, how much difficulty do you have going out to see movies, plays, or sports events?*

Optical Coherence Tomography

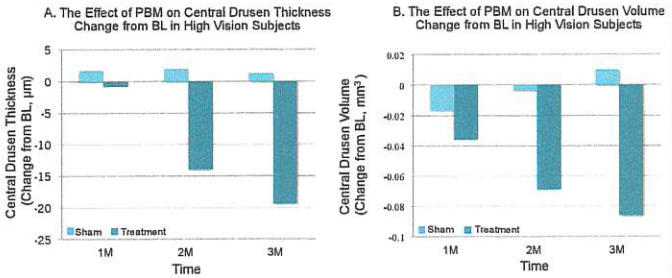
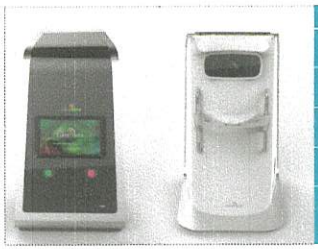


Figure 6. There was a statistically significant effect of PBM treatment on central drusen thickness (A) and central drusen volume (B) in the high vision subgroup compared to BL, (Linear mixed effects model using ranks, $p<0.05$). The development of drusen is a hallmark feature of dry AMD and significant reductions in drusen volume and thickness demonstrate disease-modifying effects.

LT-300 Light Delivery System



	Specifications
Light Source	LED
590 nm	4 mW/cm²
670 nm	50 mW/cm²
850 nm	0.6 mW/cm²
Treatment Exposure	Total of 250 sec/eye

Figure 7. Illustration of the LT-300 Light Delivery System designed for the Ophthalmology office setting.

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Summary & Conclusions

LIGHTSITE I Comparisons to TORPA II

- More dry AMD subjects with AREDs category 4 were enrolled in LIGHTSITE I
- Dry AMD subject's VA BL was more compromised in LIGHTSITE I versus TORPA II

LIGHTSITE I Conclusions:

Dry AMD patients treated with PBM demonstrated functional and anatomical improvements following PBM treatments. Over 42% of the treated dry AMD subjects had >1 line improvement in VA at 3 months. Moreover, patients classified as High Vision demonstrated enhanced PBM improvements compared to Low Vision patients suggesting PBM may be more effective in patients that are treated early. PBM improved contrast sensitivity and demonstrated reduced central drusen volume and thickness. Finally, quality of life measures were improved in subjects treated with PBM as determined by the VFQ-25 validated questionnaire. No device related adverse effects were seen. These LIGHTSITE I interim results support further clinical testing of PBM as a non-invasive treatment for dry AMD.

Final Analysis of LIGHTSITE I: A Double-Masked, Randomized, Sham-Controlled Study with Photobiomodulation in Dry Age-Related Macular Degeneration Subjects

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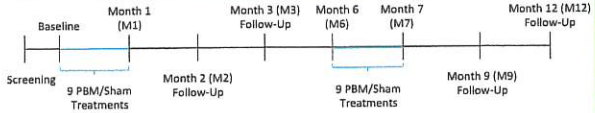
Background

Age-related macular degeneration (AMD) is the leading contributor to vision loss and blindness in adults over the age of 65. Pathological changes such as development of drusen are characteristic of the disease and contribute to visual impairment. There are no approved treatments for dry AMD other than vitamin supplementation. There is a growing body of evidence to support Photobiomodulation (PBM) in the 500-1000 nm spectrum as a novel treatment for dry AMD. PBM uses wavelengths of light to stimulate beneficial cellular activities with proven efficacy on anatomical and clinical endpoints. The purpose of this study was to evaluate PBM as a new treatment option in eyes with dry AMD.

Methods



The LIGHTSITE I study enrolled 30 dry AMD subjects. Subjects were randomized (1:1) and received either 9 PBM or sham treatments with the LT-300 device over 3-4 weeks with a second series 6 months from baseline (BL). Data presented include the topline analysis with further analyses being conducted. The LT-300 uses a multi-wavelength treatment comprised of 590 nm, 670 nm and 850 nm wavelengths applied to the subjects eyes for a total of 4-5 minutes per treatment per eye.

Statistical Analysis

Change from BL is the preferred outcome metric. Linear mixed effects models by ranks and Wilcoxon signed rank tests were used for the statistical analysis. Certain data may not be available for all time points so group mean data may not reflect equal numbers at each visit.

	PBM-Treated	Sham-Treated
Patient, (n)	15	15
Total # eyes, (n)	24	22
Mean Age, (yrs)	78.4 (72-88)	73.6 (52-90)
Gender, (M, F)	8, 7	4, 11
Duration of AMD, (yrs)	10.2 (3-28)	10.1 (2-39)
Mean BL VA Letter Score	74	71.86

This work was funded in part by the National Institutes of Health, National Eye Institute Grant # 3R43EY025508-0151

Results

Central Drusen Volume

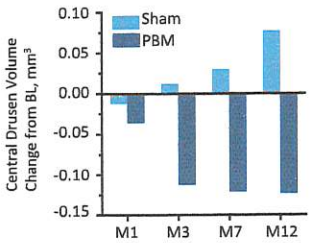


Figure 1. There was a significant effect of PBM treatment on drusen volume compared to BL, (Linear mixed effects, p = 0.05), suggesting disease-modifying effects.

AREDS Category Distribution

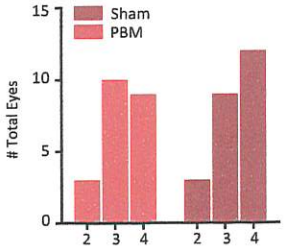
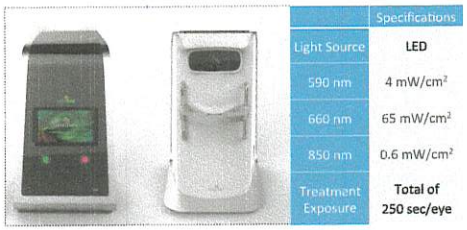


Figure 2. The AREDS categories were compared between PBM and Sham groups demonstrating similar distribution and disease status between groups.



	Specifications
Light Source	LED
590 nm	4 mW/cm²
660 nm	65 mW/cm²
850 nm	0.6 mW/cm²
Treatment Exposure	Total of 250 sec/eye

Figure 3. Illustration of the LT-300 Light Delivery System designed for the Ophthalmology office setting.

Contrast Sensitivity

Comparison	# Eyes	Group	P value	Mean Change
BL vs. M1	24	PBM	0.003*	0.35
BL vs. M1	22	Sham	0.184	0.09
BL vs. M6	23	PBM	0.032*	0.30
BL vs. M6	21	Sham	0.831	-0.04
BL vs. M7	23	PBM	0.043*	0.31
BL vs. M7	21	Sham	0.378	0.05
BL vs. M12	23	PBM	0.026*	0.31
BL vs. M12	20	Sham	0.663	0.01

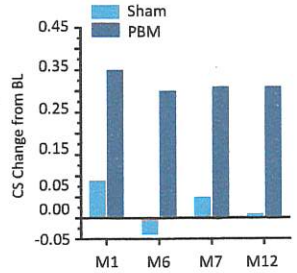


Table 1 and Figure 4. There was a significant effect of PBM treatment on Contrast Sensitivity (CS) score change of Level E (18 CPD) compared to BL, (Wilcoxon signed rank, p<0.05). The table indicates relevant p values and mean changes from BL.

Visual Acuity

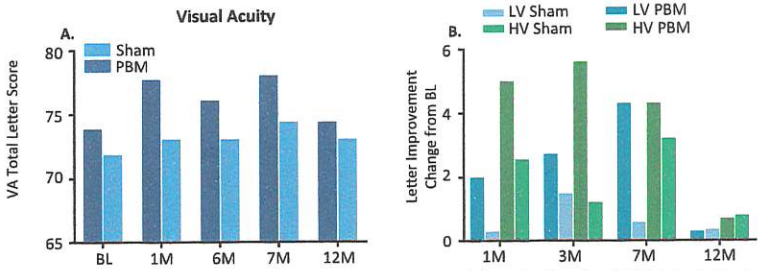


Figure 5A. Subjects showed an increase in VA letter score following PBM treatment. The largest benefit was immediately following treatment at 1 and 7 months (Wilcoxon signed rank p < 0.05). **5B.** Subjects were stratified into either high or low vision groups depending on whether their BL vision was above or below the median BL VA score 76.5. Improvements were seen up to 3 months following treatment in both the high and low vision subjects.

Summary and Conclusions

The LIGHTSITE I study investigated PBM in Dry AMD patients on both anatomical and clinical outcomes in a double masked, randomized, sham-controlled design. Dry AMD patients treated with PBM demonstrated both functional and anatomical improvements following PBM treatment. PBM-treated patients showed reductions in drusen volume and thickness demonstrating potential disease-modifying effects on key anatomical disease features. Improvements in Contrast Sensitivity and Visual Acuity were seen immediately after the 3 weeks of treatment and were maintained out to 3 to 6 months. PBM Retreatment times of 6 months are suggested to maintain clinical outcome benefits. No device related adverse effects were seen in the study. LIGHTSITE I had a total of 21 adverse events and 1 serious adverse event that were reported. PBM therapy may represent an early and cost-effective, non-invasive treatment for dry AMD patients. These results strongly support further clinical testing of PBM as a non-invasive treatment for dry AMD patients.