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● *Original Contribution*

ULTRASOUND STRAIN ELASTOGRAPHY IN ASSESSMENT OF MUSCLE STIFFNESS IN ACUTE LEVODOPA CHALLENGE TEST: A FEASIBILITY STUDY

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Abstract—To evaluate the feasibility of ultrasound strain elastography in assessing the response of muscle stiffness to the acute levodopa test, we prospectively performed strain elastography on the biceps brachii muscle (BBM) of 18 patients to diagnose Parkinson's disease. BBM and subcutaneous tissue strains (deformations) were produced by external compression with an ultrasound transducer and estimated using 2-D speckle tracking. We used the strain ratio (SR = BBM strain/reference strain) to assess BBM stiffness. The rate of increase in SR [rate = (SR after levodopa−SR before levodopa)/SR before levodopa] was used to assess the muscle stiffness response to levodopa. SR significantly increased after levodopa administration in 11 patients with Parkinson's disease ($p = 0.02$), whereas it did not in 7 patients with parkinsonian syndrome (from non-Parkinson's causes) ($p = 0.14$). The area under the receiver operating characteristic curve for the rate of increase in SR in determining Parkinson's disease was 0.96. The rate of increase in SR seems to be feasible in evaluating the effect of levodopa on muscle stiffness in the diagnosis of Parkinson's disease. (E-mail: ttyyus@sina.com) © **2016 World Federation for Ultrasound in Medicine & Biology.**

Key Words: **Acute levodopa challenge test, Muscle rigidity, Parkinson's disease, Speckle tracking, Ultrasound strain elastography.**

INTRODUCTION

Currently, the diagnosis of Parkinson's disease (PD) is based on the patient's medical history and clinical symptoms, including rest tremor, bradykinesia, postural instability and passive rigidity, because there are no quantitative measures for confirming the diagnosis. DaTscan allows visualization of decreasing dopamine transporter (DaT) function in both PD and parkinsonian syndrome, also called Parkinsonism (PS), using SPECT brain imaging. However, DaTscan is not capable of distinguishing PD from PS (*e.g.,* multisystem atrophy [MSA], progressive supranuclear palsy [PSP] [Gray et al. 2015; Perju-Dumbrava et al. 2012]).

A systematic review and practice parameter from the American Academy of Neurology (AAN), published in 2006, concluded that levodopa and apomorphine challenge tests should be considered when the diagnosis of PD is uncertain and a differentiation of PD from PS is difficult (Suchowersky et al. 2006). A challenge test is considered supportive of a diagnosis of PD if the clinical motor score, assessed with the Unified Parkinson's Disease Rating Scale (UPDRS, Part III, the standard for scoring motor abnormality and rigidity in PD), improves by more than 30% after levodopa administration (Merello et al. 2002; Rossi et al. 2000; Tolosa et al. 2006). However, such an evaluation method is subjective as it is based on physical examination of muscle rigidity by observers (Fahn and Elton 1987) and is non-quantitative. A quantitative biomarker for objectively assessing muscle response to the challenge test is preferred. We have not found any report on the use of medical imaging to evaluate the challenge test during our literature review.

Ultrasound strain elastography (SE) based on the fraction of tissue deformation under an external compression has been used to estimate change in tissue mechanical properties (stiffness) associated with tissue pathologic conditions (*e.g.,* muscle rigidity) (Brandenburg et al. 2014; Drakonaki et al. 2012; Ophir et al. 1991). The strain is higher in high-elasticity soft tissue than in low-elasticity stiffer tissue (Drakonaki et al. 2012).

Given that muscle mechanical properties associated with muscle rigidity may change after administration of

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levodopa and that SE is able to quantify tissue stiffness, we hypothesized that biceps brachii muscle (BBM) strain can be used to quantify the change in muscle stiffness in response to the Levodopa challenge test in the diagnosis of PD.

METHODS

Patients

The institutional ethics committee at Beijing Tiantian Hospital of Capital Medical University (Beijing, China) approved the study, and written informed consent was obtained from all patients.

Between July 2014 and December 2014, we prospectively enrolled 18 patients (10 men and 8 women, age range: 47–76 y, mean age: 58 ± 10 y) who were suspected of having PD according to British Brain Bank clinical criteria (Reichmann 2010). The BBM rigidity in 18 patients was assessed as I or II using the five-point UPDRS motor score criteria (0 = no rigidity, I = slight or detectable rigidity only when activated, II = mild to moderate rigidity, III = marked rigidity, IV = severe rigidity) (Fahn and Elton 1987).

Acute levodopa challenge test

All 18 patients underwent a challenge test, the standard of care for diagnosis of PD in patients with parkinsonian symptoms at the Beijing Tiantan Hospital, Capital Medical University. The challenge test was performed when the patients were *off* state (withdrawal of anti-parkinsonian medication for 12 h) and fasting. The test consists of rater-blinded assessment of parkinsonian symptoms using the UPDRS motor score before and 60 min after oral administration of single-dose levodopa (250 mg) (Albanese et al. 2001). Two experienced neurologists who were blinded to the SE study performed clinical UPDRS evaluations before and after administering levodopa separately.

On the basis of UPDRS evaluation (Merello et al. 2002), a diagnosis of PD is supported if muscle rigidity is improved >30% after administration of levodopa (positive challenge test). A diagnosis of PS is considered if muscle rigidity improves <30% after administration of levodopa (negative challenge test).

Real-time ultrasound data acquisition

All patients were imaged in the supine position with one arm relaxed, elbow extended and forearm supinated (Fig. 1). SE (Fig. 2) was performed using a Logic E9 ultrasound scanner (General Electric, USA) equipped with a L9-3 linear array transducer. Instead of conventional free-hand compression, the compression force on the BBM was produced with a sand bag (1.5 kg) tied onto the scan head. The observer used both hands to hold the transducer to maintain the transducer surface perpendicular to the skin (Fig. 1) while using as little extra force as possible. We tested sand bags of different weights (0.5, 1.0 and 1.5 kg) and chose the 1.5-kg sand bag as it was effective in producing >10% strain (deformation) in muscle tissue and constant strains on strain graphs

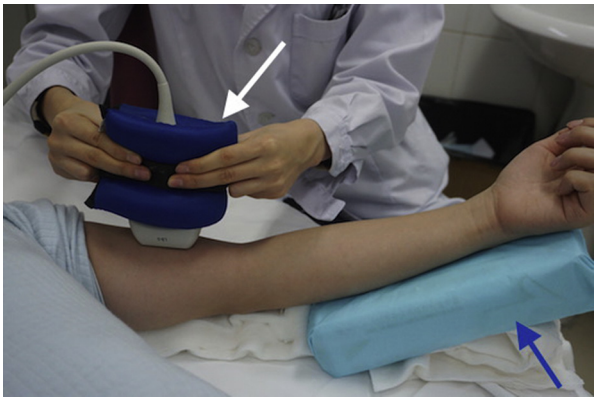

Fig. 1. Graph illustrates a 1.5-kg sandbag (*white arrow*) tied onto a linear array transducer used as the force for external compression. The transducer is placed on the mid- to lower arm, where the biceps brachii belly is located. The observer used both hands to hold the transducer to maintain its surface normal to the skin. Scanning was along longitudinal section of the biceps brachii muscle fiber. The patient was placed in the supine position. The arm muscle is relaxed when the forearm is supinated and elevated 30° using a supporting pad (*blue arrow*).

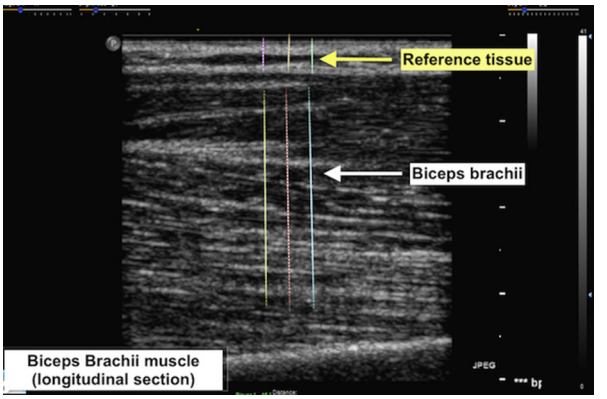

Fig. 2. Size of the region of interest for estimating BBM strain and reference subcutaneous soft tissue (reference) strain with 2-D speckle tracking software is illustrated on a longitudinal gray-scale image of the BB. BBM strain is measured in 25-mm region (*cyan, red and yellow dotted lines*) along longitudinal muscle fibers in the BBM (*white arrow*). Reference strain is measured in a 5-mm region (*green, orange and purple dotted lines*) in the subcutaneous soft tissue (*yellow arrow*). BBM (reference) strain represents the axial deformation in BBM (reference) along the direction of the emission sound beam, as well as the direction of compression using the ultrasound transducer. BBM = biceps brachii muscle.