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**Supplemental Material 1 – Protocol**

See separate file.

## **Supplemental Material 2: Battery of Upper Extremity Testing**

### **QUICKDASH**

#### QuickDASH <sup>1,2</sup>

The QuickDASH is a shorter version of the DASH Outcome Measure, which is a 30-item, self-report questionnaire that is designed to measure symptoms and physical function in people with any of a variety of musculoskeletal disorders involving the upper limb. It is often used to monitor changes in function and symptoms over time. The shorter version is valid, reliable and responsive and is popular for use in clinical programs and in research. A variety of translations are available.

### **ELEVATED ARM STRESS TEST (EAST)**

#### Elevated Arm Stress Test (EAST) <sup>3-6</sup>

Also called Roos' test, the EAST is performed by holding the arms in a position of 90 degrees of abduction and external rotation ("stick-up position"). The patient then opens and closes the hands slowly for a period of 3 minutes. Reproduction of symptoms in the entire extremity or rapid fatigue of the extremity constitutes a positive test result. Patients with thoracic outlet syndrome (TOS) typically cannot complete this test. Many authors describe this as the most reliable test for TOS. The test is of the most diagnostic benefit when symptoms occur rapidly after elevation of the arm. One study showed reproduction of symptoms in 94% of patients with neurogenic TOS. This maneuver can reproduce symptoms of other pathologies, including carpal tunnel syndrome, cubital tunnel syndrome, and rotator cuff syndrome.

### **PHALEN'S TEST**

#### Phalen's Test <sup>7,8</sup>

Phalen's test involves passive flexion of the wrist for 15 to 60 seconds. A positive test produces numbness and tingling in the distribution of the median nerve. Researchers have reported that this test is one of two clinical tests with the highest overall accuracy in testing for median nerve compression at the wrist.

### **TINEL'S TEST AT THE VOLAR WRIST**

#### Tinel's Test at the Volar Wrist <sup>9</sup>

The examiner taps over the carpal tunnel. Reproduction of paresthesias in the distribution of the median nerve is a positive response.

## **ELBOW FLEXION TEST**

### Elbow Flexion Test<sup>10</sup>

The Elbow Flexion test is one of the most sensitive and specific tests for identifying ulnar nerve compression at the cubital tunnel. With the shoulder in neutral position, manual pressure is applied to the ulnar nerve in the cubital tunnel as the elbow is placed in terminal flexion with the forearm supported in supination. Maintain the wrist in neutral. Hold the position for 60 seconds.

## **TINEL'S TEST AT THE CUBITAL TUNNEL**

### Tinel's Test at the Cubital Tunnel<sup>11</sup>

With the patient's elbow fully flexed and the wrist held in neutral position, the examiner taps over the ulnar nerve with the cubital tunnel. Reproduction of paresthesias in the distribution of the ulnar nerve is a positive response.

## **SEMMES WEINSTEIN MONOFILAMENTS TEST FOR PRESSURE THRESHOLD SCREENING**

### Semmes Weinstein Monofilaments for Pressure Threshold Screening<sup>12-14</sup>

When calibrated and applied correctly, this test is a valid test for determining sensibility detection thresholds. Studies have clearly demonstrated their ability to accurately detect intended clinical conditions. Used in standard consistent protocols, the monofilament test is able to compare patient data in individual and multicenter studies and is providing information regarding peripheral nerve changes with treatment not previously available with less sensitive and uncontrolled instruments. When calibrated correctly, it is one of the few, if not the only, sensibility measurement instrument that approaches requirements for an objective test.

The hand screen utilizes 5 monofilaments. Test sites specific to the median nerve are the tip of the thumb, index, and proximal index. Test sites specific to the ulnar nerve are the distal little finger, proximal phalanx, and ulnar base of the palm. The test site specific for the radial nerve is the dorsal aspect of the thumb web space. The examiner retests a nonresponsive test site at least three times to ensure a monofilament is not detected at that site.

## **TEN TEST**

### Ten Test<sup>15</sup>

In the Ten Test of finger pad light sensation, the patient develops a ratio between normal light moving touch and diminished moving touch. Subsequent determinations can detect serial changes. The ratios obtained can be compared with a standard scale of sensibility with a high degree of validity and reliability. The interexaminer and

intraexaminer results obtained are reliable and repeatable. Simplicity and dependability recommend this test for use in a busy clinical setting.

## **STATIC TWO-POINT DISCRIMINATION SCREENING**

### Static Two-Point Discrimination Screening <sup>16-20</sup>

Two-point discrimination is a classic test of sensibility used by hand surgeons over several decades. The test is believed by many to be a test of innervation density. Some think two-point discrimination a good predictor of patient function and manipulation. Two-point discrimination testing is most accurate at the fingertips. Normal two-point discrimination is considered less than 6 mm, fair is 6 to 10 mm, and poor is 11 to 15 mm.

## **VISUAL ANALOG PAIN SCALE (VAS)**

### Visual Analog Pain Scale <sup>21,22</sup>

The Visual Analog Scale (VAS) for pain is used to measure quantity of pain. A 10-cm line has 0 as no pain and 10 as worst pain imaginable. High test-retest reliability has been demonstrated. There is a high correlation between VAS and the numeric pain rating scale and a verbal description of pain.

The VAS is well described in research, and has been shown to be a valid, reliable and sensitive clinical measure of pain that is amenable to statistical analysis. It is simple to use. VAS showed significant positive correlation with numeric rating scales and the faces pain scale. Previous studies have shown reliability, validity and clinical sensitivity of the VAS as a measure of intensity of subjective pain.

**Supplemental Table 1: Evaluable Patient Characteristics, Disease State, Treatment Dates, Number of Days on Study, Time to Onset of CIPN (N=40)**

Subject Number	Race/Sex/Ethnicity	Weight (kg)	Height (cm)	BMI (kg/m <sup>2</sup> )	Age	Disease State	Treatment Arm	Study Treatment Start Date	Study Treatment Stop Date	Number of Days on Study	Onset of CIPN
1	W/M/NH	124.6	183.7	36.9	38	Non-Metastatic	Traditional	8/4/16	10/27/16	84	
2 <sup>a</sup>	W/F/NH	96	167.7	34.1	52	Metastatic	Investigational	8/16/16	10/7/16	58	10/1/2016 - Day 47
4	W/F/NH	69.2	160.5	26.9	77	Metastatic	Investigational	8/25/16	9/22/16	28	9/21/2016 - Day 28
5	W/F/NH	71.5	172	24.2	67	Metastatic	Traditional	8/24/16	11/16/16	84	
10	W/M/NH	99.6	188	28.2	58	Metastatic	Investigational	1/17/17	4/11/17	84	
11	W/M/NH	75.4	180	23.3	66	Metastatic	Traditional	4/12/17	7/5/17	84	
12	W/M/NH	81.2	193.5	21.7	70	Metastatic	Traditional	5/25/17	6/11/17	17	6/11/2017 - Day 17
13	W/F/NH	52.7	154.9	22	71	Metastatic	Investigational	7/5/17	9/27/17	84	
14	W/M/NH	82.9	175.3	27	61	Metastatic	Investigational	7/10/17	10/2/17	84	
15	W/F/NH	67.9	179	21.2	70	Non-Metastatic	Traditional	7/26/17	10/18/17	84	
16	W/F/NH	59.1	162.1	22.5	77	Non-Metastatic	Traditional	8/15/17	10/10/17	58	10/10/2017 - Day 57
17	W/M/NH	76.6	180.3	23.6	55	Metastatic	Investigational	10/4/17	12/12/17	69	12/9/2017 - Day 67
18	W/F/NH	62.7	165.1	23	68	Non-Metastatic	Traditional	10/11/17	1/3/18	84	
19	W/M/NH	86.5	178.9	27	83	Non-Metastatic	Investigational	11/2/17	1/26/18	85	
20	W/F/NH	60.4	155	25.1	65	Metastatic	Traditional	12/6/17	2/28/18	85	
21	W/F/NH	51	167.6	18.2	64	Metastatic	Traditional	12/8/17	3/8/18	85	
22	W/M/NH	84.9	180.3	26.1	42	Metastatic	Investigational	2/8/18	5/2/18	84	
23	W/M/NH	69.3	183.3	20.6	70	Metastatic	Investigational	2/8/18	5/7/18	88	
24	W/F/NH	65.2	154.9	27.2	61	Metastatic	Traditional	2/7/18	5/3/18	84	
25	W/M/NH	96.5	177.8	30.6	64	Non-Metastatic	Traditional	2/7/18	5/7/18	84	
28	W/M/NH	125.1	188	35.1	64	Metastatic	Traditional	7/18/18	8/21/18	34	8/21/2018 - Day 34

Subject Number	Race/Sex/Ethnicity	Weight (kg)	Height (cm)	BMI (kg/m <sup>2</sup> )	Age	Disease State	Treatment Arm	Study Treatment Start Date	Study Treatment Stop Date	Number of Days on Study	Onset of CIPN
31	W/M/NH	88	175.3	28.6	79	Non-Metastatic	Traditional	9/17/18	12/10/18	84	
34	W/M/NH	78.4	188.1	22.2	84	Non-Metastatic	Traditional	10/31/18	1/21/19	84	
35 <sup>b</sup>	W/F/NH	50.4	152.4	21.7	73	Non-Metastatic	Investigational	11/1/18	1/31/19	84	
<b>36</b>	<b>W/M/NH</b>	<b>104</b>	<b>182.9</b>	<b>31.1</b>	72	Non-Metastatic	<b>Investigational</b>	<b>12/4/18</b>	<b>1/16/19</b>	<b>43</b>	<b>1/16/2019 - Day 43</b>
37	W/M/NH	86.8	175.3	28.2	69	Non-Metastatic	Traditional	12/18/18	3/12/19	84	
39	W/F/NH	72.6	170.2	25.1	61	Metastatic	Investigational	4/1/19	6/24/19	84	
40	W/M/NH	101.4	180.3	31.2	73	Non-Metastatic	Investigational	4/25/19	7/18/19	84	
41	W/M/NH	73.3	176.5	23.5	78	Non-Metastatic	Investigational	5/30/19	8/23/19	82	
42	W/M/NH	73.5	172.7	24.6	63	Metastatic	Traditional	6/4/19	8/28/19	84	
<b>45</b>	<b>W/M/NH</b>	<b>83.2</b>	<b>190.5</b>	<b>22.9</b>	72	Non-Metastatic	<b>Traditional</b>	<b>7/25/19</b>	<b>9/19/19</b>	<b>57</b>	<b>9/19/2019 - Day 57</b>
46	W/F/NH	57.5	165.1	21.1	65	Non-Metastatic	Investigational	8/21/19	11/13/19	84	
<b>47</b>	<b>A/M/NH</b>	<b>76.7</b>	<b>180.3</b>	<b>23.6</b>	80	<b>Metastatic</b>	<b>Investigational</b>	<b>9/26/19</b>	<b>11/26/19</b>	<b>57</b>	<b>11/20/2019 - Day 56</b>
48	W/F/NH	72.3	172.7	24.2	70	Metastatic	Investigational	9/24/19	12/16/19	84	
49	W/M/NH	86	188	24.3	61	Metastatic	Investigational	10/14/19	1/7/20	84	
51	W/M/NH	85.6	177.8	27.1	79	Non-Metastatic	Traditional	12/19/19	3/12/20	84	
52	W/M/NH	56.3	172.7	18.9	75	Metastatic	Investigational	1/14/20	4/7/20	84	
<b>53</b>	<b>W/F/H</b>	<b>56.4</b>	<b>149.9</b>	<b>25.1</b>	67	<b>Metastatic</b>	<b>Investigational</b>	<b>1/15/20</b>	<b>2/5/20</b>	<b>22</b>	<b>2/4/2020 - Day 21</b>
54	W/F/NH	69.9	167.6	24.9	62	Metastatic	Traditional	1/16/20	4/21/20	84	
55	W/F/H	87.6	162.6	33.1	56	Metastatic	Investigational	6/22/20	9/15/20	84	

Abbreviations: CIPN=Chemotherapy Induced Peripheral Neuropathy, W=White, A=Asian, M=Male, F=Female, H=Hispanic, NH=Non-Hispanic

<sup>a</sup> Patient was a screen failure due to abnormal lab value (elevated bilirubin). Once resolved, the patient was reconsented, assigned a new subject number, and enrolled into study.

<sup>b</sup> Patient received Gemcitabine+Albumin-Bound Paclitaxel chemotherapy, all others received Gemcitabine+Albumin-Bound Paclitaxel+Cisplatin

Note: Patients who developed CIPN are in bold.

**Supplemental Table 2: Elevated Arm Stress Test (EAST) Right Arm**<sup>3-6</sup>

Visit	Group	Negative	Positive	Missing/Not	
				Tested	Total
1	Traditional	19 (100)	0	0	19
	Investigation	20 (95.2)	0	1 (4.8)	21
2	Traditional	19 (100)	0	0	19
	Investigation	21 (100)	0	0	21
3	Traditional	19 (100)	0	0	19
	Investigation	20 (95.2)	1 (4.8)	0	21
4	Traditional	18 (100)	0	0	18
	Investigation	18 (100)	0	1 (5.6)	18
5	Traditional	17 (100)	0	0	17
	Investigation	15 (93.8)	0	1 (6.3)	16
Total	Traditional	92 (100)	0	0	92
	Investigation	94 (95.9)	1 (1.0)	3 (3.1)	98

QuickDASH<sup>1,2</sup> - Refer to Supplemental Material 2



**Supplemental Table 3: Elevated Arm Stress Test (EAST) Left Arm**<sup>3-6</sup>

Visit	Group	Negative	Positive	Missing/Not	
				Tested	Total
1	Traditional	19 (100)	0	0	19
	Investigation	21 (100)	0	0	21
2	Traditional	19 (100)	0	0	19
	Investigation	21 (100)	0	0	21
3	Traditional	19 (100)	0	0	19
	Investigation	21 (100)	0	0	21
4	Traditional	18 (100)	0	0	18
	Investigation	18 (94.7)	0	1 (5.3)	19
5	Traditional	17 (100)	0	0	17
	Investigation	15 (93.8)	0	1 (6.3)	16
Total	Traditional	92 (100)	0	0	92
	Investigation	96 (98.0)	0	2 (2.0)	98

**Supplemental Table 4: Phalen's Test Right Arm** <sup>7,8</sup>

Visit	Group	Negative	Positive	Missing/Not	
				Tested	Total
1	Traditional	19 (100)	0	0	19
	Investigation	21 (100)	0	0	21
2	Traditional	19 (100)	0	0	19
	Investigation	21 (100)	0	0	21
3	Traditional	19 (100)	0	0	19
	Investigation	20 (95.2)	1 (4.8)	0	21
4	Traditional	18 (100)	0	0	18
	Investigation	17 (89.4)	1 (5.3)	1 (5.3)	19
5	Traditional	15 (88.2)	2 (11.7)	0	17
	Investigation	15 (93.8)	0	1 (6.3)	16
Total	Traditional	90 (97.8)	2 (2.2)	0	92
	Investigation	94 (95.9)	2 (2.0)	2 (2.0)	98

**Supplemental Table 5: Phalen's Test Left Arm** <sup>7,8</sup>

Visit	Group	Negative	Positive	Missing/Not	
				Tested	Total
1	Traditional	19 (100)	0	0	19
	Investigation	21 (100)	0	0	21
2	Traditional	19 (100)	0	0	19
	Investigation	21 (100)	0	0	21
3	Traditional	19 (100)	0	0	19
	Investigation	20 (95.2)	1 (4.8)	0	21
4	Traditional	18 (100)	0	0	18
	Investigation	18 (94.7)	0	1 (5.3)	19
5	Traditional	16 (94.1)	1 (5.9)	0	17
	Investigation	15 (93.8)	0	1 (6.3)	16
Total	Traditional	91 (98.9)	1 (1.1)	0	92
	Investigation	95 (96.9)	1 (1.0)	2 (2.0)	98

**Supplemental Table 6: Elbow Flexion Test Right Arm**<sup>10</sup>

Visit	Group	Negative	Positive	Missing/Not	
				Tested	Total
1	Traditional	19 (100)	0	0	19
	Investigation	21 (100)	0	0	21
2	Traditional	19 (100)	0	0	19
	Investigation	21 (100)	0	0	21
3	Traditional	18 (94.7)	1 (5.3)	0	19
	Investigation	21 (100)	0	0	21
4	Traditional	18 (100)	0	0	18
	Investigation	18 (94.7)	0	1 (5.3)	19
5	Traditional	16 (94.1)	1 (5.9)	0	17
	Investigation	15 (93.8)	0	1 (6.3)	16
Total	Traditional	90 (97.8)	2 (2.3)	0	92
	Investigation	96 (98.0)	0	2 (2.0)	98

**Supplemental Table 7: Elbow Flexion Test Left Arm**<sup>10</sup>

Visit	Group	Negative	Positive	Missing/Not	
				Tested	Total
1	Traditional	19 (100)	0	0	19
	Investigation	21 (100)	0	0	21
2	Traditional	19 (100)	0	0	19
	Investigation	20 (95.2)	1 (4.8)	0	21
3	Traditional	17 (89.4)	2	0	19
	Investigation	21 (100)	0	0	21
4	Traditional	17 (94.4)	1 (5.6)	0	18
	Investigation	18 (94.7)	0	1 (5.3)	19
5	Traditional	16 (94.1)	1 (5.9)	0	17
	Investigation	15 (93.8)	0	1 (6.3)	16
Total	Traditional	88 (95.7)	4 (4.3)	0	92
	Investigation	95 (6.9)	1 (1.0)	2 (2.0)	98

**Supplemental Table 8: Tinel Test Right Volar Wrist <sup>9</sup>**

Visit	Group	Negative	Positive	Missing/Not	
				Tested	Total
1	Traditional	19 (100)	0	0	19
	Investigation	21 (100)	0	0	21
2	Traditional	19 (100)	0	0	19
	Investigation	21 (100)	0	0	21
3	Traditional	19 (100)	0	0	19
	Investigation	21 (100)	0	0	21
4	Traditional	18 (100)	0	0	18
	Investigation	19 (100)	0	0	19
5	Traditional	17 (100)	0	0	17
	Investigation	15 (93.8)	0	1 (6.3)	16
Total	Traditional	92 (100)	0	0	92
	Investigation	97 (99.0)	0	1 (1.0)	98

**Supplemental Table 9. Tinel Test Left Volar Wrist <sup>9</sup>**

Visit	Group	Negative	Positive	Missing/Not	
				Tested	Total
1	Traditional	19 (100)	0	0	19
	Investigation	20 (95.2)	1 (4.8)	0	21
2	Traditional	19 (100)	0	0	19
	Investigation	21 (100)	0	0	21
3	Traditional	18 (94.7)	1 (5.3)	0	19
	Investigation	21 (100)	0	0	21
4	Traditional	18 (100)	0	0	18
	Investigation	19 (100)	0	0	19
5	Traditional	17 (100)	0	0	17
	Investigation	15 (93.8)	0	1 (6.3)	16
Total	Traditional	91 (98.9)	1	0	92
	Investigation	96 (98.0)	1 (1.0)	1 (1.0)	98

**Supplemental Table 10: Tinel Test Right Cubital Tunnel**<sup>11</sup>

Visit	Group	Negative	Positive	Missing/Not	
				Tested	Total
1	Traditional	19 (100)	0	0	19
	Investigation	21 (100)	0	0	21
2	Traditional	19 (100)	0	0	19
	Investigation	21 (100)	0	0	21
3	Traditional	18 (100)	1 (5.3)	0	19
	Investigation	20 (95.2)	1 (4.8)	0	21
4	Traditional	17 (94.4)	1 (5.6)	0	18
	Investigation	19 (100)	0	0	19
5	Traditional	17 (100)	0	0	17
	Investigation	15 (93.8)	0	1 (6.3)	16
Total	Traditional	90 (97.8)	2 (2.3)	0	92
	Investigation	96 (98.0)	1 (1.0)	1 (1.0)	98



**Supplemental Table 11: Tinel Test Left Cubital Tunnel**<sup>11</sup>

Visit	Group	Negative	Positive	Missing/Not	
				Tested	Total
1	Traditional	19 (100)	0	0	19
	Investigation	20 (95.2)	1 (4.8)	0	21
2	Traditional	19 (100)	0	0	19
	Investigation	21 (100)	0	0	21
3	Traditional	18 (94.7)	1 (5.3)	0	19
	Investigation	21 (100)	0	0	21
4	Traditional	17 (94.4)	1 (5.6)	0	18
	Investigation	19 (100)	0	0	19
5	Traditional	16 (94.1)	1 (5.9)	0	17
	Investigation	15 (93.8)	0	1 (6.3)	16
Total	Traditional	89 (96.7)	3 (3.3)	0	92
	Investigation	96 (98.0)	1 (1.0)	1 (1.0)	98

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