

# Best Conventional Therapy Versus Modular Impairment-Oriented Training for Arm Paresis After Stroke: A Single-Blind, Multicenter Randomized Controlled Trial

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**Background.** The study investigated whether passive splinting or active motor training as either individualized best conventional therapy or as standardized impairment-oriented training (IOT) would be superior in promoting motor recovery in subacute stroke patients with mildly or severely paretic arms. **Methods.** A total of 148 anterior circulation ischemic stroke patients were randomly assigned to 45 minutes of additional daily arm therapy over 3 to 4 weeks as either (a) passive therapy with inflatable splints or active arm motor therapy as either (b) individualized best conventional therapy (CONV) or (c) standardized IOT, that is Arm BASIS training for severe paresis or Arm Ability training for mild paresis. Main outcome measures included the following: Fugl-Meyer arm motor score (severely paretic arms) and the TEMPA time scores (mildly affected arms). Pre-post (immediate effects) and pre-4 weeks follow-up analyses (long-term effects) were performed. **Results.** Overall improvements were documented (mean baseline and change scores efficacy: Fugl-Meyer, arm motor scores, 24.4, +9.1 points; TEMPA, 119, -26.6 seconds;  $P < .0001$ ), but with no differential effects between splint therapy and the combined active motor rehabilitation groups. Both efficacy and effectiveness analyses indicated, however, bigger immediate motor improvements after IOT as compared with best conventional therapy (Fugl-Meyer, arm motor scores: IOT +12.3, CONV +9.2 points; TEMPA: IOT -31.1 seconds, CONV -20.5 seconds;  $P = .0363$ ); for mildly affected patients long-term effects could also be substantiated. **Conclusions.** Specificity of active training seemed more important for motor recovery than intensity (therapy time). The comprehensive modular IOT approach promoted motor recovery in patients with either severe or mild arm paresis.

**Keywords:** Stroke; Arm; Hemiparesis; Training; Rehabilitation

Hemiparesis is one of the most important predictors of long-term disability.<sup>1,2</sup> Motor function of the affected arm can explain up to 50% of the variance in functional autonomy in stroke patients.<sup>3</sup> Furthermore, both arm impairment, that is, the ability to move the arm and its segments selectively, and arm disabilities, that is, the ability to handle everyday life objects successfully, are associated with handicap situations 6 months later, that is, the degree of difficulty and help needed in daily and instrumental activities, and in social roles.<sup>4</sup>

But can they be influenced by exercise therapy? A systematic review of randomized controlled trials stated that no definite conclusions about the effectiveness of exercise therapy on arm function in stroke patients can be drawn.<sup>5</sup> The evidence suggested that more exercise therapy may be beneficial. An effect of augmented exercise therapy time (AETT) on arm activities could, however, not be substantiated in another large meta-analysis of stroke rehabilitation trials.<sup>6</sup> Similarly, for specific moderate intensity interventions the evidence is far from being conclusive: a Cochrane review including 14

randomized/quasi-randomized trials suggested that repetitive task training resulted in modest improvement in lower limb function but not upper limb function.<sup>7</sup> Functional electrical stimulation might promote motor recovery, but existing evidence is not yet unequivocal.<sup>8</sup>

Thus, the prevailing moderately intensive exercise schedules might or might not promote recovery. In contrast, massive practice in patients with at least partially preserved hand function can produce substantial and long-lasting changes in amount of arm use<sup>9,10</sup>: this subpopulation of stroke patients benefits from massive practice (6 hours per day) and parallel constraint of the less affected arm. Both the necessary massive therapy schedules and the preselection of patients do, however, restrict the potential benefits to selected stroke victims.

Given the restricted resources in our health care systems, it needs to be determined how the available moderate-intensity rehabilitation resources have to be tailored to be efficacious. It seems that both active motor therapy and a minimum exercise therapy time are key issues.<sup>11,12</sup> But within these constraints,

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would it be best to rely on the therapists' experience and intuitive selection of therapeutic elements to promote the individual patient's best possible recovery? Or is therapeutic time so precious that we have to standardize therapeutic practice and ground it firmly on neuroscientific reasoning to promote its (otherwise) small chance to modify recovery beyond natural history and spontaneous recovery? With the former we risk lacking the potential power of neuroscience knowledge and standardized work routines in daily practice; with the latter we might miss out to take advantage of experience, individual circumstances, and psychosocial characteristics.

Theoretically, training concepts could be most likely clinically efficacious if they were neuroscience based and targeted motor control deficits specifically, that is, were impairment oriented. An impairment-oriented training (IOT) would aim to be both causal, that is, improve those motor control deficits that affect daily life abilities, and comprehensive, that is, improve all relevant control deficits. By doing so, it might promote any training's efficacy and transfer to daily life even within given therapeutic time restraints.

Arm paresis shows a bimodal distribution with many patients with either mild or severe arm activity limitations and quite different motor control deficits.<sup>13-15</sup> Thus, a specific IOT concept would have to provide at least 2 training strategies to deal with arm paresis after stroke. Specific and highly structured training methods have been developed, such as the Arm Ability training for patients with mild arm paresis and the Arm BASIS training for patients with severe arm paresis.<sup>15-17</sup> Randomized controlled trials supported their clinical efficacy: the Arm Ability improved dexterity and timed performance with everyday-like arm activities in patients with mild paresis, whereas the Arm BASIS training improved the capability for selective arm movements in patients with severe paresis.<sup>18-20</sup> Together they might provide a comprehensive and efficacious impairment-oriented modular exercise therapy approach for a broad range of degree of arm paresis after brain damage. Thereby, the therapeutic needs of many stroke victims could be met.

In this study, we wanted to contrast the effects of moderately intense AETT (45 minutes per weekday over 3-4 weeks) when provided either as passive stimulation therapy with inflatable splints applied to the affected arm or as active arm motor rehabilitation therapy with active use of the affected arm during therapy session intended to promote its motor capacities (contrast "motor training intensity"). Within the active arm motor rehabilitation therapy we designed a contrast between whatever the individual therapist regarded as the best therapeutic option for a given patient's arm rehabilitation ("best conventional therapy") and the standardized highly structured IOT techniques (contrast "experimental factor"). Because patients with a broad range of severity of arm paresis were to be recruited, randomization was blocked within strata for severe and mild arm paresis. It was assumed that active motor therapy is more efficacious than passive stimulation therapy,<sup>11</sup> whereas for reasons stated above either active therapeutic regimen could have been superior. For the philosophy

and structuring of motor rehabilitation services, knowledge about the experimental factor would be of considerable importance and might help promote rational resource allocations for the benefit of many stroke patients in our societies.

## Methods

### Participants

Patients after a first clinically apparent unilateral supratentorial anterior circulation ischemic stroke in the subacute phase were recruited during inpatient rehabilitation treatment at 1 of 6 German participating departments of neurological rehabilitation: (a) the Department of Neurological Rehabilitation of the Charité—Universitätsmedizin Berlin; (b) Klinik Bavaria, Kreischa; (c) Moritz-Klinik, Bad Klosterlausnitz; (d) Wicker Klinik, Bad Wildungen; (e) the Neurological (Rehabilitation) Centre of the Segeberger Kliniken, Bad Segeberg; and (f) the Klinikum für Rehabilitation, Bad Oeynhausen.

Criteria for selection were (a) age <80 years; (b) first unilateral anterior circulation ischemic stroke between 3 weeks and 6 months prior to study entry; (c) incomplete, mild, or severe arm paresis, that is, Motricity Index<sup>21</sup> Arm Score <100 and >25; (d) no more than mild speech comprehension deficit, that is, Hemispheric Stroke Scale,<sup>22</sup> comprehension score "2" or "0" (correctly following 2 out of 3 commands); (e) no cognitive or emotional impairments that would make an adequate study participation impossible; and (f) no peripheral nerve damage or orthopedic arm problem affecting arm motion and necessitating treatment.

If the Motricity Index items shoulder abduction, elbow flexion, and precision grip had scores >19 (ie, proximal limb movements possible against gravity, able to grasp and lift a 2.5-cm cube) and if selective finger motions and precision grip were preserved, patients were classified as "mild paresis," otherwise they were classified as "severe paresis."

Type of stroke was classified according to the Bamford criteria, that is, lacunar, partial, or total anterior circulation infarct.<sup>23</sup> The NIH Stroke Scale was used for the quantification of impairment after stroke in a more general sense.<sup>24</sup> Patients were further characterized with the Ashworth Scale score for wrist and elbow flexors, a widely used measure of resistance to passive movement (and spasticity).<sup>25</sup>

All subjects gave informed consent to participate in the study that had received approval from the local ethics committee of each study center.

### Interventions

All patients were recruited during their inpatient rehabilitation treatment. Patients were randomly allocated to 1 of 3 treatment groups:

1. Inflatable splint arm therapy
2. Best conventional motor therapy

### 3. IOT either as Arm Ability training (mild paresis) or Arm BASIS training (severe paresis)

AETT consisted of one 45-minute treatment session per weekday (5 times per week) for all study participants. The subgroup “mild paresis” received additional training for 3 weeks and the subgroup “severe paresis” for 4 weeks. This difference was based on the fact that more severely affected patients take longer to recover.

*Inflatable splint arm therapy.* A standardized set of 5 different hand/arm pressure splints of various sizes was used. Hand and/or arm of the paretic arm were positioned in an antispastic position. A manual described the usage of the inflatable splints and suggested a sequence of applications that varied from day to day to enhance patient compliance.

*Conventional treatment.* During conventional treatment experienced occupational therapists and/or physiotherapists provided individualized arm rehabilitation therapy on a one-to-one basis. Based on their past therapeutic experience and individual patient characteristics they were free to select whatever they regarded the best possible physical therapy regimen. The term *best* refers to the fact that therapeutic choices were individually taken in every patient’s best interest; it does not imply that evidenced-based guidelines had been used. Study therapists were not restricted in terms of the type of therapeutic approach they choose; devices such as arm therapy robots or functional electrical stimulation could, however, not be used.

*Impairment-oriented training.* The Arm BASIS training<sup>15-17</sup> addresses the lack of selective movements in severe arm paresis. For each single degree of freedom of the arm and hand, selective movements (dynamic control with a high degree of reciprocal inhibition and as little co-contraction as possible) are systematically restored by a repetitive training of isolated motions across the full range of motion in that segment. During the first phase the therapist takes over the weight of the arm (no postural control should be carried out by the patient) and assists the movement as far as the patient cannot move on her or his own. Once the full active range of motion is achieved, the combination of dynamic and postural control is relearned for this isolated motion; only then will prespecified multijoint movements and coordination be trained.

The Arm Ability training<sup>15,16</sup> trains different abilities such as speed, aiming, dexterity, tracking, and steadiness. The selection of training tasks covers these different sensorimotor control affordances and is thereby comprehensive in terms of their relevance for motor performance in many different circumstances as encountered during daily life. In addition, variation of task difficulty is implemented in each type of training task to enhance motor learning. Work load is individually standardized in line with the baseline motor capacities of each patient. During the training, patients are continuously encouraged to try to fulfill their workload in even shorter time but without compromise for the individual

tasks’ accuracy demands. This progress (knowledge of result) is intermittently shown to the patient for each type of task during training sessions using diagrams on a PC screen (Arm Ability software).

Because the IOT was not established in the participating rehabilitation centers, study personnel had to be trained in the lead study center before patient recruitment commenced.

## Objectives

The study addressed the questions whether (a) AETT provided as either passive stimulation (splint therapy) or active arm motor could enhance motor recovery therapy (contrast “motor training intensity”), and more important, nested within this contrast (b) whether either an individualized best conventional therapeutic approach or a standardized and highly structured IOT was more able to promote recovery (contrast “experimental factor”) in a stroke population with arm paresis that could range from mild to severe.

## Outcomes

As primary outcome measure for patients with severe arm paresis, the arm motor section of the Fugl-Meyer test (FM) had been selected.<sup>26</sup> This test has been developed for hemiplegic patients. It might be viewed as a test of a hemiplegic patient’s ability to move his or her arm, including proximal arm, hand, and fingers, selectively. Using standardized guidelines for test performance and scoring, its arm motor, sensation, and passive joint motion/pain sections can reliably be applied in multicenter settings.<sup>27,28</sup>

As primary outcome measure for patients with mild arm paresis, the time scores of the TEMPA<sup>29</sup> were used. The time needed to complete activities of daily life–like tasks is separately assessed for unilateral tasks (performed with the affected and nonaffected arms) and all tasks (unilateral and bilateral tasks) and reflects any individual’s skilled (sensori)motor capacities. For the purpose of the study a weighted summary score had been used (TEMPA outcome score: sum of double weighted unilateral scores for the affected arm and summary score divided by 3:  $[2 \times \text{TEMPA}_{\text{unilateral}} + \text{TEMPA}_{\text{all}}]/3$ ).

The FM subtest passive joint motion/pain scores and Ashworth scores (measure of spasticity) were also documented (as secondary outcome measure and adverse effect measures).

Assessments were performed 3 times, once before randomization (t1), once after completion of the study therapy period (t2), and finally 4 weeks later (t3). All assessments were documented on videos. For the documentation of the FM test, frontal and side views of the patient were simultaneously captured on the video, facilitating video-based scoring.<sup>28</sup>

Because the contrasts of interest covered a broad range of severity from mild to severe arm paresis, individual standardized outcome and outcome difference scores were calculated. Thereby, the efficacy and effectiveness analyses could be based on assessment-independent (comparable) scores. For this purpose, individual standardized scores ( $[x - \text{mean}]/\text{SD}$ ) were

based on 148 pretest observations for FM motor scores and TEMPA outcome scores (66 patients with severe paresis and 82 with mild paresis). Standardized difference scores were:  $t_2 - t_1$  or  $t_3 - t_1$ . Standardized TEMPA outcome difference scores were multiplied by  $-1$ ; thus, higher scores indicate improved performance (as with FM-motor standardized differences scores).

Other motor therapy (apart from study therapy) that had individually been prescribed was additionally monitored as summary time of individual or group therapy in either occupational or physiotherapy, both between pretest and posttest and between posttest and follow-up. This type of therapy included training of arm activities, activities of daily living, and/or lower extremity rehabilitation including mobility.

### Sample Size

In 2 previous randomized controlled studies (with 3 randomized groups) that assessed Arm Ability training<sup>18</sup> and Arm BASIS training,<sup>19,20</sup> an overall study population of 60 patients was sufficient to document each treatment's efficacy. Thus, a comparable study population, that is, 120 patients (60 patients with severe paresis and 60 patients with mild paresis), was intended to be recruited to ensure sufficient statistical power to document each treatment's efficacy in the current trial. To secure the efficacy analysis, it was predetermined to substitute any patient who did not complete the study protocol. If possible within the time frame of the study, the recruitment of study patients was planned to continue beyond 120 patients to facilitate the analyses of subgroup effects.

### Randomization

Randomization was blocked within strata for "severe paresis" and "mild paresis." A random allocation sequence list was generated using a computerized random-number generator and stored outside the study centers. Assignments were enclosed in sequentially numbered, opaque, sealed envelopes and stored at the central study center in Berlin. Personnel who assessed eligibility, obtained informed consent, and enrolled a patient in the trial had no knowledge about assignment. After recruitment, the appropriate numbered, opaque, sealed envelope was opened and the randomization information given to the recruitment and training personnel of the enrolling study center (but not to the primary central rater). The code was revealed to the researchers once recruitment, data collection, and analyses were complete.

### Blinding

The primary central rater for outcome measures was blinded to treatment assignment for the duration of the study. Moreover, the rater scored the assessment videos without knowledge of time of testing (pretest, posttest, or follow-up). This was achieved by random number codes for each assessment.

### Statistical Methods

Characteristics of the study group were summarized with descriptive statistics. Differences in baseline characteristics and concurrent exercise therapy between the 3 randomized groups were analyzed with  $\chi^2$  test or 1-way analysis of variance (ANOVA) as appropriate.

Efficacy refers to whether the intervention can be successful when it is properly implemented under controlled conditions (per-protocol data). The primary analysis was an efficacy analysis and involved all patients who were randomly assigned and completed the study protocol.

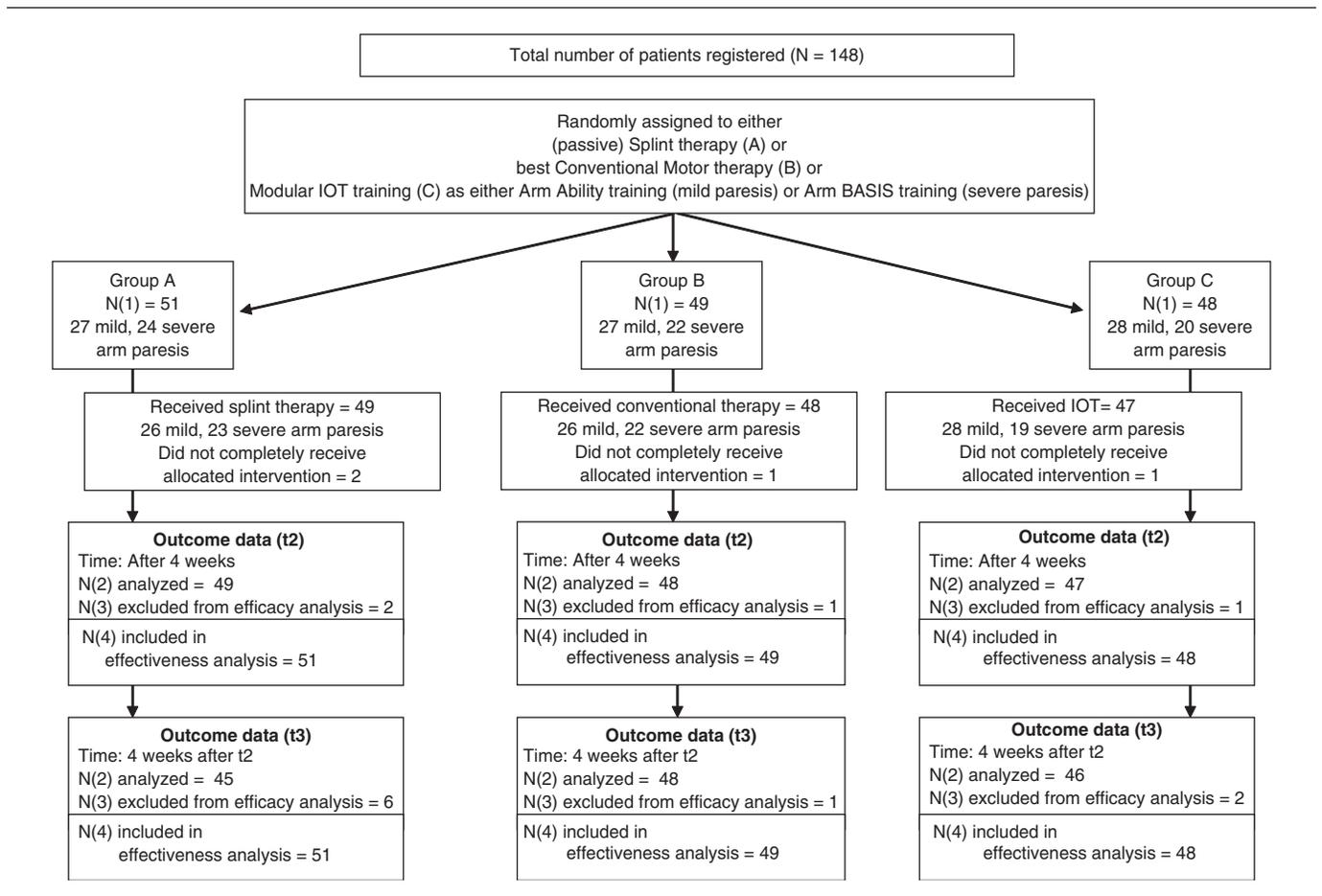
General linear models including multiple regressions within a repeated-measures ANOVA design were used to assess the effect "motor training intensity" (receiving or not receiving augmented active exercise therapy time) and type of training ("experimental factor," ie, CONV vs IOT) on motor recovery (standardized outcome scores for the FM test or TEMPA): repeated measures were pretest and posttest (or follow-up) motor scores (dependent variables, factor "time"). Independent variables were the factors "motor training intensity" (splint vs active motor training) and "type of training/experimental factor" (CONV or IOT) nested within the factor "motor training intensity." Between-group contrasts were analyzed as interactions between the factors "time" and "motor training intensity" as well as "time" and "type of training." Both severity of motor impairment at baseline (subgroups mild or severe paresis) and time since onset of stroke were used as covariates because they are known to modify recovery.<sup>9,10,15,16</sup>  $F$  values presented for these models are partial  $F$  values (based on type III sums of squares).

The analyses of secondary outcome measures included differences regarding concurrent motor therapy, any treatment effects and side effects on spasticity (Ashworth scale), or passive range of motion and joint pain (FM). These effects were analyzed with the general linear models as described above.

Effectiveness refers to whether the intervention typically is successful in actual clinical practice. An intention-to-treat analysis more closely resembles treatment effects as might be achieved in clinical practice and was therefore planned in addition. An intention-to-treat analysis (with the general linear model as described above) was planned for the primary outcome measure and effects of "motor training intensity" and the "experimental factor" (conventional therapy vs IOT). It was predefined to be based on data of all randomized patients and if necessary on the "last observation carried forward" approach for dealing with missing values in clinical trials.<sup>30</sup>

For all tested general linear models distribution assumptions had been checked by inspection of standardized residuals and estimation of Cook's distances, a commonly used estimate of the influence of data points when doing least squares regression.<sup>31</sup> Data points with large residuals (outliers) and/or high leverage may distort the outcome and accuracy of a regression. Points with a Cook's distance of 1 would have suggested closer examination, but had not been observed in the analyses.

**Figure 1**  
**Flow Chart of the Details of the Study**



## Results

Details of the number of participants who were randomly assigned, received the intended treatment, completed the study protocol, and were analyzed for the primary and secondary outcome are presented in Figure 1.

Study subjects entered the trial on average 4 to 5 weeks after stroke. The 3 groups with a total of 144 patients who completed the study protocol and were analyzed for the primary and secondary outcomes (efficacy analysis) were comparable with regard stroke type (Bamford classification) and affected hemisphere ( $\chi^2$ ,  $P > .70$ ) as well as age, time after stroke at study entry, severity of neurological impairment (NIH Stroke Scale), arm motor impairment (Motricity Index, FM, or TEMPA), and passive motion/joint pain (FM test; ANOVA,  $P > .25$ ; see Table 1). Spasticity scores (Ashworth) were low with minor differences between groups.

More male patients and fewer female patients were, however, randomized to the conventional therapy group.

Fifty-two patients were recruited in the rehabilitation center in Berlin, 46 in Kreischka, 26 in Bad Klosterlausnitz, 11 in Bad Wildungen, 9 in Bad Segeberg, and 4 in Bad Oeynhausen.

## Primary Outcome Measures

Outcome data of the per-protocol analysis (Table 2) and the intention-to-treat analysis (Table 3) are presented as change scores from pretest to posttest ( $t1 - t2$ ) and from pretest to follow-up 4 weeks after treatment ( $t1 - t3$ ). The tables provide both the standardized outcome scores (Cohen's  $d$ )<sup>32</sup> reflecting the magnitude of changes independent of the assessment measure used (FM test or TEMPA) and the raw FM test and TEMPA change scores (for the 2 subgroups with severe and arm mild paresis, respectively). The standardized outcome scores can be considered effect sizes, for example, a change score of 1 denotes a change of the magnitude of the SD of scores within the study population at baseline. Higher scores indicate more marked improvement, 0 no change, negative values deterioration.

Effects for the efficacy (per protocol) and effectiveness (intention to treat) analyses were almost identical. In the text, only data for the efficacy analysis will be mentioned. Overall improvement over time (mean and 95% confidence interval [CI] of standardized change scores,  $t1 - t2$ : 1.19 [1.01-1.38];  $F(1, 137) = 93.55$ ;  $P < .001$ ) was statistically significant,

**Table 1**  
**Characteristics of Stroke Patients**

	Study Population (n = 144)	Splint Therapy (n = 49)	Conventional Therapy (n = 48)	IOT (n = 47)	<i>P</i>
Age (mean/SD)	58.1/12.0	56.7/12.5	59.5/11.2	58.0/12.2	.5309 <sup>a</sup>
Gender (female/male)	58/86	25/24	10/38	23/24	.0034 <sup>b</sup>
Stroke (LACI, TACI, PACI)	65/22/57	23/8/18	19/6/23	23/8/16	.7005 <sup>b</sup>
Weeks after stroke (mean/SD)	4.7/3.0	5.1/3.7	4.5/2.8	4.5/2.4	.4838 <sup>a</sup>
Affected arm (left/right)	80/64	28/21	26/22	26/21	.9567 <sup>b</sup>
NIH Stroke Scale <sup>c</sup> (mean/SD)	3.8/2.6	3.6/2.8	3.9/2.7	4.0/2.3	.7306 <sup>a</sup>
MI—arm (mean/SD)	65.4/19.5	63.0/20.9	66.7/18.2	66.6/19.4	.5752 <sup>a</sup>
FM motor <sup>d</sup> (mean/SD) <sup>e</sup>	24.4/11.7	23.3/12.3	26.2/12.2	23.5/10.9	.6700 <sup>a</sup>
TEMPA-uni <sup>f</sup> (sec) (mean/SD) <sup>g</sup>	68.2/29.6	70.8/24.5	60.4/21.4	73.0/38.6	.2557 <sup>a</sup>
TEMPA-all <sup>h</sup> (sec) (mean/SD) <sup>g</sup>	221.9/66.3	226.3/64.6	210.0/50.8	229.0/80.1	.5355 <sup>a</sup>
FM joint <sup>i</sup> (mean/SD)	45.1/4.2	45.0/4.6	45.3/3.4	45.0/4.5	.9213 <sup>a</sup>
Ashworth <sup>j</sup> (mean/SD)	1.0/1.5	1.3/1.7	0.6/1.0	1.0/1.7	.0707 <sup>a</sup>

Abbreviations: IOT, impairment-oriented training; SD, standard deviation; LACI, lacunar anterior circulation infarct; TACI, total anterior circulation infarct; PACI, partial anterior circulation infarct.

<sup>a</sup>Analysis of variance (ANOVA).

<sup>b</sup> $\chi^2$  Test.

<sup>c</sup>NIH Stroke Scale (scores range from 0 [no impairment] to 36 [most severe impairment]).

<sup>d</sup>FM motor = Fugl-Meyer test, arm motor score (scores range from 0 [no] to 66 [normal selective motor control]).

<sup>e</sup>N (study population/splint/conventional/IOT) = 64/23/22/19.

<sup>f</sup>TEMPA-uni = TEMPA test, summary time score for unilateral tasks when performed with the affected arm.

<sup>g</sup>N (study population/splint/conventional/IOT) = 80/26/26/28.

<sup>h</sup>TEMPA-all = TEMPA test, summary time score for all (unilateral and bilateral) tasks.

<sup>i</sup>FM joint = Fugl-Meyer test, arm joint motion/pain score (scores range from 0 [only few degrees of range of motion/pronounced pain] to 48 [normal range of motion/no pain]).

<sup>j</sup>Ashworth scale (scores range from 0 [normal tone] to 4 [fixed rigid position]; scores presented are summary scores for wrist and elbow flexors, that is, range from 0 to 8).

whereas its interaction with “motor training intensity” was not ( $F(1, 137) = .30$ ;  $P = .5820$ ). Thus, change scores were not significantly different between those receiving passive stimulation therapy with inflatable splints applied to the affected arm and the combined groups receiving active arm motor rehabilitation therapy with active use of the affected arm during therapy session. The experimental factor (CONV vs IOT; nested within “motor training intensity”) indicated bigger improvements after IOT when compared with conventional therapy immediately after the study therapy period (mean and [95% CI] of standardized change scores, t1 – t2: CONV 1.01 [0.72-1.29]; IOT 1.51 [1.12-1.91];  $F(1, 137) = 4.47$ ;  $P < .0363$ ). That is, patients receiving IOT showed bigger improvements from pretest to posttest than those who received conventional active motor therapy. This effect was modified by severity of paresis, that is, was pronounced among patients with mild paresis with a more marked standardized effect in favor of IOT (mean of standardized change scores, t1 – t2: severe paresis, CONV 0.79, IOT 1.05; mild paresis, CONV 1.18, IOT 1.83;  $F(3, 137) = 4.35$ ;  $P < .0058$ ).

The raw change scores presented in Table 2 indicate that patients with severe arm paresis had on average a gain of 9.2 FM scale points after conventional therapy, whereas those receiving the Arm BASIS training had a gain of 12.3 points. Similarly, patients with mild arm paresis who received

conventional training could on average reduce their time needed to complete the TEMPA tasks by 20.5 seconds, whereas those who received the Arm Ability training had a reduction of 31.1 seconds on average.

Change scores from pretest (t1) to follow-up (4 weeks after the study therapy had been completed) were significantly different only among mildly paretic patients, again favoring the IOT (mean of standardized change scores, t1 – t3: severe paresis, CONV 1.10, IOT 1.18; mild paresis, CONV 1.49, IOT 2.16;  $F(3, 132) = 6.05$ ;  $P < .0007$ ). The reduction in time needed to complete the TEMPA tasks was on average 27.8 seconds in the conventional therapy group, whereas those who received the Arm Ability training had on average a reduction of 37.7 seconds.

## Secondary Outcome Measures

Upper limb passive joint motion and pain scores (FM) did not systematically change over time and were not modified by either “motor training intensity” or the experimental factor (CONV vs IOT; see Table 4). Spasticity was reduced after treatment in the subgroup with severe arm paresis, especially among those who received IOT (mean change scores on the Ashworth scale, t1 – t2: severe paresis, Splint  $-0.17$ , CONV  $-0.18$ , IOT  $-0.68$ ; mild paresis, Splint 0.04, CONV 0.0, IOT  $-0.14$ ;  $F(3, 137) = 3.17$ ;  $P = .0263$ ).

**Table 2**  
**Efficacy (Per Protocol) Analysis—Change Scores for Primary Motor Outcome Measure**

Group/Subgroup	Measure	Splint Therapy		Conventional Therapy		IOT	
		t1 – t2 <sup>a</sup> (n = 49)	t1 – t3 <sup>a</sup> (n = 45)	t1 – t2 <sup>a</sup> (n = 48)	t1 – t3 <sup>a</sup> (n = 48)	t1 – t2 <sup>a</sup> (n = 47)	t1 – t3 <sup>a</sup> (n = 46)
All	<i>d</i> <sup>b</sup>	1.07 (0.15)	1.48 (0.20)	1.01 (0.14)	1.31 (0.14)	1.51 (0.20)	1.76 (0.21)
Severe paresis <sup>c</sup>	<i>d</i> <sup>b</sup>	0.54 (0.10)	0.63 (0.14)	0.79 (0.15)	1.10 (0.16)	1.05 (0.20)	1.18 (0.24)
	FM motor <sup>d</sup>	6.3 (1.2)	7.3 (1.6)	9.2 (1.8)	12.9 (1.8)	12.3 (2.3)	13.8 (2.8)
Mild paresis <sup>c</sup>	<i>d</i> <sup>b</sup>	1.55 (0.23)	2.10 (0.27)	1.18 (0.22)	1.49 (0.23)	1.83 (0.29)	2.16 (0.30)
	TEMPA <sup>e</sup>	-27.8 (4.0)	-37.2 (4.8)	-20.5 (3.4)	-27.8 (3.6)	-31.1 (5.0)	-37.7 (5.0)
ANOVA <sup>g</sup> (Repeated Measures)							
Source	DF	t1 – t2			t1 – t3		
		F	P		F	P	
Time	1	93.55	<.0001	1	107.85	<.0001	
Time * MTR-Int	1	0.30	.5820	1	0.00	.9936	
Time * Exp (MTR-Int)	1	4.47	.0363	1	2.63	.1071	
Time * Exp * Severity (MTR-Int)	3	4.35	.0058	3	6.05	.0007	
Time * Weeks	1	11.65	.0008	1	11.56	.0009	
Error (time)	137			132			

Abbreviations: IOT, impairment-oriented training; DF, degree of freedom.

<sup>a</sup>Difference scores are presented as mean (standard error of mean).

<sup>b</sup>*d* = Standardized difference scores (Cohen's *d*; positive difference score = improvement).

<sup>c</sup>N (splint/conventional/IOT) = t1 – t2: 23/22/19; t1 – t3: 19/22/19.

<sup>d</sup>FM motor = Fugl-Meyer test, arm motor score (positive difference score = improvement).

<sup>e</sup>N (splint/conventional/IOT) = t1 – t2: 26/26/28; t1 – t3: 26/26/27.

<sup>f</sup>TEMPA = TEMPA test, summary time scores (for explanation see text "Outcomes"; negative difference score = improvement).

<sup>g</sup>ANOVA: (1) Exp = Experimental factor, that is, conventional therapy versus IOT; (2) MTR-Int = Motor training intensity, that is, splint therapy versus conventional and IOT; (3) Severity = Mild versus severe paresis; (4) Factor A (MTR-Int) = Factor A nested within factor MTR-Int.

## Other Motor Therapy

Other motor therapy time, that is, summary time of individual or group therapy in either occupational or physiotherapy, either between pretest and posttest (t1 – t2) or between posttest and follow-up (t2 – t3) was comparable across groups (mean and [95% CI], t1 – t2: 1426 [1330-1522] minutes; t2–t3: 681 [577-785] minutes). By design, the AETT was 675 minutes for patients with mild paresis and 900 minutes for patients with severe paresis (t1 – t2).

## Discussion

### Synopsis of the Key Findings

Ninety-four percent of the randomized patients completed the study (including follow-up). Aside from an imbalanced gender distribution, the randomized groups had comparable baseline characteristics. Efficacy and effectiveness analyses revealed almost identical effects (compare Tables 2 and 3). Overall, motor improvement over time was documented for the study population, modified by time since stroke, as had been expected in a subacute stroke patient population receiving rehabilitation therapy. Global effects of active motor

training intensity, that is, a differential effect between passive stimulation/splint therapy and the 2 forms of active training, could, however, not be substantiated. Differential effects were corroborated when the effects of the 2 active training strategies were compared: motor recovery rates were superior after IOT when compared with best conventional therapy. This was substantiated for the study population and its subgroups with severe or mild arm paresis. For patients with mild arm paresis, a differential effect in favor of IOT could also be documented for recovery rates from pretest to follow-up 4 weeks after discontinuation of the study treatment; this was not the case for patients with severe arm paresis.

The size and impact of the observed differences can be explained with both the standardized difference scores and the raw change scores of the 2 motor scales that were used.

Overall, the standardized IOT achieved an effect size of 1.51 after training. Compared with the effect size of 1.01 (CONV), the differential effect size in favor of IOT was 0.50, indicating an additional effect of 50% above what was achieved for this comparison group.

Our study patients with severe arm paresis had on average 24.4 FM points at baseline (scores can range from 0 to 66 [normal]). After 4 weeks of therapy, conventionally treated patients had on average a gain of 9.2 points (35% improvement),

**Table 3**  
**Effectiveness (Intention to Treat) Analysis—Change Scores for Primary Motor Outcome Measure**

Group/Subgroup	Measure	Splint Therapy		Conventional Therapy		IOT	
		t1 – t2 <sup>a</sup> (n = 51)	t1 – t3 <sup>a</sup> (n = 51)	t1 – t2 <sup>a</sup> (n = 49)	t1 – t3 <sup>a</sup> (n = 49)	t1 – t2 <sup>a</sup> (n = 48)	t1 – t3 <sup>a</sup> (n = 48)
All	<i>d</i> <sup>b</sup>	1.03 (0.14)	1.35 (0.18)	0.99 (0.14)	1.32 (0.14)	1.48 (0.20)	1.71 (0.21)
Severe paresis <sup>c</sup>	<i>d</i> <sup>b</sup>	0.51 (0.10)	0.60 (0.11)	0.79 (0.15)	1.10 (0.16)	1.00 (0.19)	1.12 (0.23)
	FM motor <sup>d</sup>	6.3 (1.2)	7.0 (1.3)	9.2 (1.8)	12.9 (1.8)	12.3 (2.3)	13.2 (2.7)
Mild paresis <sup>c</sup>	<i>d</i> <sup>b</sup>	1.49 (0.23)	2.02 (0.27)	1.15 (0.22)	1.50 (0.22)	1.83 (0.29)	2.12 (0.29)
	TEMPA <sup>e</sup>	–27.8 (4.0)	–35.8 (4.8)	–20.5 (3.4)	–27.6 (3.4)	–31.1 (5.0)	–37.1 (4.8)

ANOVA <sup>g</sup> (Repeated Measures)							
Source	DF	t1 – t2			t1 – t3		
		<i>F</i>	<i>P</i>	<i>P</i>	DF	<i>F</i>	<i>P</i>
Time	1	89.29	<.0001	<.0001	1	112.16	<.0001
Time * MTR-Int	1	0.45	.5016	.6785	1	0.17	.6785
Time * Exp (MTR-Int)	1	4.38	.0382	.1552	1	2.04	.1552
Time * Exp * Severity (MTR-Int)	3	4.65	.0040	.0001	3	7.70	.0001
Time * Weeks	1	10.90	.0012	.0014	1	10.59	.0014
Error (time)	141				141		

Abbreviations: IOT, impairment-oriented training; DF, degree of freedom.

<sup>a</sup>Difference scores are presented as mean (standard error of mean).

<sup>b</sup>*d* = Standardized difference scores (Cohen's *d*; positive difference score = improvement).

<sup>c</sup>N (splint/conventional/IOT) = t1 – t2: 24/22/20; t1 – t3: 24/22/20.

<sup>d</sup>FM motor = Fugl-Meyer test, arm motor score (positive difference score = improvement).

<sup>e</sup>N (splint/conventional/IOT) = t1 – t2: 27/27/28; t1 – t3: 27/27/28.

<sup>f</sup>TEMPA = TEMPA test, summary time scores (for explanation see text "Outcomes"; negative difference score = improvement).

<sup>g</sup>ANOVA: (1) Exp = Experimental factor, that is, conventional therapy versus IOT; (2) MTR-Int = Motor training intensity, that is, splint therapy versus conventional and IOT; (3) Severity = Mild versus severe paresis; (4) Factor A (MTR-Int) = Factor A nested within factor MTR-Int.

whereas patients receiving the Arm BASIS training had a mean gain of 12.3 (52% improvement).

The study patients with mild arm paresis had on average a TEMPA time score of 119 seconds at baseline; the norm for healthy subjects would be 52 seconds.<sup>29</sup> Accordingly, the study population had a relevant sensorimotor slowing for manual tasks at study entry. Patients receiving conventional therapy achieved on average a reduction of 20.5 seconds for the TEMPA tasks after 3 weeks of therapy, whereas those receiving the Arm Ability training had a mean reduction of 31.1 seconds, indicating a considerable improvement toward the norm.

In other words, within a few weeks of therapy the IOT group achieved a mean change (12.3 points) for patients with severe arm paresis that covered almost one fifth of the range of the FM scale (between 0 = complete paralysis to 66 = full score) and a mean benefit (–31.1 seconds) for patients with mild paresis that equals 46% of the difference between the average time needed for the TEMPA by patients with mild arm paresis in the study population at baseline (119 seconds) and the norm (52 seconds).<sup>29</sup> These effects can be regarded as substantial and clinically relevant.

With regard to secondary outcome measures (see Table 4), it can be summarized that training had an antispastic effect for the more severely affected arms, with a bigger benefit after IOT.

Other (not study related) motor therapy (occupational and physiotherapy) was comparable across groups throughout the study (see Table 5).

### Consideration of Possible Mechanisms and Explanations

The IOT strategies had specifically been developed for patients with severe (Arm BASIS training) or mild arm paresis (Arm Ability training) and have previously received support for their clinical efficacy by randomized control trials.<sup>18–20</sup> These therapeutic interventions target the deficient motor control issues specifically and comprehensively; in addition, the training is standardized and highly structured. Thus, the benefit from any AETT as provided in the study might thereby be maximized and guaranteed across individual therapists and patients. The alternative hypothesis, that the individual therapist might—based on explicit and implicit knowledge and past experience—best be able to tailor the arm rehabilitation therapy to any individual patient's needs and capacities and thereby can optimize the therapeutic outcome was not supported. The individualized approach was less successful than focusing on a neuroscience-derived training rationale; the individualization procedures embedded in the IOT techniques seem to be sufficient.

**Table 4**  
**Efficacy Analysis—Secondary Outcome Measures**

t1 – t2	Splint Therapy (n = 49)	Conventional Therapy (n = 48)	IOT (n = 47)			
Difference scores <sup>a</sup>						
FM-arm joint motion/pain						
All	0.01 (0.29)	-0.08 (0.48)	-0.04 (0.48)			
Severe paresis <sup>b</sup>	-0.30 (0.56)	-0.73 (0.96)	0.47 (0.57)			
Mild paresis <sup>c</sup>	0.36 (0.23)	0.46 (0.36)	-0.39 (0.72)			
Ashworth						
All	-0.06 (0.09)	-0.08 (0.11)	-0.36 (0.10)			
Severe paresis <sup>b</sup>	-0.17 (0.15)	-0.18 (0.21)	-0.68 (0.20)			
Mild paresis <sup>c</sup>	0.04 (0.12)	0.0 (0.08)	-0.14 (0.07)			
ANOVA <sup>d</sup> (Repeated Measures)						
Source	FM-Arm Joint Motion/Pain			Ashworth		
	DF	F	P	DF	F	P
Time	1	0.16	.6871	1	4.07	.0455
Time * MTR-Int	1	0.01	.9279	1	2.17	.1433
Time * Exp (MTR-Int)	1	0.08	.7803	1	5.27	.0232
Time * Exp * Severity (MTR-Int)	3	1.22	.3045	3	3.17	.0263
Time * Weeks	1	0.19	.6645	1	0.25	.6161
Error (time)	136			137		

Abbreviations: IOT, impairment-oriented training; DF, degree of freedom.

<sup>a</sup>Difference scores are presented as mean (standard error of mean).

<sup>b</sup>N (splint/conventional/IOT) = 23/22/19.

<sup>c</sup>N (splint/conventional/IOT) = 26/26/28.

<sup>d</sup>ANOVA: (1) Exp = Experimental factor, that is, conventional therapy versus IOT; (2) MTR-Int = Motor training intensity, that is, splint therapy versus conventional and IOT; (3) Severity = Mild versus severe paresis; (4) Factor A (MTR-Int) = Factor A nested within factor MTR-Int.

**Table 5**  
**Total Motor Therapy**

	Splint Therapy n = 49	Conventional Therapy n = 48	IOT n = 47	ANOVA F(2,141)	P
PT t1 – t2 (minutes; mean/SD)	816/422	848/432	874/428	0.22	.7996
OT t1 – t2 (minutes; mean/SD)	645/483	509/282	585/335	1.60	.2060
MT t1 – t2 (minutes; mean/SD)	1461/638	1357/539	1459/569	0.50	.6072
	n = 45	n = 48	n = 46	F(2, 138)	P
PT t2 – t3 (minutes; mean/SD)	426/445	411/432	446/370	0.08	.9188
OT t2 – t3 (minutes; mean/SD)	270/306	240/344	247/250	0.12	.8826
MT t2 – t3 (minutes; mean/SD)	696/669	651/651	693/538	0.09	.9162
Days t2 – t3 (mean/SD)	27.9/10.5	28.2/11.9	26.7/5.2	0.31	.7310

Abbreviations: IOT, impairment-oriented training; PT, physiotherapy (single and group sessions); OT, occupational therapy (single and group sessions); MT, sum of PT + OT; Days, follow-up days between t2 and t3.

The observation that the superior effect of the Arm Ability training could be sustained after the study therapy had been terminated while this was not the case for the superior immediate posttraining effects of the Arm BASIS training can be explained by the fact that mildly affected patients continue to use and foster reacquired motor skills in daily life, whereas patients with severe paresis cannot and would have to receive ongoing treatment until their arm becomes functional (or

might otherwise lose relearned motor capacities when specific treatment is withdrawn).

Although not part of the a priori hypothesis testing (and therefore not analyzed), it is of interest to note that splint therapy achieved numerically similar results or even better recovery rates (mild paresis) than conventional therapy (see Tables 2 and 3). Somatosensory stimulation could therefore be a relevant option in motor rehabilitation for patients with mild

paresis. The therapeutic potential of sensory stimulation for motor recovery has recently started to receive attention.<sup>33</sup>

### Comparison With Relevant Findings From Other Published Studies

The current data support previous randomized control trials<sup>18,19</sup> that indicated the Arm Ability and Arm BASIS training's clinical efficacy for patients with mild or severe arm paresis, respectively. The current trial adds the information that the IOT as a combined modular approach—with either the Arm BASIS training or the Arm Ability training prescribed as indicated—serves the needs of patients with a wide degree of arm paresis after stroke and can be regarded as an effective and comprehensive treatment option. The observation that specificity of training contents can be more important than augmented therapy time (AETT) is well in agreement with the previous observation that only AETT as Arm BASIS training promoted motor recovery in subacute stroke patients with severe arm paresis, whereas this was on average not the case for AETT provided as Bobath treatment.<sup>19</sup> The data are further in line with randomized control trial reports that indicated the efficacy for arm motor recovery when repetitive motor control-oriented training protocols had been technically implemented, for example, with robot therapy.<sup>34-36</sup>

### Limitations of the Study

Study subjects had on average been recruited 4 to 5 weeks after stroke. We do not know whether the differential therapeutic effects that could be demonstrated would be comparable when the training either started immediately after stroke or in the chronic phase. Furthermore, study treatment protocols with a high degree of compliance are difficult to organize for more than a few weeks in a rehabilitation context. The assessment of functionally relevant and more lasting treatment effects among patients with severe arm paresis would, however, necessitate considerably longer treatment periods.

### Clinical and Research Implications

The major clinical implication of the study might be that specificity of training can be more important for arm motor recovery after stroke than intensity (AETT) when applied in clinically relevant moderate intensities. Effect sizes for motor recovery scores were increased by the IOT by 40% to 50% on average when compared with either control condition. The standardized and highly structured modular IOT approach increased the therapeutic benefit (efficacy and effectiveness) for both patients with mild and severe arm paresis. Its effects were superior to an individualized therapeutic occupational or physiotherapeutic approach. Patients had been recruited from 6 rehabilitation centers and can be regarded as representative for subacute ischemic stroke patients. Thus, there is reason to assume that the treatment could have a clinically relevant impact on a major proportion of stroke victims.

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