정확하고 안전한 바늘근전도 검사를 위한 초음파를 이용한 요측수근굴근의 형태학적 평가

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Morphologic Evaluation of the Flexor Carpi Radialis Muscle Using Ultrasonography for Accurate and Safe Needle Electromyography

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Objective: This study aimed to determine the proper and safe needle insertion point in the flexor carpi radialis (FCR) muscle under ultrasonography guidance.

Methods: We identified the center point (CP) of the FCR as the optimal needle insertion point using ultrasonography. The location of the CP was analyzed using ratios and distances from other landmarks. The vertical distance (CP-VD) was measured by drawing an imaginary vertical line from the CP to the elbow crease. We measured the horizontal distance from the point where the imaginary vertical line from the CP meets the elbow crease to the biceps tendon at the elbow crease level (CP-HD). We presented the ratio of CP-HD to forearm circumference (HD ratio) and the ratio of CP-VD to forearm length (VD ratio) as percentages.

Results: The mean values of CP-HD and CP-VD were 2.0 ± 1.0 cm and 8.2 ± 1.1 cm, respectively. The mean HD and VD ratios were $8.4\% \pm 4.2\%$ and $32.0\% \pm 3.1\%$, respectively.

Conclusion: When performing electromyography (EMG) of the FCR muscle, it is recommended to perform EMG at the point about 2 cm medial from the biceps tendon at the elbow crease level, to nearly the proximal one-third of forearm length.

Keywords: Flexor carpi radialis; Ultrasonography; Electromyography

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Introduction

The flexor carpi radialis (FCR) muscle is the forearm superficial muscle originating in the medial epicondyle of humerus and

inserted into the base of the 2nd and 3rd metacarpal bones. As the name suggests, the contraction of FCR muscle located on the surface of volar side of forearm causes flexion and radial deviation of the wrist [1].

The FCR muscle plays an important role in the evaluation and diagnosis of the C6 and C7 nerve root lesions or pathologic conditions associated with median nerve innervations, such as pronator teres (PT) syndrome, in electromyography (EMG) [2]. Also, FCR muscle is vulnerable to myofascial pain syndrome caused by repetitive movements such as wrist flexion/extension or ulnar/radial deviation [3]. Therefore, the FCR muscle is often targeted for trigger point injection. In addition, botulinum toxin is generally injected into the FCR muscle to manage spastic wrist flexors in patients with stroke or spinal cord injury, because FCR muscle is one of the muscles associated with forearm spastic postures under hypertonicity [4].

However, when botulinum toxin A injection was performed manually without instrumental guidance such as ultrasonography, the accuracy of needle entry into the FCR muscle was as low as 41.5% [5]. Also, it is difficult to penetrate the FCR muscle with a needle accurately along with serratus anterior, flexor carpi ulnaris (FCU), flexor pollicis longus, PT, and extensor indicis proprius muscles in the upper extremity [6].

Although the optimal needle insertion position for FCR muscle is clinically important, several needle EMG methods have been introduced [7-9]. In these studies, the needle insertion point was inaccurate using fingerbreadth, and the accuracy of needle insertion was not verified by ultrasonography. Also, the optimal needle insertion point varies with the patient demographic characteristics such as height. Song et al. [10] investigated the optimal area for FCR muscle injection in cadavers. However, the study had several limitations as living musculoskeletal structures differ from those of cadavers, and the sample size was small, which prevented discussion of proper depth of needle insertion. The aim of this study was to identify the center point (CP) of FCR muscle under ultrasonography guidance and to determine the most appropriate needle insertion point, considering the anatomical location.

Materials and Methods

1) Study design and participants

We enrolled 40 healthy subjects in this cross-sectional study. The study participants were prospectively recruited as volunteers. The sample size was calculated based on a previous study [10], which determined the anatomical localization of motor points of wrist flexors. In this previous study [10], the authors concluded that the motor point of FCR muscle was located at about proximal 27% of the FCR reference line connecting the medial epicondyle and the base of the 2nd metacarpal bone. Based on the primary outcome ($p = 0.27$), a power of 80% and

a two-sided test ($\alpha = 0.05$) and, a margin of error of 20%, we determined that the sample size required was 76. Assuming a 5% loss, we estimated that the final sample size required was 80, for a total of 40 participants for the study. Subjects older than 19 years were included. Exclusion criteria were (1) inability to cooperate with the examination due to systemic disease or mental illness, (2) upper extremity amputation, and (3) a cast, splint or metal that create artifact in forearm. Both forearms were examined in all participants, and a total of 80 forearms were enrolled. Demographic characteristics including age, sex, height, weight, body mass index (BMI), and forearm length affect the morphology of FCR muscle, and therefore were collected. Especially, we analyzed data focusing on height. Because tall people have long forearms [11], we thought that height was a major factor in determining the CP of the FCR muscle. In addition, since height can be estimated approximatively, we thought it would be important during clinical examination. We defined forearm length as vertical distance from biceps tendon palpable at elbow crease to distal wrist crease, which is of sufficient consistency to be used as a reliable landmark [12]. The purpose and method of the study were explained to all subjects. All participants' informed consent was obtained. The Institutional Review Board of Soonchunhyang University Bucheon Hospital approved this study (approval number: 2020-05-029-001).

2) Sonographic examinations

A single physiatrist conducted the ultrasonography evaluation for FCR muscle using a linear array transducer (7-18 MHz, Xario SSA-660A; Toshiba, Minato, Japan). Ultrasonographic evaluation was performed in supine position with the forearm fully supinated, and the shoulder abducted about 30°. We obtained all measurable data in this supine position.

Since the shape of FCR muscle is fusiform, we assumed that the CP of the FCR muscle was an optimal needle insertion point in this study. To determine the location of CP, we located the musculotendinous junction and the origin of FCR muscle using sonographic long and short-axis views. Musculotendinous junction and origin of FCR muscle were indicated on the skin, respectively. As shown in Fig. 1A, the vertical location of CP was in the midline between origin of FCR muscle and musculotendinous junction, which was an imaginary line parallel to the elbow crease. To verify the horizontal location of CP, the FCR muscle was examined by moving the ultrasound probe horizontally over this midline. As shown in Fig. 1B, we defined the point in short-axis sonographic image where FCR muscle was located at the center of sonographic image as CP. Drawing an imaginary vertical line from CP to elbow crease, the vertical distance (CP-

Fig. 1. (A) Schematic diagram of the center point (CP) of the flexor carpi radialis (FCR) muscle in the forearm. The vertical location of the CP was along the midline between the origin of the FCR muscle and the musculotendinous junction. The horizontal location of the CP was the point where the FCR muscle was located at the center of the sonographic image. (B) Short-axis ultrasonography image of the CP of the FCR muscle. Green arrow indicates the imaginary pathway of needle entrance. CP-VD, vertical distance from center point to the elbow crease; CP-HD, horizontal distance from the biceps tendon to point where the imaginary vertical line meets the elbow crease; BT, biceps tendon; DS, depth from the skin to the superficial margin of the FCR muscle; DM, middle value of depth from skin to the superficial margin of the FCR muscle and depth from the skin to the deep margin of the FCR muscle; DD, depth from the skin to the deep margin of the FCR muscle; PL, palmaris longus; FDS, flexor digitorum superficialis; PT, pronator teres; MN, median nerve.

VD) was measured. The horizontal distance was measured from the point where the imaginary vertical line drawn from CP meets elbow crease to biceps tendon at the level of elbow crease (CP-HD) (Fig. 1A). Also, forearm circumference at CP was measured. Each person has distinct CP-HD and CP-VD due to their unique demographic characteristics. In order to suggest a representative value that is equally applicable to all people, we presented the ratio of CP-HD to forearm circumference (HD ratio) and ratio of CP-VD to forearm length (VD ratio) as a percentage. The anatomical structures that could be penetrated by imaginary needle pathway were recorded on a short-axis sonographic image obtained in CP. If the median nerve was penetrated, the depth of the median nerve was recorded as a range from the depth of the most superficial part to the deepest part of the median nerve. Also, the depth from the skin to the superficial margin of FCR muscle (DS) and the depth from the skin to the deep margin of

FCR muscle (DD) were measured. The mid-depth (DM) was defined as the median value of DS and DD (Fig. 1B).

Needle insertion points were previously suggested via 3 needle EMG methods [7-9]. Preston and Shapiro [7] and Perotto and Delagi [9] suggested that the needle should be inserted at a distance of 4 fingerbreadths distal to the center of the wrist from the midpoint between the medial epicondyle and biceps tendon at elbow crease level (point A). Lee and DeLisa [8] suggested that the needle should be inserted at the proximal third of the imaginary line connecting the FCR tendon of the wrist and medial epicondyle (point B). Perotto and Delagi [9] recommended that the needle should be inserted at a distance of 4 fingerbreadths distal from the midpoint between the medial epicondyle and biceps tendon at elbow crease level (point C). These 3 needle EMG methods and CP were marked on the skin as shown in Supplementary Fig. 1. At each point, we acquired a cross-section

tional sonographic image and analyzed the anatomical structures that could be penetrated (Fig. 2). The depth of penetration was

measured if the imaginary needle pathway penetrated the FCR muscle or median nerve. To ensure that the middle portion of

Fig. 2. (A) (Left) Schematic diagram of point A of the flexor carpi radialis (FCR) muscle in the forearm. Four fingerbreadths (FBs) distal to the center of the wrist from midpoint between the medial epicondyle and biceps tendon (BT) at the elbow crease level. (Right) Cross-sectional ultrasonography image at point A. Green arrow indicates the imaginary pathway of needle entrance. (B) (Left) Schematic diagram of point B of the FCR muscle in the forearm. Proximal third of the imaginary line connecting the FCR tendon of the wrist and medial epicondyle. (Right) Cross-sectional ultrasonography image at point B. Green arrow indicates the imaginary pathway of needle entrance. (C) (Left) Schematic diagram of point C of the FCR muscle in the forearm. Four FBs distal from the midpoint between the medial epicondyle and BT at the elbow crease level. (Right) Cross-sectional ultrasonography image at point C. Green arrow indicates the imaginary pathway of needle entrance. PL, palmaris longus; FDS, flexor digitorum superficialis; PT, pronator teres; MN, median nerve.

FCR was accurately penetrated by the imaginary needle pathway in each method, we defined the “middle portion” of the FCR muscle as the middle one-third when the muscle was divided into 3 segments in a horizontal axis. It was also recorded whether the middle portion of the FCR muscle was penetrated. In order to obtain accurate results, the ultrasound probe was carefully contacted with the skin with minimal pressure. The 4 finger-breadths length of the physiatrist who conducted ultrasonography was about 7 cm.

3) Statistical analysis

Demographic characteristics and anatomical ultrasonography parameters are expressed as mean $\pm$ standard deviation, because the number of data ($n = 80$) was sufficient to ensure a normal distribution. Ultrasonography parameters (CP-HD, HD ratio, CP-VD, VD ratio, and DM) and demographic characteristics (height, weight, and BMI) were analyzed by correlation analysis. Sex differences were identified via Student t-test and Mann-Whitney was used for data that did not follow the normal distribution. Shapiro-Wilk test was performed to confirm normal distribution. A p-value of 0.05 or less was considered statistically significant. We used IBM SPSS Statistics ver. 26.0 (IBM Corp., Armonk, NY, USA) for all statistical analyzes.

Results

This study was performed on a total of 80 forearms involving 26 males and 14 females. The mean age was 31.4 ± 7.4 years; the mean height was 169.8 ± 9.5 cm; and the mean forearm length was 25.6 ± 2.0 cm. Other demographic data are summarized in Table 1.

Ultrasonography and anatomical parameters are presented in Table 2. The mean vertical distance from CP to elbow crease (CP-VD) was 8.2 ± 1.1 cm. The mean ratio of CP-VD to forearm length (VD ratio) was $32.0\% \pm 3.1\%$. The mean horizontal distance (CP-HD) was 2.0 ± 1.0 cm and the mean ratio of CP-HD to forearm circumference (HD ratio) was $8.4\% \pm 4.2\%$. The DS and DD of FCR muscle at CP were 3.7 ± 1.3 mm and 15.6 ± 2.2 mm, respectively. The DM of FCR muscle was 9.7 ± 1.3 mm (Table 2). Correlation analysis between ultrasonography parameters and demographic characteristics was performed (Table 3). CP-VD showed a significant positive correlation with height ($R = 0.550$, $p < 0.01$, Table 3). On the other hand, the VD ratio did not show a significant correlation with any demographic characteristics. Similarly, CP-HD and HD ratio did not show a significant correlation with any demographic characteristics. Among all variables, such as CP-HD, HD ratio, CP-VD, VD

ratio, DD, DS and DM, only CP-HD, VD ratio and DM did not reveal significant differences between male and female (p-values 0.170, 0.052, and 0.947, respectively).

Table 4 demonstrates anatomical structures that could be penetrated by the imaginary needle pathway using each of the 4 different needle EMG methods [7-9]. Cross-sectional sonographic image of each point is presented in Fig. 1 and 2. The accuracy of penetration by the imaginary needle into FCR muscle was 82.5%, 20.0%, and 93.8% accuracy using methods A, B, and C, respectively. Methods A and C showed greater than 80% accuracy. However, the accuracy of penetration by the imaginary needle into the middle portion of FCR muscle was only 6.3%, 0%, and 38.8% in methods A, B, and C, respectively. Among the 3 methods, the probability of median nerve penetration was high in the order of A, C, and B (48.8%, 21.3%, 2.5%, respectively). Among the other structures, the PT, palmaris longus (PL) and flexor digitorum superficialis (FDS) muscles were also penetrated depending on the methods in question (Table 4). The median nerve penetration at CP was detected in 38 out of 80 (47.5%) forearms, showing a probability of 47.5%. In these 38 forearms, the mean

Table 1. Demographic Characteristics

Characteristic	Value ($n = 40$)
Age (y)	31.4 ± 7.4
Sex (male/female)	26/14
Height (cm)	169.8 ± 9.5
Weight (kg)	66.2 ± 11.2
Body mass index (kg/m^2)	22.8 ± 2.2
Forearm length (cm)	25.6 ± 2.0

Values are presented as mean $\pm$ standard deviation.

Table 2. Anatomical and Ultrasonographic Parameters

Variable	Total ($n = 80$)
CP-HD (cm)	2.0 ± 1.0
Forearm circumference (cm)	23.9 ± 2.2
HD ratio (%)	8.4 ± 4.2
CP-VD (cm)	8.2 ± 1.1
Forearm length (cm)	25.6 ± 2.0
VD ratio (%)	32.0 ± 3.1
DS (mm)	3.7 ± 1.3
DD (mm)	15.6 ± 2.2
DM (mm)	9.7 ± 1.3

Values are presented as mean $\pm$ standard deviation.

CP-HD, distance from the biceps tendon to the point where an imaginary vertical line meets the elbow crease; HD ratio, CP-HD/forearm circumference; CP-VD, distance from the center point to the elbow crease; VD ratio, CP-VD/forearm length; DS, depth from the skin to the superficial margin of the FCR muscle; DD, depth from the skin to the deep margin of the FCR muscle; DM, middle value of DS and DD; FCR, flexor carpi radialis.

Table 3. Correlation Coefficient (r) between Ultrasonographic Parameters and Demographic Characteristics

Parameter	Demographic characteristic						
	HD ratio	CP-VD	VD ratio	DM	Height	Weight	BMI
CP-HD	0.977*	-0.390*	-0.487*	0.096	-0.001	0.07	0.124
HD ratio	1	-0.412*	-0.461*	-0.008	-0.104	-0.085	-0.029
CP-VD		1	0.841*	-0.154	0.550*	0.361*	0.021
VD ratio			1	-0.150	0.078	-0.005	-0.083
DM				1	-0.003	0.399*	0.660*
Height					1	0.825*	0.305*
Weight						1	0.787*
BMI							1

CP-HD, distance from the biceps tendon to the point where an imaginary vertical line meets the elbow crease; HD ratio, CP-HD/forearm circumference; CP-VD, distance from the center point to the elbow crease; VD ratio, CP-VD/forearm length; DM, middle value of DS and DD; BMI, body mass index; DS, depth from the skin to the superficial margin of the FCR muscle; DD, depth from the skin to the deep margin of the FCR muscle; FCR, flexor carpi radialis.

* $p < 0.01$.

Table 4. Number of Structures Penetrated by an Imaginary Needle Pathway Using Four Different Needle Electromyography Methods (n = 80)

Method	FCR muscle (any portion of FCR)	Middle portion of FCR muscle	Median nerve	PT muscle	PL muscle	FDS muscle
A	66 (82.5)	5 (6.3)	39 (48.8)	73 (91.3)	4 (5.0)	7 (8.8)
B	16 (20.0)	0 (0)	2 (2.5)	0 (0)	72 (90.0)	78 (97.5)
C	75 (93.8)	31 (38.8)	17 (21.3)	30 (37.5)	18 (22.5)	48 (60.0)
CP	80 (100.0)	80 (100.0)	38 (47.5)	0 (0)	0 (0)	62 (77.5)

Values are presented as the number of penetrations (%).

FCR, flexor carpi radialis; PT, pronator teres; PL, palmaris longus; FDS, flexor digitorum superficialis.

Method A, 4 fingerbreadths distal to the center of the wrist from the midpoint between the medial epicondyle and biceps tendon at the elbow crease level [7]; method B, proximal third of the imaginary line connecting the flexor carpi radialis tendon of the wrist and medial epicondyle [8]; method C, 4 fingerbreadths distal from the midpoint between the medial epicondyle and biceps tendon at the elbow crease level [9]; method CP, about 2 cm medial from the biceps tendon at the elbow crease level, to nearly the proximal one-third of forearm length.

depth of the most superficial part of the median nerve was 18.61 mm and the mean depth of the deepest part was 21.31 mm.

Discussion

In the present study, 80 forearms were analyzed to propose safe and proper needle placement of FCR muscle in 40 healthy participants. According to our study, CP-VD and CP-HD were found to be approximately 8.2 cm distal, and 2 cm medial from the palpable biceps tendon at the elbow crease level, respectively. However, the precise location of FCR muscle may vary since each person has a variable forearm length. Since we hypothesized that forearm length was proportional to height [11], the correlation analysis was performed. As a result, only CP-VD showed a significant positive correlation with height, implying that as the height increases, the forearm length is longer, and accordingly, the CP-VD increases. Thus, unlike CP-VD, the CP-HD can be used regardless of height. However, the VD ratio showed no significant correlation with height, weight, and BMI. Therefore, the VD ratio can be used as a vertical distance of FCR muscle, in-

stead of CP-VD. Consequently, we conclude that the CP of FCR muscle is located approximately 2 cm medial from the biceps tendon at elbow crease level horizontally, and the proximal 32.0% of the forearm vertically regardless of height. Also, the average value DM of FCR muscle was 9.7 mm.

In a previous study, the biceps tendon and medial epicondyle were used as landmarks to localize the FCR muscle, suggesting that the FCR muscle might be located 4 fingerbreadths distal from the landmark (point A, C). Another study proposed the proximal third of imaginary line connecting the medial epicondyle of humeral origin of the FCR muscle, and the FCR tendon palpable in the lateral part of the wrist with wrist flexion (point B). These previous needle insertion points for FCR muscle appear to have been determined approximately via empirical methods or anatomical cross-sections. Method A and method C, which were presented by Preston and Perotto respectively, seem to have suggested needle insertion points based on cross-sections and the authors' experiences. In these 2 methods, it is considered a problem to suggest a fixed position without considering forearm length. Method B, presented by Lee and DeLisa [8], seems

that the needle insertion point was suggested based on the origin and insertion of the FCR muscle. In this method, they suggested that the needle should be inserted at the proximal third of the imaginary line connecting the FCR tendon of the wrist and medial epicondyle, considering forearm length. However, there was a problem that only the origin and insertion were considered and the accurate anatomy of the forearm flexors was not considered.

In the present study, we also used the biceps tendon, which is easily palpable at the elbow crease, as a landmark. However, we indicated the horizontal distance as a numerical value, and the vertical position as a proportional value based on ultrasonographic evaluation, which may be a more objective method than the other previous approaches, because our novel method did not use fingerbreadth that differs with each examiner. In addition, it considers variable heights for each examinee. VD ratio, which is approximately the proximal 1/3 of the forearm length, can be a good indicator for an intuitive approach. Additionally, the depth of FCR muscle, which was not mentioned in previous methods, was also suggested as 9.7 mm. Finally, these values did not show statistically significant differences according to sex as well as height.

As previously stated in the results, methods A and C had acceptable accuracy if used simply to penetrate FCR muscle. However, they were inaccurate if used to test or target the middle portion of FCR muscle (Table 4). Also, the accuracy of method B was substantially lower than that of methods A and C, given the anatomy of wrist flexor muscles. Wrist flexor muscles, such as FCU, PL, FCR, PT and FDS muscles, originate from medial epicondyle of humerus. The belly of FCU, PL and FCR muscles are formed proximal to the forearm, and turn into tendons distally, which are inserted into the bones of the hand. These muscles are located in the medial to lateral direction, in the order of FCU, PL, and FCR muscles in the narrow forearm space. The FCU muscle is located in the ulnar side, and the FCR muscle radially. Therefore, FCU muscle performs ulnar deviation in addition to wrist flexion, and the FCR muscle undergoes radial deviation similarly. Considering the anatomical structure, although the FCR muscle originates in the medial epicondyle similar to other wrist flexor muscles, its belly is not located on an imaginary line connecting the medial epicondyle and the FCR tendon palpable in wrist, but is located more radially from the imaginary line, because FCR muscle is pushed by PL and FCU muscles. Therefore, the point B, which is the proximal third of the imaginary line connecting the FCR tendon of the wrist and medial epicondyle, is more medially located from the muscle belly of FCR, resulting in very poor accuracy. Actually, ultrasonography reveals the muscle belly of FCR by moving the probe further radially from point B (Fig.

2B).

The methods A and C showed high accuracy in penetrating the FCR muscle, but low probability in targeting the middle portion of the FCR muscle, because the FCR muscle belly is usually located more distally than 4 fingerbreadths (A and C points). According to our ultrasonography analysis, CP-VD, which is the central point between musculotendinous junction and origin of FCR muscle, was found at about the proximal third (32%) of forearm length, and was more distally located than A and C points. Actually, in the sonographic short-axis image, the cross-sectional area of PT muscle was larger than that of FCR muscle at points A and C, whereas the FCR muscle was substantially larger at the CP (Fig. 1B, 2A, right; 2C, right).

The probability that the imaginary needle pathway in CP penetrates the median nerve was similar or higher than in the conventional method (A, 48.8%; B, 2.5%; C, 21.3%; CP, 47.5%). Therefore, it cannot be said that CP is a safer location than in previous methods. However, we can needle the FCR muscle more safely by adopting the depth established. The median nerve is formed by combining medial and lateral cords of the brachial plexus. It then passes through the arm, and the antecubital fossa to enters the forearm, driving between 2 heads of PT muscle. It traverses deeper than in the FDS muscle, and more superficially than in deep wrist flexor muscles of the forearm [2]. According to the data collected, the mean depth of the median nerve is in the range of 18.61 to 21.31 mm. The DM of CP of FCR muscle is 6.75 to 12.85 mm. The maximum DM was only 12.85 mm. Because FCR is more superficially located than the median nerve, no more than 1.3 cm depth is needed to target FCR muscle safely without piercing median nerve during needle EMG.

The study has several limitations. First, the mean age was 31.4 years old, and thus the study was targeted at relatively young people. Second, there might be slight difference between the suggested CP and the actual motor point of FCR muscle. We assumed that the actual motor point was close to the CP of the FCR muscle. Third, the average BMI of participants was 22.8 kg/m². The proper depth of needle insertion may differ in underweight or overweight and obese individuals. Fourth, we did not collect muscle mass data. Muscle mass measurement using dual energy X-ray absorptiometry is helpful in further studies. Fifth, in those without the PL muscle, the FCR belly is more likely to be located on the medial side. As mentioned earlier, this is because the FCR muscle is pushed laterally by FCU and PL muscles. Most standard textbooks of hand surgery report that the rate of absence of PL muscle was 15% [13-15]. Therefore, in such cases, it may be different from our findings. Sixth, we mea-

sured depth using ultrasonography without inserting the needle. However, when the needle is actually inserted, the shape of subcutaneous and muscle layers might be changed. Further studies involving more participants from variable age groups are required.

Conclusion

Several methods for proper needle placement have been suggested for FCR muscle. However, none of the methods have been evaluated in terms of safety and accuracy using ultrasonography. Accessing anatomical structures under ultrasonography guidance, we propose a novel method regardless of height. Also, we analyzed the accuracy of the previous methods and compared with our proposed strategy. These findings enable us to approach the CP of FCR muscle more accurately than previous methods. This study revealed that the CP of FCR muscle was approximately medial 2.0 cm from the biceps tendon at elbow crease, proximal one-third of forearm length, and at a depth of 9.7 mm. The method can be hopefully adopted more easily and safely in clinical applications.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Supplementary Materials

Further details on supplementary materials are presented online (available at <https://doi.org/10.18214/jend.2021.00017>).

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