Monitoring Response to Platelet-Rich Plasma in Patients with Alopecia Areata with Optical Coherence Tomography: A Case Series

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Alopecia areata (AA) is an autoimmune hair loss condition that is difficult to treat and frequently disruptive to the psychosocial well-being of patients. Platelet-rich plasma (PRP) is an innovative therapy that provides concentrated GFs that impart anti-inflammatory effects. Optical coherence tomography (OCT) is a noninvasive imaging modality with the potential for providing quantitative monitoring of AA response to PRP. Our objective is to share our experience using OCT to monitor the therapeutic progress of patients with AA treated with PRP. Two patients with patchy AA and one with alopecia universalis were treated with PRP three times at 6-week intervals as part of a larger clinical trial. Patients were followed from baseline to week 24 with OCT imaging. OCT demonstrates an increase in hair density associated with improvement in inflammation at week 24. Conversely, the patient with alopecia universalis did not experience any significant change in follicular activity. This case series exemplifies the potential of PRP in inflammatory regulation as well as hair regrowth in patchy AA, whereas there is no notable advantage in alopecia universalis. Our findings add evidence on the possible value of OCT in quantitatively assessing hair growth progress throughout a treatment course.


INTRODUCTION
Alopecia areata (AA) is an inflammatory, autoimmune, non-scarring hair loss condition affecting 0.1–0.2% of the American population and 2% of the world (Renert-Yuval and Guttmann-Yassky, 2017; Strazzulla et al., 2018). Disease severity ranges from isolated bald patches of the scalp to complete body hair loss. AA’s characteristically unpredictable relapse and remission pattern frequently devastate patients, greatly impact self-esteem and social development in youth, as well as increase the likelihood of psychiatric comorbidities (Wohlmut-Wieser et al., 2018).

Advances in understanding AA’s pathophysiology have motivated clinical trials using anti-inflammatory systemic and topical therapies (Jabbari et al., 2013; Wang et al., 2018). With the development of these additional treatments for AA, tools able to quantitatively discern effective therapeutic evidence are needed to better guide and advise patients. Optical imaging is an increasingly accessible, noninvasive technique that can be used for cross-sectional visualization of the skin’s microstructures. Optical coherence tomography (OCT) uses near-infrared, low-coherence interferometry to detect back-scattered photons at varying tissue depths to form high-resolution grayscale images analogous to those of ultrasound. This technology has been pivotal in the exploration of adjunct instruments for the diagnosis of both melanoma and nonmelanocytic lesions (Boone et al., 2014). OCT images reach 1.3 mm depth, provide a clear distinction between epidermal and dermal layers, as well as skin appendages such as hair follicles and also uphold comparable image quality for manual analysis of all Fitzpatrick skin types (Boone et al., 2012; Ekelem et al., 2019). Acquired data may be manipulated to provide horizontal en face viewing or vertical sections, synonymous with histology. Owing to its ability to visualize subepidermal structures, OCT can theoretically provide valuable information on the number of active hair follicles, associated appendageal structures, presence of a hair shaft, and hair shaft width.

Platelet-rich plasma (PRP) was first introduced as a regenerative aid for musculoskeletal injury and maxillofacial surgery in the 1960s (Alves and Grimalt, 2018). In vitro and in vivo studies show that VEGF, PDGF, and TGFβ lead to angiogenesis as well as differentiation and proliferation of fibroblasts to enhance wound repair (Alves and Grimalt, 2018; Li et al., 2012). The ability of PRP to induce synthesis of collagen and extracellular matrix proteins makes its benefits applicable to numerous inflammatory processes, including AA (Lynch and Bashir, 2016). The largest trial of PRP in patients with AA demonstrated a 60% complete

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Abbreviations: AA, alopecia areata; OCT, optical coherence tomography; PRP, platelet-rich plasma
remission rate after PRP, compared with only 29% receiving intralesional triamcinolone only (Trink et al., 2013). We present a case series of patients with AA treated with PRP whose treatment response was monitored both longitudinally and quantitatively using OCT.

RESULTS

Case 1 is a 60-year-old Caucasian female with an 11-year history of patchy AA and stable hypothyroidism. She reported no active hair loss or regrowth in the past 6 months, did not respond to intralesional triamcinolone injections in the past, and was not using any other concomitant medications for hair loss. Throughout her PRP treatment course, we monitored three alopecic patches and three areas of clinically unaffected scalp. OCT data demonstrated a 9 hair (16.4%) increase in the right parietal region, a 21 hair (350%) increase in the left temporal region, and a 21 hair (51.2%) increase in the frontal hairline patch from baseline to week 24 (Figure 1). Both the frontal hairline and left parietal patches showed marked clinical improvement by week 12, which was maintained or improved by week 24. OCT also demonstrated increased follicular counts of unaffected scalp regions, including the crown (18 hairs; 40%), left parietal (17 hairs; 36.2%), and right temporal regions (6 hairs; 27.3%) from baseline to week 24.

Case 2 is an otherwise healthy 69-year-old Caucasian female with a 25-year history of AA and no regrowth in the past 6 years since developing alopecia universalis. Topical and intralesional steroids were tried in the past with moderate response but not within the last 6 years. We monitored six scalp regions during her PRP treatment: midline frontal, vertex, and parietal, as well as bilateral frontal and temporal scalp. This patient did not grow any terminal hair and lacked a significant clinical response to PRP. OCT images captured small follicles only in the midline parietal region, which increased from 1 to 3 at week 24, but this was not clinically visible to the naked eye or on trichoscopy (Figure 2).

Case 3 is an otherwise healthy 58-year-old Hispanic female with patchy AA since age of 11 years, successfully treated with intralesional steroids without recurrence. In addition, she developed frontal fibrosing alopecia at age 54 years and had received intralesional and topical steroids and topical minoxidil in the past year. She discontinued all therapy before enrollment in the clinical trial with PRP for 3 months. On presentation, she had patchy AA on vertex in addition to frontal fibrosing alopecia pattern hair loss on her frontotemporal hairline. During the trial, the patient reported pruritus, tenderness, and shedding with worsening of AA peaking at week 12. At week 24, the patient reported decreased tenderness and minimal pruritus as well as hair

![Figure 1. Case 1 right parietal patch response to PRP at (a) baseline (b) week 12, and (c) week 24 with a corresponding vertical section of OCT data. The patient provided written, informed consent for publication of these images. OCT, optical coherence tomography; PRP, platelet-rich plasma.](image-url)
regrowth in patchy areas of AA. OCT data demonstrated that her vertex hair count decreased by 13 hairs (29.5%) from baseline to week 12 at the scalp vertex and then increased by 25 hairs (80.6%) by week 24 (Figure 3).

DISCUSSION
Many advances in understanding AA pathophysiology and treatment have been made in recent years. Trichoscopy remains a pillar for AA diagnosis but is limited by its inability to penetrate the skin surface. In this clinical trial, OCT provides valuable quantitative data to bolster qualitative and subjective clinical and photographic evidence of treatment response.

The cases presented highlight potential factors that may influence the PRP response rate in patients with AA. The two cases of patchy AA support the notion that patients with active inflammation or more recent patchy loss may respond to PRP, whereas longer standing diseases such as alopecia universalis with no acute activity may have limited to no response. Both cases of patchy AA demonstrate improvement in density, even in areas that were not clinically alopecic, which may represent normal hair growth or improvement of diffuse AA. The patient who concomitantly had frontal fibrosing alopecia also experienced improved inflammation and some hair regrowth in cicatricial areas. This patient also used a cooling measure with bagged ice applied to her scalp daily for 20 minutes for 3 months, the utility of which has been demonstrated with various cryotherapy tools in the literature (Jun and Lee, 2017).

Although PRP holds great therapeutic potential, standardized preparation methods to optimize platelet concentration and activation are not yet established. Differences exist in mean platelet volume and concentration, as well as the size of platelets and depth of scalp injection (Ozer et al., 2019). These factors may influence the efficacy of treatment in ways that are difficult to quantify and require further study to elucidate. The lack of internal control makes it difficult to determine with certainty whether the disease was slowed, stabilized, or improved. Other limitations in data analysis included confounding variables with concomitant therapies, possible human error in manual OCT image analysis, image artifact, or miscalibration in the relocation of scalp regions at follow-up imaging sessions. The challenges of OCT with limited depth were not relevant in this study as we were optimizing imaging for hair follicle quantification and calculation of epidermal thickness.

MATERIALS AND METHODS
This pilot study is approved by the University of California, Irvine Institutional Review Board, and is registered on ClinicalTrials.gov as NCT03376581. All patients provided written, informed consent for trial participation and consent for publication of deidentified photographs in 2017. Patients were treated with three intradermal PRP

Figure 2. Case 2 midline parietal scalp lack of significant response to PRP at (a) baseline (b) week 12, and (c) week 24 with a corresponding vertical section of OCT data. The patient provided written, informed consent for publication of these images. OCT, optical coherence tomography; PRP, platelet-rich plasma.
treatments (Eclipse PRP HC 22 ml Patient Kit, Eclipse Aesthetics, The Colony, TX) over their entire scalp at 6-week intervals. Clinical assessments were completed at weeks 6, 12, and 24 after baseline PRP treatment.

To quantitatively monitor PRP response, we used an in-line fiber-based swept-source OCT system (Thorlabs, Newton, NJ) with a 1,310 nm center wavelength and a spacer. OCT images were obtained of affected and unaffected areas, if applicable, at baseline, week 12, and 24. Scalp region relocation was achieved using individualized caps for each subject. Images were analyzed manually by two graders for follicular density using the program ImageJ (Schneider et al., 2012).

Data availability statement
Datasets related to this article will be provided upon reasonable request submitted to the corresponding author.

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CONFLICT OF INTEREST
Zhongping Chen declares financial interests in OCT Medical Imaging, which did not provide any support for this study. The authors did not receive any monetary funding from agencies in the public, commercial, or not-for-profit sectors for this project. The remaining authors state no conflict of interest.

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AUTHOR CONTRIBUTIONS
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REFERENCES


