

# Actualidades en Alopecia Frontal Fibrosante: Lo bueno, lo malo y lo feo

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CTA Lab

And

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# Lecture Overview

- Causation of FFA
- 2mm punch and mucin stain

## Postmenopausal frontal fibrosing alopecia. Scarring alopecia in a pattern distribution.

Kossard S<sup>1</sup>.

⊕ Author information ⊕ Papers ▾

### Erratum in

Arch Dermatol 1994 Nov;130(11):1407.

### Abstract

**BACKGROUND:** Recession of the frontal hairline is a common event in postmenopausal women. This has been shown not to be a marker of gross androgenization, and is usually a progressive nonscarring alopecia. Six postmenopausal women, who developed a progressive frontal scarring alopecia, were studied and their clinical and laboratory data, as well as the results of scalp biopsy specimens in all six patients, were analyzed and compared with recognized forms of scarring alopecia and recently described findings in androgenetic alopecia.

**OBSERVATIONS:** The six postmenopausal women developed a progressive frontal hairline recession that was associated with perifollicular erythema within the marginal hairline, producing a frontal fibrosing alopecia extending to the temporal and parietal hair margins. Scalp biopsy specimens from the frontal hair margin showed perifollicular fibrosis and lymphocytic inflammation concentrated around the isthmus and infundibular areas of the follicles. Immunophenotyping of the lymphocytes showed a dominance of activated T-helper cells. Clinical review of all six cases showed a progressive marginal alopecia without the typical multifocal areas of involvement seen in lichen planopilaris or pseudopelade. None of the patients had mucous membrane or skin lesions typical of lichen planus. Hormonal studies, in five patients, showed no elevated androgen abnormalities.

**CONCLUSIONS:** Progressive frontal recession in postmenopausal women may show clinical features of a fibrosing alopecia. The histologic findings are indistinguishable from those seen in lichen planopilaris. However, the absence of associated lesions of lichen planus in all six women raises the possibility that this mode of follicular destruction represents a reaction pattern triggered by the events underlying postmenopausal frontal hairline recession.

# Lichen Planopilaris (LPP)

- Miniepidemic?
  - ◆ Hair loss clinicians observing increased incidence.
  - ◆ Traditionally West Coast > East Coast

# Lichen Planopilaris

## Increasing Incidence

- ?Nanoparticle?
  - ◆ Sunscreen?
  - ◆ Lichen planus—Metals, especially dental implicated
    - ◆ Gold, mercury—dental\*
    - ◆ Nail LP associated with +metal patch test\*\*

\*Sasaki G et al. J Dermatol 23:890, 1996.

\*\*Nishizawa A et al. J Eur Acad Dermatol Venerol 27:e231, 2013.

# African people with FFA



Dlova NC *et al.* BRJ 169:939-41, 2013.

# Frontal fibrosing alopecia: possible association with leave-on facial skin care products and sunscreens; a questionnaire study.

Aldoori N<sup>1</sup>, Dobson K<sup>1</sup>, Holden CR<sup>1</sup>, McDonagh AJ<sup>1</sup>, Harries M<sup>2</sup>, Messenger AG<sup>3</sup>.

## Author information

### Abstract

**BACKGROUND:** Since its first description in 1994, frontal fibrosing alopecia (FFA) has become increasingly common, suggesting that environmental factors are involved in the aetiology.

**OBJECTIVES:** To identify possible causative environmental factors in FFA.

**METHODS:** A questionnaire enquiring about exposure to a wide range of lifestyle, social and medical factors was completed by 105 women with FFA and 100 age- and sex-matched control subjects. A subcohort of women with FFA was patch tested to an extended British standard series of allergens.

**RESULTS:** The use of sunscreens was significantly greater in the FFA group compared with controls. Subjects with FFA also showed a trend towards more frequent use of facial moisturizers and foundations but, compared with controls, the difference in frequencies just failed to reach statistical significance. The frequency of hair shampooing, oral contraceptive use, hair colouring and facial hair removal were significantly lower in the FFA group than in controls. Thyroid disease was more common in subjects with FFA than controls and there was a high frequency of positive patch tests in women with FFA, mainly to fragrances.

**CONCLUSIONS:** Our findings suggest an association between FFA and the use of facial skin care products. The high frequency of sunscreen use in patients with FFA, and the fact that many facial skin care products now contain sunscreens, raises the possibility of a causative role for sunscreen chemicals. The high frequency of positive patch tests in women with FFA and the association with thyroid disease may indicate a predisposition to immune-mediated disease.

# Frontal fibrosing alopecia in men: an association with facial moisturizers and sunscreens

DOI: 10.1111/bjd.15311

DEAR EDITOR, Frontal fibrosing alopecia (FFA) was first described by Kossard in 1994 in six postmenopausal women.<sup>1</sup> FFA remained rare during the 1990s, but in the last 10–15 years it has become increasingly common, a phenomenon observed worldwide. The recent onset and apparently rising incidence of FFA suggest involvement of environmental factors in the aetiology. We previously reported a questionnaire study in women with FFA that asked about a wide range of medical, social and environmental exposures. The results suggested an association between FFA and leave-on facial products, including moisturizers and sunscreens.<sup>2</sup> However, although the regular use of moisturizers was greater in women with FFA, these products are used by most women and we were unable to show a significant difference in their use between women with FFA and similarly aged controls. The use of primary sunscreens was significantly greater among women with FFA than in controls, but we were not able to assess whether patients were also exposed to sunscreens from other sources.

We have therefore repeated our questionnaire study in men with FFA, as we anticipated that their use of leave-on facial skincare products would be lower than in women.

As FFA is rare in men, patients were recruited from across the U.K. and one case was recruited from Belgium. In all cases the diagnosis was made by a clinician with special expertise in hair disease, and it was supported by histology in most cases. The clinical diagnosis was based on scarring alopecia affecting the frontal hairline causing recession of the hairline. Additional features included loss of eyebrows, follicular erythema of the frontal hairline and loss of sideburn and beard hair. Male controls aged 35–80 years were recruited from three sites (Sheffield, Salford and Glasgow). The patients completed a questionnaire similar to that used in our female study, but inviting more detailed information on the use of facial skincare and hair care products. Male patients with FFA were asked about the timing and distribution of hair loss, but otherwise the questionnaires completed by both groups were identical.

Seventeen men with FFA and 73 controls were recruited. The mean age of onset of hair loss in the patients with FFA was 54.5 years (range 35–77). All had loss of hair from the frontal hairline, and 16 (94%) had lost eyebrows. Twelve

men (71%) reported loss of hair from the beard and 13 (76%) reported loss of hair from the limbs. All men with FFA reported using facial moisturizers, compared with 40% in the control group. Facial moisturizers were used at least twice a week by 94% of patients with FFA, but by only 32% of controls ( $P < 0.001$ ) (Table 1). Sixteen patients reported using moisturizers for a period consistent with their use prior to the onset of FFA. The use of primary sunscreens by men with FFA was significantly more common than by controls. Overall 35% of men with FFA reported using a sunscreen at least twice a week all year round, compared with 4% of controls ( $P = 0.0012$ ).

When moisturizers containing sunscreen chemicals were included in the analysis, at least 71% of men with FFA applied a product containing a sunscreen at least twice a week all year

**Table 1** Reported use of skincare and hair care products by patients with frontal fibrosing alopecia (FFA) and controls

	Patients with		
	FFA	Controls	P-value
Number of patients	17	73	
Age (years), mean (range)	63.1 (42–80)	59.1 (37–79)	
Age at onset of hair loss (years), mean (range)	54.5 (35–77)		
Facial moisturizer <sup>a</sup>	16 (94)	23 (32)	< 0.001
Primary sunscreen <sup>b</sup>	6 (35)	3 (4)	0.0012
Sunscreen <sup>b</sup>	12 (71)	8 (11)	< 0.001
Facial cleanser <sup>a</sup>	4 (24)	5 (7)	0.066
Facial scrub <sup>a</sup>	0	0	
Facial mask <sup>a</sup>	0	0	
Aftershave <sup>a</sup>	7 (41)	28 (39)	1.00
Shampoo <sup>a</sup>	13 (76)	62 (85)	0.27
Conditioner <sup>a</sup>	4 (24)	13 (18)	0.73
Hair spray <sup>a</sup>	1 (6)	2 (3)	0.48
Hair mousse <sup>a</sup>	0	0	
Hair gel <sup>a</sup>	2 (12)	10 (14)	1.00
Hair dye <sup>c</sup>	2 (12)	3 (4)	0.26

Values are n (%) unless stated otherwise. <sup>a</sup>Twice a week or more frequently. <sup>b</sup>Twice a week or more frequently all year round. <sup>c</sup>At least once a year. Sunscreen includes exposure to sunscreen chemicals in primary sunscreens and moisturizers. Analyses were performed after excluding subjects who failed to answer the question. Frequencies in the FFA and control groups were compared using Fisher's exact test.

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# Risk factors associated with frontal fibrosing alopecia: a multicentre case–control study

**O. M. Moreno-Arrones,<sup>1</sup> D. Saceda-Corralo,<sup>1</sup> A. R. Rodrigues-Barata,<sup>1</sup> M. Castellanos-González,<sup>2</sup> M. A. Pugnaire,<sup>3</sup> R. Grimalt,<sup>4</sup> A. Hermosa-Gelbard,<sup>1</sup> C. Bernárdez,<sup>5</sup> A. M. Molina-Ruiz,<sup>6</sup> N. Ormaechea-Pérez,<sup>7</sup> P. Fernández-Crehuet<sup>8</sup> and S. Vaño-Galván<sup>1,9</sup>**

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# Alopécie frontale fibrosante post ménopausique : une réaction lichénoïde aux nanoparticules de dioxyde de titane présentes dans les follicules pileux?

Charlotte Gary<sup>1</sup>, Florence Brunet-Possenti<sup>1</sup>, Eduardo Marinho<sup>2</sup>, Lydia Descamps<sup>2</sup>, Hester Colboc<sup>3</sup>, Dominique Bazin<sup>4</sup>, Vincent Descamps<sup>1</sup>

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<sup>4</sup> Synchrotron SOLEIL, Gif-sur-Yvette



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### INTRODUCTION

L'alopécie frontale fibrosante (AFF) post ménopausique est une pathologie émergente dont l'incidence augmente dans l'ensemble des pays. Son origine reste inconnue. Nous rapportons la présence de dioxyde de titane dans les cheveux d'une patiente atteinte d'AFF.

### OBSERVATION

Une patiente âgée de 79 ans était suivie en consultation depuis 2010 pour une alopécie progressive évoluant au moins depuis 12 ans soit depuis l'âge de 69 ans prédominant au niveau fronto-temporo-pariétal avec recul progressif de la ligne d'implantation des cheveux. Elle s'associait à une alopécie des sourcils. A l'examen la peau du front était saine. Les cheveux présentaient à leur ostium folliculaire un léger érythème avec hyperkératose. Le tableau clinique était typique d'une AFF (Fig. 1). Une biopsie cutanée était réalisée confirmant le diagnostic d'alopécie cicatricielle lymphocytaire. Cette patiente avait par ailleurs une forte héliodermie témoignant d'une exposition solaire importante tout au long de sa vie.



Figure 1

### MÉTHODES ET RÉSULTATS

Une recherche de nanoparticules a été réalisée sur des follicules pileux extraits en zone atteinte par microscopie électronique à balayage par effet de champs combinée à une spectroscopie à dispersion énergétique. Un jeu de clichés de microscopie électronique à balayage sur un microscope de dernière génération a été collé sur un ensemble de cheveux mettant en évidence des dépôts anormaux de nanoparticules (Fig. 2A, 2B). En complément, les expériences de fluorescence X induites par des électrons sur le microscope électronique à balayage montraient distinctement un signal attribuable aux atomes de titane (Fig. 2C, 2D).

Cette observation met ainsi en évidence sans ambiguïté la présence de nanoparticules de dioxyde de titane au niveau des follicules pileux.

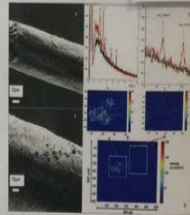


Figure 2

### DISCUSSION

L'AFF est considérée comme une forme particulière de lichen folliculaire avec histologiquement un infiltrat lymphocytaire perifolliculaire. Des études épidémiologiques récentes associent la présence de cette alopécie à l'utilisation de cosmétiques en particulier de crèmes solaires. En reprenant l'interrogatoire de cette patiente signalait l'utilisation quotidienne depuis 15 ans d'écrans solaires contenant du dioxyde de titane.

Du fait des propriétés anti-UV, la présence de nanoparticules (dioxyde de titane et oxyde de zinc) s'est très largement répandue au cours de ces dernières années dans les produits cosmétiques, et l'impact dermatologique à long terme de ces particules n'est pas encore bien connu chez l'homme. L'hypothèse formulée est que la présence de dioxyde de titane au sein du follicule pileux soit responsable d'une réaction lichénoïde. Des réactions lichénoïdes sont connues avec d'autres métaux tels que le Nickel. Des explorations complémentaires sont en cours chez cette patiente (tests épicutanés et tests in vitro de prolifération lymphocytaire et ELISPOT en présence de titane).

### CONCLUSION

Nous présentons la première observation de présence de nanoparticules dans les follicules pileux d'une patiente atteinte d'AFF post-ménopausique.

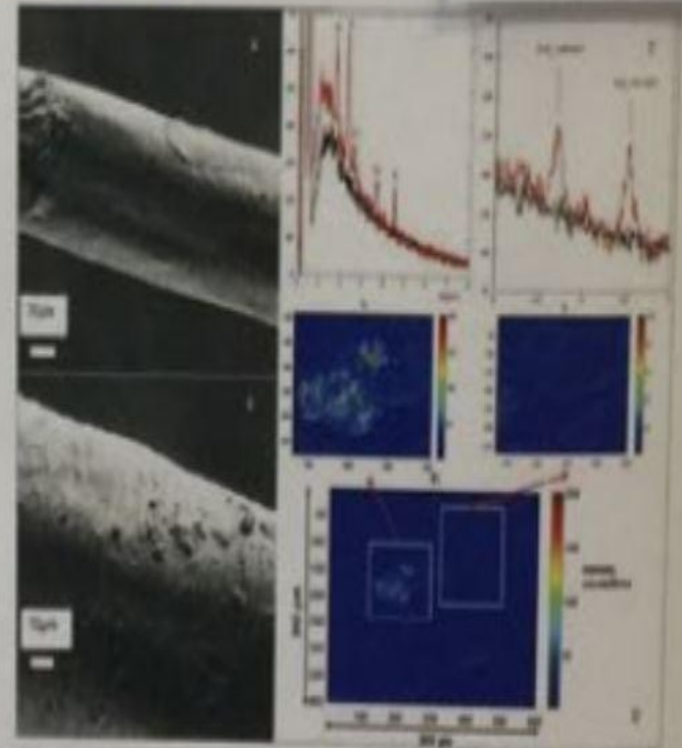
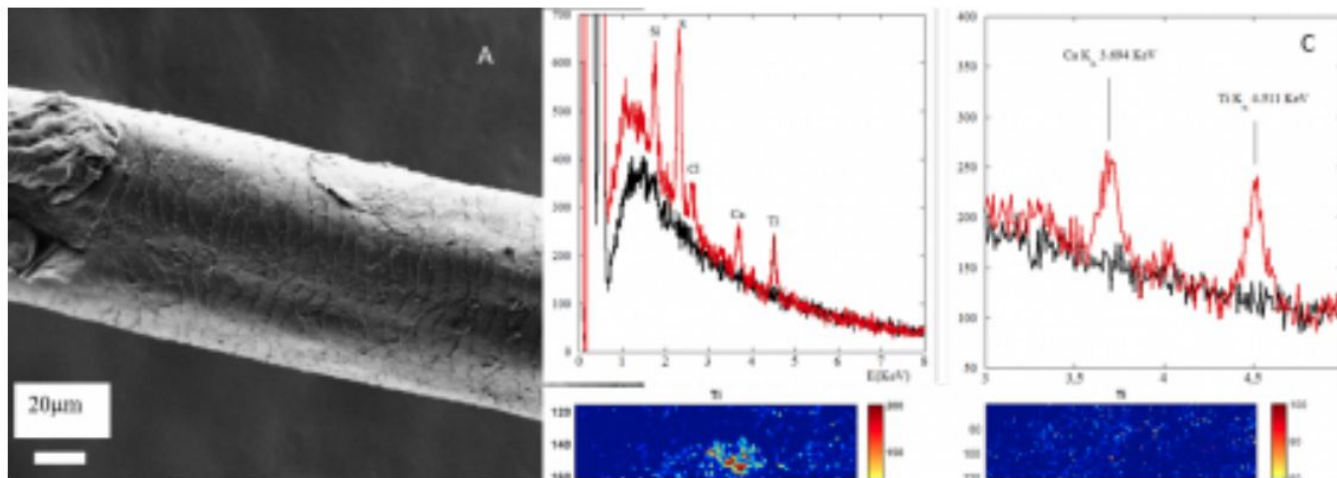


Figure 2

# Titanium on the hair shaft

Le long des follicules, à leur surface, ont ainsi été mis en évidence des agrégats de microparticules de  $\text{TiO}_2$  ( $0,5 - 1 \mu\text{m}$ ) associées à des nanoparticules de  $\text{TiO}_2$ .



Br J Dermatol. 2019 Jan 16. doi: 10.1111/bjd.17639. [Epub ahead of print]

## Identification of titanium dioxide on the hair shaft of patients with and without frontal fibrosing alopecia: A pilot study of 20 patients.

Thompson CT<sup>1,2</sup>, Chen ZQ<sup>3</sup>, Kolivras A<sup>4</sup>, Tosti A<sup>5</sup>.

 **Author information**  **Papers** ▼

### Abstract

Frontal fibrosing alopecia (FFA) has increased markedly in incidence since it was first reported in 1994. A possible role of cosmetic ingredients has been suspected, especially UV blockers, since these were added to products in the late 1980s. Daily, year-round use of facial moisturizers, most of which contain a sunscreen, has

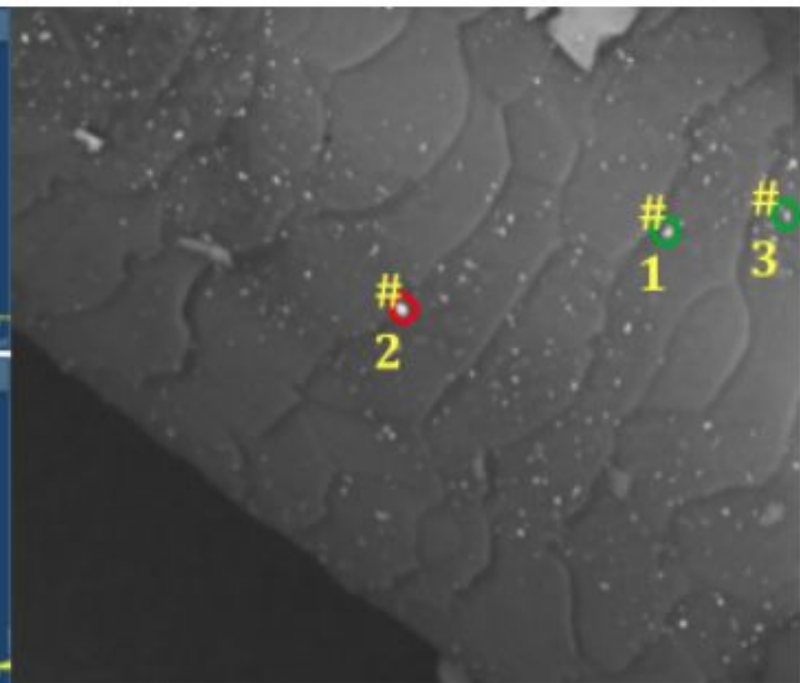


Fig. 1 Right: a backscattered electron image taken from one of typical hair shafts with SEM showing the presence of particles with brighter contrast on a hair shaft; Left: EDX spectra collected from particle 1-3 showing the presence of Ti species on particle 1 and 3.

## 20 Patient Pilot Study

- 16 Female patients with FFA      Positive Ti
- 3 Female patients without FFA      Positive Ti
- 1 Male patient without FFA      Negative Ti
  - ◆ No product usage on face or hair

# Physical Properties of $\text{TiO}_2$

- ▣ **Pigment Form—Larger particles**
  - ▣ Paint, cosmetics, food
- ▣ **Non-Pigment Form--Nanoparticles**
  - ▣ Reduces unwanted shine. “Matte” type cosmetics.
  - ▣ **Texture** – Smoother more sheer but opaque formations—conceals blemishes
  - ▣ UVA/UVB absorption and scattering.
- ▣ **Waterproof and Long-lasting**

# TiO<sub>2</sub> Nanoparticles—1990s

- 200-250nm in size but there are fragments 100nm
- Small enough to enter cells

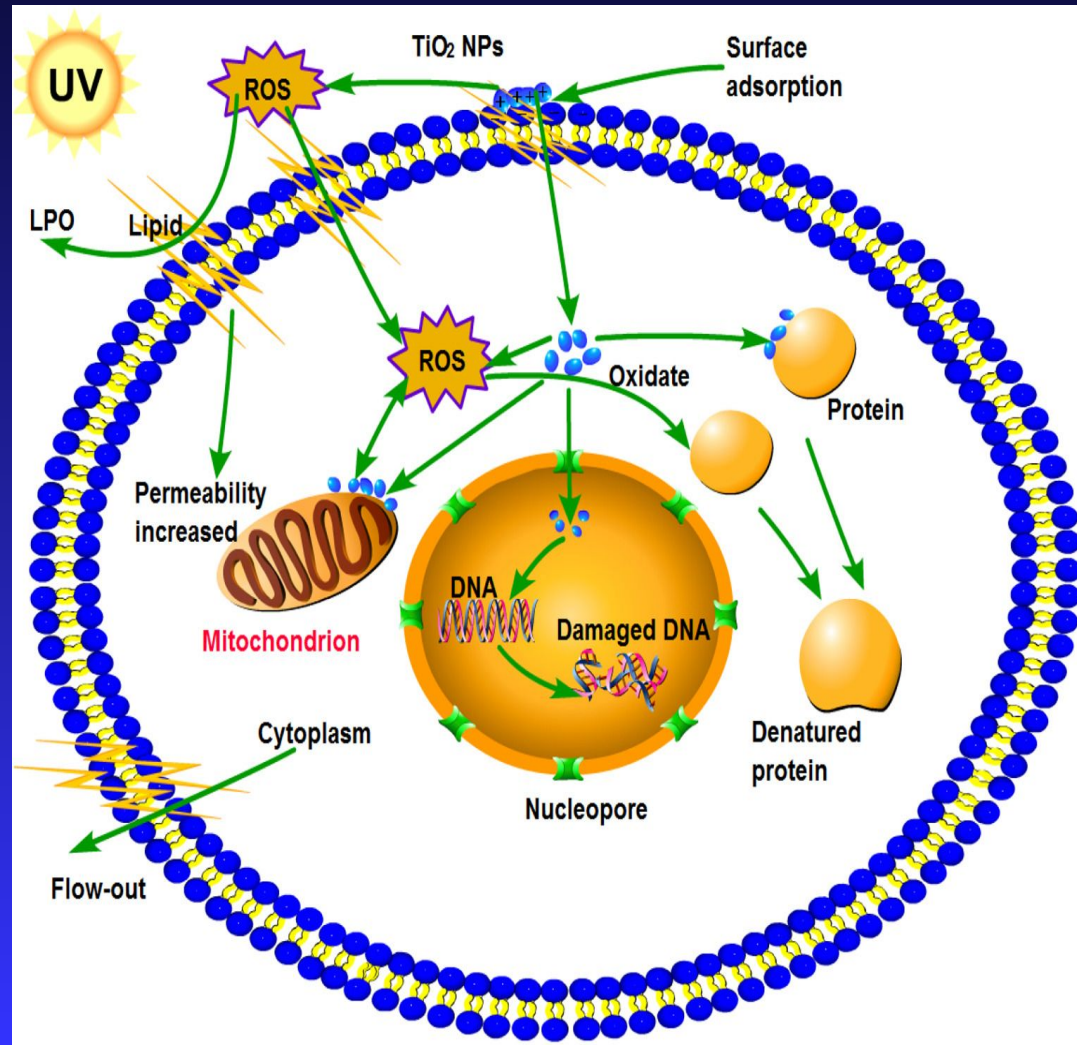
# TiO<sub>2</sub> Nanoparticle Toxicity

- 1985—Mouse study—Chronic exposure led to lung bronchioloalveolar adenomas and cystic keratinizing squamous cell carcinomas
  - ◆ 5 days/week for 2 years

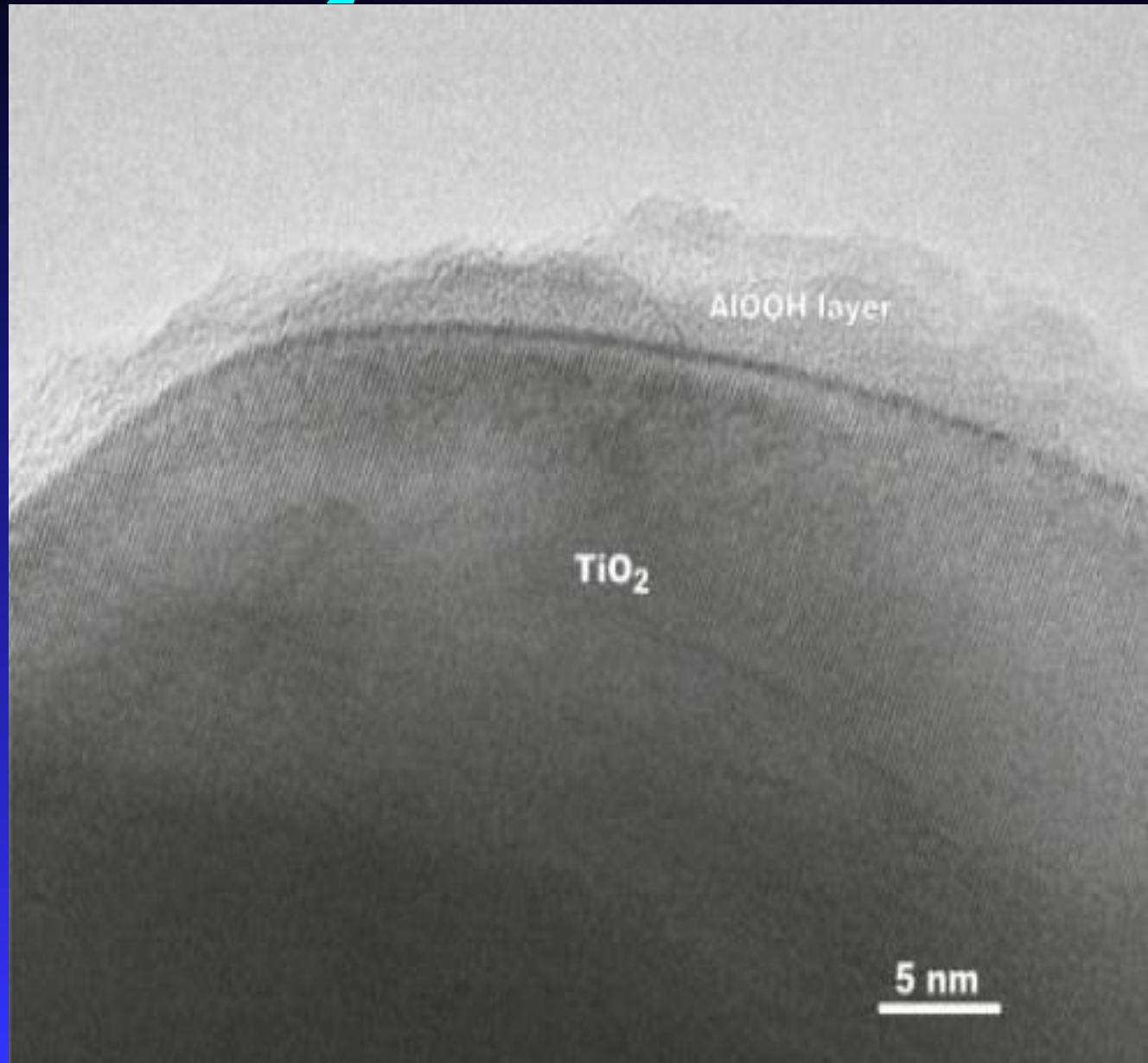
# Mechanism of $\text{TiO}_2$ nanoparticle toxicity

## □ Oxygen Radical Species upon UV exposure

- $\text{O}_2^-$ ,
- $\text{H}_2\text{O}_2$ ,
- hydroxyl  $\text{OH}^-$



# Coating of $\text{TiO}_2$ Nanoparticles

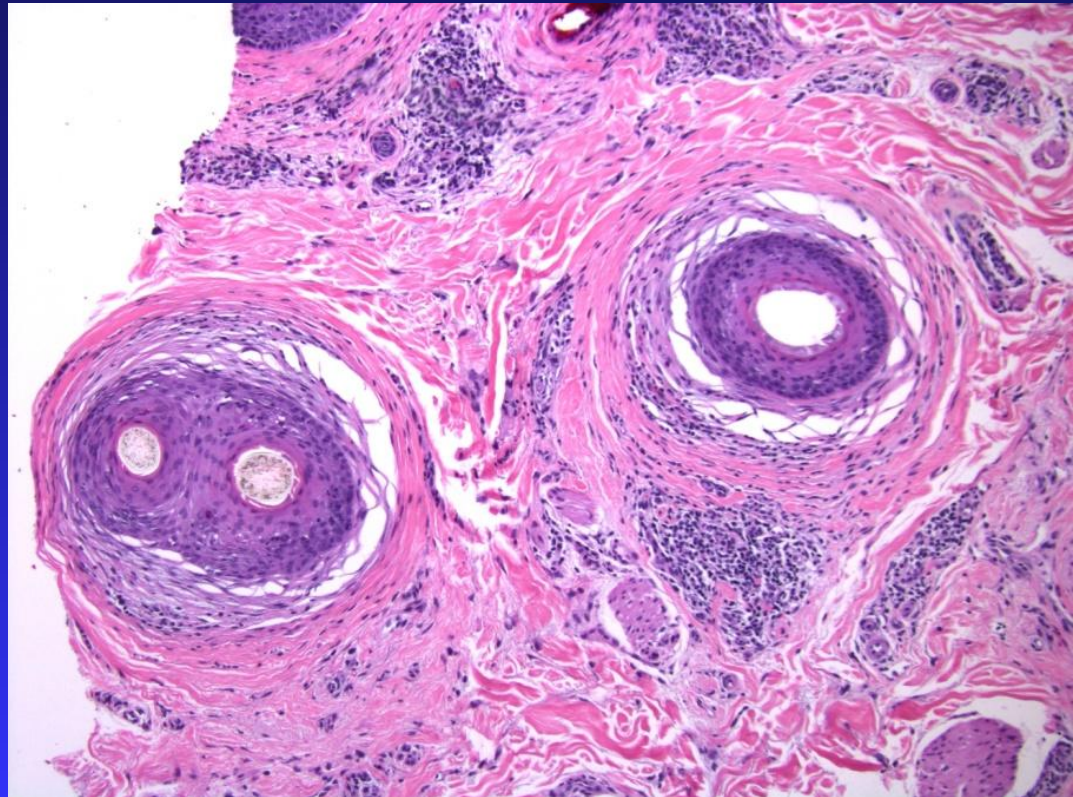


Inorganic Coatings	Organic Coatings	Natural coatings
silica	Stearate	Green tea
Alumina	butyl glycol <u>dicaprylate</u> + Stearate	Lignin
Silica + Alumina	<u>Methicone</u>	
Zirconium dioxide	<u>Dimethicone</u>	
Manganese oxide	<u>Dimethicone</u> / siloxane	
Iron oxide	<u>Dimethicone</u> / <u>methicone</u> copolymer	
Zinc oxide	Simethicone	
Aluminum hydroxide	<u>Trimethylsiloxysilicone</u>	
	<u>Polyvinyl-pyrrolidone</u>	
	Alkyl <u>silane</u>	
	Glycerin	

Is there a pathogenetic link between frontal fibrosing alopecia, androgenetic alopecia and fibrosing alopecia in a pattern distribution?

Katoulis AC, Diamanti K, Sgouros D, Liakou AI, Bozi E, Avgerinou G, Panayiotides I, Rigopoulos D.

J Eur Acad Dermatol Venereol. 2018 Jun;32(6):e218-e220. doi: 10.1111/jdv.14748. Epub 2018 Jan 15. No abstract available.



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# Sunscreen

- Avobenzone, Homosalate, Octinoxate, Octisalate, Octocrylene, Oxybenzone
- Inactive Ingredients: Sd Alcohol 40, C12-15 Alkyl Benzoate, Acrylates Octylacrylamide Copolymer, Caprylyl Glycol, Dimethyl Capramide, Aloe Barbadensis (**Aloe Vera**) Leaf Extract, Retinyl Palmitate, Tocopherol, Fragrance.

# Sunscreen

- Avobenzone, Homosalate, Octinoxate, Octisalate, Octocrylene, **Oxybenzone**
- Sd Alcohol 40, C12-15 Alkyl Benzoate, Acrylates Octylacrylamide Copolymer, Caprylyl Glycol, Dimethyl Capramide, Aloe Barbadensis (**Aloe Vera**) Leaf Extract, Retinyl Palmitate, Tocopherol, Fragrance.

**Present in 96% of the U.S. population**

# Skin Appendage Disorders

Novel Insights from Clinical Practice

## Lichen Planopilaris in the Setting of Hair Sunscreen Spray

Canavan T.N.<sup>a</sup> · McClees S.F.<sup>b</sup> · Duncan J.R.<sup>a</sup> · Elewski B.E.<sup>a</sup>

 Author affiliations

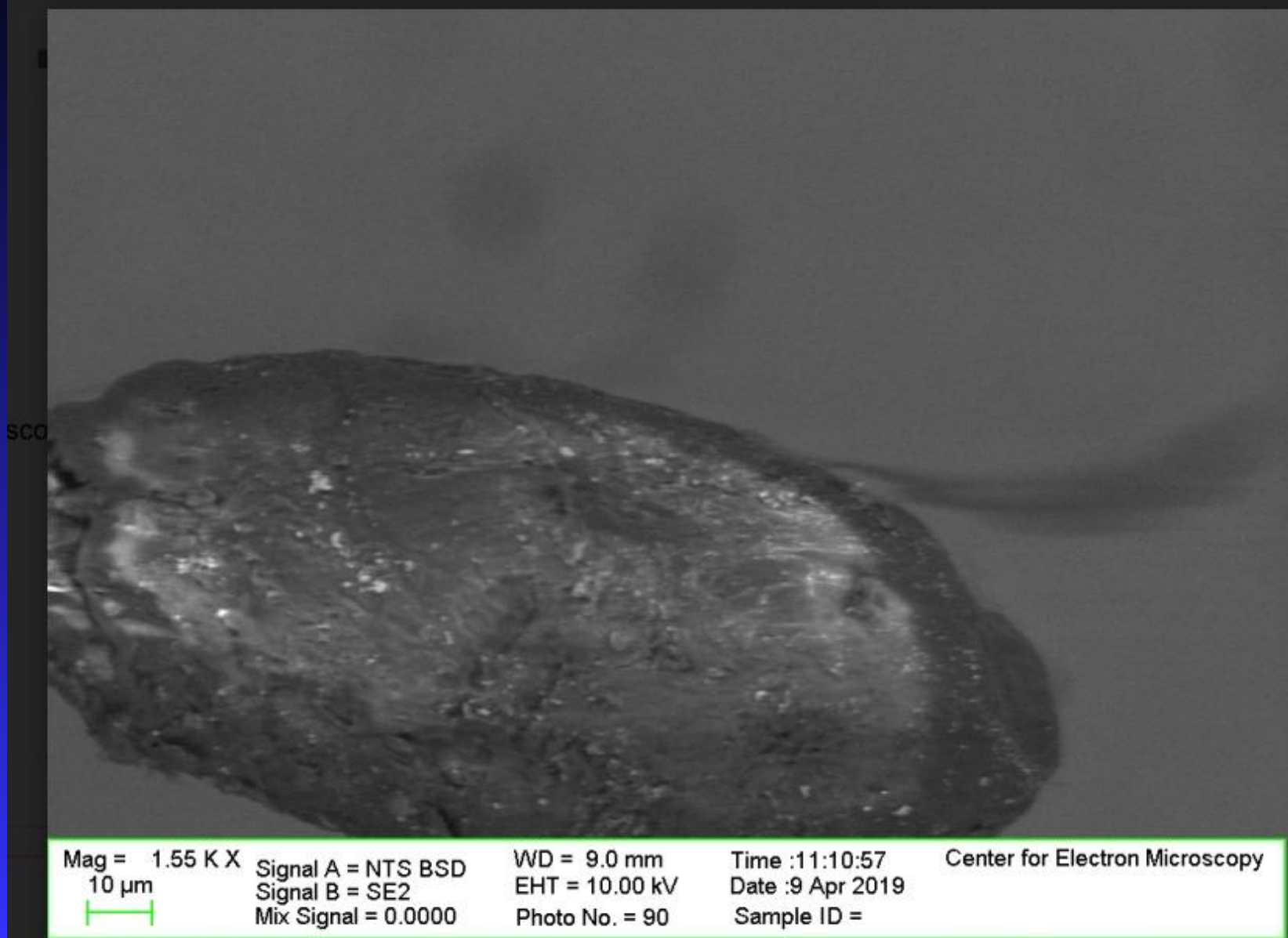
Keywords: Lichen planopilaris · Frontal fibrosing alopecia · Benzyl salicylate  
· Sunscreen · Scarring alopecia

# Argyria



Provided by Daniel Asz-Sigall, M.D.

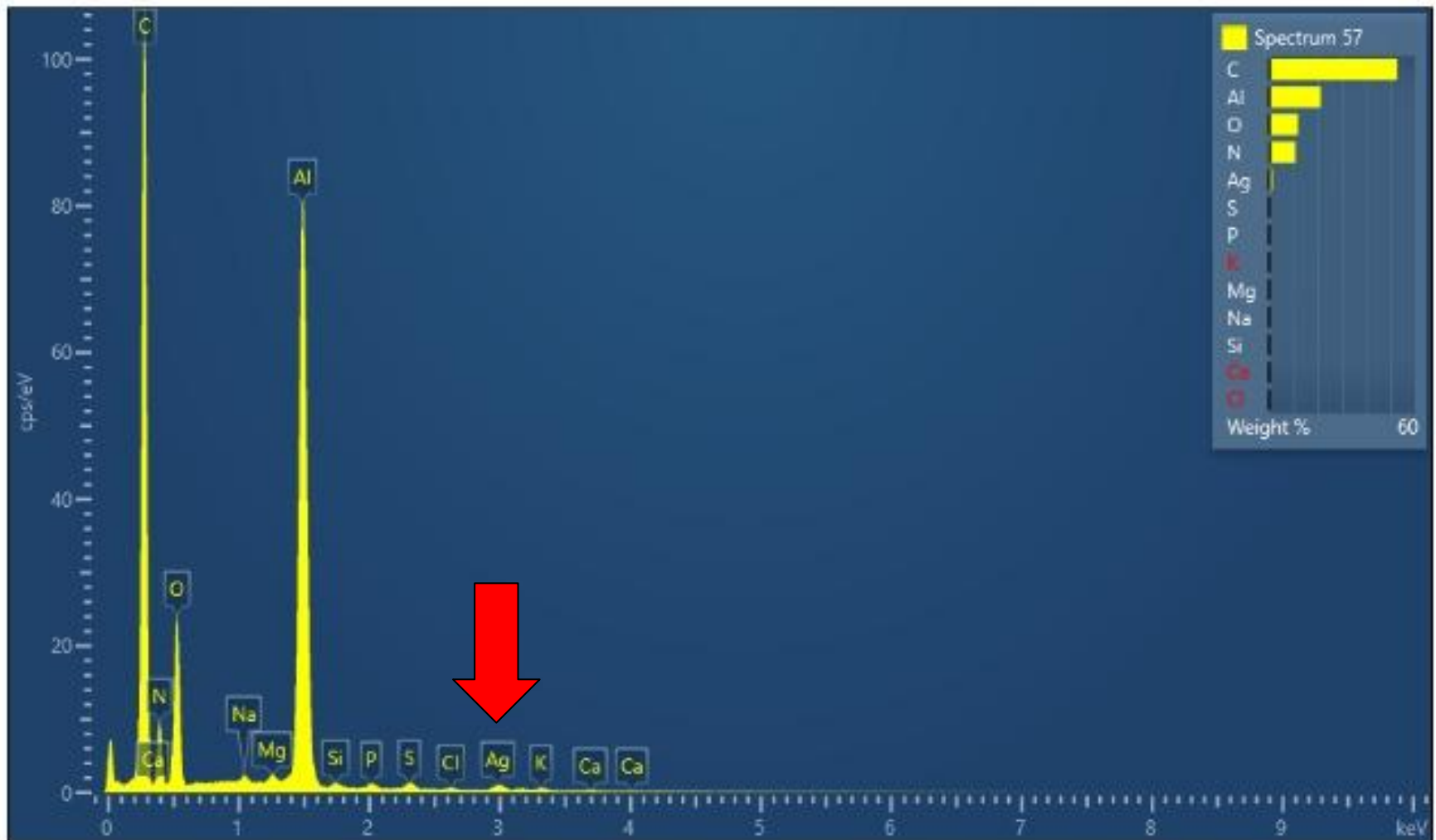
# Argyria



# Argyria

## Project 1

4/9/2019






Journal of the American Academy of Dermatology

Available online 23 December 2018

In Press, Accepted Manuscript ?



# A method for more precise sampling of the scalp and eyebrows in frontal fibrosing alopecia

Curtis T. Thompson M.D.<sup>1, 2</sup>  , Antonella Tosti M.D.<sup>3</sup>

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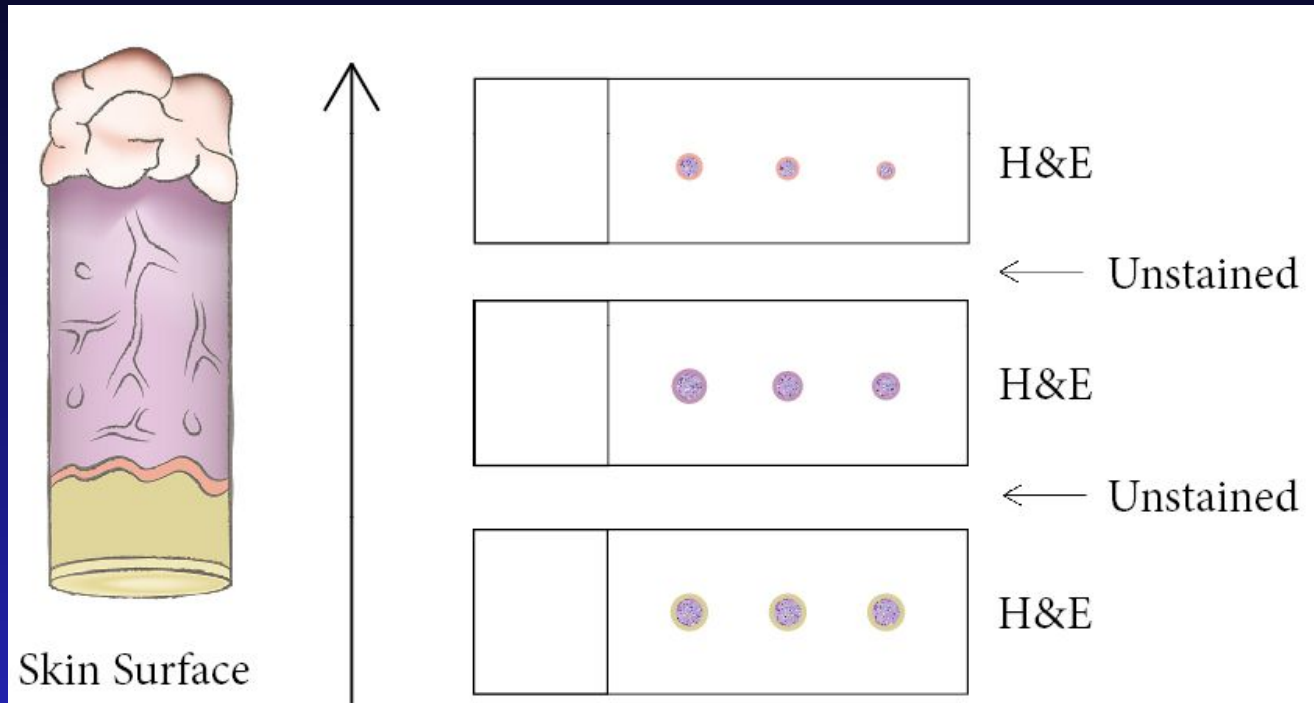
<https://doi.org/10.1016/j.jaad.2018.12.033>

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# Dermoscopic identification of disease

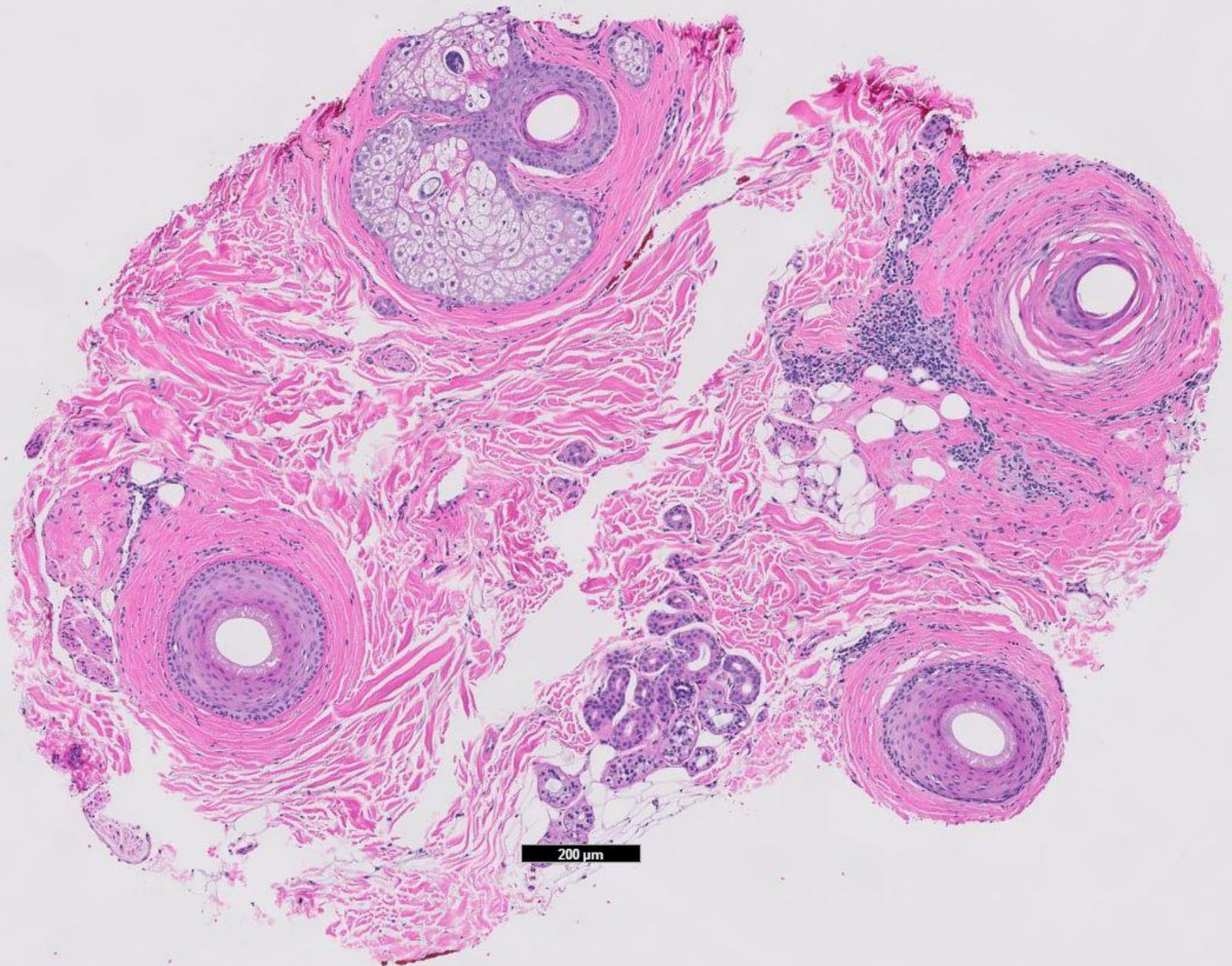


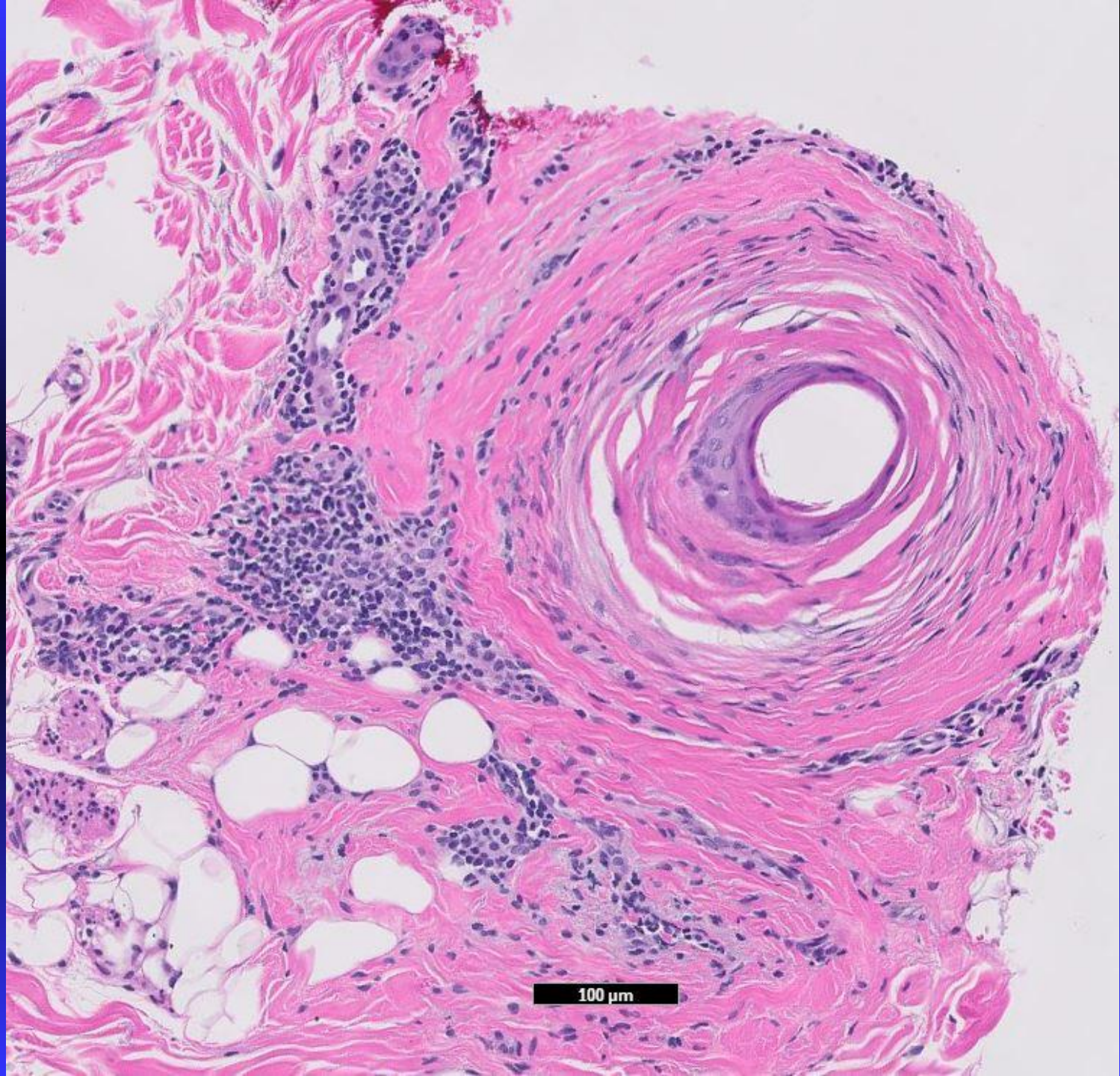
# 2mm punch—exhaust tissue

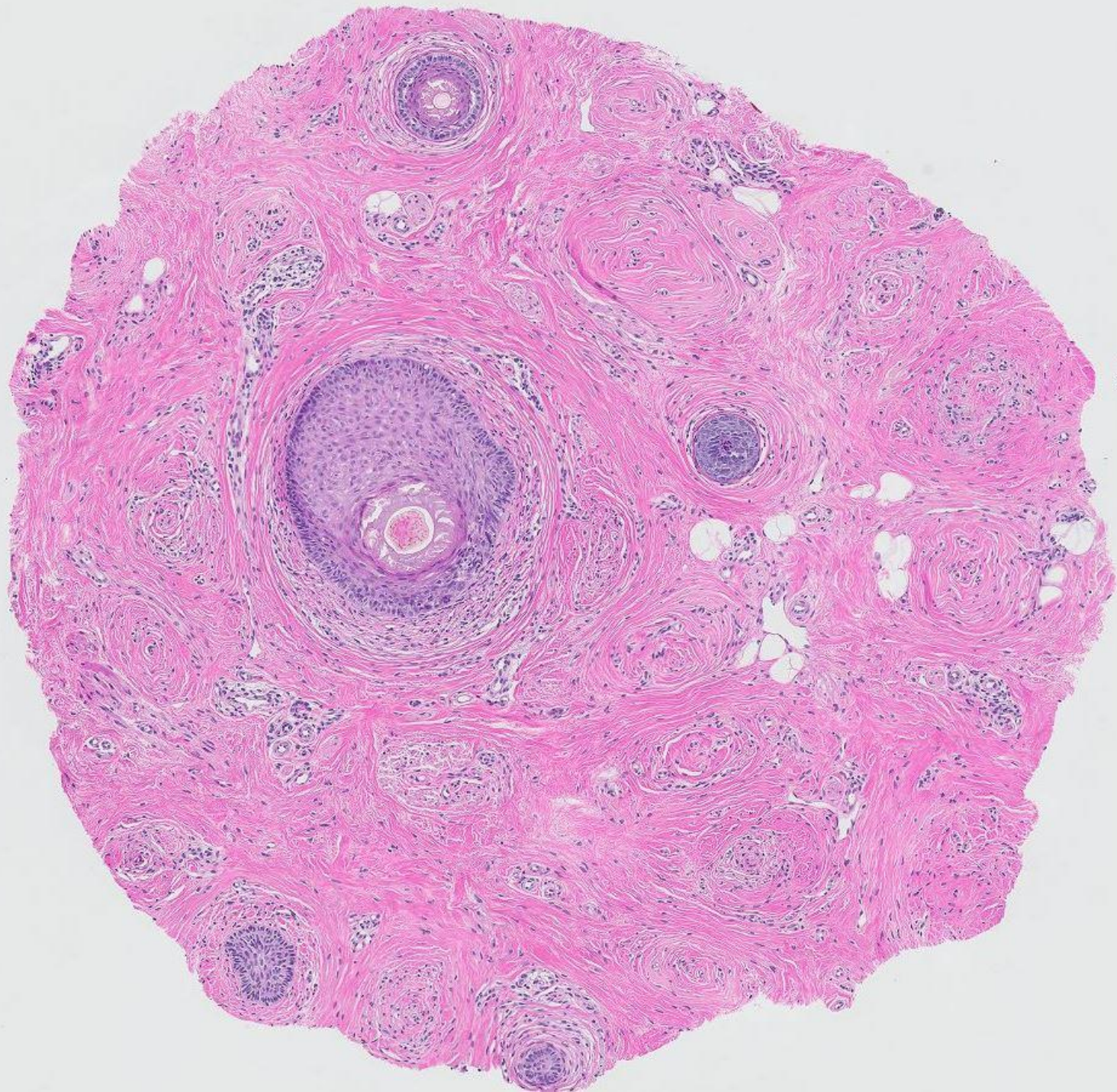


3 slides total with 9 cross  
sections; 3 sections per slide

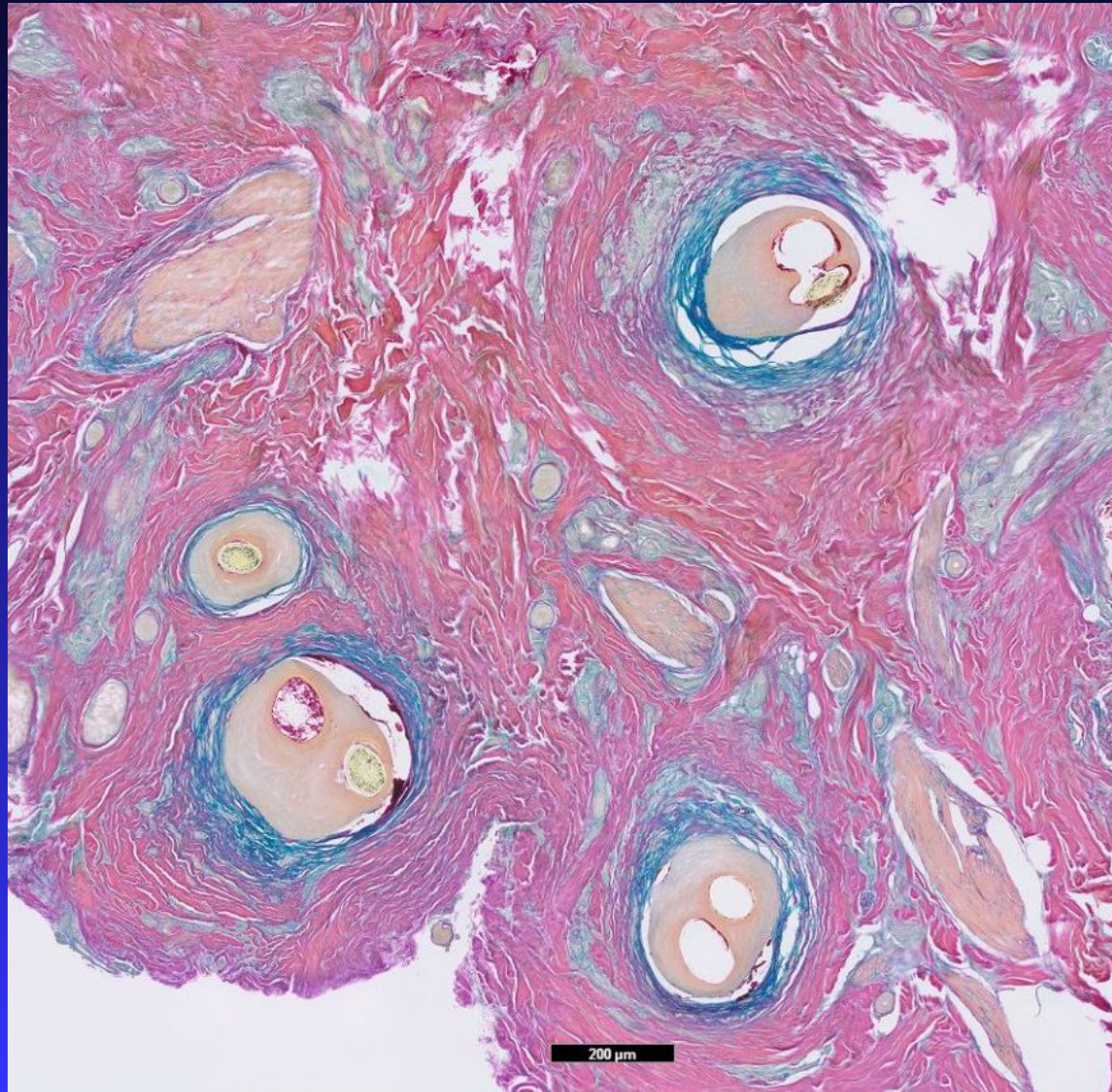
1. Tissue is embedded epidermis-down
2. Step through entire block on initial H&E stains
3. Obtain unstained slides





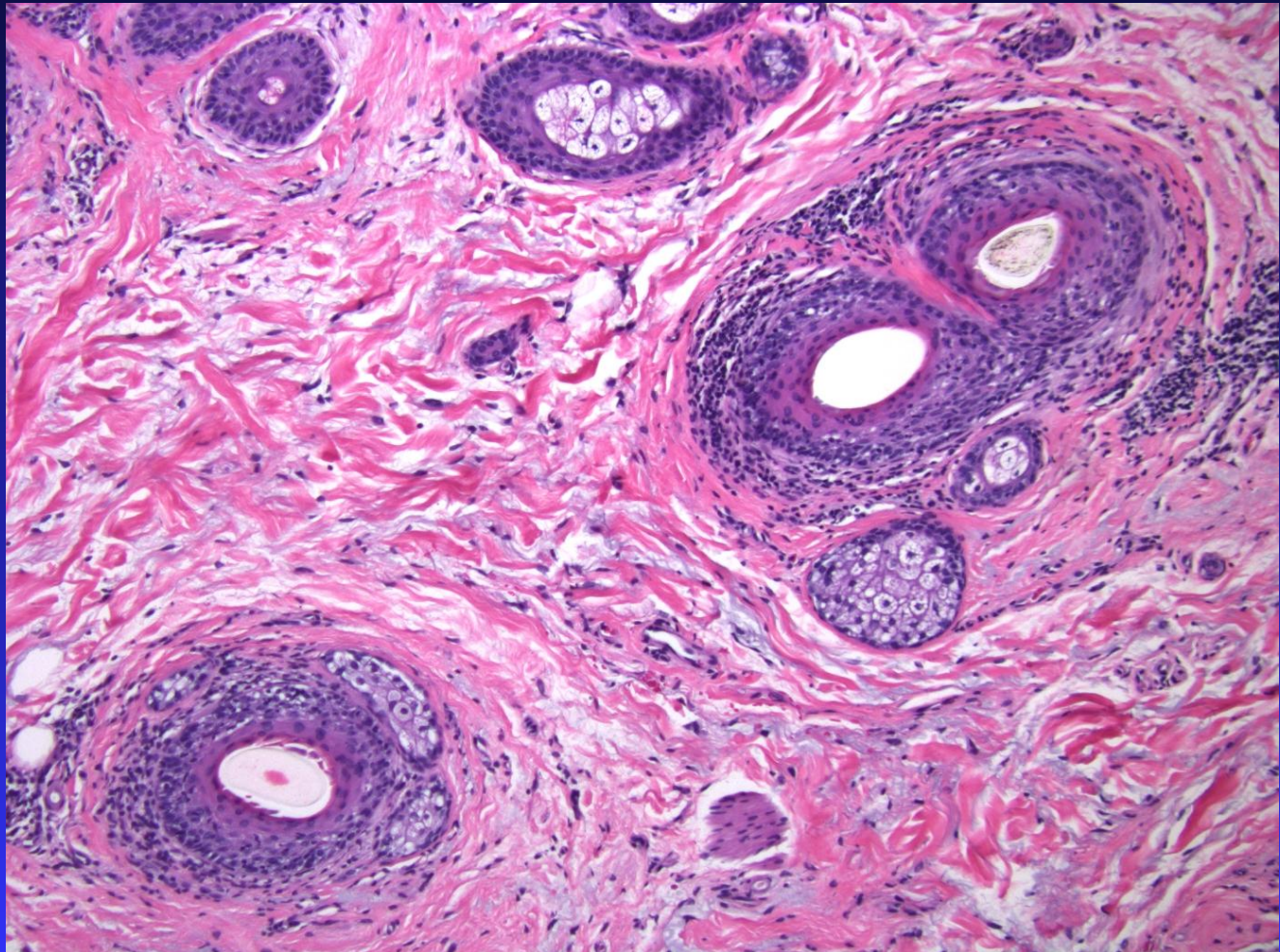


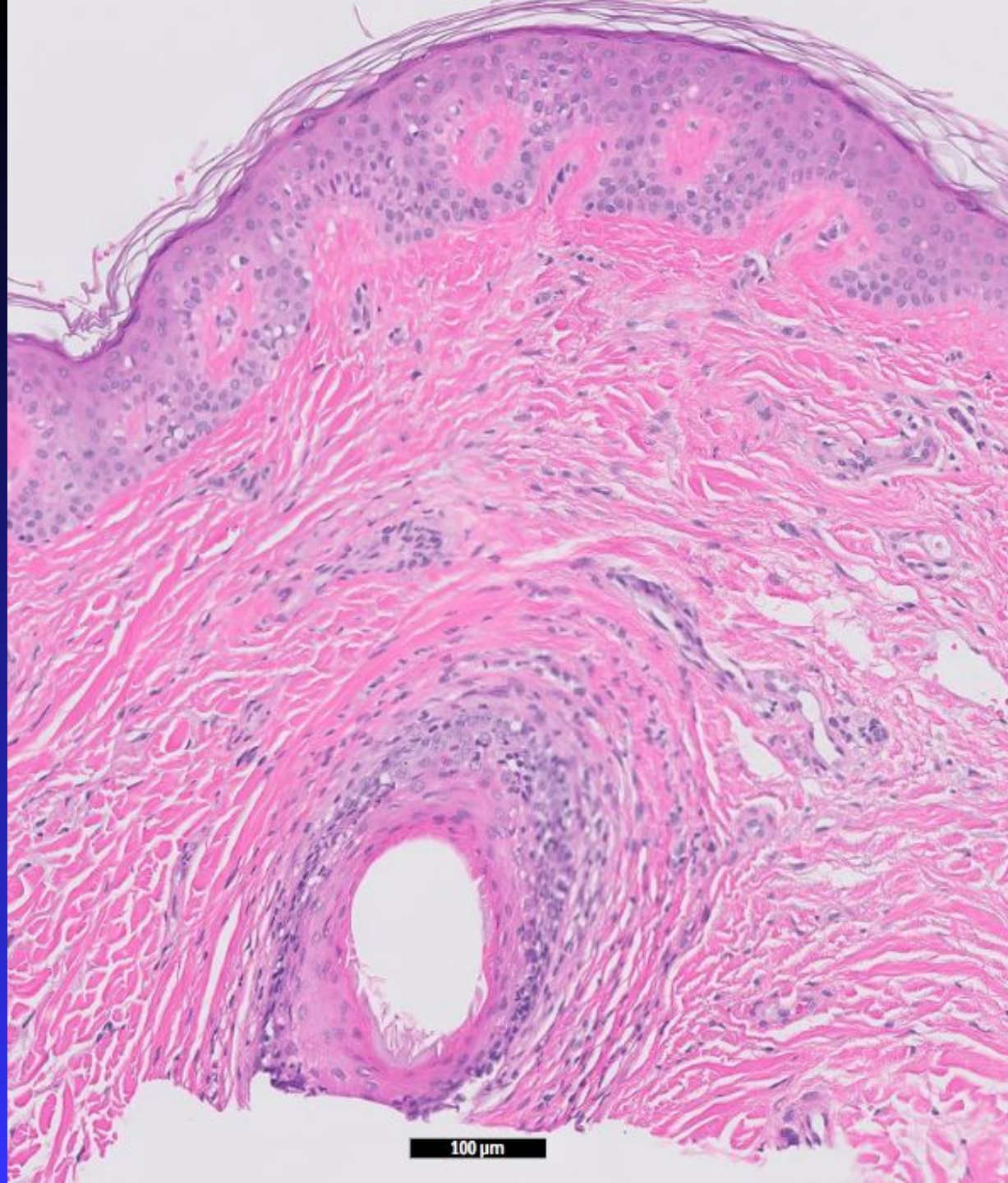
# Identification of subtle, focal scarring in FFA

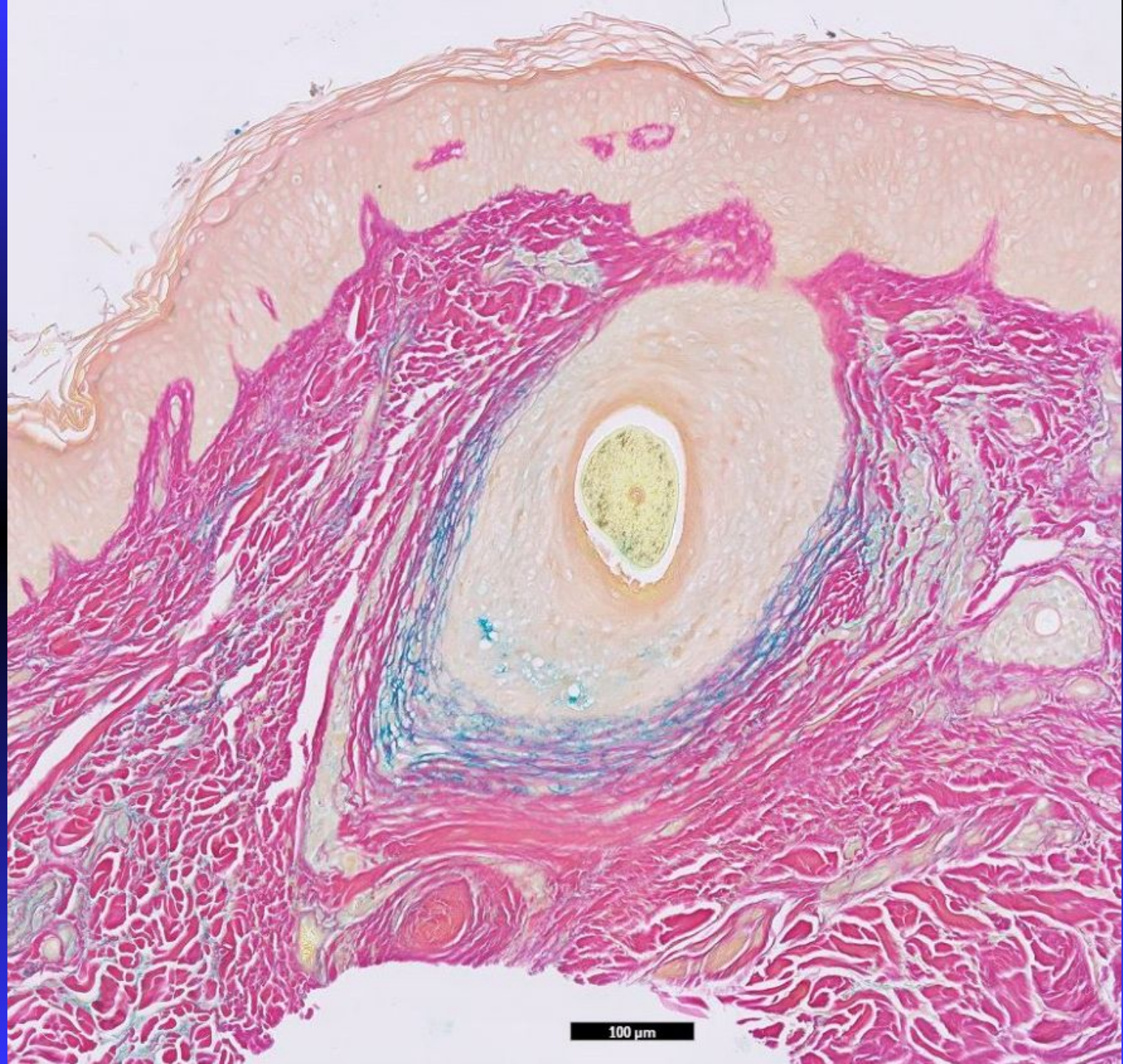


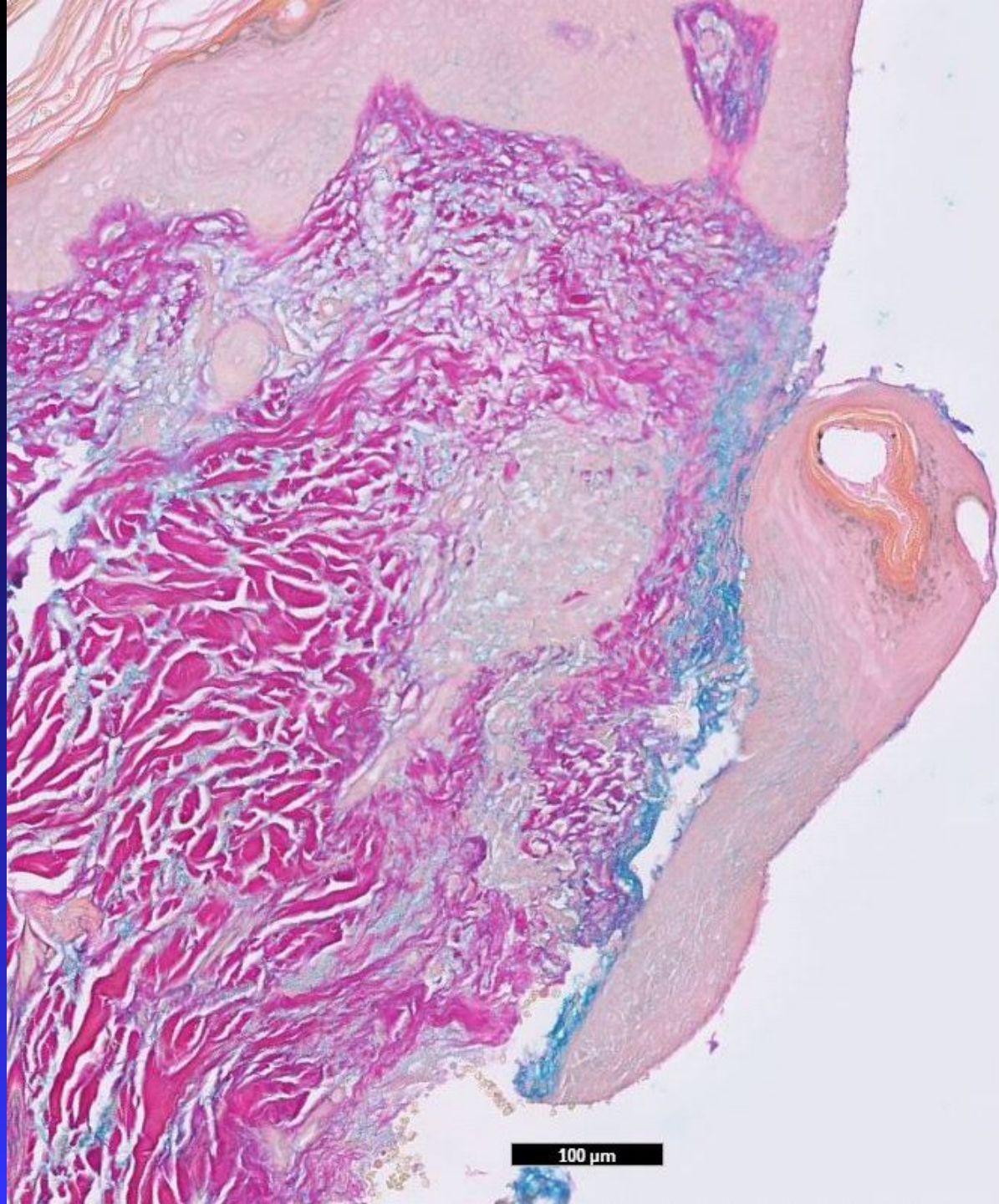
# Frontal Fibrosing Alopecia

## Histology: Minimal scarring









# Summary of FFA Update

- $\text{TiO}_2$  is a primary suspect—removing from products likely only proof
  - ◆ Concentration?
  - ◆ Preparation of nanoparticle  $\text{TiO}_2$ ?
- Other ingredients should not yet be excluded
- A 2mm punch with a mucin stain is the best tool for a histopathologic diagnosis.

# Hypotheses

- A chemical is causing a lichenoid reaction that results in IP breakdown.
- Sun protection promotes inflammation.
- Multiple entities are caused by the same chemical--FFA, LPP, FAPD, CCCA.
- Nanoparticles may be toxic.

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Thanks!

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