BACKGROUND AND OBJECTIVES
Nano-Pulse Stimulation (NPS) is the non-thermal, localized delivery of a timed series of low energy, high voltage nanosecond pulses which has been shown to induce programmed cell death and a lasting immune response in animal studies of melanoma and other non-benign tumors. This human study of benign seborrheic keratosis (SK) lesions treated with an NPS device provides evidence to guide appropriate energy parameters and protocol design decisions for planned future clinical studies of other benign and non-benign lesions.

STUDY DESIGN AND METHODS
58 adult subjects in four clinical centers were required to have at least 4 off-face lesions within study criteria for size and a clinical diagnosis of SK. A local anesthetic was injected prior to treatment. Three lesions were treated in a single session and one lesion was left untreated as a control. First five subjects were treated, then parameter adjustments were made (Learning Cohort). The subsequent 53 subjects were treated with adjusted parameters (Adjusted Cohort). Subjects returned five times over a 106-day period for physician assessment of SK lesions and the cosmetic appearance of treated areas. Visits occurring at day 7, 30, 60, 90 and 106 post-treatment included standardized photographs. At the final 106-day visit, subjects rated their satisfaction on a 5-point scale. Blinded, independent reviewers rated the degree of clearing of SK lesions based on photographs taken at 106 days post-treatment compared to baseline.

RESULTS AND CONCLUSIONS
Physician assessment of efficacy for all subjects completing the 106-day visit scored 82% of treated SK lesions as cleared or mostly cleared. At the conclusion of the study, no adverse events were reported. The most common residual skin condition was mild to moderate hyperpigmentation 106 days after treatment in 60% of lesion areas, and 2% of treated lesions were noted for hypopigmentation. The clinical NPS device demonstrates potential as a new treatment for common benign lesions. These primary lesion reduction results, along with data from pre-clinical studies that demonstrate a potential immune response, support further studies in both benign and non-benign lesions.
High Levels of Efficacy and Subject Satisfaction with Single NPS Treatment

- 58 subjects completed all treatments across four locations in the U.S.
- Learning Cohort: First 5 subjects treated, parameter adjustments made based on unsatisfactory results (15 treated lesions)
- Adjusted Cohort: Subsequent 53 subjects treated with adjusted parameters (159 treated lesions)
- Efficacy: Investigators rated 87% of treated lesions as Clear or Mostly Clear in Adjusted Cohort vs. 82% for Full Cohort. An independent, blinded photographic review of lesion images scored 71% of lesions as Clear or Mostly Clear for Full Cohort.
- Subject Satisfaction: Subjects were Satisfied or Mostly Satisfied with 82% of treated lesions in Adjusted Cohort vs. 78% for Full Cohort, closely mirroring investigator ratings.

Clinical Study Sites
1. Brian Zelickson, MD (Edina, MN)
2. George Hruza, MD (St. Louis, MO)
3. Thomas Rohrer, MD (Chestnut Hill, MA)
4. James Newman, MD (San Mateo, CA)

Examples of Clear Skin

Mostly Cleared SK with Clear Residual Skin
Location: Back
Subject: SK-TR-004 (SK #2)

Cleared SK with Clear Residual Skin
Location: Back
Subject: SK-TR-004 (SK #1)

Examples of Hyperpigmentation

Cleared SK with Hyperpigmentation
Location: Back
Subject: SK-TR-006 (SK #1)

Mostly Cleared SK with Hyperpigmentation
Location: Back
Subject: SK-TR-006 (SK #4)

60% of lesions with mild to moderate hyperpigmentation at Day 106

CLINICAL OBSERVATIONS
• Procedure well tolerated with use of local anesthesia (injected lidocaine)
• No adverse events reported
• Overlapping “passes” in center of lesion may have contributed to reports of mild to moderate hyperpigmentation

SUMMARY AND CONCLUSIONS
• Minimal clinical response in first five subjects required parameter adjustments for subsequent 53 subjects
• 87% clearance (in Adjusted Cohort of 53 subjects) of a common benign lesion establishes utility of the unique NPS mechanism for eliminating SKs or similar cellular benign lesions of the epidermis and dermis
• Improvements in residual hyperpigmentation at 286 day based on limited number of subject evaluations (see photos of SK-TR-006)
• Pre-clinical evidence of non-benign tumor efficacy (including murine melanoma) and a lasting immune response hold great promise for future human studies of malignant tissue