

Effects of different verbal instructions on change of lumbar multifidus muscle thickness in asymptomatic adults and in patients with low back pain

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Background: Spinal stabilisation exercise has been shown to be effective in the rehabilitation of low back pain (LBP). Due to the isometric nature of spinal stabilisation exercise, manual therapists use various verbal instructions to elicit lumbar multifidus muscle contraction.

Objectives: The purpose of this study was to assess whether or not three verbal instructions would alter muscle thickness of the lumbar multifidus muscle differently in asymptomatic individuals and patients with LBP.

Methods: Three verbal instructions were selected for this study: (1) swell the muscle underneath the transducer, (2) draw your belly button in towards your spinal column and (3) think about tilting your pelvis but without really doing it. Lumbar multifidus muscle thickness was determined using parasagittal ultrasound (US) imaging. Measurements of muscle thickness were collected at rest and during verbal instructions from 21 asymptomatic adults and 21 patients with LBP. Percent changes of muscle thickness during contraction and at rest were compared between groups and across verbal instructions.

Results: ANOVA results showed no significant interaction for both L4-5 and L5-S1, but a significant main effect of verbal instruction ($P = 0.049$) at L4-5. *Post hoc* analysis showed a greater increase with verbal instruction #3 than verbal instruction #2 ($P = 0.009$). There was no significant main effect of group at either segment.

Discussion: The results of the study suggest that both groups responded similarly to the three verbal instructions. Verbal instructions may increase lumbar multifidus muscle thickness by different amounts at L4-5, but by the same amount at L5-S1.

Keywords: Low back pain, Verbal instruction, Lumbar multifidus, Ultrasound imaging, Muscle activation, Muscle thickness

Introduction

Atrophy of the lumbar multifidus muscle has been demonstrated with magnetic resonance (MR) and ultrasound (US) images in patients with chronic low back pain (LBP).¹⁻⁵ Research also has demonstrated that recovery of the lumbar multifidus muscle does not occur concomitantly with pain reduction in patients with acute LBP.⁶ The finding of lumbar multifidus muscle atrophy in patients with LBP has prompted clinicians to put emphasis on lumbar multifidus activation in rehabilitation of patients with LBP. Evidence has shown that specific

spinal stabilisation exercises combined with pressure biofeedback were effective in increasing contraction of the lumbar multifidus and transversus abdominis muscles.⁷⁻⁹ However, because these stabilisation exercises are isometric and do not produce motion, it is difficult for clinicians to demonstrate them to patients. To maximise the effects of these isometric stabilisation exercises, clinicians often use various verbal instructions to facilitate muscle recruitment of lumbar multifidi.

Appropriate instructions could change muscle activity and improve the accuracy of exercise performance.¹⁰⁻¹² One electromyographic (EMG) study showed that the timing of muscle activation was modified during prone-lying hip extension when a specific verbal instruction was given.¹³

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Athletes demonstrated the ability to alter or isolate muscle activation with a simple verbal instruction.¹⁴ However, they were not able to respond to more complex instructions or to alter muscle activity during exercise at high intensities.^{14,15} Verbal instructions that focussed on activating the target muscles were found to be effective in increasing muscle activity or output force of the biceps brachii, triceps brachii and pectoralis major.^{15,16} Conversely, verbal instructions used in focussing on non-target muscle activation did not consistently decrease muscle activity of the target muscle, such as the triceps brachii, pectoralis and upper trapezius.^{12,15}

The verbal instruction used by Hides *et al.*³ to activate lumbar multifidi was described as: ‘Gently swell out your muscle under my finger without moving your spine or pelvis. Hold the contraction while breathing normally’. However, patients often express difficulty in comprehending the phrase ‘swell out your muscle’ even if they have been educated with the location of the lumbar multifidus muscle. Alternative verbal instructions, such as ‘draw your belly button towards your spine’, have been used by clinicians with the hope of achieving better activation of the lumbar multifidus muscle.⁴ These alternative verbal instructions appeared to make it easier for patients to understand the task, but it was not clear whether or not improved lumbar multifidus muscle activation was achieved using these alternative verbal instructions. Therefore, the purpose of the study was to assess whether or not three different verbal instructions would alter muscle thickness of the lumbar multifidus muscle differently in asymptomatic individuals and patients with LBP.

Methods

Participants

This study was approved by the Institutional Review Board of Texas Woman’s University (TWU) and registered with ClinicalTrials.gov (NCT02513173). Forty-two participants, 21 asymptomatic adults and 21 patients with LBP, were recruited for this study. Participants were either patients from the University of Texas Southwestern (UTSW) Medical Centre physical therapy clinic at which one investigator was employed or employees/students at TWU or UTSW. Asymptomatic participants were individuals with no existing LBP and no LBP in the past year. Participants in the LBP group were individuals who had existing LBP near the L4-S1 levels and an average pain intensity score $\geq 2/10$ on the Numeric Pain Rating Scale (NPRS) in the past week. Only participants with pain at L4-S1 were included in the study because L4, L5 and S1 are the most common painful segments found in patients with LBP.¹⁷ Exclusion criteria for all participants included previous low

back surgery, systemic joint disease (e.g. rheumatoid arthritis), cancer of the lower quadrant, neurological disorders, allergic reaction to US gel, or inability to obtain the testing position (i.e., prone lying). In addition, individuals who previously had received spinal stabilisation exercises were excluded from the study because previous training may have biased participants for specific verbal instruction. Asymptomatic participants were age- and gender-matched with the participants in the LBP group. Each participant was informed of the risks and procedures of the study, and then signed a written informed consent form.

Instrumentation and outcome measures

A Sonosite M-Turbo US scanner (Sonosite, Inc., Bothell, WA, USA) and a curvilinear transducer (3–5 MHz) were used to capture US parasagittal images of the lumbar multifidus muscles at the L4-5 and L5-S1 segments. Captured images were saved and analysed later using the ImageJ software application (National Institutes of Health, Bethesda, MD, USA).

Procedures

Eligible participants were asked to complete an intake form asking them about their age, gender and past medical history. The Modified Oswestry Low Back Pain Disability Index (OSW) questionnaire was administered to all participants to determine their perceived disability and functional limitations due to their LBP. The OSW questionnaire has been shown to be reliable and valid.^{18,19} Participants with LBP also were asked about their pain location, duration and intensity. The height and body weight of each participant was taken to determine the body mass index (BMI) because BMI has been shown to be a factor in affecting size of the multifidi.²⁰

Parasagittal US images of the lumbar multifidus muscle were captured following a testing protocol published in previous studies.^{21,22} Briefly, each participant was instructed to lie prone on an examination table with his/her arms at their sides. A pillow was placed under the participant’s abdomen to minimise the lumbar lordotic curve and an inclinometer was placed on the lumbosacral junction to ensure that the lumbar curve was less than 10°. During US imaging, one investigator (LS) was responsible for operating the US transducer and gave verbal instructions for lumbar multifidus muscle contraction. The other investigator (DT) was responsible for randomising the order of the verbal instructions as well as capturing US images. The same two investigators took all of the images of all participants in order to maintain consistency

of image acquisition. Images collected were of the right side of asymptomatic adults and the painful side of participants in the LBP group.

The spinous processes of the L4-S1 segments were first identified by palpation and marked with an erasable pen. Next, the investigator (LS) placed the transducer on the right side of asymptomatic participants or the painful side of the participants with LBP. The transducer was positioned in a cranial and caudal direction parallel with the spinous processes of the L4-S1 segments. The investigator (LS) tilted the transducer and slid it laterally away from the spinous processes until the zygapophyseal joints of L4-5 and L5-S1 could be visualised. The investigator (LS) held the transducer at this location with both hands to ensure that it was in the same plane as the zygapophyseal joints during the entire US imaging acquisition session. With this technique, parasagittal US images of the lumbar multifidus muscle were taken three times at rest and three times during contractions of the lumbar multifidus muscle for each of the three verbal instructions.²³ The first of the three muscle contractions was used to allow each patient to become familiar with the instructions, and the images of the last two muscle contractions were used for data analysis.

Prior to image acquisition, each participant was informed of the location of the lumbar multifidus muscle, the function of the transducer and the placement of the transducer. A demonstration of the transducer placement was necessary because one verbal instruction included the word 'transducer', and because the transducer was placed directly on the lumbar multifidus muscle during image acquisition. Contraction of the lumbar multifidus muscle was achieved by asking participants to generate a slow, gentle, sustained contraction without moving their spine or pelvis.^{3,5} Participants held each contraction for 3–5 seconds, and performed three contractions for each verbal instruction. Therefore, each participant performed a total of nine lumbar multifidus muscle contractions. The order of verbal instructions was selected randomly to minimise learning and fatigue effects. There were six possible variations for the order of the verbal instructions. The investigator (DT) drew one out of six cards from a pre-prepared opaque envelope before imaging acquisition. The following verbal instructions were used to elicit lumbar multifidus muscle contractions: (1) breathing normally and without moving your spine, swell the muscle underneath the transducer,⁴ (2) breathing normally and without moving your spine, draw your belly button in towards your spinal column,^{4,24} and (3) breathing normally and without moving your spine, think about tilting your pelvis but without really doing it.²⁴ Of those receiving

verbal instruction #3, eight participants (four in each group) asked for clarification on the direction of pelvic tilt. These participants were told to think about tilting the pelvis anteriorly based on the authors' clinical experience. In addition, an EMG study²⁵ demonstrated that multifidus muscle activity was significantly increased when the pelvis was in an anterior-tilted position with the trunk extended. Although the lumbar spine and pelvis were kept in a neutral position in our study, thinking about an anterior tilt may have altered or increased these participants' lumbar multifidus muscle contractions. Upon completion of US image acquisition, patients with LBP were asked to identify the verbal instruction that was most useful to contract the lumbar multifidus muscle. However, asymptomatic participants were not asked this question.

US muscle thickness measurement

Thickness of the lumbar multifidus muscle was measured off-line at L4-5 and L5-S1 using ImageJ. Electronic callipers were used to determine muscle thickness for each segment by measuring the vertical length from the most posterior portion of the zygapophyseal joint to the inner edge of the fascia between the lumbar multifidus and superficial tissue, following a previously reported protocol.²³ To determine the amount of lumbar multifidus muscle contraction, the difference between muscle thickness at rest and during muscle contraction was assessed for each verbal instruction. In order to ensure consistency of the measurements, the US images of the muscle at rest and during contraction were positioned top and bottom on the same screen during muscle thickness assessments. To minimise bias from a participant's size, a normalised value representing percent change of muscle thickness was calculated using the following formula: $\% [(thickness \text{ during contraction} / (thickness \text{ at rest})) / thickness \text{ at rest}] \times 100$.²³

Data analysis

Descriptive statistics were calculated for demographic data and muscle thickness measurements of all participants. IBM SPSS Version 19.0 (IBM Corp., Armonk, NY, USA) was used to analyse percent change (%) of lumbar multifidus muscle thickness measurements. First, a concurrent reliability analysis was performed to assess the test-retest reliability of the last two of three measurements for each verbal instruction and for the asymptomatic group and the LBP group, respectively. Next, two separate 2×3 ANOVAs with repeated measures were performed to determine differences between the two groups and across the three verbal instructions for asymptomatic participants and patients at L4-5 and L5-S1, respectively. The alpha level was

set at 0.05 for each ANOVA with repeated measures. *Post hoc* analysis was performed if significance was found.

Results

All 42 enrolled participants completed the study. Table 1 illustrates the characteristics of participants, including age, gender, BMI and the OSW scores of the asymptomatic and LBP groups, as well as patients' NPRS score and duration of LBP. Given that the patients in the LBP group were age- and gender-matched with the asymptomatic participants, there was no difference in age and gender between the two groups. Both groups were categorised as overweight because their average BMIs fell between 25 and 29.9%.²⁶ Although there was no significant difference in BMI between the two groups ($P = 0.060$), the BMI of the asymptomatic group was in the lower range of the overweight category, and the BMI of the LBP group fell in the top range. Table 2 displays the number of participants assigned to each of six possible orders of the verbal instructions. In summary, 17 participants received verbal instruction #1 first, 14 had #2 first and 11 had #3 first.

The reliability analysis revealed that our ultrasonographic image acquisition and muscle thickness measurements had good-to-excellent reliability, with ICC values ranging from 0.76 to 0.91 for L4-5, and 0.83 to 0.92 for L5-S1 (Table 3). Percent change (means and SDs) of lumbar multifidus muscle thickness at L4-5 and L5-S1 during the three verbal instructions are listed in Table 4. At L4-L5, there was no significant interaction between the two groups and the three verbal instructions ($P = 0.363$), but a significant main effect of verbal instruction ($P = 0.049$) was found. *Post hoc* analysis showed a significant difference between verbal instruction #2 and #3 ($P = 0.009$). The results indicated that both asymptomatic participants and participants with LBP achieved a higher percent change in lumbar multifidus muscle thickness at

L4-5 with verbal instruction #3 than with verbal instruction #2. At L5-S1, no significant interaction ($P = 0.374$) or main effect of verbal instruction ($P = 0.643$) was found. Further, there was no main effect of group at either segment ($P = 0.401$ for L4-5, $P = 0.294$ for L5-S1). Lastly, of 21 patients with LBP, 13 patients perceived verbal instruction #2 as the most useful to help them to contract the lumbar multifidus, 5 patients selected verbal instructions #1 and only 3 participants selected verbal instruction #3.

Discussion

The results of this study indicate that the three verbal instructions increase lumbar multifidus muscle thickness equally at L5-S1, but differently at L4-5, with the verbal instruction #2 eliciting the least muscle thickness change in all participants, regardless of existing LBP. This finding suggests that clinicians may select appropriate verbal instructions to achieve optimal lumbar multifidus contractions at L4-5. A learning effect could have contributed to the higher muscle thickness increase of verbal instructions #1 and #3 if the majority of the participants received verbal instruction #2 first. However, in this study 14 participants out of 42 received verbal instruction #2 first. Therefore, a learning effect may not have been a substantial contributor to the higher muscle thickness increase of verbal instructions #1 and #3. In addition, the fatigue factor appears negligible because 17 participants received verbal instruction #2 last (Table 2). Verbal instruction #2 originally was designed to elicit transverse abdominis muscle contraction in a supine position. Therefore, the pull of gravity may alter the ability of the lumbar multifidus muscle to contract in the prone position, thus possibly contributing to lumbar muscle thickness changes with verbal instruction #2. However, a close relationship of ability to contract lumbar multifidus and transverse abdominis muscles was noted in a prone position using clinical palpation tests.⁴

Our study also showed no significant difference in muscle thickness change between the two groups at both segments, indicating that both groups

Table 1 Characteristics of the participants for the asymptomatic group ($n = 21$) and the low back pain (LBP) group ($n = 21$).

Variables	Asymptomatic group	LBP group
Age (years)	41.6 ± 14.7	41.5 ± 14.5
Gender	Eight men 13 Women	Eight men 13 Women
BMI (kg/m ²)	25.34 ± 5.57	29.10 ± 6.95
OSW (%)	0.29 ± 1.31	29.81 ± 33.96
NPRS (out of 10)		
Now	–	2.2 ± 2.4
Worst	–	6.2 ± 2.8
Best	–	1.3 ± 2.2
Average	–	3.3 ± 2.1
Duration of LBP (weeks)	–	270.6 ± 227.3

OSW: modified Oswestry LBP disability index; NPRS: numerical pain rating scale; BMI: body mass index.

Table 2 Order of assignment for verbal instructions (VI).

Order	Asymptomatic group (n = 21)	Low back pain (LBP) group (n = 21)	All (n = 42)
VI #1 → VI #2 → VI #3	4	4	8
VI #1 → VI #3 → VI #2	4	5	9
VI #2 → VI #1 → VI #3	2	4	6
VI #2 → VI #3 → VI #1	4	4	8
VI #3 → VI #1 → VI #2	5	3	8
VI #3 → VI #2 → VI #1	2	1	3

responded similarly to the three verbal instructions. This unexpected result is in disagreement with the findings in Wallwork *et al.*'s⁵ study, in which the authors found a significant difference between groups at L5-S1. Wallwork *et al.*'s⁵ study used an instruction similar to our verbal instruction #1 in order to elicit isometric lumbar multifidus contraction. Our asymptomatic group had an increase of 4.76–6.66% at L5-S1, which was similar to Wallwork *et al.*'s⁵ asymptomatic group (6.29%). However, our LBP group had a larger increase (6.29%) than Wallwork *et al.*'s (3.05%).⁵ Although the characteristics of the participants were similar between our study and Wallwork *et al.*'s⁵ study, our asymptomatic group was slightly older (41.6 vs 33.9 years) and our patient group had a higher BMI (29.1 vs 25.1). Therefore, the difference in participants may have contributed to the differences found in the results of the two studies. Lastly, our small sample size could have affected our results. ANOVAs revealed a small effect size and power at L4-5 ($\eta^2 = 0.018$, $\beta = 0.13$) and at L5-S1 ($\eta^2 = 0.028$, $\beta = 0.18$), and these may have contributed to a non-significant finding between groups.²⁷

We could not easily explain the different muscle thickness changes found in our study at L4-5 and L5-S1, but the difference could be in part because multifidus muscle contraction is segment-specific. The segmental difference of lumbar multifidus contractions was also observed in a previous study by Wallwork *et al.*⁵ who reported an increase of 5.15%

Table 3 Test-retest reliability (ICC) of ultrasonographic measurements of muscle thickness change during three verbal instructions for asymptomatic group (n = 21) and the low back pain (LBP) group (n = 21).

Verbal instruction	Asymptomatic group		LBP group	
	L4-5	L5-S1	L4-5	L5-S1
#1	0.96	0.86	0.84	0.86
#2	0.76	0.88	0.76	0.83
#3	0.91	0.92	0.90	0.90

Verbal instruction #1: swell the muscle underneath the transducer. Verbal Instruction #2: draw your belly button in towards your spinal column. Verbal instruction #3: Think about tilting your pelvis but without really doing it.

at L4-5, but of 6.29% at L5-S1 in an asymptomatic group, as well as an increase of 2.93% at L4-5, but of 3.05% at L5-S1. We also noted a high variation of the L4-5 measurements in our study, as indicated by larger SDs than means. The high variation may discount the significant finding at L4-5. However, the high variation of muscle thickness change at L4-5 was also found in previous studies.^{5,28}

All of our participants, with or without LBP, responded to the three verbal instructions by increasing lumbar multifidus muscle thickness 1.9–6.6% at L4-5, and 4.1–6.7% at L5-S1. The increase of muscle thickness supports the use of verbal instructions to improve muscle performance, which is consistent with previous verbal instruction studies.^{5,10–13} The increase of muscle thickness changes during isometric muscle contraction is consistent with the findings in previous studies; however, the amount of the increase varies among the studies.^{5,21,23–25} Further, when comparing to Kiesel's *et al.*'s²¹ US study on thickness change of the lumbar multifidus muscle, our asymptomatic group had a smaller increase during lumbar multifidus contraction than that found in Kiesel *et al.*'s,²¹ in which percent increases of 13% on average were reported at L4-5. However, US images of muscle contraction were captured during an upper extremity arm-lift task in Kiesel *et al.*'s study,²¹ rather than during an isometric contraction, as in our study. Even so, the results from our patient group were similar to the findings in Kiesel *et al.*'s,²¹ in which the percent increase was 6% on average at L4-5 in patients with experimentally induced LBP.

It is also noted that the test-retest reliability for verbal instruction #2 had low ICC values. We do not feel that the lower ICC values came from inconsistencies in our testing or measurement protocol because the ICC values for the other two verbal instructions are high. We hypothesise that the lower ICC values likely came from the participants' inconsistent response to verbal instruction #2. In addition, verbal instruction #2 was originally designed to activate deep abdominal muscles, such as the transversus abdominis.^{4,29} Clinicians used verbal instruction #2 because the lumbar multifidus and transversus abdominis muscles are synergistic.⁴ Interestingly, the

Table 4 Percent change (means \pm SDs) of lumbar multifidus muscle thickness at L4-5 and L5-S1 during three verbal instructions for all participants ($n = 42$), the asymptomatic group ($n = 21$) and the low back pain (LBP) group ($n = 21$).

Verbal instruction	#1	#2	#3	P
		L4-L5		
All	3.85 \pm 6.54	2.23 \pm 3.50	5.24 \pm 6.44	0.049*
Asymptomatic group	3.53 \pm 6.61	2.57 \pm 3.08	3.86 \pm 5.45	
LBP group	4.17 \pm 6.60	1.89 \pm 3.91	6.61 \pm 7.17	
		L5-S1		
All	5.73 \pm 4.87	4.90 \pm 4.07	5.03 \pm 4.92	0.643
Asymptomatic group	6.66 \pm 4.78	5.72 \pm 4.51	4.76 \pm 4.74	
LBP Group	4.80 \pm 4.90	4.09 \pm 3.50	5.31 \pm 5.19	

Verbal instruction #1: swell out the muscle underneath the transducer. Verbal instruction #2: Draw your belly button in towards your spinal column. Verbal Instruction #3: think about tilting your pelvis but without really doing it.

* $P < 0.05$.

participants with LBP perceived verbal instruction #2 as the most useful to help their contraction of the lumbar multifidus even though they had the smallest increase of muscle thickness when verbal instruction #2 was given. This discrepancy may indicate a disconnection between the patients' comprehension of verbal instruction and their performance. Schmitt and Abbott³⁰ recently demonstrated a poor correlation between functional status scores and global rating of change (GROC) scores, and concurred that the GROC is not parallel with changes of functional performance. These authors challenged the ability of patients to intellectually recall their changes. Although the authors did not directly ask the participants to rate their change on the GROC, the authors did ask the participants to select the verbal instruction that they perceived would result in the most change in muscle contraction.

Learning and fatigue effects were minimised by randomising the order of verbal instructions in our study. We excluded individuals from our study if they had previous spinal stabilisation training as a patient, or if they were clinicians who were educated in delivering spinal stabilisation exercises. Previous experience with spinal stabilisation exercises may form bias towards a specific verbal instruction. Therefore, our participants had no prior knowledge of spinal stabilisation exercises. In addition, the first of the three trials was used to allow each patient to become familiar with the instructions, and the images of the last two trials were used for data analysis. As indicated in our reliability data, our participants demonstrated consistent muscle thickness change during the last two contractions for each verbal instruction. Fatigue effects were unlikely, because our participants only performed nine gentle isometric contractions. In addition, none of our participants complained of fatigue during muscle contraction.

A limitation of this study was the use of US imaging to study muscle contraction. Although the

reliability of the ultrasonographic testing protocol used in this study was shown to be good to excellent, the US imaging only captures a 2-D image and could not fully represent muscle contraction.³¹ In addition, we also recognise that direct contact of the transducer on the skin over the lumbar multifidus muscle provided additional tactile stimulation, which may have confounded the results.^{32,33} Therefore, the results may reflect the combined effects of verbal instructions and tactile pressure on the lumbar multifidus muscle.

The results of our study only addressed the verbal component of exercise instruction. However, clinicians do not solely rely on verbal commands to instruct exercises. Therefore, diagrams, pictures and non-verbal demonstrations often are incorporated to ensure that patients perform exercises correctly. Nevertheless, verbal instruction should be considered to be an important component when prescribing an isometric contraction exercise to patients. Recent systematic reviews and studies have shown conflicting evidence for the relationship between changes in lumbar multifidus and changes in LBP-related disability and for the use of lumbar multifidus morphology as a predictor to LBP recovery.^{28,29,34-36} However, stabilisation exercises, such as used in Hicks *et al.*'s⁸ study, have been used frequently by clinicians, as well as by researchers, to enhance the function of the lumbar multifidus muscle. The design of Hicks *et al.*'s⁸ stabilisation exercise programme was based on lumbar multifidus morphological studies. Further, the programme begins by eliciting spinal stabilisers (i.e. lumbar multifidus and transversus abdominis). As mentioned earlier, 2-D representation of US or MR imaging may not display a complete picture of lumbar multifidus muscle contraction.³⁰ Further, the measurement of muscle thickness changes is very small, about 3.3 mm at L4-5 in Kopenhagen *et al.*'s²³ study and 1.1 mm at L5-S1 in Wallwork *et al.*'s.⁵ This small difference may raise questions about clinical applications of ultrasonographic measurements of muscle

contraction. Nevertheless, the stabilisation function of lumbar multifidi should not be ignored in clinical management of LBP.

In conclusion, the results of the study show that the three verbal instructions may increase lumbar multifidus muscle thickness by different amounts at L4-5, but by the same amount at L5-S1. Clinicians may choose appropriate verbal instructions to achieve optimal muscle contractions. Although most of the patients with LBP reported verbal instruction #2 to be the most helpful command to activate the muscle, this verbal instruction had the least muscle thickness change on parasagittal US images at L4-5.

Disclaimer statements

Contributors SW-P: Conceiving and designing the study, obtaining IRB approval, recruiting/enrolling participants, analyzing and interpreting the data, writing the manuscript in whole JZ: Conceiving and designing the study, recruiting participants, analyzing and interpreting the data, writing the manuscript in part KB: Designing the study, recruiting participants, analyzing and interpreting the data, writing portions of the manuscript LS and DT: Designing the study, recruiting/enrolling participants, collecting the data, analyzing the data, assisting in writing the methods section.

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