Light for Improving Sleep and Treating Cancer Fatigue and Depression: A Field Study

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Acuity Brands Lighting

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Questions related to specific materials, methods, and services will be addressed at the conclusion of this presentation.

Learning Objectives

At the end of the this course, participants will be able to:

1. Learn about basics of circadian system and how circadian disruption may affect health and well being
2. Learn about lighting characteristics affecting circadian rhythms and how they differ from current lighting standards for visibility
3. Discuss research using light to treat cancer fatigue in homes and healthcare environments
4. Discuss the fixture specifications and challenges associated with developing and installing circadian lighting in hospital facilities

LEDucation

Mariana G. Figueiro, PhD, FIES

Lighting Research Center
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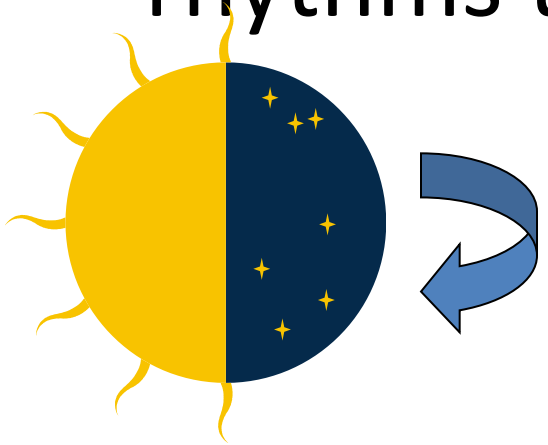
Circadian system

- Plants and animals exhibit patterns of behavioral and physiological changes over an approximately 24-hour cycle that repeat over successive days—these are circadian rhythms

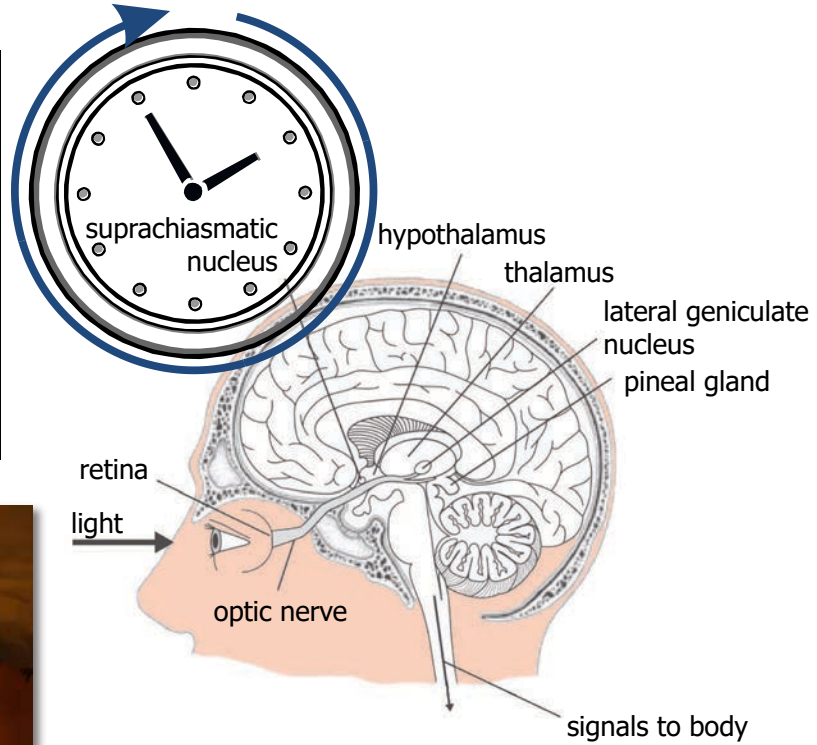
  circa = about; dies = day

- Circadian rhythms are influenced by exogenous and endogenous rhythms

Light is the primary synchronizer of circadian rhythms to local position on Earth



The natural, 24-hour, light-dark cycle



Adapted from National Library of Medicine image, 2007 (public domain)

Light is the primary synchronizer of circadian rhythms to local position on Earth

…also the major disruptor

Circadian disruption and health

- Circadian disruption has been associated with:
  - **Poor sleep, poor performance and high stress**
    - Eismann, E. A., Lush, E., & Sephton, S. E. (2010). Psychoneuroendocrinology, 35(7), 963-976.
    - Gumenyuk, V., Howard, R., Roth, T., Korzyukov, O., Drake, C.L. (2014) Sleep. March 1; 37(3): 545–556.
  - **Increased anxiety and depression**
    - Du-Quiton, J., Wood, P. A., Burch, J. B., Grutsch, J. F., Gupta, D., Tyer, K., . . . Reynolds, J. L. (2010). Psycho-Oncology, 19(2), 180-189.
  - **Increased smoking**
    - Kageyama, T., Kobayashi, T., Nishikido, N., Oga, J., & Kawashima, M. (2005). Industrial Health, 43(1), 133-141.
  - **Cardiovascular disease**
    - Young, M. E., & Bray, M. S. (2007). Sleep Medicine, 8(6), 656-667.
    - Maemura, K., Takeda, N., & Nagai, R. (2007). Journal of Pharmacological Sciences, 103(2), 134-138.
  - **Type 2 diabetes**
    - Kreier, F., Kalsbeek, A., Sauerwein, H. P., Fliers, E., Romijn, J. A., & Buijs, R. M. (2007). Experimental Gerontology, 42(1), 22-27.
  - **Higher incidence of breast cancer**
    - Schernhammer, E. S., Laden, F., Speizer, F. E., Willett, W. C., Hunter, D. J., Kawachi, I., & Colditz, G. A. (2001). Journal of the National Cancer Institute, 93(20), 1563-1568.
    - Hansen, J. (2006). Cancer Causes & Control, 17(4), 531-537.

Lighting affects three systems: Visual + non-visual + message

Amount
Spectrum
Distribution
Timing
Duration
Appearance
Visual System
Visual Performance
Performance, Well-being, Satisfaction, and Comfort
Culture, Experience, Expectations
Alerting Effects
Non-Visual Systems
Phase Shift
Amount
Spectrum
Distribution
Timing
Duration

LEDucation

Our working hypothesis

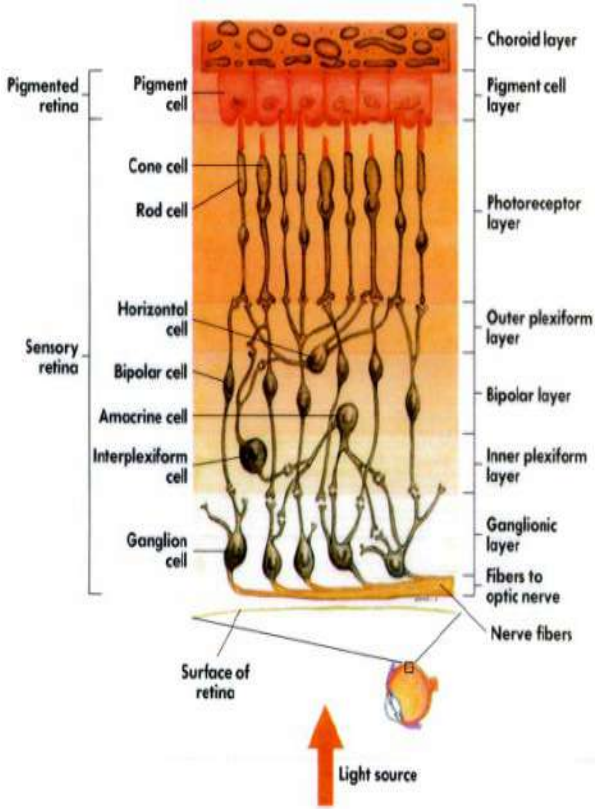
- Tailored lighting intervention designed to promote circadian entrainment can improve sleep, mood, and behavior in various populations
  - Sufferers from seasonal depression
  - Office workers
  - Submariners
  - Teenagers with delayed sleep onset
  - Older adults with early sleep onset
  - Alzheimer's disease and related dementia patients
  - Cancer patients experiencing fatigue and sleep disturbances

Specification and measurement of light stimulus

- Lighting intervention is based on known lighting characteristics affecting the circadian system outputs (e.g., biomarkers, sleep/wake cycle, self reports)
  - Amount, spectrum, timing, duration and light history
- Need to measure actual light exposure experienced by clinical populations
  - “Measurement is the first step that leads to control and eventually to improvement. If you can’t measure something, you can’t understand it. If you can’t understand it, you can’t control it. If you can’t control it, you can’t improve it.” (H. James Harrington)

Specification of light stimulus
"Melanopic lux" is NOT a correct metric

- Intrinsically photosensitive retinal ganglion cells – ipRGCs (Berson et al. 2002)
  - Located in the ganglion cell layer
  - Peak spectral sensitivity at about 480-484 nm
    - Melanopsin is believed to be the photopigment in the ipRGCs
  - Receives and sends "processed information," including spectral opponency formed at bipolar cells, to the biological clock
  - Peak sensitivity of the human circadian system is at 460 nm, *not* 480 nm



Berson, D., Dunn, F., Takao, M. (2002). Phototransduction by retinal ganglion cells that set the circadian clock. *Science*, 295, 1070-1073.

All photoreceptors (rods, cones and ipRGCs) participate in circadian phototransduction

Published in final edited form as:
Nature. 2003 July 3; 424(6944): 76–81. doi:10.1038/nature01761.

Melanopsin and rod–cone photoreceptive systems account for all major accessory visual functions in mice

S. Hattar*, R. J. Lucas†, N. Mrosovsky‡, S. Thompson†, R. H. Douglas§, M. W. Hankins†, J. Lem‖, M. Biel¶, F. Hofmann#, R. G. Foster†, and K.-W. Yau*

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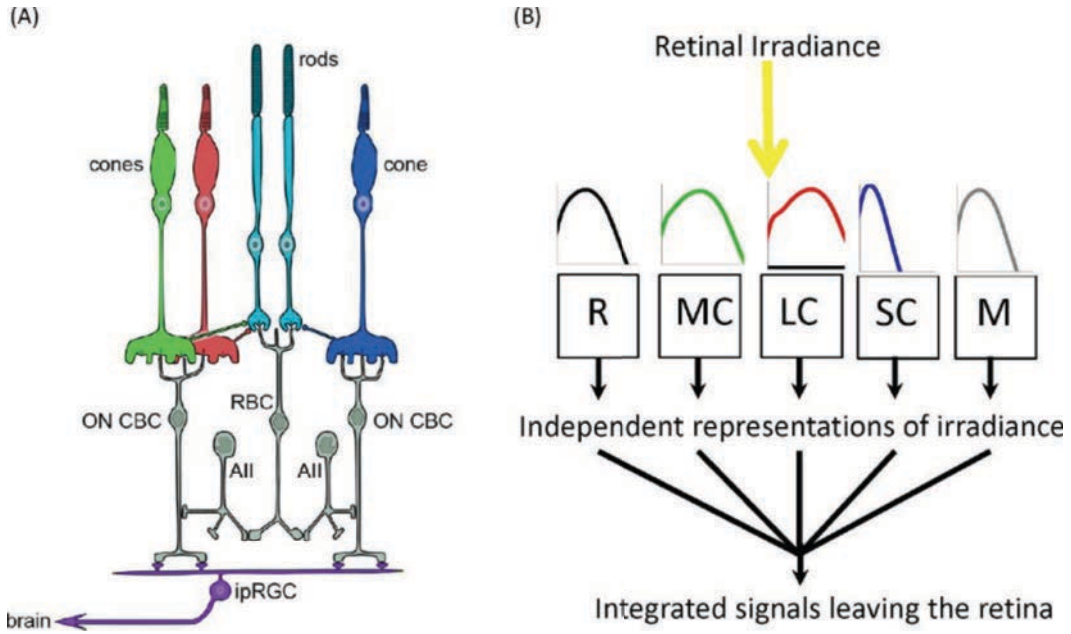
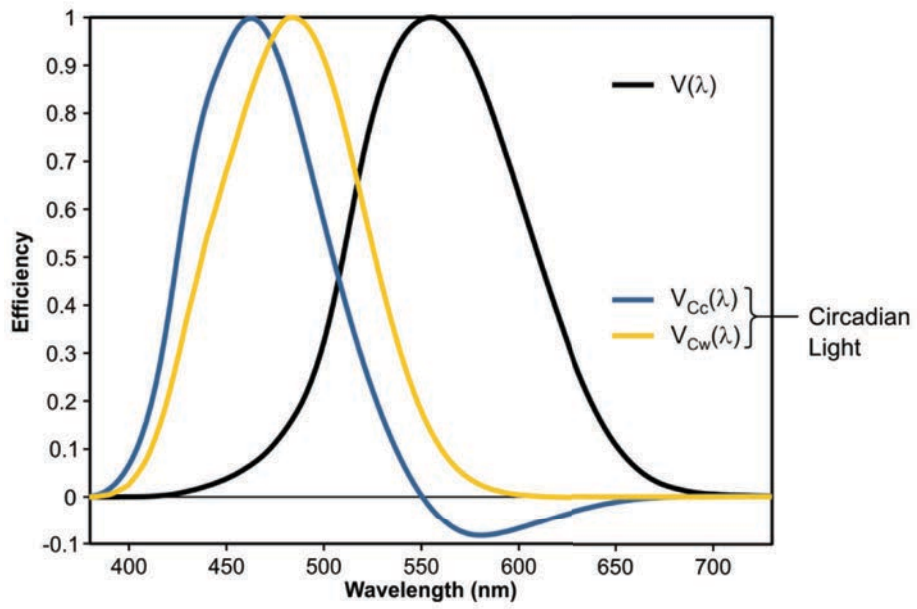


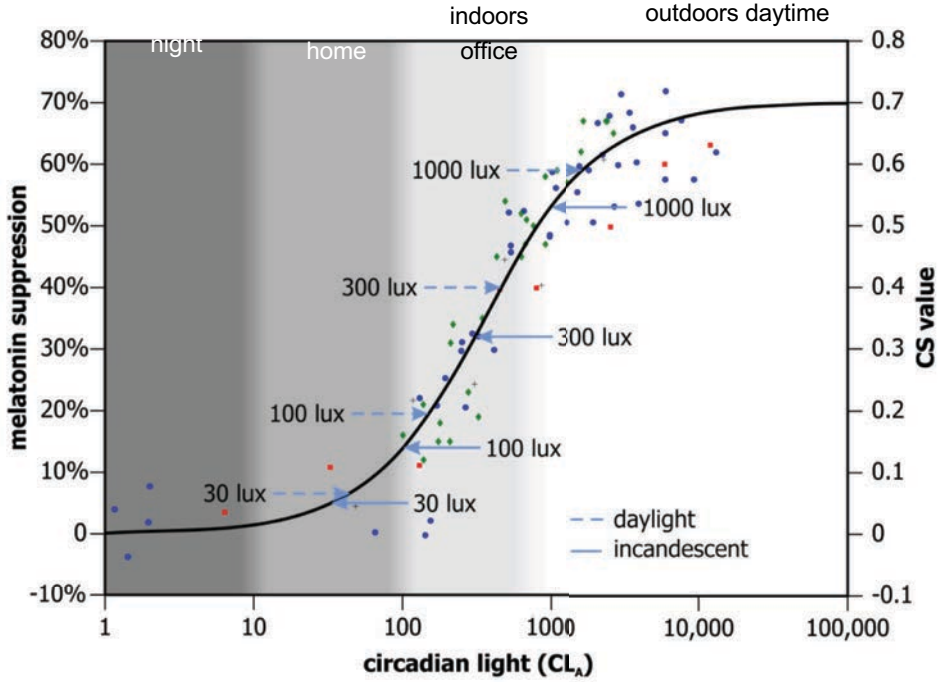
Figure from Lucas et al., 2014
Trends Neurosci. 2014 Jan; 37(1): 1–9.

Specification of the light stimulus
Circadian light (CLA) and circadian stimulus (CS)

- Spectral sensitivity



- Absolute sensitivity

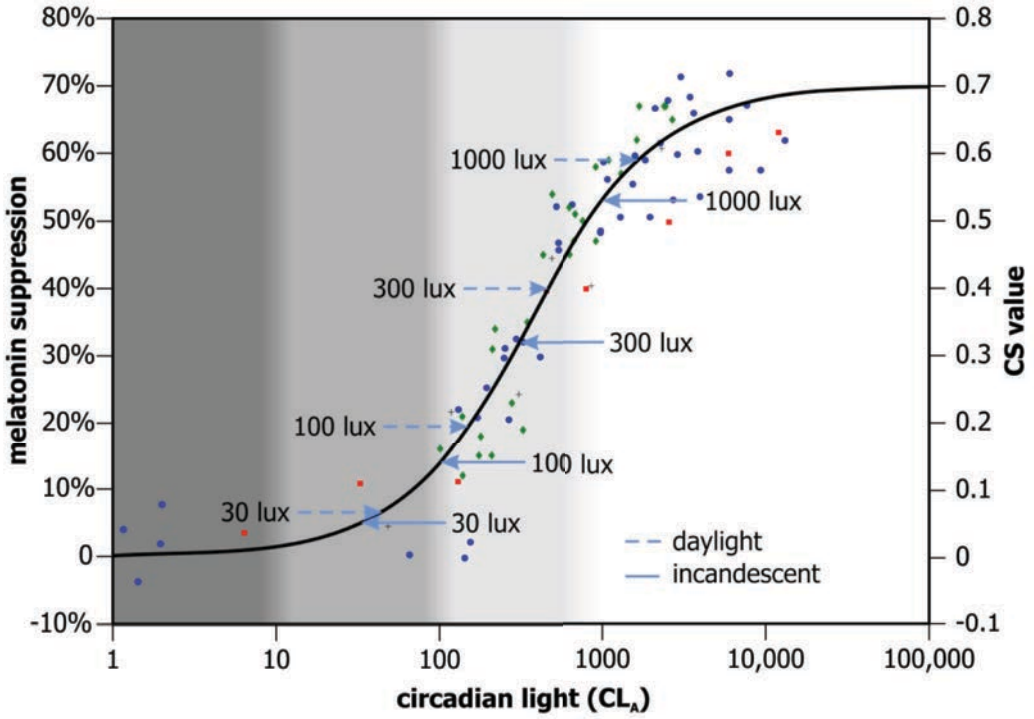


Rea, M. S., Figueiro, M. G., Bullough, J. D., & Bierman, A. (2005). A model of phototransduction by the human circadian system. *Brain Research Reviews,* 50(2), 213-228.

Rea, M. S., Figueiro, M. G., Bierman, A., & Hamner, R. (2012). Modelling the spectral sensitivity of the human circadian system. *Lighting Research and Technology,* 44(4), 386-396.

Specification of the light stimulus

- Circadian stimulus: Metric for quantifying effectiveness of light sources for activating the circadian system
- CS is equivalent to percent melatonin suppression after 1-h exposure to the light source
  - An indication of how effective the light source is for the circadian system
  - Caveat: does not take into account duration of exposure, photic history and is based on acute melatonin suppression (not phase shifting of the clock)
- Threshold = 0.1 CS; half max = 0.3 CS; saturation = 0.7 CS



LEDucation

Select Source SPD

CIE D65

(Click cell above for pull-down menu)

Illuminance (lux)

1000

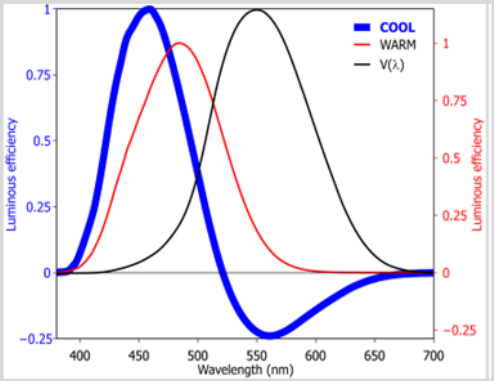
(Enter illuminance in cell above)

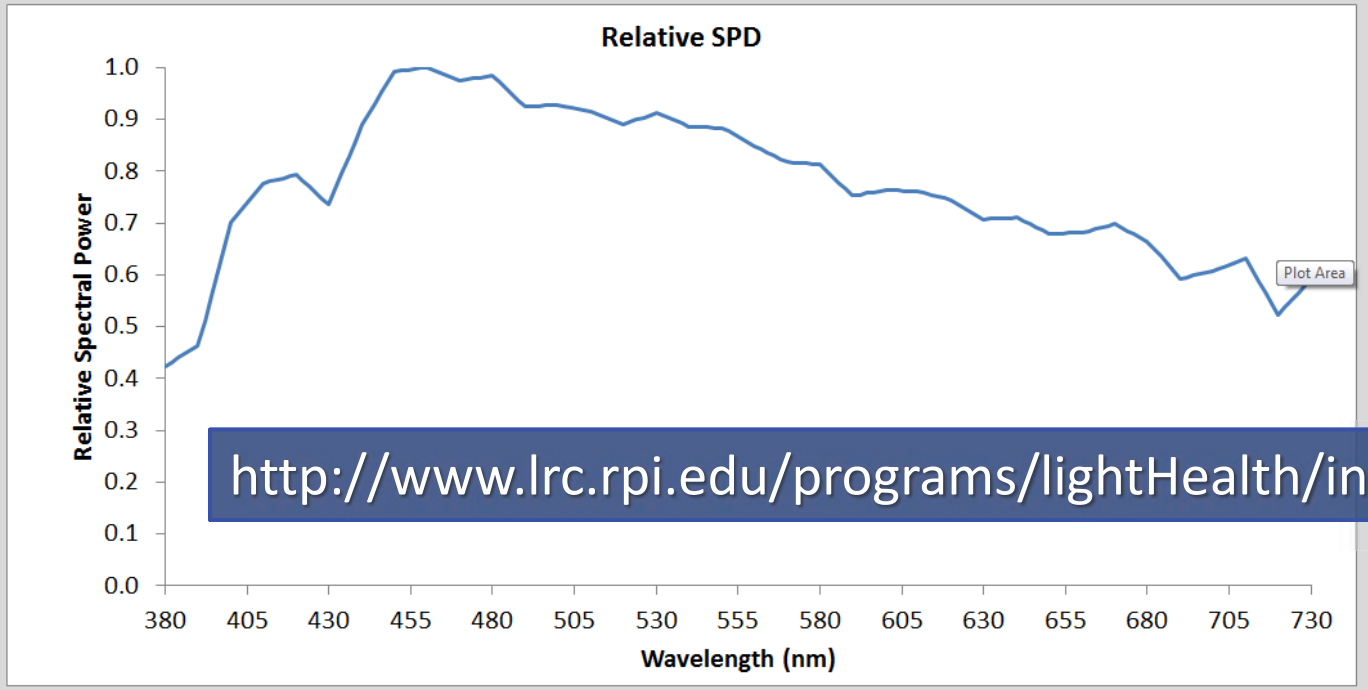
Circadian Light (CL_A)

1696 Circadian lux

Circadian Stimulus (CS)

0.594





http://www.lrc.rpi.edu/programs/lightHealth/index.asp

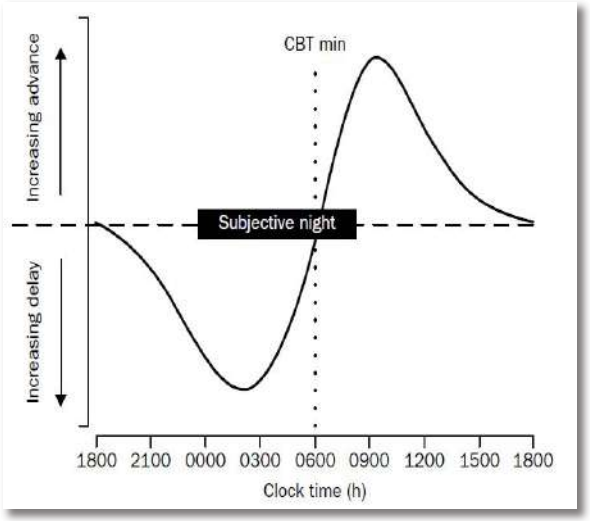
User SPD

Wavelength (nm)	Value
3.80E+02	0.09795
3.82E+02	0.10227
3.84E+02	0.10672
3.86E+02	0.1113
3.88E+02	0.11601
3.90E+02	0.12085
3.92E+02	0.12583
3.94E+02	0.13094
3.96E+02	0.13618
3.98E+02	0.14156
4.00E+02	0.14708
4.02E+02	0.15274
4.04E+02	0.15853
4.06E+02	0.16446
4.08E+02	0.17054
4.10E+02	0.17675
4.12E+02	0.18311
4.14E+02	0.18961
4.16E+02	0.19624
4.18E+02	0.20303
4.20E+02	0.20995
4.22E+02	0.21702
4.24E+02	0.22423
4.26E+02	0.23158
4.28E+02	0.23907
4.30E+02	0.24671

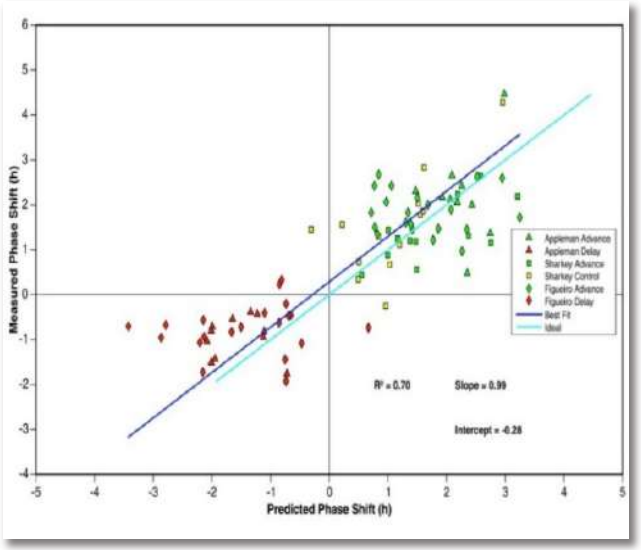
leducation.org

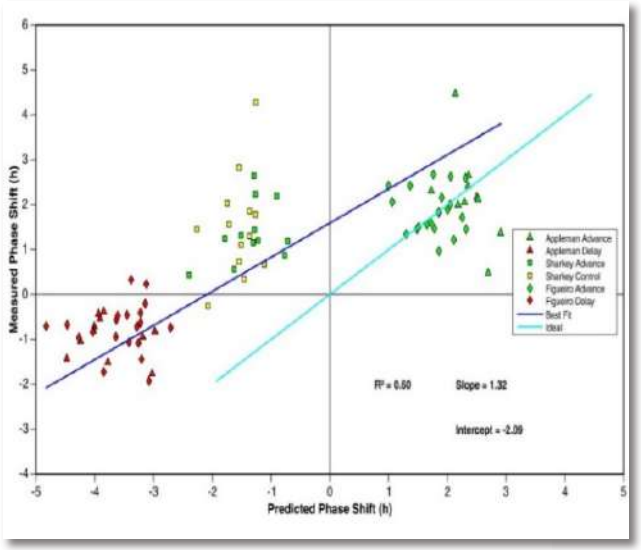
Timing and duration of exposure matters!

- Timing is critical
  - Biological morning light (after minimum core body temperature) will advance the timing of sleep
  - Biological evening light (before minimum core body temperature) will delay the timing of sleep
- But, every photon counts!



Rajaratnam S., Arendt J. (2001). Health in a 24-h Society. *The Lancet*, 358(9286), 999–1005.





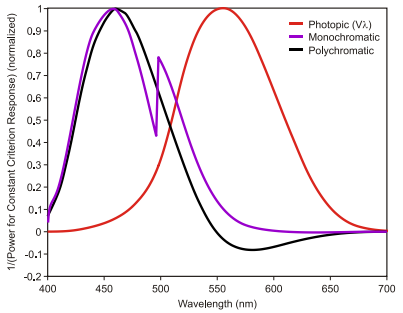
Figueiro M. G. (2016). Delayed sleep phase disorder: clinical perspective with a focus on light therapy. *Nature and Science of Sleep*, 8, 91-106.

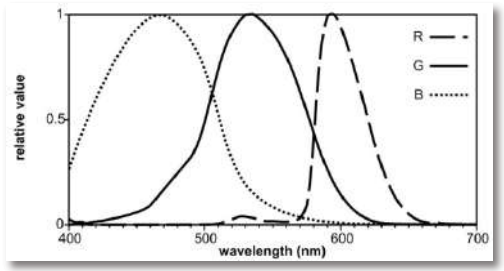
Measurement of light stimulus

- Developed a calibrated meter that measures circadian light and from that we can calculate circadian stimulus over the waking period
  - Compliance and location are still issues

Won the 2010 The Scientist's annual Top 10 Innovations contest

NIH# R01AG034157





Delivery of the correct light stimulus







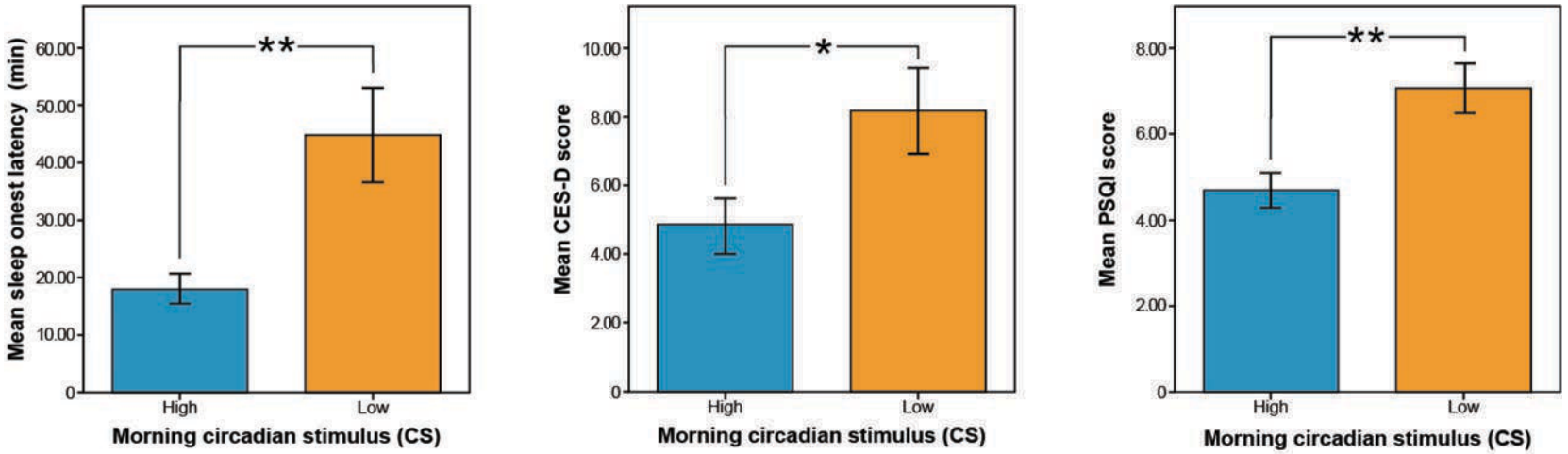



Tailored lighting intervention designed to promote circadian entrainment

- Promote entrainment in various populations by
  - Delivering high circadian stimulus (CS > 0.3) during the day, especially in the morning, and low CS (CS < 0.1) in the evening, to promote entrainment in Alzheimer's disease patients, older adults with early sleep onset, adolescents, premature infants, cancer patients undergoing treatment)

Circadian Entrainment in Office Workers

Those exposed to higher (CS > 0.3) morning (08:00 a.m. to noon) CS fell asleep faster (less sleep onset latency) and reported better sleep and feeling less depressed than those exposed to low morning CS (CS < 0.15)

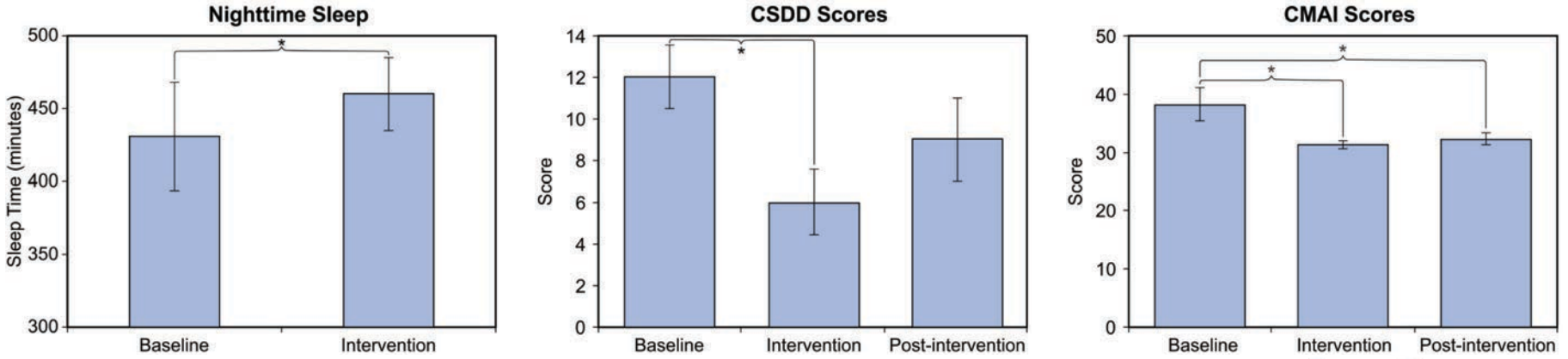


Figueiro M.G., Steverson B., Heerwagen J., Kampschroer K., Hunter C.M., Gonzales K., Rea, M.S. (2017). The impact of daytime light exposures on sleep and mood in office workers. *Sleep Health*; 3(3):204-215.

(** = $p < .01$; * = $p < 0.05$)

Circadian entrainment in persons with dementia

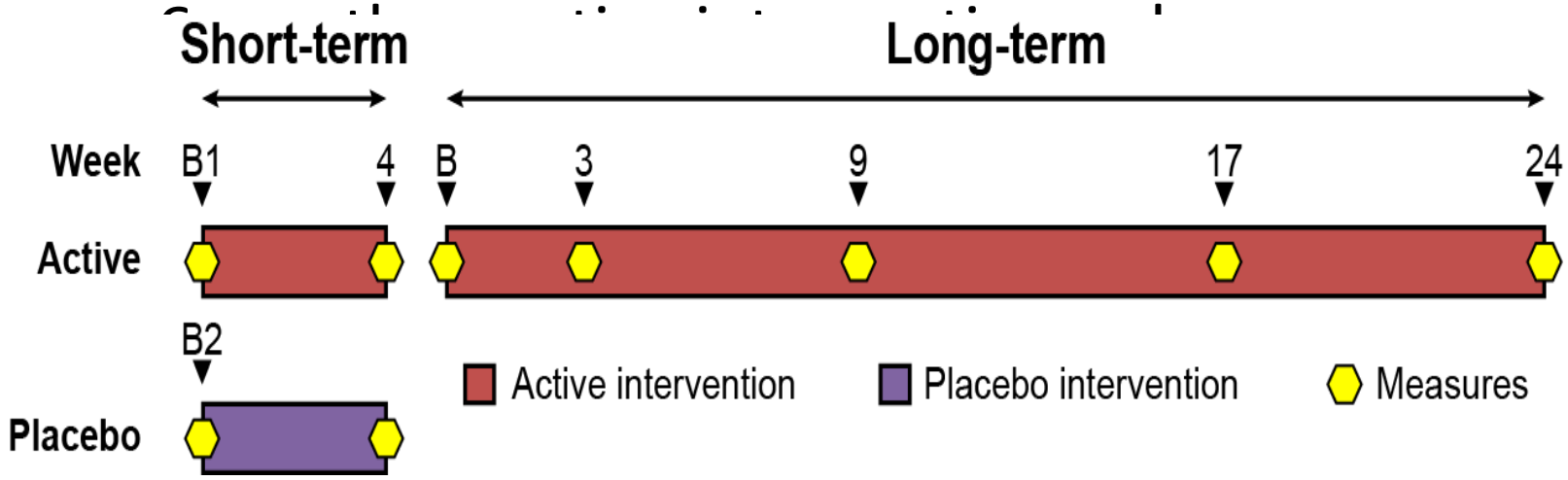
- Study tested the effectiveness of a tailored light treatment on sleep quality, agitation and depression in those with Alzheimer's disease and related dementias living in nursing homes
- High circadian stimulation during daytime hours
  - CS > 0.3 from waking to 6 pm
  - 300-400 lux at cornea of bluish-white light, CCT > 9000 K
- Results showed increase in sleep efficiency, total sleep time, reduction in agitation and depression



Sponsor: National Institute on Aging (R01AG034157)
Figueiro et al. 2014

Circadian entrainment in persons with dementia

- Two aims
  - Short-term – randomized, placebo controlled, within subjects protocol
    - (4 weeks – washout + 4 weeks)
  - Long-te



Sponsor: National Institute on Aging (R01AG034157)

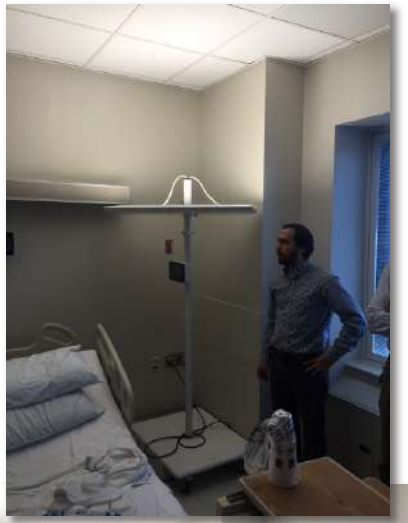
What have we learned so far?

- Light delivering the correct amount, spectrum and timing improves sleep, mood and depression in various populations
  - CS> 0.3 during the day and CS< 0.1 in the evening delivers a robust light-dark patterns for promoting entrainment
  - But we need to measure the 24-h exposure
  - Impact of light is greater in spaces where the 24-h light-dark can be controlled (e.g., nursing homes, prisons, and hospital rooms)

- Can we use this knowledge to help cancer patients?

Ambient light during stem cell transplantation

- In collaboration with Dr. William Redd (Icahn School of Medicine at Mt. Sinai) we are investigating the impact of 0.3 CS during the morning hours on:
  - Circadian markers (melatonin)
  - Fatigue
  - Depression
  - Sleep



Sponsor: National Cancer Institute
PI: Dr. Redd,

LEDucation

Sandra Stashik, PE, FIES, LEED ap

Acuity Brands Lighting

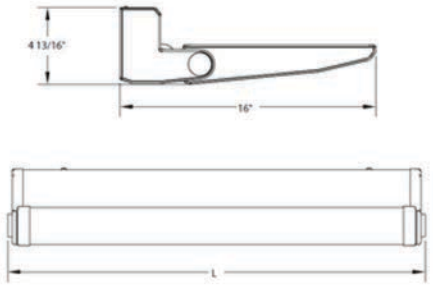
Luminaire Development Goals

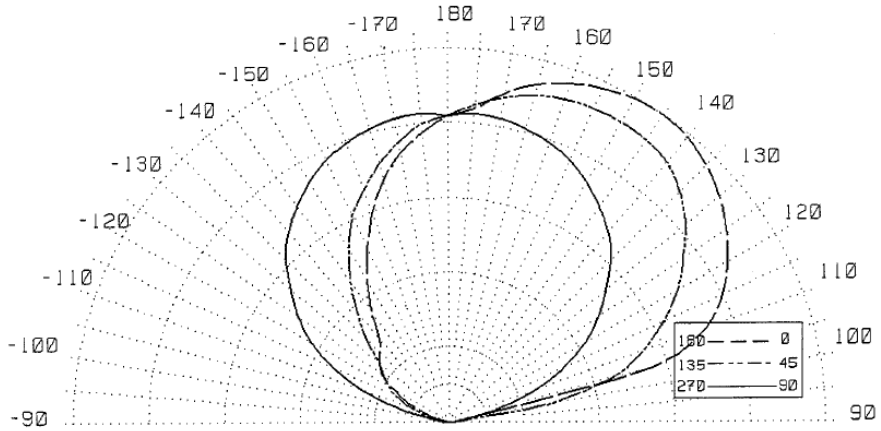
- Provide a flexible luminaire that is portable so it can be moved from room to room
- Select LED boards to provide 3500 CCT and CS > .3
- Select a control system with the ability to provide daily schedule for the luminaires on/off and intensity cycles
- Target illumination at head of bed was determined as a function of the spectrum of light source for given CS value

Luminaire Development Challenges

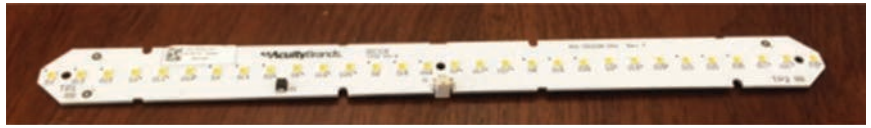
- Creating a portable luminaire to meet the project criteria while considering safety of patients and visitors
- No permanent changes to room could be made, rooms varied based on patient involvement in study
- Controls required to have a time clock function and to be easy to program by the hospital staff
- Actual location of luminaire in the rooms will vary due to furniture and current wall mounted lighting and television locations
- Deliver target CS values at patient's eye without discomfort glare
- Patient location in room varies, i.e., bed or chair

Luminaires Evaluated - Indirect





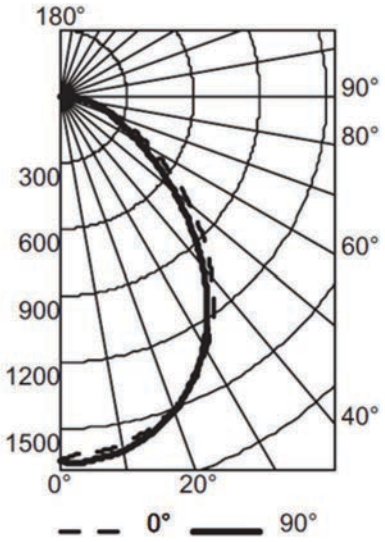
SEH1 Surface Wall / Ceiling Mount					
Nominal Length	Actual Length	Source	Lumens	Watts	Weight
12" Long	14.75"	AL1A4	6544	71w	16 lbs.
24" Long	26.12"	AL1A4	13089	141w	32 lbs.
36" Long	37.56"	AL1A4	19634	211w	48 lbs.



- Indirect asymmetric, static white luminaires, using modular LED boards with total luminous output ranging from 2000 to 19000 lm.
- Asymmetric distribution achieved by the board orientation (angled)

Luminaires Evaluated - Direct

- 1’ x 4’ LED lensed troffer
- This fixture is used to represent a general, direct-view luminaire aimed at the bed (as opposed to having light indirect – aimed to the ceiling)
- Luminaire would be positioned angled to the bed

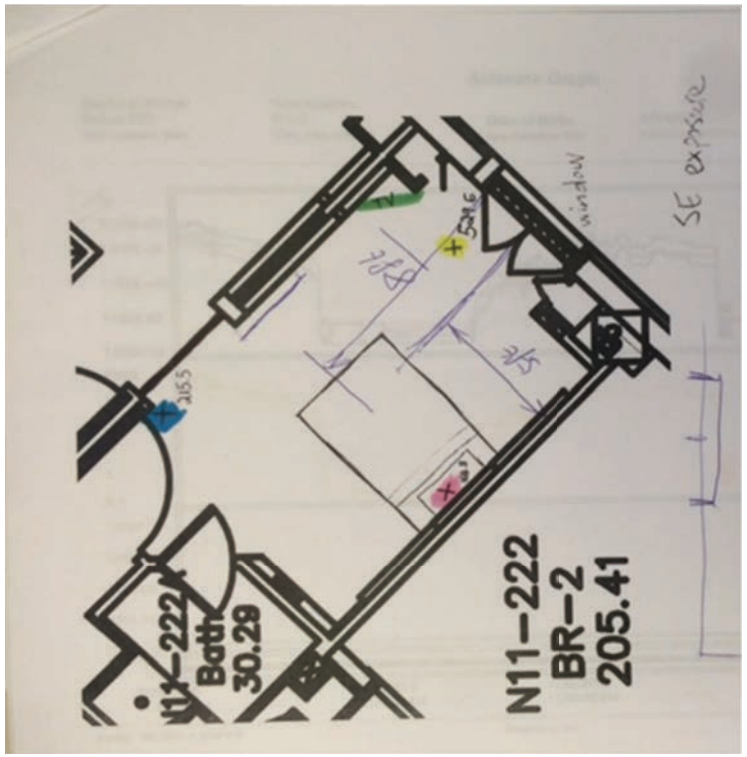


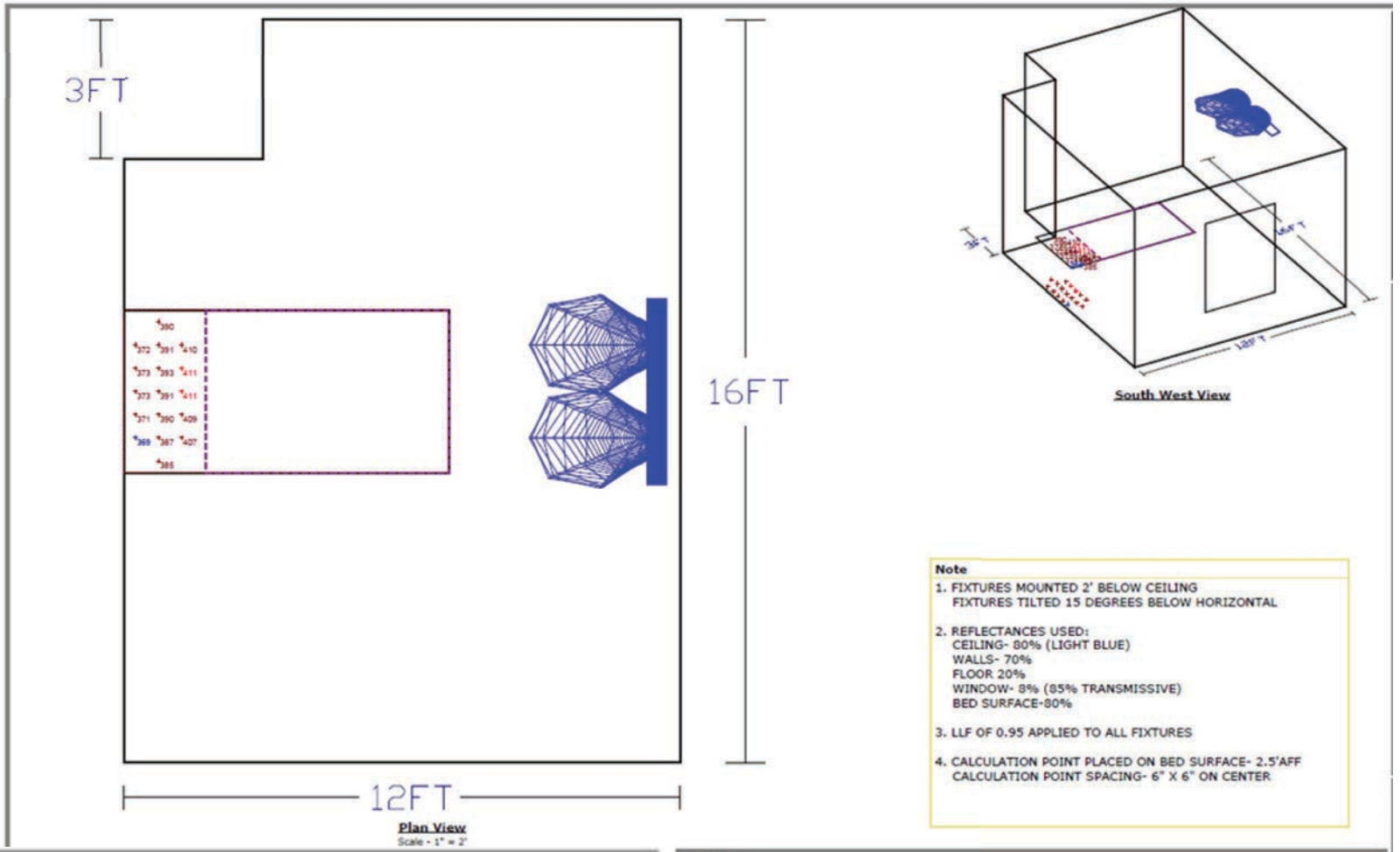
Illuminance Calculations – 6 Variations Evaluated

- Target Area: Head of Bed, horizontal
  1. 2’ Indirect Asymmetrical mounted 2’ below ceiling without optic and with 15° tilt below horizontal
  2. 1’ x 4’ lensed troffer mounted 2’ below the ceiling aimed at head of bed
  3. 3’ Indirect Asymmetrical mounted 2’ below ceiling without optic and with 15° tilt below horizontal

Illuminance Calculations – 6 Variations Evaluated

- Target Area: Head of Bed, 45° incline
  1. 2’ Indirect Asymmetrical mounted 2’ below ceiling without optic and with 15° tilt below horizontal
  2. 1’ x 4’ lensed troffer mounted 2’ below the ceiling aimed at head of bed
  3. 3’ Indirect Asymmetrical mounted 2’ below ceiling without optic and with 15° tilt below horizontal





Note

1. FIXTURES MOUNTED 2' BELOW CEILING
   FIXTURES TILTED 15 DEGREES BELOW HORIZONTAL
2. REFLECTANCES USED:
   CEILING- 80% (LIGHT BLUE)
   WALLS- 70%
   FLOOR 20%
   WINDOW- 8% (85% TRANSMISSIVE)
   BED SURFACE-80%
3. LLF OF 0.95 APPLIED TO ALL FIXTURES
4. CALCULATION POINT PLACED ON BED SURFACE- 2.5'AFF
   CALCULATION POINT SPACING- 6" X 6" ON CENTER

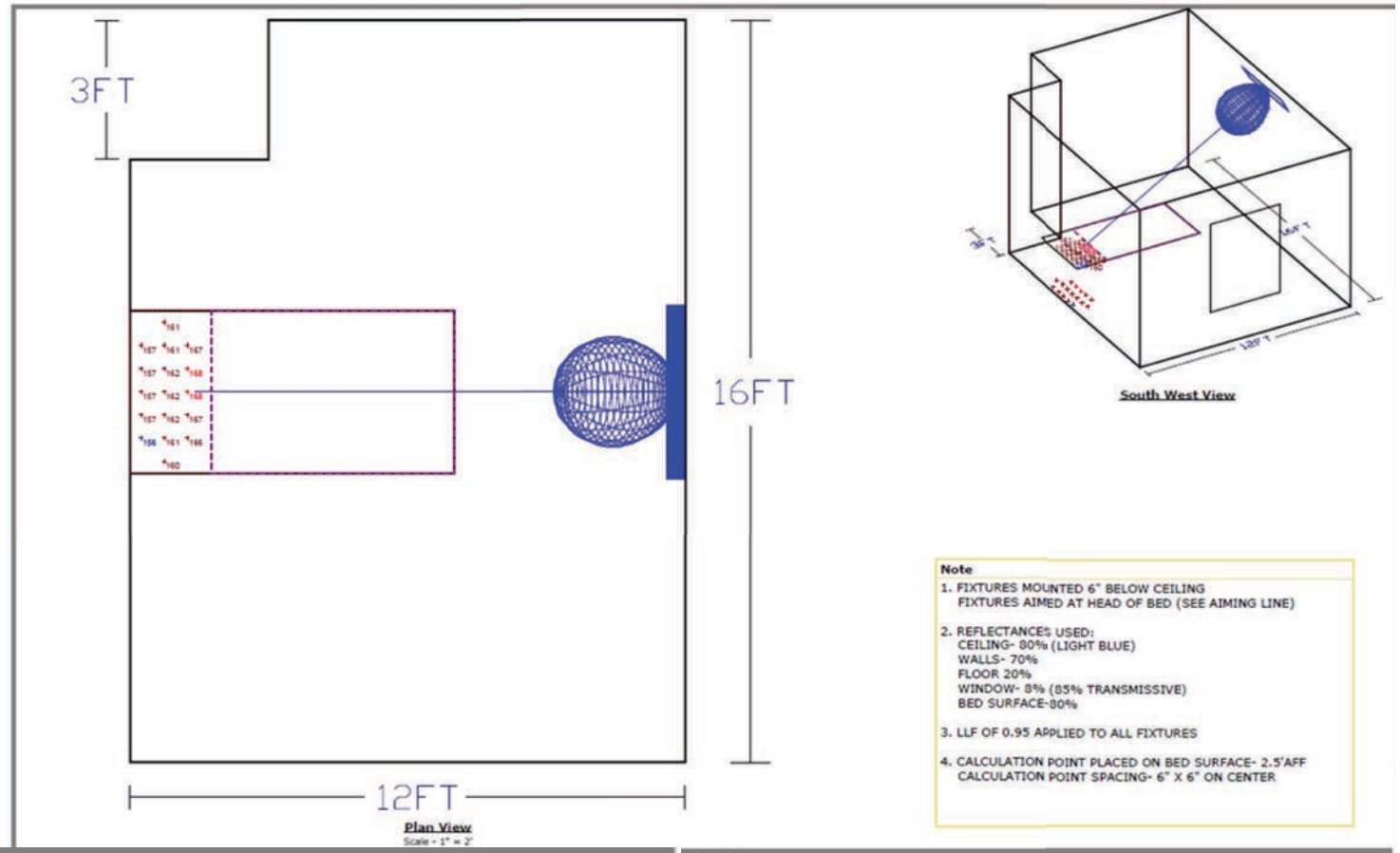
Statistics

Description	Symbol	Avg	Max	Min	Max/Min	Avg/Min
Bed	+	390 lux	411 lux	369 lux	1.1:1	1.1:1

Schedule

Symbol	Quantity	Description	Catalog Number	Lamp	Number Lamps	Filename	Lumens Per Lamp	Light Loss Factor	Wattage
▭	2	24" WALL MOUNT ASYMMETRIC UPLIGHT (4) 4SUP LED ,BOARDS. CLEAR LENS	WLAWC802 YM1A INT 24LONG AL1A2 40K MVOLT	LED@4000K	1	LTL26520_WL AWC802_WL_ 24LONG_AL1A 2_40K_MVOLT .IES	7603.642	0.95	147.5

Illuminance Calculations – Case 2



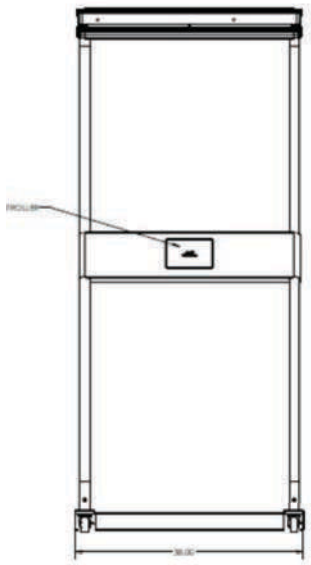
Statistics

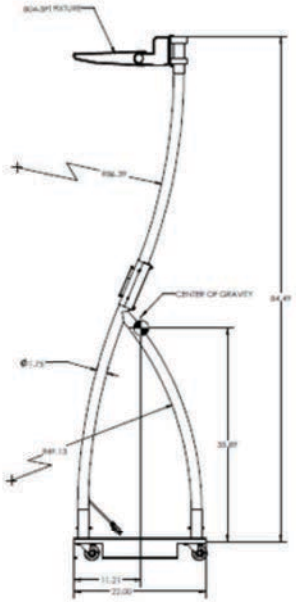
Description	Symbol	Avg	Max	Min	Max/Min	Avg/Min
Bed	+	162 lux	168 lux	156 lux	1.1:1	1.0:1

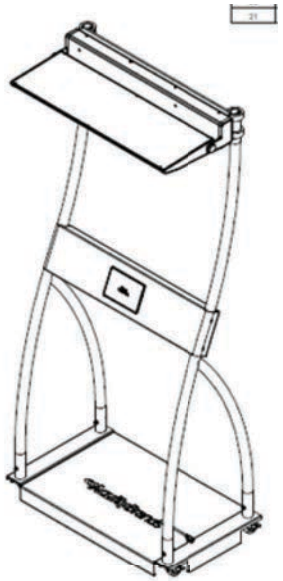
Schedule

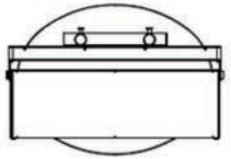
Symbol	Quantity	Description	Catalog Number	Lamp	Number Lamps	Filename	Lumens Per Lamp	Light Loss Factor	Wattage
	1	GTL 1X4, 4800 NOMINAL LUMEN, A12 LENS, NICHIA ,757D 4000K	GTL 4 48L EZ1 LP840	LED	1	GTL_4_48L_EZ 1_LP840.ies	4718.22	0.95	46.46

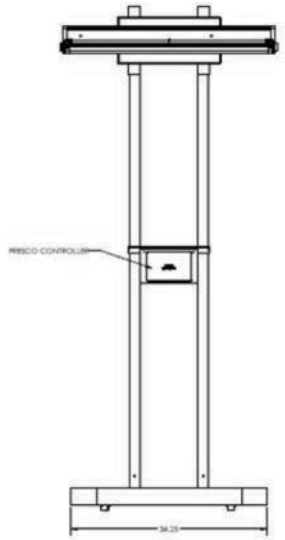
Luminaire Design - variations

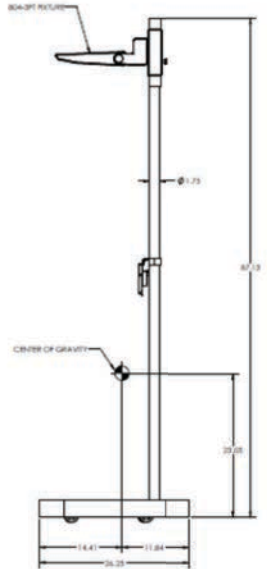


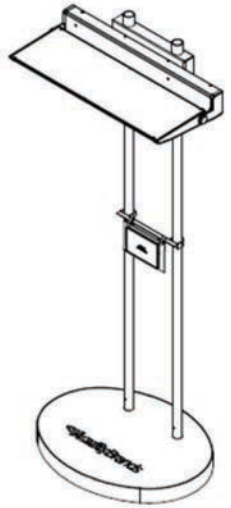




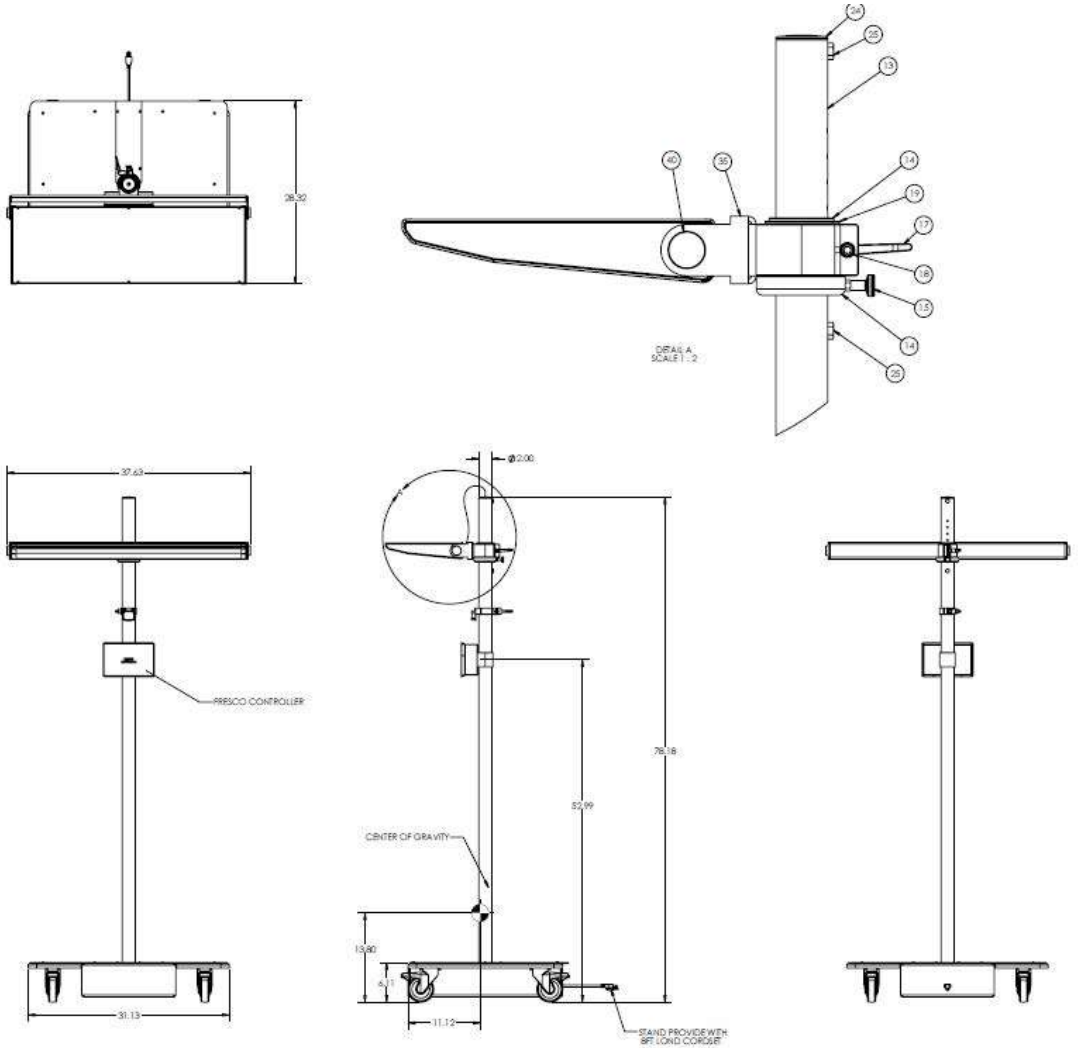








Luminaire Design - Final



Luminaire Controls and Scheduling

- LED digital drivers (2) were mounted in the base of the luminaire stand
- Touch screen controller was mounted to the pole
- Controller is preset and operated by staff only

Luminaire Design – Final – 3’-Unit

- Demonstration room with pole mounted luminaire
- Lighting controller is mounted to the pole
- Staff was trained in programming and operation
- Patients were recruited for the study (all were approached to see if they wanted to participate)

Field Measurements

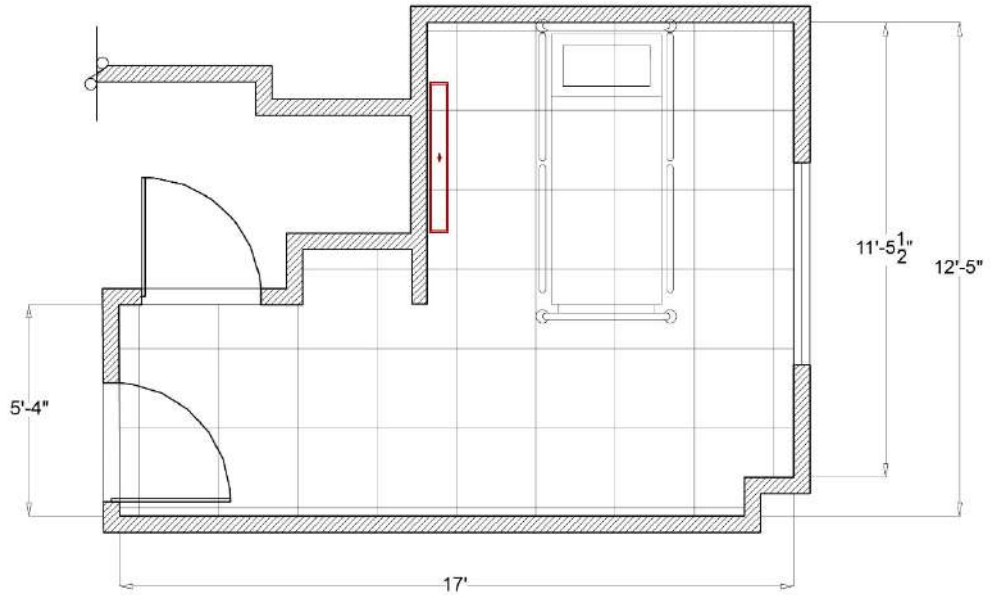
Blinds	Open	Closed	Closed	Closed	Closed	Closed	Closed	Closed	Closed	Closed
Headboard light	Off	Off	On	Off	Off	Off	Off	Off	Off	Off
Fixture %	0	0	0	100	90	80	75	70	60	55
Illuminance (lux)	91	31.7	72.2	1291	581	323	242	176	120	89.9
CS	0.191	0.065	0.083	0.451	0.305	0.21	0.176	0.141	0.116	0.101

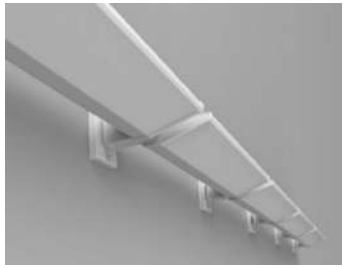
- Set point for Study 100% intensity
- Set point for Control 50%

Summary

1. Goal CS >.3 can be accomplished with a non-tunable 3500K LED
2. Design is totally flexible since the luminaire is portable and easily fits into patient rooms
3. 46 patients have participated in the study to date and only one said it was too bright
4. Patients are very satisfied with light
5. Only minor issue with fixture maintenance due to frequency of moving them over 2 years
6. Next Step – 20 rooms with fixtures mounted to wall at 2 hospitals will be implemented to further the study

New Proposed Wall Mounted Design





Calculation Summary- Illuminance (lux)					
Label	Avg	Max	Min	Avg/Min	Max/Min
General_Floor	169.35	457.5	22.3	7.59	20.52
HospitalBed	725.25	1035	387.6	1.87	2.67
Vertical_45	743.03	858.7	576.0	1.29	1.49
Vertical_90	376.88	422.8	292.9	1.29	1.44
Vertical_Bed-straigh	672.83	972.5	292.9	2.30	3.32

Luminaire Schedule					
Qty	Label	Lum. Lumens	Lum. Watts	LLF	Description
1	4 FT_ 802L	13215	148	1.000	WLAWC802L MSL4 INT AL1A2 30K MVOLT

LEDucation

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Circadian Disruption in Cancer Patients

- Research confirms that, compared to cancer-free controls, circadian activity rhythms are disrupted before and after chemotherapy and fatigue is increased; fatigue (Ancoli-Israel et al., 2013).
- The first administration of chemotherapy is associated with transient circadian disruption and repeated administration of chemotherapy results in progressively worse and more enduring rhythm impairments; disruption across cancers (Ancoli-Israel et al., 2013).
- Circadian patterns have been shown to be altered in cancer patients with advanced disease; disruption across cancers (Bower et al., 2003).
- Prostate Cancer patients display disrupted circadian activity rhythms and increased fatigue both before and after treatment; disruption and fatigue in prostate cancer (Zhu et al., 2006/2009; Savvidis et al., 2012; Stone et al., 2000).

Circadian Rhythm Disruption and Light Exposure

- Circadian Rhythm Disruption Affects:
  - Immune, metabolic, and cognitive function
  - Depression, Fatigue and Sleep
  - Risk for Cardiovascular Disease, Diabetes and Obesity
- Bright, short-wavelength (blue) light is one of the strongest synchronizers of the circadian rhythm system and can entrain disrupted rhythms

Systematic Light Exposure (sLE) and Programmed Environmental Illumination (PEI)

- Daily, 30-minute, AM administration of circadian-stimulating bright white light (BWL)
- BWL over 1,000 lux at the eye is circadian stimulating
- In research, BWL compares to dim white light (DWL), < 90 lux at the eye

Measurement Techniques

- Daysimeter
  - Light exposure
- Actigraph
  - Activity/Rest cycles
- Biomarkers
  - Saliva for cortisol
  - Urine for melatonin
  - Blood for inflammatory markers (cytokines)
- Questionnaires
  - Published with known psychometric properties
  - Measure fatigue, sleep quality, depression, quality of life, anxiety, social support, emotions, etc.

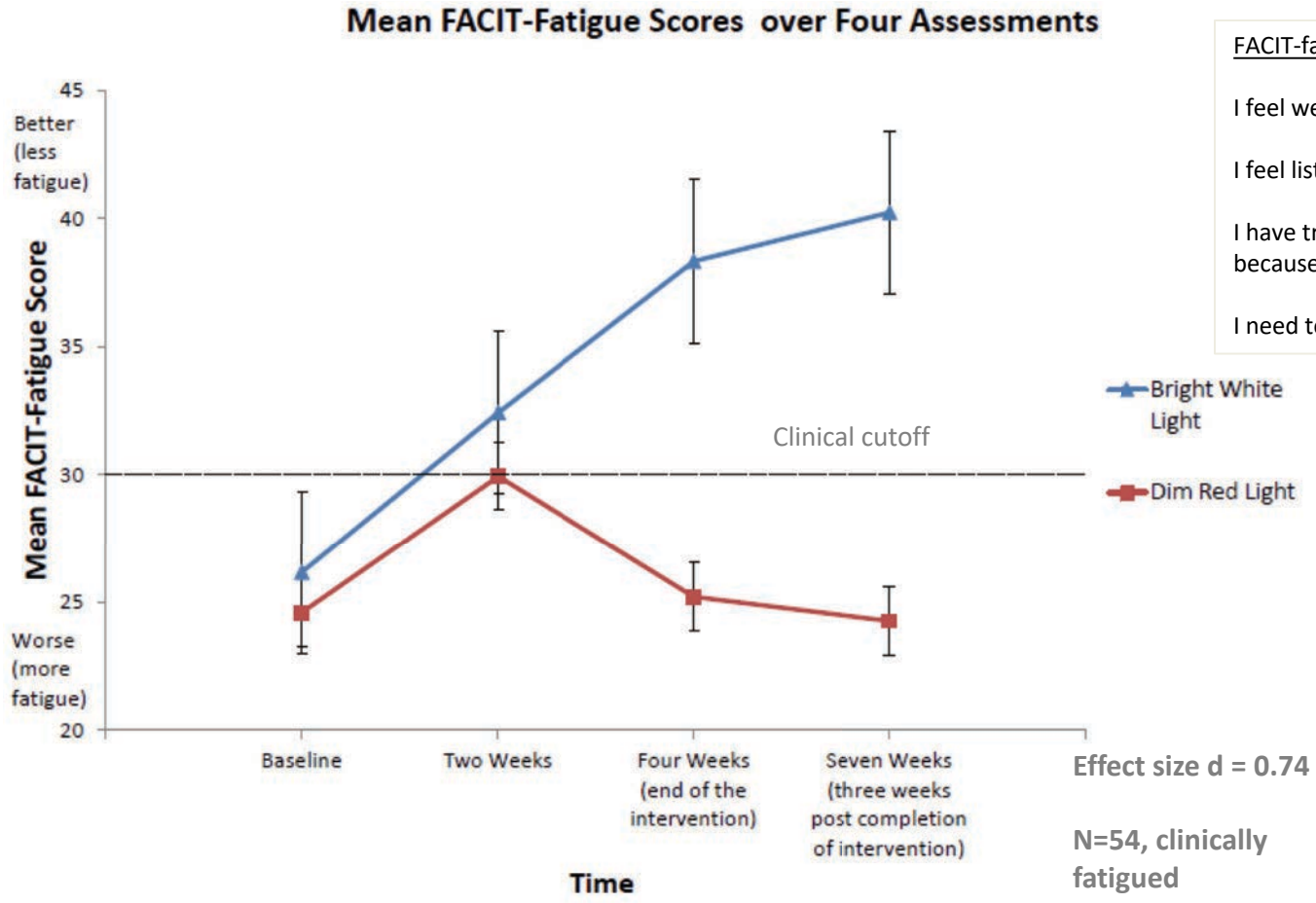
Measurement Techniques Continued

- Questionnaires
- FACIT-Fatigue
  - Fatigue; used for screening and outcome
- Pittsburgh Sleep Quality Index (PSQI)
  - Sleep problems/depressive symptoms
- Center for Epidemiological Studies Depression Scale (CES-D)
  - Depression
- Brief Symptom Inventory-18 (BSI-18)
  - Depression, Anxiety, Somatization

Initial Results for Cancer Survivors

- Ongoing Randomized Clinical Trial comparing Bright White Light (BWL, 1,000 lux) and Dim White Light (DWL, 50 lux) comparison
- Survivors of Multiple Myeloma, Hodgkin's Lymphoma, Breast Cancer, and GYN Cancers with clinically significant fatigue (FACIT-fatigue)
- First 36 patients reported here
- Linear mixed model repeated measures analysis
- Significant effect ($F(3(68)=5.93$; $p=0.0125$) BWL group had less fatigue than the DRL group

Fatigue for Cancer Survivors Receiving sLE



FACIT-fatigue example questions

I feel weak all over

I feel listless

I have trouble starting/finishing things because I am tired

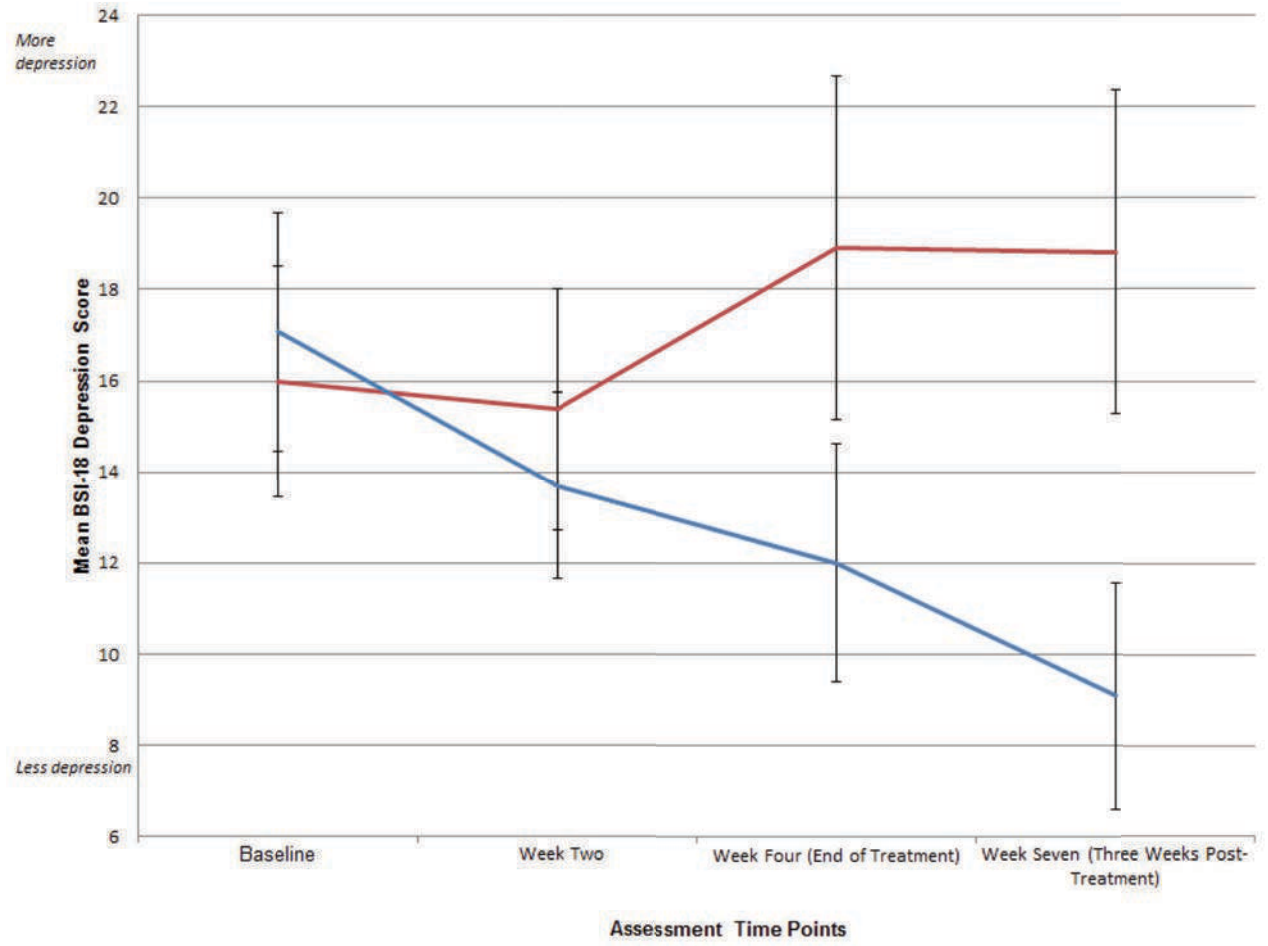
I need to sleep during the day

Effect size d = 0.74

N=54, clinically fatigued

Depression for Cancer Survivors Receiving sLE

Mean BSI-18 Depression Score



BSI-18 example questions

I feel faintness or dizziness

I feel no interest in things

I have feelings of worthlessness

I have trouble getting my breath

p = 0.0251
n = 54
Effect size = 0.97

Screened for fatigue

Sleep Efficiency for Cancer Survivors Receiving sLE

Effect size
d = 1.25

N= 54
Screened for fatigue

	Baseline (tib*)	Mid-intervention (tib)	End of Intervention (tib)	Post-intervention (tib)
Dim Red Light	82% (8.10 h)	79% (8.05 h)	79% (8.15 h)	81% (8.15 h)
Bright White Light	83% (7.63 h)	84% (7.84 h)	86% (7.61 h)	86% (8.04 h)

Effect size d=0.74

*tib = time in bed in hours

Initial Results for Cancer Patients (Ambient Light During Stem Cell Transplantation)

- Ongoing Randomized Clinical Trial comparing Ambient Bright White Light (BWL, 1,300 lux) and Ambient Dim White Light (DWL, 90 lux) comparison
- MM Patients undergoing Autogolous Stem Cell Transplant (ASCT)
- 35 patients reported here
- Linear mixed-model analyses
- BWL patients had significantly lower CES-D total scores than DWL patients (P=0.0051; Effect size (eta^2)=0.013)

Research Efforts

- Ongoing Research
  - sLE with Multiple Myeloma Stem Cell Transplant Survivors (R01)
  - sLE with Breast Cancer Patients undergoing (Neo)adjuvant Chemo (R01)
  - sPI with Multiple Myeloma Patients Undergoing ASCT (R21)
  - Biological Effects of sLE for Cancer-Related Fatigue (R21)
  - sLE to treat Obese Frailty in Prostate Cancer patients undergoing Androgen Deprivation Therapy (COH award)

Research Efforts (Continued)

- Pending Research
  - sLE to reduce/prevent Metabolic Syndrome in Breast Cancer patients during (Neo)adjuvant therapy (DOD, pending)
  - Programmed Environmental Illumination (PEI) to prevent/reduce Circadian Rhythm Disruption indicators (fatigue, depression, sleep deficiencies) from developing during HSCT

Broad Goals

- Expand light research to diverse medical conditions (e.g. depression, cardiovascular and metabolic disease)
- Understand the mechanisms whereby light intervention affects emotional, biological, cognitive and behavioral factors
- Economic impact of sLE and PEI
  - Length of stay
  - Increased treatment efficiency

LEDucation

Thank you.

leducation.org

This concludes The American Institute of Architects Continuing Education Systems Course

Current project sponsors

- National Institute on Aging
- National Cancer Institute
- National Institute of Occupational and Safety Health (CDC/NIOSH)
- General Services Administration (GSA)
- US Department of State (through GSA)
- Office of Naval Research
- The Swedish Energy Agency
- Acuity Brands