



PLATELET RICH PLASMA FOR ALOPECIA

Maryanne Makredes Senna, MD
Assistant Professor of Dermatology, Harvard Medical School

Disclosures

- Scientific Advisory Board and/or consultant for Eli Lilly, Arena Pharmaceuticals, Pfizer, L'Oreal, Kintor, Inmagene
- Research funding from Eli Lilly, Concert, Clarity, Leo, Santiste, and Follica
- Board of Directors for the Scarring Alopecia Foundation and American Hair Research Society
- Platelet rich plasma treatment of alopecia is off label.
- Only some low level laser light devices are FDA cleared or approved for the treatment of androgenetic alopecia.

Overview

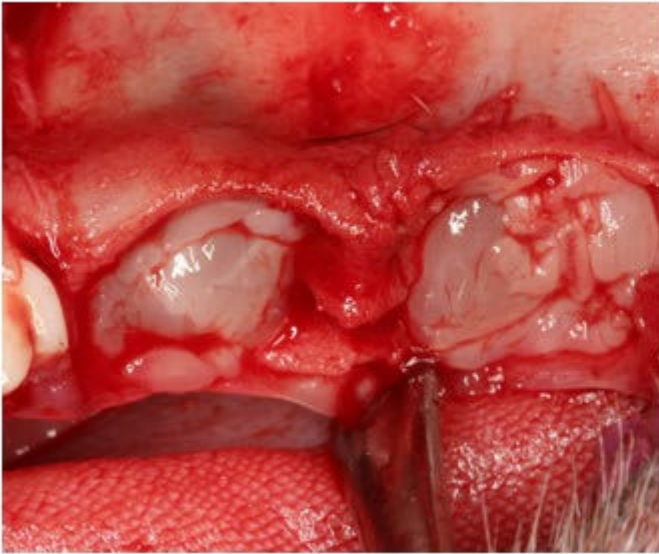
- Review background on platelet rich plasma (PRP) and low level laser light devices (LLLD) for androgenetic alopecia.
- Discuss my PRP protocol for alopecia.
- Examine some before and after photos of my patients.



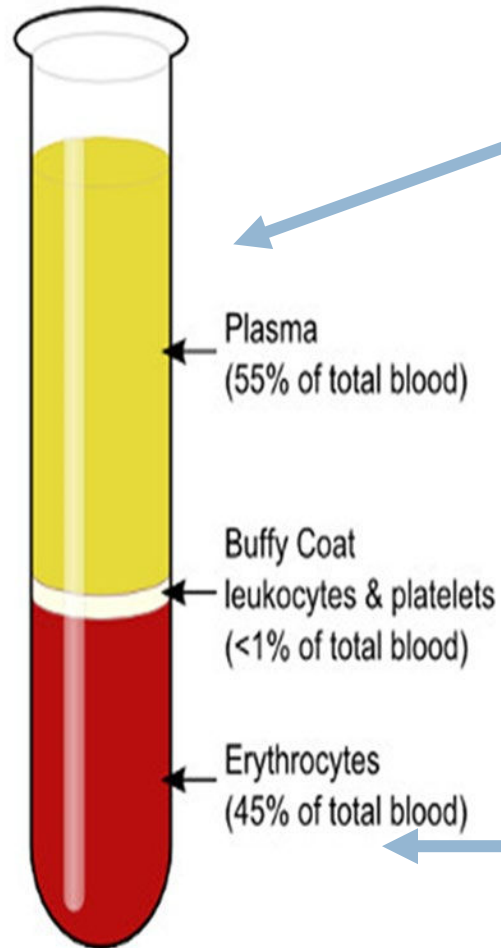
Platelet Rich Plasma (PRP)

Platelet Rich Plasma Background

- Long history of use in oral surgery, implant dentistry, wound healing and cosmetic/aesthetic surgery



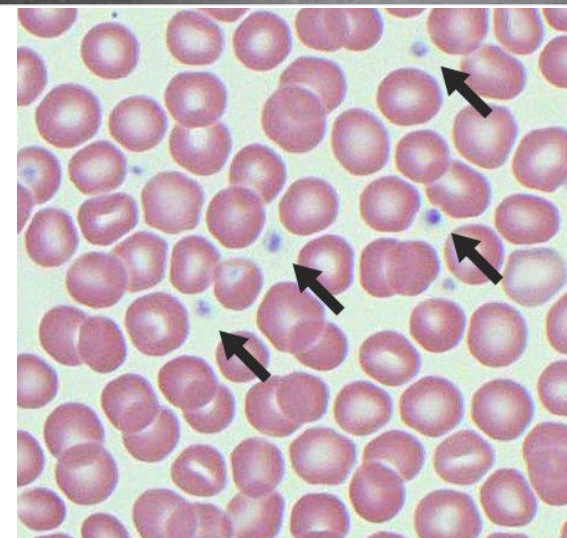
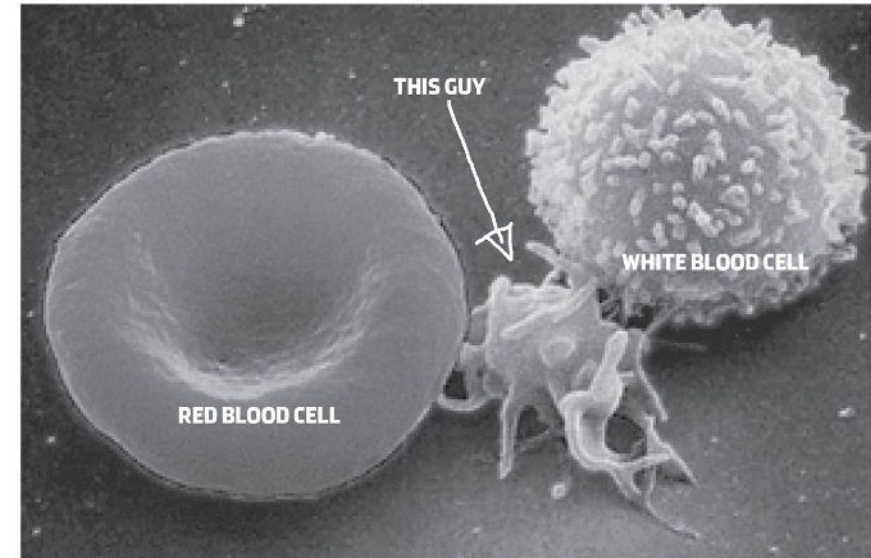
Blood Components



- Plasma: nutrient and chemical-rich liquid component that carries blood cells.
- White blood cells: help fight infection
- Platelets: involved in clotting and contain growth factors that stimulate wound healing and angiogenesis.
- Red blood cells: carry oxygen from the lungs to the rest of the body

Platelets

- Tiny jagged cells (5 times smaller than RBCs) derived from megakaryocytes in the bone marrow and lungs
- Normal range 150,000 – 400,000
- 7 day half-life in circulation
- Contain Ca^{++} , K^+ , clotting factors, adenosine diphosphate, serotonin, and **growth factors**



Platelet Growth Factors

Table 3. List of GFs identified in PRP and their suggested bio-molecular pathway in the treatment of AGA.

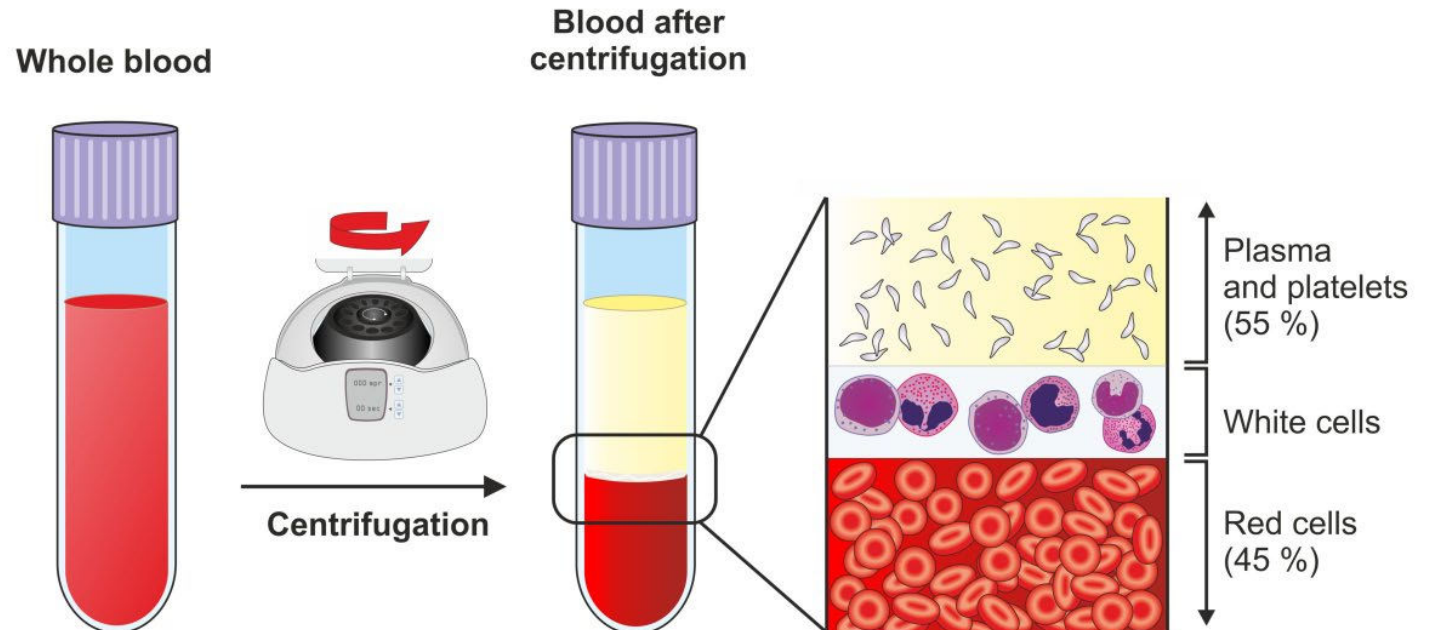
Growth Factors	Bio-Molecular Pathway in Hair Re-Growth
VEGF	Improves perifollicular angiogenesis; Elevated expression in dermal papilla cells during anagen phase; Endothelial cell-specific mitogen; Micro-vascular permeability and perifollicular vascularization;
EGF	Improves the activity and growth of follicle outer-root sheath cells by activation of Wnt/ β -catenin signaling; Cell growth modulator during follicular differentiation; Proliferation and migration of follicular outer root sheath cells;
FGF	Improves the advancement of hair follicles; Anagen phase induction via B-catenin expression; Angiogenesis; Dermal fibroblast and hair follicle mitogen;
PDGF	Up-regulate the genes associated with HF separation, induction, and control of anagen; Angiogenesis and vascularization; Hair follicle dermal stem cell proliferation; Mesenchymal stem cell mitogen;
IGF-1	Improves the migration, survival, and proliferation of HF cells; Hair follicle proliferation during development; Increase hair density and inhibit apoptosis;
HGF	Enhance the proliferation of follicular epithelial cells Hair follicle elongation; Inhibits catagen phase induction;
TGF- β	Stimulates the signaling pathways that manage the Hair cycle; Extracellular matrix synthesis; Fibroblast and mesenchymal stem cell proliferation; Hair folliculogenesis and maturation;
IL-6	Involved in WIHN through STAT3 enactment

- Promotion of perifollicular angiogenesis
- Activation of Wnt/ β -catenin signaling
- Induction of anagen growth phase
- Proliferation of hair follicle dermal stem cells
- Inhibition of catagen phase induction
- Activation of Bcl-2 protein and AKT signaling → survival of dermal papilla cells during hair cycle

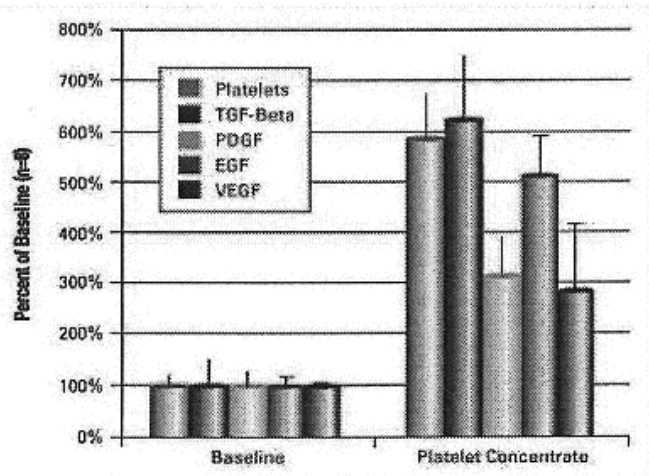
Platelet-Rich Plasma (PRP)



Heavy blood elements (WBCs, RBCs, platelets) are separated via centrifugation due to variations in size and density (sedimentation rate)



Platelet Rich Plasma (PRP)



3-5x increase in growth factor concentrations

- By separating out the other cells, PRP contains a much higher concentration of growth factors compared to baseline plasma.

Factors that affect PRP Quality and Concentration

- The amount of whole blood used
- The efficiency of platelet recovery
- The final volume of plasma in which the platelets are suspended
- The number of RBCs and WBCs in PRP

EXAMPLE:

60 mLs of whole blood = X number of platelets

Concentrate platelets into 1 mL of plasma = 60x number of platelets/mL

Theoretically produces a 60x increase in platelet concentration compared to whole blood, but 100% platelet recovery is not possible.

Most commercial systems have between 25% to >70% platelet recovery.

Platelet Concentration Can Vary Among Kits

Table 1. Composition of whole blood, Harvest platelet rich plasma (PRP), Eclipse PRP and EmCyte PRP composition averaged for all four donors with uncertainty determined using standard deviation. WBC = white blood cells; RBC = red blood cells; HCT = hematocrit; PLT = platelets.

	Average	Concentration Ratio (Compared to Whole Blood)	
Whole Blood			
WBC ($\times 10^9 \text{ L}^{-1}$)	7.0 ± 1.26		
RBC ($\times 10^{12} \text{ L}^{-1}$)	4.06 ± 0.78		
HCT (%)	35.4 ± 6.70		
PLT ($\times 10^9 \text{ L}^{-1}$)	358 ± 94		
Harvest			
WBC ($\times 10^9 \text{ L}^{-1}$)	10.8 ± 9.30	Amount of patient blood collected: 54 mLs \rightarrow 10 mL PRP	1.5 ± 1.28
RBC ($\times 10^{12} \text{ L}^{-1}$)	0.86 ± 0.41		0.21 ± 0.09
HCT (%)	6.9 ± 2.42		0.19 ± 0.09
PLT ($\times 10^9 \text{ L}^{-1}$)	<u>1242 ± 361</u>		3.8 ± 0.54
Eclipse			
WBC ($\times 10^9 \text{ L}^{-1}$)	1.8 ± 1.11	20 mLs \rightarrow 5 mLs PRP	0.3 ± 0.13
RBC ($\times 10^{12} \text{ L}^{-1}$)	0.05 ± 0.06		0.01 ± 0.02
HCT (%)	0.3 ± 0.42		0.02 ± 0.01
PLT ($\times 10^9 \text{ L}^{-1}$)	<u>662 ± 480</u>		2.0 ± 1.18
EmCyte			
WBC ($\times 10^9 \text{ L}^{-1}$)	17.5 ± 6.50	50 mLs \rightarrow 7 mLs PRP	2.5 ± 0.63
RBC ($\times 10^{12} \text{ L}^{-1}$)	0.20 ± 0.09		0.05 ± 0.02
HCT (%)	1.5 ± 0.58		0.04 ± 0.02
PLT ($\times 10^9 \text{ L}^{-1}$)	<u>2014 ± 608</u>		5.8 ± 0.80

Other PRP Considerations/Debates

- Leukocyte rich PRP versus leukocyte poor PRP
 - ▣ Do WBCs in PRP provide benefit as being anti-bacterial or could they stimulate an pro-inflammatory reaction?
 - ▣ One study found that LR-PRP had significantly higher concentrations of the catabolic protease MMP-9.

Leukocyte concentration and composition in platelet-rich plasma (PRP) influences the growth factor and protease concentrations

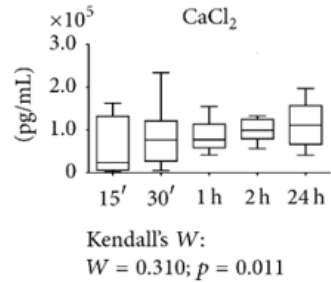
Yohei Kobayashi ^a, Yoshitomo Saita ^{a,*}, Hirofumi Nishio ^a, Hiroshi Ikeda ^a, Yuji Takazawa ^a, Masashi Nagao ^a, Tomoiku Takaku ^b, Norio Komatsu ^b, Kazuo Kaneko ^a

Journal of Orthopaedic Science 21 (2016) 683–689

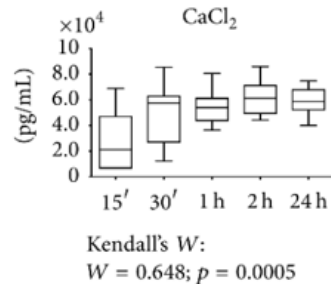
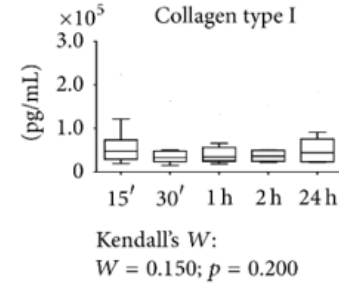
Other PRP Considerations/Debates

- Activated PRP versus Non-Activated PRP
 - When injected, platelets are activated by collagen in the scalp.
 - Alternatively, different concentrations of CaCl₂, thrombin or combination CaCl₂/thrombin can be added to “activate” the PRP before it is injected.
 - When platelets are activated by the addition of these exogenous substances, total platelet degranulation and growth factor release occurs.
 - Growth factors have a short half-life (from minutes to hours) and, if their release is not sustained over time and/or the PRP is not immediately used, GFs may be degraded before having their intended effects on the target tissue.

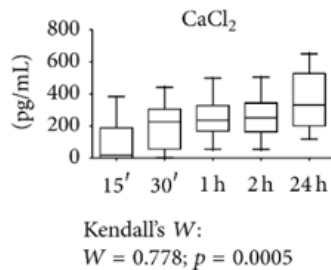
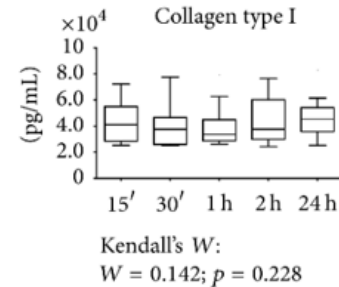
Growth Factor Concentrations and Kinetics: CaCl₂ versus Collagen Activation



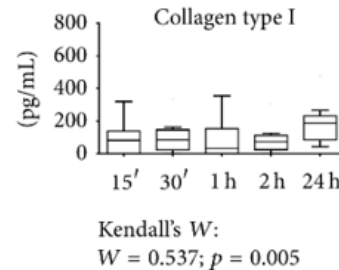
PDGF



TGF



VEGF



- PRP activated with CaCl₂ had increased release of growth factors.
- The release of growth factors with both CaCl₂ and collagen were sustained similarly over a 24 hour period.
- In vitro study—is in vivo activation different?

Lahey PRP Protocol

- 1 treatment every 4-6 weeks x 3
- Clinic follow up 3-4 months after last treatment to compare before and after photos
- Maintenance: 1 treatment every 6 months thereafter
- Can activate non-activated PRP by adding 0.17mL of 100mM stock CaCl_2 solution to final PRP product

PRP Protocol

- ALL patients at baseline are examined with trichoscopy +/- biopsy to ensure that they do not have an inflammatory alopecia.
 - ▣ Nearly 1 in 15 (6.4%) of new patients presenting to our clinic for PRP had undiagnosed cicatricial alopecia.

- ALL patients in the following photos were treated with PRP MONOTHERAPY and did NOT have telogen effluvium.

PRP Monotherapy

Before



Three months after having 3 monthly PRP injections



PRP Monotherapy

Before

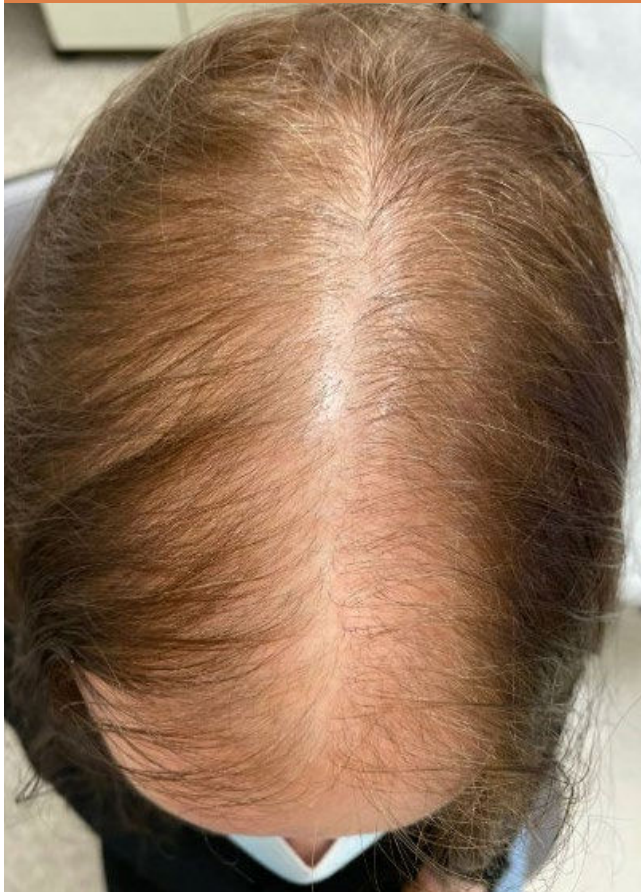


Three months after having 3 monthly PRP injections

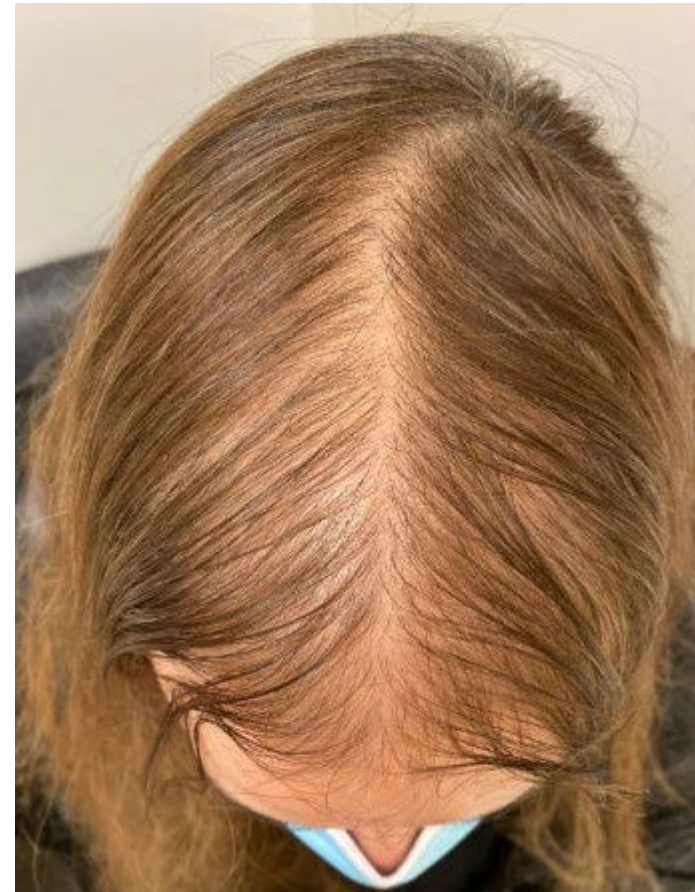


PRP Monotherapy

Before



**Three months after having 3
monthly PRP injections**



PRP Monotherapy

Before



**Three months after having
3 monthly PRP injections**



PRP Monotherapy

Before



**Three months after having 3
monthly PRP injections**





Low Level Laser Light Devices (LLLD)

Low-Level Laser Light Devices (LLLLD)

- FDA approved or cleared devices for male and female pattern hair loss, first in 2007.
- Patients can purchase themselves online without prescription.



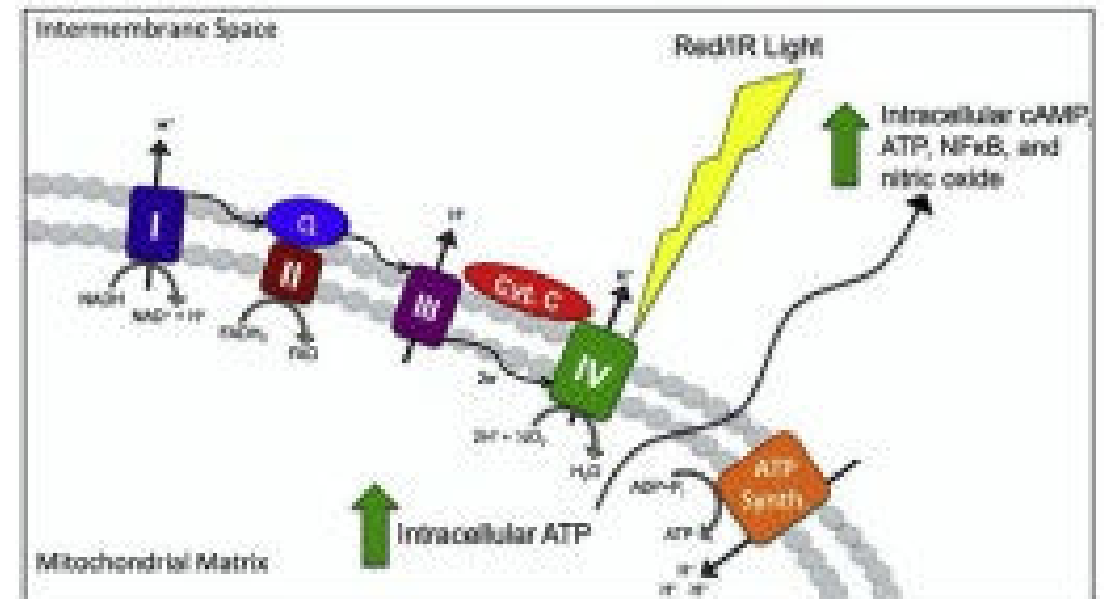
Fig. 3. Examples of in-home (ABC) and in-office (D) devices. A) Revian Red, Courtesy of Revian Red (Durham, NC); B) Theradome, Courtesy of Theradome (Silicon Valley, CA); C) HairMax, Courtesy of HairMax (Lexington International, Boca Raton, FL); D) Courtesy of Capillus (Miami, FL).

Energy-based Devices for Hair Loss

James T. Pathoulas, BA^a, Gretchen Bellefeuille, BS^a, Ora Raymond, BA^a, Bisma Khalid, MBBS, FCPS^b, Ronda S. Farah, MD^{a,*}

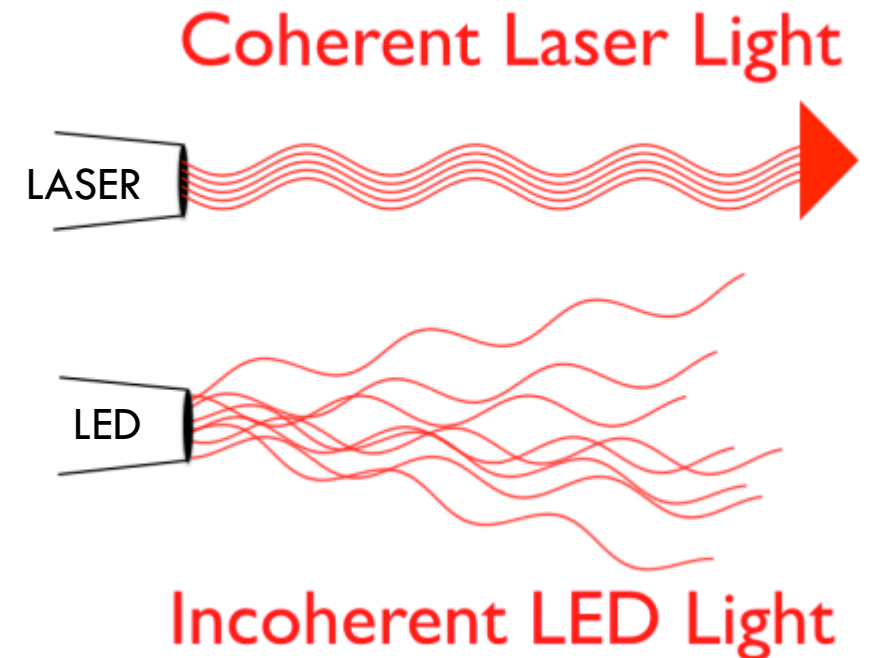
Low-Level Laser Light Devices (LLLD)

- Exact mechanism of action unknown.
 - ▣ Photo-dissociation of inhibitory nitric oxide from cytochrome C oxidase in mitochondria → ↑ATP production and cellular activity of hair follicle stem cells and keratinocytes.



LED versus Laser Devices

- Coherent and non-coherent light sources used for hair loss devices
 - ▣ Non-coherent light sources include light-emitting diodes (LEDs)
 - ▣ Coherent light sources are laser diodes
 - most at 655 nm (near infrared light)
 - ▣ Some devices use a combination of LEDs and laser diodes



LLLLD Study in Male AGA

Clin Drug Invest 2009; 29 (5)

- 6-month trial of LLLD vs sham device in 123 men with AGA.
- Treated 3x/week for 6 months.
- Subjects treated with the LLLD had a mean increase in terminal hair density of +19.8 hairs/cm², while subjects in the sham device group had a mean decrease of -7.6 hairs/cm².

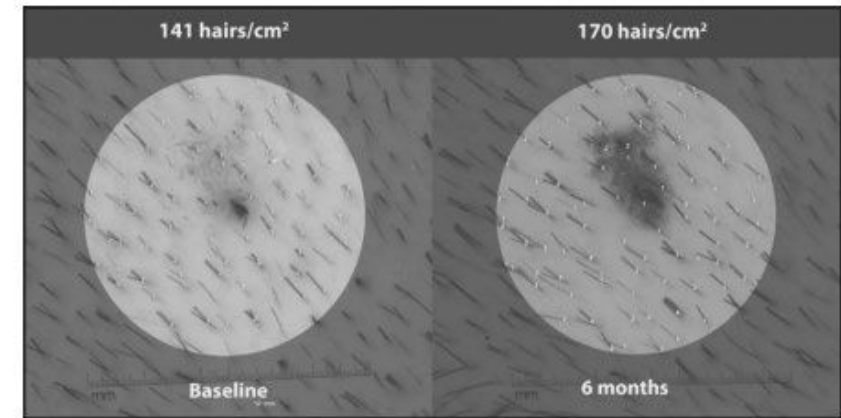


Fig. 1. Non-vellus hair density macroimages at baseline and 6 months in one patient in the HairMax LaserComb[®] group (6-month image shows evidence of ink spread).

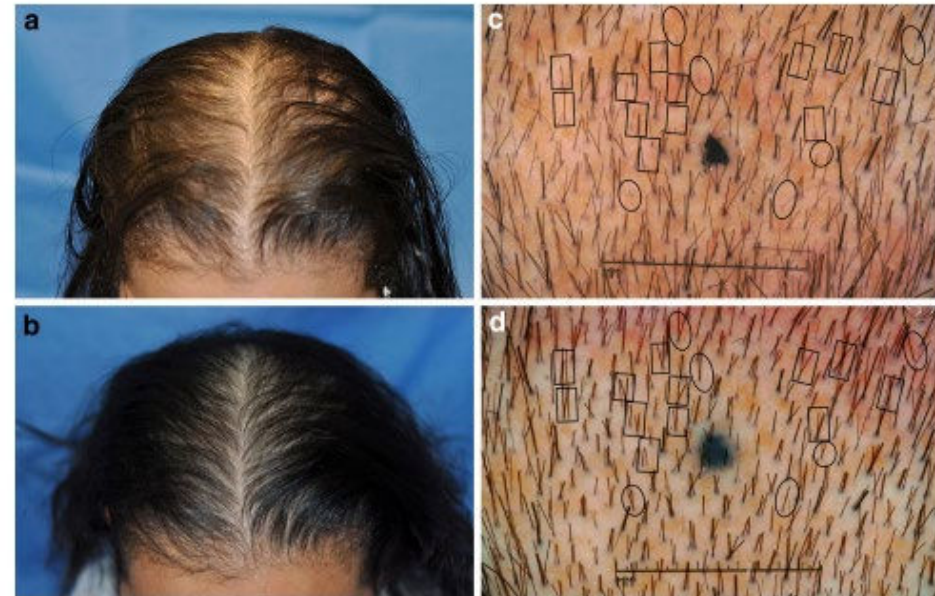
LLLD Study in Female Pattern Hair Loss

Am J Clin Dermatol 2014

- 6-month trial of LLLD vs sham device in 120 women with FPHL.
- Treated TIW x 15 mins/session.
- Mean increase in number of hairs in target area in patients treated with LLLD was 20 hairs/cm² vs 2.8 hairs/cm² in sham arm.
- No adverse events.

Fig. 3 Male and female pattern hair loss before and after lasercomb treatment. Global photographs of a female subject, at baseline (a) and after 26 weeks (b) of the 12-beam lasercomb treatment.

Macrophotographs of a male subject, at baseline (c) and after 26 weeks (d) of the 9-beam lasercomb treatment. Increased hair count through conversion of vellus or intermediate follicles to active follicles producing terminal hair (ovals) or resting telogen to active anagen follicles (rectangles) is highlighted



Low Level Laser Light Treatment

Before



After 6 months of 3x/week treatment



Table 1
Select of US Food and Drug Administration–approved photobiomodulation devices

Device	FDA Cleared	Light Source	Design	Treatment	Approximate Cost (\$)
CapillusUltra	2015	82 laser diodes	Hands-free sports cap	6 min daily	999.00
CapillusUltra+	2019	112 laser diodes	Hands-free sports cap	6 min daily	1399.00
CapillusPlus	2016	202 laser diodes	Hands-free sports cap	6 min daily	1999.00
Capillus X+	2019	244 laser diodes	Hands-free sports cap	6 min daily	2899.00
CapillusPro	2016	272 laser diodes	Hands-free sports cap	6 min daily	2999.00
CapillusRx	2016	312 Laser diodes	Hands-free sports cap	6 minutes daily	\$3499.00
HairMax Laser 272 PowerFlex Cap	2018	272 laser diodes	Hands-free sports cap	15 min, 3 times a week	1899.00
HairMax Laser 202 PowerFlex Cap	2018	202 laser diodes	Hands-free sports cap	15 minutes 3 times a week	\$1499.00
HairMax LaserBand 82	2014	82 laser diodes	Headband	Minimum 90 s, 3 times a week	799.00
HairMax LaserBand 41	2014	41 laser diodes	Headband	Minimum 3 min, 3 times a week	549.00
HairMax Ultima 12 LaserComb	2011	12 laser diodes	Comb	8 min, 3 times a week	399.00
HairMax Ultima 9 Classic LaserComb	2011	9 laser diodes	Comb	11 min, 3 times a week	199.00
iGrow Hair Growth Laser System	2012	21 laser diodes and 30 LEDs	Hands-free helmet	25 min, every other day	449.00
iRestore Essential	2016	21 laser diodes and 30 LEDs	Hands-free helmet	25 min, every other day	695.00
iRestore Professional	2019	82 laser diodes and 200 LEDs	Hands-free helmet	25 min, every other day	1195.00
Theradome Pro LH80	2017	80 laser diodes	Hands-free helmet	20 min, 2 times a week	895.00
Theradome Evo LH40	2018	40 laser diodes	Hands-free helmet	20 min, 4 times a week	595.00
Revian Red Hair Growth System	2017	100% LED, 660 and 620 nm wavelengths	Hands-free helmet	10 min daily	995.00
LaserCap LCPRO	2015	224 laser diodes	Hands-free sports cap	15–30 min, 2 times a week	2995.00
LaserCap300 MC2	2015	304 laser diodes	Hands-free cap	Not available	Not available
NutraStim Laser Hair Comb	2015	12 laser diodes	Comb	8 min, 3 times a week	279.00
illumiflow 272 Laser Cap	2017	272 laser diodes	Hands-free cap	30 min, 3 times a week	799.00
illumiflow 148 Laser Cap	2017	148 laser diodes	Hands-free cap	30 min, 3 times a week	549.00
Kiierr 148 Pro Laser Cap	2018	148 laser diodes	Hands-free sports cap	30 min, every other day	595.00
Kiierr 272 Premier Laser Cap	2018	272 laser diodes	Hands-free sports cap	30 min, every other day	845.00

Image from: Dermatologic Clinics, 2021-07-01, Volume 39, Issue 3, Pages 447-461

LED or Laser Device?

- ▣ Despite significant clinical research, the most effective parameters and device design for hair growth remain unclear.
- ▣ Need to identify the most efficacious wavelength, power, treatment time, treatment frequency, and light source.
- ▣ Devices are not covered by insurance, which limits access to patients with ability to purchase out of pocket.
- ▣ Understanding of optimal settings between various skin types is lacking.

In Summary

- PRP has been used for many years in wound healing, orthopedics, dentistry, and now for alopecia.
- Studies on efficacy are very hard to interpret since PRP preparation and treatment protocols vary so widely.
- Factors that increase PRP quality include the amount of whole blood used, the efficiency of platelet recovery, and the final volume of plasma in which the platelets are suspended.
- Data suggests that leukocyte poor PRP and CaCl₂-activated PRP are best for sustained, increased release of the right growth factors.
- Low level laser light devices can be helpful in the treatment of androgenetic alopecia in men and women, although the most effective parameters and device design for hair growth remain unclear.