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MAJOR PAPER

MR Imaging of Hair and Scalp for the Evaluation of Androgenetic Alopecia

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Purpose: Although androgenetic alopecia (AGA) is a common cause of hair loss, little is known regarding the magnetic resonance imaging (MRI) of the AGA or scalp. This study aimed to analyze whether MRI for hair and scalp (MRH) can evaluate anatomical changes in the scalp caused by AGA.

Methods: Twenty-seven volunteers were graded for the severity of AGA using the Hamilton–Norwood Scale (HNS), commonly used classification system. All subjects underwent MRH; two radiologists independently analyzed the images. As a quantitative measurement, the number of hair follicles was analyzed and compared with the HNS. As a qualitative analysis, each MRH scan was visually graded in terms of the severity of alopecia, using a 4-point MR severity score. The scores were compared with the HNS.

Results: The volunteers were divided into two groups of 12 and 15 males without and with AGA at their vertex, respectively. Inter-observer agreements for the hair count and the MR severity score were excellent. The mean hair count on MRI in the normal group was significantly higher than that in the AGA group ($P < 10^{-4}$). The MR severity score in the AGA group was significantly more severe than that in the control group ($P < 10^{-4}$). In terms of the presence or absence of thinning hair, the MR severity score was consistent with the HNS determined by a plastic surgeon in 96% of cases. MR severity scores of clinically moderate AGA cases were significantly lower than those of severe cases ($P = 0.022$).

Conclusion: MRH could depict scalp anatomy showing a clear difference between AGA and normal scalps, in both hair count and subjective visual assessment. The MR severity score was in good agreement with the clinical stages by HNS. The results support the potential of MRH as a promising imaging technique for analyzing healthy and pathological scalps.

Keywords: *magnetic resonance imaging, alopecia, scalp, hair follicle, skin*

Introduction

Hair loss is a common complaint in dermatological practice. It negatively impacts a patient's quality of life. Androgenetic alopecia (AGA) is the most common cause of hair loss, affecting up to 80% of Caucasian men aged over 70 years.[1] Additionally, the majority of cases (as many as 52% of male patients) present to clinics with complaints of hair loss, despite having a normal or even higher density of hair.[2]

Currently, there are several limitations in the diagnosis and evaluation methods of AGA, which are largely restricted to subjective assessments by physicians and patients.[1,3] With the development of newer drugs and therapeutic options, there is an increasing need for reliable and non-invasive methods for evaluating hair disorders.

Although magnetic resonance imaging (MRI) has been widely used for medical imaging, there is no report regarding the evaluation of the scalp anatomy of alopecia, because visualization of the small structures like the scalp and hair follicles has been challenging. Since MRI can non-invasively and objectively delineate tissue changes in living bodies, scalp signals are expected to change with AGA. Can MRI for hair and scalp (MRH) visualize scalp changes in AGA compared with healthy scalps? If the changes can be visualized, will the changes in MRH findings correlate with existing

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clinically used assessment methods? To answer these two clinical questions, we compared MRH findings between healthy subjects and patients with AGA. Also, MRH findings were compared with clinically assessed severity of AGA by the Hamilton–Norwood Scale (HNS), which is the most commonly used classification method.[3]

Materials and Methods

Patients

We conducted a prospective pilot study in which healthy volunteers were recruited to investigate the efficacy of MRH to evaluate androgenetic alopecia. Twenty-eight consecutive asymptomatic male volunteers were enrolled in this study. A plastic surgeon, who specializes in clinical practice of AGA and has more than 10 years of experience, examined these volunteers. The presence or degree of thinning hair was classified using the HNS. As a sub-classification of the HNS, grade IV or higher was defined as severe, and IIv and IIIv as moderate.

The volunteers prospectively underwent MRH between August 2015 and May 2017. The study was approved by the ethical committee of our institute, and written informed consents were obtained from all 28 participants (approval number: 2286). One candidate was excluded for a withdrawn consent, leaving 27 males.

Imaging protocol

Examinations were performed with a 3-T MR scanner (Achieva, Philips Healthcare, Best, The Netherlands) using a 32-channel torso coil. The participant was placed in the supine position with the head hyperextended to minimize the distance between the coil and occipitoparietal scalp for the optimization of the signal-to-noise ratio. The shoulders were elevated with a sandbag to stabilize the overextended head. To improve the reproducibility of the MRH scan, the international 10/20 system, a standard system for the positioning of electroencephalographic electrodes, was applied to determine the scan area on the scalp. A skin marker (nifedipine capsule, Adalat™, Bayer AG Leverkusen, Germany) was placed at the medial parietal region (midway between the vertex and occipital pole) to replicate the area to be scanned between participants. Localization of the marker was performed using a large field-of-view (FOV) localizer sequence. T_1-weighted sequence was performed with TR/TE = 586/23 ms, 10 slices, 2.5 mm slice thickness with 2.5 mm gap, four echo train length, reconstruction matrices of 528 × 528, and two excitations. FOV was 100 × 100 mm with an in-plane resolution of 0.19 × 0.19 mm. The acquisition time was 3 min 19 s.

Image assessment

For all 27 candidates, anonymized MR images were independently assessed by two experienced (>18 and >7 years) radiologists (SS and AM) using a picture archiving and communication system viewer (EV Insite; PSP Corp., Tokyo, Japan). In cases of disagreement, agreement was reached by consensus. The site of measurement was matched in both groups using the fiducial marker mentioned above. For each patient, one slice that was free of artifacts and closest to the marker was used for image analysis.

Data collection

As a quantitative measurement, the number of hair follicles was analyzed in each participant. Identification of hair follicles in MRH images was based on previous skin MRI studies[4,5] and scalp anatomy.[6] Specifically, the hair follicles were considered as low-signal linear structures running vertically in the scalp and did not reach the lower edge of the subcutaneous fat layer, while the hypointense linear structures reaching the lower edge of the subcutaneous fat layer were diagnosed as fibrous septa.[6–8] The results of consensus interpretation were compared with the clinical stages of AGA (HNS). As a qualitative analysis, to determine whether visually assessed MR severity score of alopecia might correlate with clinical staging, each MRH scan was visually graded into four levels of alopecia types using a classification method similar to that of basic and specific classification[9] (Table 1). The MR severity scores were compared with the clinical stages (HNS).

Statistical analysis

Intraclass correlation coefficient was calculated to assess agreement between observers for the hair follicle number count. Agreement between observers for visual grading of alopecia was assessed with Spearman's rank correlation test. The scale for the intraclass correlation coefficient and the Spearman's ρ was: <0.20 = poor, 0.21–0.40 = fair, 0.41–0.60 = moderate, 0.61–0.80 = good, and 0.81–1.00 = excellent agreement. Student's *t*-test was applied to determine the significance of differences in numbers of hair follicles between the patient groups. The MR severity scores were compared with the Fisher exact probability test. Data are expressed as means ± SD with $P = 0.05$ considered significant. Statics were performed using Stata Statistical Software Release 15 (Stata Corp., College Station, TX, USA).

Results

Using the HNS classification, the volunteers were divided into two groups: 12 healthy males with no hair loss at the

Table 1 MR severity score

Score	Hair loss types
1	No hair loss.
2	Thinning of the hair is perceptible (mild change).
3	Thinning of the hair is pronounced (moderate change).
4	Thinning of the hair around the vertex is very sparse or absent (severe change).

vertex (normal group, HNS grades I–III), and 15 males with AGA at their vertex (AGA group, HNS grade IIv, IIIv, IV–VII) (Table 2). There was no significant difference in age between the normal and AGA groups ($P = 0.75$, Table 2). All images were considered high technical quality and suitable for analysis. Representative images are shown in Figs. 1–3. The scalp image of normal subjects could demonstrate dermal structures such as dense hair follicles as well as skin layers (Figs. 1 and 2). MRH revealed that almost no hair follicle remained in the scanned region of a patient with severe AGA (Fig. 3), although fibrous septa in the hypodermis were visible. In all participants, the epidermis and dermis appeared as a dark thin layer, and the hypodermis was hyper-intense compared to the other layers of the skin (Fig. 2). The intraclass correlation coefficient for the hair follicle number count was excellent (0.88), and the inter-observer agreement was excellent for the MR severity score (Spearman's $\rho = 0.97$). A comparison of hair counts between the normal and the AGA groups is shown in Table 2. The mean hair count on MRH in the normal group was significantly higher than that in the AGA group ($P < 10^{-4}$).

Table 2 Participants included in study and results of image analyses stratified by normal and AGA groups

	Normal group	AGA group	*P*-value
Number of participants (*n*)	12	15	N/A
Age (years)	46 ± 7.1	44 ± 11	0.75*
Total hair count (count per slice)	137 ± 7.1	65 ± 37	$<10^{-4}$*
MR severity score	1.0 ± 0.0	3.2 ± 0.86	$<10^{-4}$†

Data are presented as number or mean ± standard deviation. *Student's *t*-test. †Fisher exact probability test. AGA, androgenetic alopecia.

The MR severity score (Fig. 4) in the AGA group was significantly more severe than that in the normal group ($P < 10^{-4}$, Table 2). In the normal group, all 12 subjects scored 1 (No hair loss) on MRH, and in the AGA group, 14 out of 15 patients, except for one with clinically moderate AGA (HNS IIIv), were rated as alopecia (2–4 points) by MRH (Table 3). As a result, regarding the presence or absence of thinning hair, the MR severity score was consistent with the clinical staging by the HNS in 96% (26 of 27 cases). For clinically severe cases of AGA (HNS IV–VII), all nine subjects were classified as moderate or severe, with a 3 or 4 score on the

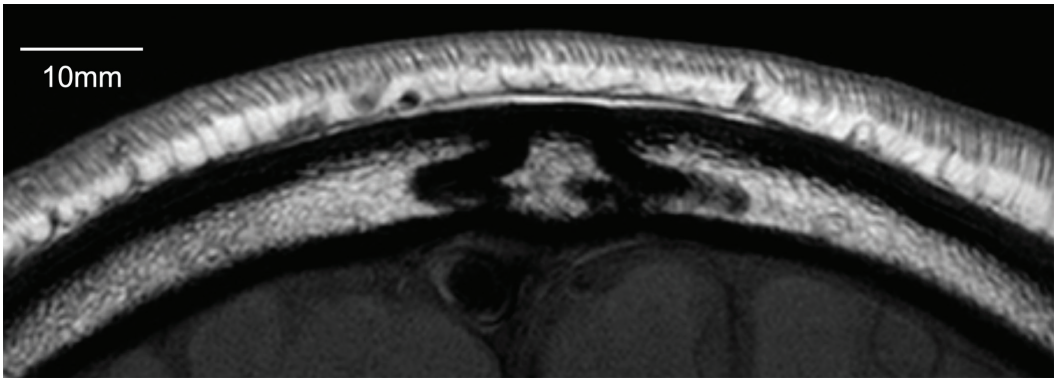

Fig. 1 Representative MR image of the normal scalp in a healthy 55-year-old male with no hair loss allowed a global anatomical analysis of the scalp and hair follicles (e.g., population and dermal penetration). The scale bar represents 10 mm.

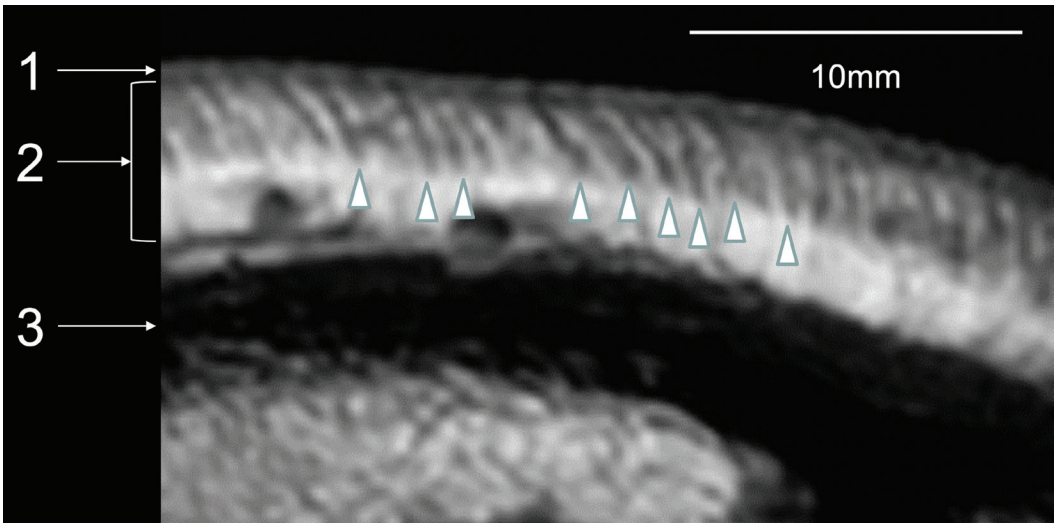

Fig. 2 Magnified MR image of the normal scalp in a healthy volunteer (the same subject as Fig. 1) demonstrating the hair follicles (arrowheads) and various skin layers. The following structures can be recognized: 1, epidermis plus dermis; 2, hypodermis; 3, skull. The scale bar represents 10 mm.

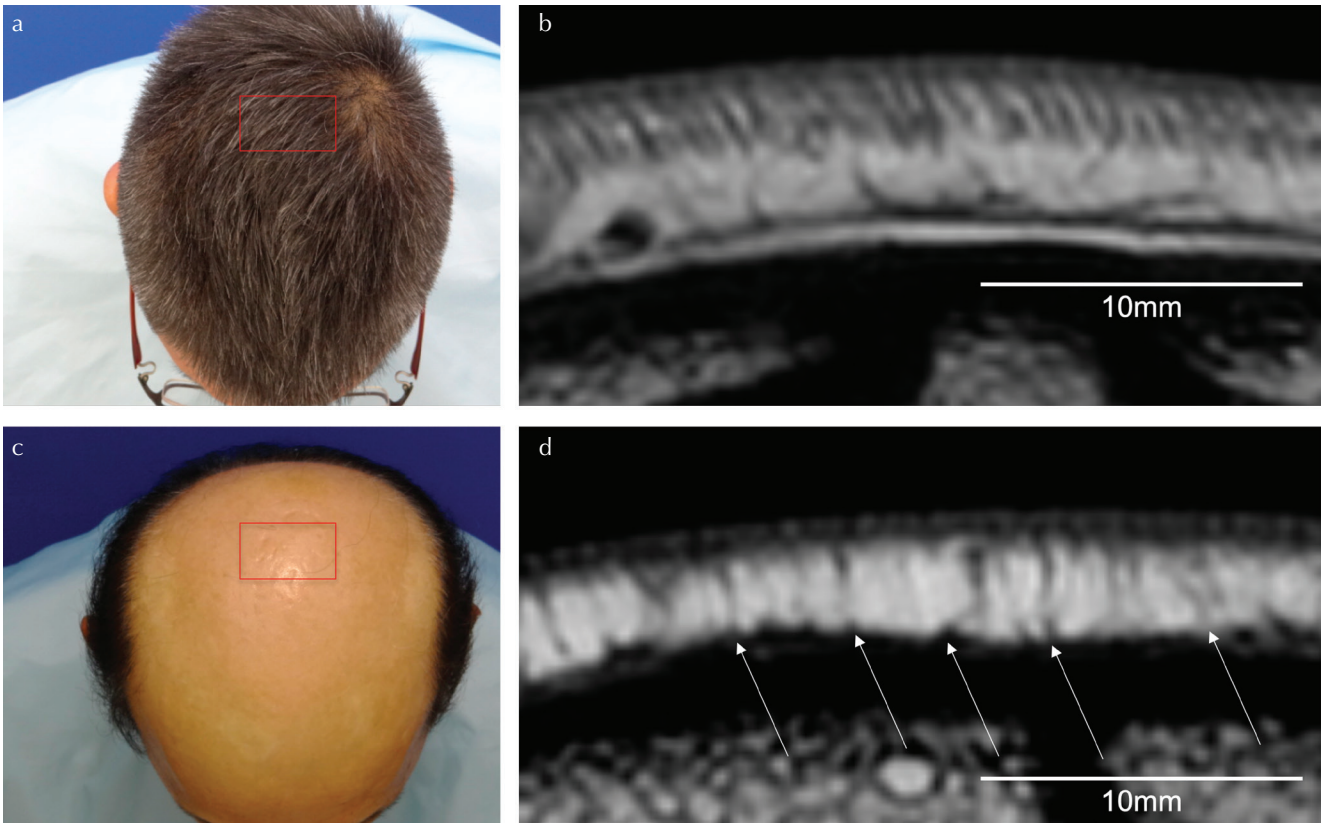

Fig. 3 Comparison of the clinical appearances and MR images of a non-alopecia volunteer (the same subject as shown in Fig. 1) and a male with the most advanced stage of androgenetic alopecia (Hamilton Norwood scale grade VII). The scanned areas are indicated by the red rectangles in (**a**) and (**c**). The scale bar represents 10 mm. (**a**) A global photograph of the normal subject showing no hair loss. (**b**) MR image of the normal scalp showing dense hair follicles. The MR severity score is 1. (**c**) Extensive hair loss with only a wreath of hair left in the back and sides of the scalp is shown on a global photograph of the male with severe alopecia. (**d**) MRI showing the absence of hair follicles, although fibrous septa in the hypodermis are seen as low-intensity lines (arrows). The MR severity score is 4.

Table 3 Number of participants stratified by MR severity scores and clinical severity

MRI severity score	Clinical Severity			Total
	Normal (HNS I–III)	Moderate (HNS IIv, IIIv)	Severe (HNS IV–VII)	
1	12	1	0	13
2	0	1	0	1
3	0	4	3	7
4	0	0	6	6
Total	12	6	9	27

visual assessment (Table 3). The MR severity scores of clinically moderate AGA cases were significantly lower than that of severe cases (2.5 ± 0.84 vs. 3.7 ± 0.50, $P = 0.022$).

Discussion

This study revealed two points. First, MRH could depict the scalp anatomy and show a clear difference between AGA and normal scalps, in both hair count and subjective visual evaluation. To the best of our knowledge, this is the first report on scalp MRI *in vivo*. The hair follicles appeared as low signal intensity on the T_1-weighted image, as previously described in non-scalp skin MRI studies.[4,5] In contrast, the hypodermis demonstrated high signal intensity on the T_1-weighted image, corresponding to fat lobules. The epidermis and dermis showed a lower signal than the subcutaneous fat, and the boundary between the two layers was unclear. The results are consistent with existing studies demonstrated that the T_1 relaxation times of the epidermis and dermis are equivalent[10] and longer than that of the hypodermis.[7]

Second, the subjective visual assessment of MRH was in good agreement with the clinical stages by HNS. In other words, the severity of AGA judged by a glance of MRH images was in excellent agreement with the HNS determined by a physician who specializes in the treatment of AGA. One advantage of MRH is that the examination can be easily performed within 10 min using a standard commercially available MRI scanner. Besides, MRH has the inherent advantage of being non-invasive without radiation exposure and can be repeated as needed. The evaluation of the scalp by MRH is

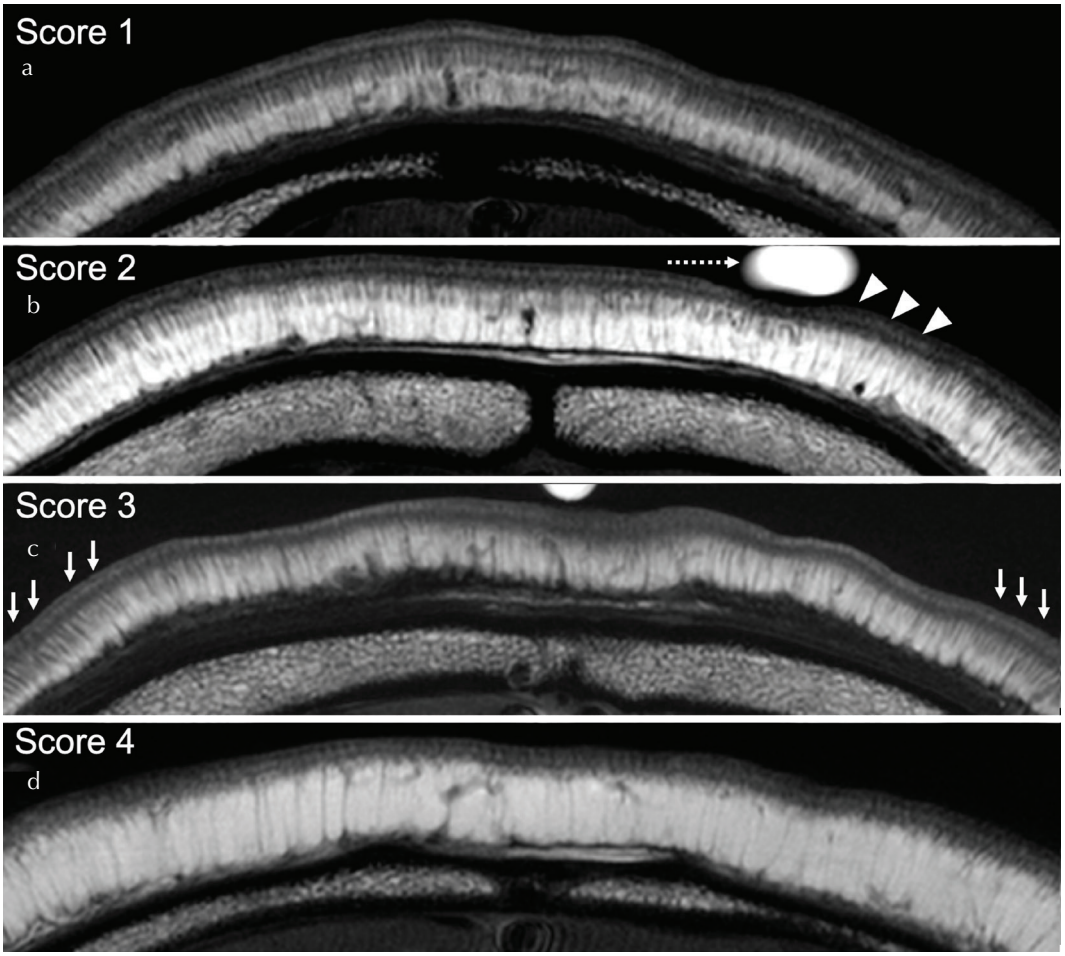

Fig. 4 Representative images of MR severity scoring. The extent of alopecia is visually scored on a four-point scale. (**a**) Score 1, no hair loss. Hair follicles are densely present throughout the scanned scalp. (**b**) Score 2, mild hair loss. Note that the hair follicles are sparse in a small area (arrowheads) near the fiducial marker (dashed arrow). Hair follicles are slightly sparse overall compared to the scalp with a score of 1. (**c**) Score 3, moderate hair loss. Hair follicles remain in some areas (arrows) but are sparse in most areas. (**d**) Score 4, severe hair loss. Few hair follicles can be identified throughout the scanned scalp, although fibrous septa in the hypodermis are visible.

not affected by hairstyle or hair length, and can visualize the anatomy of the scalp in the living body as is.

A few reports showed scalp images using ultrasound,[11–13] but the boundaries of the hair follicles in the presented images seemed more unclear than with MRH. Although direct comparative study should be performed, Sans et al.[7] advocated that MRI seemed more effective for skin imaging compared with high-resolution ultrasound, which has limited penetration (to a depth of 6–10 mm). Moreover, with serial imaging, reproducibility can be a concern since ultrasonography has the disadvantages of operator dependence.

We acknowledge several study limitations. First, the spatial resolution of MRH is still insufficient to clearly delineate all hair follicles, although our technique employed a small FOV and a unique patient position to improve image quality. According to previous pathological research, the average follicular density was approximately three follicles/mm^2.[14] Based on this data, our protocol should contain approximately 750 hair follicles per slice, because one slice contains a scan area of 250 mm^2. However, the actual number counted by MRH (137 ± 7.1) was less than one-fifth. The discrepancy is probably due to limited spatial resolution and partial volume effect. In particular, the slice thickness was set to 2.5 mm to maintain the signal-to-noise ratio; the spatial resolution in the slice direction was relatively lower than the in-plane resolution. Second, this pilot study did not evaluate other areas of the scalp than vertex, though AGA occurs in the frontotemporal area as well as the vertex, following a pattern corresponding to the HNS.[3] Although improbable, MRH findings described above may vary depending on the area examined. Finally, the current study included a small number of patients. While future studies would incorporate higher spatial resolution, various scalp locations, larger patient cohort, and different contrast, the significance of the data with high inter-observer agreement supports the potential of MRH as a new objective evaluation method for AGA.

In conclusion, we have shown that MRH could depict the scalp anatomy and show a clear difference between AGA and normal subjects, in both hair count and subjective visual evaluation. Besides, the subjective visual assessment of MRH was in good agreement with the HNS for the presence and severity of AGA. Although the visual inspection will continue to be the primary diagnostic tool for AGA, the results of this study support the potential of MRH as a promising non-invasive imaging technique for analyzing healthy or pathological scalp. MRH may also serve as a reference

method for future research on AGA and the scalp. Future MRI studies should clarify further details of anatomical changes associated with AGA. Additionally, future improvement of spatial resolution and image quality should be obtained shortly, with the development of tailored surface coil arrays and the evolving artificial-intelligence-based approach to image reconstruction, which provides higher quality images from less data.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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