

Most dermatology practices in the United States have similar or smaller staff, making this pilot applicable to a large portion of the dermatologic community. We hope this pilot initiates conversation about investing in training and education, leveraging technology, and using creative strategies to improve the alignment of CSS and physicians to optimize care delivery.

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### **In vivo identification of amyloid and mucin in basal cell carcinoma with combined reflectance confocal microscopy—optical coherence tomography device and direct histopathologic correlation**



To the Editor: The combined reflectance confocal microscopy (RCM)—optical coherence tomography (OCT) device enables simultaneous, real-time visualization of cellular features in RCM and structural features in OCT, leading to better characterization of morphologic features and improved diagnosis and depth assessment of basal cell carcinoma (BCC).<sup>1</sup>

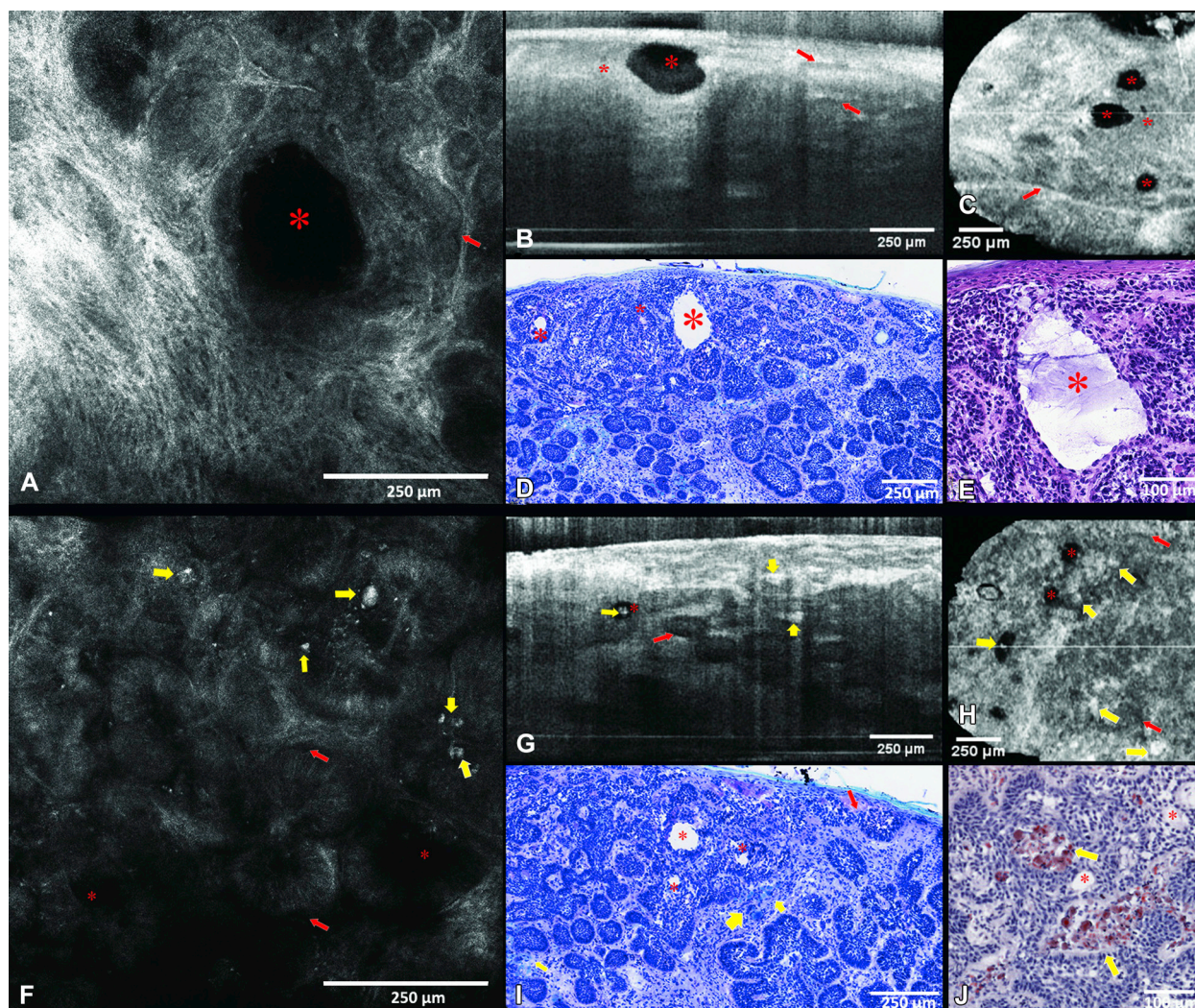
Amyloid and mucin deposits are established BCC histopathologic features. Primary cutaneous amyloidosis has been imaged with RCM,<sup>2</sup> and BCC peritumoral-mucin on RCM has been histopathologically verified.<sup>3</sup> To our knowledge, however, no prior reports have demonstrated BCC-associated amyloid on RCM or OCT, and OCT descriptions of mucin have been inferential. Herein, we report in vivo characterization of amyloid and mucin through RCM-OCT, followed by precise histopathologic correlation.

In the combined RCM-OCT device, en face or horizontal RCM images (field-of-view: 750 × 750 μm; lateral resolution: ~1 μm; optical sectioning: ~3 μm) are centered on vertical OCT images (field of view: 1000 × 2000 μm; lateral resolution: ~5 μm; optical sectioning: ~10 μm), which are postprocessed to obtain horizontal OCT.

This study was performed under the Memorial Sloan Kettering Cancer Center IRB protocol 99-099. Consecutive BCCs were prospectively investigated for the presence of: (1) amyloid (amorphous, hyper-reflective, homogenous intratumoral/peritumoral globules) and (2) mucin (intratumoral/peritumoral hyporeflective areas). Next, RCM-OCT—guided punch biopsies (2-3 mm) were obtained, followed by horizontal (for RCM) or vertical (for OCT) sectioning to permit direct histopathologic correlation using hematoxylin and eosin (H&E), toluidine blue (TB, mucin), and Congo red (amyloid) staining. The size and distribution of hyper-reflective globules and hyporeflective areas in RCM, OCT, and histopathology were analyzed using the Fiji distribution of ImageJ software (National Institutes of Health, Bethesda, MD).

Features of mucin and amyloid were identified in 6 patients (male/female ratio, 2:1; ages 24, 54, 65, 73, 78, 78 mean age, 61.5 years) with 8 BCCs (1 superficial; 6 nodular; 1 nodular-infiltrative). On histology, amyloid appeared as characteristic homogenous globules, bubble-gum pink on H&E, blue on TB, or red on Congo red. Mucin was an amorphous stringy substance, staining blue-purple-gray on H&E and magenta on TB. Hyper-reflective globules correlated with amyloid and hyporeflective areas correlated with mucin. Mucin deposition was intratumoral or peritumoral (Figs 1 and 2). Amyloid globules were distributed peritumorally (Fig 1) or within hyporeflective mucin pools (Figs 1 and 2).

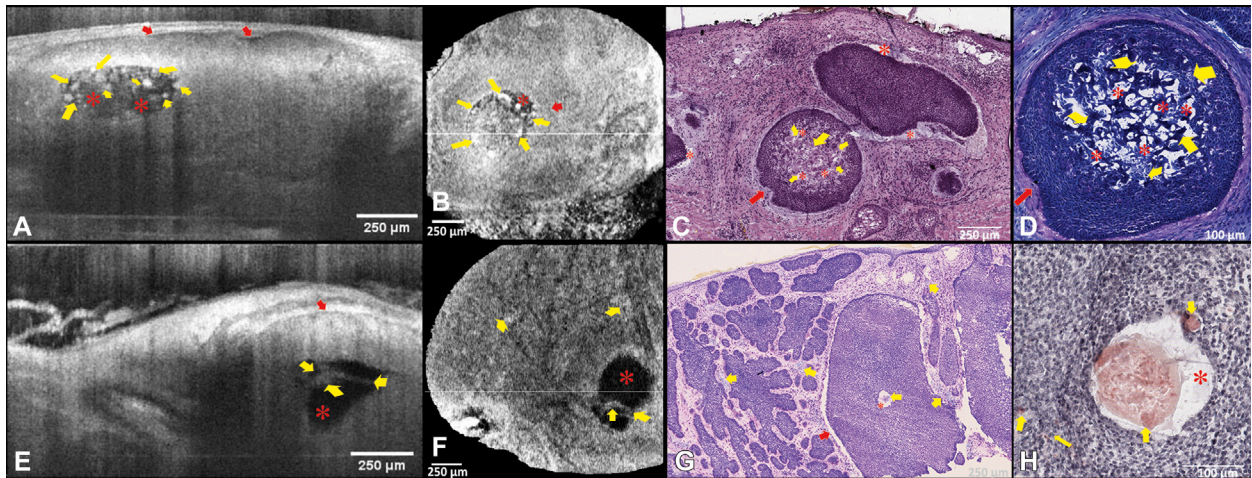
In 6 of 8 cases, we identified mucin and amyloid on RCM and OCT. In 2 cases, the features were only present in the deep dermis and therefore visualized only on OCT (8 of 8). The amyloid globule/cluster size ranged between 9 to 32 μm on horizontal RCM, 11 to 23 μm on horizontal



**Fig 1.** Case 1: Morphologic patterns of intratumoral and peritumoral mucin and stromal amyloid deposits in nodular basal cell carcinoma characterized by small- to medium-sized branching tumor lobules within the dermis. **A**, In reflectance confocal microscopy (RCM), peripheral palisading helps confirm the diagnosis along with dark peritumoral rims of mucin (red arrows), which are also seen on **(B)** vertical and **(C)** horizontal optical coherence tomography (OCT) and **(D)** in toluidine blue (TB)-stained histopathology. A large pool of mucin (red asterisk) appears as a dark oval intratumoral structure seen on **(A)** RCM and **(B, C)** OCT, and a white cavity on **(D)** TB where the mucin was washed out during processing but is clearly visualized as stringy purple-gray mucin on **(E)** hematoxylin and eosin–stained histopathology. Additional smaller mucin pools (red asterisks) are present in the plane of sectioning in **(B)** vertical and **(C)** horizontal OCT, and **(D)** low-power histopathology. **(F–I)**, Another area in the same tumor shows amyloid deposits (yellow arrows) in the superficial dermis, seen as hyper-reflective globules within peritumoral stroma on **(F)** RCM and **(G, H)** OCT, **(I)** blue peritumoral globules on TB-stained histopathology, and **(J)** red peritumoral globules on Congo red–stained histopathology. Peritumoral mucin (red arrows) is subtle but recognized as dark peritumoral rims on **(F)** RCM and **(G)** OCT as well as **(I)** white peritumoral clefts (from mucin washout during processing) on histopathology.

histology (TB/Congo red), 26 to 85  $\mu\text{m}$  on vertical OCT, and 15 to 95  $\mu\text{m}$  on vertical histology. The large mucin pool (**Fig 1**) measured 170  $\times$  220  $\mu\text{m}$  (RCM), 180  $\times$  275  $\mu\text{m}$  (OCT), and 170  $\times$  270  $\mu\text{m}$  (histology).

Amyloid and intratumoral mucin deposition are frequently observed in less aggressive nodular BCCs (up to 85% positive for amyloid).<sup>4</sup> Thus, noninvasive visualization of prominent amyloid and mucin features may be clinically relevant for the diagnosis of



**Fig 2.** Cases 2 and 3: Morphologic patterns of intratumoral amyloid deposits as well as intratumoral and peritumoral mucin deposits in nodular basal cell carcinomas confirmed on optical coherence tomography (OCT). Intratumoral deposits were present deep to the maximal imaging depth of reflectance confocal microscopy (RCM) and therefore only visualized by OCT. Case 2 shows a large intratumoral round-oval dark structure filled with hyper-reflective globules on (A) vertical and (B) horizontal OCT corresponding to a round collection of mucin (red asterisks) intermixed with amyloid globules (yellow arrows) within the center of the tumor nodule. Amyloid appeared characteristic bubble gum pink on (C) hematoxylin and eosin (H&E) and (D) blue on toluidine blue (TB). Peritumoral mucin (red arrows) is identified as a dark peritumoral rim on (A, B) OCT and corresponds to stringy amorphous material which is (C) purple-gray on H&E and (D) magenta on TB. Case 3 harbors a large tumor nodule with a central pool of mucin (red asterisk), which is (E, F) dark on OCT and amorphous, stringy, purple-gray material on (G) H&E and (H) Congo red (CR). Hyper-reflective aggregated globules (yellow arrows) noted within the mucin pool on (E, F) OCT are partially obscured by mucin on TB but (H) confirmed to be amyloid (yellow arrows) on CR-stained histopathology. Also noted is a characteristic peritumoral rim of mucin (red arrows), which appears dark on (E) OCT and white due to mucin washout on (G) H&E histopathology.

less aggressive BCCs, which in turn can help streamline management. Furthermore, given the anticipated increased use of RCM-OCT Current Procedural Terminology (American Medical Association, Chicago, IL) codes,<sup>5</sup> these features should be identified by physicians performing RCM, OCT, or both.

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**Conflicts of interest:** Dr Gill serves as a consultant to the Dermatology Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, and is also a consult investigator for an investigator-initiated study funded by DBV Technologies. Author Alessi-Fox is employed by and owns equity in Caliber Imaging and Diagnostics, Inc (formerly Lucid, Inc), the company that manufactures and sells the VivaScope confocal microscope. Dr Iftimia reports a patent

(US9655521 B2) that is assigned to Physical Sciences Inc and Memorial Sloan Kettering Cancer Center, which is related to the technology described in this study. Dr Rajadhyaksha is a former employee of and owns equity in Caliber Imaging and Diagnostics, Inc. The VivaScope is the commercial version of an original laboratory prototype that he had developed at Massachusetts General Hospital, Harvard Medical School. Dr Chen is the principal investigator of a research project sponsored by Apollo Medical Optics, Inc. Drs Sahu, Cordova, Navarrete-Dechent, González, and Marghoob have no disclosures or conflicts of interest to report. This research was completed without financial support from Caliber Imaging and Diagnostics, Inc, Memorial Sloan-Kettering Cancer Center, Physical Sciences Inc, or Apollo Medical Optics, Inc, and data were acquired and processed from patients by co-authors unaffiliated with any commercial entity.

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### Dermatology education in geriatric fellowship programs: A nationwide survey of program directors



*To the Editor:* The growing elderly population has led to calls for more effective health care for aging adults. There is a critical role for dermatology within geriatrics and geriatrics training programs to manage common skin diseases in older people,<sup>1</sup> prevent drug-related iatrogenic complications,<sup>2</sup> and detect cutaneous signs of elder abuse.<sup>3</sup> In a previous study, geriatrics education in dermatology programs was

explored, and gaps were found in holistic treatment, including communication, ethical issues, and safe prescribing.<sup>4</sup> However, little is known about formal dermatology curricula and education in geriatric fellowship programs. Building upon a prior study that examined dermatology education in internal medicine residency programs,<sup>5</sup> we aimed to characterize and identify gaps in dermatology education in geriatric fellowship programs.

During May-June 2019, the program directors of all 154 Accreditation Council for Graduate Medical Education—accredited geriatric fellowship programs were invited to complete study surveys by using the REDCap software platform. Descriptive statistics and multiple logistic regression models were performed in SPSS version 24 (IBM Corporation, Armonk, NY).

Fifty-five (35.7%) out of the 154 programs responded to the survey. All fellowships were 1 year in length, and responding programs were representative of the national distribution (Table I). Twenty-two (40%) geriatrics programs did not offer dermatology clinical experience, and only 3 (5.5%) programs had an identified dermatology subspecialty coordinator (ie, a physician guiding the curriculum). Five (9.1%) programs had mandatory dermatology clinic rotations, and 3 (5.5%) had longitudinal dermatology experiences throughout the year. Most clinical experiences (70.9%) comprised <5 half-day clinic sessions over the course of the fellowship. The most common dermatology learning experiences offered were formal dermatology didactic lectures and board review, with few educational experiences in procedural skills or inpatient dermatology (Table I).

Overall, 60% (33/55) of the responding programs were at institutions with a dermatology residency program. The presence of a dermatology residency program was associated with a higher odds of having >5 half-day dermatology clinic sessions for geriatrics fellows (odds ratio 4.12, 95% confidence interval 1.01-16.76; Table II). The presence of a dermatology residency program was also associated with a nonsignificant increase in odds of having outpatient clinical experiences and dermatology faculty discussants at teaching conferences (Table II). Multivariate logistic regression revealed no statistically significant associations between fellowship program demographics (eg, geographic region, setting, hospital type, and number of fellows per year) and presence of dermatology clinical experience.

This study provides insight into dermatology education in geriatric fellowship programs, highlighting gaps in dermatology education and offering opportunities to strengthen dermatology exposure for geriatrics trainees. Almost half of the responding programs did not offer dermatology experiences in