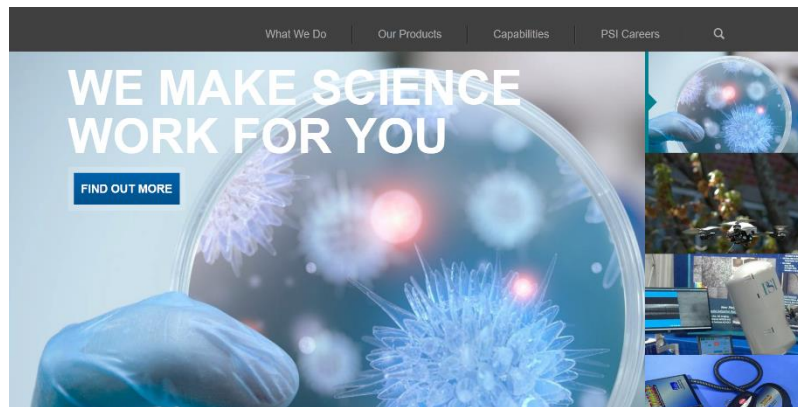


# Guiding skin cancer therapy with combined Confocal-OCT imaging

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# Clinical Need Addressed: Guidance of Non-surgical Skin Cancer Therapy Approaches

- Non-Melanoma skin cancers (NMSCs): >5 million new cases every year
- Over 60% of the NMSCs are on the head and neck areas
- Surgery is the standard of care for NMSCs
- Surgery is expensive and not desirable for head and neck
- Non-surgical approaches are rapidly advancing: laser ablation, radiotherapy, PDT, etc.
- **Therapy guidance is needed for improved outcome**

After Mohs Surgery



After Reconstructive Surgery



After Laser Therapy



**Solution: Hand-held RCM-OCT imaging - early diagnosis and margins assessment**

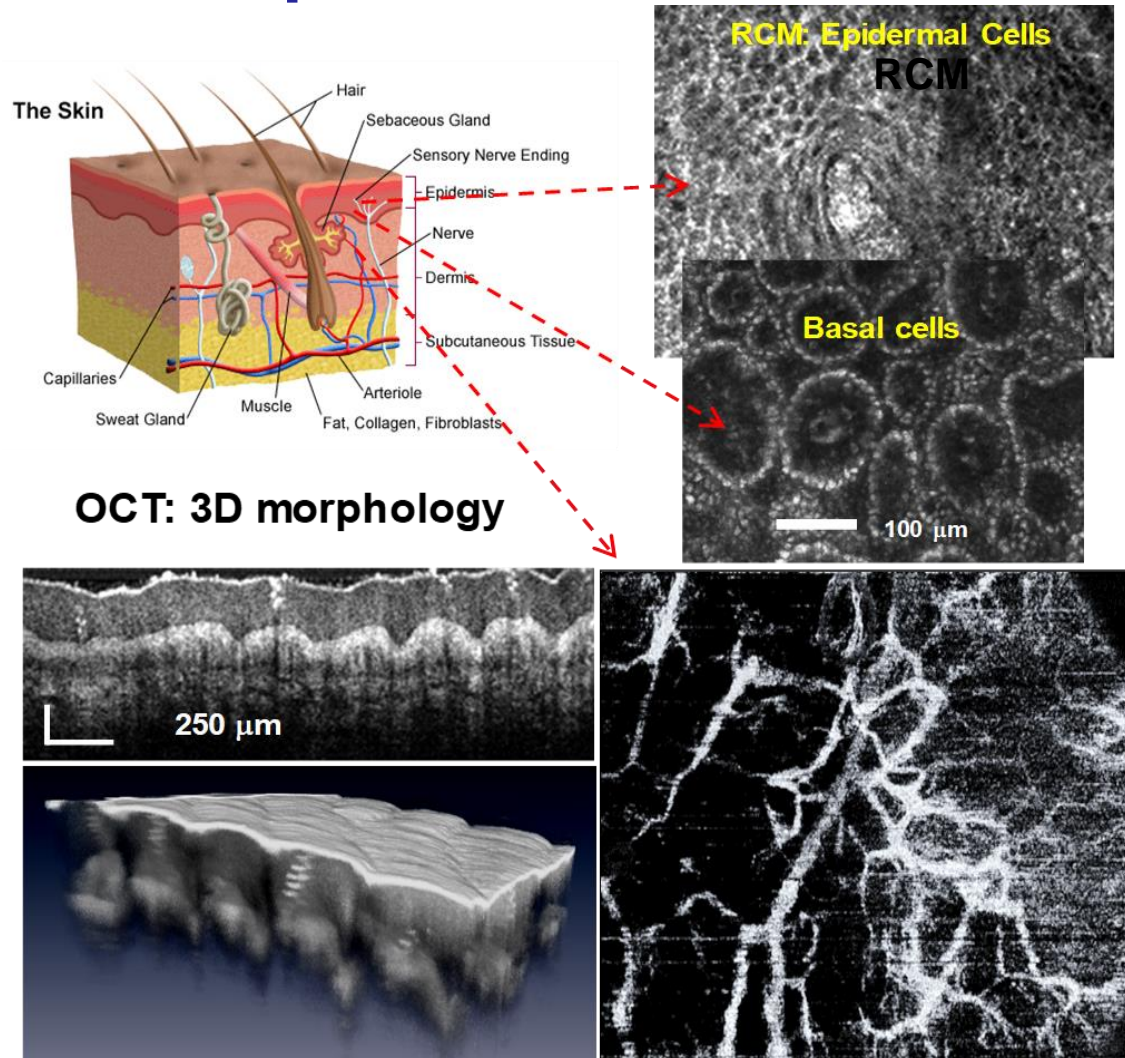
# RCM-OCT Capabilities

## RCM capabilities:

- *Enface* imaging of the superficial epithelium with high resolution, similar to histology slides

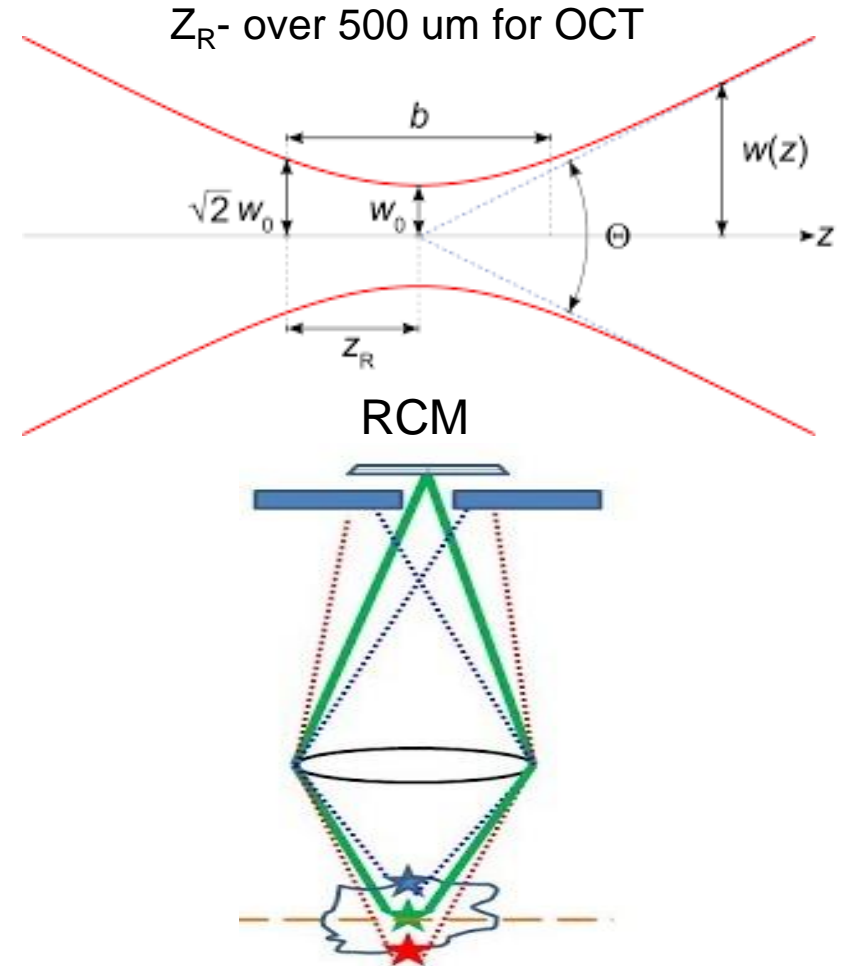
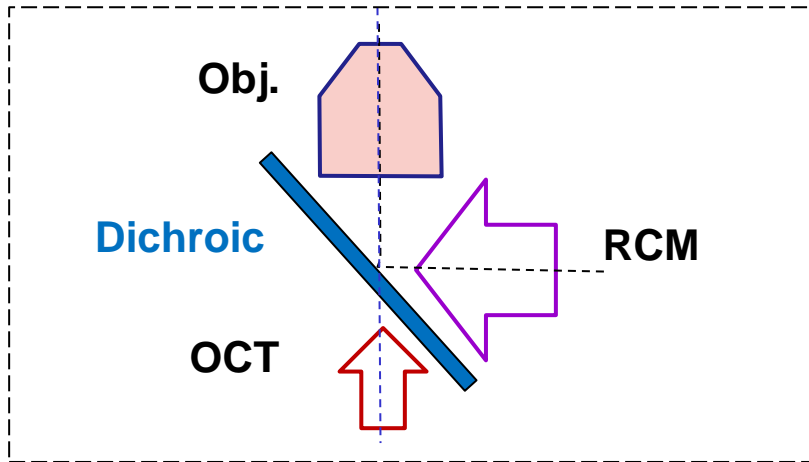
## OCT capabilities:

- Cross-sectional imaging of the deeper layers, to  $\geq 1.5$  mm
- Visualizes the dermal-epidermal junction-crucial for skin cancer therapy decisions
- Visualization of skin perfusion- tissue viability



# Same optical path RCM-OCT Implementation

US Patent: 9655521B2

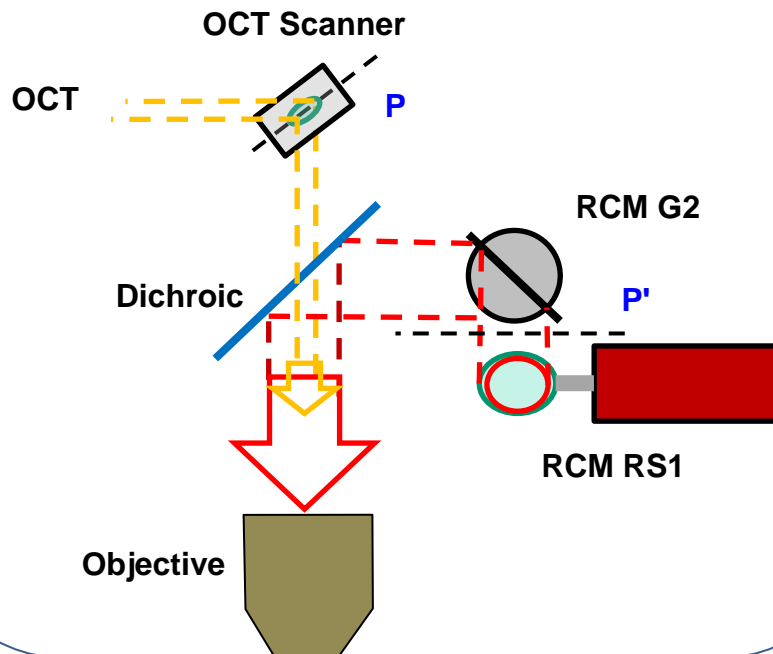


- OCT underutilizes the NA – enabling a larger imaging depth
- RCM fully utilizes the NA of the imaging objective and a confocal gate:  $\mu\text{m}$  scale sectioning

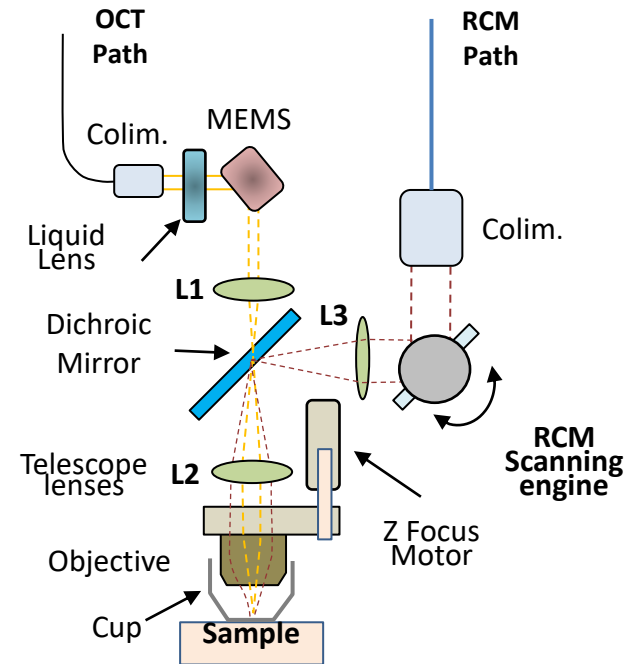
# HH Probe Implementation

- Fiber based - both RCM and OCT- improved alignment stability

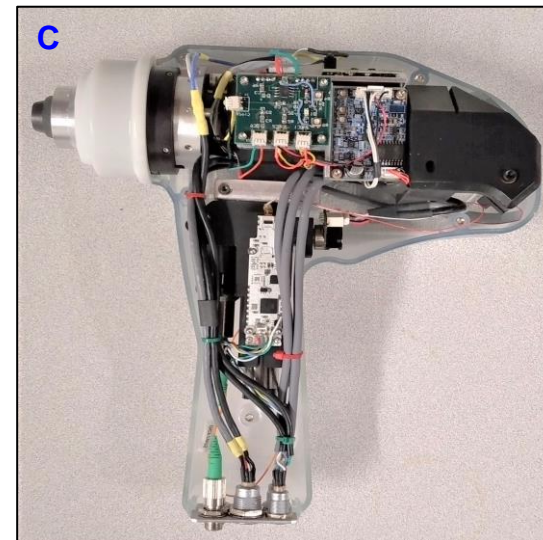
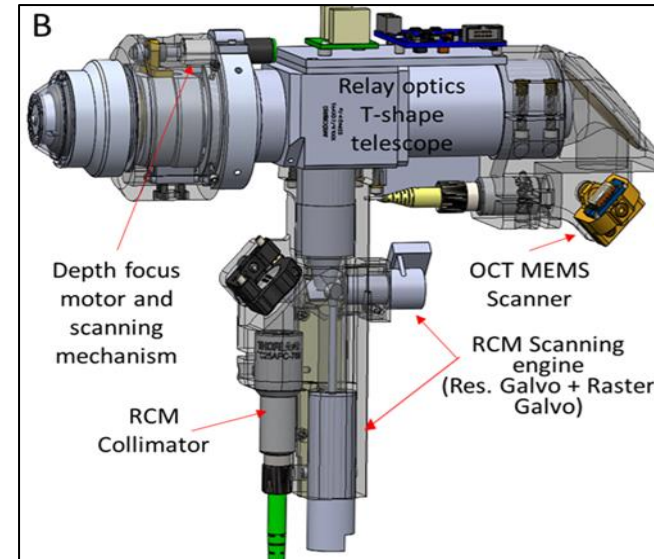
**A** OCT: Dual-axis MEMS –small format package



**B**



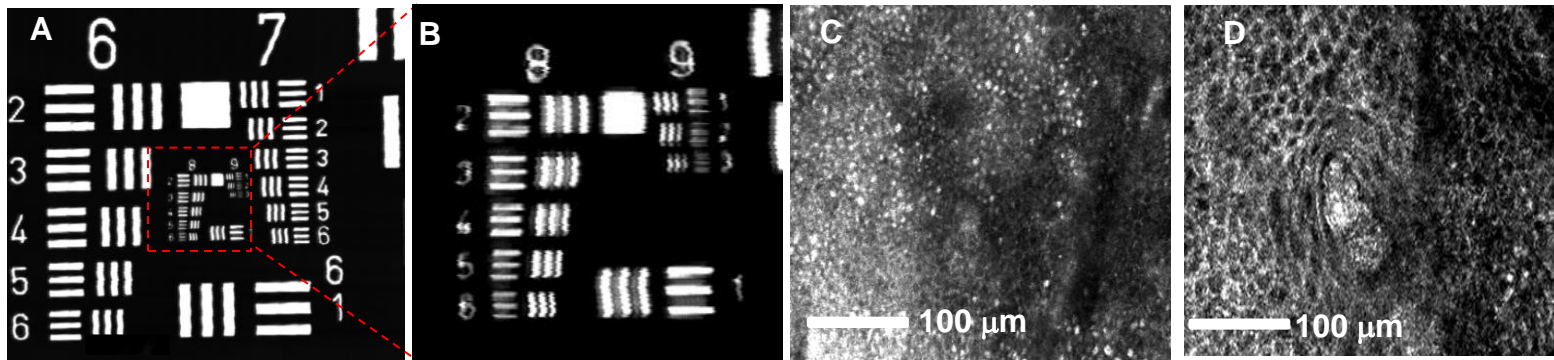
# Instrument Implementation



# Imaging performance assessment

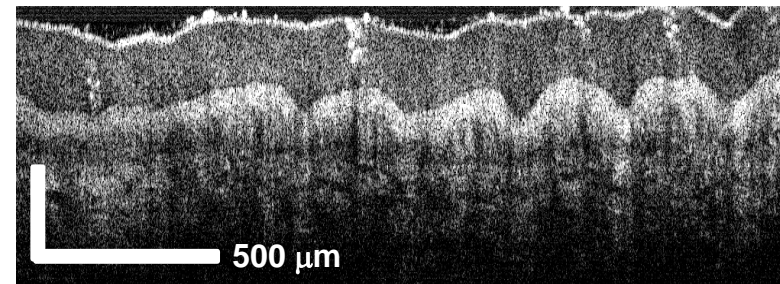
## Objectives:

- Determine axial-lateral resolution in each imaging mode
- Determine imaging depth



## Results:

- Resolution: RCM:  $<0.68 \mu\text{m}$  lateral  
OCT:  $\sim 6 \mu\text{m}$  lateral
- Imaging depth:  $\sim 250 \mu\text{m}$  in RCM mode  
 $\sim 1.25\text{mm}$  in OCT mode



## Clinical Evaluation/Study Objectives

- Reflectance Confocal Microscopy (RCM) and Optical Coherence Tomography (OCT) have the ability to **identify Basal Cell Carcinoma (BCC)** and estimate their **invasion depth**
- Laser ablation has been shown to **treat superficial and early nodular BCCs** under the guidance of RCM, while **radiation therapy (RT)** has shown to be effective in treating deeper lesions

### AIMS

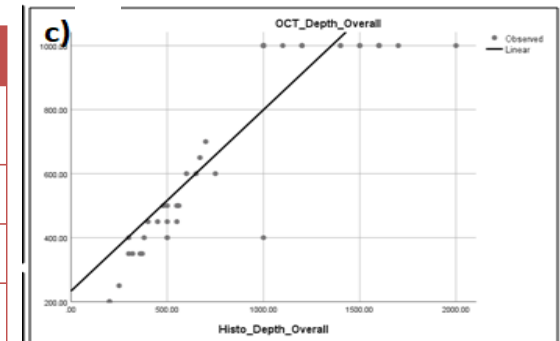
- **Aim 1:** Use RCM-OCT to select thin BCCs for either laser ablation or radiation therapy and establish laser fluence or RT dose
- **Aim 2:** To use RCM-OCT to monitor the outcome of the treated BCCs



# RCM-OCT Clinical Evaluation

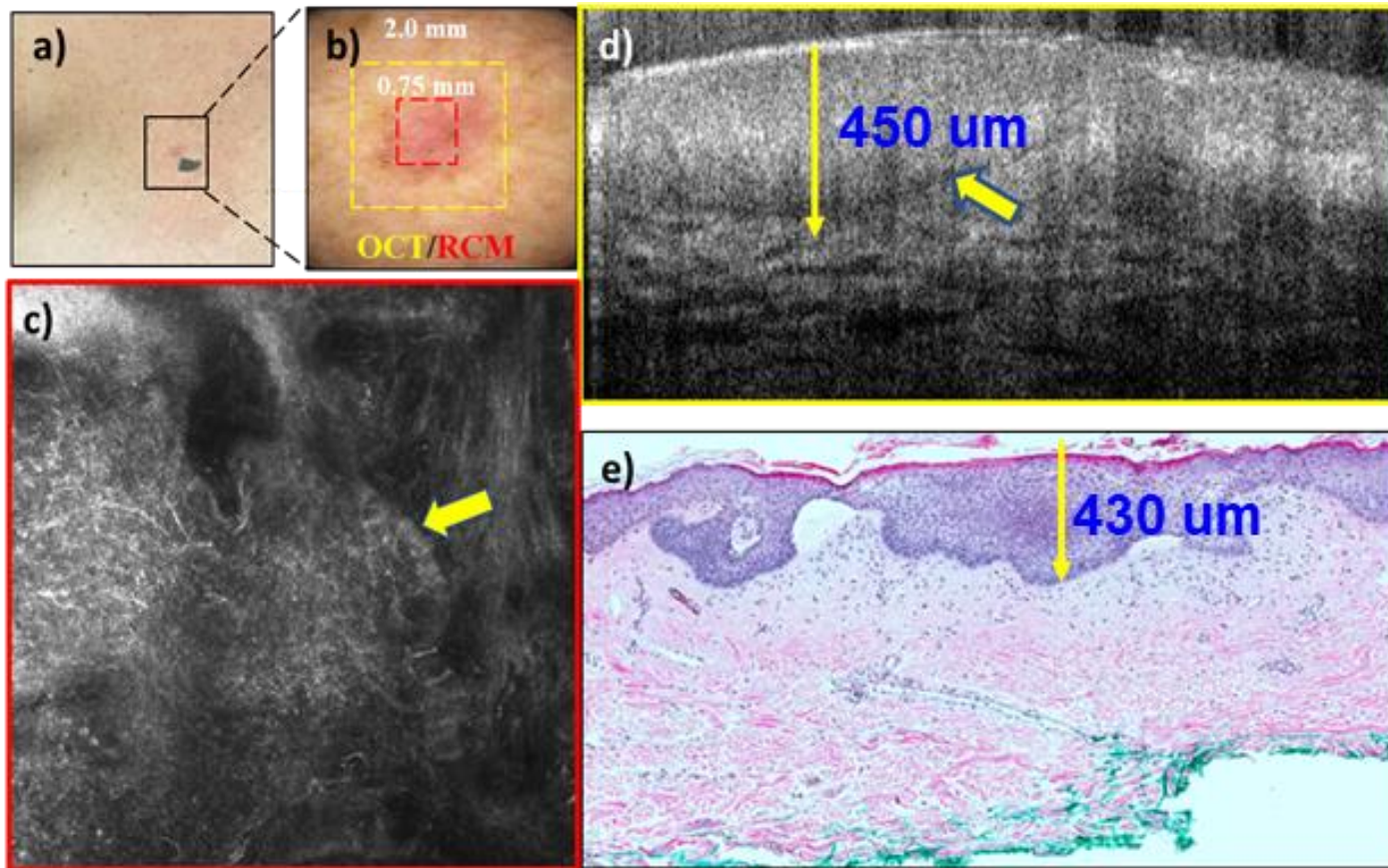
1. >100 patients were evaluated to date
2. Combined RCM/OCT imaging features, as shown in the table below, enabled accurate identification of NMSC presence and invasion depth evaluation, both confirmed by histopathology
3. High specificity (94.1%) was observed in the clinically suspicious lesions (n=185), in intact skin

RCM Features	OCT Features
Epidermal streaming	<u>Hyporeflexive</u> or gray structures attached to the dermal-epidermal junction (DEJ)
Tumor nests	Disruption of the DEJ
Cordlike structures	<u>Hyporeflexive</u> or gray ovoid structures in the dermis
Nuclear palisading at tumor edge	Dark <u>peritumoral rim</u> (clefting)
Dark peritumoral rim (clefting)	Hyper-reflective <u>peritumoral stroma</u>
Stroma with plump cells and bright dots	Hypo- and hyper-reflective streaks in dermis
Horizontal vessels	Branched vessels



<b>R value</b>	<b>0.86</b>
R <sup>2</sup> value	0.75
p value	< 0.0001
Level of significance	0.05

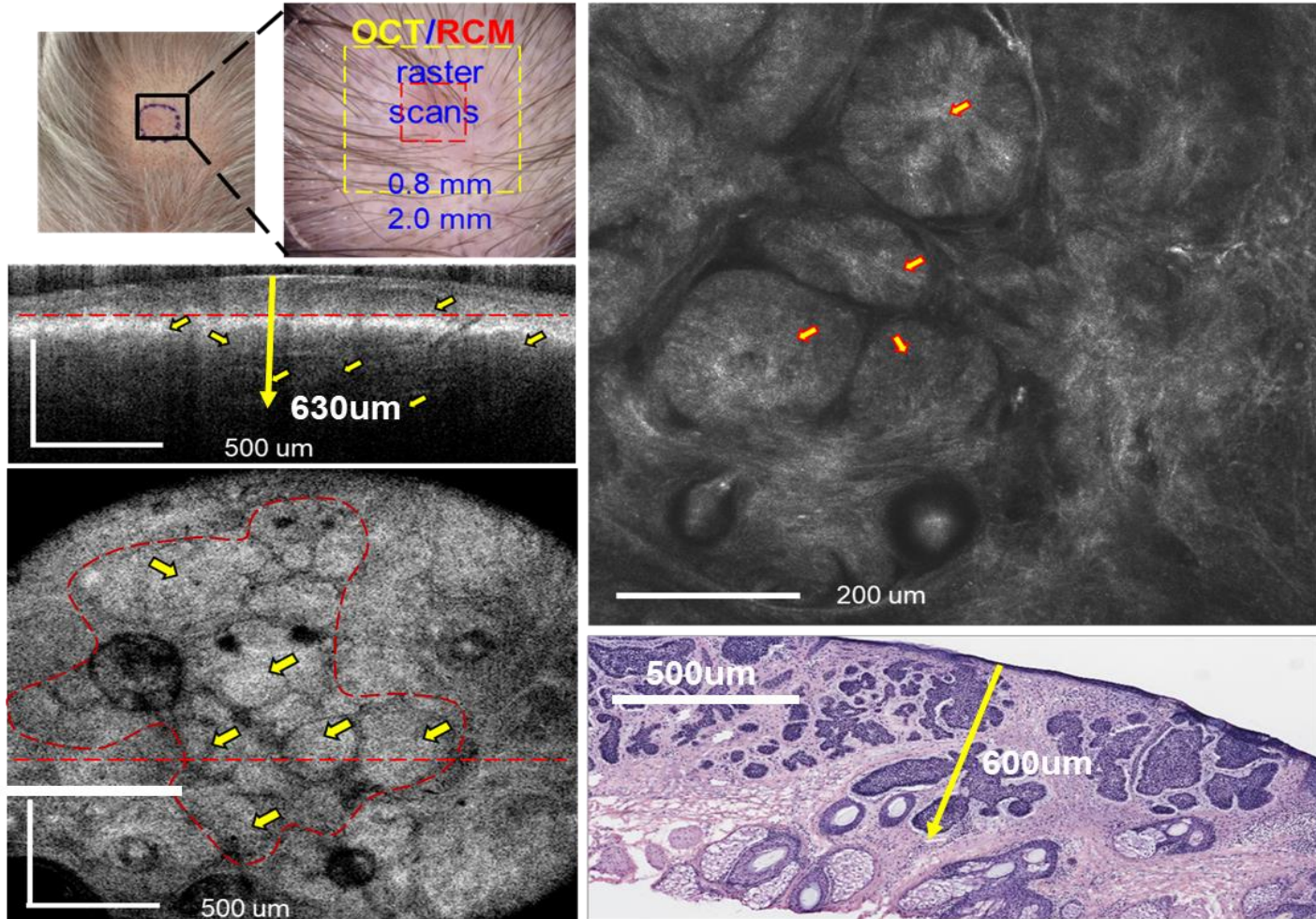
# BCC RCM-OCT features: Example 1



**Nuclear palisading at the tumoral edge**

**Peritumoral rim, hypo and hyper reflective streaks in the dermis**

# BCC RCM-OCT features: Example 2



**Ovoid structures in the dermis, hypo and hyper reflective streaks in the dermis**

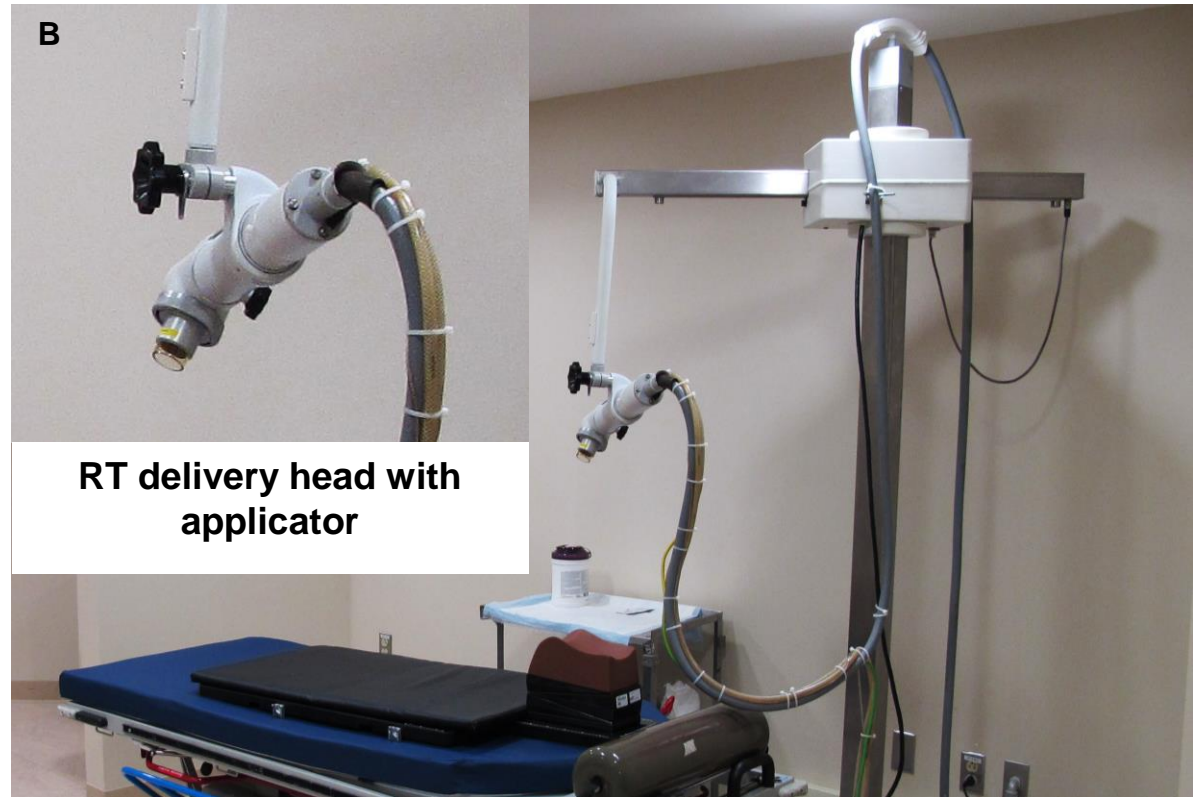
**Multiple tumor nests, dark peritumoral rims**

# Clinical Machines

**Erbium-YAG laser (2940)**



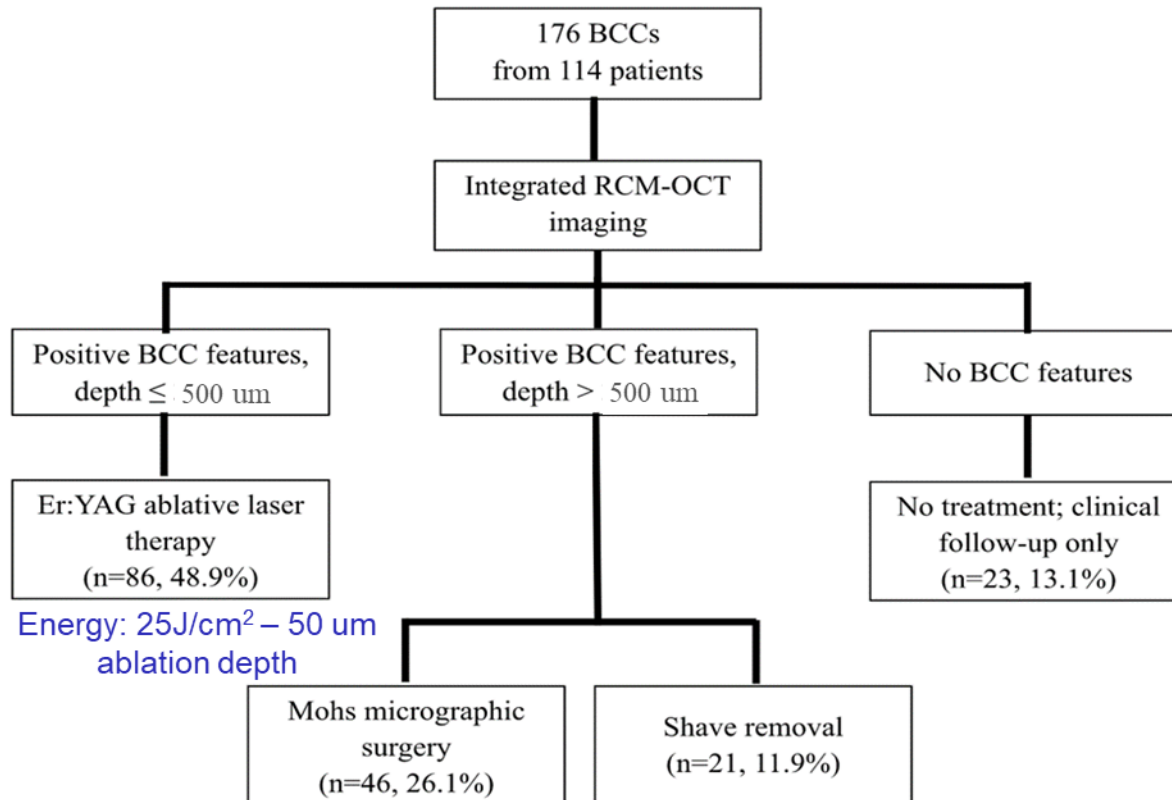
**Varian GammaMed Ir-192 afterloading source and Varian BrachyVision™ planning software**



# Laser Ablation Clinical Study

## Study Goals:

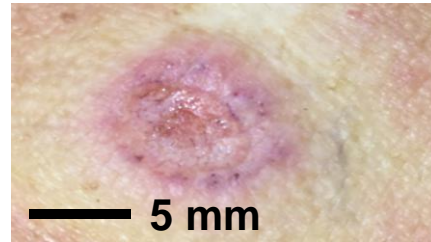
1. Test RCM/OCT capability to delineate tumor margins with high accuracy (micron scale)
2. Determine if improved cosmetic are obtained as compared to Mohs surgery, while and therapy results are the same (less than 5% recurrence)



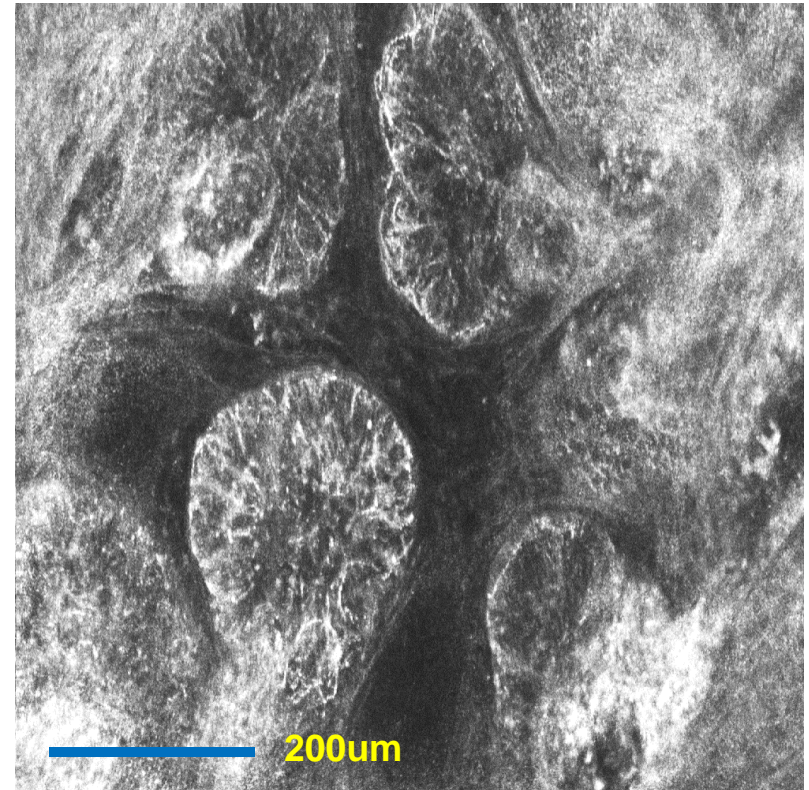
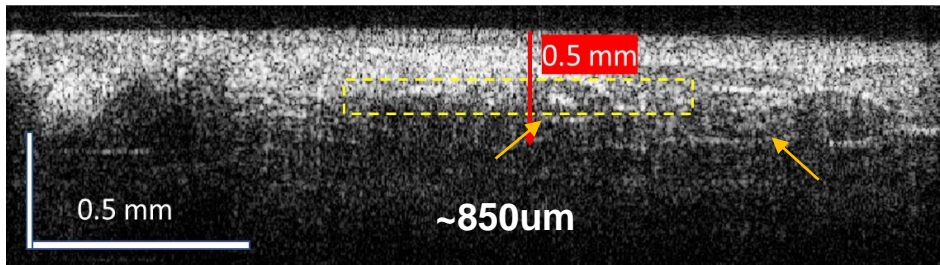
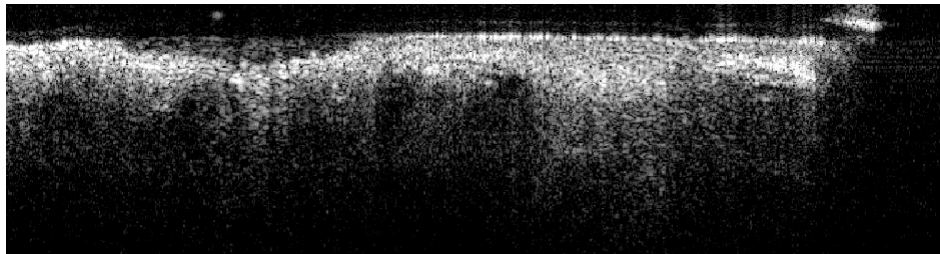
# Ablation of BCC on the back



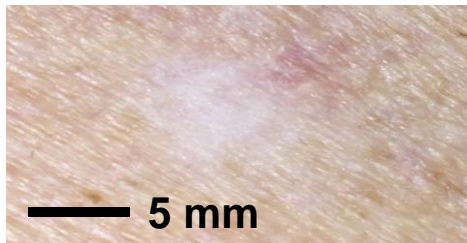
**Pre-ablation**  
11/21/2019



**Ablation**  
11/21/2019

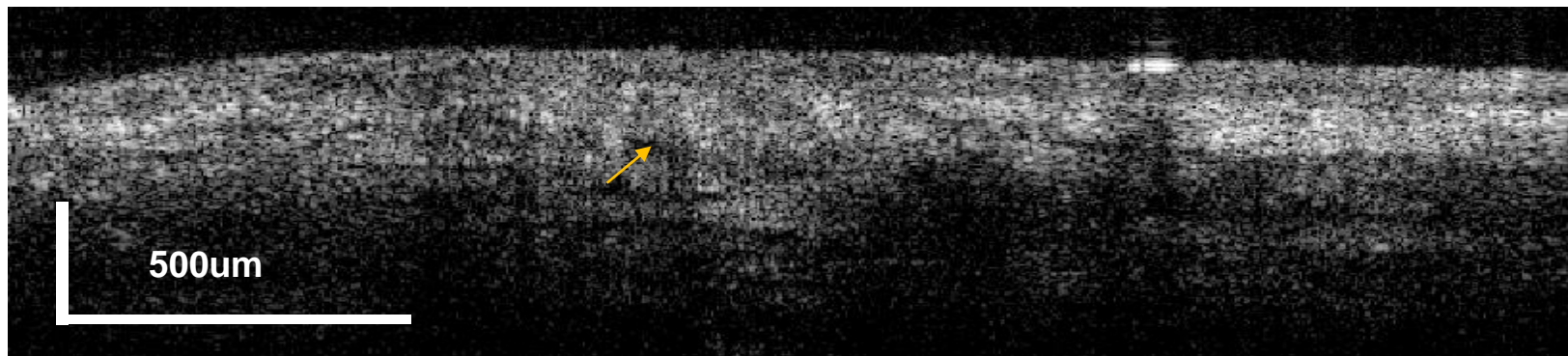
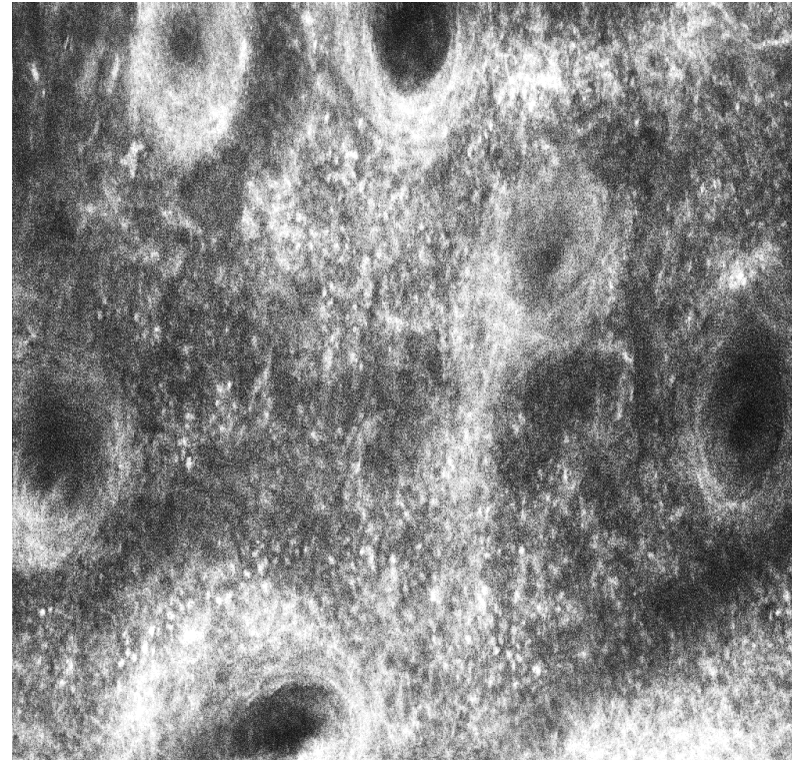


# Post Ablation Results



5 mm

**Post-ablation  
11/18/2021**



500um

# Laser Ablation Summary

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- 100 % of clinically diagnosed unequivocal BCCs were confirmed to be BCCs on RCM-OCT (n=53)
- 23 of 123 (18.7%) biopsy proven BCCs did not reveal any residual tumor on RCM-OCT and were spared any further intervention but continued RCM-OCT monitoring
- Tumors <500 microns treated with laser ablation had a recurrence rate of 3.5%
- Our study suggests RCM-OCT may potentially facilitate BCC triage for appropriate management at bedside, thus may also help streamline the management of BCC.



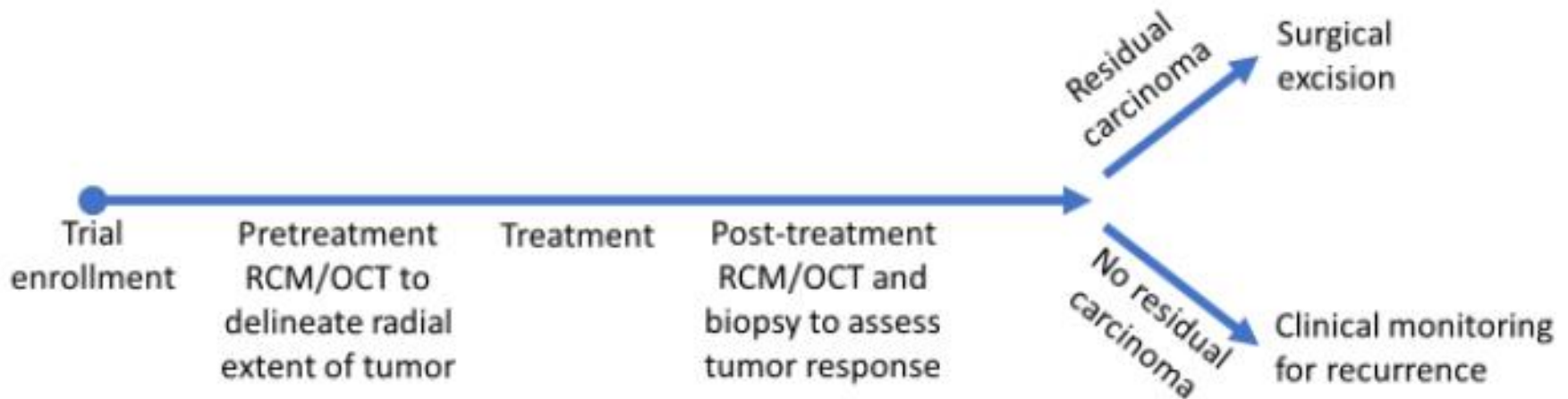
# RT Clinical Study

## Primary objective

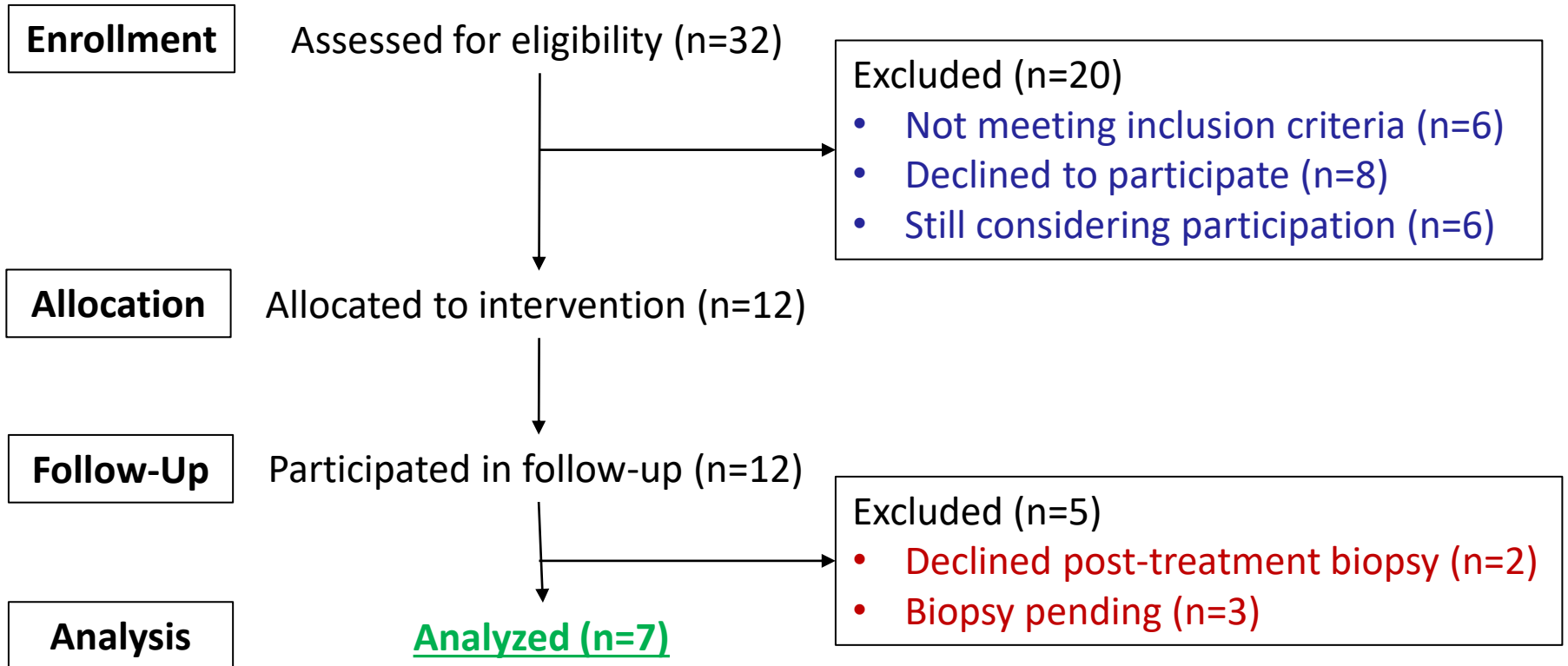
- Determine histologic response rate of early-stage basal cell carcinoma to RCM/OCT-guided radiotherapy 6 weeks after completing treatment

## Secondary objectives

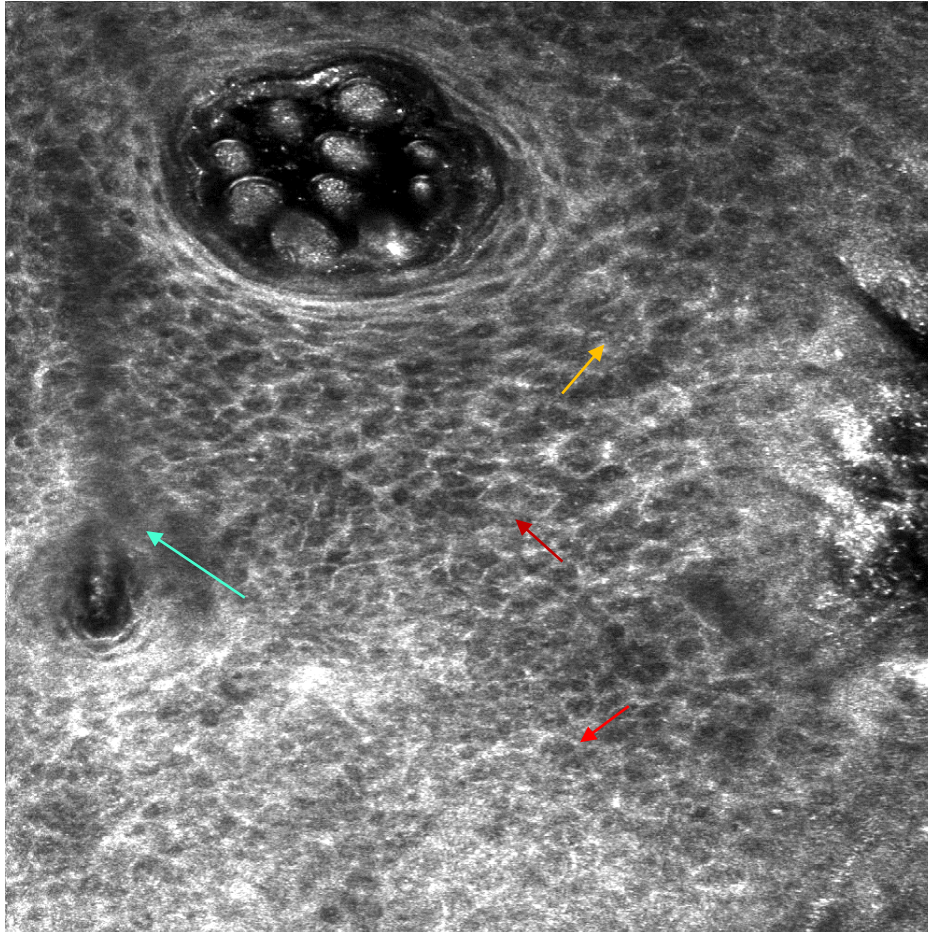
- Adverse event frequency and severity
- Quality of life before and after radiotherapy
- Primary tumor recurrence rate 3 years after completing treatment



# RT Enrolment



# BCC on the nose: Pre-treatment Evaluation

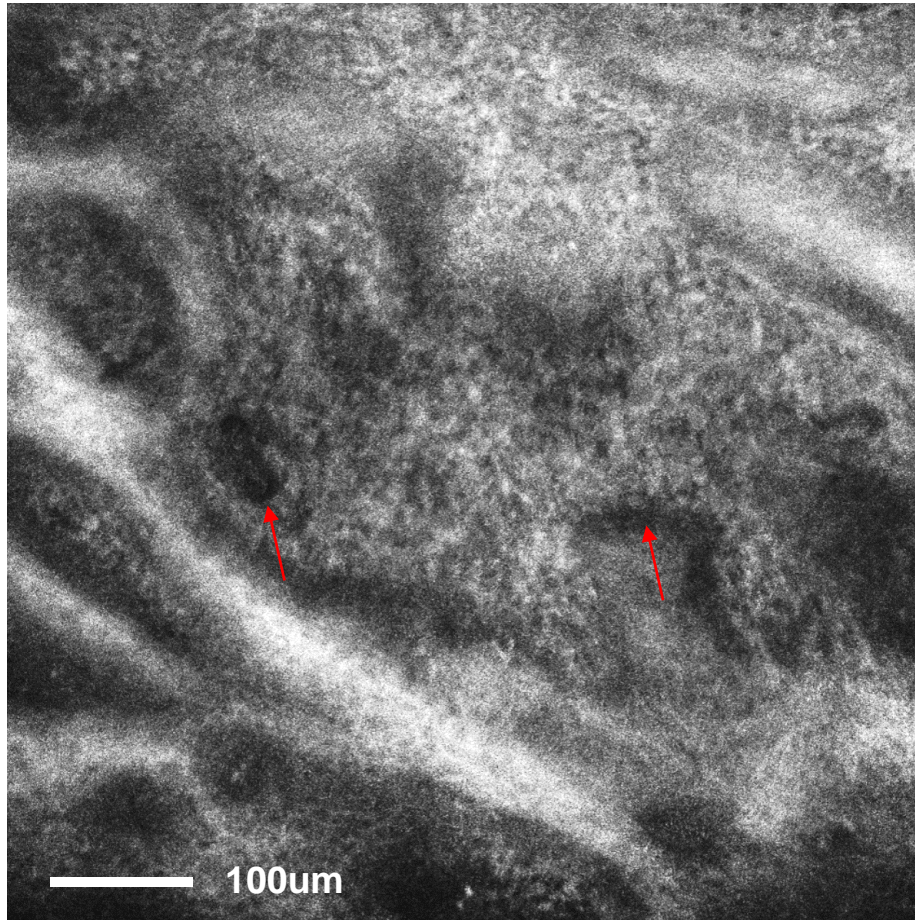


Red=Target using standard/clinical method  
Black=Target using RCM/OCT imaging

**ARROW LEGEND:**

Green - Hair follicles; Orange- Tumor  
RED- BLOOD VESSEL

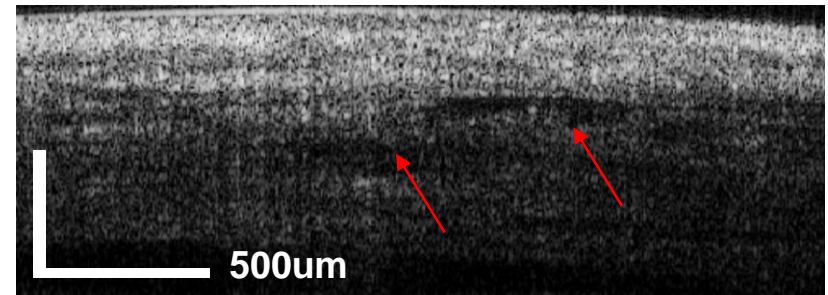
# Post-treatment Evaluation



12 weeks post-treatment



RCM/OCT guided biopsy confirms no residual carcinoma  
Complete resolution of grade 2 radiation dermatitis at 12 weeks



**ARROW LEGEND:**

**RED-** Large BLOOD VESSELS

## RT Summary

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- All patients enrolled underwent pretreatment post treatment imaging with RCM/OCT, radiotherapy
- All patients that underwent biopsy (n=7) had no evidence of residual carcinoma
- High grade adverse events infrequent
  - 1 grade 3 adverse event, radiation dermatitis
  - Other adverse events were grade 1-2
- Quality of life assessments – improved compared to Mohs!
- Clinical target volume typically smaller using RCM/OCT definition
- No recurrence to date

- Designed and built common optical path RCM/OCT instrument
- Demonstrated that RCM/OCT imaging capabilities complement each-other allowing for:
  - ✓ Imaging the epithelial layer at the sub-cellular scale and visualizing tissue morphology up to 1.5 mm in depth with micron scale
  - ✓ Assess cancer presence and spreading in depth and laterally
- Demonstrated the RCM/OCT may be a suitable tool for:
  - ✓ Reliably diagnosing skin lesions
  - ✓ Non-surgical therapy guidance

# Acknowledgements

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Dr. C. Barker, Rad Oncologist, MSKCC –RT Clinical Lead  
Dr. Chih-Shan Jason Chen, Surgeon, MSKCC- Laser therapy Clinical Lead  
Drs. Larissa Pastore, M. Cordova and A. Sahu, MSKCC - Imaging specialists  
Mr. G. Maguluri, Dr. M. Mujat, PSI - Software Development  
Mr. J. Grimble, Ms. Aliana Caron, PSI- Mechanical design and Fabrication

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# Questions?



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