

# Computerized Arm Training Improves the Motor Control of the Severely Affected Arm After Stroke

## A Single-Blinded Randomized Trial in Two Centers

S. Hesse, MD; C. Werner, MA; M. Pohl, MD; S. Rueckriem, PT; J. Mehrholz, PT; M.L. Lingnau, MA

**Background and Purpose**—To compare a computerized arm trainer (AT), allowing repetitive practice of passive and active bilateral forearm and wrist movement cycle, and electromyography-initiated electrical stimulation (ES) of the paretic wrist extensor in severely affected subacute stroke patients.

**Method**—A total of 44 patients, 4 to 8 weeks after stroke causing severe arm paresis (Fugl–Meyer Motor Score [FM, 0 to 66] <18), were randomly assigned to either AT or ES. All patients practiced 20 minutes every workday for 6 weeks. AT patients performed 800 repetitions per session with the robot and ES patients performed 60 to 80 wrist extensions per session. The primary outcome measure was the blindly assessed FM (0 to 66), and the secondary measures were the upper limb muscle power (Medical Research Council [MRC] sum, 0 to 45) and muscle tone (Ashworth score sum, 0 to 25), assessed at the beginning and end of treatment and at 3-month follow-up.

**Results**—The AT group had a higher Barthel Index score at baseline, but the groups were otherwise homogenous. As expected, FM and MRC sum scores improved overtime in both groups but significantly more in the robot AT group. The initial Barthel Index score had no influence. In the robot AT group, FM score was 15 points higher at study end and 13 points higher at 3-month follow-up than the control ES group. MRC sum score was 15 points higher at study end and at 3-month follow-up compared with the control ES group. Muscle tone remained unchanged, and no side effects occurred.

**Conclusion**—The computerized active arm training produced a superior improvement in upper limb motor control and power compared with ES in severely affected stroke patients. This is probably attributable to the greater number of repetitions and the bilateral approach. (*Stroke*. 2005;36:1960-1966.)

**Key Words:** rehabilitation ■ stroke

Each year, >1 million patients experience a stroke in the European community, and ≈30% of the survivors experience a severe upper limb paresis without volitional distal activity.<sup>1</sup> Their prognosis for regaining functional hand activity 6 months later is very poor.<sup>2</sup> More Bobath therapy does not improve outcome,<sup>3</sup> and the patients do not meet the criteria for entering active training programs.<sup>4</sup> Electromyography (EMG) biofeedback<sup>5</sup> and treatment on a rocking chair<sup>6</sup> showed positive effects on upper limb motor control for this subgroup of severely affected patients.

Robots are a new treatment option. The MIT-Manus<sup>7</sup> and the MIME robots<sup>8</sup> work on shoulder–elbow movement, and randomized studies have shown a positive effect on motor power of the affected shoulder and elbow muscles, although motor control improved to a lesser extent.<sup>9,10</sup>

The Bi-Manu-Track robotic arm trainer (AT) works on more distal arm movements, practicing bilateral elbow pro-

supination and wrist flexion–extension.<sup>11</sup> In chronic patients, a 4-week training program reduced wrist and finger spasticity.

The present trial studied the effect of the Bi-Manu-Track on subacute stroke patients experiencing severe arm paresis. The control group received electrical muscle stimulation (ES) of the paretic wrist extensors. Although less effective in severely affected patients,<sup>12–14</sup> the authors chose ES in line with national stroke rehabilitation guidelines on the basis of positive systematic reviews of the literature.<sup>15,16</sup> The robot group was expected to have a better outcome because of a higher repetition rate and the bilateral approach.

## Methods

### Subjects

Subjects were recruited from 2 rehabilitation centers over an 8-month period, who met the following criteria:

Received January 24, 2005; final revision received May 27, 2005; accepted June 17, 2005.

From the Klinik Berlin (S.H., C.W., M.L.L.), Neurological Rehabilitation, Charité, Berlin, Germany; and Klinik Bavaria (M.P., S.R., J.M.), Neurological Rehabilitation, Kreischa, Germany.

Reha-Stim Company, Berlin, Germany, holds the national patent on the Bi-Manu-Track. The company is owned by Dr Beate Brandl-Hesse, the spouse of S.H.

Correspondence to Stefan Hesse, MD, Klinik Berlin, Kladower Damm 223, 14089 Berlin, Germany. E-mail bhesse@zedat.fu-berlin.de

© 2005 American Heart Association, Inc.

Stroke is available at <http://www.strokeaha.org>

DOI: 10.1161/01.STR.0000177865.37334.ce

- first time supratentorial stroke;
- stroke interval before study onset 4 to 8 weeks;
- severe upper limb paresis with no or only a palpable volitional activity of the wrist and finger extensors (ie, Medical Research Council [MRC] 0 or 1);
- an initial upper limb Fugl-Meyer Motor Score (0 to 66) of <18;
- absent or moderate elbow, wrist, and finger spasticity;
- able to understand the meaning of the study; and
- written informed consent to participate in the approved study.

The exclusion criteria were: apraxia (ie, 1 fault in the tasks waving goodbye, saluting, and making a fist with the nonaffected hand after verbal instruction and demonstration, and using an eraser, comb, and screwdriver with the objects handed to the patient and verbally instructed);

- shoulder pain insensitive to standard therapy;
- hand swelling sufficient to prevent fist formation;
- painful arthritis of the wrist or finger joints; and
- forearm skin ulcers.

### Allocation

A total of 44 lots (A or B) had been prepared in 2 sealed envelopes, 22 lots for each center. Just before the first session, the patient drew a lot out of the envelope presented by an independent person, who then informed the therapists.

Power calculation ( $\alpha$  0.05;  $\beta$  0.8) assumed a mean Fugl-Meyer Motor Score (FM, 0 to 66) of 14 (SD 6.0), a clinically relevant difference of 5 points and a drop-out rate of 20%.

### Intervention

In addition to their standard inpatient rehabilitation program, the patients practiced with an AT (AT group; Bi-Manu-Track) or ES of their paretic wrist extensors (ES group; Bentrifit M13 and F12) for 20 minutes every workday for 6 weeks (30 sessions).

The AT<sup>11</sup> enabled the mirror-like practice of 2 movement cycles: forearm pro-supination and wrist flexion extension. The patients sat at a height-adjustable table with their elbows bent at 90° and put their forearms in the mid-position into an arm trough. Each hand grasped a handle; a strap led the paretic hand in place. To switch movement direction, the device was tilted 90° downward and the handles position changed. Three computer-controlled modes were offered: (1) passive-passive, with both arms being moved by the machine; (2) active-passive, with the nonaffected arm driving the affected side; and (3) active-active, with both arms actively moving against resistance. Within 1 session, each patient practiced 200 of the elbow and 200 of the wrist cycles, totaling 400 cycles, or 800 repetitions, half in mode 1 and half in mode 2. Additionally, the patients could practice 25 to 50 repetitions in mode 3.

In the ES group, the patients sat at a height-adjustable table with their elbows bent 90° and their forearms in pro-nation. Four- to 7-s trains of monophasic exponential pulses (75 Hz; 0.5 ms; 0 to 80 mA) were applied by 2 self-adhesive flexible electrodes (2.5×3 cm). The intensity was set to produce maximum wrist extension. Patients performed 60 to 80 wrist extensions per session, with an interstimulus interval between 8 and 15 s.

If the patient could volitionally activate the wrist extensor muscle during the study, an EMG-initiated ES was applied. A third flexible self-adhesive electrode, placed between the 2 stimulation electrodes, recorded the volitional muscular activity. The EMG activity level required to trigger the ES was continuously adjusted near the patients' highest level. Again, 60 to 80 wrist extensions were practiced per session.

Both treatments (AT or ES) were performed by the same therapists and in the same room to limit external influences. After help with the set-up (2 to 3 minutes for AT and ES), the patients practiced themselves, and a therapist remained within shouting distance in case of problems. AT patients received additional help tilting the device and exchanging the handles, which took another 1 to 2 minutes.

The ongoing standard rehabilitation program comprised 5 45-minute sessions of physiotherapy (PT) and 4 30-minute sessions of occupational therapy (OT) based on the neurodevelopmental tech-

nique concept every week. Restoration of stance and gait and activities of daily living competence were primary targets. Upper limb exercises took ≈20% of PT and OT, mostly devoted to tone-inhibiting maneuvers and improving proximal muscle control (eg, weight acceptance over the shoulder girdle).

### Outcome Measures

The primary outcome variable was the Fugl-Meyer Motor Score of the upper extremity (FM, 0 to 66).<sup>17</sup> The sensitive, reliable, and valid test included items related to movements of the shoulder, elbow, and forearm (proximal part) and the wrist and hand (distal part). A proximal shoulder/elbow (FM-prox, 0 to 42) and a distal hand/wrist (FM-dist, 0 to 24) subscore were calculated.

Secondary outcome measures were the muscle power and tone of the affected extremity. The MRC scale (0 to 5) evaluated the power of the shoulder abductors, flexors, and extensors of the elbow, the wrist, the fingers, and the thumb. A total motor power score (MRC sum, 0 to 45) included a proximal (MRC-prox, 0 to 15) and a distal subscore (MRC-dist, 0 to 30).

The modified Ashworth scale (AS, 0 to 5) assessed the tone of the shoulder adductors, the flexors of the elbow, wrist, fingers, and the thumb.<sup>18</sup> A total (AS sum, 0 to 25), proximal (AS-prox, 0 to 10), and distal (AS-dist, 0 to 15) scores were calculated. Data were assessed at study onset (Tbegin), after 4 weeks (T4weeks), at the end of treatment (Tend), and 3 months later (Tfollow-up).

The FM assessment was entirely videographed with the patient sitting on a chair with a mirror placed in an angle of 45° to his/her paretic shoulder. A blinded therapist rated the videos of all patients at the end of the trial. The treating therapists rated the secondary outcome variables.

### Statistical Analysis

An intention-to-treat analysis was performed. If a subject dropped out, assessment continued, or if this was not possible, the last score was used. Homogeneity of the groups before study onset was tested by Mann-Whitney *U* test. Two-factor (intervention-AT, ES- and time-Tbegin, T4weeks, Tend, Tfollow-up) ANOVA, with Barthel Index (BI) as baseline covariant, was performed.  $\alpha$  was set to 0.05.

### Results

Of 914 stroke patients admitted during this period, 44 patients entered the trial. Twenty-one of the AT and 22 of the ES group completed treatment, and 19 (20) patients were available at 3-month follow-up (Figure 1). At baseline, BI was higher in the AT group, but the groups were otherwise well matched (Table 1).

Each AT patient practiced a total of 12 000 cycles or 24 000 repetitions. Twelve (9) patients additionally practiced 25 to 50 elbow (wrist) cycles in mode 3 after 3 to 4 weeks. Side effects did not occur.

Each ES patient practiced a total of 1800 to 2400 wrist extensions. Only 3 of 22 patients were able to use EMG-initiated ES after 2 to 5 weeks. Three patients developed hand swelling, which responded to treatment.

As expected, FM score improved in both groups over time ( $F=25.8$ ;  $P<0.001$ ) but significantly more in the AT group (factor group  $F=6.3$  and  $P=0.016$  and interaction of the factors group and time  $F=10.6$  and  $P<0.001$ ). The initial BI had no influence. Mean FM score was  $15.0\pm 3.3$  (95% CI, 8.3 to 21.7) greater in AT group than ES group at study end and  $13.4\pm 5.1$  (95% CI, 3.0 to 23.6) at follow-up (Table 2). The subscores FM-prox and FM-dist improved in the AT group to a similar extent (Table 3; Figure 2). Among the neglect patients (5 cases in both groups), only 2 in the AT group and 1 in the ES group improved their FM

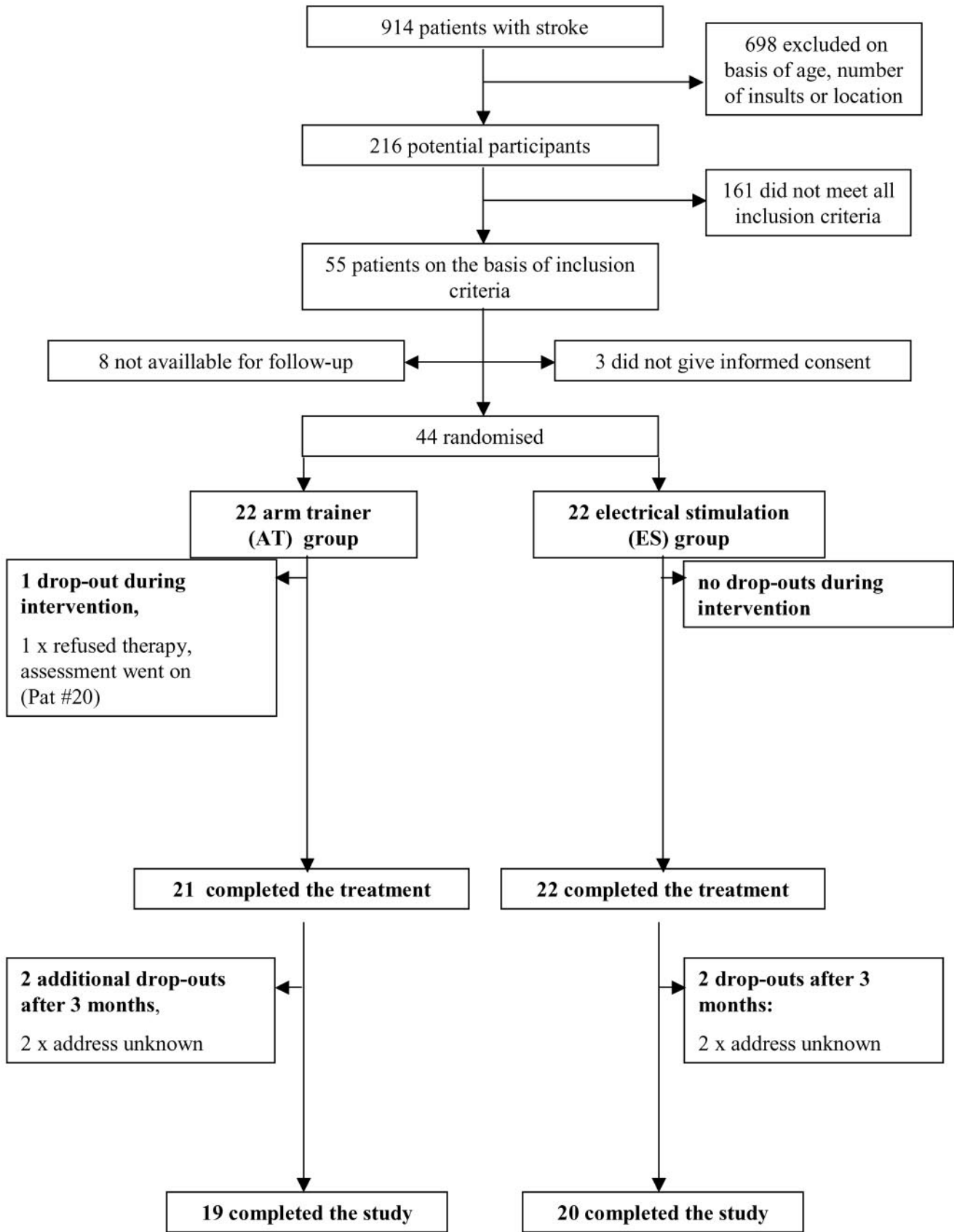


Figure 1. Flow diagram.

**TABLE 1. Clinical Data and Initial Assessment Scores in Means (SD) and Median (IQR) for Both Groups**

	AT Group	ES Group
No.	22	22
Diagnosis	20 ischemic, 2 hemorrhagic	20 ischemic, 2 hemorrhagic
Hemiparesis	14 left, 8 right	11 left, 11 right
Stroke interval, weeks	5.1 (±1.3)	5.5 (±1.4)
Age, years	65.4 (±11.5) range: 33–80	64.0 (±11.6) range 34–80
Sex	12 females; 10 males	12 females; 10 males
Neglect	5	5
BI (0–100)	48 (±26)*	36 (±18)
Upper limb motor control	7.9 (±3.4)	7.3 (±3.3)
Fugl-Meyer Motor Score (0–66)		
Upper limb motor strength	2 (0.75–4.75)	2.5 (0.25–6.75)
MRC Sum Score (0–45) median (IQR)		
Upper limb spasticity	0 (0–2.5)	0 (0–1)
Modified Ashworth Sum Score (0–25) median (IQR)		

IQR indicates interquartile range.  
 \*Significant difference in favor of AT group at study onset.

score >5 points during the intervention (ie, the presence of a neglect syndrome seemed to negatively influence the outcome).

The upper limb motor power (MRC sum) significantly improved in both groups over time (F=38.9; P<0.001) but

significantly more in the AT group (interaction of the factors group and time F=13.5; P<0.001). Mean MRC sum was 15.0±3.0 (95% CI, 8.9 to 21.1) higher in the AT group at study end and 14.7±3.2 (95% CI, 8.2 to 21.3) at 3-month follow-up. The muscle tone (AS sum) remained constant in both groups.

**TABLE 2. Mean (SD) and Median (IQR) Scores, Mean Differences (SD) and Approximate CIs for the AT and ES Group**

Outcome		Fugl-Meyer-Score (0–66)	Total MRC (0–45)	Total Ashworth (0–25)
Week 0	AT	Mean (SD)	7.9 (±3.4)	2.9 (±2.6)
		Median (IQR)	7 (5.75–8.5)	2.5 (0.75–5.25)
	ES	Mean (SD)	7.3 (±3.3)	3.5 (±3.3)
		Median (IQR)	6.5 (4.75–9.25)	2.5 (0.25–6.75)
Week 4	AT	Mean (SD)	19.8 (±12.5)	19.2 (±10.0)
		Median (IQR)	19.5 (8.5–27.5)	22 (8–27)
	ES	Mean (SD)	9.8 (±7.1)	6.0 (±7.0)
		Median (IQR)	9 (4–12)	3.5 (0–11)
Week 6	AT	Mean (SD)	24.6 (±14.9)	21.8 (±10.5)
		Median (IQR)	28 (10.75–32.25)	22.5 (11–27.75)
	ES	Mean (SD)	10.4 (±7.5)	6.8 (±8.3)
		Median (IQR)	9 (4.75–11.25)	3.5 (0–12.5)
Mean group difference week 6 95% CI		15.0 (±0.3.3)* 8.3–21.7	15.0 (±3.0)* 8.9–21.1	NS
Week 18	AT	Mean (SD)	30.0 (±16.8)	22.6 (±11.1)
		Median (IQR)	31 (11–38)	22 (12–27)
	ES	Mean (SD)	16.6 (±14.9)	7.9 (±9.0)
		Median (IQR)	12 (4.5–23.5)	6 (0–13)
Mean group difference week 18 95% CI		13.4 (±5.1)* 3.0–23.6	14.7 (±3.2)* 8.2–21.3	NS

IQR indicates interquartile range.  
 \*Significant difference (P<0.001) between groups in favor of AT.

**TABLE 3. Mean (SD) Scores of the Proximal and Distal Sections of All 3 Variables for the AT and ES Groups**

Outcome		Fugl-Meyer-Score Prox (0–42), Dist (0–24)	MRC-Score Prox (0–15), Dist (0–30)	Ashworth-Score Prox (0–10), Dist (0–15)
Week 0	AT Proximal	7.5 (±2.9)	2.6 (±1.5)	0.8 (±1.1)
	AT Distal	0.4 (±0.5)	0.3 (±0.5)	0.7 (±1.6)
	ES Proximal	7.1 (±3.1)	3.0 (±2.5)	0.4 (±0.6)
	ES Distal	0.2 (±0.4)	0.5 (±0.5)	0.4 (±0.5)
Week 4	AT Proximal	15.2 (±7.6)	7.3 (±3.9)	0.9 (±0.3)
	AT Distal	4.6 (±2.3)	11.9 (±8.0)	0.4 (±3.1)
	ES Proximal	8.6 (±5.5)	3.5 (±3.1)	1.2 (±0.5)
	ES Distal	1.2 (±1.9)	2.5 (±3.8)	0.7 (±0.3)
Week 6	AT Proximal	15.6 (±6.0.9)	12.1 (±3.9)	0.9 (±1.3)
	AT Distal	9.0 (±4.8)	9.7 (±5.3)	0.8 (±1.4)
	ES Proximal	9.8 (±5.9)	4.4 (±2.2)	0.6 (±0.7)
	ES Distal	0.6 (±0.8)	2.4 (±2.2)	1.2 (±1.3)
Week 18	AT Proximal	20.2 (±8.6)	12.7 (±5.3)	0.8 (±1.4)
	AT Distal	9.8 (±6.0)	9.9 (±5.9)	0.6 (±1.4)
	ES Proximal	14.7 (±9.2)	5.1 (±4.1)	0.5 (±0.6)
	ES Distal	1.9 (±2.2)	2.8 (±3.9)	1.3 (±1.4)

## Discussion

Subacute stroke patients with severe upper limb paresis, but without neglect, showed a significantly better upper limb motor control and muscle strength after robot arm training compared with the wrist ES.

Arm function improved over time with ES of the paretic wrist extensor, as currently recommended by national guidelines based on positive literature reviews,<sup>15,16</sup> but this study is not designed to show whether ES added anything to the conventional therapy that patients were also receiving. With the robot, patients practiced a total of 24 000 repetitions, evenly divided between 4 different movement directions, whereas the ES group practiced a total of 1800 to 2400 repetitions of wrist extension only. This ES intensity followed the literature.<sup>12</sup> More stimulations per session could have resulted in an excessive muscle fatigue as a well known effect of ES because of its reversed motor unit recruitment pattern.<sup>19</sup> The higher treatment intensity and patients' more active participation are the most likely explanations for the enhanced result from robotic training<sup>20</sup>; the contribution of the unique feature of the robot itself to the outcome remains unclear at the present moment. Potential risks of excessive training (eg, focal dystonia<sup>21</sup> or impaired sensorimotor function,<sup>22</sup> as seen in experimental animals) did not occur.

With the AT, the patients practiced bilaterally, which has been shown by a pilot functional MRI study to enhance activation of primary motor cortex compared with unilateral paretic hand movement in the early recovery stage of 2 patients.<sup>23</sup> Further arguments in favor of a bilateral approach after stroke are the controlled trials of Feys et al and Carrough et al, who showed a superior treatment effect of a bilateral repetitive shoulder stimulation on a rocking chair and of a coupled protocol of EMG-triggered ES and bilateral coordination training.<sup>6,24</sup>

Controlled trials with the MIT-Manus in acute stroke patients consistently reported a significantly stronger proximal muscle

strength in the robot group during treatment.<sup>9</sup> Among patients with a plegic hand (n=56), FM-shoulder and wrist-hand subscores did not improve after 20 1-hour treatment sessions.<sup>9</sup>

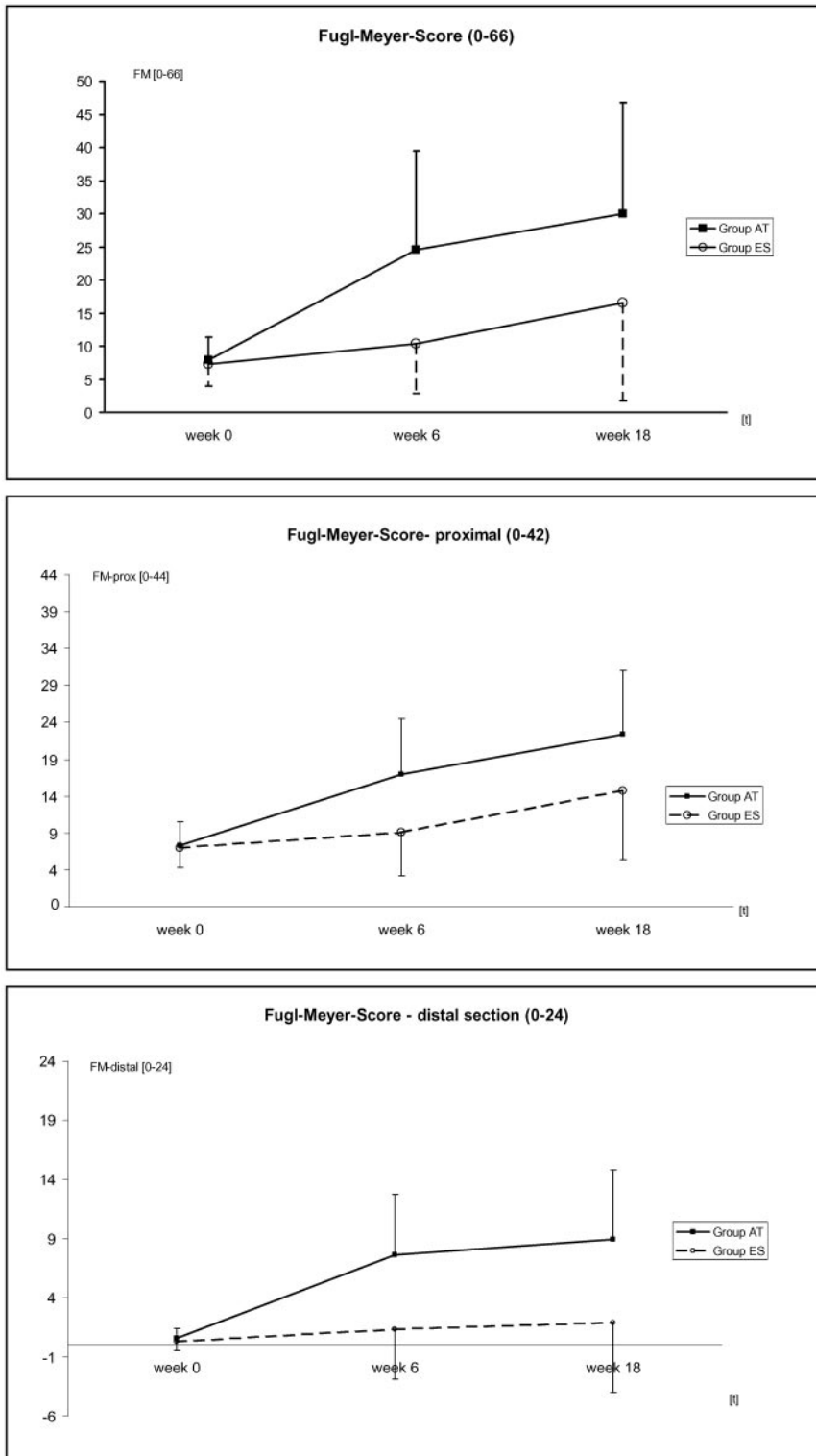
In the present study, the proximal and distal motor control improved in the robot group, suggesting a generalized treatment effect. One may speculate that the more distal approach resulted in a more powerful activation of the sensorimotor cortex given their larger cortical representation. The recently suggested competition between proximal and distal arm segments for plastic brain territory after stroke<sup>25</sup> would recommend shifting the emphasis of treatment from the shoulder to the forearm, hand, and fingers.

The limitations of this study include the higher level of competence in daily living in the AT group at study onset and the nonblinded assessment of the secondary outcome variables. The duration of therapy devoted to hand function during the conventional rehabilitation program was not recorded; this would have revealed whether patients with a higher initial BI, for instance, had more hand therapy, which would have favored the AT group. Further actual concomitant therapies were not monitored, and the omission of a specific measure of activity limited the clinical relevance of the study.

In conclusion, 30 20-minute sessions of robotic training improved upper limb motor control and muscle strength compared with ES of the paretic wrist extensors in subacute stroke patients with severe upper limb paresis. Confirmation of this finding within a large multicenter trial is warranted.

## Acknowledgments

The study was sponsored by a grant of the BMBF. Suppliers were Reha-Stim, Kastanienallee, Berlin, Germany, and Bentrionic GmbH, Kreillerstr., München, Germany. Stephen Kirker, Cambridge, UK, rephrased the final draft of this article.



**Figure 2.** Mean (SD) Fugl-Meyer-Score (FM, 0 to 66, top), proximal (FM-prox, 0 to 42, middle) and distal (FM-dist, 0 to 24, bottom) subscores of both groups at study begin, end, and at follow-up.

## References

1. Nakayama H, Jorgensen HS, Raaschou HO, Olsen TS. Recovery of upper extremity function in stroke patients: the Copenhagen Study. *Arch Phys Med Rehabil.* 1994;75:852–857.
2. Kwakkel G, Kollen BJ, an der Grond J, Prevo AJ. Probability of regaining dexterity in the flaccid upper limb. The impact of severity of paresis and time since onset in acute stroke. *Stroke.* 2003;34:2181–2186.
3. Parry RH, Lincoln NB, Vass CD. Effect of severity of arm impairment on response to additional physiotherapy early after stroke. *Clin Rehabil.* 1999;13:187–198.
4. Taub E, Miller NE, Novak TA, Cook EW, Fleming WC, Nepomuceno CS, Connell JS, Crago JE. Technique to improve chronic motor deficit after stroke. *Arch Phys Med Rehabil.* 1993;74:347–354.
5. Crow JJ, Lincoln NB, Nouri FM, De Weerd W. The effectiveness of EMG biofeedback in the treatment of arm function after stroke. *Int Disabil Res.* 1989;11:155–160.
6. Feys HM, De Weerd WJ, Selz BE, Cox Steck GA, Spichiger R, Vereeck LE, Putman KD, van Hoydonck GA. Effect of a therapeutic intervention for the hemiplegic upper limb in the acute phase after stroke. 1998;29: 785–792.

7. Hogan N, Krebs HI, Charnarong J, Sharon A. Interactive robotics therapist. Cambridge, Massachusetts Institute of Technology: US Patent No. 5466213; 1995.
8. Burgar CG, Lum PS, Shor P, van der Loos HF. Development of robots for rehabilitation therapy: the Palo Alto VA/Stanford experience. *J Rehabil Res Dev*. 2000;37:663–673.
9. Volpe BT, Krebs HI, Hogan N, Edelman L, Diels C, Aisen M. A novel approach to stroke rehabilitation. *Neurology*. 2000;54:1938–1944.
10. Lum PS, Burgar CG, Shor PC, Majmundar M, van der Loos M. Robot-assisted movement training compared with conventional therapy techniques for the rehabilitation of upper-limb motor function after stroke. *Arch Phys Med Rehabil*. 2002;83:952–959.
11. Hesse S, Schulte-Tiggens G, Konrad M, Bardeleben A, Werner C. Robot-assisted arm trainer for the passive and active practice of bilateral forearm and wrist movements in hemiparetic subjects. *Arch Phys Med Rehabil*. 2003;84:915–920.
12. Hummelsheim H, Amberger S, Mauritz KH. The influence of EMG-initiated electrical muscle stimulation on motor recovery of the centrally paretic hand. *Eur J Neurol*. 1996;3:245–254.
13. Chae J, Bethoux F, Bohine T, Dobos L, Davis T, Friedl A. Neuro-muscular stimulation for upper extremity motor and functional recovery in acute hemiplegia. *Stroke*. 1998;29:975–979.
14. Powell J, Pandyan AD, Granat M, Cameron M, Stott DJ. Electrical stimulation of wrist extensors in poststroke hemiplegia. *Stroke*. 1999;30:1384–1389.
15. De Kroon JR, van der Lee JH, Ijzerman MJ, Lankhorst GJ. Therapeutic electrical stimulation to improve motor control and functional abilities of the upper extremity after stroke: a systematic review. *Clin Rehabil*. 2002;16:350–360.
16. Platz T. Evidenzbasierte Arm rehabilitation. Eine systematische Literaturübersicht. *Nervenarzt*. 2003;74:841–849.
17. Fugl-Meyer AR, Jasko L, Leyman I, Olsson S, Steglind S. The post-stroke patient. A method for evaluation of physical performance. *Scand J Rehabil Med*. 1975;7:13–31.
18. Bohannon RW, Smith MB. Interrater reliability of a modified Ashworth scale of muscle spasticity. *Phys Ther*. 1987;67:206–207.
19. Bigland-Ritchie B, Zijdwind I, and Thomas CK. Muscle fatigue induced by stimulation with and without doublets. *Muscle Nerve*. 2000;23:1348–1355.
20. Kwakkel G, Wagenaar RC, Twisk JWR, Lankhorst GJ, Koetsier JC. Intensity of leg and arm training after primary middle-cerebral-artery stroke: a randomised trial. *Lancet*. 1999;354:191–196.
21. Byl NN, Merzenich MM, Jenkins WM. A primate genesis model of focal dystonia and repetitive strain injury: I. Learning-induced dedifferentiation of the representation of the hand in the primary somatosensory cortex in adult monkeys. *Neurology*. 1996;47:508–520.
22. Bland ST, Schallert T, Strong R, Aronowski J, Grotta JC. Early exclusive use of the affected forelimb after moderate transient focal ischemia in rats. *Stroke*. 2000;31:1144–1152.
23. Staines WR, McIlroy WE, Graham SJ, Black SE. Bilateral movement enhances ipsilesional cortical activity in acute stroke: a pilot functional MRI study. *Neurology*. 2001;56:401–404.
24. Carraugh JH, Kim S. Two coupled motor recovery protocols are better than one. *Stroke*. 2002;33:1589–1593.
25. Muelbacher W, Richards C, Ziermann U, Wittenberg G, Weltz D, Borojerdi B, Cohen L, Hallett M. Improving hand function in chronic stroke. *Arch Neurol*. 2002;59:1278–1282.