

SciBase comments  
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## Point-of-care detection of melanoma

Advancing the management of skin cancer and dermatological conditions with evidence-based AI driven technology



# Diagnosing standard / Ground truth

- The ground truth must be reliable with minimal error and potential sources of bias.
- The level of inaccuracy in the diagnostic standard directly impacts the observed accuracy of the device tested.
- The diagnostic standard for melanoma should be histopathology
  - though imperfect it is still the most accurate and established reference standard available.
- In the PMA approval of the Nevisense device, the prospective clinical study included:
  - Local histopathologist
  - A panel of at least 3 histopathologists (dermatopathologists)
  - A plan (further expert panel) to address disagreements.

# Acceptable thresholds for Sensitivity & Specificity

- Acceptable thresholds for sensitivity and NPV should be high in order to guide the clinician in not missing any skin cancers, especially melanoma.
- Studies should be prospective, adequately powered and require that the observed sensitivity confidence interval lower bound exceeds 90%
- Performance goals for accuracy should depend on device indications for use and the intended user group.
  - If a skin lesion analyzer is not intended for use by an experienced dermatologist, for a certain preselected lesion type, or is intended for use as a ‘screener’ or standalone diagnostic tool, the accuracy requirements and clinical validation study size/scope would need to be greater.

# Patient characteristics

- Sufficient numbers of subjects should be included in studies to allow for subgroup analyses.
- A validation study should address the diversity of ethnicity, gender, age groups, low/intermediate/high risk populations, and Fitzpatrick skin types that are characteristic of the intended patient population.
- To adequately evaluate device performance, a broad range of atypical lesions need to be included with various sizes and level of suspicion.
  - Adequate numbers of small lesions and early-stage melanomas need to be included in any prospective study.

# Balance of Increased Access with Risk Mitigation

- A wider group of users outside of dermatologists increases the risk that:
  - skin lesions that should be analyzed or biopsied are missed,
  - the wrong lesion type is selected for the device, resulting in inaccurate results
  - the user lacks the competence needed to combine the output of the device with other relevant clinical or historical signs and make a correct clinical management decision.
- To safely increase access, FDA would need to increase device accuracy requirements and the size and scope of any clinical validation study would need to be much greater.