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High Intensity Focused Ultrasound (HIFU) treatment of Cutaneous Neurofibromas (cNF): Preliminary results from a prospective dual-center clinical investigation.

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Introduction & Objectives:

Neurofibromatosis Type I (NF1) is among the most common single-gene inherited conditions worldwide and predisposes to multiple forms of benign and malignant neoplasms. The most common tumor in NF1 patients is cutaneous neurofibroma (cNF). The benign cNF can appear in numbers up to several hundred on the skin of NF1 patients. cNF may cause pain, social and functional limitations. Treatment options include surgical removal or the use of various devices that cause tissue destruction showing limited efficacy and often leave cutaneous scarring. High intensity focused ultrasound (HIFU) is capable of controlled and targeted thermo-mechanical treatment to small intradermal volumes containing neoplastic cells, without inflicting damage to the surrounding tissue. The objectives of this study were to investigate safety, local tolerability, and efficacy of high intensity focused ultrasound (HIFU) for treatment of NF1 associated cNFs.

Materials & Methods:

Twenty adult patients having at least 8 eligible cNFs were recruited in two centers. Focused ultrasound treatment utilizing a 20 MHz HIFU-device with integrated dermoscopic guidance was performed using a handpiece with a focus depth of 2.3 mm below the skin surface. Single dose acoustic energy of 0.7 J/dose of pulse duration 250 ms/dose was manually positioned with distance of 1-2 mm between each applied dose, at repetition frequency of 1-2 seconds until the full cNF including a 1 mm perilesional margin was covered. No anesthetic was applied. Primary endpoint was evaluation of safety and tolerance of the HIFU-treatment. Post-treatment effects were assessed immediately after treatment and at follow-up visits including on-site clinical evaluation, patients' evaluation and clinical photography for 9 months. Further evaluation of the included cNFs was performed by ultrasound scanning (US) in one center and histopathology in the other center.

Results:

A total of 147 cNFs (mean 7.35/patient; diameter 2-9 mm) were treated. Mild wheal-and-flare reaction was observed immediately after treatment. Occasionally, erosions/crusts were observed and rarely dyspigmentation after 1 week and 3, 6 and 9 months post-treatment respectively. Regarding the primary endpoint, no serious adverse events occurred, and no significant scarring was observed. The median reduction in cNF thickness measured by ultrasound scanning was 0.53 mm with a range of -100% to +19%. Visual rating of treated cNFs by the clinical investigator at 9 months showed that 45 out of 92 cNFs (49%) had full or substantial reduction; biopsied lesions excluded. During treatment the patient-reported pain-score was median 3.5 (range 1-7) on a 0-10 point scale. No pain was reported post-treatment.

Conclusion:

HIFU treatment is a new non-invasive, rapid, and tolerable treatment modality. This study demonstrates the safety,

local tolerability, efficacy, and feasibility of HIFU for the treatment of cNFs. The variation in cNF reduction after HIFU-treatment and the occasional erosions and crusts in the treatment area indicate that dosing needs to be further adjusted. Follow-up clinical studies to optimize the dose response in adults with NF1 are underway with a goal of applying this therapy to both established and developing cNFs in the future.