Title of Entry: Three-dimensional Innervation Zone Imaging from Noninvasive High-Density Surface EMG Recordings

Innovation: The study develops a novel 3D innervation zone (IZ) imaging approach (3DIZI) by combining the bioelectric activity imaging and surface EMG decomposition approaches to image the 3D IZ distribution or propagating internal muscle activities in target muscles from high-density surface EMG (HD-sEMG) recordings. This research is innovative because it represents the first effort to noninvasively localize IZs and propagating muscle activities in the 3D muscle space from HD-sEMG recordings, which is of great significance for a variety of application in research and clinical diagnosis for neuromuscular diseases such as ALS and muscle spasticity. This research will also lead to an advanced IZ-guided Botulinum neurotoxin (BTX) injection approach in treating muscle spasticity, which is not currently available in clinic.

Description: The incidence of spasticity is reported to be 20%-40% in post-stroke patients, which not only has downstream effects on the patients’ quality of life, also lays substantial burden on the caregivers and the society. Botulinum neurotoxin (BTX) is considered as an effective treatment for post-stroke spasticity. BTX acts on the neuromuscular junction and the effectiveness of the BTX injection depends on the proximity of the injection site to the neuromuscular junction indicated by the innervation zone (IZ). The location of IZs varies between muscles and individuals, and currently there is no consensus about techniques used to localize IZs in the 3D muscle space.

Bioelectrical activity imaging approaches have been successfully used to localize bioelectrical activities in the brain and heart from scalp EEG and body surface ECG recordings respectively. Similar to EEG and ECG recordings, surface EMG signals are composed of superimposed action potentials of many muscle fibers and are the summation of each motor unit action potentials (MUAPs). Previous studies have demonstrated the feasibility of utilizing bioelectrical activity imaging approaches to localize the internal muscle activities from noninvasive high-density surface EMG (HD-sEMG) recordings, but currently available muscle activity imaging approaches suffer from low accuracy and specificity which limit their application and prevent them from being utilized to accurately localize innervation zones of muscles.

A novel 3D innervation zone imaging approach (3DIZI) was developed by combining the surface EMG decomposition and bioelectrical activities imaging methods to image the distribution of IZs in the 3D space of the target muscles from noninvasive HD-sEMG recordings. The developed 3DIZI approach was validated using 128-channel surface EMG and intramuscular EMG signals simultaneously recorded from the biceps of two healthy male subjects.

Data Acquirement: Surface EMG signals were recorded with 2 flexible 64-channel surface electrode array (TMSi, Enschede, The Netherlands), as shown in Fig. 1(a). Intramuscular EMG was recorded with a fine wire electrode (hook wire electrode, VIASYS Healthcare, Madison, WI) inserted into the middle section of the biceps. A sampling rate of 2 KHz was used for simultaneous surface and intramuscular EMG recordings with a 136-channel Refa system (TMSi, Enschede, Netherlands). The depth of the inserted wire electrode in the biceps was estimate with ultrasound as 1.53 cm (green circle) from the skin surface as shown in Fig. 2(b). Computational Model: A computational upper arm model was constructed from a general MR image data set and modified to match the ultrasound images of the subject’s right upper arm. The model consists of the skin, fat, biceps, triceps, compact bone and cancellous bone and was meshed into a finite element model for computation as shown in Fig. 2. Surface EMG Decomposition: Our newly developed K-means clustering and Convolution Kernel Compensation (KmCKC) algorithm was employed to decompose the 128-channel surface EMG signals into their constituent MUAP trains. A total of 10 MUAP trains were successfully decomposed from the 128-channel surface EMG signals of the 1st subject. The correlation between each reconstructed MUAP train and the simultaneously recorded intramuscular EMG signals was calculated and a high correlation indicates the corresponding MUAP train decomposed from the HD-sEMG signals was also simultaneously recorded by the inserted wire electrode. The correlation calculation results showed that only the 3rd and 6th MUAP trains, as shown in Fig. 3, have high correlation with the intramuscular EMG signals. IZ Localization: The surface location of each IZ was identified from the corresponding bipolar MUAPs by checking their phase change during propagation. By incorporating the identified surface location of each IZ, the 3D IZ location in the biceps was accurately localized from the corresponding decomposed MUAPs train using our recently developed internal muscle activity imaging algorithm. 3DIZI Validation: Fig. 1 and Fig. 3 shows that the insertion location of the wire electrode in the subject #1 is very close to the IZs of both MU3 and MU6. The large overlap between the reconstructed IZs of MU3 and MU6 and the fact that both IZs fully cover the location of the inserted wire electrode, as shown in Fig. 4. Similar results were also achieved on the subject #2. Results on both subjects demonstrate the high accuracy of the 3DIZI in localizing the IZs in the 3D space of muscles.

The well-developed 3DIZI approach can be utilized to noninvasively and accurately image the 3D distribution of IZs in target muscles of specific patients with muscle spasticity to guide the BTX injection. Such a muscle-specific and patient-specific 3D IZ image approach can also be employed to advance the understanding of the mechanisms of the spasticity.
**Supporting Material:**

**Fig. 1:** shows (a) position of 128-channel surface EMG recording electrodes (2 flexible $8 \times 8$ arrays with the electrode diameter of 5 mm, and the center-to-center electrode distance of 8.5 mm) and wire electrode (green star) over the subject’s right upper arm, and (b) location of the inserted wire electrode (green circle) in the ultrasound image of the upper arm. Note that the wire electrode is inserted at the midpoint of the 48th and 96th surface EMG electrodes.

**Fig. 2:** Computational model of (a) the bones and muscles, and (b) the entire upper arm. The entire model consists of 225,462 tetrahedron elements and 39,605 nodes. The conductivity values assigned to the skin, fat, muscle, compact bone and cancellous bone are $4.55 \times 10^{-4}$ S/m, 0.0379 S/m, 0.2455 S/m, 0.02 S/m and 0.075 S/m, respectively.

**History of Dissemination:**

**Fig. 3:** (a1) and (a2) show monopolar and bipolar MUAPs of the MU#3, and (b1) and (b2) show monopolar and bipolar MUAPs of the MU#6, decomposed from 128-channel surface EMG recordings. The red rectangles in (a2) and (b2) indicate the locations of innervation zones of the MU#3 and MU#6, which are very close to the 48th and 96th surface EMG electrode locations.

**Fig. 4:** shows (a) top view and (b) frontal view of reconstructed innervation zones of the MU#3 and MU#6 and their overlap. White and yellow dots represent the innervation zone of the MU#3 and MU#6 respectively, blue dots represent their overlap area. The two green stars represent the locations of 48th and 96th surface EMG electrodes and the purple dot represents the location of the inserted wire electrode.