Imaging Techniques for Neurofibromatosis Type 1-Associated Cutaneous Neurofibromas: Existing Approaches and Advancements

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Background

Neurofibromatosis type 1 (NF1) is a tumor predisposition syndrome caused by pathogenic variants in the NF1 gene. Cutaneous neurofibromas (cNFs), the predominant manifestation of NF1, can number in the thousands, resulting in substantial discomfort and disfigurement. A major limitation in advancing therapies is a lack of validated approaches for evaluating cNFs. Standardized measurement techniques must be applied to reliably assess the efficacy of treatments for these tumors.

Objective

This review presents the available data on existing and emerging techniques for identifying, measuring, and tracking cNFs.

Methods

A comprehensive search across PubMed, Google Scholar, and clinicaltrials.gov was performed. Sources were assessed for the purpose of imaging and readouts addressing reliability, reproducibility, feasibility, and capabilities when assessing cNFs.

Results

Seven manuscripts published from 2008-2022 and eight clinical studies focused on cNF imaging techniques were identified. These measurement techniques included calipers, digital imaging, high-frequency ultrasound sonography (HFUS), spatial frequency domain imaging (SFDI), and optical coherence tomography (OCT).

Calipers prove useful for cNFs measuring at least 5 mm; however, time required for measurement of each cNF, measurement variability, and lack of raw data storage are limiting factors. 2D digital imaging is accessible to clinics and patients as phone cameras can be utilized, allowing crowdsourcing of data and potential supplementation of medical grade images for cNF assessment. 3D image capture, including whole-body imaging, facilitates longitudinal tracking of cNFs. HFUS demonstrates high measurement reliability and allows visualization of cNF features below the skin surface. New techniques applied to other dermatologic conditions such as SFDI and OCT are being repurposed for cNFs to enable earlier detection of cNFs and augment trials focused on preventative treatment. The cost of each technique, user training, and median time for image or measurement acquisition and analysis varied significantly (Figure 1).

Conclusion

Accurate and efficient detection, tracking, and evaluation of change for cNFs are critical to address the unmet medical need of these tumors. Calipers, 2D/3D imaging, and HFUS have shown utility in this context. SFDI and OCT can potentially detect nascent cNFs. However, the need to assess tumors involving dermis beneath and above the skin surface and the variable phenotype of cNFs (in size, morphology, color, location, growth rate, abutment with other tumors) make imaging challenging. With a growing array of cNF therapeutic options in development, further work is needed to pinpoint optimal imaging technique applications aligned with specific cNF study goals.

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